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# Intramolecular chaperone-assisted dual-anchoring activation (ICDA): a suitable preorganization for electrophilic halocyclization

# Table of Contents

Supplementary Methods ..... 2
1. General information ..... 2
2. Limitation and mechanism of electrophilic intramolecular halocyclization ..... 3
3. Analyzation of different rate-determining step (RDS) of electrophilic intramolecular halocyclization ..... 5
4. Detailed description of electrophilic halogenation reagents and natural oxidative halogenation strategy ..... 6
5. Mechanism of typical enzyme catalysis and selected examples ..... 7
6. Optimization of BCTC-induced electrophilic intramolecular bromolactonization ..... 9
7. Flow protocol for the intramolecular halocyclization of olefins ..... 13
7.1 Introduction ..... 13
7.2 Materials for the construction of flow apparatus ..... 13
7.3 General procedure for the 1 mmol scale synthesis ..... 13
7.4 General procedure for the 5.7 mmol (1.01 g) scale synthesis ..... 14
8. A catalytic asymmetric version of the halocyclization ..... 16
9. Studies of kinetic isotope effects (KIE) and intermolecular completive reactions. ..... 20
9.1 Studies of kinetic isotope effects (KIE) ..... 20
9.2 Intermolecular competition bromocyclization ..... 21
9.3 The valuation of nucleophilicity parameters (*N*) ..... 26
9.4 Investigation of relative reaction rates of cholorolactonization, bromolactonization and iodolactonization ..... 27
10. Computational calculation for mechanistic studies ..... 28
10.1 General Computational Procedures ..... 28
10.2 Proton Affinity (*PA)* ..... 28
10.3 Halogen Affinity (*HalA*) ..... 29
10.4 Quantitative calculation of halenium affinity (*HalA)* values and NPA (X=Cl, Br) ..... 30
10.5 NMR evidence for excluding the transfer of $H^+$ as the initial step ..... 32
10.6 Potential energy surface calculation and the topological analysis of the electron charge density ..... 33
10.7 Cartesian coordinates of optimized structures ..... 34
11. X-ray crystallographic data ..... 62
12. General procedures and analytical data of five- and six-membered heterocyclic compounds ..... 63
13. Procedures and analytical data of medium and large ring lactones ..... 77
14. Procedures and analytical data of difluoromethyl-containing oxazoline compounds ..... 82
15. Comparison of different published methodology for bromocyclization ..... 84
16. General procedure for generating unsaturated substrates and characterization of new substrates ..... 87
17. References ..... 102

# Supplementary Methods

## 1. General information

**General Experimental Procedures:** All reactions were monitored by TLC or GC-MS analysis. Flash column chromatography was performed over silica gel (200-300 mesh). Analytical thin-layer chromatography (TLC) was carried out on GF254 pre-coated silica gel plate. Visualization was accomplished by UV light (254 nm). All experiments were conducted in sealed tubes under atmosphere unless noted otherwise.

**Materials:** Unless noted otherwise, all reagents and starting materials were purchased from commercial sources and used as received. $CDCl_3$ and DMSO-$d_6$ were purchased from *Energy Chemical*. All chemicals were purchased from Adamas Reagent, Ltd, Bide Pharmatech Ltd, Energy chemical company, Alfa Aesa chemical company and so forth.

**Instrumentation:** $^{1}H$ NMR (400 MHz), $^{13}C$ NMR (100 MHz) and $^{19}F$ NMR (376 MHz) spectra were recorded on a Quantum-I Plus 400 NMR spectrometer with $CDCl_3$ or DMSO-$d_6$ as solvent and tetramethylsilane (TMS) as the internal standard. $^{1}H$ NMR chemical shifts (in ppm) were referenced to $CDCl_3$ ($\delta$ = 7.26 ppm) as internal standards. $^{13}C$ NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ ($\delta$ = 77.16 ppm). Data are reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet, br = broad), coupling constant (in Hz), and integration. GC analysis was performed on 7890A-5975C/Agilent. HR-MS spectra were recorded on a Waters Xevo G2QTOF/UPLC mass spectrometer using electrospray ionization. Crystallographic data were obtained from a Bruker D8 VENTURE diffractometer. The enantiomeric excesses (*ee*) of the products were determined by high performance liquid chromatography (HPLC) analysis employing Daicel Chiralpak OD-H and AD-H columns.

## 2. Limitation and mechanism of electrophilic intramolecular halocyclization

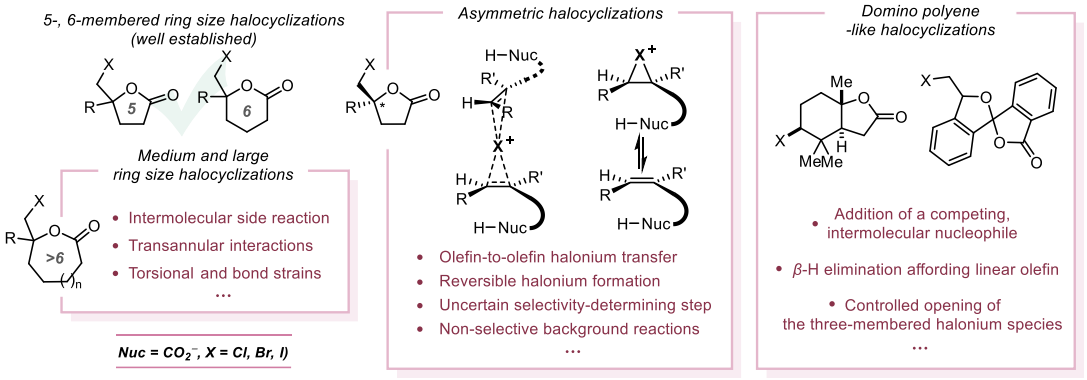



**Figure S1.** Mainly categories and limitations of electrophilic (asymmetric catalytic) intramolecular halocyclization.

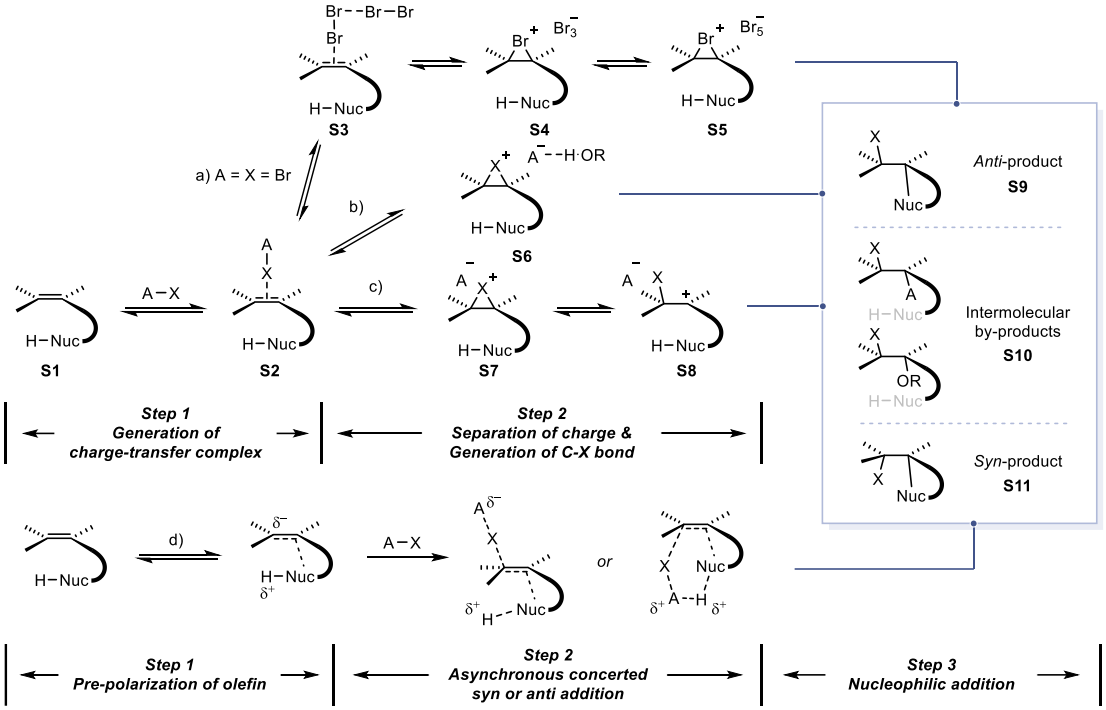



**Figure S2.** Summary of solvent-, substrate-, reagent-, and nucleophile-depended reaction mechanism of electrophilic intramolecular halocyclization.

The addition of electrophilic reagents to olefins is perhaps one of the most fundamental transformations for the rapid construction of complex organic molecules. Indeed, by the early 1930s, the electrophilic functionalization of olefins had already become a classic transformation detailed in textbooks.[1] Amongst all these examples, halogen electrophiles are most commonly utilized in these addition reactions. The incorporation of a halogen atom in a molecule can modify both its physical and biological activities, often through alterations in steric and electronic properties.[2] The versatility of incorporating a halogen atom into a molecule lies in the ability of alkyl halides to serve as precursors or sites for constructing various bonds like C–C, C–N, and C–O, among others.[3] This is especially so for halocyclization reactions, a sub-class of

halofunctionalization reactions, whereby heterocyclic rings are the resultant products. Typically, these reactions proceed via the intramolecular addition of a heteronucleophile to a carbon–carbon double bond in the presence of an electrophilic halogen source.

The basic mechanism of the halogenation of olefins by electrophilic halogen source has been extensively studied over the last century.[1] Analogously, a general mechanism of halocyclization is presented in Figure S2. The initial step entails the exothermic complexation of olefin **S1** with elemental halogen, leading to the generation of a charge-transfer complex.[4] In polar, protic solvents, solvation strongly promotes ion-pair formation. The charge-transfer complex decomposes into an ion-pair complex (**S6**) with the assistance of hydrogen bonds from the solvent (Brønsted-acid-induced activation).[5] This intermediate ion-pair decomposes, yielding either solvent adducts (e.g., **S10**) or halocyclization products (e.g., **S11**). When elemental halogen reacts with olefins in non-polar solvents, the formation of the ion-pair complex is facilitated by the coordination of the halide anion (halogen-bond-induced activation) with one or more equivalents of elemental halogen (e.g., through 1:2 (**S4**), 1:3 (**S5**), or higher-order olefin-halogen complexes).[3] In non-polar, aprotic solvents (e.g., dichloromethane), these reactions proceed via the formation of a haliranium ion or a classical halomethyl carbenium ion, which decomposes to form either ion-pair adducts (e.g., **S10**) or halocyclization products (e.g., **S11**).

Besides the stepwise mechanism first proposed in 1937 by Kimball[6], and further developed by Fahey[7,8], Olah[9-11], and Brown[12], Borhan suggested a nucleophile-assisted alkene activation (NAAA) enabled $Ad_E3$-type process that electron donation from the nucleophilic addition partner activates the alkene for electrophilic attack (i.e., prepolarization).[13] It is important to mention that NAAA describes the interaction of the nucleophile with the olefin, irrespective of the presence or absence of an electrophile. $Ad_E3$ denotes the transition state requiring the presence of the electrophile and that of the nucleophile. In a manner of speaking, NAAA relates to the ability of the olefin to undergo an $Ad_E3$-type reaction, with higher rates being the result of more effective NAAA.

*Note: The mechanism of electrophilic intramolecular halocyclization relies heavily on the type of solvent, electrophilic halogenation reagent, intramolecular nucleophile and substituents on unsaturated C=C bonds. For example, enhancing the electron richness of the olefin via π-donor substituent(s) and increasing the leaving group ability of the halenium ion donor may shift the mechanism from the NAAA enabled $Ad_E3$-type process to a classical stepwise halomethyl carbenium ion route.[13] Hence, it is not advisable to suggest and define the route of an electrophilic intramolecular halocyclization reaction hastily while the deliberate exploration may offer both mechanistic insight and the promise of new handles on stereocontrol in the classic process of electrophilic addition to alkenes.*

## 3. Analyzation of different rate-determining step (RDS) of electrophilic intramolecular halocyclization

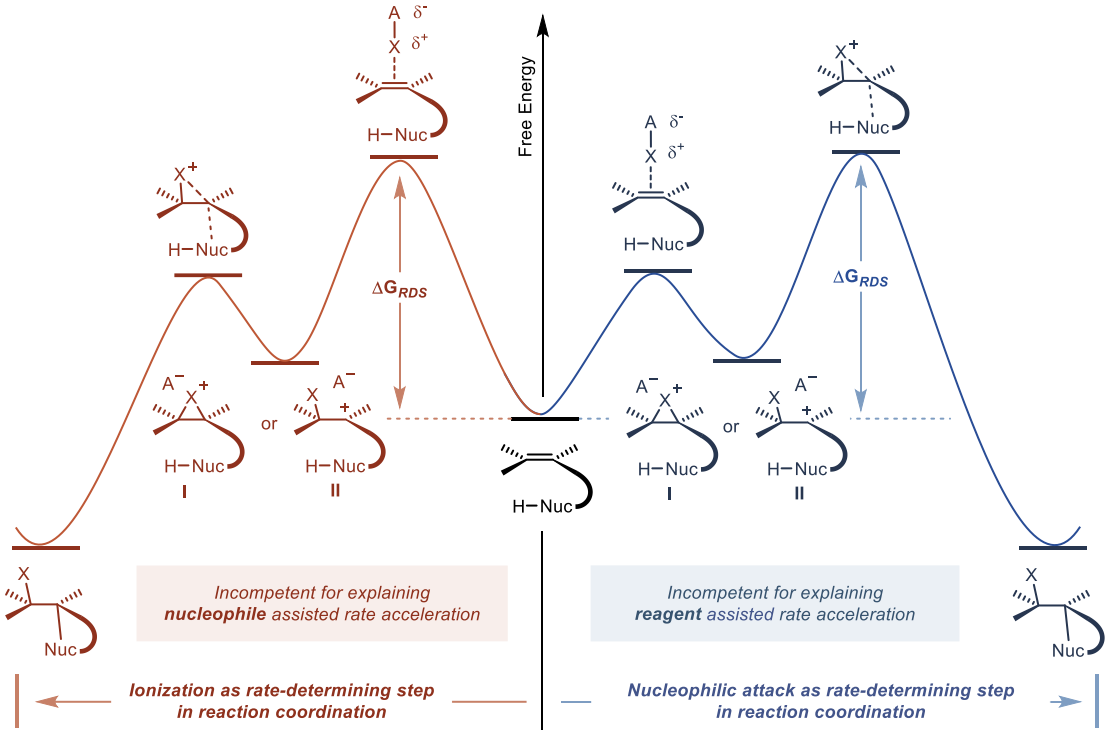



**Figure S3.** Analyzation of different rate-determining step (RDS) of electrophilic intramolecular halocyclization

Due to the rapid rate and high reactivity of the intermediate species, identifying the rate-determining step (RDS) of the overall halocyclization reaction under different circumstances poses a significant challenge.

**Ionization as the rate-determining step (RDS):** If the initial step involves solely the olefin and the halenium ion source, the formation of intermediates **I** and **II** (separation of charge) will define the barrier for the rate-determining step. Nonetheless, the relative reaction rates shown in Fig. 2 against this possibility due to the inevitable influence of intramolecular nucleophiles on the reaction rate.

**Nucleophilic attack as the rate-determining step (RDS):** If the second step (nucleophilic attack) was assumed to be the rate-determining step in halofunctionalization of olefins, in this scenario, the formation of the charged ion-pair species **I** and **II** should be reversible. and the capture of the ion-pair by a nucleophile is both rate-limiting and product-determining with respect to enantioselectivity. To some extent, this scenario could explain the intramolecular nucleophile dependent reaction rate. Hence, the completive reaction of bromolactonization and iodolactonization should have shown a similar reaction rate. Namely, the ratio of **2a-I:2a-Br** and **2a-Br:2a-Cl** in Fig. 2d should be approximately 1:1 instead of 1.34:1 and >20:1, respectively. These observations implied that the ICDA enhanced halocyclization of olefins does not generate the classical intermediates **I** or **II**.

# 4. Detailed description of electrophilic halogenation reagents and natural oxidative halogenation strategy

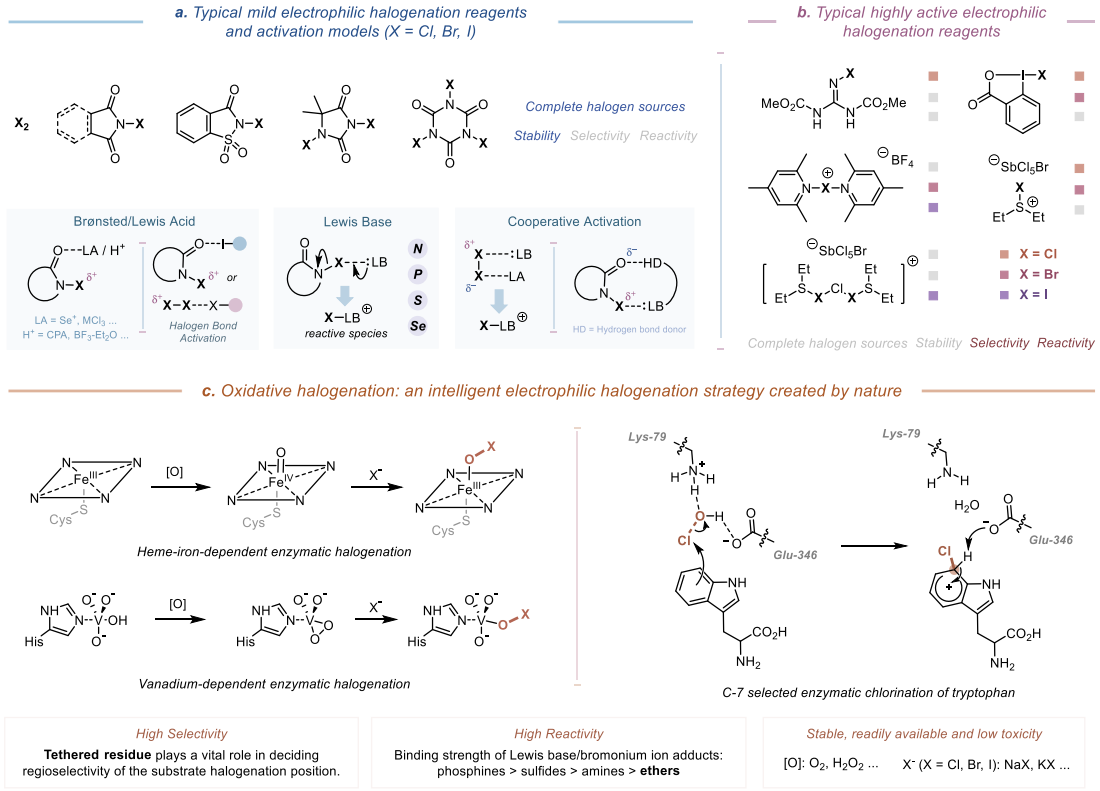



**Figure S4. a.** Typical mild electrophilic halogenation reagents and activation models, **b.** Typical highly active electrophilic halogenation reagents, **c.** Natural oxidative halogenation strategy.

Over the last few decades, a multitude of halogenation reagents have been developed for electrophilic halogenation various synthetic transformations. [14] Numerous organic transformations are well-documented with commercially available NX-type reagents, acknowledged as significant precursors of halogen(I) compounds (Figure S4a, top). In the NX-type reagents, the halogen atoms are covalently bonded to the nitrogen centers. Since all bonding phenomena are interactions between an electron-rich species (Lewis base) and an electron-poor species (Lewis acid), these reagents can be conceptualized as Lewis-base-coordinated halogen(I) species. Within this coordination, the interaction between the halogen atom and the Lewis base (e.g., succinimide) is strong yet less polarized, resulting in low reactivity of the electrophilic halogen.[15] To enhance the electrophilicity and chemical reactivity of halenium ions and their equivalents in a reaction mixture, the introduction of exogenous additives was employed as a powerful strategy to polarize strong N–X covalent bond or generate a thermodynamically stable halogen(I) intermediate through noncovalent interactions (Figure S4a,bottom). Generally, the activation model can be categorized into three types: (a) Lewis/Brønsted-acid-induced activation, (b) Lewis-base-induced activation, and (c) Lewis/Brønsted-acid-Lewis-base-coordinated activation.

# 5. Mechanism of typical enzyme catalysis and selected examples

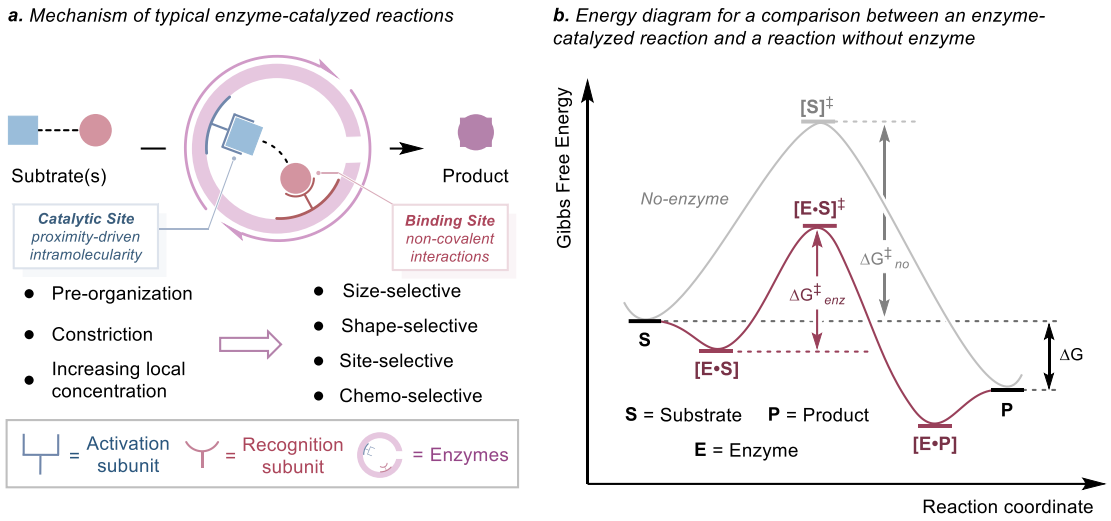



**Figure S5. a.** Mechanism of typical enzyme-catalyzed reactions, **b.** Energy diagram for comparing an enzyme-catalyzed reaction and a reaction without enzyme.[16]

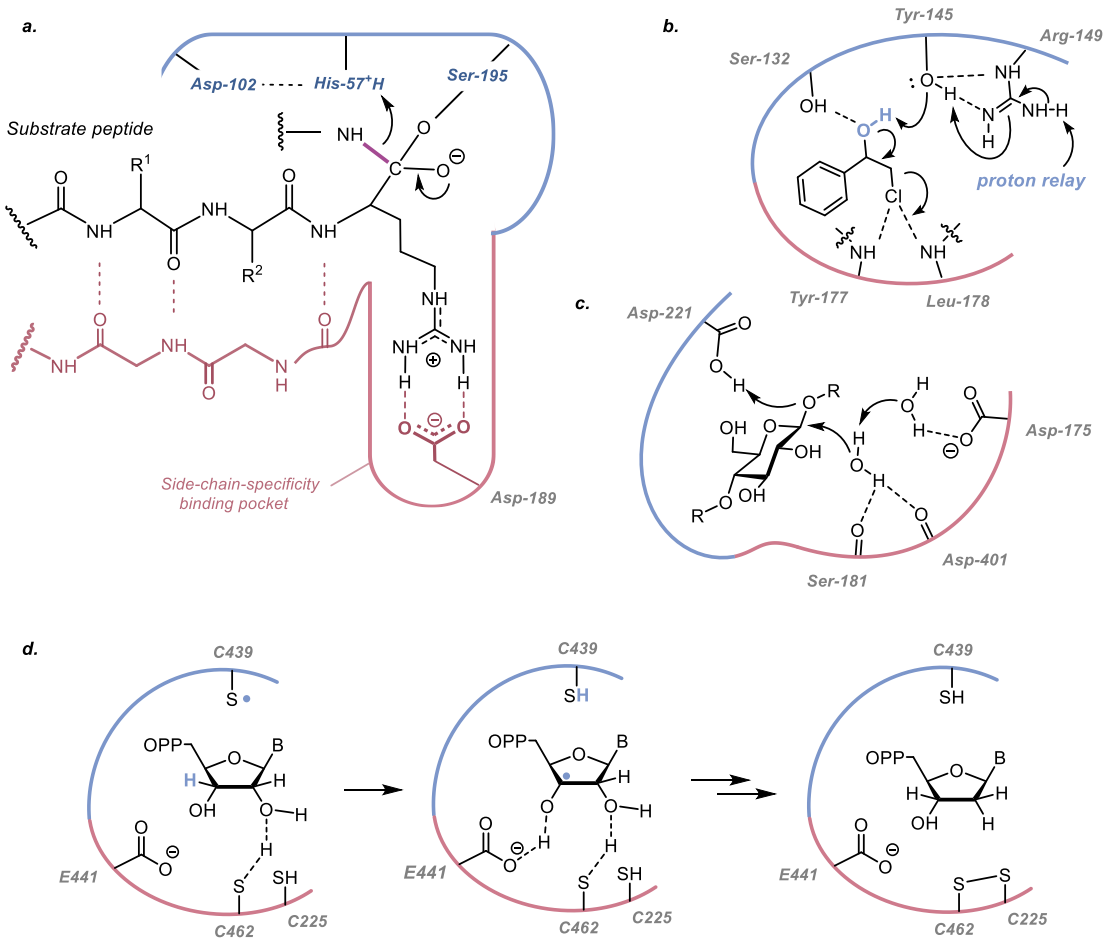


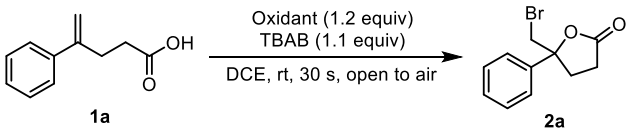

**Figure S6.** Selected examples of enzyme-catalyzed reactions: **a.** Trypsin-mediated hydrolysis of peptide bonds.[17] **b.** Haloalcohol dehalogenases catalyzed dehalogenation of vicinal haloalcohols.[18] **c.** enzymatic glycoside hydrolysis.[19] **d.** Ribonucleotide reductases (RNRs) catalyzed deoxygenation of nucleotides.[20]

Enzymes are remarkable catalysts and often serve as the benchmark for both catalytic activity and selectivity. The confined microenvironment of enzyme catalyst distinctly comprises two functional regions: the catalytic site and the binding site (Figure S5a). Essentially, the geometric constraints in confined binding pocket plays a vital role in recognizing, controlling, blocking and expediting. In 1946, Pauling suggested the specific reason why enzymes cause the catalysis under mild reaction conditions like in living cells.[21] An enzyme (**E**) binds with a substrate (**S**) to create a complex (**[E·S]**) through a lock-and-key interaction, which activates the substrate to lead to a transition state (**[E·S]**$^{‡}$) for the reaction to proceed, where the activation energy ($\Delta G_{enz}^{‡}$) is greatly lowered by the stabilizing action by the enzyme, in comparison with that ($\Delta G_{no}^{‡}$) of a reaction without enzyme via a transition state [S]$^{‡}$ (Figure S5b). The enzymatic catalysis normally brings about the rate acceleration of $10^{6}$–$10^{12}$ fold; however, in certain instances, this rate acceleration could even reach $10^{20}$ fold.[22] The processes depicted in Figure S6 exemplify some classical enzymatic reactions involving carboxylate anion residues.

# 6. Optimization of BCTC-induced electrophilic intramolecular bromolactonization

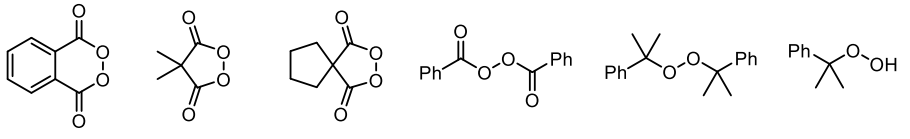
**Table S1.** Screening of the optimal oxidant[a] and a brief summary for electrophile-mediated halolactonization.

***a.*** *Screening of the optimal oxidant[a]*



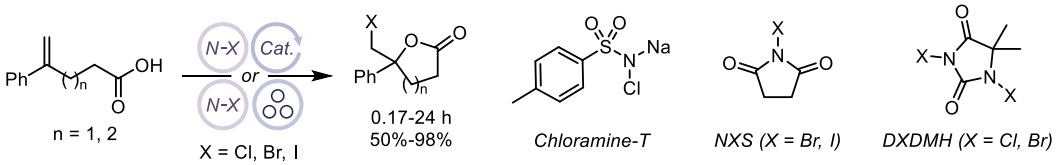

**1a** **2a**

| Entry | Oxidant | Yield of **2a**[b] | Entry | Oxidant | Yield of **2a**[b,c] |
|---|---|---|---|---|---|
| 1 | PPO | >96 | 8 | DCP | <5 |
| 2 | MPO-1 | 91 | 9 | TBPB | <5 |
| 3 | MPO-2 | 90 | 10 | CHP | <5 |
| 4 | BPO | <5 | 11 | TBHP | <5 |
| 5 | BPO | 90%[c] | 12 | DTBP | <5 |
| 6 | LPO | <5 | 13 | TBPA | <5 |
| 7 | LPO | 60%[c] | 14 | 30% $H_2O_2$ (aq) | <5 |

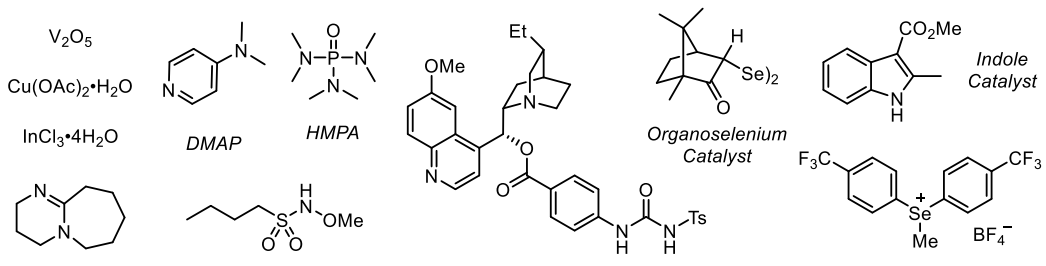



***b.*** *Selected synthetic methodologies for halolactonization*

*N-X*

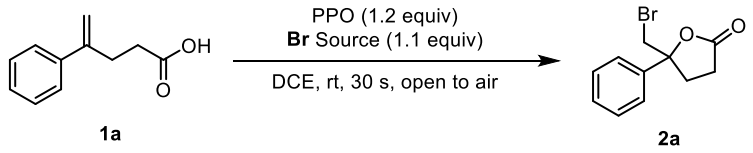



*Cat.*



[a] Reaction conditions: **1a** (0.1 mmol, 1 equiv.), oxidant (0.12 mmol, 1.2 equiv.), TBAB (0.11 mmol, 1.1 equiv.), and DCE (1 mL), rt, 30 s. [b] Yields of isolated products. [c] Reaction time: 17 h. PPO = phthaloyl peroxide; BPO = benzoyl peroxide; MPO = malonoyl peroxide; DCP = dicumyl peroxide; CHP = cumene hydroperoxide; TBPB = *tert*-butyl peroxybenzoate, LPO = lauroyl peroxide; TBHP = *tert*-butyl hydroperoxide; DTBP = di-*tert*-butyl peroxide; TBPA = *tert*-butyl peroxyacetate; TBAB = tetrabutylammonium bromide; TBACl = tetrabutylammonium chloride; TBAI = tetrabutylammonium iodide, DCE = 1,2-dichloroethane. See also Supplementary Tables S2, S3, S4, S5.

**Table S2.** Screening of the optimal Br source.[a]

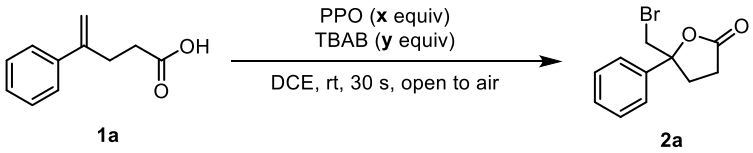



**1a** **2a**

| Entry | **Br** Resource | Yield of **2a**[b] |
|---|---|---|
| 1 | TBAB | >96% |
| 2 | LiBr | 31% |
| 3 | NaBr | 35% |
| 4 | KBr | 19% |
| 5 | CsBr | 13% |
| 6 | NBS | 6% |

[a] Reaction conditions: **1a** (0.1 mmol, 1 equiv.), PPO (0.12 mmol, 1.2 equiv.), Br source (0.11 mmol, 1.1 equiv.), and DCE (1 mL), rt, 30 s. [b] Yields of isolated products.

**Table S3.** Screening of the optimal amount of PPO and TBAB.[a]

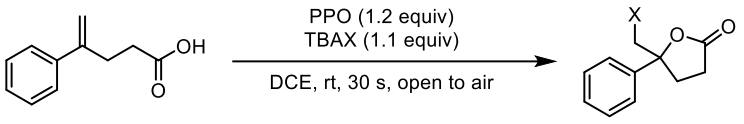



**1a** **2a**

| Entry | **x** (equiv) | **y** (equiv) | Yield of **2a**[a] |
|---|---|---|---|
| 1 | 1.1 | 1.1 | 90% |
| 2 | 1.1 | 1.0 | 85% |
| 3 | 1.0 | 1.0 | 73% |

[a] Yields of isolated products.

**Table S4.** Investigation of the chlorolactonization and iodolactonization.[a]

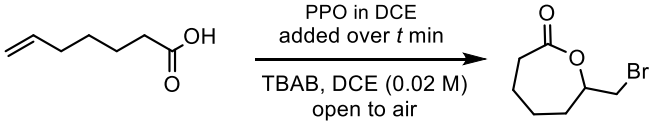



**1a** **2a-X**

| Entry | X = Cl, Br, I | Yield of **2a**[b] |
|---|---|---|
| 1 | TBAI | >96 |
| 2 | TBACl | 35 |
| 3[c] | TBACl | 76 |

[a] Reaction conditions: **1a** (0.1 mmol, 1 equiv.), PPO (0.11 mmol, 1.1 equiv.), TBACl or TBAI (0.11 mmol, 1.1 equiv.), and DCE (1 mL), rt, 30 s. [b] Yields of isolated products. [c] Reaction conditions: **1a** (0.1 mmol, 1 equiv.), PPO (0.24 mmol, 2.4 equiv.), TBACl (0.22 mmol, 2.2 equiv.), and DCE (1 mL), rt, 30 s.

**Table S5.** Screening of the optimal condition for the construction of medium-sized and large-sized rings.




**11a** **12a**

| Entry | *t* (min) | Reaction Time (min)[a] | PPO (equiv) | TBAB (equiv) | Yield **12a**[b] |
|---|---|---|---|---|---|
| 1[c] | 0.5 | 0.5 | 1.2 | 1.2 | 24% |
| 2[d,e] | 30 | 30 | 1.2 | 1.2 | 45% |
| 3[d,e] | 30 | 30 | 2 | 2 | 62% |
| 4[d,f] | 30 | 60 | 2 | 2 | 63% |
| 5[d,e] | 60 | 60 | 2 | 2 | 62% |
| 6[g] | 30 | 30 | 2 | 2 | trace |

[a] Reaction time includes the process of adding the DCE solution of PPO. [b] Yields of isolated products. [c] Reaction conditions: **11a** (0.1 mmol, 1 equiv.), PPO (0.12 mmol, 1.2 equiv.), TBAB (0.12 mmol, 1.2 equiv.), and DCE (1 mL), 25 °C, 30 s. [d] Reaction conditions: **11a** (0.1 mmol), TBAB in DCE (4 mL), PPO in DCE (1mL) was added over *t* min at 25 °C. [e] Quenched with $Na_2S_2O_3$ (aq.) after addition. [f] Further stirred for another 30 min, then quenched with $Na_2S_2O_3$ (aq.). [g] BPO was employed as oxidant instead of PPO.

**Optimization of BTCT-induced electrophilic halocyclization of 1a.** 4-Phenyl-4-pentenoic acid **1a** was selected as the model substituted alkene for our optimization studies. The corresponding bromolactonization product **2a** was produced in nearly quantitative yield (>96%) in 30 s at room temperature under the optimal reaction condition (Table S1, entry 1). No significant decrease in yield was observed when alkyl cyclic diacyl peroxide malonoyl peroxides (MPO-1 and MPO-2) were employed as oxidants (Table S1, entries 2 and 3). In consideration of extensive applications of redox system (the cooperation of stoichiometric oxidant and halogen anion) in halolactonization, a series of commercially available and readily accessed oxidants were assessed critically and comprehensively. Benzoyl peroxide (BPO) and dilauroyl peroxide (LPO), act as the

open-chain analog of cyclic diacyl peroxides, were first examined, resulting in the formation of **2a** with yields of less than 5% within 30 seconds. Only extending the reaction time to 17 hours could afford an increasing generation of **2a** in yield to 90% and 60%, respectively (Table S1, entries 4 to 7). Compared with the excellent yields that obtained in 30s by employing PPO and MPO, the significant decrease in yield indicates that the intramolecular chaperone-like carboxylate anion of BCTC acts like enzyme residue and can accelerate the reaction by orders of magnitude. The employment of other commercially available oxidants, including dialkyl peroxides, alkyl hydroperoxide and $H_2O_2$(aq) give negative results (Table S1, entries 8 to 14). Changing the $Br^-$ source from TBAB to LiBr, NaBr, KBr, CsBr or *N*-bromosuccinimide (NBS) were detrimental (Table S2). Reducing the amount TBAB or PPO resulted in a sightly diminish in the yield of **2a** (Table S3). Both tetrabutylammonium iodide (TBAI) and tetrabutylammonium chloride (TBACl) were found to be suitable for this protocol, thus funishing **2a-Cl** and **2a-I** in good to excellent yield (Table S4).

**Optimization of BTCT-induced electrophilic halocyclization of 11a.** Synthetically, as a consequence of enthalpic (e.g., transannular interactions, torsional and bond strains) and entropic influences, the construction of seven-membered, medium-sized rings (MSR, typically eight-eleven membered ring structures) and large-sized rings are significantly more challenging than that of small-ring compounds (Table S5, entry 1). In order to minimize the potential undesired intermolecular addition of carboxylic acids to olefins, we employed the high dilution and slow addition methodology to for the preparation of seven-membered and medium-sized rings. A slow addition of PPO to the mixture of **11a** and TBAB in DCE was found effective, in which case we could obtain 56% yield of **12a** in 30 min (Table S5, entry 2). Increasing the equivalents of PPO and TBAB could offer a further increase in yielding **12a** (Table S5, entry 3, 62%). A longer addition time or reaction time shows no beneficial influence on the yield of **12a** (Table S5, entries 4 and 5). In stark contrast, BPO displayed inactive reactivity and inferior result was obtained (Table S5, entry 6), further demonstrating the importance of ICDA in the spatial adjustment of reactive conformation.

# 7. Flow protocol for the intramolecular halocyclization of olefins

## 7.1 Introduction

While the commendable thermostability and shock resistance of PPO has been demonstrated, the application of stoichiometric quantities of peroxides for oxidative transformations may pose safety concerns arising from the elevated energy content of peroxide-containing compounds.[23] Thus, devising a protocol for the continuous formation of phthaloyl peroxide in flow would minimize the accumulation of peroxide and eliminate the necessity for isolating and recrystallizing substantial quantities of phthaloyl peroxide. This would represent an enhancement over previous batch techniques.

## 7.2 Materials for the construction of flow apparatus

Column compression endcaps (0.250", 4.6mm dist. cone) IDEX (cat.: 4-1v).

Female to female luer lock adapter (10-32 cone) IDEX (cat.: P-659).

Fingertight fittings (10-32 cone) IDEX (cat.: F-120).

Inline check valve (1/4-28 FB,10-32 cone) IDEX (cat.: CV-3335).

Mesh Sieves (140 and 325 mesh) Alfa Aesar (cat.: 39989 and 39994).

PFA tubing 1/16 x 0.020 x 5 ft (cut into three 12" lengths) IDEX (cat.: 1512).

Sodium percarbonate (ground using a mortar and pestle) Sigma Aldrich (cat.: 371432-500g).

Stainless steel frits (10 μm pore size) IDEX (cat.: A-107x).

Stainless steel spheres (60-125 μm) ThermoFisher (cat.: 436).

Stainless steel tubing (316 smooth-bore; 0.25" OD, 0.21" ID, 0.02" wall, 1' length purchased, cut into 15 cm lengths) McMaster-Carr (cat.: 89785K222).

The construction of flow apparatus was similar with the general procedure reported by Siegel in 2015.[23]

## 7.3 General procedure for the 1 mmol scale synthesis

To a 20 mL graduated cylinder was added phthaloyl chloride (530 μL, 710 mg, 3.5 mmol). Anhydrous DCM was added to bring the final volume to 17.5 mL, producing a 0.2 M solution. The flow apparatus was manually purged with anhydrous DCM (2 mL dead volume). The solution of phthaloyl chloride was taken up into a 20 mL syringe and affixed to the luer port. A flow rate of 10 mL/h was dialed into the syringe pump. The first 4 mL (roughly twice the dead volume of the packed bed reactor) that passed through the apparatus was discarded. After 4 mL, the feed was connected through an inlet adapter to a 100 mL round bottom flask containing **1a** (1 mmol, 0.1 M in DCM), adding the remaining 11.5 mL of the peroxide solution (2.3 equiv.). Upon completing the addition of phthaloyl chloride solution, the mixture was quenched with $Na_2S_2O_3$ (aq.) and extracted with DCM for three times. The combined organic layer was dried over $Na_2SO_4$, filtrated, and concentrated in vacuo and purified via silica gel flash chromatography to offer the desired product in 86% yield.

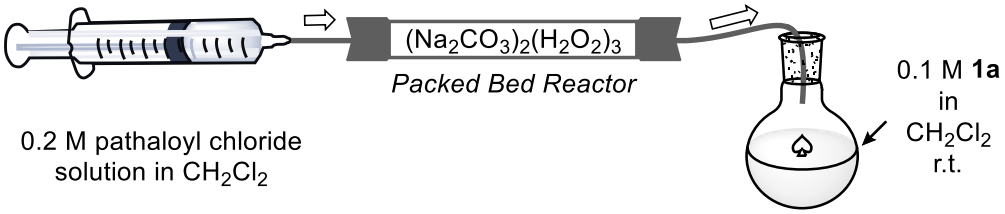



**Figure S7.** Schematic for the combination of flow and batch reactions using in-situ generated phthaloyl peroxide.

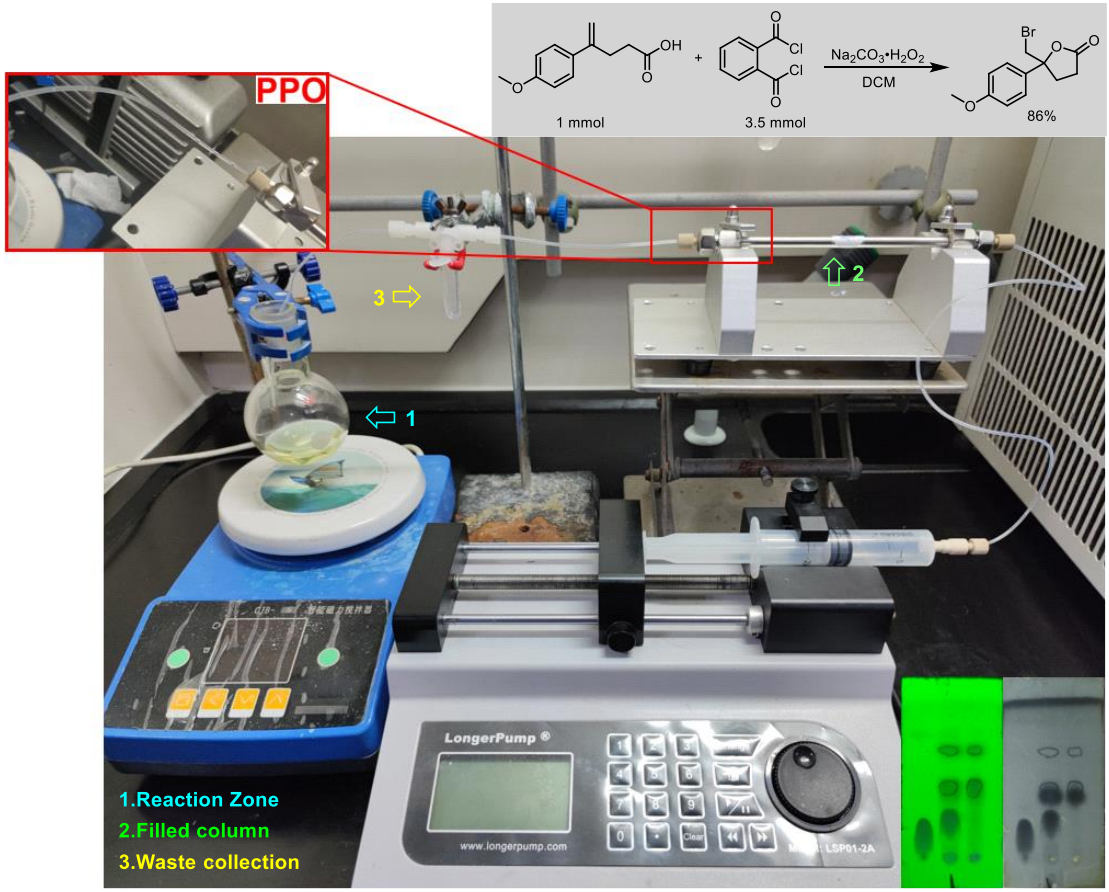



**Figure S8** Picture of the combination of flow and batch reactions using in-situ generated phthaloyl peroxide (1 mmol scale synthesis).

## 7.4 General procedure for the 5.7 mmol (1.01 g) scale synthesis

To a 100 mL graduated cylinder was added phthaloyl chloride (2.3 mL, 3.05 g, 15 mmol). Anhydrous DCM was added to bring the final volume to 75 mL, producing a 0.2 M solution. The flow apparatus was manually purged with anhydrous DCM (2 mL dead volume). The solution of phthaloyl chloride was taken up into a 100mL round bottom flask and linked with LongerPum. A flow rate of 10 mL/h was dialed into the syringe pump. The first 4 mL (roughly twice the dead volume of the packed bed reactor) that passed through the apparatus was discarded. After 4 mL, the feed was connected through an inlet adapter to a 250 mL flask containing **1a** (1 mmol, 0.1 M in DCM), adding 20 mL of the peroxide solution (2.4 equiv.). after the addition of 20 mL of phthaloyl chloride solution, the noneffective sodium percarbonate was replaced by fresh sodium percarbonate, and this process was repeated for two more times. Alternatively, the operation process could be simplified by employing a larger stainless steel tubin (1.00" OD, 0.92" ID, 0.04" wall, 20 cm lengths, corresponded to 13.0-13.4 g of sodium percarbonate) and a flow rate of

40mL/h. Upon completing the addition of phthaloyl chloride solution, the mixture was quenched with $Na_2S_2O_3$ (aq.) and extracted with DCM for three times. The combined organic layer was dried over $Na_2SO_4$, filtrated, and concentrated in vacuo and purified via silica gel flash chromatography to offer the desired product in 89% yield.

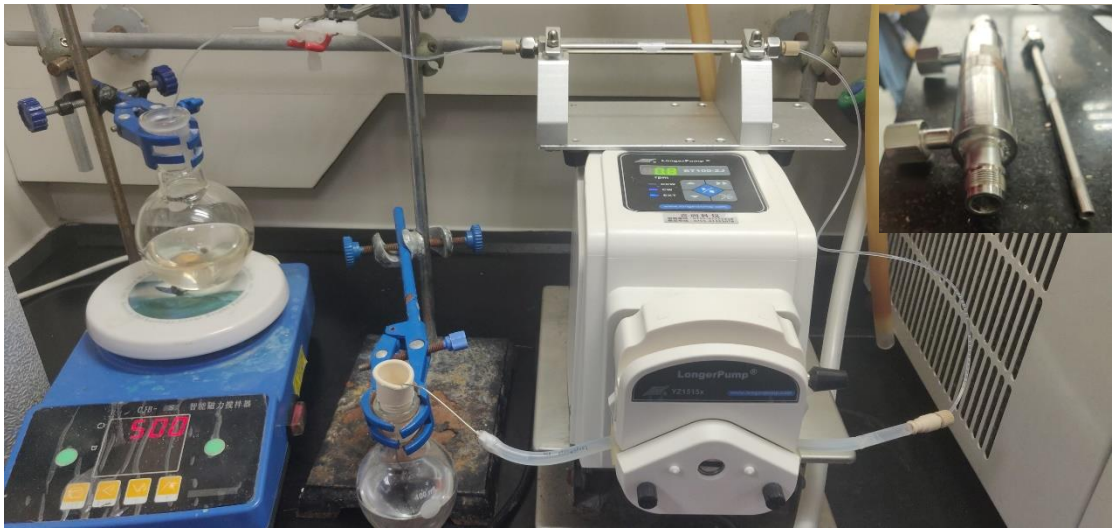
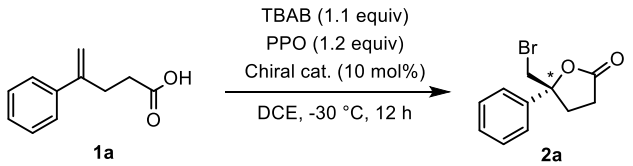


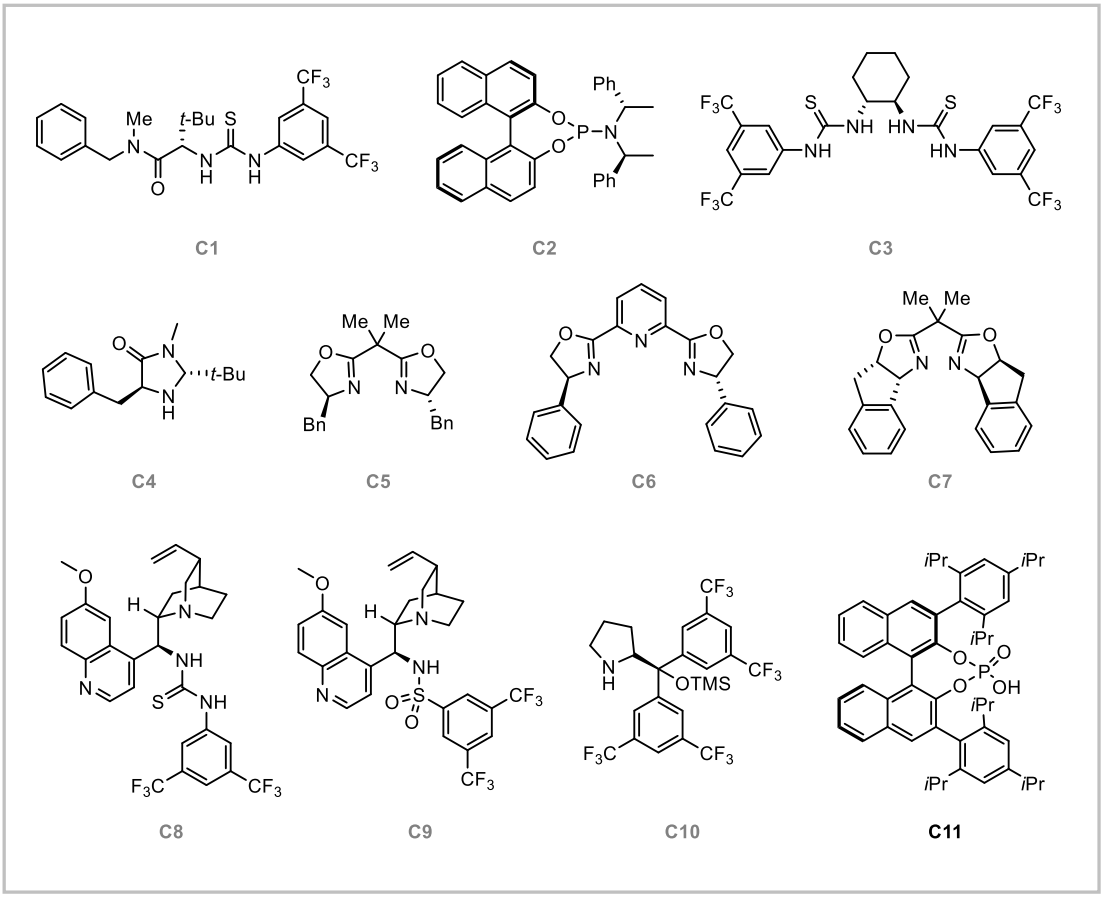

**Figure S9.** Picture of the combination of flow and batch reactions using in-situ generated phthaloyl peroxide (1 g scale synthesis).

# 8. A catalytic asymmetric version of the halocyclization

**Table S6** Screening of the chiral catalyst for asymmetric halocyclization of **1a**.[a]




| Entry | Chiral cat. | Yield of **2a** (%)[b] | *ee* of **2a** (%) |
|---|---|---|---|
| 1 | **C1** | 83 | 0 |
| 2 | **C2** | 93 | 0 |
| 3 | **C3** | 54 | 0 |
| 4 | **C4** | 82 | 0 |
| 5 | **C5** | 79 | 0 |
| 6 | **C6** | 80 | 0 |
| 7 | **C7** | 93 | 0 |
| 8 | **C8** | 54 | 0 |
| 9 | **C9** | 81 | 0 |
| 10 | **C10** | 86 | 0 |
| 11 | **C11** | 80 | 27 |



[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), Chiral cat. (0.01 mmol, 10 mol%), PPO (0.12 mmol, 1.2 equiv.), TBAB (0.11 mmol, 1.1 equiv.), and DCE (2 mL), -30 °C, 12 h. [b] Yields of isolated product.

**General procedure for catalytic asymmetric halocyclization of 1a.** In a dried sealed 10 mL Schlenk tube, **1a** (0.10 mmol, 1.0 equiv.), **C11** (7.5 mg, 0.01 mmol, 10 mmol %) and TBAB (0.11 mmol, 1.1 equiv.) were dissolved in dry DCE (1 mL), and the mixture was cooled to -30 °C. Then a solution of PPO (0.12 mmol, 1.2 equiv.) in dry DCE (1 mL) was added slowly during 12 hours. According to the same workup procedure for racemic sample, the residue was purified by chromatography (petroleum ether:ethyl acetate = 3:1) to give product **2a** (80% yield, 25% *ee*) as colorless oil.

**Optical rotation**: $[\alpha]_D^{25}$ +3.9 (*c* 0.7, $CHCl_3$, 25% ee).

**HPLC analysis**: DAICEL CHIRALPAK IC, *n*-hexane/isopropanol = 85/15, 0.6 mL/min, λ = 214 nm, $t_1$ = 25.7 min (major), $t_2$ = 30.4 min (minor).

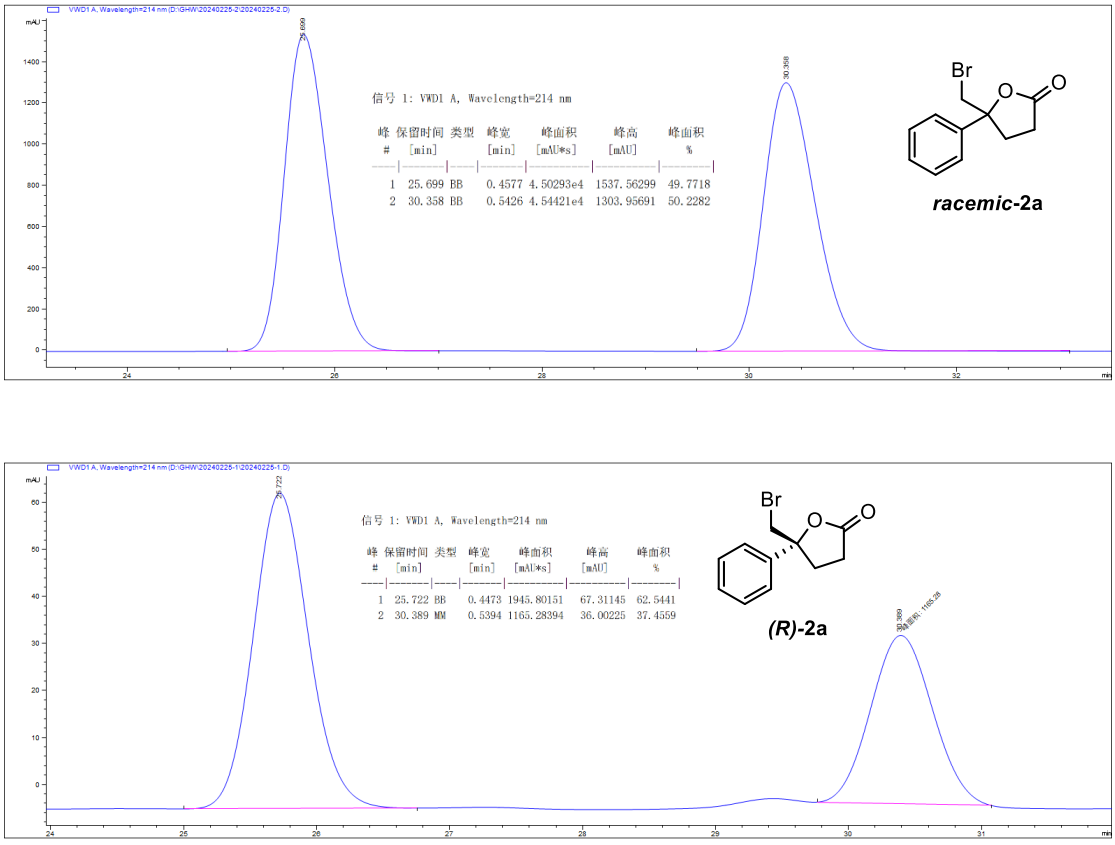



**Figure S10.** HPLC spectrum of racemic and chiral sample **2a**.

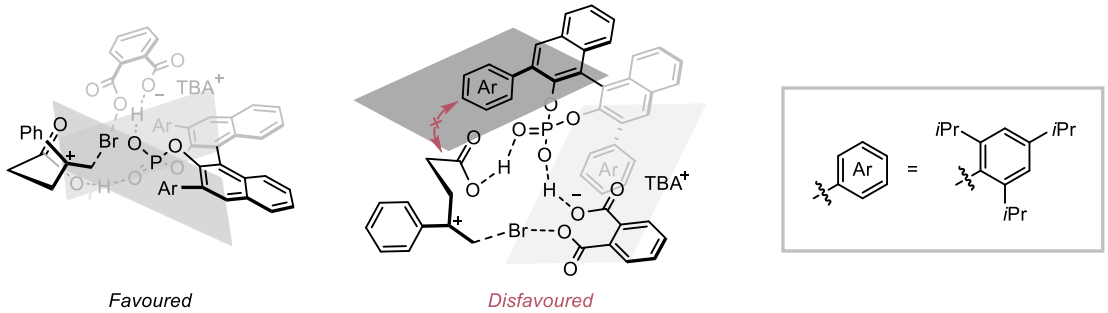
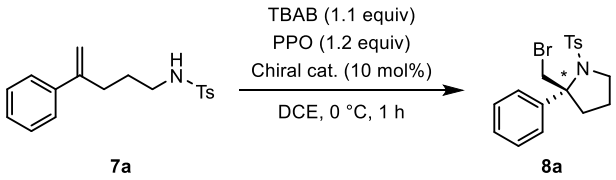


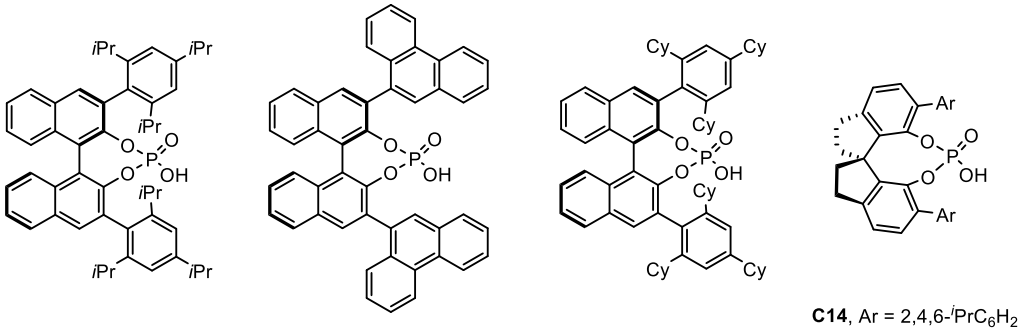

**Figure S11.** The possible transition state of BCTC-induced enantioselective halocyclization

**Table S7** Screening of the chiral catalyst for asymmetric halocyclization of **7a**.[a]




**7a** **8a**

| Entry | Chiral cat. | Yield of **8a** (%)[b] | *ee* of **8a** (%) |
|---|---|---|---|
| 1 | **C11** | 74 | 36 |
| 2 | **C12** | 81 | 13 |
| 3 | **C13** | 80 | 10 |
| 4 | **C14** | 83 | 25 |
| 5 | **C15** | 77 | 18 |




[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), Chiral cat. (0.01 mmol, 10 mol%), PPO (0.12 mmol, 1.2 equiv.), TBAB (0.11 mmol, 1.1 equiv.), and DCE (2 mL), 0 °C, 1 h. [b] Yields of isolated product.

**General procedure for catalytic asymmetric halocyclization of 7a.** In a dried sealed 10 mL Schlenk tube, **7a** (0.10 mmol, 1.0 equiv.), **C11** (0.01 mmol, 10 mmol %) and TBAB (0.11 mmol, 1.1 equiv.) were dissolved in dry DCE (1 mL), and the mixture was cooled to 0 °C. Then a solution of PPO (0.12 mmol, 1.2 equiv.) in dry DCE (1 mL) was added slowly in ten portions within 1 hour. According to the same workup procedure for racemic sample, the residue was purified by chromatography (petroleum ether:ethyl acetate = 5:1) to give product **8a** (74% yield, 36% *ee*) as colorless oil.

**Optical rotation**: $[\alpha]_D^{25}$ +2.3 (*c* 0.8, $CHCl_3$, 36% ee).

**HPLC analysis**: DAICEL CHIRALPAK AD-H, *n*-hexane/isopropanol = 90/10, 1.0 mL/min, λ = 220 nm, $t_1$ (major) = 20.4 min, $t_2$ (minor) = 15.4 min, *ee* = 36%.

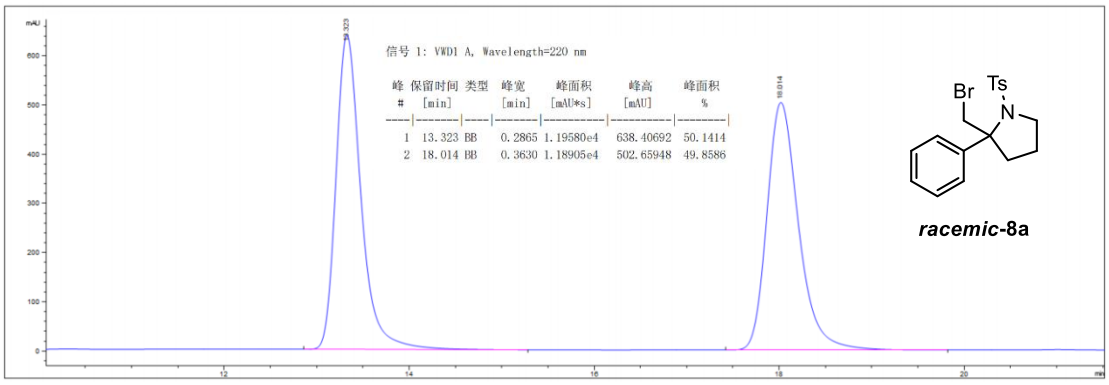



**Figure S12.** HPLC spectrum of racemic sample **8a**.

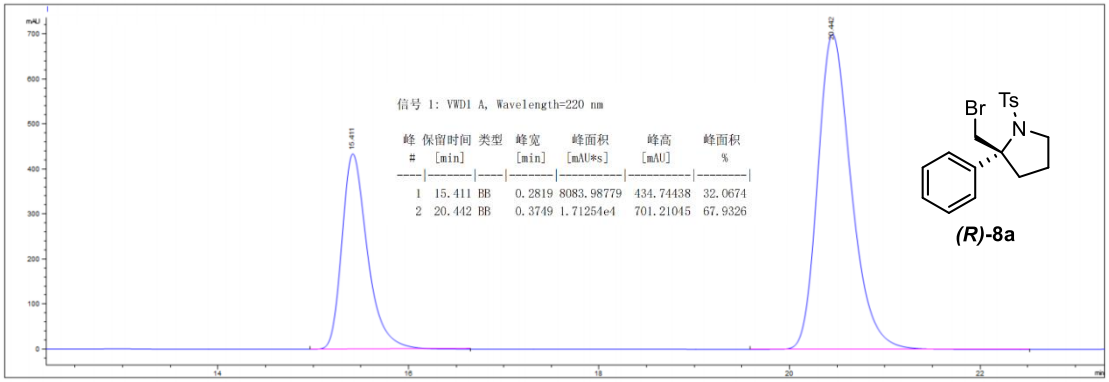



**Figure S13.** HPLC spectrum of chiral sample **8a**.

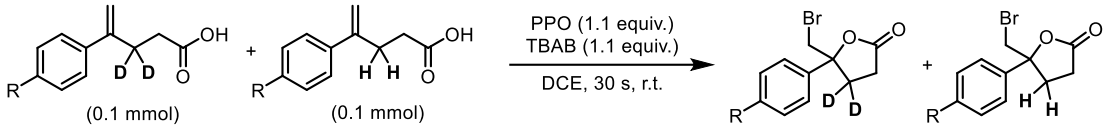
# 9. Studies of kinetic isotope effects (KIE) and intermolecular completive reactions.

## 9.1 Studies of kinetic isotope effects (KIE)

**General procedure for intermolecular KIE studies.** In a dried Schlenk tube, **1** (0.1 mmol), **1-$D_2$** (0.1 mmol) and TBAB (1 equiv., 0.1 mmol) were added in DCE (1mL) at 25 °C. Subsequently, PPO (1.1 equiv., 0.1 mmol) was added and the reaction was performed at same temperature for 30 s. After the reaction was completed, the solvent was evaporated and the residue was purified by column chromatography (petroleum ether:ethyl acetate = 3:1) to give the expected product.

**General procedure for intramolecular KIE studies.** In a dried Schlenk tube, **1a-D** (0.1 mmol) and TBAB (1.1 equiv., 0.11 mmol) were added in DCE (1mL) at 25 °C. Subsequently, PPO (1.2 equiv., 0.11 mmol) was added and the reaction was performed at same temperature for 30 s. After the reaction was completed, the solvent was evaporated and the residue was purified by column chromatography (petroleum ether:ethyl acetate = 3:1) to give the expected product.

**Table S8.** Intermolecular KIE experiment of electrophilic bromolactonization.




| R | Run 1 | Run 2 | Run 3 | KIE |
|---|---|---|---|---|
| H | 1.12 | 1.10 | 1.08 | 1.10±0.02 |
| OMe | 1.20 | 1.17 | 1.22 | 1.20±0.03 |

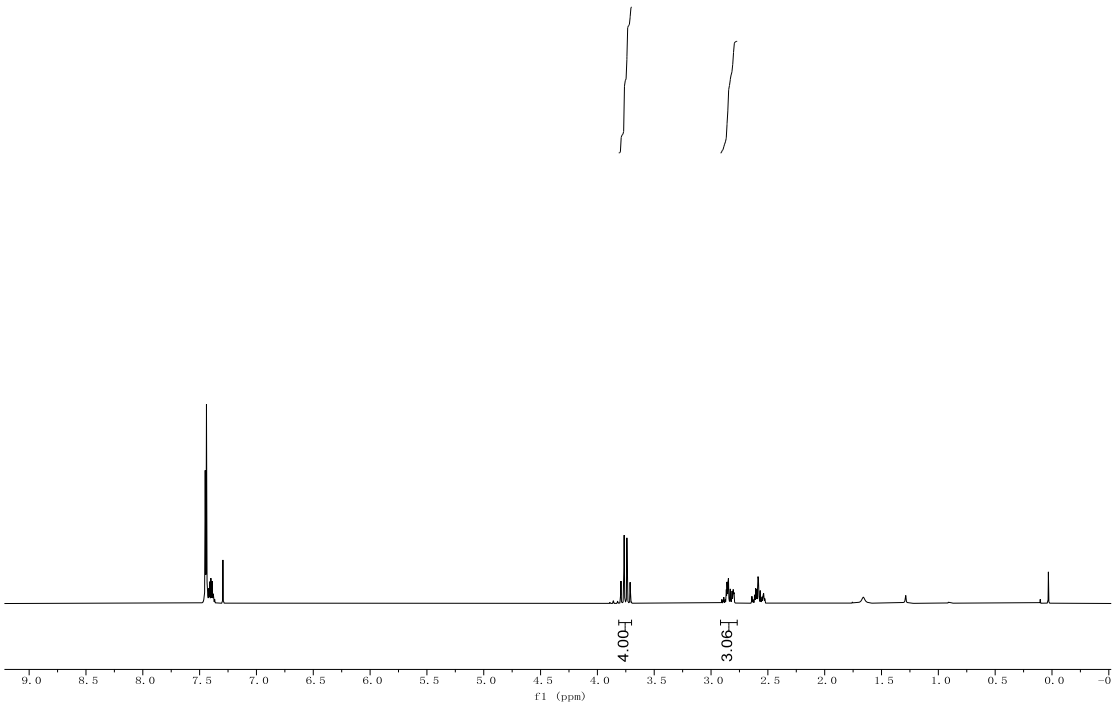


**Figure S14.** $^{1}$H NMR spectrum of intermolecular KIE of **1a** and **1a-D$_2$**.

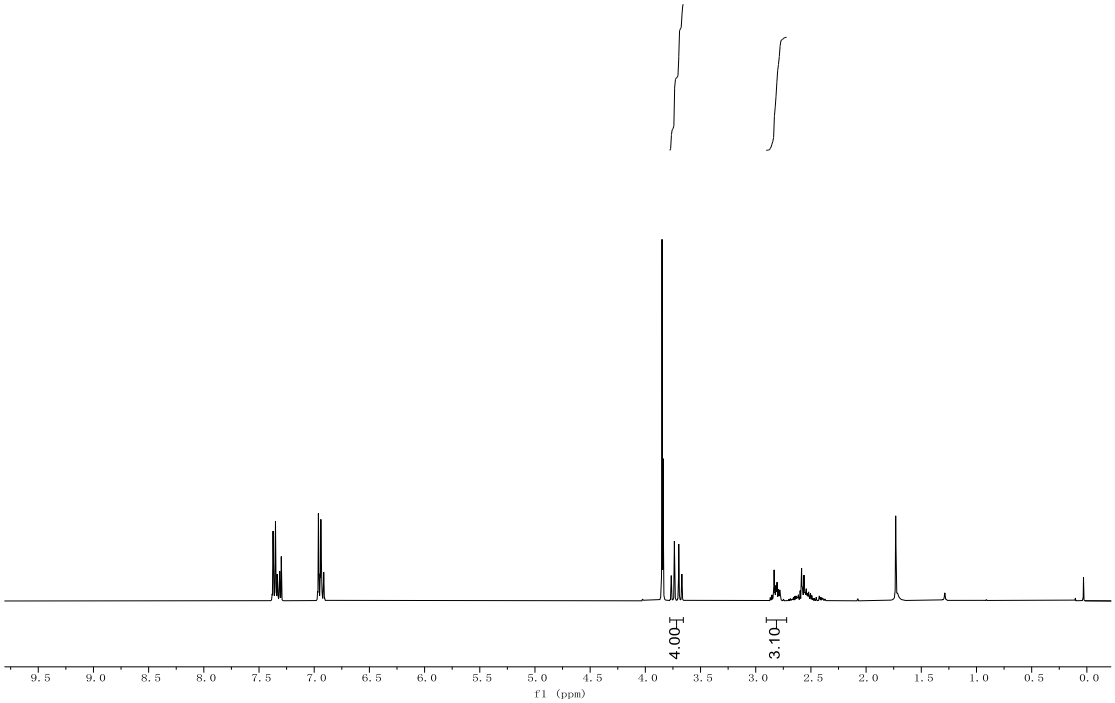



**Figure S15.** $^{1}$H NMR spectrum of intermolecular KIE of **1b** and **1b-D$_2$**.

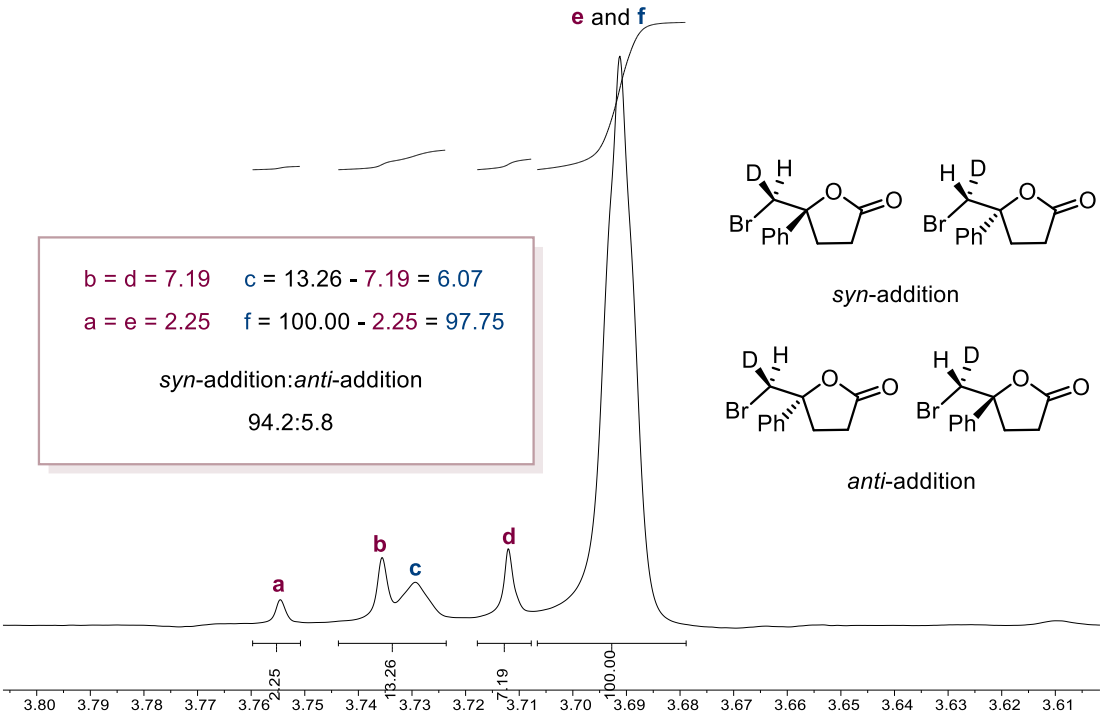



**Figure S16.** $^{1}$H NMR spectrum of intramolecular KIE of **1a** and **1a-D**.

## 9.2 Intermolecular competition bromocyclization

**Table S9.** Competition experiments of intermolecular electrophilic bromolactonization.

| Entry | A : B | Run 1 | Run 2 | Run 3 | Ratio |
|---|---|---|---|---|---|
| 1 | **1a** : **3a** | 2.21 : 1 | 2.43 : 1 | 2.30 : 1 | 2.313±0.111 |
| 2 | **1a** : **5f** | 2.53 : 1 | 2.76 : 1 | 2.61 : 1 | 2.833±0.117 |
| 3 | **1a** : **5g** | 3.38 : 1 | 3.40 : 1 | 3.35 : 1 | 3.376±0.025 |
| 4 | **1a** : **5i** | 7.80 : 1 | 7.27 : 1 | 7.57 : 1 | 7.547±0.266 |
| 5 | **1a** : **7a** | >20 : 1 | >20 : 1 | >20 : 1 | >20 |
| 6 | **3a** : **5f** | 1.22 : 1 | 1.15 : 1 | 1.14 : 1 | 1.170±0.044 |
| 7 | **3a** : **5g** | 1.61 : 1 | 1.69 : 1 | 1.78 : 1 | 1.693±0.085 |
| 8 | **5f** : **5g** | 1.59 : 1 | 1.66 : 1 | 1.47 : 1 | 1.573±0.096 |

**General procedure for intermolecular competition bromocyclization.** In an oven dried Schlenk tube equipped with a stirring bar and substrate A (1 equiv.), substrate B (1 equiv.) and TBAB (1 equiv.) were dissolved in DCE (0.1 M for TBAB), followed by the addition of PPO (1.1 equiv.) at ambient temperature. The solution is stirred for 2 min before quenched by saturated sodium bicarbonate solution. Then the solution was diluted with DCM and the combined organic layers were dried over anhydrous $Na_2SO_4$ and evaporated in vacuo. The residue was purified by column chromatography over silica gel or using $^1H$ NMR the to give the competition ratios.

Intermolecular competition bromocyclization of **1a** and **3a**: *product **2a**=17.9 mg; product **3a**=7.3 mg.*

Intermolecular competition bromocyclization of **1a** and **5f**: *product **2a**=55.5 mg; product **6f**=24.4 mg.*

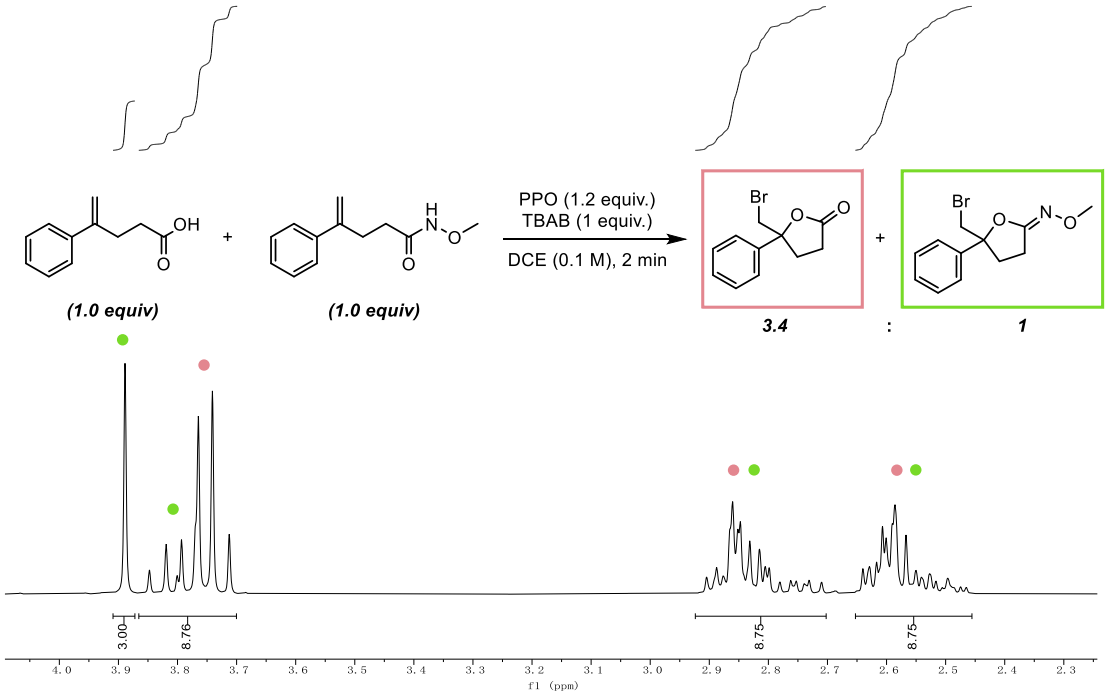



**Figure S17.** Intermolecular competition bromocyclization of **1a** and **5g**.

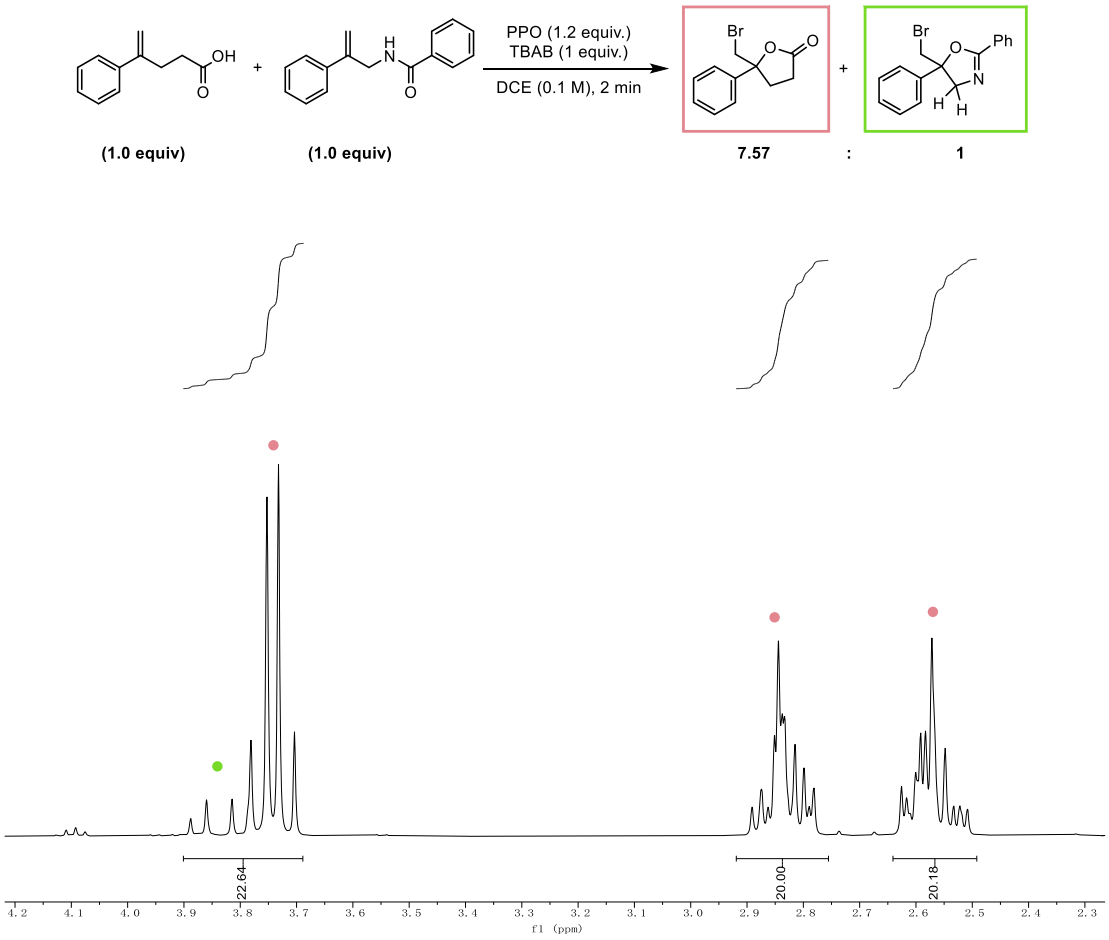



**Figure S18.** Intermolecular competition bromocyclization of **1a** and **5i**.

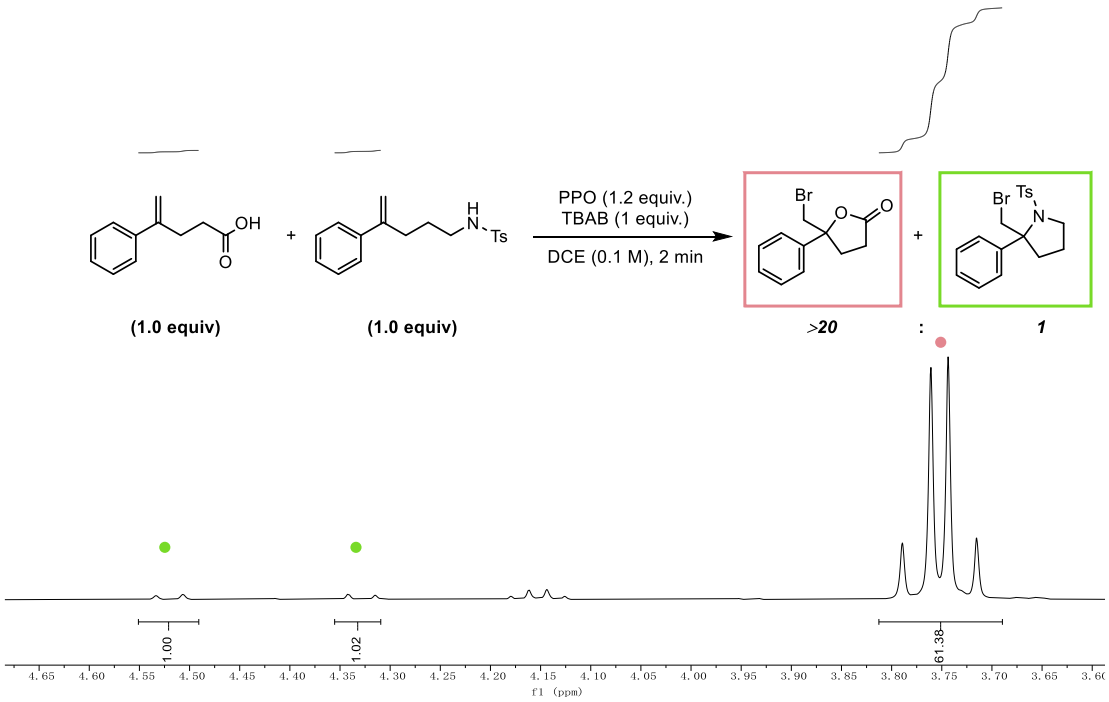



**Figure S19.** Intermolecular competition bromocyclization of **1a** and **7a**.

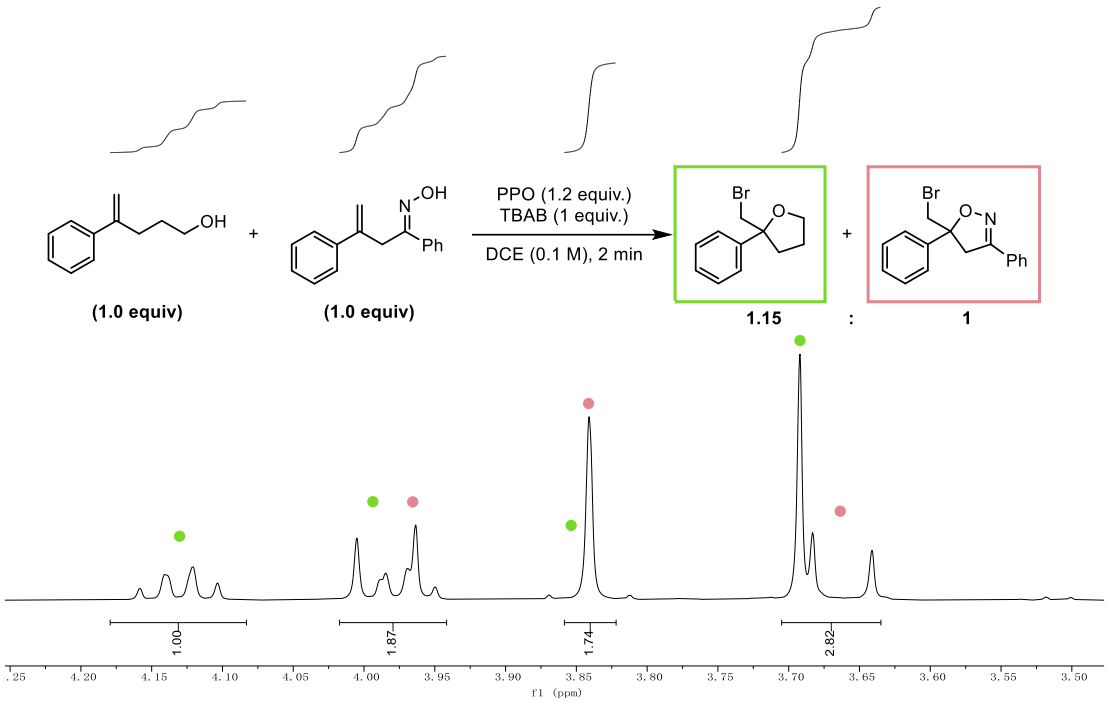



**Figure S20.** Intermolecular competition bromocyclization of **3a** and **5f**.

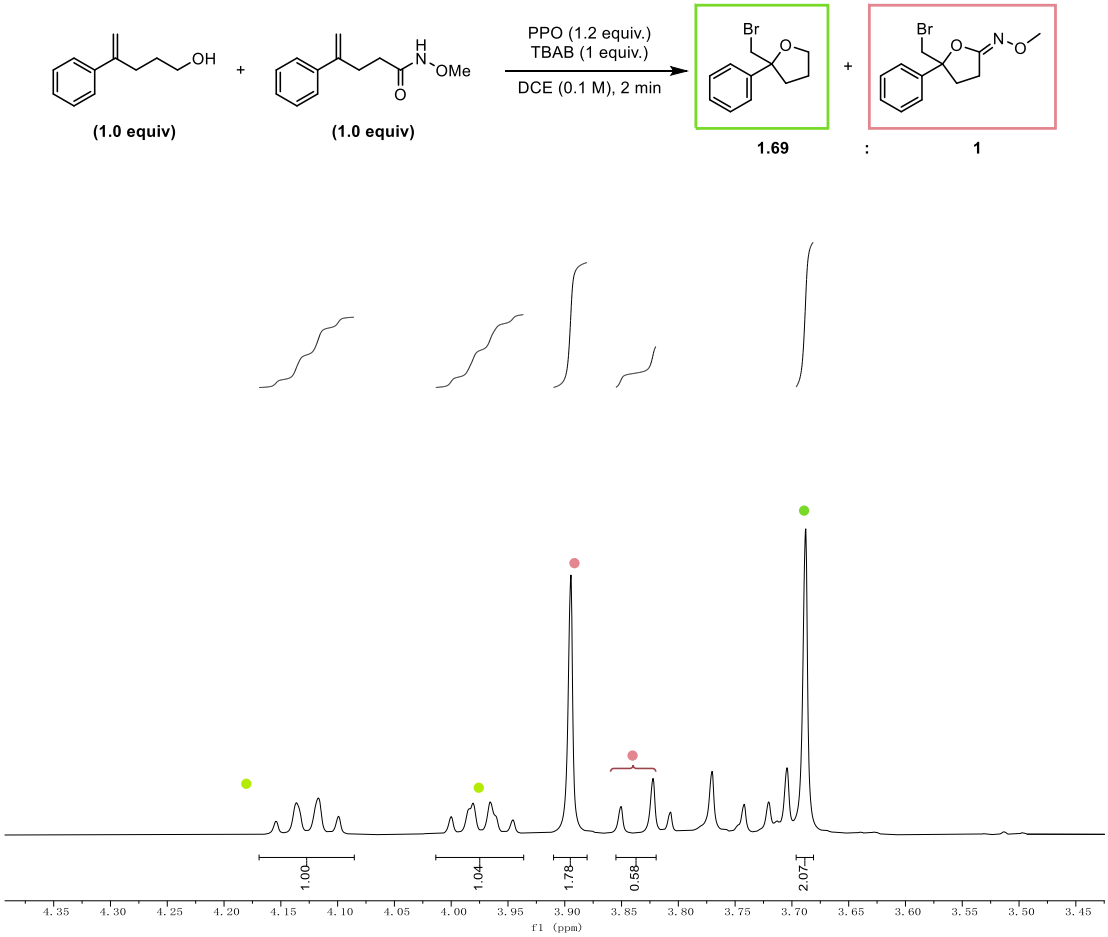



**Figure S21.** Intermolecular competition bromocyclization of **3a** and **5g**.

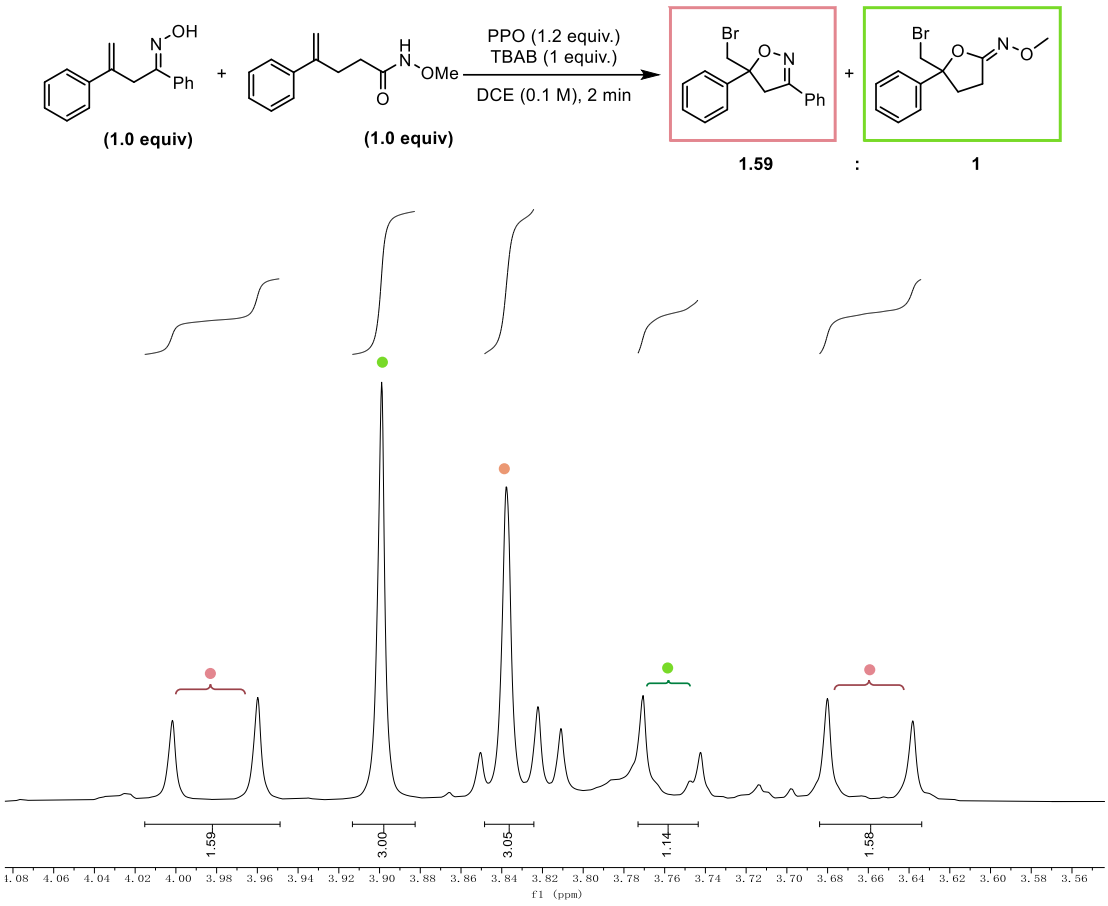



**Figure S22.** Intermolecular competition bromocyclization of **5f** and **5g**.

## 9.3 The valuation of nucleophilicity parameters (*N*)

The nucleophilicity parameters (*N*) of six molecules (**1a**, **3a**, **5f**, **5g**, **5i**, **7a**) were predicted with the aid of the *r*SPOC model developed by Luo et.al.[24] The experimental data could be partially explained in a reasonable manner by comparing the nucleophilicity of attacking groups. For example, the *N* value of acetic acid in DCM is 11.27, while the *N* value of *N*-methoxyacetamide in DCM is 9.99. As a result, the bromocyclization of **1a** was faster than than of **5i** in intermolecular competition reaction. By that analogy, the relative reaction rate of **1a** (*N* = 11.27 for acetic acid) and **5g** (*N* = 9.72 for *N*-methylbenzamide)**,** as well as **5i** (*N* = 9.99 for *N*-methoxyacetamide) and **5g** (*N* = 9.72 for *N*-methylbenzamide)**,** could also been explained (Figure S23, top). Finally, the rate of bromoamination of **7a** was lowest, which was attributed to the low nucleophilicity of *N*,4-dimethylbenzenesulfonamide (*N* = 7.72). Nevertheless, the predicted nucleophilicity parameters *N* were inconsistent with the result of the intermolecular competition bromocyclization involving **3a** and **5f** (Figure S23, bottom). Moreover, a diametrically inverse in ratio was observed in comparing the halocyclization rates of alkenoic acid **1a** and alkenols **3a**. Namely, the halolactonization of **1a** was 2.3 times faster than haloetherification of **3a** under the effect of ICDA, whereas previous work reported that the haloetherification of **3a** was 4.7 times faster than halolactonization of **1a**.[13] Fundamentally, a comprehensive consideration of more factors (including dual-anchoring promoted conformational adjustment, geometric constraint, steric hindrance, p*K*a value, tautomerization) is ineluctably necessary when comparing the relative rates of intermolecular competition reactions.

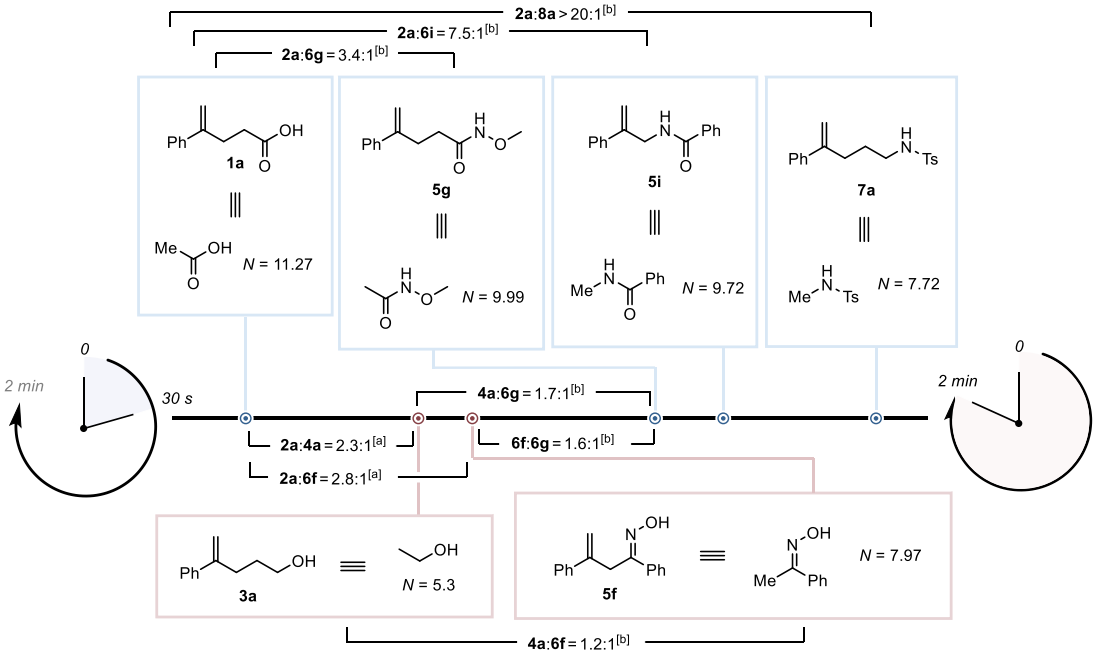



**Figure S23.** The relation between nucleophilicity parameters *N* and reaction rate. [a] Isolated yield. [b] $^{1}$H NMR yield.

## 9.4 Investigation of relative reaction rates of cholorolactonization, bromolactonization and iodolactonization

**General procedure for competition reaction:** In an oven dried Schlenk tube equipped with a stirring bar and TBAX (1.1 equiv. for each $X^-$ source), PPO (2.4 equiv.) were dissolved in DCE (0.1 M for **1a**), followed by the addition of **1a** (1.0 equiv.) at ambient temperature. The solution is stirred for 30 s before quenched by saturated sodium bicarbonate solution. Then the solution was diluted with DCM and the combined organic layers were dried over anhydrous $Na_2SO_4$ and evaporated in vacuo. The residue was purified by column chromatography over silica gel and the ratio was confirmed by $^1H$ NMR.

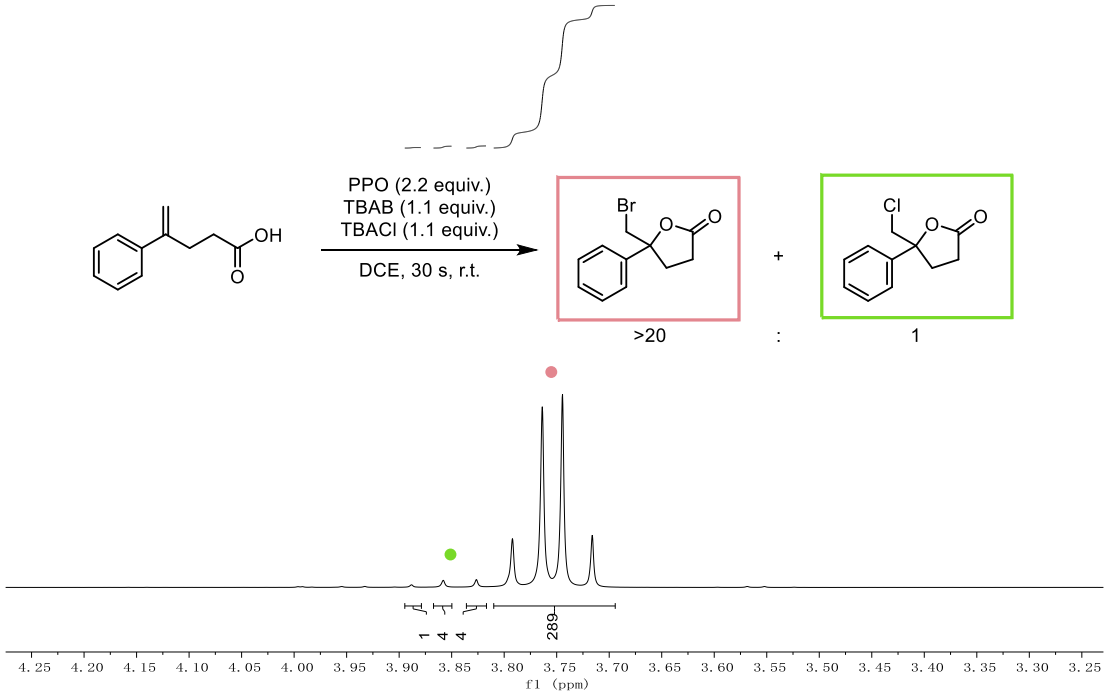



**Figure S24.** Competition cholorolactonization and bromolactonization of **1a**.

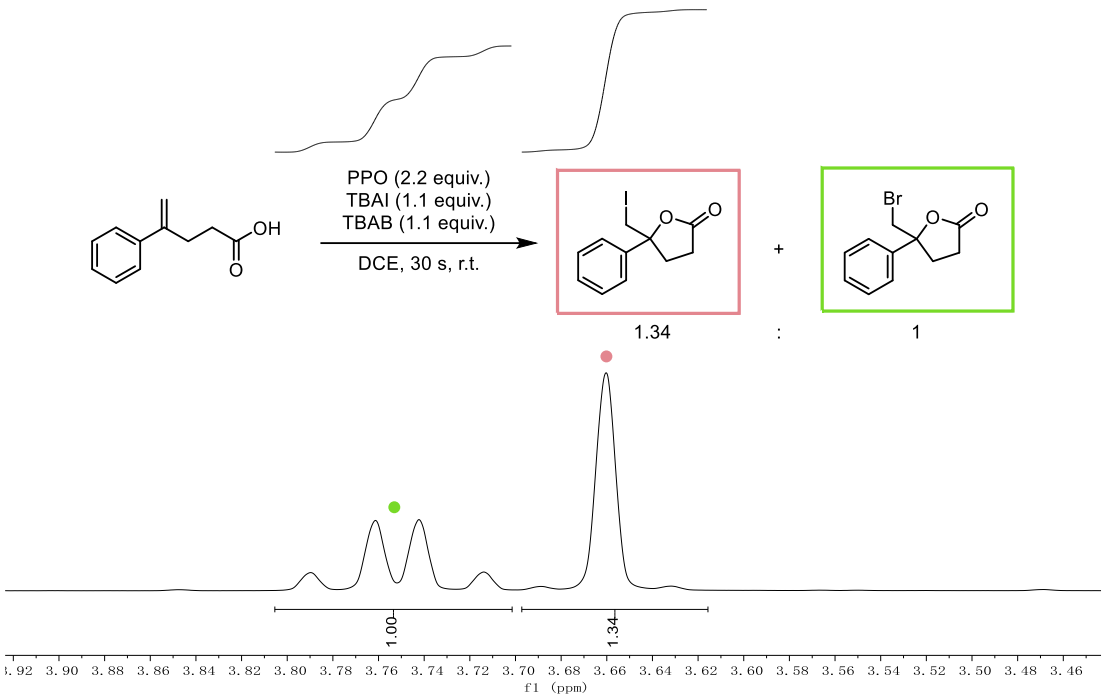



**Figure S25.** Competition bromolactonization and iodolactonization of **1a**.

# 10. Computational calculation for mechanistic studies

## 10.1 General Computational Procedures

All *ab initio* and DFT calculations were performed using Gaussian suite of programs.[61] Geometries of all species were fully optimized using M062X functional[62] with dispersion correction[63] (M062X-D3) and 6-311G(d) basis set in the gas phase. Harmonic vibrational frequency calculations at the same level of theory were performed to ensure that either a minimum (for intermediates) or a first-order saddle point (for transition states) was obtained. More accurate electronic energies were calculated using M062X-D3/6-311++G(d,p) method in dichloroethane solvent via SMD model[64]. Unless otherwise specifies, the energies reported in this paper are Gibbs free energies under 298.15 K and 1 atm with solvent effect corrections. The 3D structures of intermediates and transition states were illustrated using the CYLview software.[67] The visualization of halogen bond was carried out by independent gradient model based on Hirshfeld partition of moleculardensity (IGMH).[68] The topological analysis of the electron charge density performed for the theoretical models of the structure was determined using Bader's theory of "atoms in molecules" (AIM)[69] by Multiwfn.[65,66]

## 10.2 Proton Affinity (*PA)*

Proton affinities (*PA*), describing the ability of a molecule to accept a proton (basicity) in a chemical reaction, representing one of the most fundamental intrinsic properties of chemical compounds.[25] Pragmatically, the prediction of *PA* is important for rationalizing the biological functions of nucleic bases and amino acids, and for designing of strong and hyperstrong organic bases in chemical reaction. Experimentally, a gargantuan number of *PA* values of Brønsted bases have been explored by means of ion-cyclotron resonance, proton NMR and others for reference.

Nevertheless, compared with the gargantuan number of chemical substances in existence, the proportion of which *PA* value has been measured is extremely small, therefore inestimable resources would cost to perfect the experimental *PA* value of the database. More importantly, on the other hand, unless performing careful additional spectroscopic measurements, anchor bases with benchmark accuracy indispensable for establishing the absolute basicity scale is difficult to achieve by common experimental techniques alone. However, information not retrieved by experimental research could be provided by theoretical methods, which has demonstrated remarkable ability to assist chemists in the prediction of the absolute basicity scale and in the purposeful design of strong and hyperstrong organic bases in silico, at molecular and supramolecular levels.

It is defined for a gas-phase reaction[25], where a protonated conjugate acid (**B**H$^+$) dissociates into gaseous base (**B**) and the free proton (H$^+$):

$$\mathrm{PA}(\mathbf{B}) = \Delta H\,[\mathbf{B}\mathrm{H}^+(\mathrm{g}) \rightarrow \mathbf{B}\,(\mathrm{g}) + \mathrm{H}^+(\mathrm{g})] = \Delta E + RT \tag{1}$$

where $\Delta E$ represents the difference in the total energies of the products and a reactant of reaction, $T$ is the absolute temperature, and $R$ is the ideal gas constant. The total energy of a polyatomic molecule $E$ can be expressed as

$$E = E_{\mathrm{ele}} + E_{\mathrm{ZPV}} + E_{\mathrm{vib}} + E_{\mathrm{rot}} + E_{\mathrm{trans}} \tag{2}$$

where $E_{\mathrm{ele}}$ stands for the electronic energy, $E_{\mathrm{ZPV}}$ is the zero point vibrational energy of normal vibrational modes at a temperature of T = 0, and $E_{\mathrm{trans}}$ and $E_{\mathrm{rot}}$ are translational and rotational contributions to the total energy, respectively. Furthermore, $\mathrm{E_{vib}}$ is a vibrational energy change from 0 to 298.15 K. Employing statistical mechanics, one obtains that the contributions of the $E_{\mathrm{rot}}$ and $E_{\mathrm{trans}}$ energies for a nonlinear molecule are equal, (3/2)RT each. The energies $E_{\mathrm{ZPV}}$ and $E_{\mathrm{vib}}$ are given by eq (3):

$$E_{\mathrm{ZPV}}(\mathrm{T}) = \frac{1}{2}\sum_{i=1}^{3n-6} h\omega_i \text{ and } E_{\mathrm{vib}} = \sum_{i=1}^{3n-6} h\omega_i/\left(\mathrm{e}^{h\omega_i/\mathrm{RT}} - 1\right) \tag{3}$$

where $n$ is the number of atoms in a molecule. Combining eqs (2) and (3) and taking into account that proton (H$^+$) possesses only translational energy, (3/2)RT, it follows that the PA of the base **B** can be calculated by using the following equation:

$$\mathrm{PA}(\mathbf{B}) = [E_{\mathrm{ele}}(\mathbf{B}) - E_{\mathrm{ele}}(\mathbf{B}\mathrm{H}^+)] + [E_{\mathrm{ZPV}}(\mathbf{B}) - E_{\mathrm{ZPV}}(\mathbf{B}\mathrm{H}^+)] + [E_{\mathrm{vib}}(\mathbf{B}) - E_{\mathrm{vib}}(\mathbf{B}\mathrm{H}^+)] + (5/2)RT \tag{4}$$

## 10.3 Halogen Affinity (*HalA*)

Because of the parallels between protonation and halogenation chemistry, the evaluation of gas phase Halenium Affinity (*HalA*) is essentially similar to the reported methods used for derivation of *PA*. This thermodynamic parament is defined as the molar enthalpy change for a given Lewis base upon its attachment to a halenium ion.[25] Significantly, the computationally evaluated *HalA* have an accurate consistent with known experimental data in estimating and predicting of reactivity (*NAAA*), chemo-selectivity (multiple nucleophilic sites) and site selectivity (electron-rich aromatic compounds) of electrophilic halogenation reactions.[13,26]

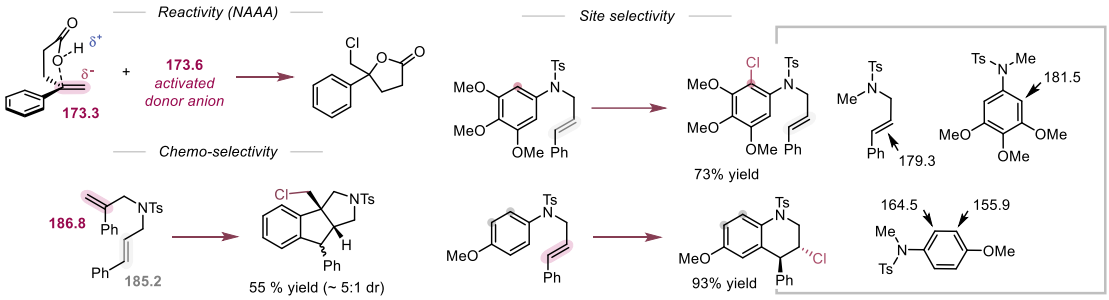



**Figure S26.** Application of *HalA* values in explaining and predicting reactivity, chemo-selectivity and site selectivity.

The acceptor fragment may be neutral or anionic (i.e., the X─LB complex is cationic or neutral), leading to two distinct cases:

$$\text{neutral acceptor: } \Delta H_{\text{rxn}}(X^+ + :LB \rightarrow X{-}LB^+)$$

$$\text{anionic acceptor: } \Delta H_{\text{rxn}}(X^+ + :LB^- \rightarrow X{-}LB)$$

The HalA values in kcal/mol are derived at T = 298.15 K (unless noted otherwise) as in eqs (5) and (6):

$$HalA = -\Delta E_{(\text{elec})} - \Delta\text{ZPE} - \Delta E'_{(\text{vib})} + (5/2)RT \tag{5}$$

$$\text{E}'_{\text{vib}}(T) = \sum_{i=1}^{3n-6} Nhv_i/\left(\text{e}^{Nhv_i/RT} - 1\right) \tag{6}$$

where $\Delta E_{(\text{elec})}$ = $E_{(\text{elecronic})}$(X─LB adduct) – [$E_{(\text{elecronic})}$(:LB) +$E_{(\text{elecronic})}$($X^+$)]; zero point energy change ΔZPE = ZPE(X─LB adduct) – ZPE(:LB); $\Delta E'_{(\text{vib})} = E'_{(\text{vib})}$(X─LB adduct) – $E'_{(\text{vib})}$(:LB), i.e., difference in temperature dependence of vibrational energy; $N$ is Avogadro's number, $h$ is Planck's constant, and $v_i$ is the $i^{\text{th}}$ vibrational frequency. Finally, the (5/2)$RT$ quantity accounts for translational degrees of freedom and the ideal gas value for the change from two particles to one. The energy used for the free halenium ion is the value calculated for its (6-electron, $s^2p^4$) triplet ground state.

## 10.4 Quantitative calculation of halenium affinity (*HalA)* values and NPA (X=Cl, Br)

In this section, to quantitatively elucidate the characteristic of BCTC, we resorted to compare the halenium affinity (*HalA*) parameter of several Lewis base/bromonium ion adducts. For the *HalA* values described in this report we have employed M06L/6-31G*/SMD($CHCl_3$) or M06L/6-31G*/SMD(DCE) level of theory. To ensure the accuracy of the parameters, the calculated *HalA* values of anions of commonly employed halenium sources and olefin compounds were compared with reported research[25], and a good agreement was achieved (Figure S27a, errors at the 95% confidence limit). Reasonably, due to the relatively weak interaction between "hard" oxygen and "soft" bromine atom, the *HalA* value of anion of benzoyl hypobromite (BPO-Br, 160.4 kcal/mol) is lower than that of other halenium sources. Anomalously, however, the *HalA* value of anion of BCTC-Br (170.2 kcal/mol) is apparently higher than that of BPO-Br, and even higher than that of

DBDMH. That is because, the introduction of intramolecular chaperone-like carboxylate anion slightly increases the O−Br bond strength of BCTC-Br.

Furthermore, the intermolecular $Br^+$ competition experiments between tetra-*n*-butylammonium succinimidate (anionic acceptor) and *N*-bromophthalimide (NBP), BCTC-Br, 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) and BPO-Br were set up (Figure S27b), respectively. According to the definition of *HalA* parament, the anion with higher *HalA* value owing a greater ability to capture a bromonium ion, thus owing a stronger tend to form the corresponding electrophilic bromination reagent. From this point of view, reasonably designed intramolecular bromonium competition could verified the accuracy of the theoretical research. Experimentally, due to the distinct disparity in $^1H$ chemical shift of tetra-*n*-butylammonium succinimidate (2.41 ppm) and NBS (2.96 ppm), the proton NMR was employed as a powerful tactic to visualize the $Br^+$ competition experiments. As shown in Figure S27b, the $^1H$ chemical shift decreased from 2.41 ppm to 2.53, 2.57, 2.61 and 2.68 ppm when tetra-*n*-butylammonium succinimidate was mixed 1:1 with NBP, BCTC-Br, DBDMH and BPO-Br, respectively, indicating the distance of $Br^+$ and NBS-$N^-$ decreased during competition reactions. Namely, the capacity to capture $Br^+$ attenuated sequentially from NBP to BPO-Br, which accords with the *HalA*(Br) of anion of NBS versus other anions (Δ*HalA*(Br) = -2.9, -5.9, -10.8 and -15.7 kcal/mol). Distinctly, according to the *HalA* values and intermolecular $Br^+$ competition experiments, BPO-Br should own a better reactivity that BCTC-Br in the electrophilic bromocyclization, while the *HalA(Br)* values of anion of BCTC-Br even higher than some specific air-stable electrophilic bromination reagents.

To further investigate the electrophilicity of the Br nucleus, we conducted a computational study to calculate the NPA charges of BPO-Br and BCTC-Br on Br atom and O atom. For the NPA values described in this report we have employed M06L/6-31G*/SMD($CHCl_3$) level of theory. The result in Figure S27c shows that the Br atom in BCTC-Br carries lower positive charge (0.240) than that in BPO-Br (0.304). The cationic character of the Br atom was consistent with the theoretical and experimental results description in Figure S27a and Figure S27b. Namely, the lower the positive charge on the Br atom, the higher the *HalA*(Br) value of the corresponding anion, and vice versa. Apparently, the installation of intramolecular chaperone-like carboxylate anion reduced the electrophilicity of corresponding hypobromite unit in BCTC-Br. Subsequently, NPA charges on Br atom and O atom were calculated for hypobromite complexes of BPO-Br (in blue line) and BCTC-Br (in red line) while changing the O−Br distance from 1.80 to 2.10 Å. In each case (same O−Br length), the intramolecular chaperone-like carboxylate anion could observably and permanently decrease the positive charge on the Br atom, whereas there was only slightly influence in the positive charge on the O atom. These observations implied that the role of

tethered carboxylate anion in BCTC was analogous to that of the "Trojan Horse". Trojan-like camouflage & approach: the reactivity of "hard-soft" O−X bond was constrained (hid soldiers) and BCTC was positioned proximity to π-bond via hydrogen bond interaction (across the wall of the castle). Subsequently, ICDA provided strict conformational control in a precisely tailored environment and accelerated the $X^+$ transformation (transported soldiers into castle).

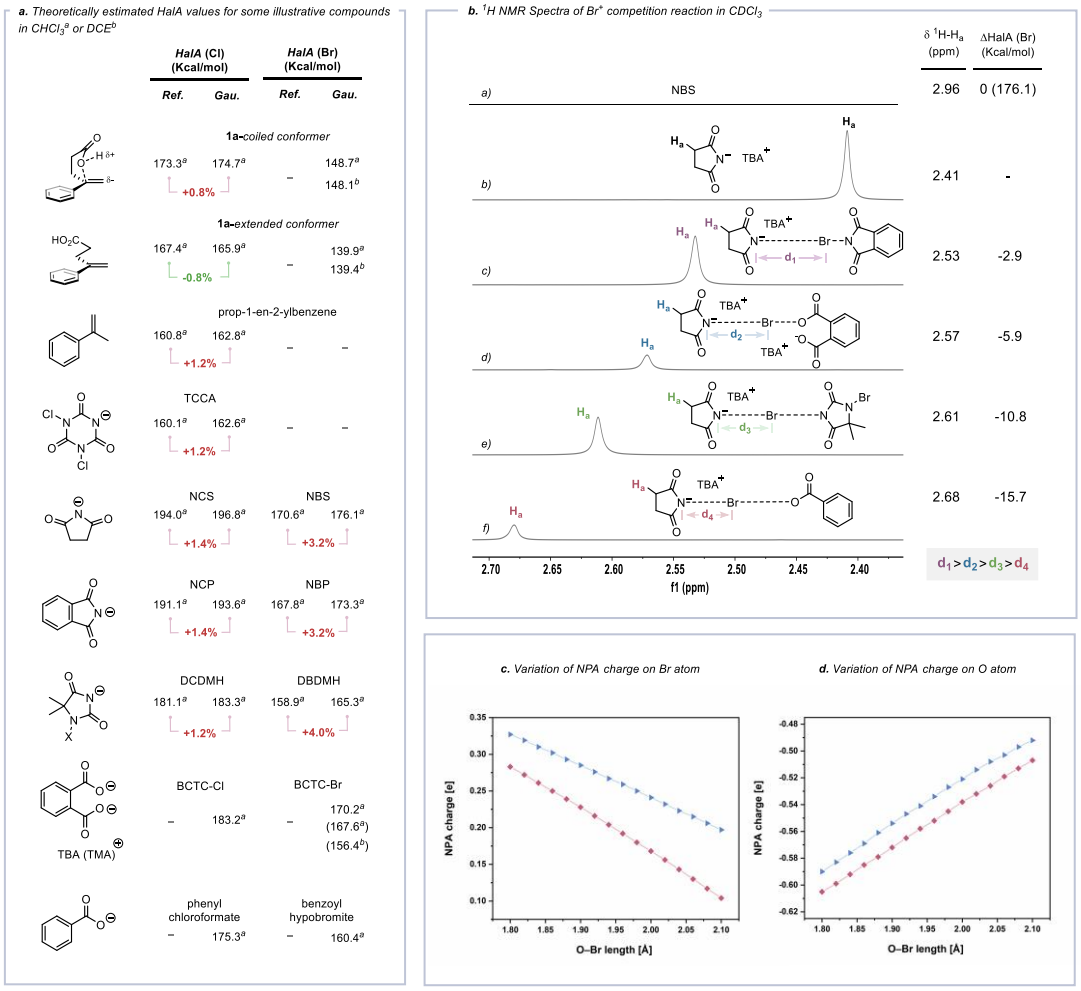



**Figure S27. a**. *HalA* values of two alkenes, BCTC-Br, benzoyl hypobromite and some classical electrophilic bromination reagents. **b**. $^1$H NMR spectra of competition reactions between succinimide anion and several neutal donors (d1 > d2 > d3 > d4), ($CDCl_3$, rt, dark, 30 s): a) *N*-Bromosuccinimide, b) Succinimide anion, c) 1:1 Mixture of succinimide anion and NBP, d) 1:1 Mixture of succinimide anion and Y, e) 1:1 Mixture of succinimide anion and DBDMH, f) 1:1 Mixture of succinimide anion and benzoyl hypobromite. **c**. Variation of NPA charge of Br atom and O atom.

## 10.5 NMR evidence for excluding the transfer of $H^+$ as the initial step

The classical two-steps mechanism begins with electrophilic halenium delivery to form an open β-halo-carbenium ion or a bridged halonium ion, followed by the attack of intramolecular nucleophile to obtain the cyclization products. Although not specifically stated, the deprotonation progress should occur between the electrophilic bromination and intramolecular attack. On the other hand, detail mechanism calculation by Yeung and co-workers reveals that in some case the deprotonation occurs before the electrophilic bromination.[27] Recently, Borhan and co-workers

reported that changing the attacking group from carboxylic acid to the most nucleophilic carboxylate anion substrate could accomplish corresponding chlorolactonization in two minutes.[13] In order to understand the process of this lightning-like reaction rate by utilizing our protocol, it is essential to ascertain whether the short reaction time (in 30s) is mainly ascribed to the rapid in-situ deprotonation of carboxylic acid and carboxylate anion. Since the basicity of the nucleophile could influence the activity of olefin via 'through-space' interaction, the chemical shifts of $\mathbf{H_a}$ and $\mathbf{H_b}$ would be well correlated with the nucleophilicity of the remotely tethered group (Supplementary Figures S28a and S28d). In this respect, competition reactions were set up between 4-phenylpent-4-enoic acid **1a** and tetra-*n*-butylammonium benzoate as well as 4-phenylpent-4-enoic acid and TBAB to study the possible transfer of hydrogen ion. Results shown in Supplementary Figures S28b and S28c indicated that adding tetra-*n*-butylammonium benzoate or TBAB could increase the basicity of remotely tethered group of **1a**, however, failed to form the ionic compound tetra-n-butylammonium 4-phenylpent-4-enoate in-situ. From this point of view, the deprotonation could be thought of as occurring after the formation of C−X bond.

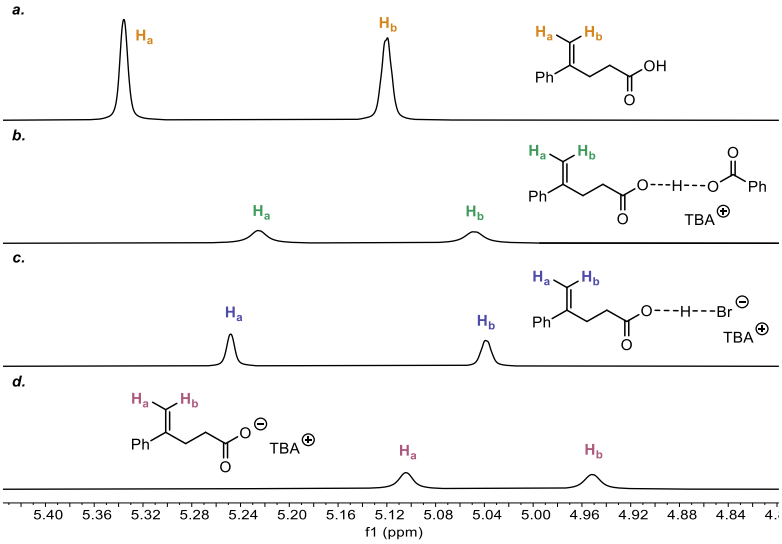



**Figure S28.** $^1$H NMR Spectrum of **a**. **1a**; **b**. 1:1 mixture of **1a** and tetra-*n*-butylammonium benzoate; **c**. 1:1 mixture of **1a** and TBAB; **d**. tetra-*n*-butylammonium 4-phenylpent-4-enoate.

## 10.6 Potential energy surface calculation and the topological analysis of the electron charge density

**Table S10.** Some bond critical point properties (in a.u.) of halogen bond valuation at the M062X-D3/6-311G(d) level of theory calculated by Multiwfn.[65]

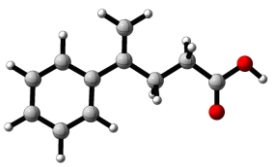
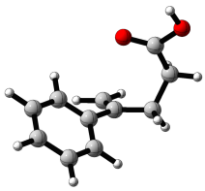
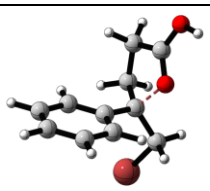
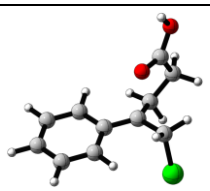
| Complexes | $\rho$ | $\nabla^2\rho$ | $V_b$ | $G_b$ | $H_b$ | $\lvert V_b\rvert/G_b$ |
|---|---|---|---|---|---|---|
| C–Br (**INT1**) | 0.0554 | 0.0665 | -0.0386 | 0.0276 | -0.0110 | 1.3986 |
| Br–O (**INT1**) | 0.1054 | 0.1595 | -0.1096 | 0.0747 | -0.0349 | 1.4672 |
| C–Br (**TS1**) | 0.1315 | -0.0387 | -0.1228 | 0.0566 | -0.0662 | 2.1696 |
| Br–O (**TS1**) | 0.0292 | 0.0975 | -0.0223 | 0.0234 | 0.0010 | 0.9630 |
| C–Br (**INT2**) | 0.1344 | -0.0461 | -0.1274 | 0.0580 | -0.0695 | 2.1966 |
| Br–O (**INT2**) | 0.0216 | 0.0724 | -0.0160 | 0.0170 | 0.0011 | 0.9412 |

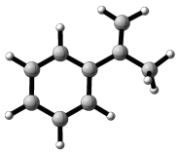
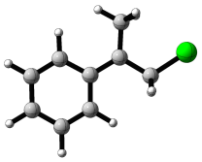
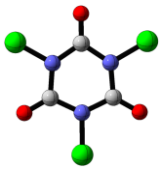
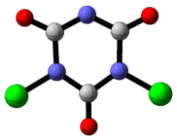
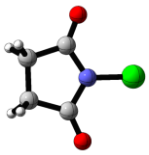
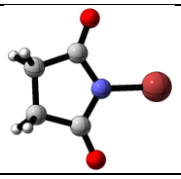
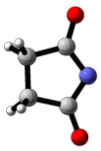
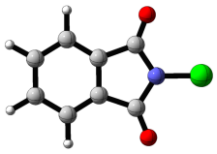
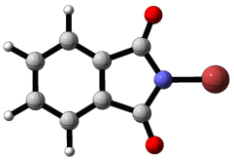
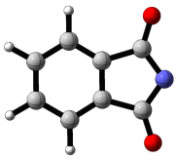
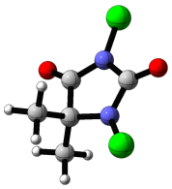
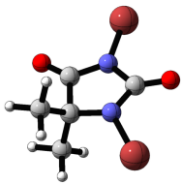
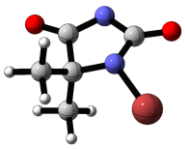
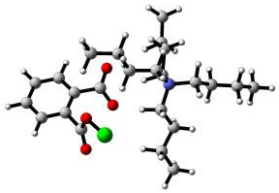
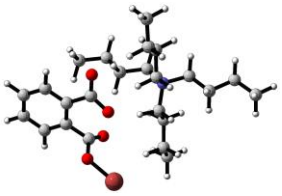
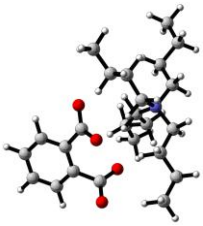
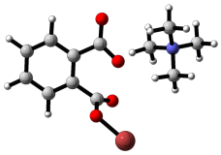
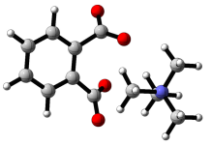
The theory of "atoms in molecules" (AIM) has been used to clarify the nature of interactions in halogen bond system.[70-72] The theory analyzes the topology of the electron density $\rho$, and the Laplacian $\nabla^2$at the critical points. More recently, kinetic energy density $G_c$ and potential energy density $V_c$ at the critical point, obtained from AIM analysis has been used for understanding the bonding. The ratio $|V_c|/G_c$ is claimed to be a better descriptor of bonding. When $|\boldsymbol{V_c}|/\boldsymbol{G_c} < \mathbf{1}$, interactions in a chemical system are characteristic of closed-shell interactions; those with $|\boldsymbol{V_c}|/\boldsymbol{G_c} > \mathbf{2}$ are typically covalent interactions; and when $\mathbf{1} < |\boldsymbol{V_c}|/\boldsymbol{G_c} < \mathbf{2}$, they are of intermediate character.

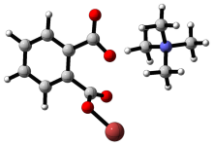
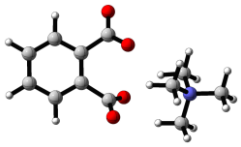
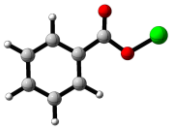
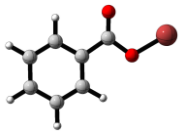
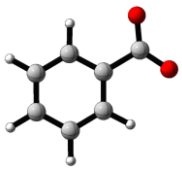
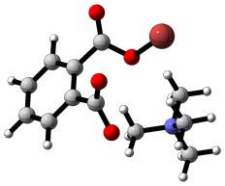
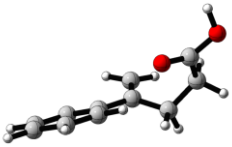
For potential energy surface calculation, geometries of substrate, BCTC, **INT1**, **TS1** and **INT2** species were fully optimized using M062X functional[62] with dispersion correction[63] (D3) and 6-311G(d) basis set in the gas phase, while geometries of BCTC-H, **INT3**, **TS2** and product were fully optimized using same level of theory but in dichloroethane (DCE) solvent. Harmonic vibrational frequency calculations at the same level of theory were performed to ensure that either a minimum (for intermediates) or a first-order saddle point (for transition states) was obtained. More accurate electronic energies were calculated using M062X-D3/6-311++G(d,p) method in dichloroethane solvent via SMD model[64].

## 10.7 Cartesian coordinates of optimized structures

**Table S11.** Optimized Structures of the studied species for *HalA* valuation.

| Species | Optimized Structures | Species | Optimized Structures |
|---|---|---|---|
| **1a-***coiledconformer*_neutral |  | **1a-***extendedconformer*_neutral |  |
| **1a**-Br_cation |  | **1a**-Cl_cation |  |

| | | | |
|---|---|---|---|
| Prop-1-en-2-ylbenzene_neutral |  | Prop-1-en-2-ylbenzene-Cl _cation |  |
| TCCA_neutral |  | TCCA_anion |  |
| NCS_neutral |  | NBS_neutral |  |
| NCS/NBS_anion |  | NCP_neutral |  |
| NBP_neutral |  | NCP/NBP_anion |  |
| DCDMH_neutral |  | DBDMH_neutral |  |
| DCDMH/ DBDMH _anion |  | BCTC-Cl _TBA_neutral |  |
| BCTC-Br _TBA_neutral |  | BCTC-Br/-Cl _TBA_anion |  |
| BCTC-Br_TMA _neutral |  | BCTC-Br _TMA_anion |  |

| | | | |
|---|---|---|---|
| BCTC-Br_TMA _DCE_neutral |  | BCTC-Br_TMA _DCE_anion |  |
| Phenylchloroformate _neutral |  | Benzoylhypobromite _neutral |  |
| Phenylchloroformate/ Benzoylhypobromite _anion |  | Active_BCTC-Br_TMA |  |
| Active_**1a** _neutral |  | | |

**Cartesian coordinates**

**1a**-*coiledconformer*_neutral

| | | | |
|---|---|---|---|
| H | -1.41470400 | 1.17861200 | -1.95290700 |
| C | -1.78633200 | 0.56072500 | -1.14283500 |
| C | -2.78840600 | -1.01299800 | 0.92705000 |
| C | -1.06826300 | 0.47990900 | 0.06655400 |
| C | -2.98984300 | -0.12408000 | -1.30295400 |
| C | -3.49712200 | -0.91667100 | -0.26874900 |
| C | -1.58770700 | -0.32447800 | 1.09370100 |
| H | -3.53234200 | -0.03828400 | -2.23831400 |
| H | -4.43077600 | -1.45599000 | -0.39960400 |
| H | -1.02801300 | -0.42613600 | 2.01579300 |
| H | -3.16429500 | -1.63705300 | 1.73159000 |
| C | 0.18511700 | 1.26435900 | 0.26865100 |
| C | 0.40498200 | 1.92110800 | 1.42202600 |
| H | 1.32411800 | 2.48404100 | 1.58721500 |
| H | -0.32449100 | 1.93001300 | 2.22565000 |
| C | 1.22265900 | 1.28500900 | -0.83387400 |
| H | 0.85747500 | 0.77762600 | -1.73692400 |
| H | 1.42852100 | 2.32227400 | -1.11632500 |
| C | 2.58551000 | 0.64534900 | -0.42901000 |
| H | 3.01419000 | 1.21289400 | 0.40099900 |
| H | 3.25216900 | 0.69864100 | -1.29350200 |
| C | 2.50994500 | -0.79741800 | 0.02478000 |
| O | 3.44462700 | -1.58629700 | -0.67222300 |
| H | 3.30322700 | -2.49395800 | -0.34735300 |
| O | 1.75183500 | -1.21839900 | 0.94367900 |

**1a**-*extendedconformer*_neutral

| | | | |
|---|---|---|---|
| H | -2.48449500 | 2.10628200 | -0.54394100 |
| C | -2.62036900 | 1.05401900 | -0.29940900 |
| C | -2.99071200 | -1.64636300 | 0.22780100 |
| C | -1.50627000 | 0.27960500 | 0.06783500 |
| C | -3.88939900 | 0.49644000 | -0.38863400 |
| C | -4.08374600 | -0.85858800 | -0.12140600 |
| C | -1.71899300 | -1.08633200 | 0.31543500 |
| H | -4.73161500 | 1.12157900 | -0.68145300 |
| H | -5.07753800 | -1.29672400 | -0.19542400 |
| H | -0.88272100 | -1.72459600 | 0.59378600 |
| H | -3.12472300 | -2.70719800 | 0.43370400 |
| C | -0.15412800 | 0.87695100 | 0.17417800 |
| C | 0.01675100 | 2.19570600 | 0.36272600 |
| H | 1.00248100 | 2.64940100 | 0.42615600 |
| H | -0.82360300 | 2.87609800 | 0.48127300 |
| C | 1.01029500 | -0.07343100 | 0.07513600 |
| H | 0.98046500 | -0.77615600 | 0.92084800 |
| H | 0.88521800 | -0.71196600 | -0.81156100 |
| C | 2.37925600 | 0.57323500 | 0.03632500 |
| H | 2.57591100 | 1.15842500 | 0.94562700 |
| H | 2.46341900 | 1.29227800 | -0.79057900 |
| C | 3.48331800 | -0.43270700 | -0.10486500 |
| O | 4.68772800 | 0.17310600 | -0.16714900 |
| H | 5.35434500 | -0.53510800 | -0.25594300 |
| O | 3.35062700 | -1.63854600 | -0.15700500 |

**1a**-Br_cation

| | | | |
|---|---|---|---|
| H | -0.53728400 | 1.08858000 | -2.15700400 |
| C | -0.57460300 | 1.59951600 | -1.19559500 |
| C | -0.72028400 | 2.92453300 | 1.24553500 |
| C | -0.42750300 | 0.87326700 | -0.00506800 |
| C | -0.79611200 | 2.96993200 | -1.16263600 |
| C | -0.86365000 | 3.63741500 | 0.05953900 |
| C | -0.50972000 | 1.54816000 | 1.21700200 |
| H | -0.91310000 | 3.51897500 | -2.09431500 |
| H | -1.02854500 | 4.71249100 | 0.08552300 |
| H | -0.39344800 | 1.01687700 | 2.15893600 |
| H | -0.76928900 | 3.43842500 | 2.20289000 |
| C | -0.17593300 | -0.60666600 | -0.08656700 |
| C | -0.34417900 | -1.43038500 | 1.18704400 |
| H | 0.17314600 | -2.38836500 | 1.06730800 |
| H | 0.07776100 | -0.93993200 | 2.06528700 |
| C | -1.84643200 | -1.66208500 | 1.29468300 |
| H | -2.37367900 | -0.82523000 | 1.77793000 |
| H | -2.14999600 | -2.57707900 | 1.81027600 |
| C | -2.24499000 | -1.66813400 | -0.12270300 |
| O | -3.37476300 | -2.12885800 | -0.52605100 |
| H | -3.48808200 | -2.02739000 | -1.49963800 |
| O | -1.40032900 | -1.17174500 | -0.93741800 |
| C | 1.00859900 | -1.00421900 | -0.94118300 |
| H | 1.02869300 | -0.47123800 | -1.89325100 |
| H | 1.02556400 | -2.08207100 | -1.11952200 |
| Br | 2.64336700 | -0.54706300 | 0.01037200 |

**1a**-Cl_cation

| | | | |
|---|---|---|---|
| H | -1.76557000 | 1.33287700 | -1.25769300 |
| C | -2.00652600 | 0.42165600 | -0.71737400 |
| C | -2.69018500 | -1.89390300 | 0.69412800 |
| C | -1.03739300 | -0.20825300 | 0.10557100 |
| C | -3.28978500 | -0.08350000 | -0.80458500 |
| C | -3.63476300 | -1.24066800 | -0.10146200 |
| C | -1.41002600 | -1.38520900 | 0.80335900 |
| H | -4.02908600 | 0.42061600 | -1.42135400 |
| H | -4.64466100 | -1.63827100 | -0.17821300 |
| H | -0.68094100 | -1.92421500 | 1.40216200 |
| H | -2.95881200 | -2.80293200 | 1.22583600 |
| C | 0.28632000 | 0.32018600 | 0.21421000 |
| C | 1.18811600 | -0.00478000 | 1.35719000 |
| H | 1.20253700 | 0.88079700 | 2.01114500 |
| H | 0.78753200 | -0.81891600 | 1.96277300 |
| C | 2.60500200 | -0.32914900 | 0.89839300 |
| H | 3.16269300 | -0.88964300 | 1.65365700 |

| | | | |
|---|---|---|---|
| H | 3.19915100 | 0.57091700 | 0.68992400 |
| C | 2.49313900 | -1.09344200 | -0.37879300 |
| O | 3.54565200 | -1.81449900 | -0.70629900 |
| H | 3.38442500 | -2.24735500 | -1.57132000 |
| O | 1.47677800 | -1.01753300 | -1.07335300 |
| C | 0.69284500 | 1.50289600 | -0.61735900 |
| H | 0.29655700 | 1.47123000 | -1.63309400 |
| H | 1.77612400 | 1.62151200 | -0.66381200 |
| Cl | 0.05353800 | 2.97909600 | 0.19397200 |

Prop-1-en-2-ylbenzene_neutral

| | | | |
|---|---|---|---|
| C | -1.96554900 | 1.15235700 | 0.12867800 |
| C | -2.61182700 | -0.07674400 | -0.00600500 |
| C | -1.85065300 | -1.23513700 | -0.13028900 |
| C | -0.45992900 | -1.16597000 | -0.12439200 |
| C | 0.20887600 | 0.06315900 | -0.00559800 |
| C | -0.57858300 | 1.21979500 | 0.13179800 |
| C | 1.68727500 | 0.12461500 | -0.01281500 |
| C | 2.35851300 | 1.26586500 | -0.23920200 |
| C | 2.43715100 | -1.15338400 | 0.22322900 |
| H | -2.54797000 | 2.06538800 | 0.24276100 |
| H | -3.69916800 | -0.12938800 | -0.00465100 |
| H | -2.33974600 | -2.20283500 | -0.23100900 |
| H | 0.11345000 | -2.08559400 | -0.22452000 |
| H | -0.09566700 | 2.18630300 | 0.26560500 |
| H | 3.44672900 | 1.28591100 | -0.22803100 |
| H | 1.86376500 | 2.20940800 | -0.45993800 |
| H | 2.29031000 | -1.86794200 | -0.59826400 |
| H | 3.51294600 | -0.96873700 | 0.30682400 |
| H | 2.10371800 | -1.65984500 | 1.13880200 |

Prop-1-en-2-ylbenzene-Cl_cation

| | | | |
|---|---|---|---|
| C | -2.97054900 | 0.95443300 | 0.00010500 |
| C | -3.42992800 | -0.36566700 | -0.00003400 |
| C | -2.52800400 | -1.43763200 | -0.00014700 |
| C | -1.17262200 | -1.19440900 | -0.00009700 |
| C | -0.67204200 | 0.14254200 | 0.00005600 |
| C | -1.61493100 | 1.21152100 | 0.00012000 |
| C | 0.72108600 | 0.39915700 | 0.00020100 |
| C | 1.30317400 | 1.74002000 | -0.00024800 |
| C | 1.65350600 | -0.76456300 | 0.00019800 |
| Cl | 3.39038200 | -0.38395400 | -0.00001700 |
| H | -3.67910900 | 1.77811200 | 0.00019600 |
| H | -4.49979800 | -0.56427300 | -0.00006300 |
| H | -2.89680300 | -2.45950500 | -0.00027500 |
| H | -0.49073600 | -2.04079100 | -0.00018100 |
| H | -1.27799500 | 2.24284100 | 0.00022500 |
| H | 0.58887200 | 2.55976400 | -0.00045900 |
| H | 1.97770000 | 1.83977400 | 0.86409000 |
| H | 1.97755900 | 1.83923400 | -0.86476800 |
| H | 1.46292700 | -1.39006000 | 0.88097000 |
| H | 1.46274900 | -1.39029500 | -0.88036900 |

TCCA_neutral

| | | | |
|---|---|---|---|
| N | 1.27827800 | 0.39780000 | -0.00092900 |
| C | 1.07120600 | -0.98893000 | 0.00003600 |
| N | -0.29453800 | -1.30575600 | -0.00015500 |
| C | -1.39182900 | -0.43290100 | -0.00026300 |
| N | -0.98336900 | 0.90828700 | -0.00036000 |
| C | 0.32112300 | 1.42238400 | 0.00010700 |
| O | 0.58576600 | 2.59433800 | 0.00104500 |
| O | 1.95391500 | -1.80397100 | 0.00060300 |
| O | -2.53909000 | -0.78964000 | -0.00026900 |
| Cl | 2.90241600 | 0.90253400 | -0.00026100 |
| Cl | -0.66953700 | -2.96473500 | 0.00020300 |
| Cl | -2.23348600 | 2.06152800 | 0.00004600 |

TCCA_anion

| | | | |
|---|---|---|---|
| N | -1.14231800 | -0.13916600 | 0.00019600 |
| C | -0.00000100 | -0.93522600 | -0.00007000 |
| N | 1.14231700 | -0.13916400 | 0.00012800 |
| C | 1.19198300 | 1.31118900 | -0.00000400 |
| N | -0.00000100 | 1.92626800 | -0.00025000 |
| C | -1.19198400 | 1.31119100 | -0.00006600 |
| O | -2.28849700 | 1.84900600 | 0.00001700 |
| O | 0.00000100 | -2.14932600 | -0.00031600 |
| O | 2.28849700 | 1.84900100 | 0.00003800 |
| Cl | -2.63436900 | -1.00141100 | 0.00007400 |
| Cl | 2.63437000 | -1.00140800 | 0.00006800 |

NCS_neutral

| | | | |
|---|---|---|---|
| C | -0.42997800 | 1.19279500 | 0.00016500 |
| C | -1.87447600 | 0.76360400 | 0.00165200 |
| C | -1.87447700 | -0.76360300 | -0.00177800 |
| C | -0.42998000 | -1.19279500 | 0.00010300 |
| N | 0.31357900 | 0.00000000 | 0.00005700 |
| O | 0.04516600 | 2.30298400 | -0.00074000 |
| O | 0.04516400 | -2.30298500 | 0.00075500 |
| H | -2.36207900 | 1.19365500 | 0.88292400 |
| H | -2.36613800 | 1.19828900 | -0.87501000 |
| H | -2.36185400 | -1.19363600 | -0.88318500 |
| H | -2.36636400 | -1.19830200 | 0.87474800 |
| Cl | 2.01130700 | -0.00000100 | -0.00005000 |

NBS_neutral

| | | | |
|---|---|---|---|
| C | 0.91549800 | 1.18762700 | -0.00046900 |
| C | 2.36322000 | 0.76323600 | -0.00198600 |
| C | 2.36322000 | -0.76323900 | 0.00193500 |
| C | 0.91549800 | -1.18762800 | 0.00064900 |

| | | | |
|---|---|---|---|
| N | 0.16950900 | 0.00000100 | 0.00011300 |
| O | 0.44760700 | 2.30203500 | 0.00098200 |
| O | 0.44760300 | -2.30203400 | -0.00111300 |
| Br | -1.68853900 | 0.00000000 | -0.00000800 |
| H | 2.84910900 | 1.19480500 | -0.88358700 |
| H | 2.85388700 | 1.20024700 | 0.87419300 |
| H | 2.84922100 | -1.19480200 | 0.88347800 |
| H | 2.85377600 | -1.20025500 | -0.87430300 |

NCS/NBS_anion

| | | | |
|---|---|---|---|
| C | -0.75620500 | 1.22150600 | -0.00218200 |
| C | 0.75620400 | 1.22150600 | 0.00221200 |
| C | 1.10944100 | -0.27648300 | -0.00016500 |
| N | 0.00000000 | -1.06671600 | -0.00004000 |
| C | -1.10944100 | -0.27648400 | -0.00017300 |
| O | -2.28328100 | -0.66766400 | 0.00105700 |
| O | 2.28328100 | -0.66766400 | -0.00082700 |
| H | -1.20283500 | 1.69977700 | -0.88405500 |
| H | -1.20933500 | 1.70490600 | 0.87347400 |
| H | 1.20282400 | 1.69957900 | 0.88419900 |
| H | 1.20934500 | 1.70510200 | -0.87332800 |

NCP_neutral

| | | | |
|---|---|---|---|
| C | 0.81706600 | 0.69935300 | 0.00002300 |
| C | 0.81706600 | -0.69935200 | 0.00002600 |
| C | -0.57911200 | -1.18956500 | 0.00007000 |
| N | -1.34644500 | -0.00000100 | 0.00000400 |
| C | -0.57911100 | 1.18956600 | 0.00007300 |
| Cl | -3.03643400 | 0.00000000 | -0.00006900 |
| O | -1.02461900 | 2.31375700 | 0.00004800 |
| O | -1.02461600 | -2.31375800 | 0.00004900 |
| C | 1.99800100 | 1.42179200 | -0.00001300 |
| C | 3.19492000 | 0.69811200 | -0.00003900 |
| C | 3.19492000 | -0.69811100 | -0.00004100 |
| C | 1.99800100 | -1.42179100 | -0.00001200 |
| H | 1.99127800 | 2.50961300 | -0.00001600 |
| H | 4.14265600 | 1.23201000 | -0.00006400 |
| H | 4.14265500 | -1.23201000 | -0.00006700 |
| H | 1.99127700 | -2.50961300 | -0.00001300 |

NBP_neutral

| | | | |
|---|---|---|---|
| C | -3.74372700 | -0.69829900 | -0.00024700 |
| C | -3.74372700 | 0.69830000 | -0.00025000 |
| C | -2.54714200 | 1.42215700 | -0.00008500 |
| C | -1.36645800 | 0.69896100 | 0.00011400 |
| C | -1.36645800 | -0.69896100 | 0.00010800 |
| C | -2.54714300 | -1.42215600 | -0.00008400 |
| C | 0.03246100 | 1.18428300 | 0.00040000 |
| N | 0.80234800 | -0.00000100 | 0.00012100 |
| C | 0.03246200 | -1.18428500 | 0.00039600 |
| O | 0.47128700 | -2.31227400 | 0.00033300 |
| O | 0.47128700 | 2.31227300 | 0.00033200 |
| Br | 2.65159200 | 0.00000100 | -0.00020900 |
| H | -4.69171600 | -1.23183200 | -0.00038700 |
| H | -4.69171600 | 1.23183400 | -0.00039500 |
| H | -2.54046100 | 2.51000400 | -0.00008800 |
| H | -2.54046300 | -2.51000300 | -0.00009000 |

NCP/NBP_anion

| | | | |
|---|---|---|---|
| C | -2.52450000 | -0.69857900 | 0.00009500 |
| C | -2.52450100 | 0.69857700 | 0.00009700 |
| C | -1.32162100 | 1.41654400 | -0.00001500 |
| C | -0.13943900 | 0.69474600 | -0.00018100 |
| C | -0.13943800 | -0.69474700 | -0.00018100 |
| C | -1.32162100 | -1.41654600 | -0.00001900 |
| C | 1.31142100 | 1.10926900 | -0.00036300 |
| N | 2.11341900 | 0.00000100 | 0.00025100 |
| C | 1.31142300 | -1.10926800 | -0.00034600 |
| O | 1.67969900 | -2.29104400 | 0.00020700 |
| O | 1.67969500 | 2.29104600 | 0.00021000 |
| H | -3.47479000 | -1.23216900 | 0.00020200 |
| H | -3.47479000 | 1.23216600 | 0.00020400 |
| H | -1.31492500 | 2.50708500 | -0.00000700 |
| H | -1.31492500 | -2.50708600 | -0.00001100 |

DCDMH_neutral

| | | | |
|---|---|---|---|
| N | 1.22946600 | -0.13864000 | 0.01836100 |
| C | 0.24486700 | -1.16271300 | -0.07517800 |
| N | -0.91978700 | -0.45435300 | -0.26529000 |
| C | -0.79701600 | 0.99753400 | -0.01173100 |
| C | 0.73053700 | 1.14978600 | -0.00639700 |
| O | 1.35594900 | 2.18221900 | 0.00088300 |
| Cl | 2.88382000 | -0.51199300 | 0.01015400 |
| O | 0.43788900 | -2.35036200 | -0.02667800 |
| Cl | -2.40694400 | -1.26080000 | 0.00654800 |
| C | -1.33180000 | 1.39441500 | 1.35825500 |
| C | -1.42320700 | 1.80356800 | -1.13353600 |
| H | -2.42065700 | 1.27962900 | 1.38356300 |
| H | -0.89438200 | 0.78334700 | 2.15549600 |
| H | -1.09308900 | 2.44521000 | 1.55013900 |
| H | -1.22564500 | 2.86874600 | -0.97871500 |
| H | -1.02328800 | 1.50802400 | -2.10855300 |
| H | -2.50857700 | 1.65307600 | -1.13949100 |

DBDMH_neutral

| | | | |
|---|---|---|---|
| C | -0.09238600 | -0.90742900 | -0.06362800 |
| N | 1.00818200 | -0.10362900 | -0.18992900 |
| C | 0.74488900 | 1.33483200 | -0.01484800 |

| | | | |
|---|---|---|---|
| C | -0.79279300 | 1.34088800 | -0.00062900 |
| N | -1.17432800 | 0.01843800 | 0.00264000 |
| O | -0.18232100 | -2.11016900 | -0.03579900 |
| O | -1.50344300 | 2.31848600 | 0.01946700 |
| Br | 2.71006600 | -0.83755400 | 0.00976800 |
| C | 1.25339100 | 1.85812800 | 1.32089600 |
| C | 1.27258600 | 2.13975900 | -1.18881700 |
| Br | -2.94012500 | -0.55382600 | 0.00753500 |
| H | 2.34903600 | 1.84447500 | 1.33630000 |
| H | 0.92280100 | 2.89226000 | 1.45982100 |
| H | 0.88323300 | 1.25541100 | 2.15754300 |
| H | 0.97005100 | 3.18665700 | -1.08832200 |
| H | 2.36795000 | 2.10002500 | -1.20702700 |
| H | 0.89403800 | 1.75223100 | -2.14008000 |

DCDMH/DBDMH_anion

| | | | |
|---|---|---|---|
| C | 0.21776700 | 1.54959100 | -0.08483200 |
| N | -0.15783400 | 0.20476000 | -0.39210700 |
| C | 0.93106500 | -0.69806900 | -0.02995800 |
| C | 2.07041400 | 0.35297100 | 0.01125200 |
| N | 1.58413100 | 1.61391200 | 0.01246500 |
| O | -0.59211100 | 2.46550100 | -0.00847300 |
| O | 3.25258700 | 0.00091400 | 0.06755800 |
| Br | -1.95348000 | -0.30524000 | 0.00482900 |
| C | 0.79834900 | -1.32063600 | 1.35474400 |
| C | 1.16548500 | -1.75820900 | -1.08921400 |
| H | -0.00720200 | -2.06531800 | 1.38318800 |
| H | 1.73869500 | -1.81810800 | 1.62105900 |
| H | 0.58806000 | -0.55817100 | 2.11497900 |
| H | 2.09269600 | -2.30309800 | -0.87643700 |
| H | 0.33908700 | -2.48145300 | -1.11490400 |
| H | 1.25408500 | -1.30638300 | -2.08406400 |

BCTC-Cl_TBA_neutral

| | | | |
|---|---|---|---|
| C | -6.00660300 | 0.75860600 | -1.04330800 |
| C | -5.34973900 | 1.95576500 | -1.32939500 |
| C | -3.96059900 | 2.01851300 | -1.27629700 |
| C | -3.20376600 | 0.89483000 | -0.94498300 |
| C | -3.87578300 | -0.30110100 | -0.65771600 |
| C | -5.27092200 | -0.37039800 | -0.69701500 |
| C | -3.12614700 | -1.53667400 | -0.27812700 |
| O | -2.75820400 | -1.33559700 | 1.03647500 |
| O | -3.03961600 | -2.57723300 | -0.87442100 |
| Cl | -1.87530700 | -2.67229500 | 1.74262500 |
| C | -1.68836100 | 0.93510700 | -0.95633300 |
| O | -1.12743400 | -0.19934400 | -0.96165000 |
| O | -1.14173300 | 2.06467900 | -0.96625100 |
| H | -7.09283500 | 0.70383900 | -1.08468000 |
| H | -5.92594800 | 2.84074000 | -1.59543200 |
| H | -3.42547000 | 2.94089100 | -1.49573300 |
| H | -5.77405200 | -1.30669400 | -0.45907400 |
| N | 2.17446200 | 0.00905200 | 0.69420200 |
| C | 1.54130300 | 0.52107300 | 1.98059200 |
| C | 3.65573100 | -0.18729300 | 0.98913100 |
| C | 1.50099700 | -1.31632500 | 0.36231800 |
| C | 1.93746300 | 0.98623300 | -0.44326600 |
| C | 4.61123300 | -0.12757900 | -0.18761100 |
| C | 6.00286200 | -0.57117100 | 0.24968100 |
| C | 7.02284900 | -0.45922000 | -0.86766900 |
| C | 2.10171000 | -2.12043000 | -0.76951200 |
| C | 1.20998500 | -3.32037400 | -1.07545400 |
| C | 1.76720800 | -4.18415300 | -2.19091100 |
| C | 0.05543900 | 0.78583400 | 1.90250800 |
| C | -0.45628100 | 1.44035800 | 3.17964900 |
| C | -1.94246400 | 1.73659700 | 3.08757700 |
| C | 2.31012500 | 2.41951400 | -0.13054800 |
| C | 2.26129600 | 3.25669800 | -1.40279900 |
| C | 2.54850800 | 4.72378200 | -1.14646900 |
| H | 2.08631100 | 1.43537300 | 2.23987000 |
| H | 1.78422400 | -0.23188200 | 2.74131100 |
| H | 3.92929800 | 0.58537600 | 1.71605600 |
| H | 3.72169500 | -1.15316400 | 1.50559700 |
| H | 0.46492200 | -1.05721700 | 0.11786000 |
| H | 1.52192400 | -1.89211000 | 1.29646700 |
| H | 2.51984200 | 0.60992100 | -1.28907100 |
| H | 0.87462300 | 0.90895300 | -0.70916700 |
| H | 4.27380800 | -0.75770500 | -1.01873200 |
| H | 4.66352800 | 0.89790400 | -0.57973700 |
| H | 6.32549100 | 0.03171100 | 1.11181500 |
| H | 5.95371400 | -1.61013500 | 0.60926500 |
| H | 8.01577300 | -0.78743000 | -0.53977100 |
| H | 6.73885800 | -1.07541800 | -1.73040800 |
| H | 7.11643300 | 0.57566700 | -1.22098400 |
| H | 3.11162500 | -2.47386300 | -0.51426900 |
| H | 2.19287800 | -1.50798000 | -1.67768700 |
| H | 0.20548600 | -2.96152900 | -1.34224100 |
| H | 1.08415000 | -3.92411900 | -0.16367400 |
| H | 1.11358800 | -5.03856600 | -2.40037800 |
| H | 2.75921200 | -4.58058900 | -1.93610800 |
| H | 1.87079100 | -3.61289300 | -3.12246200 |
| H | -0.50171700 | -0.14195400 | 1.72399900 |
| H | -0.17238100 | 1.44102100 | 1.05136400 |
| H | 0.09965000 | 2.37319500 | 3.36317700 |
| H | -0.25359200 | 0.79017000 | 4.04484000 |
| H | -2.31750900 | 2.22465700 | 3.99498900 |
| H | -2.52254900 | 0.81671600 | 2.93836500 |
| H | -2.15898600 | 2.39692900 | 2.23712700 |
| H | 1.60485600 | 2.84326200 | 0.59908800 |
| H | 3.31198100 | 2.48628800 | 0.32385000 |
| H | 2.98262500 | 2.85395100 | -2.13062100 |
| H | 1.26675000 | 3.13938600 | -1.85543500 |
| H | 2.51304600 | 5.30868500 | -2.07287700 |
| H | 1.81385300 | 5.15692800 | -0.45556100 |

| | | | |
|---|---|---|---|
| H | 3.54272400 | 4.86815300 | -0.70245400 |

BCTC-Br_TBA_neutral

| | | | |
|---|---|---|---|
| C | -5.43804800 | -1.23132900 | 0.74210600 |
| C | -4.98517100 | -2.47022100 | 0.28767300 |
| C | -3.72786200 | -2.57782900 | -0.29832900 |
| C | -2.90837400 | -1.45950400 | -0.45347100 |
| C | -3.37291000 | -0.22288200 | 0.01155500 |
| C | -4.63356200 | -0.10409900 | 0.60236600 |
| C | -2.50189400 | 0.99619500 | -0.05061600 |
| O | -1.76822500 | 1.40699500 | 0.82092100 |
| O | -2.87580300 | 1.67313100 | -1.16377500 |
| C | -1.52381800 | -1.57045900 | -1.06128600 |
| O | -0.94344200 | -0.46331100 | -1.26325300 |
| O | -1.07691200 | -2.72321000 | -1.26944500 |
| H | -6.41985900 | -1.14004400 | 1.20320900 |
| H | -5.61669400 | -3.35126700 | 0.39243800 |
| H | -3.34296900 | -3.53439500 | -0.64890600 |
| H | -4.97898700 | 0.86690000 | 0.95539700 |
| Br | -1.93574300 | 3.29359000 | -1.45857100 |
| N | 2.30136400 | -0.40760100 | 0.51180200 |
| C | 1.72880600 | -1.10935600 | 1.72776900 |
| H | 2.35357200 | -1.99728400 | 1.87974600 |
| H | 1.91635900 | -0.43765500 | 2.57280000 |
| C | 2.09205000 | -1.23812200 | -0.74912500 |
| H | 2.61351100 | -0.69317300 | -1.54365900 |
| H | 1.01739300 | -1.18293500 | -0.97511700 |
| C | 1.59472400 | 0.91888700 | 0.27397100 |
| H | 2.06725500 | 1.34331300 | -0.61915800 |
| H | 0.56341100 | 0.66970200 | -0.00314900 |
| C | 3.77959800 | -0.20922500 | 0.79010400 |
| H | 4.20898300 | -1.21594900 | 0.82604300 |
| H | 3.85234900 | 0.20165200 | 1.80268200 |
| C | 2.56053600 | -2.67475000 | -0.68796300 |
| H | 2.03226700 | -3.22115600 | 0.10676900 |
| H | 3.63609800 | -2.74772000 | -0.46536200 |
| C | 0.26697500 | -1.47593500 | 1.63301000 |
| H | 0.09419000 | -2.16312600 | 0.79371800 |
| H | -0.34688300 | -0.58623200 | 1.43366700 |
| C | 2.26372300 | -3.35596600 | -2.02089300 |
| H | 2.78007300 | -2.81656100 | -2.82940900 |
| H | 1.18612100 | -3.26101300 | -2.21644100 |
| C | -0.20389000 | -2.13361600 | 2.92503900 |
| H | 0.41075500 | -3.02389700 | 3.13027900 |
| H | -0.03785700 | -1.44832300 | 3.77071600 |
| C | 1.64715300 | 1.88675400 | 1.43641300 |
| H | 2.67274400 | 1.98957900 | 1.82280600 |
| H | 1.03158700 | 1.51495100 | 2.26833100 |
| C | 1.13257400 | 3.25816500 | 1.01569400 |
| H | 1.75979200 | 3.64421900 | 0.19699400 |
| H | 0.12075400 | 3.14493000 | 0.60424600 |
| C | 1.11609200 | 4.24649400 | 2.16628400 |
| H | 2.11834500 | 4.38878400 | 2.59257000 |
| H | 0.46062200 | 3.90036700 | 2.97593300 |
| H | 0.75100600 | 5.22952300 | 1.84657700 |
| C | 2.67575700 | -4.81570400 | -2.02922000 |
| H | 2.45425000 | -5.28973600 | -2.99253900 |
| H | 2.14303800 | -5.38278300 | -1.25474500 |
| H | 3.75175000 | -4.93491500 | -1.84227600 |
| C | -1.66847100 | -2.52445900 | 2.85500300 |
| H | -1.85128400 | -3.21711300 | 2.02301300 |
| H | -2.30624300 | -1.64520400 | 2.69246100 |
| H | -2.00262700 | -3.01279600 | 3.77820600 |
| C | 4.53278300 | 0.66461500 | -0.18907700 |
| H | 4.37815000 | 0.32414400 | -1.22253700 |
| H | 4.16752100 | 1.70037800 | -0.14048100 |
| C | 6.02489800 | 0.64764400 | 0.12621400 |
| H | 6.39722900 | -0.38564300 | 0.06480500 |
| H | 6.18020400 | 0.96368900 | 1.16859500 |
| C | 6.82270100 | 1.53962100 | -0.80610200 |
| H | 6.70943100 | 1.22656000 | -1.85193300 |
| H | 7.89219100 | 1.51516600 | -0.56804900 |
| H | 6.49272700 | 2.58425300 | -0.73916200 |

BCTC-Br/-Cl_TBA_anion

| | | | |
|---|---|---|---|
| O | -1.95076700 | 1.43103200 | 0.48839400 |
| C | -2.97361300 | 1.02588400 | -0.13448200 |
| O | -3.69234100 | 1.66897200 | -0.93762700 |
| C | -3.44573100 | -0.37454100 | 0.23080700 |
| C | -4.69346900 | -0.49108800 | 0.85700500 |
| C | -5.17045600 | -1.71346700 | 1.32443500 |
| C | -4.39367300 | -2.86052300 | 1.16575400 |
| C | -3.15518200 | -2.75897800 | 0.53718000 |
| C | -2.66868900 | -1.53918400 | 0.05407800 |
| C | -1.34907400 | -1.53933700 | -0.70444400 |
| O | -1.24783000 | -0.69539900 | -1.63995200 |
| O | -0.49327100 | -2.39485100 | -0.34857400 |
| H | -5.29843200 | 0.40962800 | 0.97610900 |
| H | -6.14477700 | -1.76998900 | 1.81146400 |
| H | -4.75279900 | -3.82560500 | 1.52437800 |
| H | -2.52622400 | -3.63923400 | 0.40172500 |
| C | -1.52879400 | 3.94691300 | -2.33795900 |
| C | -0.17869200 | 3.79702600 | -1.66067900 |
| C | 0.28046300 | 2.34338400 | -1.64141700 |
| C | 1.61636100 | 2.20938500 | -0.93954100 |
| N | 1.94642700 | 0.81246000 | -0.43706100 |
| C | 1.82730300 | -0.12920300 | -1.62843500 |
| C | 2.35570000 | -1.53337400 | -1.44547900 |
| C | 1.95787500 | -2.37069800 | -2.65578600 |
| C | 2.37721800 | -3.82116200 | -2.51239000 |
| C | 3.36672400 | 0.86875400 | 0.09461000 |
| C | 3.76075000 | -0.17101700 | 1.12742600 |
| C | 5.26317400 | -0.11634700 | 1.37918000 |
| C | 5.70355800 | -1.08334900 | 2.46223700 |

| | | | |
|---|---|---|---|
| C | 0.95275200 | 0.38962900 | 0.62808800 |
| C | 0.81409400 | 1.34205100 | 1.79461600 |
| C | 0.01042000 | 0.66403700 | 2.89774000 |
| C | -0.40976000 | 1.63057300 | 3.98778700 |
| H | -1.86877200 | 4.99068300 | -2.33170900 |
| H | -1.48470300 | 3.62126000 | -3.38642100 |
| H | -2.28670700 | 3.32971900 | -1.83014200 |
| H | -0.25120600 | 4.15432200 | -0.62110600 |
| H | 0.57667300 | 4.43401600 | -2.15053000 |
| H | 0.34908900 | 1.95993100 | -2.66873300 |
| H | -0.49438800 | 1.75335300 | -1.13225500 |
| H | 1.66261300 | 2.85689200 | -0.05711600 |
| H | 2.45547200 | 2.48588000 | -1.59132300 |
| H | 0.74818100 | -0.19009400 | -1.84301800 |
| H | 2.34777300 | 0.38117200 | -2.45028100 |
| H | 3.44993600 | -1.54794900 | -1.31986900 |
| H | 1.89204800 | -1.99323600 | -0.56421800 |
| H | 0.86586900 | -2.30613300 | -2.75771500 |
| H | 2.39144500 | -1.93875900 | -3.57171400 |
| H | 2.08772200 | -4.41587100 | -3.38719500 |
| H | 3.46490400 | -3.92088200 | -2.39025600 |
| H | 1.90257000 | -4.27531300 | -1.63261800 |
| H | 3.49451600 | 1.87007700 | 0.52292200 |
| H | 4.01243400 | 0.81247700 | -0.79120800 |
| H | 3.48126700 | -1.18218400 | 0.81197300 |
| H | 3.22690000 | 0.01376100 | 2.06990400 |
| H | 5.55292600 | 0.90930100 | 1.65445400 |
| H | 5.79490400 | -0.33838200 | 0.44120200 |
| H | 6.78652600 | -1.03938700 | 2.62676700 |
| H | 5.44999300 | -2.11826800 | 2.19906100 |
| H | 5.21387400 | -0.86063200 | 3.41895100 |
| H | -0.01585700 | 0.29955800 | 0.12965200 |
| H | 1.25595300 | -0.61206500 | 0.94535100 |
| H | 1.78949900 | 1.67837500 | 2.18321600 |
| H | 0.26392700 | 2.23377900 | 1.46789400 |
| H | -0.88277100 | 0.22369900 | 2.43376600 |
| H | 0.59601900 | -0.16613000 | 3.32335500 |
| H | -0.96003700 | 1.12306800 | 4.78925000 |
| H | 0.45430900 | 2.13257000 | 4.44595800 |
| H | -1.06753100 | 2.40914200 | 3.57959200 |

BCTC-Br_TMA_neutral

| | | | |
|---|---|---|---|
| C | -4.18630000 | -1.25066700 | 0.85762900 |
| C | -3.85976500 | -2.44527300 | 0.21616700 |
| C | -2.60525400 | -2.60077300 | -0.36600100 |
| C | -1.66502600 | -1.57126900 | -0.33428600 |
| C | -1.99939200 | -0.38204600 | 0.32724700 |
| C | -3.25624800 | -0.21640900 | 0.91419900 |
| C | -0.98658100 | 0.71293400 | 0.49366000 |
| O | -0.17025200 | 0.81418700 | 1.38005600 |
| O | -1.30502400 | 1.67382400 | -0.40821600 |
| C | -0.30660100 | -1.72222200 | -0.99089200 |
| O | 0.35162000 | -0.63990800 | -1.08332600 |
| O | 0.04803500 | -2.86306700 | -1.35505100 |
| H | -5.16632700 | -1.12107500 | 1.31328800 |
| H | -4.58816800 | -3.25349200 | 0.16847200 |
| H | -2.32253900 | -3.52377800 | -0.86996400 |
| H | -3.50109900 | 0.71764300 | 1.41855500 |
| Br | -0.19360200 | 3.21360800 | -0.33805100 |
| N | 3.35779800 | -0.93846800 | 0.34588600 |
| C | 2.36347600 | -1.44765400 | 1.33966000 |
| H | 2.56110500 | -2.50703600 | 1.51854800 |
| H | 2.47516400 | -0.87667400 | 2.26421800 |
| C | 3.28535500 | -1.76958100 | -0.89820100 |
| H | 4.00070200 | -1.36549200 | -1.61863500 |
| H | 2.26048600 | -1.71738500 | -1.28408900 |
| C | 3.02648300 | 0.48253500 | 0.01095900 |
| H | 3.78079300 | 0.85544800 | -0.68616800 |
| H | 2.03170700 | 0.48906900 | -0.44085900 |
| C | 4.72811500 | -1.01559400 | 0.92351900 |
| H | 4.94787800 | -2.05642300 | 1.17153400 |
| H | 4.76682900 | -0.39838200 | 1.82419200 |
| H | 3.55099700 | -2.79693300 | -0.63817900 |
| H | 1.36697500 | -1.29666700 | 0.92186900 |
| H | 5.44316400 | -0.64759900 | 0.18420800 |
| H | 3.03921400 | 1.06761500 | 0.93393200 |

BCTC-Br/-Cl_TMA_anion

| | | | |
|---|---|---|---|
| O | -0.25675700 | 1.80186000 | -0.02441000 |
| C | 0.95885900 | 1.84370200 | 0.34308900 |
| O | 1.56056900 | 2.80739800 | 0.86304600 |
| C | 1.79387400 | 0.62090300 | -0.01334900 |
| C | 2.91724800 | 0.84031600 | -0.82080700 |
| C | 3.69568800 | -0.21009800 | -1.30152700 |
| C | 3.35753800 | -1.52071100 | -0.96750400 |
| C | 2.24885100 | -1.75130800 | -0.15666100 |
| C | 1.46498300 | -0.70468200 | 0.34360800 |
| C | 0.34532200 | -1.05452500 | 1.31681500 |
| O | 0.18133200 | -0.28040900 | 2.28926800 |
| O | -0.29398100 | -2.12288200 | 1.06734600 |
| H | 3.17404300 | 1.87011100 | -1.07442400 |
| H | 4.56126700 | -0.00697100 | -1.93320400 |
| H | 3.95613200 | -2.35599600 | -1.33273400 |
| H | 1.96589700 | -2.76786500 | 0.11837300 |
| C | -3.20845000 | 1.30923500 | -0.98076800 |
| N | -2.89123300 | -0.07047400 | -0.51040700 |
| C | -2.56343000 | -0.01799000 | 0.95274400 |
| C | -4.05090200 | -0.97105300 | -0.73530700 |
| C | -1.69826700 | -0.57652200 | -1.26573700 |
| H | -3.42317400 | 1.27580300 | -2.05228600 |
| H | -4.08237900 | 1.67322600 | -0.43401700 |
| H | -1.71958100 | 0.66691500 | 1.07403100 |
| H | -3.45508400 | 0.32808300 | 1.48344800 |
| H | -4.28287800 | -0.99477900 | -1.80331100 |

| | | | |
|---|---|---|---|
| H | -4.90911400 | -0.59408400 | -0.17299800 |
| H | -0.90328000 | 0.16514600 | -1.11206000 |
| H | -1.39271200 | -1.53189200 | -0.82992500 |
| H | -3.78666100 | -1.97229800 | -0.38718400 |
| H | -2.24855000 | -1.01492500 | 1.27405900 |
| H | -2.33288300 | 1.93294200 | -0.77609100 |
| H | -1.97959900 | -0.67144200 | -2.31840300 |

BCTC-Br_TMA_DCE_neutral

| | | | |
|---|---|---|---|
| C | -4.21200300 | -1.18727700 | 0.88491900 |
| C | -3.91368300 | -2.38015400 | 0.22618100 |
| C | -2.66860300 | -2.54990900 | -0.37237300 |
| C | -1.70930000 | -1.53763200 | -0.33938800 |
| C | -2.01643100 | -0.34974300 | 0.33785500 |
| C | -3.26340000 | -0.16970500 | 0.94210100 |
| C | -0.98550500 | 0.72853100 | 0.50275800 |
| O | -0.18135800 | 0.82510600 | 1.40027400 |
| O | -1.27448500 | 1.68613500 | -0.41316100 |
| C | -0.35965800 | -1.70660900 | -1.01194600 |
| O | 0.32981000 | -0.64239800 | -1.07345300 |
| O | -0.04590500 | -2.84444900 | -1.42095900 |
| H | -5.18392700 | -1.04627600 | 1.35412600 |
| H | -4.65620900 | -3.17530600 | 0.17846000 |
| H | -2.40820300 | -3.47205500 | -0.88981800 |
| H | -3.48677000 | 0.76236400 | 1.46003300 |
| Br | -0.12700300 | 3.19840500 | -0.34915000 |
| N | 3.36101400 | -0.98421200 | 0.35340500 |
| C | 2.36008000 | -1.45383900 | 1.35883600 |
| H | 2.54211700 | -2.51165400 | 1.56164600 |
| H | 2.48456200 | -0.86486800 | 2.27027600 |
| C | 3.26286800 | -1.83077600 | -0.87736600 |
| H | 3.98567200 | -1.45507700 | -1.60543900 |
| H | 2.23847700 | -1.75653600 | -1.26044900 |
| C | 3.06512800 | 0.43879100 | -0.00104700 |
| H | 3.82224800 | 0.77949900 | -0.71109200 |
| H | 2.06649400 | 0.46662500 | -0.44297000 |
| C | 4.73221700 | -1.08820700 | 0.92617900 |
| H | 4.92335200 | -2.13090900 | 1.18886100 |
| H | 4.78967100 | -0.45754500 | 1.81613500 |
| H | 3.50463800 | -2.86009100 | -0.60243300 |
| H | 1.36520900 | -1.29602900 | 0.93844600 |
| H | 5.45117800 | -0.75042600 | 0.17662300 |
| H | 3.10473400 | 1.03760900 | 0.91212700 |

BCTC-Br_TMA_DCE_anion

| | | | |
|---|---|---|---|
| O | -0.03813100 | 1.48390300 | -0.60854900 |
| C | 1.05431900 | 1.76248000 | -0.04170100 |
| O | 1.40690000 | 2.86427000 | 0.45196300 |
| C | 2.09176900 | 0.64308300 | -0.01193100 |
| C | 3.44366000 | 0.98024800 | -0.13958500 |
| C | 4.44098800 | 0.01025500 | -0.22230100 |
| C | 4.08677500 | -1.33741100 | -0.16625300 |
| C | 2.74470000 | -1.68806600 | -0.02785200 |
| C | 1.73713200 | -0.71957000 | 0.06024900 |
| C | 0.31720900 | -1.19059100 | 0.31716000 |
| O | -0.18488500 | -0.84202000 | 1.41979400 |
| O | -0.19485700 | -1.94778700 | -0.55108500 |
| H | 3.69484600 | 2.04097600 | -0.17429800 |
| H | 5.48596600 | 0.30163400 | -0.33190500 |
| H | 4.85170100 | -2.11199300 | -0.22919100 |
| H | 2.46065100 | -2.74129000 | 0.01683000 |
| C | -2.72250500 | 0.90576300 | 0.91462400 |
| N | -3.35069800 | -0.01513000 | -0.08375100 |
| C | -3.25143400 | -1.42097000 | 0.41604300 |
| C | -4.78013400 | 0.35170500 | -0.27523700 |
| C | -2.62439900 | 0.09306500 | -1.38640900 |
| H | -2.76320800 | 1.92155900 | 0.51651900 |
| H | -3.29924300 | 0.83470500 | 1.84092100 |
| H | -2.18598700 | -1.67393100 | 0.49939500 |
| H | -3.75445200 | -1.47318400 | 1.38514700 |
| H | -4.83363600 | 1.38557200 | -0.62412100 |
| H | -5.30040600 | 0.24944600 | 0.68006700 |
| H | -1.56806600 | -0.12857500 | -1.21369700 |
| H | -3.07873200 | -0.61577900 | -2.08369100 |
| H | -5.22000100 | -0.31963400 | -1.01661600 |
| H | -3.75445800 | -2.07225900 | -0.30364400 |
| H | -1.68477400 | 0.58640000 | 1.06069000 |
| H | -2.73601100 | 1.11538800 | -1.75396600 |

Phenylchloroformate_neutral

| | | | |
|---|---|---|---|
| C | 2.43869400 | -1.42363900 | 0.00018900 |
| C | 3.34639200 | -0.36530800 | -0.00007600 |
| C | 2.88823000 | 0.95170000 | -0.00026800 |
| C | 1.52436500 | 1.21231400 | -0.00019000 |
| C | 0.61038500 | 0.15071400 | 0.00006600 |
| C | 1.07191900 | -1.17244100 | 0.00025000 |
| C | -0.82340900 | 0.51113300 | 0.00016500 |
| O | -1.58096300 | -0.64096800 | -0.00034100 |
| O | -1.28527300 | 1.62507900 | 0.00049400 |
| Cl | -3.27840400 | -0.35601800 | -0.00011400 |
| H | 2.79722300 | -2.45074400 | 0.00035900 |
| H | 4.41578700 | -0.56816500 | -0.00013300 |
| H | 3.59630600 | 1.77774500 | -0.00047000 |
| H | 1.14782400 | 2.23249400 | -0.00032600 |
| H | 0.36614300 | -1.99875600 | 0.00046600 |

Benzoylhypobromite_neutral

| | | | |
|---|---|---|---|
| C | 3.57296300 | 0.90347200 | -0.00005500 |
| C | 3.99505900 | -0.42554700 | -0.00002600 |
| C | 3.05856100 | -1.45846600 | 0.00003500 |
| C | 1.69904400 | -1.16914800 | 0.00003500 |
| C | 1.27389500 | 0.16548100 | 0.00001300 |

| | | | |
|---|---|---|---|
| C | 2.21654300 | 1.20136500 | -0.00002200 |
| C | -0.15440700 | 0.56066500 | 0.00003500 |
| O | -0.56944700 | 1.69671000 | 0.00008200 |
| O | -0.94562300 | -0.55007100 | -0.00003100 |
| H | 4.30341300 | 1.70994900 | -0.00009300 |
| H | 5.05864500 | -0.65708300 | -0.00003800 |
| H | 3.38924100 | -2.49496800 | 0.00008500 |
| H | 1.86729800 | 2.23128200 | -0.00001900 |
| Br | -2.78390300 | -0.19015300 | -0.00001500 |
| H | 0.96862800 | -1.97385600 | 0.00007700 |

Phenylchloroformate /benzoylhypobromite_anion

| | | | |
|---|---|---|---|
| O | -2.36254500 | 1.13244900 | -0.04926800 |
| C | -1.81619700 | -0.00000300 | -0.00001700 |
| O | -2.36252700 | -1.13245400 | 0.04928700 |
| C | -0.28302200 | 0.00000100 | -0.00000700 |
| C | 0.43413300 | -1.19993500 | -0.01784900 |
| C | 1.82704500 | -1.20564500 | -0.02241600 |
| C | 2.52939000 | 0.00000100 | 0.00000500 |
| C | 1.82704200 | 1.20564800 | 0.02242100 |
| C | 0.43413100 | 1.19993800 | 0.01784100 |
| H | -0.13795800 | -2.12702700 | -0.03047200 |
| H | 2.37099600 | -2.15079500 | -0.04230400 |
| H | 3.61937800 | 0.00000600 | 0.00000900 |
| H | 2.37099400 | 2.15079700 | 0.04230500 |
| H | -0.13796000 | 2.12702900 | 0.03045400 |

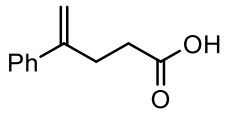
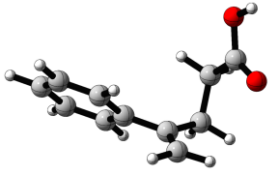
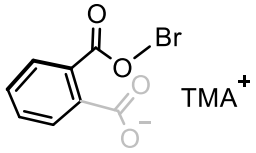
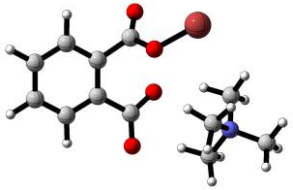
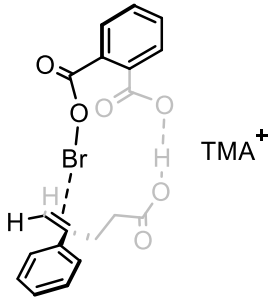
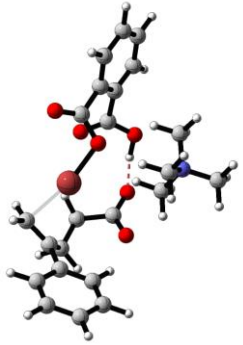
Active_BCTC-Br_TMA

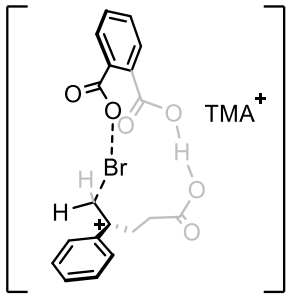
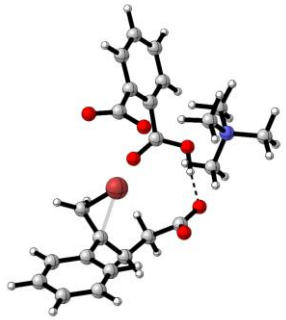
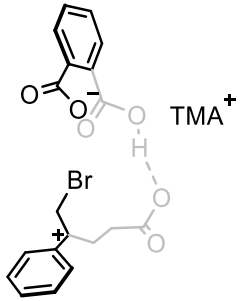
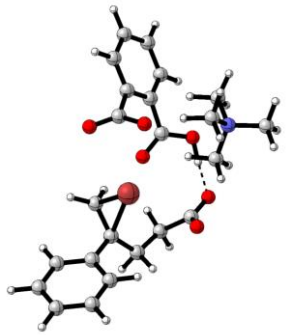
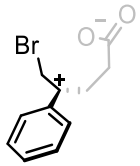
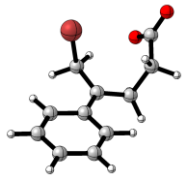
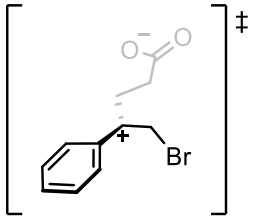
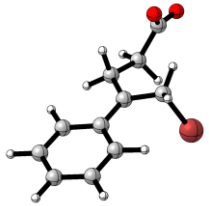
| | | | |
|---|---|---|---|
| Br | -1.68664600 | -2.26332800 | 0.05680000 |
| O | -0.39625300 | -0.87529600 | -0.59528000 |
| C | 0.80122600 | -1.36433200 | -0.94246900 |
| C | 1.90027400 | -0.41836300 | -0.53679400 |
| O | 0.99366900 | -2.38525700 | -1.53811000 |
| C | 1.89989000 | 0.17523100 | 0.73015400 |
| C | 2.90144200 | -0.11053100 | -1.45141900 |
| C | 0.88114200 | -0.25263500 | 1.75556700 |
| C | 2.87812100 | 1.11073400 | 1.05097600 |
| C | 3.88487300 | 0.81574400 | -1.12129900 |
| H | 2.89514700 | -0.60080500 | -2.41854900 |
| O | 0.67822400 | -1.41444200 | 1.99960300 |
| O | 0.27203700 | 0.76971500 | 2.32307200 |
| C | 3.86877700 | 1.43018800 | 0.12680700 |
| H | 2.86649100 | 1.57194800 | 2.03219700 |
| H | 4.66274400 | 1.05716400 | -1.83660300 |
| H | 4.63521300 | 2.15176100 | 0.38631100 |
| C | -2.47350700 | 1.39470600 | 0.71694000 |
| N | -1.91757200 | 2.28970700 | -0.35954700 |
| C | -2.57225300 | 3.62018900 | -0.27630100 |
| C | -0.44163500 | 2.43645700 | -0.18264100 |
| C | -2.18709100 | 1.66241100 | -1.68613000 |
| H | -1.96452200 | 0.43818700 | 0.65525600 |
| H | -2.29605800 | 1.82614900 | 1.69880900 |
| H | -3.64850000 | 3.49124400 | -0.37693800 |
| H | -2.34618500 | 4.05802000 | 0.69418500 |
| H | 0.00922700 | 1.46104800 | -0.33837600 |
| H | -0.23449000 | 2.76088900 | 0.83437700 |
| H | -3.26369600 | 1.56087400 | -1.81263600 |
| H | -1.77291300 | 2.29643800 | -2.46963200 |
| H | -3.53807100 | 1.26348100 | 0.54999500 |
| H | -0.07039300 | 3.15438200 | -0.91388600 |
| H | -2.19454500 | 4.25956000 | -1.07331000 |
| H | -1.71278800 | 0.68163400 | -1.69697600 |

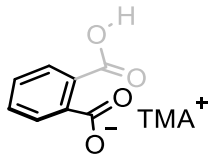
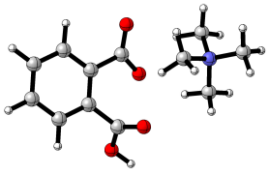
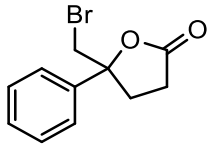
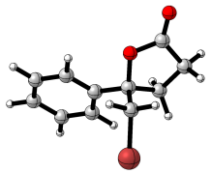
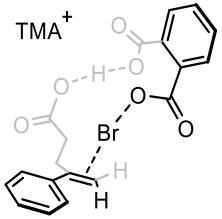
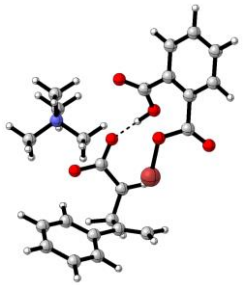
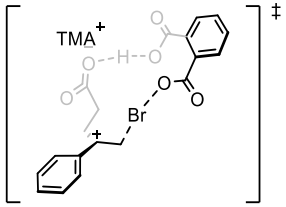
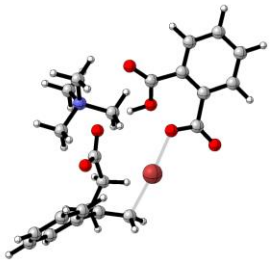
Active_**1a**_neutral

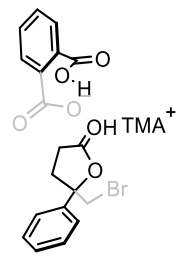
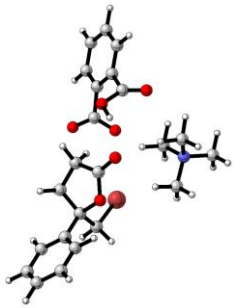
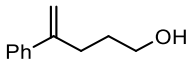
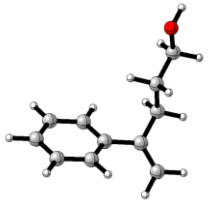
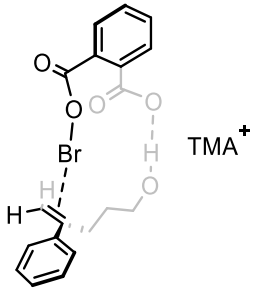
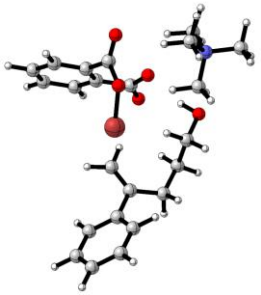
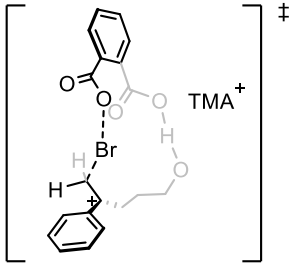
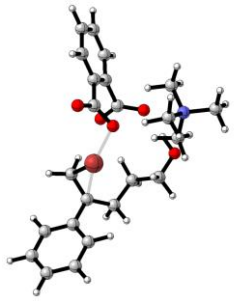
| | | | |
|---|---|---|---|
| H | 0.19975300 | -1.45536100 | 0.61326900 |
| C | 1.15474700 | -0.98026200 | 0.36721900 |
| C | 3.58433600 | 0.25517300 | -0.35935900 |
| C | 1.19023500 | 0.40877300 | 0.07309000 |
| C | 2.32097800 | -1.73305700 | 0.30071700 |
| C | 3.54106300 | -1.12490100 | -0.08273800 |
| C | 2.42230100 | 1.00279200 | -0.28232700 |
| H | 2.28063900 | -2.79668400 | 0.54500500 |
| H | 4.44896200 | -1.71711600 | -0.13172400 |
| H | 2.49124200 | 2.07720800 | -0.47164900 |
| H | 4.53787000 | 0.74099100 | -0.64677400 |
| C | -1.14787700 | 0.83948200 | 1.11434100 |
| H | -1.14694500 | 1.65766000 | 1.84610600 |
| H | -0.87458500 | -0.06441500 | 1.65337400 |
| C | -2.56839200 | 0.67234300 | 0.55110000 |
| H | -3.27842000 | 0.67108400 | 1.39248200 |
| H | -2.87208600 | 1.50003100 | -0.09415000 |
| C | -2.75280000 | -0.63367400 | -0.22772700 |
| O | -4.03729000 | -0.93509700 | -0.57083800 |
| O | -1.77467100 | -1.40013900 | -0.35816000 |
| H | -4.09980400 | -1.35430200 | -1.49948600 |
| C | -0.16824800 | 2.35991200 | -0.61164100 |
| H | 0.65226000 | 2.76101100 | -1.18709400 |
| H | -1.01730800 | 3.01055300 | -0.44786500 |
| C | -0.04732500 | 1.20862300 | 0.13407400 |

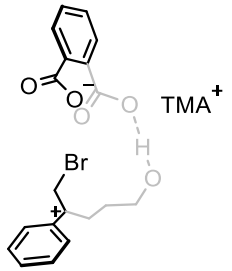
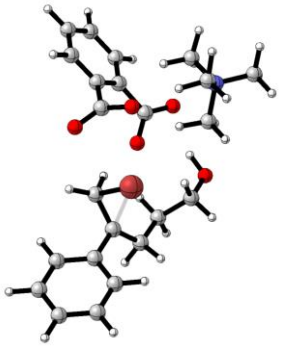
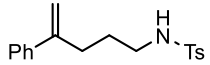
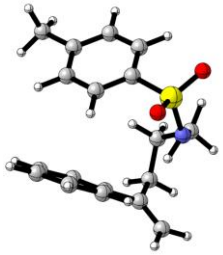
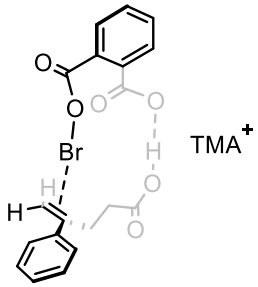
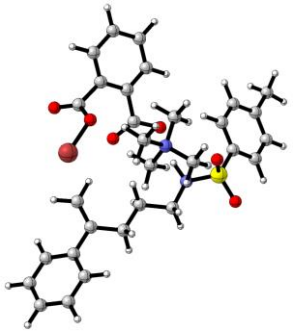
**Table S12.** Absolute energies (a.u.) of the studied species calculated at the M062X-D3/6-311G(d) and absolute solvated energies calculated by M062X-D3/6-311++G(d,p)/SMD(DCE)

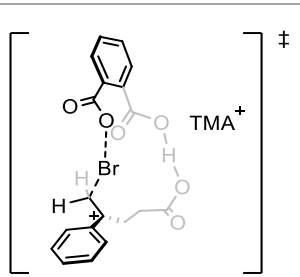
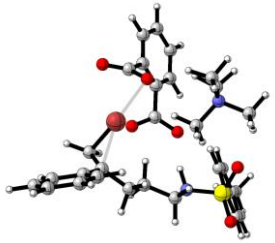
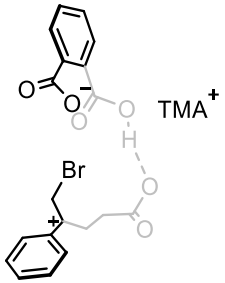
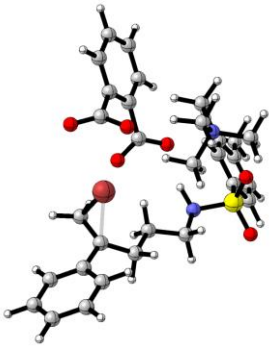
| | Species | Optimized Structures | Sum of electronic and thermal Free Energies (a.u.) | Thermal Correction to Gibbs Free Energy by Shermo (a.u.)[a] | Solvent corrected electronic Energies (a.u.) |
|---|---|---|---|---|---|
| **1a** |  |  | -576.569491 | 0.170378 | -576.7841336 |
| BCTC_Br |  |  | -3396.308293 | 0.229129 | -3396.608111 |
| **anti_INT1_$CO_2H$** |  |  | -3972.872591 | 0.425997 | -3973.406738 |

| | | | | | |
|---|---|---|---|---|---|
| **anti_TS1_$CO_2H$** |  |  | -3972.865272 | 0.428345 | -3973.407892 |
| **anti_INT2_$CO_2H$** |  |  | -3972.867431 | 0.427368 | -3973.407357 |
| **anti_INT3_$CO_2H$[b]** |  |  | -3150.103757 | 0.15556 | -3150.289349 |
| **anti_TS2_$CO_2H$[b]** |  |  | -3150.101481 | 0.155794 | -3150.287562 |

| | | | | | |
|---|---|---|---|---|---|
| BCTC_H[b] |  |  | -822.777412 | 0.23971 | -823.097358 |
| **2a**[b] |  |  | -3150.193533 | 0.160021 | -3150.375316 |
| **syn_INT1_$CO_2H$** |  |  | -3972.893196 | 0.42765 | -3973.414578 |
| **syn_TS1_$CO_2H$** |  |  | -3972.871854 | 0.427797 | -3973.4021 |

| | | | | | |
|---|---|---|---|---|---|
| **syn_INT2_$CO_2H$** |  |  | -3972.946644 | 0.429603 | -3973.485106 |
| **3a** |  |  | -502.495312 | 0.188488 | -502.7303372 |
| **anti_INT1_OH** |  |  | -3898.81055 | 0.445654 | -3899.353359 |
| **anti_TS1_OH** |  |  | -3898.778295 | 0.447407 | -3899.34388 |

| | | | | | |
|---|---|---|---|---|---|
| **anti_INT2_OH** |  |  | -3898.786003 | 0.448428 | -3899.349164 |
| **7a** |  |  | -1301.387657 | 0.313002 | -1301.764208 |
| **anti_INT1_NHTs** |  |  | -4697.705933 | 0.567753 | -4698.386554 |

| | | | | | |
|---|---|---|---|---|---|
| **anti_TS1_NHTs** |  |  | -4697.674483 | 0.570354 | -4698.37592 |
| **anti_INT2_NHTs** |  |  | -4697.676546 | 0.569343 | -4698.375824 |

[a] Lu, T.; Chen, Q. Shermo: A general code for calculating molecular thermochemistry properties. *Comput. Theor. Chem.* **2021**, *1200*, 113249.

[b] Optimized using M062X-D3/6-311G(d)/SMD(DCE) level of theory.

**Cartesian coordinates**

**1a**

| | | | |
|---|---|---|---|
| H | -1.54786500 | 1.04586000 | 1.93645500 |
| C | -1.87759300 | 0.49385500 | 1.06310900 |
| C | -2.77408900 | -0.89831000 | -1.16427200 |
| C | -1.09694000 | 0.49320700 | -0.09750300 |
| C | -3.09305300 | -0.17846800 | 1.10551200 |
| C | -3.54644600 | -0.87719900 | -0.00808000 |
| C | -1.56060400 | -0.22293000 | -1.20604000 |
| H | -3.68891800 | -0.15425700 | 2.01111600 |
| H | -4.49186500 | -1.40639000 | 0.02735400 |
| H | -0.94751900 | -0.26329500 | -2.09990100 |
| H | -3.11189500 | -1.45115600 | -2.03375400 |
| C | 0.19937100 | 1.22290200 | -0.16054900 |
| C | 0.54949200 | 1.91640000 | -1.24312200 |
| H | 1.51658700 | 2.40186300 | -1.30713700 |
| C | 1.12792900 | 1.09200600 | 1.02493700 |
| H | 0.60635000 | 1.35360800 | 1.94904500 |
| H | 1.96127700 | 1.78720500 | 0.91639400 |
| C | 1.67326800 | -0.33094000 | 1.15140500 |
| H | 2.17856500 | -0.47531400 | 2.11200900 |
| H | 0.87834900 | -1.07867300 | 1.10463500 |
| C | 2.69134200 | -0.63088400 | 0.07863700 |
| H | -0.11963500 | 2.02000000 | -2.09071700 |
| O | 2.88113400 | -1.95469900 | -0.07043100 |
| O | 3.29974700 | 0.18166100 | -0.56007700 |
| H | 3.56347100 | -2.07298400 | -0.74563900 |

BCTC_Br

| | | | |
|---|---|---|---|
| C | 1.39051200 | 1.17253000 | 0.52706000 |
| O | -0.12748400 | -0.84639100 | 0.98440500 |
| O | 1.40632900 | 1.89149800 | 1.47052900 |
| O | 0.54609200 | 1.33264900 | -0.55316200 |
| C | 0.56005000 | -1.67133700 | 0.32652800 |
| O | 0.19350800 | -2.76876100 | -0.11984600 |
| C | 2.37520000 | 0.09582300 | 0.18496000 |
| C | 1.99258800 | -1.23771700 | 0.04193900 |
| C | 3.70090900 | 0.48214100 | 0.00331000 |
| C | 2.95424800 | -2.17859600 | -0.30978200 |
| C | 4.65408800 | -0.47001200 | -0.33649200 |
| H | 3.97898500 | 1.52264300 | 0.13015700 |
| C | 4.27831100 | -1.80056600 | -0.49832900 |
| H | 2.63233400 | -3.20696300 | -0.42459000 |
| H | 5.68734800 | -0.17257800 | -0.47503700 |
| H | 5.02172600 | -2.54356300 | -0.76548100 |
| Br | -0.77509100 | 2.59764100 | -0.31047800 |
| N | -3.20942800 | -1.15703400 | -0.03509400 |
| C | -4.62480300 | -1.13887100 | -0.48554500 |
| H | -4.72121900 | -1.75733600 | -1.37660800 |
| H | -5.25584300 | -1.53429300 | 0.30908200 |
| H | -4.91393100 | -0.11397300 | -0.71319700 |
| C | -3.03688300 | -0.23650000 | 1.13524100 |
| H | -3.25039200 | 0.77951000 | 0.80574100 |
| H | -3.73908600 | -0.53781600 | 1.91209100 |
| H | -2.00119600 | -0.32391200 | 1.46646500 |
| C | -2.31872900 | -0.69989500 | -1.15247900 |
| H | -2.71551600 | 0.23573000 | -1.54486700 |
| H | -1.32222700 | -0.54995400 | -0.74203500 |
| H | -2.30820400 | -1.46925600 | -1.92274000 |
| C | -2.82785300 | -2.55009700 | 0.37048600 |
| H | -3.39376400 | -2.80803800 | 1.26512400 |
| H | -3.08911400 | -3.22275400 | -0.44610100 |
| H | -1.74908700 | -2.58901500 | 0.53758900 |

**anti_INT1_$CO_2H$**

| | | | |
|---|---|---|---|
| H | -3.49431300 | 1.37558900 | 0.60895300 |
| C | -4.12693600 | 0.84946700 | -0.09927400 |
| C | -5.69397900 | -0.54279000 | -1.93859600 |
| C | -4.06312700 | -0.54906800 | -0.14796400 |
| C | -4.95431200 | 1.53685600 | -0.97825000 |
| C | -5.73978700 | 0.84700200 | -1.89663100 |
| C | -4.85781100 | -1.23587000 | -1.07425900 |
| H | -4.99122900 | 2.62002200 | -0.93993200 |
| H | -6.39351800 | 1.38861500 | -2.57138500 |
| H | -4.85137300 | -2.31991200 | -1.09364600 |
| H | -6.31635600 | -1.08809700 | -2.63889600 |
| C | -3.06728100 | -0.84935500 | 2.21911700 |
| H | -3.55728100 | -1.64982500 | 2.78707700 |
| H | -3.65900600 | 0.05197600 | 2.36852700 |
| C | -1.66792300 | -0.61118500 | 2.80097300 |
| H | -1.71371900 | -0.68660400 | 3.89048100 |
| H | -0.93136800 | -1.35411100 | 2.48177900 |
| C | -1.10581100 | 0.78111500 | 2.46947500 |
| O | 0.03332500 | 1.04370400 | 2.95071000 |
| O | -1.79763200 | 1.54710800 | 1.78148200 |
| H | 1.40460100 | 0.71101500 | 2.47861200 |
| C | -2.56071600 | -2.44096800 | 0.35865300 |
| H | -2.78264500 | -2.88204000 | -0.60480800 |
| H | -2.03346600 | -3.06338300 | 1.07251600 |

| | | | |
|---|---|---|---|
| C | -3.17365800 | -1.28972700 | 0.77401200 |
| Br | -0.67007500 | -1.22875400 | -0.44946200 |
| O | 1.13943000 | -0.57020100 | -1.00441100 |
| C | 2.01166900 | -1.54619900 | -1.28811200 |
| C | 3.39101800 | -1.18415100 | -0.80481600 |
| O | 1.76364400 | -2.55341900 | -1.88647300 |
| C | 3.58045800 | -0.63625300 | 0.46853400 |
| C | 4.47650000 | -1.36685800 | -1.65452100 |
| C | 2.41915600 | -0.55163900 | 1.42595700 |
| C | 4.85228800 | -0.23093300 | 0.85991800 |
| C | 5.74830600 | -0.97197000 | -1.25370000 |
| H | 4.30941000 | -1.81543700 | -2.62746100 |
| O | 1.70543300 | -1.49776300 | 1.64033400 |
| O | 2.29737200 | 0.64236000 | 1.97164500 |
| C | 5.93411700 | -0.39866500 | 0.00024200 |
| H | 4.98954000 | 0.19980300 | 1.84545600 |
| H | 6.59296200 | -1.11200200 | -1.91851200 |
| H | 6.92501900 | -0.09114400 | 0.31485400 |
| C | 0.21983000 | 2.40468900 | 0.21710600 |
| N | 1.17863100 | 2.94409300 | -0.81183900 |
| C | 1.18253900 | 4.42783000 | -0.74693800 |
| C | 2.55178600 | 2.41910600 | -0.54734000 |
| C | 0.73581100 | 2.48632000 | -2.16100500 |
| H | 0.25221800 | 1.32088000 | 0.17139700 |
| H | 0.51278600 | 2.72474100 | 1.21382700 |
| H | 0.16972000 | 4.79130600 | -0.91169700 |
| H | 1.52294100 | 4.73100500 | 0.24142200 |
| H | 2.52823700 | 1.34310400 | -0.69092700 |
| H | 2.82197100 | 2.62997100 | 0.48466500 |
| H | -0.26345700 | 2.87439600 | -2.35137900 |
| H | 1.43453800 | 2.85887600 | -2.90960300 |
| H | -0.77980700 | 2.75932100 | -0.01379100 |
| H | 3.24649600 | 2.88647500 | -1.24512600 |
| H | 1.85169500 | 4.82145200 | -1.51111400 |
| H | 0.72222600 | 1.39689900 | -2.15903200 |

**anti_TS1_$CO_2H$**

| | | | |
|---|---|---|---|
| H | -3.81561500 | 1.55828600 | -0.22997300 |
| C | -4.45905600 | 0.70979000 | -0.44753500 |
| C | -6.04038300 | -1.51004700 | -1.02698400 |
| C | -4.08642200 | -0.55686600 | 0.01489100 |
| C | -5.60866000 | 0.85549700 | -1.20672400 |
| C | -6.40364600 | -0.25348700 | -1.49344500 |
| C | -4.87742900 | -1.66598000 | -0.27920600 |
| H | -5.88737100 | 1.83463400 | -1.57800900 |
| H | -7.30585800 | -0.13532900 | -2.08245300 |
| H | -4.60765200 | -2.64879200 | 0.09215900 |
| H | -6.65931700 | -2.37255400 | -1.24428400 |
| C | -2.83287800 | 0.18493400 | 2.09455500 |
| H | -3.44446600 | -0.39558600 | 2.80215600 |
| H | -3.37686400 | 1.10552200 | 1.89172800 |
| C | -1.48586100 | 0.53669400 | 2.70590800 |
| H | -1.63317900 | 0.82886700 | 3.74854900 |
| H | -0.77707100 | -0.29357200 | 2.71912800 |
| C | -0.80130400 | 1.72260200 | 1.99245300 |
| O | 0.34673000 | 2.00973700 | 2.43753800 |
| O | -1.40714200 | 2.28561300 | 1.07032800 |
| H | 1.58448600 | 1.08460900 | 2.28971900 |
| C | -2.03268200 | -1.86232800 | 0.76186300 |
| H | -2.34023900 | -2.69690900 | 0.14383500 |
| H | -1.34162700 | -2.08880300 | 1.56742400 |
| C | -2.86911400 | -0.67852000 | 0.85679000 |
| Br | -1.13265100 | -0.54153200 | -0.39355300 |
| O | 1.30473700 | -0.31694500 | -1.35734300 |
| C | 1.60704900 | -1.55655600 | -1.25084600 |
| C | 2.94959400 | -1.79217600 | -0.56625800 |
| O | 0.95127200 | -2.51753100 | -1.62817500 |
| C | 3.22499600 | -1.21117400 | 0.67694800 |
| C | 3.94988100 | -2.51220500 | -1.20999400 |
| C | 2.11227400 | -0.56131900 | 1.44207200 |
| C | 4.49736200 | -1.30238000 | 1.23403400 |
| C | 5.21913200 | -2.61693600 | -0.64857400 |
| H | 3.72133900 | -2.98373900 | -2.15968000 |
| O | 1.04544700 | -1.11121100 | 1.61135200 |
| O | 2.41721700 | 0.62898800 | 1.92246500 |
| C | 5.49752300 | -2.00525200 | 0.56947100 |
| H | 4.69220400 | -0.83669800 | 2.19409800 |
| H | 5.99341600 | -3.17529100 | -1.16365300 |
| H | 6.48627800 | -2.08423300 | 1.00722400 |
| C | 1.01994200 | 2.62041700 | -0.39077900 |
| N | 2.23243800 | 2.82142500 | -1.25876700 |
| C | 2.62482300 | 4.25189700 | -1.23175500 |
| C | 3.35441100 | 1.97187800 | -0.74752800 |
| C | 1.90672800 | 2.39694800 | -2.65294800 |
| H | 0.80789100 | 1.55518400 | -0.38181100 |
| H | 1.21903500 | 2.95528200 | 0.62443300 |
| H | 1.78522700 | 4.85581900 | -1.57257600 |
| H | 2.87939700 | 4.52405700 | -0.20904200 |
| H | 3.04786700 | 0.93395500 | -0.86328300 |
| H | 3.51233300 | 2.19085400 | 0.30602100 |
| H | 1.10298600 | 3.02958900 | -3.02765900 |
| H | 2.79571000 | 2.51598600 | -3.27227900 |
| H | 0.18573700 | 3.17746400 | -0.81068600 |
| H | 4.24670800 | 2.18858900 | -1.33492300 |
| H | 3.48385700 | 4.40296400 | -1.88453900 |
| H | 1.59672300 | 1.35166700 | -2.61366100 |

**anti_INT2_$CO_2H$**

| | | | |
|---|---|---|---|
| H | -4.17380200 | 1.57875400 | -0.47306100 |
| C | -4.71111500 | 0.63551900 | -0.47831100 |
| C | -6.04440200 | -1.80698400 | -0.52658800 |
| C | -4.10800100 | -0.49836000 | 0.07215000 |
| C | -5.96514900 | 0.54111800 | -1.06059900 |
| C | -6.63605800 | -0.68020900 | -1.08185900 |

| | | | |
|---|---|---|---|
| C | -4.77850100 | -1.71995600 | 0.04430100 |
| H | -6.42133900 | 1.41980400 | -1.50111700 |
| H | -7.61837200 | -0.75099100 | -1.53432200 |
| H | -4.32796400 | -2.60257200 | 0.48538400 |
| H | -6.56363600 | -2.75801600 | -0.53832500 |
| C | -2.74884800 | 0.59205800 | 1.90605300 |
| H | -3.45795600 | 0.13939600 | 2.61493200 |
| H | -3.20495600 | 1.52529100 | 1.57202500 |
| C | -1.43046700 | 0.91177800 | 2.59738300 |
| H | -1.65814000 | 1.30894300 | 3.59076300 |
| H | -0.79943500 | 0.03893900 | 2.75981700 |
| C | -0.58968600 | 1.99156700 | 1.88018100 |
| O | 0.56212800 | 2.18518000 | 2.37058000 |
| O | -1.09861100 | 2.58675100 | 0.92274800 |
| H | 1.74466700 | 1.21439300 | 2.30439100 |
| C | -1.82706700 | -1.48200000 | 0.61323600 |
| H | -2.09646700 | -2.36647100 | 0.04864700 |
| H | -1.01548100 | -1.59483600 | 1.32314900 |
| C | -2.78576300 | -0.38154000 | 0.75056200 |
| Br | -1.26114400 | -0.11173900 | -0.66640200 |
| O | 1.37420600 | -0.49201200 | -1.52429200 |
| C | 1.40648500 | -1.68740700 | -1.09123000 |
| C | 2.71249800 | -2.02328500 | -0.36742700 |
| O | 0.54103300 | -2.55281300 | -1.19153200 |
| C | 3.08502400 | -1.33015600 | 0.79229500 |
| C | 3.60713900 | -2.93654800 | -0.91460200 |
| C | 2.07195300 | -0.45518100 | 1.45335100 |
| C | 4.34326000 | -1.51232100 | 1.35991900 |
| C | 4.86014500 | -3.13282300 | -0.34029300 |
| H | 3.31468800 | -3.48872000 | -1.80134300 |
| O | 0.89786700 | -0.76260800 | 1.48277100 |
| O | 2.54202100 | 0.64698000 | 1.99988100 |
| C | 5.23497400 | -2.41599800 | 0.79189400 |
| H | 4.60602400 | -0.95823200 | 2.25448000 |
| H | 5.54871600 | -3.84630500 | -0.78036400 |
| H | 6.21129200 | -2.56891600 | 1.23760200 |
| C | 1.36969700 | 2.46417700 | -0.51076900 |
| N | 2.59624100 | 2.54576400 | -1.37812400 |
| C | 3.12725100 | 3.93093800 | -1.34504300 |
| C | 3.62744000 | 1.58671800 | -0.86983200 |
| C | 2.23230000 | 2.16004700 | -2.77422700 |
| H | 1.06812400 | 1.41946900 | -0.48255800 |
| H | 1.59179600 | 2.81211400 | 0.49554400 |
| H | 2.34745100 | 4.61646700 | -1.67324200 |
| H | 3.41551500 | 4.16895100 | -0.32276600 |
| H | 3.22789400 | 0.58427100 | -1.01720400 |
| H | 3.78830400 | 1.77148100 | 0.19053700 |
| H | 1.49909000 | 2.87323500 | -3.14899900 |
| H | 3.13075300 | 2.18986200 | -3.39066900 |
| H | 0.58538500 | 3.08116200 | -0.94294600 |
| H | 4.54577000 | 1.73135100 | -1.43893500 |
| H | 3.99120800 | 4.00201800 | -2.00489600 |
| H | 1.81940200 | 1.15091200 | -2.74010600 |

**anti_INT3_$CO_2H$**

| | | | |
|---|---|---|---|
| C | -2.95583800 | -1.08660900 | -0.15633500 |
| C | -1.56689100 | -1.73706400 | -0.43703900 |
| H | -1.11864500 | -1.26411000 | -1.31264800 |
| H | -1.73223400 | -2.78472200 | -0.69984800 |
| C | -0.59111600 | -1.74256600 | 0.79273700 |
| H | -1.25494800 | -1.72827000 | 1.66286200 |
| H | 0.02490100 | -2.63641600 | 0.80083800 |
| C | 0.20399700 | -0.51663700 | 0.79374400 |
| C | -0.52628600 | 0.72173100 | 1.20895400 |
| H | -1.52152700 | 0.47778800 | 1.56881000 |
| H | 0.03357500 | 1.32429100 | 1.91974500 |
| O | -3.69164700 | -1.04661800 | -1.15294900 |
| O | -3.18968300 | -0.71624800 | 1.01516700 |
| Br | -0.80727600 | 1.82149600 | -0.39113400 |
| C | 1.56414700 | -0.46527900 | 0.38626300 |
| C | 2.35087600 | 0.69485300 | 0.61156800 |
| C | 2.15459100 | -1.57109800 | -0.27825000 |
| C | 3.66754500 | 0.73352200 | 0.20678000 |
| H | 1.93790900 | 1.54945800 | 1.13184400 |
| C | 3.46550200 | -1.51064300 | -0.70364800 |
| H | 1.56960000 | -2.45609100 | -0.49298500 |
| C | 4.22294800 | -0.36500400 | -0.45453500 |
| H | 4.26819200 | 1.61371800 | 0.39848400 |
| H | 3.90507900 | -2.35018900 | -1.22720200 |
| H | 5.25657200 | -0.32611500 | -0.77939900 |

**anti_TS2_CO2H**

| | | | |
|---|---|---|---|
| C | -3.16802000 | -1.28569000 | 0.24467200 |
| C | -2.10300000 | -1.17164400 | -0.88606500 |
| H | -2.16868000 | -0.17632100 | -1.33115900 |
| H | -2.39361300 | -1.86824700 | -1.67426500 |
| C | -0.66942100 | -1.52388500 | -0.46691000 |
| H | -0.78389700 | -2.21582800 | 0.39705200 |
| H | -0.14144900 | -2.06626600 | -1.24583400 |
| C | 0.17620600 | -0.48875200 | 0.14353100 |
| C | -0.52324900 | 0.57711800 | 0.91917000 |
| H | -1.52015600 | 0.25408400 | 1.20564500 |
| H | 0.02686500 | 0.93592300 | 1.78220600 |
| O | -4.34251600 | -1.15916300 | -0.12825800 |
| O | -2.72967500 | -1.48863200 | 1.40310800 |
| C | 1.59886200 | -0.52276700 | 0.09390500 |
| C | 2.37279700 | 0.52743300 | 0.65612400 |
| C | 2.27923600 | -1.61532700 | -0.50460700 |
| C | 3.74965900 | 0.48612900 | 0.61199600 |
| H | 1.89709900 | 1.38801800 | 1.10748900 |
| C | 3.65731400 | -1.65954600 | -0.52036000 |
| H | 1.72693000 | -2.43975700 | -0.93283200 |
| C | 4.39254600 | -0.60849900 | 0.03002200 |
| H | 4.32938700 | 1.29868500 | 1.03124700 |

| | | | |
|---|---|---|---|
| H | 4.16589400 | -2.50569000 | -0.96471300 |
| H | 5.47597300 | -0.64170200 | 0.00509200 |
| Br | -0.70326900 | 2.08377300 | -0.32878900 |

BCTC_H

| | | | |
|---|---|---|---|
| O | -0.34482500 | 0.06805400 | 1.39397800 |
| C | 0.19856300 | 1.03995000 | 0.80997200 |
| O | -0.27111400 | 2.17360800 | 0.62502300 |
| C | 1.57909300 | 0.75542600 | 0.22024900 |
| C | 2.46166300 | 1.80467000 | -0.01596300 |
| C | 3.74795200 | 1.56105600 | -0.48189000 |
| C | 4.16400600 | 0.25529500 | -0.72307700 |
| C | 3.28680900 | -0.80067100 | -0.50641200 |
| C | 1.99478800 | -0.54988000 | -0.04805600 |
| O | 0.08421400 | -1.89558200 | -0.63394200 |
| H | 2.10852800 | 2.80977100 | 0.18337000 |
| H | 4.43005500 | 2.38714900 | -0.65110800 |
| H | 5.16853000 | 0.05756900 | -1.07996300 |
| H | 3.60107300 | -1.82134800 | -0.69652000 |
| C | -3.17196800 | 1.12379100 | 0.79126000 |
| N | -3.13840400 | 0.09712500 | -0.30358800 |
| C | -2.85079500 | -1.24669300 | 0.29398700 |
| C | -4.45181200 | 0.07740800 | -0.99670100 |
| C | -2.05710200 | 0.42298800 | -1.29678800 |
| H | -3.43250600 | 2.08427000 | 0.34937100 |
| H | -3.93079500 | 0.81474700 | 1.51025600 |
| H | -1.93428400 | -1.14857100 | 0.87651100 |
| H | -3.69929500 | -1.53267600 | 0.91536100 |
| H | -4.59966200 | 1.03325200 | -1.49747000 |
| H | -5.24054100 | -0.08188600 | -0.26304500 |
| H | -1.11448100 | 0.05630100 | -0.90585300 |
| H | -2.28882800 | -0.09410700 | -2.22727900 |
| H | -4.45699200 | -0.72927500 | -1.72813300 |
| H | -2.70447300 | -1.96006500 | -0.51560800 |
| H | -2.18307800 | 1.17741800 | 1.24411200 |
| H | -2.01712400 | 1.50053800 | -1.43691300 |
| C | 1.05629900 | -1.71002300 | 0.05732200 |
| O | 1.48899000 | -2.62975300 | 0.92991400 |
| H | 0.85960800 | -3.36347800 | 0.90484000 |

**2a**

| | | | |
|---|---|---|---|
| H | -0.69410000 | -1.82931500 | -1.80400000 |
| C | -1.33942900 | -1.55271800 | -0.97784700 |
| C | -2.99252600 | -0.86087800 | 1.14862700 |
| C | -0.82635100 | -0.79955600 | 0.07935800 |
| C | -2.66809400 | -1.96314400 | -0.96657600 |
| C | -3.49822100 | -1.61704200 | 0.09614300 |
| C | -1.66122000 | -0.45491400 | 1.14121400 |
| H | -3.05434000 | -2.55553200 | -1.78850400 |
| H | -4.53417800 | -1.93691600 | 0.10439000 |
| H | -1.27771300 | 0.13304700 | 1.96818600 |
| H | -3.63238700 | -0.58740400 | 1.98011900 |
| C | 0.60983800 | -0.32551800 | 0.03714000 |
| C | 0.77720300 | 0.90609000 | -0.86558500 |
| H | 0.39831700 | 0.69224400 | -1.86249100 |
| C | 1.28913100 | -0.16158500 | 1.40719000 |
| H | 1.14946000 | 0.83541800 | 1.82233100 |
| H | 0.86983400 | -0.88866800 | 2.10396200 |
| C | 2.74264600 | -0.50580500 | 1.10494200 |
| H | 3.27229600 | -0.99100600 | 1.92240800 |
| H | 3.32728000 | 0.36396100 | 0.79198900 |
| C | 2.63772300 | -1.44432200 | -0.07470900 |
| O | 1.40365800 | -1.34005100 | -0.62926100 |
| O | 3.45848400 | -2.18987600 | -0.51928600 |
| H | 1.82259000 | 1.20533900 | -0.92665400 |
| Br | -0.19909700 | 2.47070300 | -0.22579200 |

**syn_INT1_CO2H**

| | | | |
|---|---|---|---|
| C | -2.57295800 | -1.85734100 | -0.39300400 |
| O | -2.20292200 | 0.10182800 | 1.59277400 |
| O | -2.49171800 | -3.01368600 | -0.11483300 |
| H | 4.17110000 | -2.93551100 | -1.26083800 |
| C | 4.25566300 | -1.85562400 | -1.29537500 |
| C | 4.59379700 | 0.89234900 | -1.36798400 |
| C | 3.76741200 | -1.08372100 | -0.23195800 |
| C | 4.88514700 | -1.26387700 | -2.38101400 |
| C | 5.05161800 | 0.11708300 | -2.42662600 |
| C | 3.96429500 | 0.30219100 | -0.27601300 |
| H | 5.26088400 | -1.88420800 | -3.18699200 |
| H | 5.55173100 | 0.57907500 | -3.27059000 |
| H | 3.60668700 | 0.91648600 | 0.54383400 |
| H | 4.74496600 | 1.96722300 | -1.38005400 |
| C | 3.06006300 | -1.72399700 | 0.91182200 |
| C | 2.43353800 | -2.90583200 | 0.75861900 |
| H | 1.96403200 | -3.39623000 | 1.60503900 |
| C | 3.08977400 | -1.07895500 | 2.29122900 |
| H | 3.48198600 | -1.83566800 | 2.97674900 |
| H | 3.78939100 | -0.24450000 | 2.31129500 |
| C | 1.73662500 | -0.58689200 | 2.82590700 |
| H | 1.81883300 | -0.45156400 | 3.90978500 |
| H | 0.94153800 | -1.31805600 | 2.66816400 |
| C | 1.29264400 | 0.77404900 | 2.27059600 |
| O | 2.18389600 | 1.55991600 | 1.88618200 |
| O | 0.05971300 | 1.03333500 | 2.26640400 |
| H | -1.32452800 | 0.47701600 | 1.94817300 |
| H | 2.41185200 | -3.44308500 | -0.18185200 |
| O | -1.53741700 | -1.06449500 | -0.75768200 |
| C | -2.81319300 | 0.89051000 | 0.75033500 |
| O | -2.54411700 | 2.05843200 | 0.53952600 |
| C | -3.85197100 | -1.08033000 | -0.46141600 |
| C | -3.95146500 | 0.22243800 | 0.03418500 |
| C | -4.95345900 | -1.68950300 | -1.05356300 |
| C | -5.14419300 | 0.92203500 | -0.11371400 |

| | | | |
|---|---|---|---|
| C | -6.14822900 | -0.99140800 | -1.18000500 |
| H | -4.85856300 | -2.70700900 | -1.41471000 |
| C | -6.24087700 | 0.31692700 | -0.71642100 |
| H | -5.20320800 | 1.93683900 | 0.26236400 |
| H | -7.00480400 | -1.46709400 | -1.64322000 |
| H | -7.17095600 | 0.86426400 | -0.81770400 |
| Br | 0.14799000 | -1.67756100 | -0.20189000 |
| C | 1.82898600 | 3.63526900 | -1.00994600 |
| H | 1.86014500 | 4.72373300 | -0.97953200 |
| H | 2.52821500 | 3.21495100 | -0.28732600 |
| H | 2.06221600 | 3.27735000 | -2.01228600 |
| C | 0.43713800 | 1.67776300 | -0.72153700 |
| H | 1.23664300 | 1.29139700 | -0.09905000 |
| H | -0.52589700 | 1.32977300 | -0.36521100 |
| H | 0.58873300 | 1.39822700 | -1.76438400 |
| C | -0.56672900 | 3.73163900 | -1.54583400 |
| H | -1.53553800 | 3.35292700 | -1.22159400 |
| H | -0.54572600 | 4.81906800 | -1.48578900 |
| H | -0.35165500 | 3.40923800 | -2.56397700 |
| C | 0.17698800 | 3.63705800 | 0.77245500 |
| H | 0.19798100 | 4.72761900 | 0.76111100 |
| H | -0.79903700 | 3.25624500 | 1.05890300 |
| H | 0.93668300 | 3.21456500 | 1.42603400 |
| N | 0.46621100 | 3.17542000 | -0.63051300 |

**syn_TS1_CO2H**

| | | | |
|---|---|---|---|
| C | -2.69123600 | -1.57104600 | -0.83917300 |
| O | -2.23810300 | -0.24511400 | 1.70589100 |
| O | -2.67567700 | -2.77536300 | -0.94250000 |
| H | 2.63822800 | -0.26466100 | -1.79086200 |
| C | 3.64480000 | -0.12057100 | -1.41004100 |
| C | 6.19787700 | 0.27752700 | -0.38282700 |
| C | 3.99209400 | -0.69023500 | -0.17763300 |
| C | 4.56093600 | 0.64942500 | -2.10861200 |
| C | 5.84352900 | 0.84813300 | -1.59827100 |
| C | 5.27378100 | -0.47903600 | 0.33113000 |
| H | 4.28045500 | 1.09202300 | -3.05824000 |
| H | 6.56259000 | 1.44286200 | -2.14998600 |
| H | 5.56627500 | -0.92431400 | 1.27494700 |
| H | 7.19577000 | 0.42118300 | 0.01512800 |
| C | 3.00279000 | -1.51708500 | 0.53756900 |
| C | 2.21668900 | -2.42577400 | -0.21826800 |
| H | 1.89610400 | -3.30992800 | 0.32302700 |
| C | 3.07425900 | -1.72280500 | 2.02881000 |
| H | 3.41718700 | -2.74209600 | 2.23325200 |
| H | 3.77851900 | -1.02186100 | 2.47615300 |
| C | 1.68421600 | -1.47026200 | 2.61721800 |
| H | 1.68980700 | -1.44613400 | 3.70713200 |
| H | 0.96124600 | -2.23312400 | 2.31248200 |
| C | 1.20821000 | -0.12858600 | 2.05742800 |
| O | 1.89552100 | 0.28318200 | 1.07724300 |
| O | 0.22812200 | 0.44904500 | 2.55196500 |
| H | -1.41976700 | 0.09549700 | 2.13916000 |
| H | 2.57285700 | -2.62369400 | -1.22214700 |
| O | -1.69465400 | -0.74990300 | -1.01198500 |
| C | -2.92735300 | 0.73019500 | 1.15222600 |
| O | -2.70015800 | 1.91095300 | 1.32278200 |
| C | -3.99020300 | -0.84313900 | -0.54322900 |
| C | -4.07699400 | 0.25330700 | 0.32103400 |
| C | -5.13263500 | -1.27083400 | -1.21335800 |
| C | -5.28351900 | 0.93631100 | 0.46065900 |
| C | -6.33891000 | -0.59840600 | -1.05889200 |
| H | -5.05361400 | -2.13856100 | -1.85802900 |
| C | -6.41405800 | 0.51367200 | -0.22644600 |
| H | -5.32346700 | 1.79130500 | 1.12607500 |
| H | -7.21988600 | -0.94022600 | -1.59080500 |
| H | -7.35169300 | 1.04417500 | -0.10545600 |
| Br | 0.21440600 | -1.63587100 | -0.69887700 |
| C | 1.76266600 | 2.87863500 | -0.61942200 |
| H | 2.26594100 | 3.79673000 | -0.31694200 |
| H | 2.11941300 | 2.02575200 | -0.04237900 |
| H | 1.91238600 | 2.70563000 | -1.68481100 |
| C | -0.40217600 | 1.74927900 | -0.72577400 |
| H | -0.10909700 | 0.98934400 | -0.00833400 |
| H | -1.47277400 | 1.91680200 | -0.68356400 |
| H | -0.09897800 | 1.45065700 | -1.72801900 |
| C | -0.25290600 | 4.14086800 | -1.17459800 |
| H | -1.31004000 | 4.25083300 | -0.93921800 |
| H | 0.28120000 | 5.05968200 | -0.93536200 |
| H | -0.13184700 | 3.90255300 | -2.23044600 |
| C | 0.07713700 | 3.30517700 | 1.09400600 |
| H | 0.58069700 | 4.23920200 | 1.34308900 |
| H | -0.99389500 | 3.36556300 | 1.27341500 |
| H | 0.47065000 | 2.46634500 | 1.66764700 |
| N | 0.29959500 | 3.02757700 | -0.36208900 |

**syn_INT2_CO2H**

| | | | |
|---|---|---|---|
| C | -2.28916000 | -1.60383700 | -0.80585400 |
| O | -2.15216300 | -0.50241100 | 1.93827500 |
| O | -1.69045900 | -2.63363900 | -1.12191800 |
| H | 4.31037300 | 1.00271100 | 1.65008900 |
| C | 4.86604900 | 0.14185500 | 1.30000900 |
| C | 6.28071800 | -2.08546500 | 0.41704600 |
| C | 4.24561300 | -0.78251500 | 0.46390700 |
| C | 6.18546600 | -0.05274300 | 1.69806900 |
| C | 6.89589600 | -1.16229900 | 1.25743400 |
| C | 4.96282300 | -1.89622300 | 0.02314400 |
| H | 6.65707500 | 0.66657500 | 2.35799500 |
| H | 7.92294700 | -1.31142700 | 1.57004600 |
| H | 4.48379000 | -2.62734600 | -0.62181600 |
| H | 6.82546300 | -2.95706800 | 0.07292200 |
| C | 2.82246500 | -0.58406600 | -0.02421700 |
| C | 2.90994500 | -0.06646400 | -1.46079100 |
| H | 3.39927300 | -0.79882000 | -2.09892000 |

| | | | |
|---|---|---|---|
| C | 1.92480100 | -1.83596600 | 0.14987100 |
| H | 1.75145900 | -2.34441100 | -0.79924000 |
| H | 2.40472200 | -2.53346800 | 0.83618900 |
| C | 0.62360600 | -1.28781900 | 0.72548600 |
| H | 0.19184500 | -1.87107600 | 1.53787000 |
| H | -0.15894500 | -1.18141300 | -0.03622900 |
| C | 0.96728400 | 0.09409700 | 1.17896300 |
| O | 2.19760100 | 0.45078600 | 0.76327200 |
| O | 0.29217700 | 0.88879200 | 1.79325600 |
| H | -1.47566000 | 0.16188600 | 2.16014600 |
| H | 3.46184900 | 0.87100700 | -1.48634600 |
| O | -1.88694800 | -0.40909300 | -0.88551900 |
| C | -3.21153300 | 0.10239400 | 1.39799000 |
| O | -3.40331900 | 1.29463700 | 1.50103800 |
| C | -3.69818700 | -1.74719300 | -0.22226500 |
| C | -4.15284100 | -0.86515400 | 0.76282500 |
| C | -4.57687300 | -2.70230500 | -0.71898300 |
| C | -5.47313700 | -0.89977300 | 1.19972700 |
| C | -5.89598900 | -2.75051500 | -0.27834100 |
| H | -4.20282100 | -3.39866700 | -1.46124100 |
| C | -6.34926300 | -1.84414600 | 0.67527800 |
| H | -5.80345500 | -0.19758800 | 1.95807600 |
| H | -6.57518100 | -3.49350000 | -0.68289000 |
| H | -7.37801200 | -1.87715600 | 1.01627900 |
| Br | 1.15066300 | 0.26487000 | -2.23023100 |
| C | 0.43525400 | 3.55555400 | -0.27851700 |
| H | 0.79973100 | 4.50986500 | 0.10130400 |
| H | 0.85187400 | 2.73293000 | 0.30068000 |
| H | 0.69842100 | 3.43636000 | -1.32825700 |
| C | -1.55897500 | 2.21610100 | -0.70030300 |
| H | -1.10635800 | 1.39489500 | -0.15949800 |
| H | -2.63525500 | 2.16580000 | -0.56649400 |
| H | -1.28635700 | 2.14981100 | -1.75124400 |
| C | -1.65674700 | 4.64820300 | -0.89896200 |
| H | -2.73858600 | 4.59448900 | -0.79230300 |
| H | -1.28769000 | 5.59100800 | -0.49698400 |
| H | -1.38613300 | 4.55832200 | -1.94965700 |
| C | -1.42153300 | 3.61693200 | 1.29830200 |
| H | -1.09085400 | 4.58540900 | 1.67357900 |
| H | -2.49729700 | 3.49499000 | 1.39406000 |
| H | -0.92638300 | 2.80692600 | 1.82801600 |
| N | -1.05032100 | 3.51914400 | -0.14773900 |

**3a**

| | | | |
|---|---|---|---|
| H | -0.49790300 | -0.68705900 | 1.87159500 |
| C | -1.19754000 | -0.58724600 | 1.04891400 |
| C | -3.01331800 | -0.35776800 | -1.03629700 |
| C | -1.05643000 | 0.46435800 | 0.13762800 |
| C | -2.23789700 | -1.50022600 | 0.92950500 |
| C | -3.15137300 | -1.38843400 | -0.11302500 |
| C | -1.97402700 | 0.55600900 | -0.91355200 |
| H | -2.33451300 | -2.30228100 | 1.65274300 |
| H | -3.95910300 | -2.10479500 | -0.21063300 |
| H | -1.85213100 | 1.33942800 | -1.65356900 |
| H | -3.71001900 | -0.27126600 | -1.86267100 |
| C | 0.04254300 | 1.45854800 | 0.27646200 |
| C | -0.16523400 | 2.75079400 | 0.02233700 |
| H | 0.63654600 | 3.47675300 | 0.10463800 |
| C | 1.39998600 | 0.94658100 | 0.69691700 |
| H | 1.33288300 | 0.48453000 | 1.68917600 |
| H | 2.08041100 | 1.79646600 | 0.80275900 |
| C | 1.98057500 | -0.06590000 | -0.29337400 |
| H | 1.30993000 | -0.92206500 | -0.40609300 |
| H | 2.07795900 | 0.39382500 | -1.28107900 |
| H | -1.14380300 | 3.12765200 | -0.25411200 |
| C | 3.33912600 | -0.57300500 | 0.14478500 |
| H | 3.25474600 | -1.05497900 | 1.12947700 |
| H | 4.03870200 | 0.26912500 | 0.24404400 |
| O | 3.78948000 | -1.49263700 | -0.83200700 |
| H | 4.65198600 | -1.82650300 | -0.57202200 |

**anti_INT1_OH**

| | | | |
|---|---|---|---|
| H | -3.42032000 | 2.42619800 | -1.03278800 |
| C | -4.17675100 | 1.65334100 | -0.94466000 |
| C | -6.10238300 | -0.33805500 | -0.76955700 |
| C | -4.05461900 | 0.67361500 | 0.04577600 |
| C | -5.23821000 | 1.63131800 | -1.84150900 |
| C | -6.20657600 | 0.63665200 | -1.75593800 |
| C | -5.03638400 | -0.31884800 | 0.12180200 |
| H | -5.30774300 | 2.39211600 | -2.61115400 |
| H | -7.03789500 | 0.62322000 | -2.45166800 |
| H | -4.96351800 | -1.06987900 | 0.90102000 |
| H | -6.85662300 | -1.11307100 | -0.68951600 |
| C | -2.63008600 | 1.97316600 | 1.71514200 |
| H | -3.50703300 | 2.16732700 | 2.34409400 |
| H | -2.62652900 | 2.79448100 | 0.98754900 |
| C | -1.35554500 | 2.04446800 | 2.55507200 |
| H | -1.42289000 | 2.88607300 | 3.25001200 |
| H | -1.23084900 | 1.14544300 | 3.16446300 |
| O | 1.07700900 | 2.25813700 | 2.46340400 |
| H | 1.23704700 | 1.32699600 | 2.71055400 |
| C | -2.22389000 | -0.46241900 | 1.20675600 |
| H | -2.49964300 | -1.37782900 | 0.69057300 |
| H | -1.37556100 | -0.52212000 | 1.88148600 |
| C | -2.90176100 | 0.66894400 | 0.99139600 |
| Br | -0.35008300 | -0.36498500 | -1.28355300 |
| O | 1.39321300 | -0.63289600 | -1.85198800 |
| C | 2.19079700 | -1.50876100 | -1.14194500 |
| C | 1.53786600 | -2.52919300 | -0.25620300 |
| O | 3.34669000 | -1.49746900 | -1.45562200 |
| C | 1.12885100 | -2.23358700 | 1.04582100 |
| C | 1.36111700 | -3.80617800 | -0.78008100 |
| C | 1.36475600 | -0.83555800 | 1.59511700 |
| C | 0.52380200 | -3.22267600 | 1.81003200 |

| | | | |
|---|---|---|---|
| C | 0.75458700 | -4.78990400 | -0.00546300 |
| H | 1.69292200 | -4.02814900 | -1.78867400 |
| O | 0.85865400 | -0.53210200 | 2.68857500 |
| O | 2.05443300 | -0.10053400 | 0.84858900 |
| C | 0.33339900 | -4.49776400 | 1.28766400 |
| H | 0.21410700 | -2.96410000 | 2.81629400 |
| H | 0.61389900 | -5.78417900 | -0.41378600 |
| H | -0.13847500 | -5.26631000 | 1.88956600 |
| C | 2.33858600 | 2.37100300 | -0.48420000 |
| N | 3.82186700 | 2.24895900 | -0.69528700 |
| C | 4.44167500 | 3.58844000 | -0.51402500 |
| C | 4.42170000 | 1.29418600 | 0.29482800 |
| C | 4.08206900 | 1.74038600 | -2.07428900 |
| H | 1.87924400 | 1.41987700 | -0.72994300 |
| H | 2.14502000 | 2.58129900 | 0.56851500 |
| H | 4.02654600 | 4.27612900 | -1.24903700 |
| H | 4.21509000 | 3.94049700 | 0.49095500 |
| H | 4.02098400 | 0.30171800 | 0.11460200 |
| H | 4.12853500 | 1.60686500 | 1.29459300 |
| H | 3.62189600 | 2.42026300 | -2.79010700 |
| H | 5.15874300 | 1.69713300 | -2.23562000 |
| H | 1.97917000 | 3.16783200 | -1.13575900 |
| H | 5.50383600 | 1.32308400 | 0.16848900 |
| H | 5.51924700 | 3.50712500 | -0.64807100 |
| H | 3.65148100 | 0.74308100 | -2.16141400 |
| C | -0.10861000 | 2.23451900 | 1.69837700 |
| H | -0.17514800 | 3.19849100 | 1.17749200 |
| H | -0.05201900 | 1.44851200 | 0.93551700 |

**anti_TS1_OH**

| | | | |
|---|---|---|---|
| H | -3.79367300 | 1.58916800 | -0.94444300 |
| C | -4.45638200 | 0.73255100 | -0.88249300 |
| C | -6.11502000 | -1.49663300 | -0.77311300 |
| C | -4.14106100 | -0.32251000 | -0.02119500 |
| C | -5.58028200 | 0.66486300 | -1.69049200 |
| C | -6.41492200 | -0.44902900 | -1.63429000 |
| C | -4.97867700 | -1.43853900 | 0.02601800 |
| H | -5.80476400 | 1.47864200 | -2.36988700 |
| H | -7.29568600 | -0.49905700 | -2.26379500 |
| H | -4.76130500 | -2.25374000 | 0.70756500 |
| H | -6.76356000 | -2.36320900 | -0.72188300 |
| C | -2.88811400 | 0.96065500 | 1.79341200 |
| H | -3.68780200 | 0.75379400 | 2.51867000 |
| H | -3.23822700 | 1.84095100 | 1.24474400 |
| C | -1.56714400 | 1.26208200 | 2.51510800 |
| H | -1.76351300 | 1.50317600 | 3.56181400 |
| H | -0.88165900 | 0.40915700 | 2.51543800 |
| O | 0.41688800 | 2.66436600 | 2.46650200 |
| H | 0.96351900 | 1.85754700 | 2.29537100 |
| C | -2.17988400 | -1.40282000 | 1.12561000 |
| H | -2.48050100 | -2.34007500 | 0.67278900 |
| H | -1.49167700 | -1.46258400 | 1.96486000 |
| C | -2.96047500 | -0.23779000 | 0.87562400 |
| Br | -1.05624200 | -0.43670400 | -0.29048800 |
| O | 1.05569600 | -0.14346000 | -1.26081400 |
| C | 1.63922700 | -1.25755200 | -1.58954600 |
| C | 2.60985300 | -1.82504400 | -0.55859000 |
| O | 1.50629500 | -1.82690900 | -2.65864100 |
| C | 2.61374300 | -1.49614500 | 0.80743200 |
| C | 3.56770700 | -2.71966400 | -1.04779500 |
| C | 1.60760100 | -0.59756100 | 1.53090000 |
| C | 3.58863800 | -2.06615500 | 1.63225900 |
| C | 4.53798800 | -3.26567100 | -0.22237500 |
| H | 3.51973000 | -2.97346800 | -2.10029000 |
| O | 0.64865000 | -1.17626600 | 2.06540800 |
| O | 1.88612500 | 0.62950200 | 1.58157400 |
| C | 4.54879600 | -2.93217900 | 1.12926000 |
| H | 3.57768200 | -1.82517900 | 2.69048400 |
| H | 5.27598000 | -3.95045100 | -0.62578400 |
| H | 5.29688500 | -3.35456400 | 1.79206500 |
| C | 1.56927900 | 2.75877700 | -0.42537000 |
| N | 2.86066500 | 2.62851300 | -1.17698400 |
| C | 3.57121800 | 3.93174000 | -1.18263300 |
| C | 3.71763900 | 1.59073200 | -0.51671800 |
| C | 2.56267600 | 2.19726900 | -2.57790200 |
| H | 1.14046900 | 1.76198500 | -0.35517500 |
| H | 1.76177000 | 3.13598900 | 0.57661900 |
| H | 2.92280900 | 4.68938700 | -1.62038300 |
| H | 3.81316900 | 4.20170800 | -0.15626700 |
| H | 3.19830800 | 0.64052400 | -0.57890700 |
| H | 3.83060100 | 1.84147100 | 0.53455300 |
| H | 2.02166100 | 3.00022600 | -3.07785000 |
| H | 3.50372300 | 2.00544300 | -3.09203600 |
| H | 0.92950300 | 3.44490700 | -0.98180300 |
| H | 4.67581500 | 1.56434500 | -1.03546400 |
| H | 4.48442800 | 3.83946300 | -1.76918300 |
| H | 1.95238900 | 1.29387400 | -2.52668200 |
| C | -0.83470500 | 2.44847200 | 1.88386800 |
| H | -1.42328900 | 3.36298500 | 2.01904400 |
| H | -0.75439400 | 2.27568500 | 0.79770200 |

**anti_INT2_OH**

| | | | |
|---|---|---|---|
| H | -4.56613200 | 1.74941300 | -0.39970500 |
| C | -4.95204200 | 0.73796600 | -0.33242400 |
| C | -5.92287000 | -1.86510100 | -0.21859100 |
| C | -4.13101600 | -0.28824800 | 0.14417800 |
| C | -6.24003200 | 0.46004800 | -0.76095100 |
| C | -6.72992400 | -0.84292400 | -0.69999100 |
| C | -4.62326400 | -1.59292400 | 0.19523000 |
| H | -6.86329600 | 1.25822700 | -1.14642500 |
| H | -7.73873900 | -1.05866100 | -1.03196900 |
| H | -4.00516300 | -2.39751700 | 0.57661800 |
| H | -6.29923700 | -2.87979500 | -0.16767800 |
| C | -2.71410100 | 1.06765100 | 1.75047000 |

| | | | |
|---|---|---|---|
| H | -3.44470200 | 0.67624100 | 2.47296200 |
| H | -3.17952700 | 1.98212200 | 1.36691300 |
| C | -1.40747700 | 1.37971800 | 2.48604200 |
| H | -1.67409100 | 1.78974900 | 3.46406600 |
| H | -0.82424600 | 0.47818900 | 2.66913400 |
| O | 0.68334500 | 2.62487500 | 2.50942600 |
| H | 1.27360500 | 1.85098900 | 2.41898500 |
| C | -1.70915400 | -0.98149000 | 0.48284600 |
| H | -1.91974800 | -1.92346500 | -0.00924600 |
| H | -0.79475200 | -0.94637500 | 1.07812600 |
| C | -2.76899000 | 0.01036700 | 0.66678300 |
| Br | -1.42721800 | 0.31812900 | -0.97685300 |
| O | 1.34001400 | -0.48114400 | -1.62832500 |
| C | 1.13436100 | -1.59558300 | -1.05939300 |
| C | 2.29015200 | -2.12000900 | -0.20871600 |
| O | 0.12443800 | -2.30368600 | -1.14932000 |
| C | 2.79638100 | -1.42375000 | 0.89800400 |
| C | 2.90896600 | -3.30555200 | -0.60146000 |
| C | 2.11252100 | -0.18201300 | 1.43994500 |
| C | 3.93081200 | -1.89759500 | 1.55466900 |
| C | 4.03259800 | -3.78151100 | 0.06627100 |
| H | 2.49586600 | -3.85280800 | -1.44248100 |
| O | 0.86365400 | -0.12614300 | 1.33018900 |
| O | 2.82364200 | 0.70984800 | 1.95510500 |
| C | 4.55091100 | -3.07266000 | 1.14551700 |
| H | 4.30732800 | -1.32898200 | 2.39805200 |
| H | 4.50281100 | -4.70487000 | -0.25585600 |
| H | 5.42680200 | -3.43830000 | 1.67070100 |
| C | 1.91952600 | 2.30004300 | -0.52071800 |
| N | 3.15800400 | 2.19967500 | -1.36314400 |
| C | 3.94363300 | 3.45206000 | -1.23542600 |
| C | 3.98712900 | 1.03352200 | -0.90680900 |
| C | 2.75578000 | 1.96883000 | -2.78225000 |
| H | 1.40420300 | 1.34136900 | -0.58823300 |
| H | 2.19940500 | 2.49854000 | 0.51156600 |
| H | 3.32266100 | 4.29554600 | -1.53447300 |
| H | 4.24499800 | 3.56553800 | -0.19551900 |
| H | 3.41225100 | 0.13526400 | -1.12592500 |
| H | 4.14707900 | 1.11460900 | 0.16747700 |
| H | 2.18521700 | 2.83099600 | -3.12724600 |
| H | 3.65635100 | 1.85384600 | -3.38503500 |
| H | 1.31073700 | 3.11230100 | -0.92105900 |
| H | 4.92510700 | 1.04912700 | -1.46183900 |
| H | 4.82308300 | 3.39106100 | -1.87523800 |
| H | 2.15342500 | 1.05917300 | -2.80557800 |
| C | -0.49942500 | 2.39774300 | 1.79198600 |
| H | -1.01919500 | 3.36144700 | 1.72730100 |
| H | -0.28311200 | 2.06327500 | 0.77558800 |

**7a**

| | | | |
|---|---|---|---|
| H | 1.39923100 | 2.27139400 | 1.76309000 |
| C | 1.57281100 | 2.13804600 | 0.70132000 |
| C | 1.99718200 | 1.83785100 | -2.02718200 |
| C | 2.21387800 | 0.98479100 | 0.23730800 |
| C | 1.17618100 | 3.13708900 | -0.17984800 |
| C | 1.38889600 | 2.99380500 | -1.54695800 |
| C | 2.40103500 | 0.84440600 | -1.14429000 |
| H | 0.69890300 | 4.03163100 | 0.20530300 |
| H | 1.07490500 | 3.77114300 | -2.23428600 |
| H | 2.85218300 | -0.06019700 | -1.53991100 |
| H | 2.14269300 | 1.69819300 | -3.09204800 |
| C | 2.69604000 | -0.06247600 | 1.18195400 |
| C | 3.81535000 | -0.74528000 | 0.92819800 |
| H | 4.16369200 | -1.52144600 | 1.60086900 |
| C | 1.88095600 | -0.34234400 | 2.42526900 |
| H | 1.80226000 | 0.56838300 | 3.02744900 |
| H | 2.42626600 | -1.06418600 | 3.03979400 |
| C | 0.46804100 | -0.88043100 | 2.15268500 |
| H | -0.02579400 | -1.04096900 | 3.11585900 |
| H | -0.12831000 | -0.13619900 | 1.61676600 |
| H | 4.43264900 | -0.53500200 | 0.06193800 |
| C | 0.46820200 | -2.20656200 | 1.38243300 |
| H | -0.48382100 | -2.72792400 | 1.50188500 |
| H | 1.23372000 | -2.87430300 | 1.78954400 |
| N | 0.70875900 | -2.08745200 | -0.05585800 |
| H | 1.47183800 | -1.48618700 | -0.33712300 |
| S | -0.56156700 | -2.01258500 | -1.10706400 |
| O | -1.33697600 | -3.22191300 | -0.93161800 |
| O | 0.02539700 | -1.63816000 | -2.37721700 |
| C | -1.59351300 | -0.67413500 | -0.54093800 |
| C | -2.67369200 | -0.95376900 | 0.28745000 |
| C | -1.24302600 | 0.63384600 | -0.85249200 |
| C | -3.40824600 | 0.10042400 | 0.81576100 |
| H | -2.93668800 | -1.98436000 | 0.49522700 |
| C | -1.99325600 | 1.67371900 | -0.32127400 |
| H | -0.40169300 | 0.83179600 | -1.50737000 |
| C | -3.07828300 | 1.42469200 | 0.52255300 |
| H | -4.25470400 | -0.10922700 | 1.46187300 |
| H | -1.72701400 | 2.69688700 | -0.56649300 |
| C | -3.89989400 | 2.56136200 | 1.07023500 |
| H | -4.36202000 | 2.29671000 | 2.02225500 |
| H | -3.29170000 | 3.45438700 | 1.22192700 |
| H | -4.70218100 | 2.82338200 | 0.37505500 |

**anti_INT1_NHTs**

| | | | |
|---|---|---|---|
| H | -4.41539100 | -3.35835300 | 0.96240900 |
| C | -5.13448700 | -3.16263600 | 0.17475800 |
| C | -7.00347700 | -2.69668300 | -1.81844000 |
| C | -4.76894600 | -2.37683700 | -0.92376400 |
| C | -6.41552400 | -3.69181700 | 0.28518400 |
| C | -7.35767100 | -3.45863500 | -0.70920600 |
| C | -5.72461200 | -2.16749200 | -1.92534000 |
| H | -6.67598200 | -4.29069000 | 1.15108200 |
| H | -8.35493100 | -3.87589000 | -0.62754100 |

| | | | |
|---|---|---|---|
| H | -5.44825900 | -1.60458200 | -2.80979400 |
| H | -7.72297000 | -2.52507400 | -2.61150300 |
| C | -2.27781500 | -2.59053900 | -0.41231900 |
| H | -2.41191900 | -3.64829600 | -0.66760000 |
| H | -2.37760200 | -2.54396100 | 0.68147900 |
| C | -0.87735900 | -2.13105800 | -0.79828300 |
| H | -0.71303500 | -2.27965300 | -1.86966900 |
| H | -0.76965700 | -1.05643800 | -0.63334000 |
| H | 1.46390100 | -1.28589600 | -0.59942900 |
| C | -3.21266000 | -0.60500500 | -1.61872100 |
| H | -4.05353900 | -0.03531300 | -2.00095500 |
| H | -2.23770400 | -0.14032800 | -1.71944000 |
| C | -3.40508000 | -1.78903200 | -1.03192800 |
| Br | -3.23299100 | 2.34566600 | 0.59539400 |
| O | -1.51987600 | 3.01030800 | 0.39730600 |
| C | -1.23890500 | 3.50693800 | -0.86506900 |
| C | 0.22341700 | 3.83096700 | -0.92410900 |
| O | -2.06537100 | 3.75991700 | -1.67362400 |
| C | 1.19648400 | 2.82933500 | -0.93747300 |
| C | 0.58096200 | 5.17599500 | -0.97279400 |
| C | 0.78863300 | 1.35663000 | -0.94309200 |
| C | 2.53716100 | 3.20020400 | -0.97949600 |
| C | 1.92377200 | 5.53060500 | -1.02086000 |
| H | -0.19215500 | 5.93646200 | -0.97739900 |
| O | -0.39067900 | 1.12132600 | -1.24836500 |
| O | 1.67444900 | 0.53814500 | -0.59336700 |
| C | 2.90225700 | 4.54095500 | -1.02169200 |
| H | 3.28245700 | 2.41327300 | -0.99352600 |
| H | 2.20407900 | 6.57678100 | -1.06244100 |
| H | 3.95008500 | 4.81653200 | -1.06506100 |
| C | -0.43564000 | 0.10249600 | 1.75683100 |
| N | 0.19711600 | 0.87022800 | 2.87819900 |
| C | 0.61856600 | -0.08039600 | 3.94987300 |
| C | 1.39928200 | 1.59361000 | 2.35199100 |
| C | -0.77579200 | 1.85738700 | 3.42200000 |
| H | -0.76882400 | 0.79408700 | 0.98571800 |
| H | 0.32528000 | -0.55632100 | 1.34852300 |
| H | -0.26574700 | -0.59779500 | 4.31976000 |
| H | 1.32809500 | -0.78599500 | 3.52029400 |
| H | 1.06311400 | 2.31878400 | 1.61292000 |
| H | 2.06184000 | 0.86612300 | 1.88669600 |
| H | -1.66877500 | 1.32882400 | 3.75238500 |
| H | -0.31626200 | 2.37760800 | 4.26157300 |
| H | -1.27973900 | -0.46053800 | 2.15574100 |
| H | 1.88261300 | 2.09980200 | 3.18717200 |
| H | 1.08000300 | 0.48709700 | 4.75710500 |
| H | -1.03181700 | 2.56276400 | 2.63403200 |
| C | 0.19125900 | -2.87085700 | -0.00573500 |
| H | 0.21771400 | -3.93372400 | -0.25157200 |
| H | -0.03409200 | -2.79823500 | 1.06765700 |
| N | 1.50898500 | -2.28192300 | -0.31985100 |
| S | 2.63916300 | -2.46215100 | 0.86322200 |
| O | 2.59346500 | -3.84087800 | 1.31714600 |
| O | 2.49195300 | -1.41199000 | 1.88364200 |
| C | 4.16726600 | -2.16152600 | 0.01438900 |
| C | 5.04252700 | -3.22061100 | -0.16431800 |
| C | 4.45985900 | -0.87812400 | -0.43828700 |
| C | 6.24943500 | -2.98536100 | -0.81497800 |
| H | 4.77892700 | -4.20440800 | 0.20528700 |
| C | 5.66331200 | -0.67174300 | -1.09332500 |
| H | 3.74213500 | -0.07502300 | -0.30467700 |
| C | 6.57387400 | -1.71583000 | -1.28810700 |
| H | 6.94594900 | -3.80480800 | -0.95789200 |
| H | 5.90449900 | 0.31961700 | -1.46511000 |
| C | 7.87431400 | -1.45763600 | -2.00194800 |
| H | 8.46107600 | -0.69738000 | -1.48095000 |
| H | 8.47921800 | -2.36204400 | -2.07080700 |
| H | 7.69477900 | -1.09348100 | -3.01627600 |

**anti_TS1_NHTs**

| | | | |
|---|---|---|---|
| H | -4.55505000 | -2.13809000 | 1.44869300 |
| C | -5.20613600 | -2.21960600 | 0.58525800 |
| C | -6.89904700 | -2.37480900 | -1.61466300 |
| C | -4.73473800 | -1.84761100 | -0.67762300 |
| C | -6.51331300 | -2.65071600 | 0.74611100 |
| C | -7.36260300 | -2.73155100 | -0.35507900 |
| C | -5.59200900 | -1.92959500 | -1.77669300 |
| H | -6.87388600 | -2.92009400 | 1.73176300 |
| H | -8.38388600 | -3.07118200 | -0.22858400 |
| H | -5.23585400 | -1.67412500 | -2.76834400 |
| H | -7.55318200 | -2.44178000 | -2.47582600 |
| C | -2.25670800 | -2.34598200 | -0.27499400 |
| H | -2.51440700 | -3.35539300 | -0.61953900 |
| H | -2.38476700 | -2.37223100 | 0.81215400 |
| C | -0.82241700 | -1.98570600 | -0.64789500 |
| H | -0.62094100 | -2.25212200 | -1.68976200 |
| H | -0.67332600 | -0.90485200 | -0.59082300 |
| H | 1.49305400 | -1.09285200 | -0.42036900 |
| C | -2.98115800 | -0.45022300 | -1.85319800 |
| H | -3.76595000 | -0.02635000 | -2.46775900 |
| H | -1.96318800 | -0.34766800 | -2.22148700 |
| C | -3.32125000 | -1.43535100 | -0.86052800 |
| Br | -2.95680400 | 0.60767100 | -0.13942600 |
| O | -1.64446500 | 2.53762200 | 0.75037400 |
| C | -1.60238900 | 3.22523200 | -0.33996400 |
| C | -0.21935300 | 3.75072300 | -0.69659600 |
| O | -2.55005800 | 3.48786000 | -1.06246000 |
| C | 0.86487700 | 2.89593600 | -0.94124500 |
| C | -0.01966700 | 5.12929400 | -0.71467300 |
| C | 0.68964000 | 1.38616900 | -1.00753200 |
| C | 2.13070000 | 3.43868800 | -1.15394600 |
| C | 1.24459600 | 5.66360900 | -0.94034200 |
| H | -0.87103000 | 5.78102500 | -0.54828000 |
| O | -0.34783900 | 0.95855900 | -1.53852500 |
| O | 1.62034200 | 0.68719700 | -0.50881900 |

| | | | |
|---|---|---|---|
| C | 2.32586900 | 4.81557100 | -1.15691300 |
| H | 2.95962100 | 2.76078800 | -1.32863300 |
| H | 1.38453900 | 6.73933000 | -0.94874300 |
| H | 3.31432800 | 5.22507700 | -1.33554700 |
| C | -0.07617900 | 0.28374800 | 2.08179800 |
| N | 0.51193700 | 1.29722000 | 3.01463100 |
| C | 1.31709100 | 0.60303100 | 4.05730900 |
| C | 1.39002300 | 2.21852300 | 2.22393200 |
| C | -0.58864900 | 2.09198600 | 3.63325900 |
| H | -0.60094200 | 0.83088000 | 1.30099500 |
| H | 0.74381200 | -0.29748800 | 1.67220800 |
| H | 0.66395600 | -0.07140200 | 4.61014300 |
| H | 2.10226500 | 0.03117300 | 3.56581600 |
| H | 0.74726300 | 2.79347800 | 1.56118600 |
| H | 2.07932600 | 1.61977400 | 1.63059500 |
| H | -1.19739300 | 1.42490600 | 4.24325100 |
| H | -0.14757200 | 2.86615100 | 4.26060000 |
| H | -0.75794100 | -0.34521400 | 2.65780600 |
| H | 1.91471500 | 2.87216100 | 2.92008500 |
| H | 1.73488600 | 1.34959900 | 4.73172800 |
| H | -1.17818000 | 2.52896800 | 2.82522500 |
| C | 0.22073700 | -2.65282700 | 0.23775500 |
| H | 0.24437300 | -3.73707000 | 0.11210600 |
| H | -0.00906200 | -2.45270500 | 1.29427500 |
| N | 1.52639200 | -2.10214500 | -0.15636000 |
| S | 2.74278900 | -2.35152100 | 0.93005600 |
| O | 2.70149300 | -3.75026500 | 1.32245500 |
| O | 2.70014700 | -1.34630600 | 1.99782400 |
| C | 4.19199400 | -2.03632900 | -0.04251000 |
| C | 5.07330100 | -3.07962600 | -0.27429700 |
| C | 4.42066700 | -0.75202900 | -0.53050200 |
| C | 6.22293500 | -2.82828100 | -1.01655000 |
| H | 4.85736800 | -4.06438400 | 0.12289700 |
| C | 5.56678400 | -0.53094700 | -1.27729900 |
| H | 3.69940600 | 0.04172000 | -0.35798200 |
| C | 6.48320600 | -1.55833100 | -1.52661600 |
| H | 6.92416500 | -3.63503100 | -1.20267600 |
| H | 5.75622400 | 0.46008100 | -1.67830000 |
| C | 7.72415500 | -1.28071500 | -2.33317800 |
| H | 8.35986600 | -0.54884100 | -1.82884900 |
| H | 8.31134300 | -2.18623400 | -2.48834900 |
| H | 7.46854700 | -0.87066300 | -3.31286800 |

**anti_INT2_NHTs**

| | | | |
|---|---|---|---|
| H | -4.61709000 | -2.20713500 | 1.43204700 |
| C | -5.22997700 | -2.28542200 | 0.54058700 |
| C | -6.82302600 | -2.43637500 | -1.73311200 |
| C | -4.71985000 | -1.86542800 | -0.69143900 |
| C | -6.52768500 | -2.76204500 | 0.63466400 |
| C | -7.32670900 | -2.84080600 | -0.50387900 |
| C | -5.52572500 | -1.94474000 | -1.82813600 |
| H | -6.92012000 | -3.06908800 | 1.59683200 |
| H | -8.34075600 | -3.21568900 | -0.42969300 |
| H | -5.13771500 | -1.64974100 | -2.79664700 |
| H | -7.43814200 | -2.50092300 | -2.62270500 |
| C | -2.24812700 | -2.33771900 | -0.23830000 |
| H | -2.49222800 | -3.33132500 | -0.63446500 |
| H | -2.39731200 | -2.41453800 | 0.84376300 |
| C | -0.81438700 | -1.94630100 | -0.57390600 |
| H | -0.59739300 | -2.16603600 | -1.62360700 |
| H | -0.68173000 | -0.86718300 | -0.47485300 |
| H | 1.50760600 | -1.06673200 | -0.38279700 |
| C | -2.96199600 | -0.37547300 | -1.76227100 |
| H | -3.73927300 | 0.04226700 | -2.39074700 |
| H | -1.93549200 | -0.23985900 | -2.09721200 |
| C | -3.31054800 | -1.40946500 | -0.80336200 |
| Br | -3.04191000 | 0.57878600 | -0.02293600 |
| O | -1.58252700 | 2.62038200 | 0.84988200 |
| C | -1.60277800 | 3.17447200 | -0.30415700 |
| C | -0.26080400 | 3.74118400 | -0.75217600 |
| O | -2.57777900 | 3.28873900 | -1.03855100 |
| C | 0.84787600 | 2.91483700 | -0.98624300 |
| C | -0.11192500 | 5.12223900 | -0.84957200 |
| C | 0.71062200 | 1.40221300 | -0.97329600 |
| C | 2.08631300 | 3.48640200 | -1.26862600 |
| C | 1.12463500 | 5.68636900 | -1.14804500 |
| H | -0.97865700 | 5.75443800 | -0.68646100 |
| O | -0.35399500 | 0.93459500 | -1.41520300 |
| O | 1.68034200 | 0.73639900 | -0.50939400 |
| C | 2.22998500 | 4.86724900 | -1.35341600 |
| H | 2.93286300 | 2.82813000 | -1.43360500 |
| H | 1.22464600 | 6.76428800 | -1.21967400 |
| H | 3.19628200 | 5.30149600 | -1.58644400 |
| C | -0.01855200 | 0.34408100 | 2.10327800 |
| N | 0.56886000 | 1.37359700 | 3.01966600 |
| C | 1.43625800 | 0.70350300 | 4.02730800 |
| C | 1.38197400 | 2.33186900 | 2.20255800 |
| C | -0.53409800 | 2.12564400 | 3.68577300 |
| H | -0.59088600 | 0.87716500 | 1.34518800 |
| H | 0.80468100 | -0.20880100 | 1.66120100 |
| H | 0.82847000 | 0.00462400 | 4.60118200 |
| H | 2.22072000 | 0.15872100 | 3.50540200 |
| H | 0.69001100 | 2.87943200 | 1.56606900 |
| H | 2.07564400 | 1.76260700 | 1.58551600 |
| H | -1.10105000 | 1.43162600 | 4.30601300 |
| H | -0.09507200 | 2.90363900 | 4.30989500 |
| H | -0.65465100 | -0.31147300 | 2.70142900 |
| H | 1.90368000 | 3.00354600 | 2.88369200 |
| H | 1.85369700 | 1.46168900 | 4.68888500 |
| H | -1.16022600 | 2.55752000 | 2.90341200 |
| C | 0.23483900 | -2.62613100 | 0.29255300 |
| H | 0.25631700 | -3.70916000 | 0.15616800 |
| H | 0.01924500 | -2.43448600 | 1.35367100 |
| N | 1.53621000 | -2.07367300 | -0.11431900 |

| | | | |
|---|---|---|---|
| S | 2.76761800 | -2.33345700 | 0.95343200 |
| O | 2.71243600 | -3.73043100 | 1.35051500 |
| O | 2.75453600 | -1.32366500 | 2.01623300 |
| C | 4.20543400 | -2.04393400 | -0.04399000 |
| C | 5.06744600 | -3.10135900 | -0.28469700 |
| C | 4.44485200 | -0.76569200 | -0.54254500 |
| C | 6.20836100 | -2.87084900 | -1.04686800 |
| H | 4.84365800 | -4.08077400 | 0.12123200 |
| C | 5.58174500 | -0.56548800 | -1.30913200 |
| H | 3.73905500 | 0.04008600 | -0.36301900 |
| C | 6.47882000 | -1.60748000 | -1.56786000 |
| H | 6.89455500 | -3.68882600 | -1.23997000 |
| H | 5.77888500 | 0.42064700 | -1.71832000 |
| C | 7.71053000 | -1.35232900 | -2.39574700 |
| H | 8.36638700 | -0.62951700 | -1.90429300 |
| H | 8.28029500 | -2.26772500 | -2.55786400 |
| H | 7.44542400 | -0.94087900 | -3.37232600 |

# 11. X-ray crystallographic data

Crystal data and structure refinement for **2aa** (CCDC 2308651)

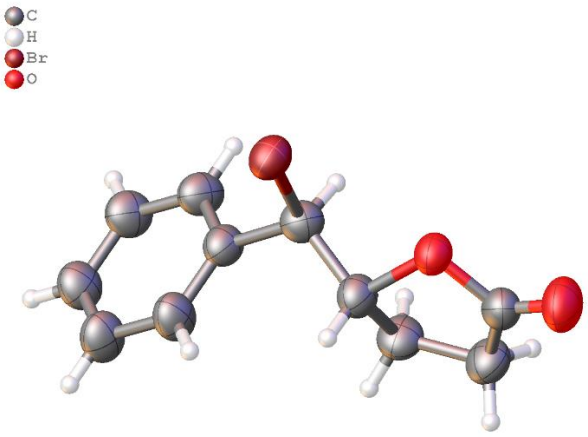


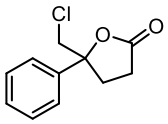

**Figure S29.** Crystal data and structure refinement for 20190328-zx.

| | |
|---|---|
| Identification code | 20190328-zx |
| Empirical formula | $C_{11}H_{11}BrO_2$ |
| Formula weight | 255.11 |
| Temperature/K | 293(2) |
| Crystal system | monoclinic |
| Space group | $P2_1/c$ |
| a/Å | 8.7528(2) |
| b/Å | 11.8433(2) |
| c/Å | 10.7335(2) |
| α/° | 90 |
| β/° | 106.057(2) |
| γ/° | 90 |
| Volume/Å$^3$ | 1069.25(4) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.585 |
| μ/mm$^{-1}$ | 5.014 |
| F(000) | 512.0 |
| Crystal size/mm$^3$ | 0.10 × 0.14 × 0.12 |
| Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 10.518 to 134.152 |
| Index ranges | $-10 \le h \le 10$, $-13 \le k \le 14$, $-9 \le l \le 12$ |
| Reflections collected | 3538 |
| Independent reflections | 1913 [$R_{int}$ = 0.0158, $R_{sigma}$ = 0.0203] |
| Data/restraints/parameters | 1913/0/147 |
| Goodness-of-fit on F$^2$ | 1.041 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0308, $wR_2$ = 0.0850 |
| Final R indexes [all data] | $R_1$ = 0.0323, $wR_2$ = 0.0869 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.37/-0.36 |

## 12. General procedures and analytical data of five- and six-membered heterocyclic compounds

**General procedure for intramolecular bromocyclization.** To a solution of substrate (0.3 mmol, 1.0 equiv.) and TBAB (0.33 mmol, 1.1 equiv.) in DCE (3 mL) was added PPO (0.36 mmol, 1.2 equiv.) at room temperature. The solution was stirred at room temperature for 30s to 10 min. Saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with DCM (15 mL × 3). After completion of the reaction as monitored by TLC, the combined extracts were washed by brine (10 mL) and dried over $Na_2SO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography to yield the corresponding cyclized products.

**5-(chloromethyl)-5-phenyldihydrofuran-2(3*H*)-one (2a-Cl)**



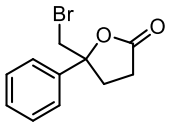

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.31 (m, 2H), 3.81 (q, *J* = 12.1 Hz, 1H), 2.88 – 2.72 (m, 1H), 2.62 – 2.45 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.83, 140.71, 128.92, 128.74, 124.94, 52.23, 31.47, 29.07.

These data are consistent with that previously reported.[28]

**5-(Bromomethyl)-5-phenyldihydrofuran-2(3*H*)-one (2a-Br)**



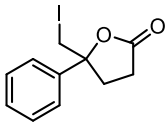

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.50 – 7.31 (m, 5H), 3.87 – 3.51 (m, 2H), 2.97 – 2.73 (m, 2H), 2.67 – 2.45 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.64, 140.89, 129.00, 128.82, 125.05, 86.57, 41.15, 32.53, 29.22.

These data are consistent with that previously reported.[29]

**5-(Iodomethyl)-5-phenyldihydrofuran-2(3*H*)-one (2a-I)**



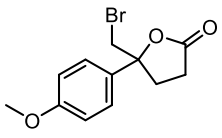

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.31 (m, 3H), 3.63 (s, 1H), 2.84 – 2.68 (m, 1H), 2.68 – 2.48 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.45, 140.69, 128.92, 128.68, 124.95, 86.13, 34.05, 29.32, 16.43.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (2b)**



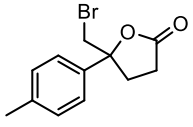

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.25;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.42 – 7.31 (m, 2H), 7.00 – 6.90 (m, 2H), 3.84 (d, *J* = 1.3 Hz, 3H), 3.80 – 3.63 (m, 2H), 2.91 – 2.73 (m, 2H), 2.57 (tdd, *J* = 10.7, 8.9, 2.5 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.73, 159.75, 132.56, 126.33, 114.18, 86.44, 55.42, 41.25, 32.26, 29.22.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(p-tolyl)dihydrofuran-2(3*H*)-one (2c)**



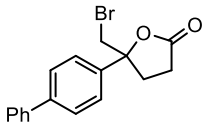

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.32 – 7.27 (m, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 3.82 – 3.58 (m, 2H), 2.88 – 2.69 (m, 2H), 2.61 – 2.45 (m, 2H), 2.35 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.73, 138.67, 137.75, 129.56, 124.91, 86.56, 41.19, 32.40, 29.18, 21.15.

These data are consistent with that previously reported.[29]

**5-([1,1'-Biphenyl]-4-yl)-5-(bromomethyl)dihydrofuran-2(3*H*)-one (2d)**



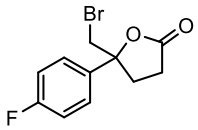

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (dd, *J* = 17.5, 7.7 Hz, 4H), 7.47 (dd, *J* = 15.5, 7.9 Hz, 4H), 7.38 (t, *J* = 7.3 Hz, 1H), 3.85 – 3.68 (m, 2H), 2.92 – 2.73 (m, 2H), 2.68 – 2.48 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.55, 141.66, 140.09, 139.68, 128.96, 127.81, 127.56, 127.14, 125.49, 86.44, 41.03, 32.46, 29.16.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(4-fluorophenyl)dihydrofuran-2(3*H*)-one (2e)**



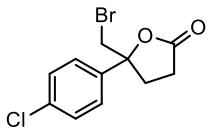

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.34 (m, 2H), 7.09 (t, *J* = 8.6 Hz, 2H), 3.68 (q, *J* = 11.3 Hz, 2H), 2.89 – 2.70 (m, 2H), 2.65 – 2.45 (m, 2H); **$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.34, 162.77 (d, *J* = 248.5 Hz), 136.66 (d, *J* = 3.3 Hz), 127.02 (d, *J* = 8.3 Hz), 115.91 (d, *J* = 21.8 Hz), 86.16, 40.95, 32.52, 29.14 .

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -112.86 (p, *J* = 7.3 Hz).

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(4-chlorophenyl)dihydrofuran-2(3*H*)-one (2f)**



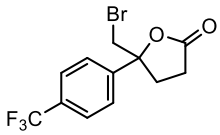

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.41 – 7.31 (m, 4H), 3.75 – 3.59 (m, 2H), 2.89 – 2.70 (m, 2H), 2.60 – 2.45 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.22, 139.34, 134.80, 129.11, 126.54, 86.06, 40.70, 32.49, 29.07.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3*H*)-one (2g)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.27;

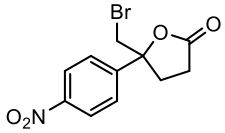
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 3.78 – 3.65 (m, 2H), 2.93 – 2.74 (m, 2H), 2.55 (qd, *J* = 11.2, 9.9, 4.0 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.08, 144.82, 131.07 (q, *J* = 32.7 Hz), 125.99 (q, *J* = 3.7 Hz), 125.63, 123.83 (q, *J* = 272.3 Hz), 86.06, 40.46, 32.65, 29.00.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -62.73.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(4-nitrophenyl)dihydrofuran-2(3*H*)-one (2h)**



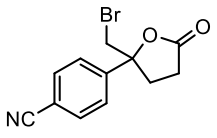

**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.37;

**$^1$H NMR** (400 MHz, DMSO-$d_6$) δ 8.45 – 8.11 (m, 2H), 7.83 – 7.61 (m, 2H), 4.21 (d, *J* = 11.3 Hz, 1H), 4.14 (d, *J* = 11.4 Hz, 1H), 2.96 – 2.68 (m, 2H), 2.67 – 2.36 (m, 2H).

**$^{13}$C NMR** (101 MHz, DMSO-$d_6$) δ 175.89, 149.28, 147.64, 127.03, 124.09, 86.46, 41.01, 33.38, 28.77.

These data are consistent with that previously reported.[29]

**4-(2-(Bromomethyl)-5-oxotetrahydrofuran-2-yl)benzonitrile (2i)**



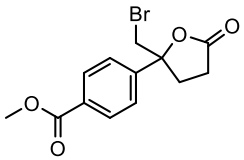
**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, DMSO-$d_6$) δ 8.02 – 7.86 (m, 2H), 7.78 – 7.61 (m, 2H), 4.19 (d, *J* = 11.3 Hz, 1H), 4.11 (d, *J* = 11.3 Hz, 1H), 2.91 – 2.67 (m, 2H), 2.62 – 2.41 (m, 2H).

**$^{13}$C NMR** (101 MHz, DMSO-$d_6$) δ 175.94, 147.35, 132.97, 126.59, 118.99, 111.44, 86.44, 41.08, 33.28, 28.76.

These data are consistent with that previously reported.[32]

**Methyl 4-(2-(bromomethyl)-5-oxotetrahydrofuran-2-yl) benzoate (2j)**



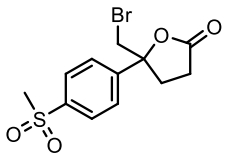
**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.28

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.13 – 7.96 (m, 2H), 7.48 (dd, *J* = 8.5, 2.9 Hz, 2H), 3.90 (t, *J* = 2.7 Hz, 3H), 3.70 (s, 2H), 2.81 (tt, *J* = 13.5, 5.6 Hz, 2H), 2.64 – 2.44 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.20, 166.36, 145.61, 130.54, 130.14, 125.13, 86.23, 52.39, 40.54, 32.57, 29.02.

**HRMS-ESI(m/z)** calc'd for $[C_{13}H_{13}BrO_4+Na]^+$, 334.9889; found, 334.9890.

**5-(Bromomethyl)-5-(4-(methylsulfonyl)phenyl)dihydrofuran-2(3*H*)-one (2k)**



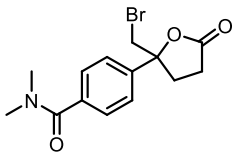
**TLC** (hexane:ethyl acetate, 50:50 v/v): $R_f$ = 0.25;

**$^1$H NMR** (400 MHz, DMSO-$d_6$) δ 8.02 – 7.90 (m, 2H), 7.74 – 7.63 (m, 2H), 4.15 (d, *J* = 11.3 Hz, 1H), 4.07 (d, *J* = 11.3 Hz, 1H), 3.22 (s, 3H), 2.89 – 2.63 (m, 2H), 2.61 – 2.33 (m, 2H).

**$^{13}$C NMR** (101 MHz, DMSO-$d_6$) δ 175.59, 147.22, 140.53, 127.30, 126.16, 86.11, 43.47, 40.83, 32.97, 28.38.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{13}BrO_4S+Na]^+$, 354.9610; found, 354.9609.

**4-(2-(Bromomethyl)-5-oxotetrahydrofuran-2-yl)-*N*,*N*-dimethylbenzamide (2l)**



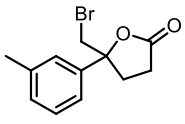
**TLC** (hexane:ethyl acetate, 50:50 v/v): $R_f$ = 0.31;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.42 (s, 4H), 3.74 – 3.60 (m, 2H), 3.08 (s, 3H), 2.95 (s, 3H), 2.86 – 2.69 (m, 2H), 2.59 – 2.44 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.30, 170.70, 142.11, 136.82, 127.62, 125.11, 86.20, 40.67, 39.55, 35.37, 32.45, 28.99.

**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{16}BrNO_3+Na]^+$, 348.0506; found, 348.0207.

**5-(Bromomethyl)-5-(m-tolyl)dihydrofuran-2(3*H*)-one (2m)**



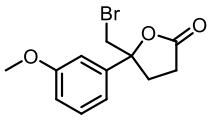
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.35 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 1.9 Hz, 1H), 7.27 – 7.20 (m, 2H), 3.85 – 3.70 (m, 2H), 2.94 – 2.80 (m, 2H), 2.67 – 2.54 (m, 2H), 2.44 (s, 3H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.72, 140.79, 138.79, 129.49, 128.83, 125.64, 122.04, 86.58, 41.23, 32.49, 29.20, 21.64.

These data are consistent with that previously reported.[30]

**5-(Bromomethyl)-5-(3-methoxyphenyl)dihydrofuran-2(3*H*)-one (2n)**



**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.28;

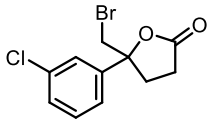
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.31 (t, *J* = 8.1 Hz, 1H), 6.99 – 6.91 (m, 2H), 6.90 – 6.84 (m, 1H), 3.81 (s, 3H), 3.75 – 3.66 (m, 2H), 2.86 – 2.73

(m, 2H), 2.61 – 2.47 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.58, 159.95, 142.46, 130.05, 117.16, 113.97, 111.01, 86.42, 55.48, 41.09, 32.52, 29.17.

These data are consistent with that previously reported.[29]

**5-(Bromomethyl)-5-(3-chlorophenyl)dihydrofuran-2(3*H*)-one (2o)**



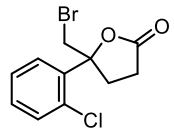
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 2.1 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.26 – 7.22 (m, 1H), 3.83 – 3.51 (m, 2H), 2.86 – 2.67 (m, 2H), 2.58 – 2.45 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.23, 142.88, 134.98, 130.28, 128.97, 125.41, 123.26, 85.92, 40.65, 32.49, 29.02.

These data are consistent with that previously reported.[31]

**5-(Bromomethyl)-5-(2-chlorophenyl)dihydrofuran-2(3*H*)-one (2p)**



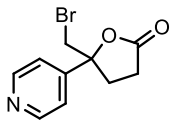
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 1H), 7.25 – 7.15 (m, 3H), 5.29 (q, *J* = 1.5 Hz, 1H), 5.04 (d, *J* = 1.2 Hz, 1H), 2.86 – 2.72 (m, 2H), 2.47 (dd, *J* = 8.6, 6.9 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.37, 138.28, 131.46, 130.18, 130.12, 127.60, 127.52, 86.53, 39.14, 31.81, 29.14.

These data are consistent with that previously reported.[27]

**5-(Bromomethyl)-5-(pyridin-4-yl)dihydrofuran-2(3*H*)-one (2q)**



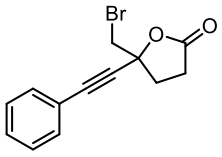
**TLC** (hexane:ethyl acetate, 50:50 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.71 – 8.56 (m, 2H), 7.39 – 7.27 (m, 2H), 3.75 – 3.61 (m, 2H), 2.89 – 2.71 (m, 2H), 2.62 – 2.40 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.84, 150.49, 149.59, 119.86, 85.29, 39.75, 32.39, 28.81.

**HRMS-ESI(m/z)** calc'd for $[C_{10}H_{10}BrNO_2+Na]^+$, 277.9787; found, 277.9784.

**5-(Bromomethyl)-5-(phenylethynyl)dihydrofuran-2(3*H*)-one (2r)**



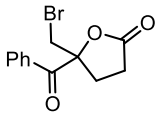
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.28;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.47 – 7.41 (m, 2H), 7.40 – 7.30 (m, 3H), 3.84 – 3.72 (m, 2H), 2.84 (dt, *J* = 17.7, 9.5 Hz, 1H), 2.72 (ddd, *J* = 17.7, 9.2, 4.7 Hz, 1H), 2.67 – 2.53 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.09, 131.96, 129.47, 128.51, 121.07, 87.80, 85.13, 79.09, 37.99, 33.65, 29.03.

**HRMS-ESI(m/z)** calc'd for $[C_{13}H_{11}BrO_2+Na]^+$, 300.9835; found, 300.9832.

**5-Benzoyl-5-(bromomethyl)dihydrofuran-2(3*H*)-one (2s)**



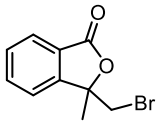
**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.27;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.13 – 7.97 (m, 2H), 7.63 – 7.53 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 3.94 (d, *J* = 11.2 Hz, 1H), 3.74 (d, *J* = 11.2 Hz, 1H), 2.88 (ddd, *J* = 13.2, 9.5, 6.0 Hz, 1H), 2.71 (ddd, *J* = 16.5, 9.4, 5.9 Hz, 1H), 2.57 – 2.37 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 196.69, 175.04, 133.93, 130.07, 128.76, 89.79, 37.03, 29.89, 28.16.

These data are consistent with that previously reported.[33]

**3-(Bromomethyl)-3-methylisobenzofuran-1(3*H*)-one (2t-Br)**



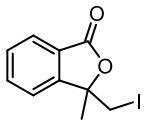
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 3.66 (d, *J* = 2.7 Hz, 2H), 1.76 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.8, 150.1, 133.2, 128.8, 125.3, 124.9, 120.4, 83.5, 36.8, 23.2.

These data are consistent with that previously reported.[78]

**3-(Iodomethyl)-3-methylisobenzofuran-1(3*H*)-one (2t-I)**



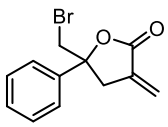
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 3.73 – 3.53 (m, 2H), 1.87 (s, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.94, 151.93, 136.18, 134.46, 129.94, 126.38, 126.01, 125.84, 121.22, 84.20, 25.15, 12.44.

These data are consistent with that previously reported.[77]

**5-(Bromomethyl)-3-methylene-5-phenyldihydrofuran-2(3*H*)-one (2u)**



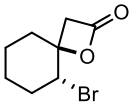
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.33;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.47 – 7.30 (m, 5H), 6.27 (t, *J* = 2.9 Hz, 1H), 5.68 (t, *J* = 2.6 Hz, 1H), 3.72 (d, *J* = 1.5 Hz, 2H), 3.57 (dt, *J* = 17.2, 2.7 Hz, 1H), 3.26 (dt, *J* = 17.2, 2.8 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.85, 140.83, 134.22, 128.92, 128.77, 125.00, 122.87, 83.31, 41.61, 38.90.

These data are consistent with that previously reported.[34]

**5-Bromo-1-oxaspiro[3.5]nonan-2-one (2v)**



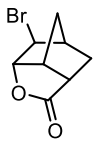
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.34 (dd, *J* = 6.9, 3.8 Hz, 1H), 3.44 (d, *J* = 16.4 Hz, 1H), 3.10 (d, *J* = 16.4 Hz, 1H), 2.37 – 2.28 (m, 1H), 2.24 (ddd, *J* = 13.0, 7.0, 3.7 Hz, 1H), 1.89 (ddt, *J* = 13.5, 9.3, 6.5 Hz, 2H), 1.80 – 1.68 (m, 2H), 1.60 – 1.48 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.15, 78.37, 54.71, 47.20, 32.91, 32.64, 22.45.

These data are consistent with that previously reported.[32]

**6-Bromohexahydro-2*H*-3,5-methanocyclopenta[*b*]furan-2-one (2w)**



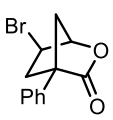
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.86 (d, *J* = 5.1 Hz, 1H), 3.79 (d, *J* = 2.3 Hz, 1H), 3.18 (t, *J* = 5.0 Hz, 1H), 2.61 (d, *J* = 3.9 Hz, 1H), 2.55 – 2.47 (m, 1H), 2.32 – 2.23 (m, 1H), 2.17 – 1.99 (m, 1H), 1.81 – 1.64 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 178.2, 86.6, 52.5, 44.9, 44.5, 36.5, 34.7, 33.0.

These data are consistent with that previously reported.[32]

**6-Bromo-4-phenyl-2-oxabicyclo[2.2.1]heptan-3-one (2x)**



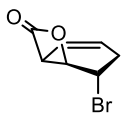
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.39 (hept, *J* = 6.7, 5.8 Hz, 5H), 4.97 (s, 1H), 4.39 – 4.22 (m, 1H), 2.92 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.76 (d, *J* = 11.0 Hz, 1H), 2.67 (d, *J* = 11.1 Hz, 1H), 2.49 (dd, *J* = 14.5, 3.6 Hz, 1H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 176.01, 134.07, 128.78, 128.30, 127.30, 81.85, 55.07, 43.48, 43.46, 41.93, 41.02.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{11}BrO_2+Na]^+$, 288.9835; found, 288.9835.

**5-Bromo-7-oxabicyclo[4.2.0]oct-2-en-8-one (2y)**



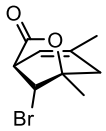
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.33;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.05 (dt, *J* = 9.3, 4.3 Hz, 1H), 5.90 (ddt, *J* = 9.9, 6.6, 1.7 Hz, 1H), 4.94 (dd, *J* = 5.4, 2.7 Hz, 1H), 4.55 (q, *J* = 3.3 Hz, 1H), 4.34 – 4.20 (m, 1H), 2.72 (ddt, *J* = 4.5, 3.3, 1.3 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 166.21, 128.31, 118.37, 70.74, 49.25, 41.57, 28.02.

These data are consistent with that previously reported.[13]

**8-Bromo-3,5-dimethyl-6-oxabicyclo[3.2.1]oct-2-en-7-one (2z)**



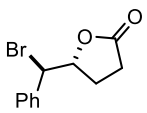
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.64 – 5.46 (m, 1H), 4.21 (dd, *J* = 4.5, 1.0 Hz, 1H), 3.23 (dd, *J* = 7.0, 4.5 Hz, 1H), 2.49 (ddd, *J* = 18.8, 2.1, 1.1 Hz, 1H), 2.28 (d, *J* = 18.8 Hz, 1H), 1.74 (d, *J* = 1.5 Hz, 3H), 1.48 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 172.03, 137.68, 115.69, 84.81, 49.44, 45.50, 39.55, 22.10, 21.87

These data are consistent with that previously reported.[13]

**5-(Bromo(phenyl)methyl)dihydrofuran-2(3*H*)-one (2aa)**



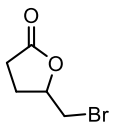
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.33;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.52 – 7.23 (m, 5H), 4.92 (d, *J* = 5.5 Hz, 1H), 4.89 – 4.76 (m, 1H), 2.53 – 2.25 (m, 2H), 2.25 – 2.09 (m, 1H), 2.08 – 1.90 (m, 1H).

**$^{13}$C NMR** (100 MHz, Chloroform-*d*) δ 176.1, 137.0, 129.2, 129.0, 128.6, 82.1, 55.3, 28.4, 25.8.

These data are consistent with that previously reported.[37]

**5-(Bromomethyl)dihydrofuran-2(3*H*)-one (2ab)**



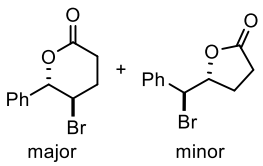
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.83 – 4.60 (m, 1H), 3.50 (d, *J* = 5.0 Hz, 2H), 2.69 – 2.45 (m, 2H), 2.45 – 2.29 (m, 1H), 2.15 – 1.95 (m, 1H).

**$^{13}$C NMR** (100 MHz, Chloroform-*d*) δ 175.2, 76.9, 33.2, 27.4, 25.2.

These data are consistent with that previously reported.[29]

**5-Bromo-6-phenyltetrahydro-2*H*-pyran-2-one (major) and 5-(bromo(phenyl)-methyl)dihydrofuran-2(3*H*)-one (minor) (2ac, 2ac′)**




**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.34;

Major: Minor = 2.3:1

Major: **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.53 – 7.28 (m, 5H), 5.56 (d, *J* = 6.4 Hz, 1H), 4.47 – 4.31 (m, 1H), 3.01 – 2.29 (m, 1H), 2.77 – 2.65 (m, 1H), 2.46 – 2.34 (m, 1H), 2.32 – 2.20 (m, 1H).

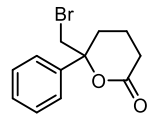
**$^{13}$C NMR** (150 MHz, Chloroform-*d*) δ 169.1, 137.3, 129.1, 128.8, 126.4, 85.6, 47.2, 28.4, 27.6.

Minor: **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.53 – 7.28 (m, 5H), 5.07 – 4.97 (m, 1H), 4.96 – 4.84 (m, 1H), 2.57 – 2.46 (m, 3H), 2.32 – 2.20 (m, 1H).

**$^{13}$C NMR** (150 MHz, Chloroform-*d*) δ 176.1, 137.1, 128.9, 128.8, 128.3, 81.7, 55.5, 28.6, 26.4.

These data are consistent with that previously reported.[37]

**6-(Bromomethyl)-6-(4-bromophenyl)tetrahydro-2*H*-pyran-2-one (2ad)**



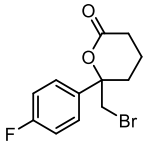
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 (tdd, *J* = 8.5, 6.0, 2.3 Hz, 5H), 3.79 – 3.56 (m, 2H), 2.56 – 2.44 (m, 2H), 2.44 – 2.32 (m, 2H), 1.89 – 1.78 (m, 1H), 1.66 – 1.55 (m, 1H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 170.61, 140.34, 129.11, 128.64, 125.47, 85.26, 41.66, 30.14, 29.20, 16.31.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(4-fluorophenyl)tetrahydro-2*H*-pyran-2-one (2ae)**



**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.29;

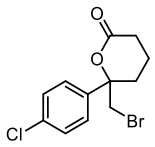
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 (dd, *J* = 8.1, 4.7 Hz, 2H), 7.19 – 6.97 (m, 2H), 3.62 (q, *J* = 11.2 Hz, 2H), 2.57 – 2.26 (m, 5H), 1.85 (dq, *J* = 11.6, 4.1, 3.6 Hz, 1H), 1.60 (ddd, *J* = 11.4, 5.7, 3.2 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.26, 162.71 (d, *J* = 248.5 Hz), 136.22 (d, *J* = 3.3 Hz), 127.52 (d, *J* = 8.2 Hz), 116.07 (d, *J* = 21.6 Hz), 84.92, 41.50 (d, *J* = 1.4 Hz), 30.21, 29.21, 16.37.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -112.85 (p, *J* = 7.3 Hz).

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(4-chlorophenyl)tetrahydro-2*H*-pyran-2-one (2af)**



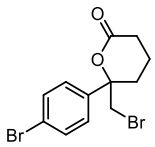
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.35 (q, *J* = 8.4 Hz, 4H), 3.74 – 3.54 (m, 2H), 1.85 (ddd, *J* = 14.5, 7.3, 3.8 Hz, 1H), 1.67 – 1.48 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.12, 138.97, 134.77, 129.29, 127.06, 84.88, 41.24, 30.21, 29.21, 16.36.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(4-bromophenyl)tetrahydro-2*H*-pyran-2-one (2ag)**



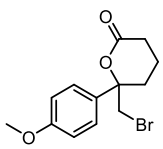
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 3.66 – 3.36 (m, 2H), 2.34 (td, *J* = 12.3, 11.3, 7.1 Hz, 2H), 2.23 (dddd, *J* = 19.1, 14.3, 9.7, 3.5 Hz, 2H), 1.73 (ddd, *J* = 14.5, 7.2, 3.8 Hz, 1H), 1.45 (dtt, *J* = 14.1, 7.2, 2.7 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.13, 139.52, 132.27, 127.37, 122.95, 84.93, 41.14, 30.19, 29.21, 16.37.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(4-methoxyphenyl)tetrahydro-2*H*-pyran-2-one (2ah)**



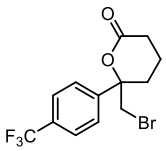
**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H), 6.96 – 6.86 (m, 7H), 3.81 (s, 4H), 3.69 – 3.56 (m, 3H), 2.49 – 2.30 (m, 6H), 1.83 (ddq, *J* = 14.9, 7.6, 3.8 Hz, 2H), 1.67 – 1.56 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.73, 159.71, 132.20, 126.85, 114.41, 85.08, 55.45, 41.87, 29.92, 29.15, 16.35.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(4-(trifluoromethyl)phenyl)tetrahydro-2*H*-pyran-2-one (2ai)**



**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.32;

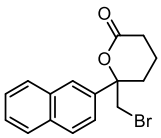
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 3.72 – 3.55 (m, 2H), 2.59 – 2.46 (m, 2H), 2.46 – 2.35 (m, 2H), 1.88 (ddd, *J* = 15.4, 7.4, 4.0 Hz, 1H), 1.67 – 1.45 (m, 1H).

**$^{13}$C NMR** (100 MHz, Chloroform-*d*) δ 169.7, 144.4, 130.9 (q, *J* = 34.1 Hz), 126.0, 126.0 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 271.0 Hz), 84.8, 40.8, 30.3, 29.1, 16.3.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -62.68.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)-6-(naphthalen-2-yl)tetrahydro-2*H*-pyran-2-one (2aj)**



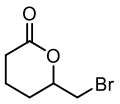
**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.94 – 7.79 (m, 4H), 7.53 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 1H), 3.75 (s, 2H), 2.61 – 2.38 (m, 4H), 1.86 (ddd, *J* = 14.7, 7.6, 3.8 Hz, 1H), 1.70 – 1.51 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.65, 137.63, 133.19, 133.02, 129.13, 128.50, 127.69, 127.02, 126.95, 125.41, 122.57, 85.42, 41.50, 30.22, 29.27, 16.41.

These data are consistent with that previously reported.[36]

**6-(Bromomethyl)tetrahydro-2*H*-pyran-2-one (2ak)**



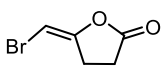
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.49 (dq, *J* = 9.5, 4.7 Hz, 1H), 3.61 – 3.38 (m, 2H), 2.59 (dt, *J* = 17.9, 5.7 Hz, 1H), 2.54 – 2.32 (m, 1H), 2.23 – 2.03 (m, 1H), 2.01 – 1.78 (m, 2H), 1.77 – 1.58 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 170.47, 78.66, 33.91, 29.46, 26.39, 18.22.

These data are consistent with that previously reported.[36]

**(*E*)-5-(Bromomethylene)dihydrofuran-2(3*H*)-one (2al)**



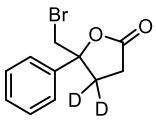
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.96 (t, *J* = 2.4 Hz, 1H), 2.93 – 2.84 (m, 2H), 2.76 – 2.68 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 174.24, 152.60, 85.42, 27.23, 24.87.

These data are consistent with that previously reported.[59]

**5-(Bromomethyl)-5-phenyldihydrofuran-2(3*H*)-one-4,4-$d_2$ (2a-$D_2$)**



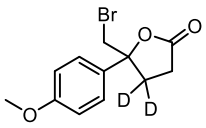
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.48 – 7.30 (m, 5H), 3.80 – 3.63 (m, 2H), 2.78 (d, *J* = 18.1 Hz, 1H), 2.52 (d, *J* = 18.0 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.43, 140.64, 128.81, 128.63, 124.87, 86.39, 41.21, 29.10.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_9D_2BrO_2+Na]^+$, 278.9961; found, 278.9964.

**5-(Bromomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one-4,4-$d_2$ (2b-$D_2$)**



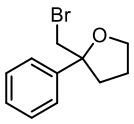
**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.9 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 3.73 – 3.61 (m, 2H), 2.81 – 2.70 (m, 1H), 2.51 (d, *J* = 17.0 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 175.73, 159.79, 132.58, 126.35, 114.22, 86.33, 55.44, 41.23, 29.05.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{11}D_2BrO_3+Na]^+$, 309.0066; found, 309.0065.

**2-(Bromomethyl)-2-phenyltetrahydrofuran (4a)**



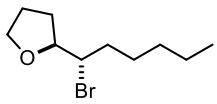
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.43 (dt, *J* = 8.1, 1.5 Hz, 3H), 7.36 (td, *J* = 7.9, 7.5, 1.6 Hz, 3H), 7.29 (dd, *J* = 7.1, 1.7 Hz, 1H), 4.10 (q, *J* = 8.4, 7.6 Hz, 1H), 3.94 (q, *J* = 7.8, 7.0 Hz, 1H), 3.65 (s, 3H), 2.49 – 2.39 (m, 2H), 2.27 (dddd, *J* = 12.6, 7.7, 5.3, 1.5 Hz, 2H), 2.06 (dddt, *J* = 13.9, 7.1, 5.5, 3.6 Hz, 2H), 1.92 – 1.79 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 144.11, 128.40, 127.52, 125.70, 85.40, 68.79, 42.30, 36.58, 26.29.

These data are consistent with that previously reported.[38]

**2-(1-Bromohexyl)tetrahydrofuran (4b)**



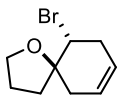
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 3.98 (tt, *J* = 10.2, 5.7 Hz, 2H), 3.91 (t, *J* = 7.1 Hz, 1H), 3.81 (td, *J* = 7.8, 5.6 Hz, 1H), 2.08 – 1.73 (m, 6H), 1.60 (dt, *J* = 14.7, 5.9 Hz, 1H), 1.41 (tt, *J* = 8.1, 4.6 Hz, 1H), 1.36 – 1.20 (m, 4H), 0.88 (t, *J* = 6.7 Hz, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 81.86, 69.03, 60.17, 35.05, 31.33, 29.67, 27.53, 26.30, 22.60, 14.13.

These data are consistent with that previously reported.[39]

**(±)-10-Bromo-1-oxaspiro[4.5]dec-7-ene (4c)**



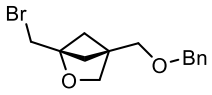
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.45;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.65 (dt, *J* = 9.2, 3.0 Hz, 1H), 5.56 (dt, *J* = 10.3, 2.8 Hz, 1H), 4.28 (t, *J* = 6.0 Hz, 1H), 3.93 (t, *J* = 6.6 Hz, 2H), 3.03 – 2.86 (m, 1H), 2.58 – 2.40 (m, 2H), 2.25 – 2.08 (m, 2H), 2.01 – 1.88 (m, 2H), 1.79 – 1.67 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 125.47, 124.24, 82.76, 69.05, 55.63, 36.83, 35.18, 33.69, 25.92.

**HRMS-ESI(m/z)** calc'd for $[C_9H_{13}BrO+Na]^+$, 239.0042; found, 239.0039.

**4-((Benzyloxy)methyl)-1-(bromomethyl)-2-oxabicyclo[2.1.1]hexane (4d)**



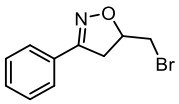
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.35 (qt, *J* = 7.4, 5.8 Hz, 5H), 4.56 (s, 2H), 3.80 (s, 2H), 3.73 (s, 2H), 3.65 (s, 2H), 1.83 – 1.76 (m, 2H), 1.76 – 1.69 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 138.21, 128.44, 127.69, 127.44, 85.69, 73.29, 71.72, 68.69, 49.03, 43.24, 31.74.

**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{17}BrO_2+Na]^+$, 319.0305; found, 319.0304.

**5-(Bromomethyl)-3-phenyl-4,5-dihydroisoxazole (6a)**



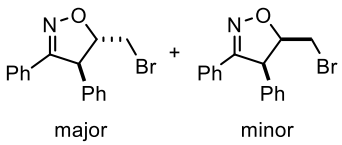
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.72 – 7.61 (m, 2H), 7.42 (dd, *J* = 5.2, 2.0 Hz, 3H), 5.01 (dddd, *J* = 10.5, 8.3, 6.4, 4.2 Hz, 1H), 3.64 – 3.47 (m, 2H), 3.47 – 3.28 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 156.18, 130.52, 129.13, 128.92, 126.92, 79.83, 39.74, 33.30.

These data are consistent with that previously reported.[28]

**5-(Bromomethyl)-3,4-diphenyl-4,5-dihydroisoxazole (6b, 6b′)**




**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.30;

major:minor=2:1

Major: **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.76 – 7.53 (m, 2H), 7.48 – 7.12 (m, 8H), 4.85 – 4.70 (m, 2H), 3.76 – 3.59 (m, 1H), 3.51 – 3.44 (m, 1H).

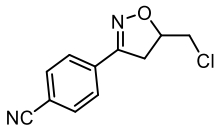
**$^{13}$C NMR** (150 MHz, Chloroform-*d*) δ 157.9, 138.3, 130.2, 129.4, 128.7, 127.5, 127.4, 88.3, 58.6, 32.5.

Minor: **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.76 – 7.53 (m, 2H), 7.48 – 7.12 (m, 8H), 5.13–5.02 (m, 1H) 4.85 – 4.70 (m, 1H), 3.42 – 3.36 (m, 1H), 3.05 – 2.92 (m, 1H).

**$^{13}$C NMR** (150 MHz, Chloroform-*d*) δ 160.7, 132.1, 130.2, 129.1, 128.6, 128.4, 128.3, 128.0, 127.2, 85.0, 56.2, 27.4.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{14}BrNO+H]^+$, 316.0332,; found, 249.0125.

**4-(5-(Chloromethyl)-4,5-dihydroisoxazol-3-yl)benzonitrile (6c-Cl)**



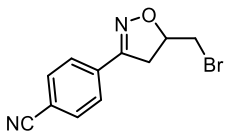

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.82 – 7.74 (m, 2H), 7.74 – 7.66 (m, 2H), 5.08 (dtd, *J* = 10.8, 6.8, 4.1 Hz, 1H), 3.74 (dd, *J* = 11.4, 4.1 Hz, 1H), 3.62 (dd, *J* = 11.4, 7.0 Hz, 1H), 3.50 (dd, *J* = 17.0, 10.7 Hz, 1H), 3.35 (dd, *J* = 17.0, 6.7 Hz, 1H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 155.05, 133.43, 132.68, 127.35, 118.38, 113.82, 80.67, 44.85, 37.94.

These data are consistent with that previously reported.[28]

**4-(5-(Bromomethyl)-4,5-dihydroisoxazol-3-yl)benzonitrile (6c-Br)**



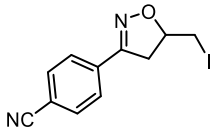

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 5.08 (dtd, *J* = 11.0, 7.2, 4.1 Hz, 1H), 3.60 (dd, *J* = 10.5, 4.1 Hz, 1H), 3.55 – 3.41 (m, 2H), 3.32 (dd, *J* = 17.0, 6.7 Hz, 1H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 154.93, 133.39, 132.64, 127.31, 118.35, 113.75, 80.53, 39.03, 33.12.

These data are consistent with that previously reported.[28]

**4-(5-(Iodomethyl)-4,5-dihydroisoxazol-3-yl)benzonitrile (6c-I)**



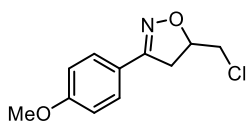

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 1H), 4.97 (dddd, *J* = 10.7, 8.7, 6.8, 4.0 Hz, 1H), 3.58 – 3.38 (m, 2H), 3.33 – 3.16 (m, 2H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 154.66, 133.45, 132.63, 127.29, 118.35, 113.72, 81.24, 40.56, 7.28.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_9IN_2O+H]^+$, 312.9832; found, 312.9833.

**5-(Chloromethyl)-3-(4-methoxyphenyl)-4,5-dihydroisoxazole (6d-Cl)**



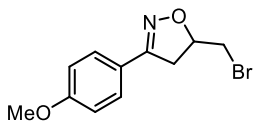

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 5.00 – 4.90 (m, 1H), 3.84 (s, 3H), 3.71 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.58 – 3.41 (m, 2H), 3.31 (dd, *J* = 16.9, 6.3 Hz, 1H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.35, 155.83, 128.45, 121.64, 114.28, 79.64, 55.50, 44.96, 38.95.

These data are consistent with that previously reported.[28]

**5-(Bromomethyl)-3-(4-methoxyphenyl)-4,5-dihydroisoxazole (6d-Br)**




**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;

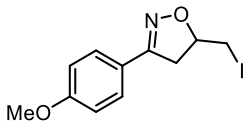
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.66 – 7.55 (m, 2H), 6.99 – 6.86 (m, 2H), 5.03 – 4.90 (m, 1H), 3.84 (d, *J* = 1.2 Hz, 3H), 3.60 – 3.54 (m, 1H), 3.49 (dd, *J* = 16.9, 10.4 Hz, 1H), 3.42 – 3.36 (m, 1H), 3.33 – 3.26 (m, 1H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.35, 155.71, 128.44, 121.63, 114.28, 79.55, 55.50, 39.95, 33.38.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_{12}BrNO_2+H]^+$,270.0124; found, 270.0124.

**5-(Iodomethyl)-3-(4-methoxyphenyl)-4,5-dihydroisoxazole (6d-I)**

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;



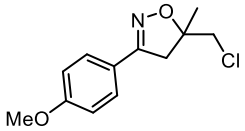
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.9 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.90 (dddd, *J* = 10.4, 9.1, 6.4, 4.1 Hz, 1H), 3.85 (s, 3H), 3.54 – 3.37 (m, 2H), 3.26 – 3.16 (m, 2H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.36, 155.50, 128.46, 121.73, 114.31, 80.31, 55.53, 41.37, 7.88.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_{12}INO_2+H]^+$, 317.9985; found, 317.9985.

**5-(Chloromethyl)-3-(4-methoxyphenyl)-5-methyl-4,5-dihydroisoxazole (6e-Cl)**

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;



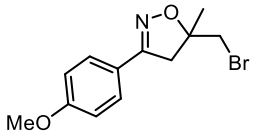
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 3.66 – 3.54 (m, 2H), 3.49 (d, *J* = 16.9 Hz, 1H), 3.07 (d, *J* = 16.9 Hz, 1H), 1.60 (s, 3H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.23, 156.10, 128.27, 122.10, 114.24, 86.30, 55.49, 49.30, 44.09, 23.77.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{14}ClNO_2+H]^+$, 240.0786; found, 240.0786.

**5-(Bromomethyl)-3-(4-methoxyphenyl)-5-methyl-4,5-dihydroisoxazole (6e-Br)**

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;

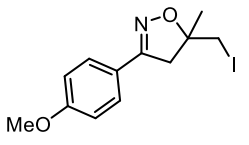


**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 3.84 (s, 2H), 3.57 – 3.43 (m, 3H), 3.09 (d, *J* = 16.9 Hz, 1H), 1.65 (s, 3H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.22, 156.01, 128.25, 122.07, 114.23, 85.99, 55.48, 44.88, 38.45, 24.29.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{14}BrNO_2+H]^+$, 284.0281; found, 284.0281.

**5-(Iodomethyl)-3-(4-methoxyphenyl)-5-methyl-4,5-dihydroisoxazole (6e-I)**



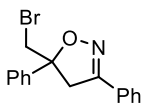
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 3.51 – 3.34 (m, 3H), 3.12 (d, *J* = 16.8 Hz, 1H), 1.70 (s, 3H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 161.21, 155.82, 128.25, 122.13, 114.24, 85.82, 55.50, 46.12, 25.13, 14.07.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{14}INO_2+Na]^+$, 353.9961; found, 353.9961.

**5-(Bromomethyl)-3,5-diphenyl-4,5-dihydroisoxazole (6f)**



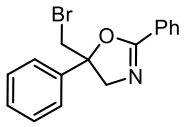
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.75 – 7.65 (m, 2H), 7.60 – 7.51 (m, 2H), 7.45 – 7.38 (m, 5H), 7.38 – 7.32 (m, 1H), 3.96 (d, *J* = 16.7 Hz, 1H), 3.81 (s, 2H), 3.63 (d, *J* = 16.8 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 156.38, 141.55, 130.39, 129.26, 128.83, 128.76, 128.45, 126.79, 125.61, 89.03, 45.31, 39.67.

These data are consistent with that previously reported.[28]

**5-(Bromomethyl)-2,5-diphenyl-4,5-dihydrooxazole (6g)**



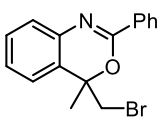
**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.34;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.14 – 7.99 (m, 2H), 7.56 – 7.38 (m, 7H), 7.34 (ddt, *J* = 8.3, 5.7, 1.8 Hz, 1H), 4.51 (d, *J* = 14.9 Hz, 1H), 4.29 (d, *J* = 14.9 Hz, 1H), 3.85 (d, *J* = 11.2 Hz, 1H), 3.78 (d, *J* = 11.2 Hz, 1H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 162.99, 141.81, 131.68, 128.87, 128.56, 128.39, 128.38, 127.49, 125.02, 87.09, 65.98, 40.24.

These data are consistent with that previously reported.[29]

**4-(Bromomethyl)-4-methyl-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (6h)**



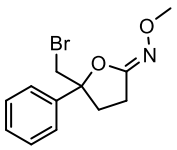
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.23 (dt, *J* = 7.0, 1.5 Hz, 2H), 7.55 – 7.43 (m, 3H), 7.37 (dd, *J* = 3.9, 1.6 Hz, 2H), 7.24 (dt, *J* = 5.4, 4.0 Hz, 1H), 7.18 (dd, *J* = 7.9, 1.3 Hz, 1H), 3.78 (d, *J* = 11.2 Hz, 1H), 3.56 (d, *J* = 11.2 Hz, 1H), 1.94 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 156.32, 139.20, 132.44, 131.71, 129.71, 128.42, 128.40, 127.16, 126.91, 125.68, 123.36, 78.21, 39.86, 25.02.

These data are consistent with that previously reported.[60]

**5-(Bromomethyl)-5-phenyldihydrofuran-2(3*H*)-one *O*-methyl oxime (6i)**



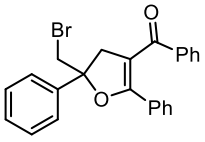
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.60;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.71 – 7.29 (m, 5H), 3.86 (d, *J* = 7.9 Hz, 3H), 3.83 – 3.68 (m, 2H), 2.90 – 2.64 (m, 2H), 2.62 – 2.40 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 156.90, 140.36, 128.81, 128.60, 125.21, 90.40, 62.49, 39.88, 33.35, 26.45.

These data are consistent with that previously reported.[31]

**(5-(Bromomethyl)-2,5-diphenyl-4,5-dihydrofuran-3-yl)(phenyl)methanone (6j)**



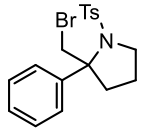
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.40;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 7.3 Hz, 2H), 7.47 – 7.40 (m, 4H), 7.39 – 7.30 (m, 3H), 7.22 (td, *J* = 7.3, 1.8 Hz, 2H), 7.09 (dt, *J* = 13.9, 7.6 Hz, 4H), 3.90-3.84 (m, 2H), 3.82 (d, *J* = 15.1 Hz, 1H), 3.72 (d, *J* = 15.3 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 193.18, 164.33, 142.34, 138.79, 131.30, 130.22, 129.76, 129.42, 128.99, 128.81, 128.40, 127.76, 127.73, 125.16, 112.18, 88.04, 44.02, 41.51.

These data are consistent with that previously reported.[35]

**2-(Bromomethyl)-2-phenyl-1-tosylpyrrolidine (8a)**



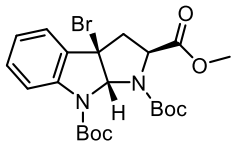
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 2H), 7.23 (t, *J* = 4.0 Hz, 5H), 7.08 (d, *J* = 7.8 Hz, 2H), 4.48 (d, *J* = 10.7 Hz, 1H), 4.28 (d, *J* = 10.7 Hz, 1H), 3.69 (q, *J* = 7.7 Hz, 1H), 3.61 (q, *J* = 8.2, 7.7 Hz, 1H), 2.68 (dt, *J* = 14.4, 7.6 Hz, 1H), 2.36 (s, 3H), 2.24 (dt, *J* = 13.5, 6.9 Hz, 1H), 2.03 (dt, *J* = 13.2, 6.5 Hz, 1H), 1.94 (dt, *J* = 13.2, 7.2 Hz, 1H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.75, 141.16, 137.14, 129.07, 128.21, 127.54, 127.26, 127.17, 71.77, 50.45, 41.93, 39.55, 23.05, 21.57.

These data are consistent with that previously reported.[38]

**1,8-Di-*tert*-Butyl 2-methyl (2*S*,3a*R*,8a*R*)-3a-bromo-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*]indole-1,2,8-tricarboxylate (8b)**



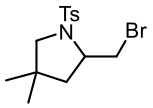
**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.40;

$^1$H NMR (400 MHz, Chloroform-*d*) δ 7.51 (dd, *J* = 33.9, 7.7 Hz, 1H), 7.39 – 7.27 (m, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.39 (s, 1H), 3.88 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.74 (s, 3H), 3.20 (dd, *J* = 12.6, 6.3 Hz, 1H), 2.82 (dd, *J* = 12.6, 10.3 Hz, 1H), 1.58 (s, 9H), 1.39 (s, 9H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 171.64, 152.32, 141.64, 132.95, 130.74, 124.55, 123.35, 117.68, 83.91, 82.42, 81.60, 59.85, 59.59, 52.53, 42.46, 28.39.

These data are consistent with that previously reported.[76]

**2-(Bromomethyl)-4,4-dimethyl-1-tosylpyrrolidine (8c-Br)**



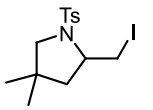
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.92 (dd, *J* = 9.7, 3.1 Hz, 1H), 3.86 (tdd, *J* = 8.4, 7.3, 3.0 Hz, 1H), 3.52 (dd, *J* = 9.7, 8.6 Hz, 1H), 3.21 – 3.10 (m, 2H), 2.42 (s, 3H), 1.87 (ddd, *J* = 12.9, 7.3, 1.3 Hz, 1H), 1.70 (dd, *J* = 12.9, 8.2 Hz, 1H), 1.04 (s, 3H), 0.52 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 143.81, 135.08, 129.83, 127.64, 62.01, 60.14, 45.99, 37.64, 37.56, 26.21, 25.93, 21.66.

These data are consistent with that previously reported.[38]

**2-(Iodomethyl)-4,4-dimethyl-1-tosylpyrrolidine (8c-I)**



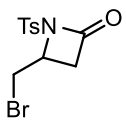
**TLC** (hexane:ethyl acetate, 90:10 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.75 (dd, *J* = 9.4, 2.9 Hz, 1H), 3.68 (tdd, *J* = 8.8, 7.0, 2.8 Hz, 1H), 3.36 (t, *J* = 9.1 Hz, 1H), 3.19 (d, *J* = 2.5 Hz, 2H), 2.42 (s, 3H), 1.90 (dd, *J* = 12.8, 7.1 Hz, 1H), 1.59 (dd, *J* = 12.8, 8.4 Hz, 1H), 1.03 (s, 3H), 0.50 (s, 3H).

**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 143.82, 134.98, 129.84, 127.62, 62.14, 60.22, 47.89, 37.62, 26.12, 25.97, 21.70, 13.36.

These data are consistent with that previously reported.[38]

**4-(Bromomethyl)-1-tosylazetidin-2-one (8d)**



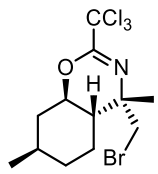
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.93 – 7.82 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 4.28 (ddt, *J* = 7.5, 6.0, 3.1 Hz, 1H), 3.86 (dd, *J* = 10.9, 3.0 Hz, 1H), 3.62 (dd, *J* = 10.9, 7.5 Hz, 1H), 3.12 (dd, *J* = 16.1, 5.9 Hz, 1H), 2.94 (dd, *J* = 16.1, 3.2 Hz, 1H), 2.45 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 162.32, 145.76, 135.38, 130.22, 127.58, 53.26, 42.58, 32.43, 21.84.

These data are consistent with that previously reported.[56]

**(4*S*,4a*S*,7*R*)-4-(Bromomethyl)-4,7-dimethyl-2-(trichloromethyl)-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*e*][1,3]oxazine (8e)**



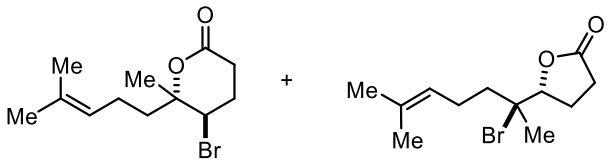
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.40;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.02 (td, *J* = 11.0, 4.6 Hz, 1H), 3.63 (d, *J* = 10.3 Hz, 1H), 3.50 (d, *J* = 10.3 Hz, 1H), 2.25 (dddd, *J* = 12.3, 4.9, 3.6, 1.8 Hz, 1H), 1.86 (ddd, *J* = 11.7, 10.7, 3.4 Hz, 1H), 1.81 – 1.74 (m, 2H), 1.62 – 1.51 (m, 1H), 1.34 – 1.26 (m, 1H), 1.25 (s, 3H), 1.16 – 1.05 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 153.48, 75.84, 56.23, 42.25, 41.30, 40.06, 34.12, 31.10, 24.64, 22.40, 22.05.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{17}BrCl_3NO+Na]^+$, 397.9452; found, 397.9451.

**5-Bromo-6-methyl-6-(4-methylpent-3-en-1-yl)tetrahydro-2*H*-pyran-2-one (major) and 5-(2-bromo-6-methylhept-5-en-2-yl)dihydrofuran-2(3*H*)-one (minor) (10a, 10a′)**




**1.2** : **1**

**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

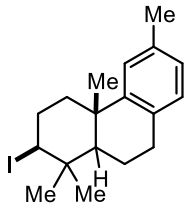
Major: Minor = 1.2:1

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.08 (dtq, *J* = 10.0, 7.1, 1.4 Hz, 2H), 4.45 (t, *J* = 7.3 Hz, 1H), 4.27 (dd, *J* = 9.0, 4.4 Hz, 1H), 2.83 – 2.55 (m, 4H), 2.48 – 2.24 (m, 4H), 2.21 – 1.99 (m, 4H), 1.94 – 1.74 (m, 4H), 1.73 (s, 3H), 1.69 – 1.66 (m, 6H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.52 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 176.61, 169.49, 133.04, 133.00, 122.71, 85.20, 84.56, 70.83, 50.06, 41.94, 40.22, 28.66, 28.54, 27.19, 25.78, 25.76, 24.48, 24.01, 23.61, 21.92, 17.81, 17.79.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{19}BrO_2+Na]^+$, 297.0461; found, 297.0463.

**2-Iodo-1,1,4a,6-tetramethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (10b)**




d.r. >95:5

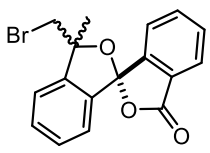
**TLC** (hexane:ethyl acetate, 98:2 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.99 (d, *J* = 1.6 Hz, 1H), 6.97 – 6.89 (m, 2H), 4.28 (dd, *J* = 12.9, 4.2 Hz, 1H), 2.94 – 2.81 (m, 2H), 2.57 (qd, *J* = 13.4, 3.6 Hz, 1H), 2.45 (dq, *J* = 13.9, 3.9 Hz, 1H), 2.30 (s, 3H), 2.17 (dt, *J* = 13.3, 3.5 Hz, 1H), 1.99 (ddt, *J* = 13.1, 5.5, 2.4 Hz, 1H), 1.81 (dtd, *J* = 13.0, 11.0, 7.3 Hz, 1H), 1.64 – 1.51 (m, 2H), 1.25 (s, 3H), 1.14 (s, 3H), 1.10 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 148.70, 135.31, 131.65, 129.09, 126.62, 125.13, 53.79, 50.15, 41.98, 39.69, 38.24, 34.54, 33.24, 30.65, 25.00, 21.87, 21.40, 21.32.

These data are consistent with that previously reported.[57]

**3'-(bromomethyl)-3'-methyl-3*H*,3'*H*-1,1'-spirobi[isobenzofuran]-3-one (10c)**




d.r. = 1.15:1

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.96 – 7.89 (m, 2H), 7.73 – 7.59 (m, 5H), 7.53 – 7.46 (m, 3H), 7.38 – 7.27 (m, 4H), 6.92 (dq, *J* = 7.7, 1.1 Hz, 2H), 3.93 – 3.81 (m, 2H), 3.80 – 3.67 (m, 2H), 1.85 (s, 3H), 1.84 (s, 3H).

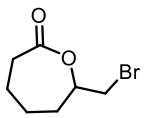
**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.96, 167.79, 146.52, 144.48, 144.40, 136.82, 136.45, 134.93, 134.90, 131.22, 131.20, 130.71, 130.50, 129.62, 129.37, 127.46, 127.31, 125.17, 125.02, 124.48, 123.66, 122.87, 122.67, 122.33, 120.88, 114.05, 113.63, 88.88, 88.41, 40.02, 39.54, 26.78, 25.09.

**HRMS-ESI(m/z)** calc'd for $[C_{17}H_{13}BrO_3+H]^+$, 345.0121; found, 345.0122.

## 13. Procedures and analytical data of medium and large ring lactones

**General procedure for intramolecular medium- and large-sized bromocyclization.** Substrate (0.3 mmol) and TBAB (0.6 mmol, 2.2 equiv.) were added into a dried Schlenk tube in DCE (12 mL) at 25 °C. Subsequently, a solution of PPO (0.6 mmol, 2.2 equiv.) in DCE (3 mL) was added slowly over 30 min at same temperature. After addition, the reaction was completed and the solvent was evaporated. The residue was purified by column chromatography (petroleum ether:ethyl acetate = 4:1) to give the expected product.

**7-(bromomethyl)oxepan-2-one (12a)**



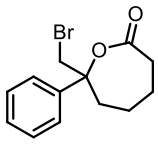
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 4.44 (dt, *J* = 8.6, 5.9 Hz, 1H), 3.52 (dd, *J* = 10.6, 5.6 Hz, 1H), 3.41 (dd, *J* = 10.6, 6.1 Hz, 1H), 2.76 – 2.66 (m, 1H), 2.64 – 2.51 (m, 1H), 2.24 – 2.14 (m, 1H), 2.07 – 1.90 (m, 2H), 1.63 (qd, *J* = 12.1, 9.0 Hz, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 174.25, 79.36, 34.86, 34.40, 33.09, 28.02, 22.90.

These data are consistent with that previously reported.[58]

**7-(bromomethyl)-7-phenyloxepan-2-one (12b)**



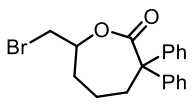
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.47 – 7.39 (m, 1H), 7.39 – 7.30 (m, 2H), 3.62 (d, *J* = 10.7 Hz, 1H), 3.47 (d, *J* = 10.7 Hz, 0H), 2.75 – 2.65 (m, 1H), 2.55 (ddt, *J* = 14.2, 6.6, 1.5 Hz, 1H), 2.38 (ddd, *J* = 15.8, 12.9, 3.3 Hz, 1H), 1.97 (dd, *J* = 13.7, 2.4 Hz, 0H), 1.93 – 1.87 (m, 0H), 1.85 – 1.75 (m, 0H), 1.75 – 1.67 (m, 0H), 1.58 (tdd, *J* = 14.6, 3.5, 1.6 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 174.53, 139.00, 129.27, 128.60, 126.31, 84.09, 44.90, 36.78, 35.33, 24.09, 22.91.

**HRMS-ESI(m/z)** calc'd for $[C_{13}H_{15}BrO_2+Na]^+$, 305.0148; found, 305.0149.

**7-(bromomethyl)-3,3-diphenyloxepan-2-one (12c)**



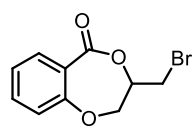
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.32;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.49 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.44 – 7.38 (m, 1H), 7.31 – 7.26 (m, 2H), 7.25 – 7.16 (m, 3H), 6.92 – 6.85 (m, 2H), 4.32 – 4.20 (m, 1H), 3.42 (dd, *J* = 10.7, 6.3 Hz, 1H), 3.31 (dd, *J* = 10.7, 4.9 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.67 – 2.58 (m, 1H), 2.04 – 1.89 (m, 3H), 1.84 – 1.71 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 174.16, 146.84, 137.99, 129.41, 128.55, 128.01, 127.91, 127.81, 126.88, 78.41, 61.52, 35.51, 34.74, 32.50, 23.53.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_{11}BrO_3+Na]^+$: 381.0461; found, 381.0459.

**3-(bromomethyl)-2,3-dihydro-5*H*-benzo[*e*][1,4]dioxepin-5-one (12d)**



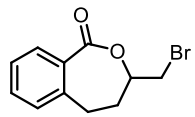
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.91 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.51 (ddd, *J* = 8.3, 7.2, 1.8 Hz, 1H), 7.13 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H), 7.03 (dd, *J* = 8.3, 1.1 Hz, 1H), 4.85 – 4.70 (m, 1H), 4.57 (dd, *J* = 12.6, 1.8 Hz, 1H), 4.45 (dd, *J* = 12.7, 7.8 Hz, 1H), 3.60 (dd, *J* = 11.0, 5.0 Hz, 1H), 3.52 (dd, *J* = 11.0, 6.7 Hz, 1H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 167.07, 155.43, 135.29, 133.95, 123.16, 120.95, 119.06, 75.33, 73.18, 28.47.

These data are consistent with that previously reported.[58]

**3-(bromomethyl)-4,5-dihydrobenzo[*c*]oxepin-1(3*H*)-one (12e)**



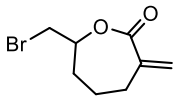
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.48 (td, *J* = 7.5, 1.4 Hz, 1H), 7.37 (td, *J* = 7.6, 1.1 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 4.25 (dq, *J* = 11.6, 5.9 Hz, 1H), 3.57 (dd, *J* = 10.8, 6.1 Hz, 1H), 3.49 (dd, *J* = 10.8, 5.3 Hz, 1H), 3.01 (ddd, *J* = 14.0, 11.5, 8.7 Hz, 1H), 2.81 (ddd, *J* = 14.2, 5.8, 2.2 Hz, 1H), 2.28 – 2.07 (m, 2H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.41, 137.70, 133.04, 131.22, 130.41, 128.85, 127.68, 77.11, 32.86, 32.64, 29.51.

These data are consistent with that previously reported.[58]

**7-(bromomethyl)-3,3-diphenyloxepan-2-one (12f)**



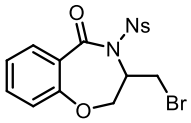
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.35;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.72 (s, 1H), 5.45 (d, *J* = 1.6 Hz, 1H), 4.36 (dtd, *J* = 10.0, 5.7, 1.5 Hz, 1H), 3.54 (dd, *J* = 10.7, 5.6 Hz, 1H), 3.44 (dd, *J* = 10.7, 5.9 Hz, 1H), 2.52 (ddd, *J* = 14.7, 6.8, 3.4 Hz, 1H), 2.39 – 2.29 (m, 1H), 2.10 (dt, *J* = 14.2, 5.0 Hz, 1H), 1.95 (dtt, *J* = 13.3, 6.3, 3.6 Hz, 1H), 1.79 (dtd, *J* = 13.7, 9.8, 3.8 Hz, 1H), 1.69 (dtt, *J* = 13.1, 6.3, 2.8 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 171.31, 142.47, 123.98, 79.00, 34.23, 32.37, 31.47, 26.37.

**HRMS-ESI(m/z)** calc'd for $[C_8H_{11}BrO_4+Na]^+$, 240.9835; found, 240.9828.

**3-(bromomethyl)-4-((4-nitrophenyl)sulfonyl)-3,4-dihydrobenzo[*f*][1,4]oxazepin-5(2*H*)-one (12g)**



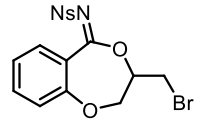
**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.40;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.43 – 8.34 (m, 2H), 8.33 – 8.21 (m, 2H), 7.93 (dt, *J* = 8.6, 1.5 Hz, 1H), 7.48 (td, *J* = 7.9, 1.8 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 2H), 5.09 (ddd, *J* = 18.2, 11.4, 5.1 Hz, 2H), 4.23 (d, *J* = 13.0 Hz, 1H), 3.61 – 3.42 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 165.57, 156.47, 150.81, 144.76, 135.57, 134.07, 130.48, 124.13, 122.65, 120.30, 118.10, 69.70, 57.16, 27.84.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{13}BrN_2O_6S+H]^+$, 440.9751; found, 440.9743.

**N-(3-(bromomethyl)-2,3-dihydro-5*H*-benzo[*e*][1,4]dioxepin-5-ylidene)-4-nitrobenzenesulfonamide (12g′)**



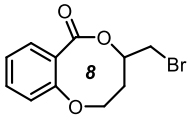
**TLC** (hexane:ethyl acetate, 80:20 v/v): $R_f$ = 0.65;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.40 – 8.31 (m, 2H), 8.26 – 8.18 (m, 2H), 7.84 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.55 (td, *J* = 7.8, 1.8 Hz, 1H), 7.14 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 4.94 – 4.85 (m, 1H), 4.58 – 4.46 (m, 2H), 3.64 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.57 (dd, *J* = 11.4, 6.2 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.48, 156.59, 150.17, 147.39, 136.44, 133.48, 128.70, 124.17, 124.06, 121.80, 119.58, 79.16, 73.97, 27.31.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{13}BrN_2O_6S+H]^+$, 440.9751; found, 440.97446.

**4-(bromomethyl)-3,4-dihydro-2*H*,6*H*-benzo[*b*][1,5]dioxocin-6-one (12h)**



**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.40;

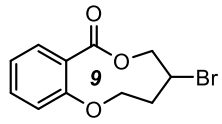
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.52 (dt, *J* = 7.9, 1.7 Hz, 1H), 7.40 (tt, *J* = 8.6, 1.6 Hz, 1H), 7.08 – 7.00 (m, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 4.62 (tdd, *J* = 7.6, 4.8, 1.9 Hz, 1H), 4.39 – 4.25 (m, 2H), 3.53 (ddd, *J* = 11.0, 6.3, 1.4 Hz, 1H),

3.46 (dd, *J* = 10.9, 5.2 Hz, 1H), 2.34 (dddd, *J* = 17.0, 7.7, 4.0, 2.0 Hz, 1H), 2.02 (tt, *J* = 14.4, 3.1 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 169.87, 157.20, 122.10, 119.79, 116.62, 75.25, 65.30, 35.15, 32.81.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_{11}BrO_3+Na]^+$: 292.9784; found, 292.9797.

**4-bromo-2,3,4,5-tetrahydro-7*H*-benzo[*b*][1,5]dioxonin-7-one (12h′)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.55;

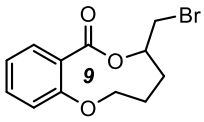
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.57 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.43 (td, *J* = 7.8, 1.8 Hz, 1H), 7.16 (td, *J* = 7.5, 1.1 Hz, 1H), 7.09 (dd, *J* = 8.1, 1.0 Hz, 1H), 5.04 – 4.91 (m, 1H), 4.47 – 4.41 (m, 1H), 4.41 – 4.37 (m, 1H), 4.32 (t, *J* = 10.3 Hz, 1H), 3.98 (ddd, *J* = 11.7, 6.2, 2.7 Hz, 1H), 2.60 (ddt, *J* = 15.2, 8.9, 2.9 Hz, 1H), 2.40 (dddd, *J* = 15.7, 9.8, 6.2, 1.9 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.27, 159.95, 133.20, 129.32, 126.01, 124.23, 122.59, 75.12, 69.64, 45.50, 39.73.

**HRMS-ESI(m/z)** calc'd for $[C_{11}H_{11}BrO_3+Na]^+$: 292.9784; found, 292.9780.

**5-(bromomethyl)-2,3,4,5-tetrahydro-7*H*-benzo[*b*][1,5]dioxonin-7-one (12i)**

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.50;

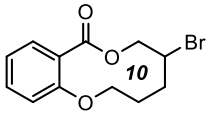



**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.42 (td, *J* = 7.8, 1.8 Hz, 1H), 7.14 (td, *J* = 7.5, 1.1 Hz, 1H), 7.08 (dd, *J* = 8.1, 1.1 Hz, 1H), 5.11 – 5.02 (m, 1H), 4.28 (ddd, *J* = 11.2, 7.8, 2.3 Hz, 1H), 4.00 (ddd, *J* = 11.3, 6.9, 2.4 Hz, 1H), 2.14 (ddt, *J* = 11.9, 8.0, 3.9 Hz, 1H), 2.08 – 1.96 (m, 2H), 1.93 – 1.82 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 169.01, 160.01, 133.04, 129.48, 126.28, 123.87, 122.35, 77.04, 76.55, 33.50, 30.69, 26.80.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{13}BrO_3+Na]^+$, 306.9940; found, 306.9947.

**5-bromo-3,4,5,6-tetrahydro-2*H*,8*H*-benzo[*b*][1,5]dioxecin-8-one (12i′)**



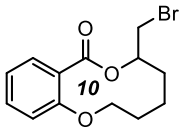

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.60;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.45 (td, *J* = 7.8, 1.8 Hz, 1H), 7.18 – 7.06 (m, 2H), 5.12 – 4.81 (m, 1H), 4.42 – 4.19 (m, 2H), 4.19 – 4.03 (m, 2H), 2.41 (tt, *J* = 6.3, 3.1 Hz, 2H), 2.25 – 2.01 (m, 1H), 1.81 (ddq, *J* = 12.5, 10.7, 4.1 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.33, 158.75, 133.07, 129.45, 126.35, 123.82, 122.01, 74.31, 69.30, 47.07, 34.82, 28.91;

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{13}BrO_3+Na]^+$, 306.9940; found, 306.9945.

**6-(bromomethyl)-3,4,5,6-tetrahydro-2*H*,8*H*-benzo[*b*][1,5]dioxecin-8-one (12j)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.55;

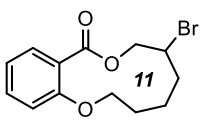
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.60 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.44 (td, *J* = 7.8, 1.8 Hz, 1H), 7.21 – 7.12 (m, 2H), 5.21 – 5.06 (m, 1H), 4.21 – 4.03 (m, 2H), 3.57 (h, *J* = 5.9 Hz, 2H), 2.17 – 2.03 (m, 1H), 2.02 – 1.82 (m, 1H), 1.82 – 1.70 (m, 2H), 1.70 – 1.57 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.67, 158.76, 132.88, 129.77, 127.35, 124.07, 123.16, 75.51, 73.29, 33.77, 30.48, 30.41, 19.64.

**HRMS-ESI(m/z)** calc'd for $[C_{13}H_{15}BrO_3+Na]^+$, 321.0097; found, 321.0097.

**6-bromo-2,3,4,5,6,7-hexahydro-9*H*-benzo[*b*][1,5]dioxacycloundecin-9-one (12j′)**



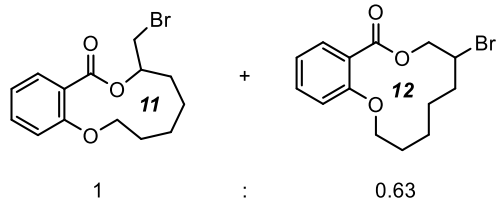


**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.60;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.51 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.45 (td, *J* = 7.9, 1.8 Hz, 1H), 7.05 (td, *J* = 7.5, 1.0 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 5.09 (dd, *J* = 10.8, 4.3 Hz, 1H), 4.39 (ddt, *J* = 11.4, 7.9, 4.1 Hz, 1H), 4.27 (ddd, *J* = 8.4, 4.9, 2.9 Hz, 1H), 4.20 (t, *J* = 10.7 Hz, 1H), 3.97 (td, *J* = 9.3, 2.0 Hz, 1H), 2.55 (dddd, *J* = 15.1, 9.6, 5.6, 3.8 Hz, 1H), 2.12 – 1.70 (m, 4H); **$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.22, 157.28, 132.49, 128.66, 123.99, 121.41, 114.46, 69.56, 67.84, 46.44, 33.88, 25.56, 22.81.

**HRMS-ESI(m/z)** calc'd for $[C_{13}H_{15}BrO_3+Na]^+$, 321.0097; found, 321.0091.

**7-(bromomethyl)-2,3,4,5,6,7-hexahydro-9*H*-benzo[*b*][1,5]dioxacycloundecin-9-one and 7-bromo-3,4,5,6,7,8-hexahydro-2*H*,10*H*-benzo[*b*][1,5]dioxacyclododecin-10-one (12k, 12k′)**



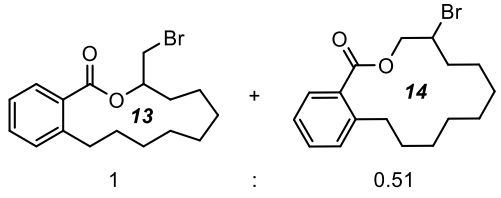

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.60;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.53 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.42 (dtd, *J* = 10.3, 7.6, 1.9 Hz, 2H), 7.04 – 6.89 (m, 5H), 5.31 – 5.23 (m, 1H), 4.74 (dd, *J* = 10.9, 4.0 Hz, 1H), 4.41 – 4.33 (m, 1H), 4.31 – 4.23 (m, 1H), 4.20 – 4.12 (m, 2H), 3.95 (dtd, *J* = 25.9, 8.9, 3.2 Hz, 3H), 3.61 – 3.51 (m, 3H), 2.33 – 2.23 (m, 1H), 2.20 – 2.10 (m, 1H), 2.02 (ddq, *J* = 10.5, 6.8, 3.7 Hz, 1H), 1.93 – 1.67 (m, 4H), 1.66 – 1.58 (m, 1H), 1.57 – 1.46 (m, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.46, 167.42, 157.96, 157.88, 133.54, 132.58, 131.67, 129.38, 124.11, 121.37, 120.91, 120.49, 115.49, 112.79, 74.63, 70.81, 69.38, 68.88, 47.77, 35.82, 33.42, 29.51, 26.43, 26.27, 25.83, 25.48, 25.41, 22.20.

**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{17}BrO_3+Na]^+$, 335.0254; found, 335.0256.

**3-(bromomethyl)-4,5,6,7,8,9,10,11-octahydrobenzo[*c*][1]oxacyclotridecin-1(3*H*)-one and 4-bromo-3,4,5,6,7,8,9,10,11,12-decahydro-1*H*-benzo[*c*][1]oxacyclotetradecin-1-one (12l, 12l′)**



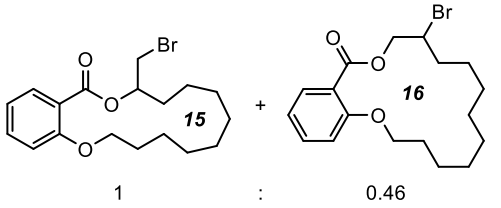

**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.62;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.62 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.42 (dtd, *J* = 10.1, 8.1, 1.8 Hz, 2H), 7.03 – 6.79 (m, 3H), 5.23 (p, *J* = 5.7 Hz, 1H), 4.75 (dd, *J* = 10.9, 3.7 Hz, 1H), 4.38 (t, *J* = 10.4 Hz, 1H), 4.28 (ddt, *J* = 10.7, 7.7, 3.9 Hz, 0H), 4.03 (dqd, *J* = 24.9, 8.9, 7.6, 3.7 Hz, 3H), 3.64 – 3.45 (m, 2H), 2.25 (ddt, *J* = 15.0, 10.1, 4.8 Hz, 1H), 1.84 (q, *J* = 6.3, 5.4 Hz, 3H), 1.80 – 1.63 (m, 3H), 1.64 – 1.52 (m, 3H), 1.52 – 1.38 (m, 4H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 168.35, 167.28, 157.70, 157.22, 133.39, 132.79, 131.77, 130.94, 121.87, 120.61, 120.18, 120.09, 112.58, 112.13, 74.43, 69.03, 68.05, 66.83, 50.04, 33.73, 33.39, 29.82, 27.47, 26.65, 25.69, 24.57, 24.34, 24.29, 24.08, 23.82, 23.58, 21.99.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{21}BrO_3+Na]^+$, 363.0567; found, 363.0565.

**11-(bromomethyl)-2,3,4,5,6,7,8,9,10,11-decahydro-13*H*-benzo[*b*][1,5]dioxacyclopentadecin-13-one and 11-bromo-3,4,5,6,7,8,9,10,11,12-decahydro-2*H*,14*H*-benzo[*b*][1,5]dioxacyclohexadecin-14-one (12m, 12m′)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.65;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.76 – 7.71 (m, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.47 – 7.37 (m,

3H), 7.01 – 6.89 (m, 6H), 5.46 (qd, *J* = 5.9, 2.7 Hz, 2H), 4.72 (dd, *J* = 11.3, 4.0 Hz, 1H), 4.47 (dd, *J* = 11.4, 8.6 Hz, 1H), 4.29 (tt, *J* = 8.7, 4.0 Hz, 1H), 4.20 (dt, *J* = 8.9, 4.1 Hz, 2H), 4.08 (q, *J* = 4.6 Hz, 2H), 3.94 (td, *J* = 9.3, 3.1 Hz, 2H), 3.60 – 3.51 (m, 4H), 2.08 (ddd, *J* = 15.1, 7.9, 4.2 Hz, 1H), 1.90 – 1.68 (m, 11H), 1.58 (tdd, *J* = 13.1, 7.8, 4.9 Hz, 8H), 1.33 (tdt, *J* = 30.5, 11.5, 5.6 Hz, 22H).

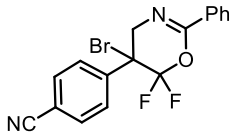
**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 166.55, 166.15, 158.41, 157.81, 133.53, 132.80, 131.75, 130.42, 121.70, 120.34, 120.00, 119.89, 112.87, 112.45, 71.71, 69.64, 68.57, 67.91, 51.08, 35.29, 33.23, 32.86, 28.55, 28.05, 27.45, 27.37, 26.97, 26.75, 26.60, 25.99, 25.91, 25.19, 25.06, 24.97, 24.10

**HRMS-ESI(m/z)** calc'd for $[C_{18}H_{25}BrO_3+Na]^+$, 391.0880; found, 391.0871.

## 14. Procedures and analytical data of difluoromethyl-containing oxazoline compounds

**General procedure for PPO-induced bromocyclization of difluoroalkenes.** To a solution of 1a (0.3 mmol, 1.0 equiv.) and TBAB (0.60 mmol, 2.0 equiv.) in DCE (3 mL) was added PPO (0.60 mmol, 2.0 equiv.) at room temperature. The solution was stirred at room temperature for 10 min. Saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with DCM (15 mL × 3). After completion of the reaction as monitored by TLC, the combined extracts were washed by brine (10 mL) and dried over $Na_2SO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography to yield the corresponding cyclized products.

**4-(5-bromo-6,6-difluoro-2-phenyl-5,6-dihydro-4*H*-1,3-oxazin-5-yl)benzonitrile (14a′)**



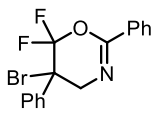
**TLC** (hexane:ethyl acetate, 60:40 v/v): $R_f$ = 0.50;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.01 – 7.94 (m, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 4.60 (dt, *J* = 18.1, 3.5 Hz, 1H), 4.53 (dt, *J* = 18.0, 3.7 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 151.16, 140.26, 132.49, 132.36, 129.68, 129.06, 128.64, 127.80, 120.56 (t, *J* = 263.6 Hz), 117.97, 113.67, 55.96, 55.34 (t, *J* = 27.2 Hz). **$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -74.65.

**HRMS-ESI(m/z)** calc'd for $[C_{17}H_{11}BrF_2N_2O+K]^+$: 416.9634; found, 416.9629.

**5-bromo-6,6-difluoro-2,5-diphenyl-5,6-dihydro-4*H*-1,3-oxazine (14b′)**



**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.45;

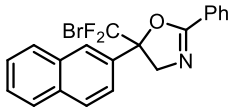
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.04 – 7.98 (m, 2H), 7.76 – 7.68 (m, 2H), 7.56 – 7.49 (m, 1H), 7.48 – 7.35 (m, 5H), 4.65 (dt, *J* = 18.1, 3.3 Hz, 1H), 4.55 (dt, *J* = 18.0, 3.7 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 151.01, 135.34, 132.04, 130.21, 129.66, 128.78, 128.55, 128.15, 127.79, 121.01 (t, *J* = 263.4 Hz), 56.79 (t, *J* = 26.9 Hz), 56.23.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -74.94.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{12}BrF_2NO+Na]^+$: 373.9963; found, 373.9961.

**5-(bromodifluoromethyl)-5-(naphthalen-2-yl)-2-phenyl-4,5-dihydrooxazole (14c)**



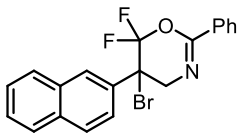
**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.30;

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.17 – 8.12 (m, 2H), 8.09 (d, *J* = 1.9 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.89 – 7.84 (m, 1H), 7.65 (dq, *J* = 8.7, 1.5 Hz, 1H), 7.61 – 7.48 (m, 5H), 4.92 (d, *J* = 15.6 Hz, 1H), 4.54 (d, *J* = 15.6 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 162.62, 133.89, 133.49, 132.79, 132.15, 128.74, 128.57, 128.54, 127.80, 127.20, 126.84, 126.81, 126.71, 124.23 (t, *J* = 312.8 Hz), 123.94, 90.72 (t, *J* = 24.8 Hz), 64.89. **$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -58.91 (d, *J* = 169.0 Hz), -60.15 (d, *J* = 169.3 Hz).

These data are consistent with that previously reported.[55]

**5-bromo-6,6-difluoro-5-(naphthalen-2-yl)-2-phenyl-5,6-dihydro-4*H*-1,3-oxazine (14c′)**



**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.35;

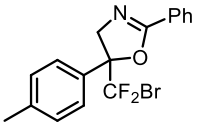
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.11 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.87 (dd, *J* = 14.6, 6.0 Hz, 4H), 7.54 (p, *J* = 8.5, 7.8 Hz, 3H), 7.45 (t, *J* = 7.7 Hz, 2H), 4.80 (d, *J* = 18.0 Hz, 1H), 4.68 (dt, *J* = 18.1, 3.7 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 151.08, 133.41, 132.62, 132.49, 132.05, 130.16, 128.85, 128.68, 128.55, 127.80, 127.60, 126.91, 126.73, 126.14 (d, *J* = 2.6 Hz), 121.13 (t, *J* = 263.6 Hz), 57.03 (t, *J* = 27.0 Hz), 56.22.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -74.42.

**HRMS-ESI(m/z)** calc'd for $[C_{20}H_{14}BrF_2NO+K]^+$: 439.9864; found, 439.9856.

**5-(bromodifluoromethyl)-2-phenyl-5-(*p*-tolyl)-4,5-dihydrooxazole (14d)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.40;

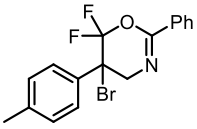
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.10 – 8.05 (m, 2H), 7.58 – 7.52 (m, 1H), 7.51 – 7.43 (m, 4H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.79 (d, *J* = 15.5 Hz, 1H), 4.40 (d, *J* = 15.5 Hz, 1H), 2.38 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 162.56, 139.42, 133.64, 132.05, 129.27, 128.68, 128.51, 124.27 (t, *J* = 312.6 Hz), 90.52 (t, *J* = 24.7 Hz), 64.83, 21.29.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -59.30 (d, *J* = 168.0 Hz), -60.44 (d, *J* = 167.8 Hz).

These data are consistent with that previously reported.[55]

**5-bromo-6,6-difluoro-2-phenyl-5-(*p*-tolyl)-5,6-dihydro-4*H*-1,3-oxazine (14d′)**




**TLC** (hexane:ethyl acetate, 75:25 v/v): $R_f$ = 0.45;

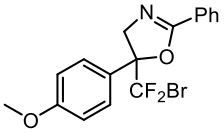
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.03 – 7.96 (m, 2H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.43 (dd, *J* = 8.3, 6.8 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 4.62 (dt, *J* = 18.0, 3.3 Hz, 1H), 4.53 (dt, *J* = 18.0, 3.7 Hz, 1H), 2.36 (s, 3H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 151.01, 139.82, 132.39, 132.01, 130.25, 129.47, 128.54, 128.02, 127.79, 121.05 (t, *J* = 263.3 Hz), 56.84 (t, *J* = 26.8 Hz), 56.22, 21.22.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -75.06.

**HRMS-ESI(m/z)** calc'd for $[C_{17}H_{14}BrF_2NO_2+Na]^+$: 404.0074; found, 404.0069.

**5-(bromodifluoromethyl)-5-(4-methoxyphenyl)-2-phenyl-4,5-dihydrooxazole (14e)**




**TLC** (hexane:ethyl acetate, 70:30 v/v): $R_f$ = 0.30;

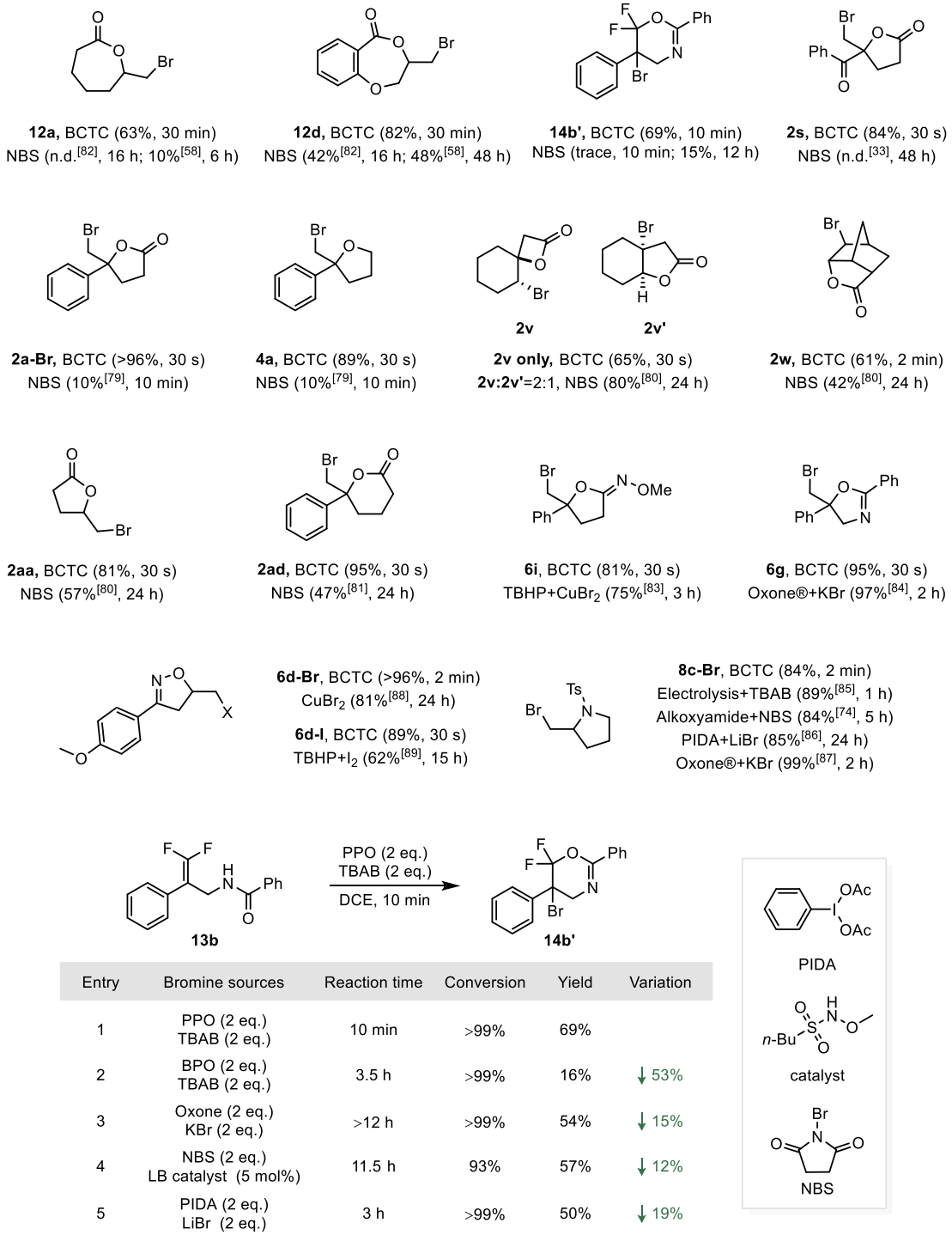
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.12 – 7.99 (m, 2H), 7.62 – 7.41 (m, 5H), 6.95 (d, *J* = 8.6 Hz, 2H), 4.79 (d, *J* = 15.5 Hz, 1H), 4.40 (d, *J* = 15.5 Hz, 1H), 3.82 (s, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 162.55, 160.38, 132.05, 128.66, 128.49, 128.42, 128.33, 126.83, 124.37 (t, *J* = 312.6 Hz), 113.94, 90.39 (t, *J* = 24.7 Hz), 64.76, 55.41.

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -59.48 (d, *J* = 167.9 Hz), -60.51 (d, *J* = 167.6 Hz).

These data are consistent with that previously reported.[55]

# 15. Comparison of different published methodology for bromocyclization




| Entry | Bromine sources | Reaction time | Conversion | Yield | Variation |
|---|---|---|---|---|---|
| 1 | PPO (2 eq.)<br>TBAB (2 eq.) | 10 min | >99% | 69% | |
| 2 | BPO (2 eq.)<br>TBAB (2 eq.) | 3.5 h | >99% | 16% | ↓ 53% |
| 3 | Oxone (2 eq.)<br>KBr (2 eq.) | >12 h | >99% | 54% | ↓ 15% |
| 4 | NBS (2 eq.)<br>LB catalyst (5 mol%) | 11.5 h | 93% | 57% | ↓ 12% |
| 5 | PIDA (2 eq.)<br>LiBr (2 eq.) | 3 h | >99% | 50% | ↓ 19% |

**Figure S30.** Comparison of different published methodology for bromocyclization.

Construction of medium-sized and large-sized rings: The utilization of just NBS was also incapable for these transformations. Taking the synthesis of **12a** as example (Figure R3), less than 10% yield of desired product was obtained even employing an unsuitable catalyst. That is, the construction of medium-sized and large-sized rings relies more heavily on the synergistic

collaboration of NBS with structurally specific organocatalysts (e.g., sulfur-based zwitterionic organocatalyst) or an extra co-catalyst (e.g., DMAP). Notably, our protocol has a clear advantage over previous reports in synthesizing seven-membered lactone **12d** (Figure S30).

Synthesis of difluoromethylene unit containing compounds: The bromocyclization of **13b** was unsatisfactory when replacing PPO and TBAB with NBS in darkness condition for 10min and relative low yield in 12 h (Figure S30).

Halolactonization and haloetherification: In this respect, the utilization of just NBS was incapable for the synthesis of **2s** while the π-bond of corresponding substrate **1s** was relative sluggish. Furthermore, utilizing the BCTC model exhibited a higher efficient and selectivity than just using NBS during synthesizing **2a-Br**, **4a**, **2u**, **2v**, **2w**, **2aa** and **2ad** using thermochemistry (Figure S30)

The scope of intramolecular nucleophile moieties: In the part of haloxygenation and haloaminocyclization, we illustrated the experimental results of yield and time of our BCTC model and eight literatures. The results shown in Figure S30 certify the excellent synthetic ability of BCTC model in constructing diverse heterocyclic rings with high efficiency.

In conclusion, we demonstrated that the BCTC model is superior to just using NBS in the synthesis of five-membered to seven-membered lactones, substituted tetrahydrofuran as well as difluoromethylene unit containing compounds. Furthermore, the ICDA enhanced halocyclization is proved as a powerful and better protocol for the fast and high-yielding construction of seven types of heterocyclic units.

**General procedure for bromocyclization in entry 3.** To a solution of **13b** (0.25 mmol, 1.0 equiv.) and Oxone (307 mg, 0.50 mmol, 2.0 equiv.) in acetonitrile (1 mL) was added KBr (59.5 mg, 0.50 mmol, 2.0 equiv.) under argon atmosphere at room temperature. The solution was stirred at room temperature for 3 h. Saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). After completion of the reaction as monitored by TLC, the combined extracts were washed by brine (10 mL) and dried over $Na_2SO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography to yield the corresponding cyclized products.

This methodology was previously employed for intramolecular bromoamination of *N*-alkenyl sulfonamides and *N*-alkenoxyl sulfonamides.[73]

**General procedure for bromocyclization in entry 4.** To a mixture of **13b** (0.1 mmol, 1.0 equiv.) and catalyst (0.005 mmol, 0.05 equiv.) in heptane (5 mL) at 25 °C was added *N*-bromosuccinimide (0.2 mmol, 2.0 equiv.). The reaction tube was covered with aluminium foil and the resulting mixture was stirred at room temperature. After completion of the reaction as monitored by TLC, the reaction was quenched with saturated aqueous $Na_2SO_3$ solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash silica-gel column chromatography to yield the corresponding cyclized products.

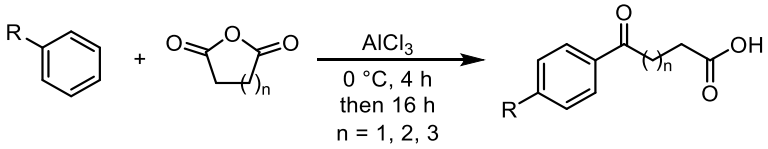
This methodology was previously employed for intramolecular bromolactonization, bromoetherification and bromoamination.[74]

**General procedure for bromocyclization in entry 5.** A solution of **13b** (0.1 mmol, 1 equiv.) and LiBr (0.2 mmol, 16.7 mg, 2.0 equiv.) in DCM (2.5 mL) at room temperature. PIDA (0.2 mmol, 78 mg, 2.0 equiv.) was added, and the solution was stirred at room temperature. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure to give the

crude product, which was purified by flash silica-gel column chromatography to yield the corresponding cyclized products.

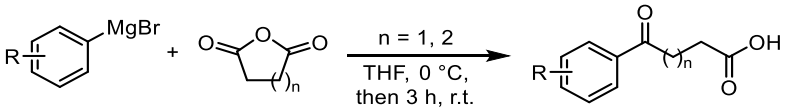
This methodology was previously employed for intramolecular bromocyclization of guanidines.[75]

## 16. General procedure for generating unsaturated substrates and characterization of new substrates

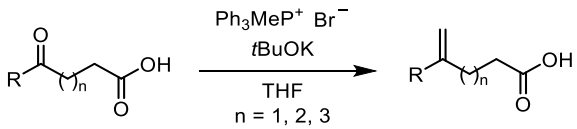



A 100 mL, three-necked, round-bottomed flask is charged with powdered dihydrofuran-2,5-dione (1.0 equiv.) and arene (1.0 equiv.) under dry nitrogen. The resulting white mixture was cooled to 0 °C before anhydrous aluminum trichloride (1.2 equiv.) was added in one portion. The reaction mixture was stirred over a period of 4 h before allowing it to warm to room temperature for 16 h. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice. The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated. Product was engaged in the next step without further purification.


To a solution of succinic anhydride (1.2 g, 12 mmol, 1.2 equiv.) in DCM (125 mL) in a 250mL round-bottom flask fitted with a thermometer, and solvent addition funnel was added aluminum trichloride (2.3 g, 17 mmol). The reaction mass was cooled under stirring to 15 °C and a solution of trimethyl(phenylethynyl)silane (2.0 mL, 10 mmol) in 10 mL of DCM was added dropwise and the reaction mixture was stirred for 16 h at rt. The reaction was poured in ice and 10 mL of concentrated hydrochloric acid was added under stirring at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM twice (2 × 50 mL). The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated to give the expected compound.

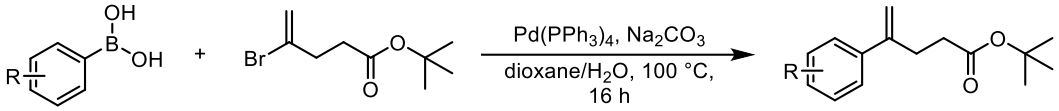



To the solution of glutaric anhydride (1.0 equiv.) in THF under a $N_2$ atmosphere was added dropwise the corresponding Grignard reagent (1.2 equiv.) at 0 °C. The solution was warmed to room temperature and stirred for a further 3 hours. The reaction was quenched with 10% HCl, and THF was removed under vacuum. The resulting aqueous solution was extracted with DCM. The combined organic layers were washed with brine, dried ($Na_2SO_4$) and evaporated under vacuum to give a white solid and used without other purification.




Under nitrogen, to a solution of *t*BuOK (2.6 equiv.) in dry THF (0.5 M) was added bromo(methyl)triphenylphosphorane (1.3 equiv.) in portions at 0 °C. The mixture was stirred at 0 °

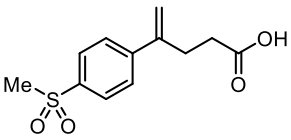
C for 30 min and a solution of ketone (1.0 equiv.) in dry THF (1 M) was added dropwise and the reaction was stirred at 0 °C for 1 h and at rt overnight. The solvent was removed in vacuo and the residue diluted with DCM and aqueous NaOH (1 M). The aqueous layer was separated, washed with dichloromethane, and acidified to pH 1 with concentrated HCl. DCM was added and the organic compound was extracted twice with DCM. The organic layer was washed with water, dried over $MgSO_4$ and concentrated. The crude product was purified by $SiO_2$ column chromatography (DCM/MeOH: 100/0 to 95/5 to 9/1) to give pure enoic acid. NMR data of **1a**[28], **1b**[29], **1c**[29], **1d**[29], **1e**[29], **1f**[29], **1g**[28], **1m**[29], **1n**[29], **1r**[30], **1t**[28], **1ad**[31], **1ae**[31], **1af**[31], **1ag**[31], **1ah**[31], **1ai**[31], **1aj**[31] were correspond to the reported values.




A mixture of methyl 4-bromopent-4-enoate (193 mg, 1.0 mmol, 1.0 eq), aryl boronic acid (1.2 mmol, 1.2 eq), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol, 0.05 eq), and $Na_2CO_3$ (233 mg, 2.2 mmol, 2.2 eq) in dioxane/$H_2O$ (7:1, v/v) (8 mL) was stirred at 100 °C under $N_2$ for 16 h. The solvent was removed under reduced pressure and the residue was diluted with water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by flash column chromatography (hexane/EtOAc) to give the corresponding ester.

To a solution of corresponding ester (1.0 eq) in DCM (0.5 M) was added TFA (32.36 eq). Then the mixture was stirred at 20 °C for 2 hours. The reaction solution was concentrated in vacuum. The residue was purified by reversed phase flash chromatography to give the corresponding pure enoic acid. NMR data of **1h**[29], **1i**[29], **1j**[29], **1p**[27] **1q**[32]were correspond to the reported values.

**4-(4-(methylsulfonyl)phenyl)pent-4-enoic acid** (**1k**)

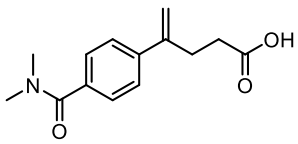



**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H), 7.59 – 7.54 (m, 2H), 5.43 (s, 1H), 5.26 (t, *J* = 1.6 Hz, 1H), 3.06 (s, 3H), 2.88 – 2.83 (m, 2H), 2.56 – 2.49 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 178.59, 146.28, 145.21, 139.47, 127.72, 127.15, 116.16, 44.62, 32.71, 29.88.

**HRMS-ESI(m/z)** calc'd for $[C_{12}H_{14}O_4S+Na]^+$, 277.0505; found, 277.0506.

**4-(4-(dimethylcarbamoyl)phenyl)pent-4-enoic acid** (**1l**)

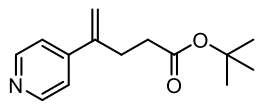



**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.85 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 5.31 (s, 1H), 5.10 (d, *J* = 1.2 Hz, 1H), 3.08 (s, 3H), 2.97 (s, 3H), 2.78 (t, *J* = 7.9 Hz, 2H), 2.44 (dd, *J* = 8.8, 6.7 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 177.17, 171.81, 145.98, 142.00, 134.87, 127.34, 126.05, 113.86, 39.74, 35.57, 32.88, 30.04.

**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{17}NO_3+Na]^+$, 270.1101; found, 277.1100.

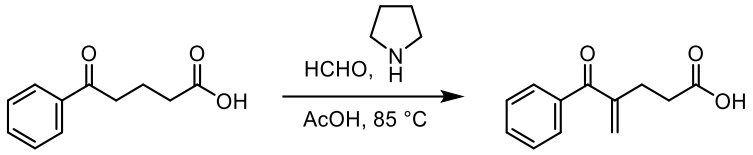
***tert*-butyl 4-(pyridin-4-yl)pent-4-enoate** (precursor of **1m**)



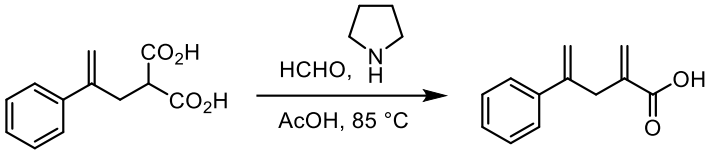

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.54 (dd, *J* = 4.5, 1.7 Hz, 2H), 7.27 (dd, *J* = 4.5, 1.7 Hz, 2H), 5.46 (s, 1H), 5.22 (t, *J* = 1.7 Hz, 1H), 2.75 (ddd, *J* = 7.8, 6.7, 1.5 Hz, 2H), 2.37 (dd, *J* = 8.6, 6.7 Hz, 2H), 1.41 (s, 8H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 172.06, 150.06, 148.18, 144.88, 120.82, 115.71, 80.65, 34.03, 29.61, 28.13.

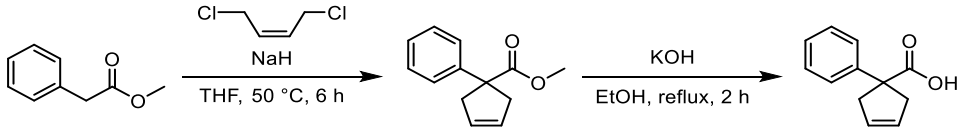
**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{19}NO_2+H]^+$, 234.1489; found, 234.1486.




To a solution of keto acid (3.0 mmol, 1.0 eq) in acetic acid (6 mL) was added pyrrolidine (0.1 mL, 1.2 mmol, 0.4 eq) and formaldehyde solution (36.5-38% in $H_2O$, 1 mL, 13.2 mmol, 4.4 eq) at room temperature. The mixture was then stirred for 48 h at 85 °C. After evaporation of acetic acid, water and EtOAc were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the corresponding α, β-unsaturated ketone **1s** as a yellow solid. NMR data correspond to the reported value.[33]



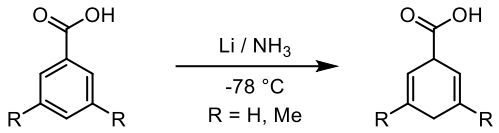

To a solution of di-acid (3.0 mmol, 1.0 eq.) in acetic acid (6 mL) was added pyrrolidine (0.1 mL, 1.2 mmol, 0.4 eq.) and formaldehyde solution (36.5-38% in $H_2O$, 1 mL, 13.2 mmol, 4.4 eq.) at room temperature. The mixture was then stirred for 24 h at 85 °C. After evaporation of acetic acid, water and EtOAc were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the corresponding enoic acid. NMR data correspond to the reported value.[34]




To a cooled (0 °C) solution of methyl phenylacetate (6.0 g, 39.6 mmol) in THF (80 mL) and *N*,*N*'-dimethylpropyleneurea (20 mL) was carefully added NaH (1.9 g, 79.7 mmol) and the mixture was stirred at 50 °C. After 2 h, the resultant mixture was allowed to cool to room temperature, and cis-1,4-dichloro-2-butene (5.2 mL, 47.3 mmol) was added dropwise. The resultant mixture was then stirred at 50 °C for 3 h. After cooling to room temperature, the mixture was quenched with saturated ammonium chloride and extracted with ethyl acetate (2 × 25 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated under reduced pressure. Flash chromatography on silica gel (97:3 hexanes:ethyl acetate) affords the corresponding ester as a yellow oil.

To a carboxylate ester was added a solution of KOH 1 M in ethanol (5 equiv.), and the reaction was heated at reflux for 2 h. The reaction mixture was cooled to rt and partially concentrated under reduced pressure. The residue was added water and extracted twice with dichloromethane. The aqueous layer was acidified until pH = 1 with HCl (3M) and extracted twice with dichloromethane. The combined organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure to afford the corresponding carboxylic acid. NMR data correspond to the

reported value.[35]



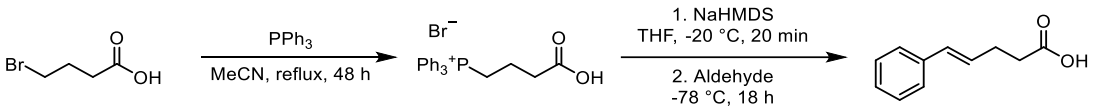

Benzoic acid (7.0 g, 57.3 mmol) was charged in a flame dried 250 mL three neck flask. One of the necks was connected to nitrogen inlet at atmospheric pressure while a condenser was attached to the center neck. The flask was purged with nitrogen for 1-2 min while rested in a -78 ºC bath (acetone/dry ice). The third neck of the flask was then closed with a glass adapter and ammonia gas was condensed until the total volume was 100 mL. To a vigorously stirred solution of benzoic acid in liquid ammonia was added 1.19 g (172.0 mmol, 3.0 equiv.) of lithium (cut into small pieces prior to addition) in portions over a period of 30 min. After the addition was complete, the solution was stirred for another 30 min and quenched carefully by addition of solid ammonium chloride (~15 g) until the solution turned into a white gel. The flask was gradually warmed to room temperature over 20 min while the ammonia was removed under a stream of nitrogen gas. The resulting solid residue (free of ammonia) was dissolved in distilled water (30 mL) and cooled on an icewater bath. The solution was acidified to pH=2 using concentrated HCl (12 M). The product was extracted in dichloromethane (3 × 20 mL). The organics were separated, dried over anhydrous $Na_2SO_4$, filtered, concentrated. Pure **1y** was obtained as colorless oil in 98% yield (8.1 g). It was used immediately for further steps without prolonged storage. NMR data correspond to the reported value.[13]

*Note: Compound **1y** undergoes rapid oxidation at room temperature. It can be stored as a frozen solution in argon purged benzene at -80 ºC for about 2-3 weeks.*

Commercially available 3,5-dimethylbenzoic acid was recrystallized from hot ethyl acetate and dried prior to use. 3,5-Dimethylbenzoic acid (5.0 g, 33.0 mmol) was charged in a flame dried 250 mL three neck flask. One of the necks was connected to nitrogen inlet at atmospheric pressure while a condenser was attached to the center neck. The flask was purged with nitrogen for 1-2 min while rested in a -78 ºC bath (acetone/dry ice). The third neck of the flask was then closed with a glass adapter and ammonia gas was condensed until the total volume was 150 mL. To a vigorously stirred suspension of 3,5-dimethylbenzoic acid in liquid ammonia was added sodium (3.0 g, 130.4 mmol, 4.0 equiv.), in portions over a period of 30 min (part of the sodium clumps were cut into smaller pieces and immediately added). After the addition was complete, the solution was stirred for another 30 min and quenched carefully by addition of solid ammonium chloride (~12 g) at -78 ºC until the solution turned into a white gel. The flask was gradually warmed to room temperature over 20 min while the ammonia was removed under a stream of nitrogen gas. The resulting solid residue (free of ammonia) was dissolved in distilled water (30 mL) and cooled on an ice-water bath. The solution was acidified to pH=2 using concentrated HCl (12 M). The product was extracted in dichloromethane (3 × 20 mL). The organics were separated, dried over anhydrous $Na_2SO_4$, filtered, and concentrated. The crude white solid was recrystallized from hot ethyl acetate to yield 4.51 g of pure 1t as a crystalline white solid (89% yield). Crystalline **1z** (devoid of impurities) can be stored in a freezer at -20 ºC under argon atmosphere for over a year without any traces of re-aromatization. NMR data correspond to the reported value.[13]

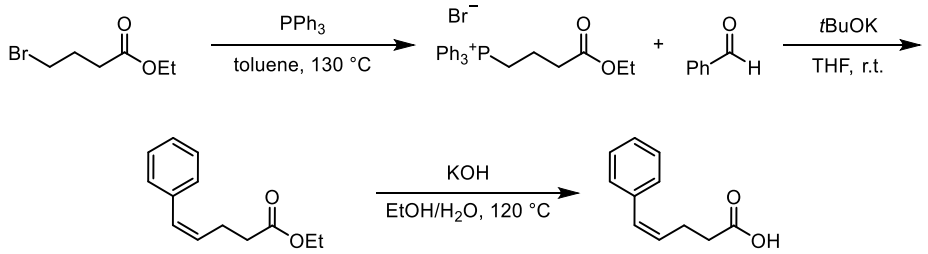
*Note: If the commercially available 3,5-dimethylbenzoic acid is not purified prior to use, **1z** is obtained as a yellowish solid. The resulting impurities can then be removed by multiple*

*recrystallizations from hot ethyl acetate, however with a significant drop in isolated yield.*



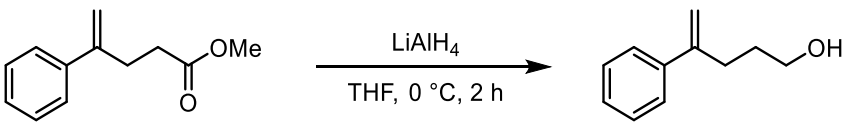

A mixture of 4-bromobutyric acid (8.38 g, 50 mmol, 1.0 eq) and triphenylphosphine (13.11 g, 50 mmol, 1.0 eq) was heated at reflux temperature in MeCN (60 mL) for 48 h. Upon termination, the solvent was removed in vacuo. The residue was washed with DCM (50 mL), filtered and washed with more DCM (3 × 50 mL) to afford (3-carboxypropyl)triphenylphosphonium bromide.

(3-Carboxypropyl)triphenylphosphonium bromide (924 mg, 2.16 mmol, 1.08 eq) was suspended in THF (12 mL) at -20 °C. NaHMDS (2.16 mL, 4.32 mmol, 2.16 eq) was added dropwise into the suspension and further stirred for 20 min. The reaction mixture was then cooled to -78 °C and the benzaldehyde (2.0 mmol, 1.0 eq) was added. After 18 h, the solvent was removed in vacuo. $H_2O$ (60 mL) was added to the residue and extracted with diethyl ether (3 × 20 mL). The diethyl ether layers were discarded while the $H_2O$ layer was acidified to pH 2 using HCl (1 M). The acidified aqueous layer was further extracted with ethyl acetate (3 × 20 mL). The organic layers were combined, dried over sodium sulfate, filtered and concentrated to dryness. The alkenoic acid was purified over silica gel using ethyl acetate:hexane (1:1). NMR data correspond to the reported value.[37]

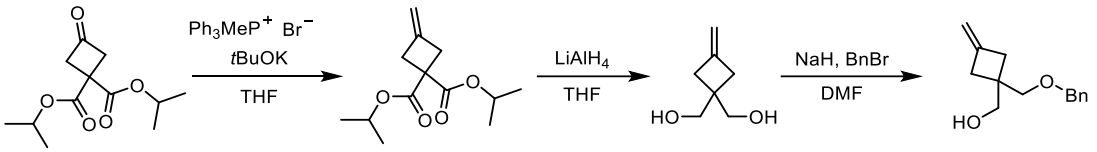



A solution of ethyl-4-bromobutyrate (2.9 mL, 20 mmol) and triphenylphosphine (5.3 g, 20 mmol) in toluene (25 mL) was stirred at 130 °C for 12 h. After the solution was cooled to ambient temperature, white precipitates were collected and then dissolved in DCM. To the resulting solution was added $Et_2O$ until the precipitates disappeared, and DCM was then remomved under reduced pressure. Subsequently, the precipitates were collected to give (4-ethoxy-4-oxobutyl)triphenylphosphonium bromide as a white solid in 49% yield (4.4 g).

A mixture of (4-ethoxy-4-oxobutyl)triphenylphosphonium bromide (4.3 g, 9.5 mmol) and potassium tert-butoxide (1.1 g, 9.5 mmol) in THF (20 mL) was stirred at 0 ºC for 30 min. The resulting mixture was allowed to warm to ambient temperature and stirred for additional 1 h. The solution was again cooled to 0 ºC, and benzaldehyde (0.80 mL, 7.9 mmol) was added dropwise. The solution was stirred at ambient temperature for 5 h. The resulting mixture was quenched with $H_2O$, and then the aqueous layers were extracted with $Et_2O$ (20 mL × 3). The organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residual oil was purified by flash silica gel column chromatography using hexane/EtOAc (v/v = 10:1) to afford ethyl (*Z*)-5-phenylpent-4-enoate as a white solid in 46% yield (0.74 g). NMR data correspond to the reported value.[37]



To a solution of ester (1.0 mmol, 1.0 eq) in THF (10 mL) was added $LiAlH_4$ (76 mg, 2.0 mmol, 2.0 equiv.) at 0 °C under $N_2$. The resulting mixture was stirred at 0 °C for 10 min and then was warmed to 25 °C and stirred for another 3 h. After TLC revealed the absence of the starting material, the reaction was quenched with crushed ice (ca. 300 mg) at 0 °C. The mixture was further stirred for 2 h and filtered through a thin pad of silica gel and eluted with EtOAc (20 mL). The filtrate was concentrated in vacuo and purified by a short column (hexane/EtOAc 3:1) to give alcohol. NMR data correspond to the reported value.[38]

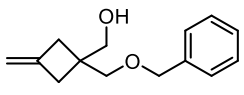



To a suspension of methyltriphenylphosphonium bromide (970 mg, 2.72 mmol) in THF (8 mL) at 0 °C was added potassium *tert*-butoxide (1.0 M/THF) (2.72 mL, 2.72 mmol). The ice bath was removed and the reaction mixture was stirred at room temperature for 1h. The resulting yellow solution was cooled to 0 °C and a solution of diisopropyl 3-oxocyclobutane-1,1-dicarboxylate (506 mg, 2.09 mmol,) in THF (4 mL) was added dropwise via cannula. The ice bath was removed and the reaction mixture was stirred at room temperature for 1.5 h. The reaction was quenched with saturated $NH_4Cl$ and extracted with EtOAc. The organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (0-50% EtOAc/hexanes). The product was not dried under high vacuum due to volatility.

To a solution of diisopropyl 3-methylenecyclobutane-1,1-dicarboxylate (502 mg, 2.09 mmol) in THF (6 mL) at 0 °C was added a solution of lithium aluminum hydride (2.0 M/THF, 3.13 mL, 6.27 mmol) dropwise. The reaction mixture was warmed to room temperature and stirred for 0.5 h. The reaction mixture was diluted with ether and cooled to 0 °C. The reaction was quenched by the careful addition of 0.24 mL of $H_2O$, followed by 0.24 mL of 15% NaOH, and finally 0.72 mL of $H_2O$. The resulting mixture was warmed to room temperature and stirred for 15 min. Magnesium sulfate was added and the solids were filtered off. The filter cake was washed with ether and the filtrate was concentrated to afford the product as a colorless oil (180 mg, 67%) that was used without purification.

Sodium hydride (60% dispersion in oil, 1.1 equiv.) was washed in triplicate with hexanes. After decanting the solvent, dry DMF was added (0.7 M). The mixture was cooled to 0 ºC, and diol (1.0 equiv.) was added slowly. After stirring for 10 min, benzyl bromide (1.0 equiv.) was added cautiously. The mixture was allowed to acclimate to room temperature and stirred for 18 h. The reaction was quenched upon addition of water (100 mL) and subsequently extracted with EtOAc (6 × 30 mL). The organic layer was dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure to afford a yellow oil. Flash chromatography (25% EtOAc/hexane) gave the product **3d**.

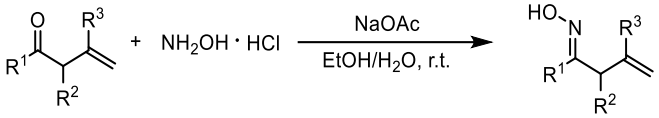
**(1-((benzyloxy)methyl)-3-methylenecyclobutyl)methanol** (**3d**)



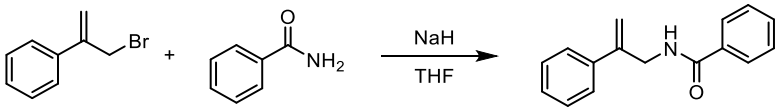

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 4.85 (p, *J* = 2.4 Hz, 2H), 4.54 (s, 2H), 3.71 (s, 2H), 3.60 (s, 2H), 2.68 (s, 1H), 2.56 – 2.48 (m, 2H), 2.48 – 2.39 (m, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 144.25, 138.01, 128.60, 127.90, 127.71, 108.33, 73.68, 69.05, 38.62, 37.18.

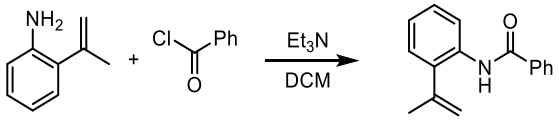
**HRMS-ESI(m/z)** calc'd for $[C_{14}H_{18}O_2+Na]^+$, 241.1199; found, 241.1205.



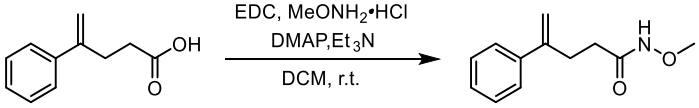

To a solution of hydroxylamine hydrochloride (5 equiv.) in water was added a solution of sodium acetate (7 equiv.) in ethanol. The mixture was stirred at room temperature while the unsaturated ketone (1 equiv.) was added as a solution in ethanol. The mixture wasstirred overnight and concentrated in vacuo. Then, the mixture was extracted with ethyl acetate 3 times and the combined extracts were washed with water and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford the unsaturated oxime. NMR data correspond to the reported value.[40,41]



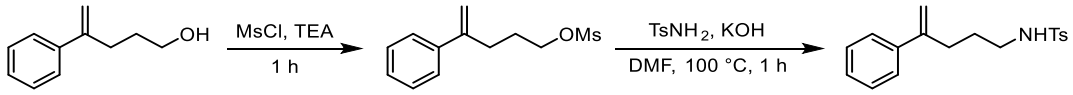

A solution of benzamide (532 mg, 4.40 mmol) in dry THF (10 mL) was added slowly to a suspension of NaH (320 mg, 8.00 mmol, 60% in oil) and the resulting mixture was stirred at room temperature for 1 h. The resulting bright yellow suspension was cooled to 0 °C and a solution of the corresponding bromide (4.00 mmol) in dry THF (4 mL) was added dropwise. Then, the reaction was warmed to room temperature overnight with stirring. The resulting solution was poured into an ice/water mixture (10 mL) and extracted with $Et_2O$ (3 × 20 mL). The combined organic extracts were washed with brine (2 × 15 mL), dried $MgSO_4$, and the filtrate was concentrated in vacuo and purified by silica gel chromatography (10% EtOAc in hexane) to afford the corresponding products. NMR data correspond to the reported value.[42]




In a 100 mL single-neck flask, o-propenyl aniline (0.99 g, 7.4 mmol) and triethylamine (1.53 g, 11.1 mmol) were dissolved in 15 mL of dichloromethane. Under an ice bath, a dichloromethane solution of benzoyl chloride (1.0 mL, 8.9 mmol) was slowly added dropwise. The reaction was completed in about 1 hour. After silica gel column chromatography, the corresponding amide (3.89 g) was obtained. NMR data correspond to the reported value.[43]

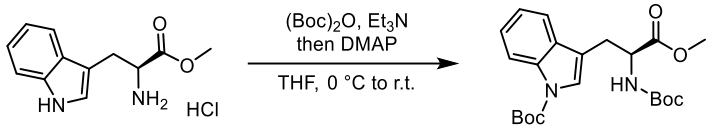



4-Phenylpent-4-enoic acid (2.0 g, 11.35 mmol) was added to a solution of EDC (3.26 g, 17 mmol) in DCM (114 mL) at 0 ºC. The mixture was stirred for 10 min and DMAP (139 mg, 1.13 mmol), methoxyamine hydrochloride (1.14 g, 13.6 mmol) and $Et_3N$ (3.95 mL, 28.4 mmol.) were added. The resulting mixture was stirred until starting material was consumed. Then, $NH_4Cl$ (sat.) (50 mL) was added and the aqueous phase was extracted with DCM (3 × 50 mL). The organic layers were dried, filtered, concentrated and purified by flash chromatography to give N-methoxy-4-phenylpent-4-enamide. NMR data correspond to the reported value.[44]

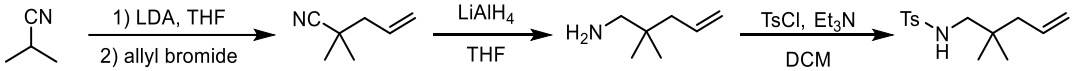


To a solution of alcohol F (1.0 mmol, 1.0 eq) and triethylamine (418 µL, 3.0 mmol, 3.0 eq) in DCM (5 mL) was added MsCl (116 µL, 1.5 mmol, 1.5 eq) at 0 °C. The resulting mixture was stirred at 0 °C for 10 min and then was warmed to 25 °C and stirred for another 2 h. After TLC revealed the absence of the starting material, the reaction was quenched with water (4 mL) and extracted with DCM (3 × 5 mL). The combined organic extracts were dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by flash column chromatography (hexane/EtOAc 3:1) to give the corresponding product.

A solution of $TsNH_2$ (256 mg, 1.5 mmol, 1.5 eq) and KOH (84 mg, 1,5 mmol, 1.5 eq) in DMF (5 mL) was stirred at 100 °C for 0.5 h. Then to the mixture was added a solution of 4-phenylpent-4-en-1-yl methanesulfonate (1.0 mmol, 1.0 eq) in DMF (1 mL) dropwise. After addition the mixture was stirred at 100 °C for 1 h and was cooled to 25 °C. The reaction mixture was diluted with water (10 mL) and extracted with $Et_2O$ (3 × 15 mL). The combined organic extracts were washed with water (3 × 10 mL) and brine, dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by flash column chromatography (DCM/hexane 2:1 to pure DCM) to give the desired product. NMR data correspond to the reported value.[38]




To a magnetically stirred ice-cold solution of HCl salt of *L*-Trp-OMe (8 g, 31.4mmol,1.0 equiv.) and $Et_3N$ (6.6 mL,47.4 mmol,1.5 equiv.) in dry DCM (150 mL) was added Boc anhydride (7.3 mL, 31.7mmol, 1.0equiv) dropwise. The resulting mixture was stirred at room temperature overnight. After 12 h, the solvent was washed with 1 N HCl, washed with brine, and finally dried over anhydrous $Na_2SO_4$. To a magnetically stirred ice-cold solution of the above crude product and DMAP (3.84g, 31.4mmol,2 equiv.) in dry THF (100 mL) was added Boc anhydride (7.2 mL,31.4 mmol,1.0 equiv.) dropwise. The resulting mixture was stirred at room temperature overnight. After12 h, the solvent was evaporated under reduced pressure. The resultant residue was dissolved in ethyl acetate, washed with 1 N aq. HCl, washed with brine, and finally dried over anhydrous sodium sulfate. The product was purified by column chromatography (ethylacetate/hexanes) as thick colorless oil. NMR data correspond to the reported value.[45]

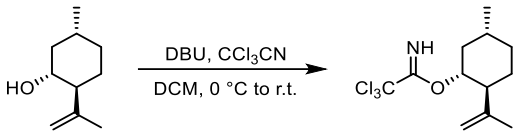



Isobutyronitrile (2.674 g, 40 mmol) was added to a solution of LDA (48 mmol) in THF (100 mL) at 0 ºC. After stirring 2 h at 0 ºC, allyl bromide (4.18 mL, 48 mmol) in THF (20 mL) was added. The reaction was treated with water (20 mL) after 3 h and extracted with diethyl ether (3 × 50 mL). The organic layers were combined, washed with brine and dried with $MgSO_4$. Evaporation of the solvent gave nitrile alkene product (4.0 g, crude), which was used directly in the next step.

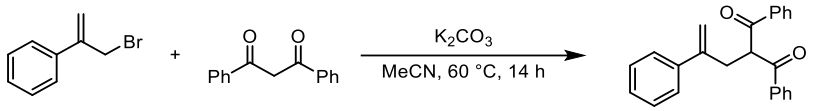
Nitrile alkene (4.0 g, crude) in diethyl ether (80 mL) was treated with $LiAlH_4$ (3.04 g, 80 mmol) at room temperature. The reaction was refluxed for 2 h and then cooled in an ice bath. Water (3.04 mL), 15% aqueous NaOH (3.04 mL) and water (9.12 mL) was slowly added to the reaction. The reaction mixture was stirred at room temperature for 15 minutes, and the solid was filtered off. Evaporation of the filtrate gave amine (3.66 g, 32.4 mmol) in 81% yield (over 2 steps).

A mixture of amine (1.44 g, 12.7 mmol) and triethylamine (3.48 mL, 25 mmol) in DCM (40

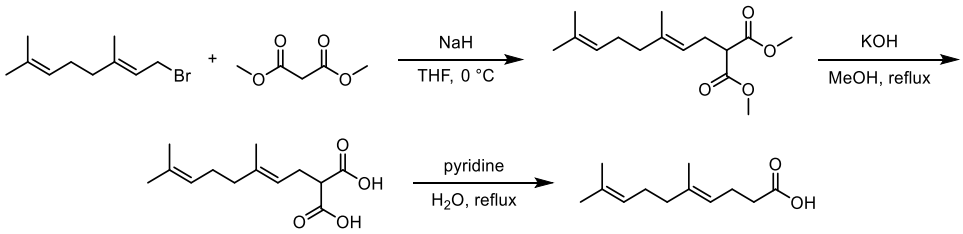
mL) was treated with TsCl (2.29 g, 12 mmol) at 0 ºC. The reaction was stirred at room temperature for 12 h. The mixture was washed with 10% $NaHCO_3$ (30 mL), brine (30 mL) and dried with $MgSO_4$. The solvent was evaporated and the residue was purified through silica gel flash column chromatography (eluent: hexanes: ethyl acetate= 5:1) to give the desired product (3.05 g, 11.4 mmol) in 90% yield. NMR data correspond to the reported value.[46]




To a stirred mixture of alcohol (10 mmol, 1 equiv.) in 20 mL of dichloromethane, was added trichloroacetonitrile (1.5 mL, 15 mmol, 1.5 equiv.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1.5 mL, 110 mmol, 1.0 equiv.). The resulting reaction mixture was continuously stirred at room temperature. After 12 h, the reaction mixture was diluted with water, the aqueous phase was separated and extracted with dichloromethane. The combined organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography with triethylamine-treated silica gel using 3% of triethylamine in hexane as eluent to give the desired product. NMR data correspond to the reported value.[38]




$K_2CO_3$ (308.14 mg, 2.0 equiv, 2.23 mmol) was added to a stirred solution of 1,3-diphenylpropane-1,3-dione (250 mg, 1.0 equiv, 1.11 mmol) in 6 mL of MeCN at room temperature for 20 minutes. Then, (3-bromoprop-1-en-2-yl)benzene (230.67 mg, 1.1 equiv, 1.11 mmol) was added to the mixture. Later heated the reaction mixture at 60°C for 14 h. After the completion of reaction on TLC, the reaction mixture was cooled to RT diluted with water and extracted with ethyl acetate. The combined organic layer was dried over $Na_2SO_4$, filtered and concentrated then purified by column chromatography using hexane/ ethyl acetate (96:4) as the eluent to give 1,3-diphenyl-2-(2-phenylallyl)propane-1,3-dioneas a colorless liquid in 82% yield (309 mg). NMR data correspond to the reported value.[47]

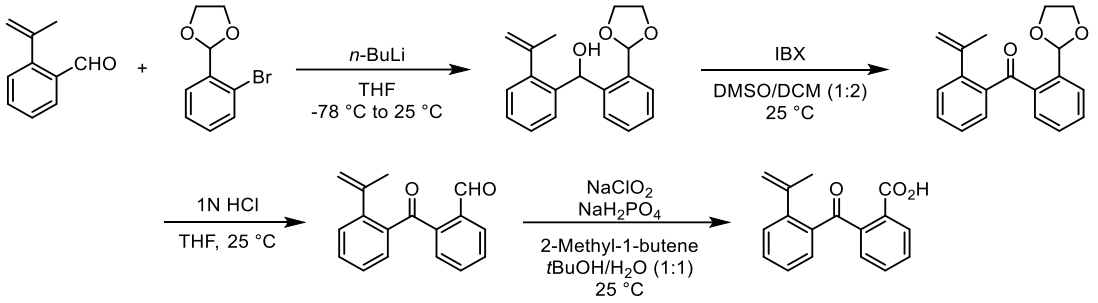



Solid NaH (60% dispersion in mineral oil, 477 mg, 11.9 mmol) was added to a stirred solution of dimethyl malonate (1.35 mL, 11.5 mmol) in THF (25 mL) at 0 °C and the reaction was allowed to stir for 30 min. Geranyl bromide (1.09 mL, 9.44 mmol) then was added dropwise to the reaction. The resulting mixture was allowed to stir overnight while slowly warming to rt and subsequently was quenched by addition of saturated $NH_4Cl$. The resulting mixture was extracted with EtOAc (3 times), dried ($Na_2SO_4$), and filtered, and the filtrate was concentrated in vacuo. Final purification by flash column chromatography (3% EtOAc in hexanes) afforded diester (1.53 g, 81%) as a yellow oil.

To a stirred solution of dimethyl ester (1.27 g, 6.36 mmol) in MeOH (24 mL), 5 N KOH (3.8

mL, 19.0 mmol) was added. The resulting solution was heated at reflux for 1 h, and the solvent then was removed in vacuo. The resulting residue was dissolved in $H_2O$, acidified with 2 N HCl to pH=2, and extracted with $Et_2O$ (4 times). The combined organicextracts were dried ($Na_2SO_4$), filtered, and concentrated in vacuo to provide dicarboxylic acid (905 mg, 83%) as a pale yellow solid, which was used without further purification.

A stirred solution of dicarboxylic acid (1.46 g, 8.47 mmol) in pyridine (3.4 mL) and $H_2O$ (0.15 mL) was heated at reflux for 2 h. The reaction miture then was allowed to cool to rt, diluted with $H_2O$, acidified with2 N HCl to pH 2, and extracted with DCM (5 times). The combined organic extracts were dried ($Na_2SO_4$), filtered, and concentrated in vacuo to afford the desired monocarboxylic acid. NMR data correspond to the reported value.[48]




To a solution of 2-(2-bromophenyl)-1,3-dioxolane (3.3 mmol) in THF (3.0 mL) was added *n*-BuLi (2.4 M in hexane, 1.5 mL, 3.6 mmol) dropwise over 30 minutes at -78 °C. After 30 minutes, a solution of 2-(prop-1-en-2-yl)benzaldehyde (3.0 mmol) in THF (3.0 mL) was added dropwise over 30 minutes at -78 °C. The resultant mixture was stirred for 6 hours at 25 °C. Then, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution and was extracted with ethyl acetate (10 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was loaded on a thin plug of silica gel and eluted with hexane/ethyl acetate (5: 1) to yield (2-(1,3-dioxolan-2-yl)phenyl)(2-(prop-1-en-2-yl)phenyl)methanol, which was directly used in the next step without further purification.

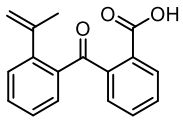
To a solution of (2-(1,3-dioxolan-2-yl)phenyl)(2-(prop-1-en-2-yl)phenyl)methanol (2.0 mmol) in DMSO:DCM (1:2 v/v, 5.0 mL) was added 2-iodoxybenzoic acid (IBX, 4.0 mmol) portionwise at 25 °C. The resultant mixture was stirred for 12 hours. Then, the reaction mixture was filtered through a thin plug of celite and the filtrate was concentrated under reduced pressure. The residue was loaded on a thin plug of silica gel and eluted with hexane/ethyl acetate (10: 1) to yield (2-(1,3-dioxolan-2-yl)phenyl)(2-(prop-1-en-2-yl)phenyl)methanone, which was directly used in the next step without further purification.

To a solution of (2-(1,3-dioxolan-2-yl)phenyl)(2-(prop-1-en-2-yl)phenyl)methanone (1.8 mmol) in THF (2.0 mL) was added 1 N HCl solution (3.6 mL). The resultant mixture was stirred for 12 hours. Then, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate (10 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting crude 2-(2-(prop-1-en-2-yl)benzoyl)benzaldehyde was used in next step without further purification.

To a solution of 2-(2-(prop-1-en-2-yl)benzoyl)benzaldehyde (1.5 mmol) in *t*-BuOH (3.0 mL) was added 2-methy-2-butene (27.0 mmol), water (3.0 mL), $NaH_2PO_4$ (12.0 mmol), and $NaClO_2$ (6.0 mmol) sequentially. The resultant mixture was stirred for 12 hours. Then the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution and extracted with ethyl acetate (10 mL × 3).

The combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography (hexane/ethyl acetate/acetic acid 100: 20: 1) to afford **9c**.

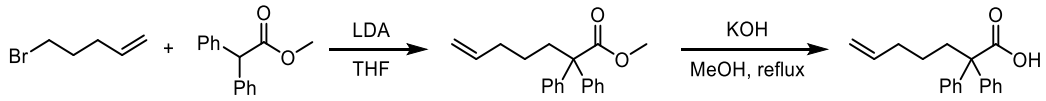
**2-(2-(prop-1-en-2-yl)benzoyl)benzoic acid** (**9c**)



**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.51 (s, 1H), 7.97 – 7.89 (m, 1H), 7.61 – 7.53 (m, 2H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.40 (td, *J* = 6.0, 2.7 Hz, 2H), 7.32 – 7.26 (m, 2H), 5.10 – 4.98 (m, 1H), 4.91 (s, 1H), 2.01 (s, 3H).

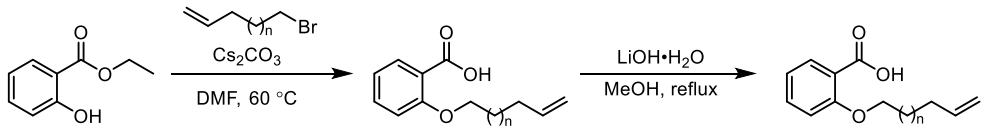
**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 197.66, 172.14, 146.02, 145.09, 142.01, 136.06, 132.14, 131.97, 131.37, 130.44, 130.00, 129.56, 129.34, 126.92, 115.82, 23.53.

**HRMS-ESI(m/z)** calc'd for $[C_{17}H_{14}O_3+Na]^+$, 289.0836; found, 289.0836.




To a solution of diisopropylamine (4.0 mL, 28.7 mmol) in THF (37 mL) was added *n*-butyllithium (16.1 mL, 26.5 mmol) at 0ºC. After being stirred for 20 minutes at same temperature, a solution of methyl diphenylacetate (5.00 g, 22.1 mmol) in THF (37 mL) was added at -78 ºC. After being stirred for 15 minutes at same temperature, 5-bromo-1-pentene was added at -78ºC. After being stirred for 15hours at room temperature, the reaction mixture was quenched by the addition of saturated ammonium chloride aq and concentrated in vacuo. The aqueous portion was extracted with ethyl acetate. The organic portion was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by flash column chromatography to give ester.

To a carboxylate ester was added a solution of KOH 1 M in ethanol (5 equiv.), and the reaction was heated at reflux for 2 h. The reaction mixture was cooled to rt and partially concentrated under reduced pressure. The residue was added water and extracted twice with dichloromethane. The aqueous layer was acidified until pH = 1 with HCl (3M) and extracted twice with dichloromethane. The combined organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure to afford the corresponding carboxylic acid. NMR data correspond to the reported value.[49]

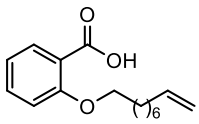



Ethyl salicylate (2.0 g, 12 mmol) was dissolved in anhydrous DMF (20 mL) and treated with $Cs_2CO_3$ (19.6 g, 60 mmol). Allyl bromide (1.53 mL, 18 mmol) was added and the mixture was stirred at 60 °C for 4 h. The reaction was quenched with 1M HCl and extracted with EtOAc (3 × 20 mL). The combined organics were washed with $H_2O$ (15 mL), brine (15 mL), dried over $MgSO_4$, filtered and concentrated. Flash column chromatography, eluting with EtOAc/PE (0-10 %) afforded ester as a clear oil.

The ester (3.0 g, 15 mmol) was dissolved in MeOH (10 mL). An aqueous solution of LiOH (11 mL, 8M) was added and the mixture allowed to stir for 12 h. The reaction was quenched with 10% citric acid (15 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), $H_2O$ (10 mL), dried over $MgSO_4$ and concentrated. Then

purified the residue by column chromatography. NMR data of **11d**[50], **11h**[50], **11i**[50], **11j**[51], **11k**[51] correspond to the reported value.

**2-(non-8-en-1-yloxy)benzoic acid** (**11l**)

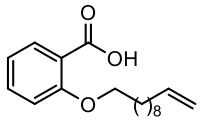


**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.16 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.64 – 7.48 (m, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 5.78 (ddt, *J* = 16.9, 9.8, 6.7 Hz, 1H), 5.03 – 4.88 (m, 2H), 4.23 (t, *J* = 6.6 Hz, 2H), 2.03 (q, *J* = 6.8 Hz, 2H), 1.90 (p, *J* = 6.9 Hz, 2H), 1.47 (p, *J* = 7.0 Hz, 2H), 1.35 (tt, *J* = 14.0, 11.1, 4.4 Hz, 7H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 165.59, 157.65, 139.01, 135.13, 133.78, 122.17, 117.65, 114.42, 112.64, 70.29, 33.76, 29.09, 28.79, 25.87.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{22}O_3+Na]^+$, 285.1462; found, 185.1465.

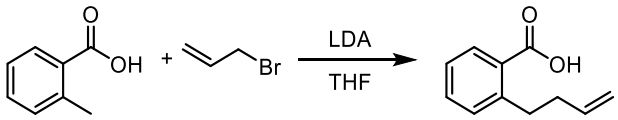
**2-(undec-10-en-1-yloxy)benzoic acid** (**11m**)



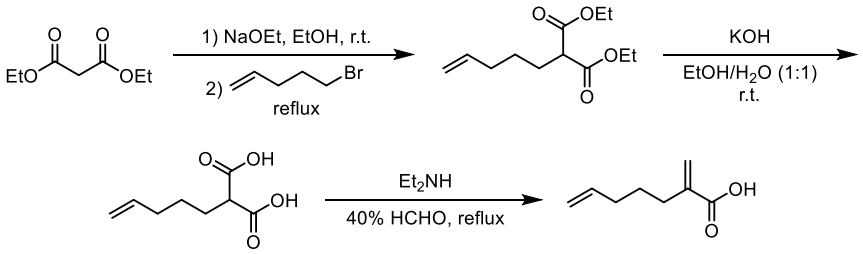
**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 10.40 (s, 1H), 8.12 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.51 (ddd, *J* = 8.8, 7.3, 1.9 Hz, 1H), 7.14 – 6.93 (m, 2H), 5.77 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.02 – 4.79 (m, 2H), 4.21 (t, *J* = 6.6 Hz, 2H), 2.00 (tdd, *J* = 8.1, 6.0, 1.5 Hz, 2H), 1.87 (dt, *J* = 14.8, 6.7 Hz, 2H), 1.50 – 1.40 (m, 2H), 1.36 – 1.22 (m, 10H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 165.69, 157.63, 139.10, 135.06, 133.58, 121.98, 117.54, 114.16, 112.63, 70.21, 33.76, 29.35, 29.32, 29.16, 29.03, 28.86, 25.83.

**HRMS-ESI(m/z)** calc'd for $[C_{18}H_{26}O_3+Na]^+$, 313.1775; found, 313.1781.




To a solution of 2-methylbenzoic acid (3.0 g, 22.03 mmol, 1.0 equiv.) in anhydrous THF (20 mL) at 0 ºC under N2 atmosphere, LDA (27.5 mL, 55.09 mmol, 2.5 equiv. 2.0 M solution in THF/n-heptane/ethylbenzene) was added dropwise over 10 minutes. The resulting mixture was stirred at 0 °C for 3 h, and then allyl bromide (6.66 g, 55.09 mmol, 2.5 equiv.) was added slowly. The reaction mixture was stirred at room temperature for overnight, then it was quenched with water slowly. After acidified with 1 M HCl to pH 1, the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine, dried with $Na_2SO_4$, filtered and concentrated under vacuum. Then purified the residue by column chromatography to give 2-(but-3-en-1-yl)benzoic acid. NMR data correspond to the reported value.[52]

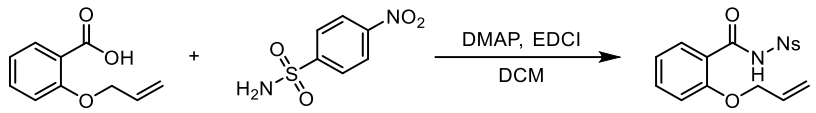



To a 250-mL, three-necked, round-bottomed flask equipped with a reflux condenser and magnetic stir bar was charged with dry ethanol (150 mL). Under a stream of argon, sodium metal (2.2 g, 95.7 mmol), pre-washed with dry n-hexane, was added in several small portions over 5 min. The mixture was then heated to reflux until all the sodium metal was dissolved. The resulting NaOEt/EtOH solution was cooled to room temperature, and diethyl malonate (13.0 mL, 85.2

mmol) was added through a syringe. After stirring for 30 min, the reaction mixture was slowly added 4-bromo-1-butene (9.7 mL, 95.7 mmol). Upon addition, some white precipitates were formed, and heat was generated gradually. After the addition, the reaction mixture was heated to reflux. After 6 h, the mixture was cooled, and EtOH was removed by rotary evaporation. The yellow residue was taken up with 5% aqueous HCl (60 mL), and extracted with diethyl ether (60 mL × 2). The combined organic layers were washed with brine (60 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography to give corresponding product (16.1 g, 75.0 mmol, 88% yield) as a yellow oil.

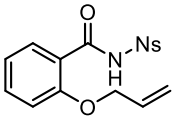
In a 250-mL Erlenmeyer flask equipped with a magnetic stir bar, potassium hydroxide (2.7 g, 48.6 mmol) was dissolved in a 1:1 mixture of EtOH/$H_2O$ solution (80 mL). After 5 min, malonate (2.6 g, 12.1 mmol) was transferred to the stirring mixture with EtOH (5 mL). The mixture was stirred vigorously at room temperature. After 10 h, the mixture was diluted with 50 mL of water, and EtOH was removed under vacuum. After cooling down the aqueous residue to room temperature, the basic solution was washed with diethyl ether once (60 mL). Over an ice-water bath, the aqueous layer was acidified with 10% HCl solution until a milky appearance was observed (pH paper indicated pH value < 2). The acidic solution was washed with diethyl ether (80 mL × 3). The combined organic layers were further washed with brine (80 mL), and concentrated in vacuo (below 30 °C) to afford the diacid intermediate as a white solid.

In a 50-mL round-bottomed flask, the diacid was taken up with 40% formaldehyde solution (30 mL). Over an ice-water bath, diethylamine (1.3 mL, 12.1 mmol) was added with stirring. After 5 min, the reaction flask was assembled with a water condenser, and the reaction mixture was heated to reflux. After 12 h, the mixture was cooled down to room temperature, and was added DCM (50 mL) and saturated $NaHCO_3$ solution (40 mL). The organic layer was further extracted with saturated $NaHCO_3$ solution (40 mL × 2). The combined aqueous layers were acidified with 6, HCl solution until a milky appearance was observed (pH paper indicated pH value < 2). The acidic solution was washed with diethyl ether (50 mL × 3). The combined organic layers were further washed with water (50 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to afford acrylic acid (0.95 g, 7.5 mmol) as a yellow oil. NMR data correspond to the reported value.[53]




A mixture of acid (18 mmol), $NsNH_2$ (18 mmol), EDC•HCl (23 mmol), and DMAP (27 mmol) in anhydrous DCM (10 mL) was stirred at room temperature overnight. The crude product obtained was purified by column chromatography to afford compound **11g**.

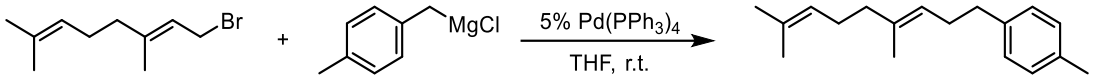
**2-(allyloxy)-*N*-((4-nitrophenyl)sulfonyl)benzamide** (**11g**)



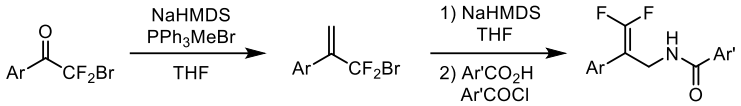

**$^1$H NMR** (400 MHz, DMSO-$d_6$) δ 12.41 (s, 0H), 8.47 (d, $J$ = 8.8 Hz, 1H), 8.24 (d, $J$ = 8.9 Hz, 1H), 7.49 (ddd, $J$ = 8.8, 7.5, 2.0 Hz, 1H), 7.38 (dd, $J$ = 7.6, 1.9 Hz, 1H), 7.11 (d, $J$ = 8.4 Hz, 1H), 6.99 (t, $J$ = 7.5 Hz, 1H), 6.01 (ddt, $J$ = 17.5, 10.3, 5.0 Hz, 1H), 5.38 (dq, $J$ = 17.4, 1.9 Hz, 1H), 5.25 (dq, $J$ = 10.6, 1.8 Hz, 1H), 4.63 – 4.55 (m, 2H).

**$^{13}$C NMR** (101 MHz, DMSO-$d_6$) δ 165.46, 155.99, 150.36, 144.68, 133.44, 133.04, 129.58, 129.39, 124.56, 122.59, 120.64, 117.42, 113.26, 68.85.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{14}N_2O_6S+Na]^+$, 385.0465; found, 385.0467.



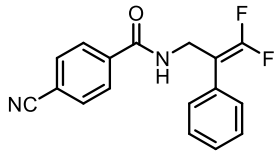

To an oven-dried 100 mL round-bottom flask with a magnetic stirring bar was added [$Pd(Ph_3P)_4$] (0.25 mmol, 5 mol%) and dry THF (20 mL). The solution was cooled to 0 ºC prior to addition of allylic bromide (5.0 mmol, 1.0 eq.). The solution was stirred for 5 minutes and was treated with the Grignard reagent (7.5 mmol in 1.0M THF solution, 1.5 eq.). The reaction mixture was allowed to proceed at room temperature for another 24 hours before quenching with ice water 30 mL. The aqueous layer was extracted with diethyl ether (2 × 30 mL), and the combined organic extracts were washed with water (30 mL) and brine (30 mL) and dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residual crude product was purified by column chromatography to afford the desired product. NMR data correspond to the reported value.[54]




To a solution of 2.5 g of $PPh_3MeBr$ (7.0 mmol, 1.4 equiv.) in 55 mL of anhydrous THF at –78 °C, 3.5 mL of NaHMDS solution (2M in THF, 7 mmol, 1.4 equiv.) was added dropwise. After complete addition, the solution was warmed to 0 °C and stirred for an hour. A solution of the corresponding bromodifluoro acetophenone (5 mmol, 1 equiv.) in 4 mL of anhydrous THF was then added dropwise. After complete addition, the reaction was allowed to warm to room temperature, and stirred for an additional hour. After this, the reaction was quenched with 10 mL of aqueous 1M HCl and diluted with 50 mL of $Et_2O$. The aqueous and organic layers were separated, and the aqueous layer was extracted with 20 mL of additional ether. The organic layers were combined, dried with $Na_2SO_4$, and the solvent was removed under reduced pressure. To the residue was added a minimal amount of DCM to dissolve the oil, then the solution was passed through a silica plug with 1:9 EtOAc/hexane as eluent. The solvent was removed under reduced pressure, and the resulting residue was purified once again by silica plug with 1/9 EtOAc/hexane as eluent. The solvent was then removed under reduced pressure, and the resulting oil was used in the next step without further purification.

To a stirred solution of allylic $CF_2Br$ (1 mmol, 1 equiv.) in dry THF (5 mL), was added 0.60 mL of NaHMDS solution (2M in THF, 1.2 mmol, 1.2 equiv.) over 1 min. After addition, the solution was heated to 40 °C and stirred overnight. After cooled to room temperature, the reaction was quenched with Ar'$CO_2H$ (1.1 mmol, 1.1 equiv.), where a solid precipitate is immediately observed. To this slurry, Ar'COCl (2.4 mmol, 2.4 equiv.) was added dropwise over 1 min. After stirring for an additional 2 hours at ambient temperature, the reaction is quenched with saturated $NaHCO_3$ (10 mL) and diluted with 20 mL of diethyl ether. The aqueous and organic layers were separated, and the aqueous layer was extracted with 20 mL of diethyl ether. The organic layers were combined, dried with $Na_2SO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography ($Et_2O$/pentane) to yield product. Trace benzoyl chlorides were removed from purified product by dissolving the mixture in 30 mL of $Et_2O$ and washing with 25% aqueous ammonia (3 × 20 mL). After drying of the organic layer with $Na_2SO_4$, the solvent was removed under reduced pressure to yield pure **13a-13e**. NMR data of **13c**, **13d** and **13e** correspond to the reported value.[55]

**4-cyano-*N*-(3,3-difluoro-2-phenylallyl)benzamide** (**13a**)



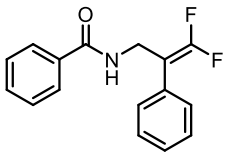
**$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.58 – 7.50 (m, 4H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.42 – 7.35 (m, 1H), 7.31 – 7.25 (m, 2H), 6.29 (d, *J* = 6.1 Hz, 1H), 4.42 (dt, *J* = 5.5, 2.5 Hz, 2H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.72, 155.36 (dd, *J* = 296.8, 294.0 Hz), 136.56 (d, *J* = 3.2 Hz), 133.79, 132.51, 132.01, 128.95 (t, *J* = 4.0 Hz), 128.78, 126.98, 118.59, 111.56, 90.61 (dd, *J* = 19.0, 13.7 Hz), 36.80 (d, *J* = 3.1 Hz).

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -83.81 (d, *J* = 27.1 Hz), -83.90 (d, *J* = 27.5 Hz).

**HRMS-ESI(m/z)** calc'd for $[C_{17}H_{12}F_2NO_2+Na]^+$, 321.0810; found, 321.0809.

***N*-(3,3-difluoro-2-phenylallyl)benzamide** (**13b**)



**$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.63 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.43 – 7.33 (m, 3H), 7.33 – 7.27 (m, 0H), 6.27 (d, *J* = 6.8 Hz, 0H), 4.50 (dt, *J* = 5.1, 2.4 Hz, 1H).

**$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 167.70, 154.79 (t, *J* = 292.5 Hz), 134.23, 131.72, 131.43, 128.89, 128.67, 128.29 (t, *J* = 3.5 Hz), 128.04, 127.00, 90.62 (t, *J* = 16.8 Hz), 37.44 (t, *J* = 3.4 Hz).

**$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -87.20.

**HRMS-ESI(m/z)** calc'd for $[C_{16}H_{13}F_2NO+H]^+$, 274.1038; found, 274.1038.

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