– SUPPORTING INFORMATION –

Terpene Cyclase Mimicking Chlorine-Induced Polyene Cyclizations

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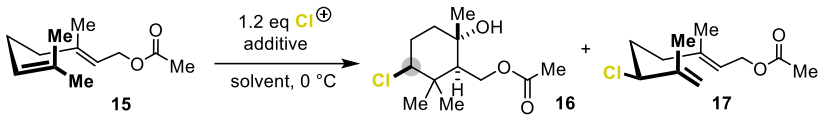
Content

1. General Information

Solvents used in reactions were p.A. grade. Solvents for chromatography were technical grade and distilled prior to use. 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP) was purchased from Fluorochem with a purity >99%, dried over magnesium sulfate and distilled prior to use. Reagents were purchased at the highest commercial quality available and used without further purification. For better handling in all reactions the preformed morpholine-HFIP was used instead of the free base morpholine (**14**). Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on Merck silica gel aluminium plates with F-254 indicator using UV light as the visualizing agent (UV), ceric ammonium molybdate (CAM), and heat as developing agents. Silica gel Merck 60 (particle size 40 – 60 µm) was used for flash column chromatography. Solvent mixtures are understood as volume/volume (v/v). NMR spectra were recorded on a Bruker AVANCE III HD 400, a Bruker AV300, a Bruker AV400, a Bruker AV500, a Bruker AV500-cryo, a Varian MERCURYplus 300 and a Varian MERCURYplus 400 spectrometer. The spectra were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$ @ 7.26 ppm, $CDCl_3$ @ 77.16 ppm ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, q = quartet, p = pentet, quint = quintet (with 1:2:3:2:1 intensity), hept = heptet, m = multiplet, br = broad. In addition, the following abbreviations were used: EtOAc = ethyl acetate, MeCN = acetonitrile, DCM = dichloromethane, DCE = 1,2-dichloroethane, DMSO = dimethyl sulfoxide, TFE = 1,1,1-trifluoroethanol, HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol, PFTB = perfluoro-*tert*-butyl alcohol, TLC = thin layer chromatography, rt = room temperature, sat = saturated, aq = aqueous, eq = equivalent, NCS = *N*-chloro-succinimide, DCDMH = dichlorodimethylhydantione, TClCA = trichlorocyanuric acid, NCM = *N*-chloro-morpholine, TFA = trifluoroacetic acid, FA = formic acid. Melting points were measured on a Büchi 510 or Büchi M-560 and are not calibrated. IR spectra were recorded on a JASCO FT/IR-4100 (ATR, KBr and Film) and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were conducted on a Thermo Scientific LTQ-FT Ultra (ESI HRMS), a ThermoFisher Scientific LTQ Orbitrap XL spectrometer (ESI HRMS), a Finnigan MAT 8230 spectrometer (EI HRMS) or a Bruker Daltonics MicrOTOF spectrometer (ESI HRMS).

2. Optimization of the Reaction Conditions

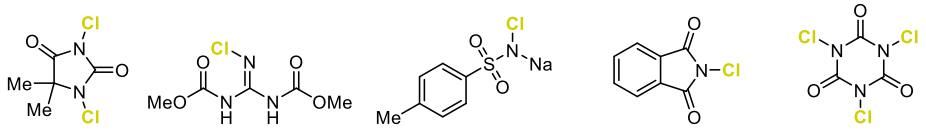


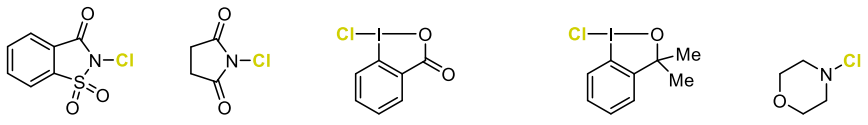
HFIP (1.00 mL, 0.1 M) was cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the corresponding reagent (120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

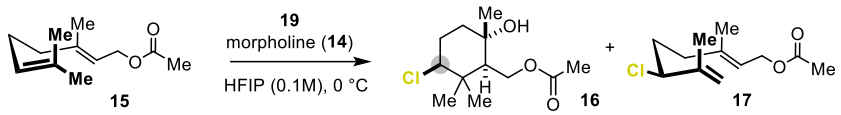
Table S1. Screening of chlorine sources.

entry	reagent	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	DCDMH (**13**)	86 : 14	8	52
2	Palau'Chlor (**S1**)	83 : 17	9	37
3	Chloramine T (**S2**)	76 : 24	8	53
4	Cl-Phthalimide (**S3**)	84 : 16	9	48
5	TCICA (**S4**)	85 : 15	10	44
6	Cl-Saccharin (**23**)	86 : 14	11	63
7	NCS (**S5**)	88 : 12	9	54
8	Cl-Benziodoxole (**20**)	---	< 5	< 5
9	Cl-Benziodoxolone (**19**)	84 : 16	19	41
10	NCM (**18**)	86 : 14	10	52

[a]determined from the ^{1}H-NMR spectra of the crude mixture.


DCDMH (**13**) Palau'Chlor (**S1**) Chloramine T (**S2**) *N*-chlorophthalimide (**S3**) TCICA (**S4**)


N-chlorosaccharin (**23**) NCS (**S5**) chlorobenziodoxole (**19**) chlorobenziodoxolone (**20**) NCM (**18**)

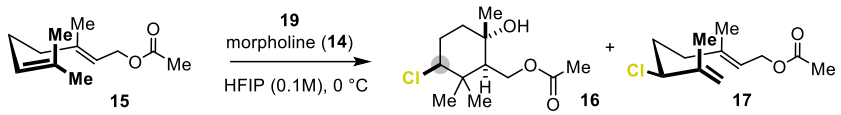


HFIP (1.00 mL, 0.1 M) was cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the chloro benziodoxolone **19** in varying quantitites. The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S2. Chlorocyclization of geranyl acetate (**15**) with varying amounts of chloro benziodoxolone **19**.

entry	eq of **19**	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	0.6	85:15	6[b]	31
2	1.0	84:16	11	35
3	1.2	84:16	19	41
4	1.8	85:15	14	30
5	2.4	84:16	13	27
6	3.6	83:17	13	30

[a]determined from the ^{1}H-NMR spectra of the crude mixture. [b]25% of **15** recovered

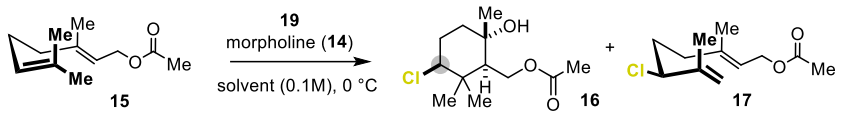


HFIP (1.00 mL, 0.1 M) was cooled to 0 °C before adding the morpholine-HFIP salt in varying quantities and the chlorinating reagent **19** (33.9 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S3. Chlorocyclization of geranyl acetate (**15**) with varying amounts of morpholine (**14**).

entry	eq of **14**	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	0	83:17	19	21
2	0.6	83:17	16	29
3	1.0	84:16	14	31
4	1.4	84:16	19	41
5	1.8	80:20	14	44
6	2.4	87:13	10	49
7	3.6	85:15	9	54

[a]determined from ^{1}H-NMR spectra of the crude mixture with internal standard.

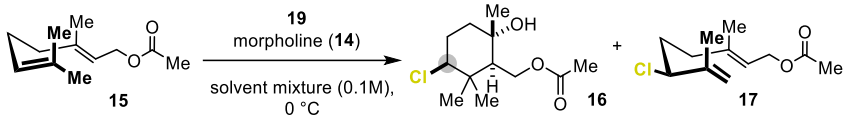


The solvent (1.00 mL, 0.1 M) was cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq.) and the chlorinating reagent **19** (33.9 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S4. Chlorocyclization of geranyl acetate (**15**) in different solvents.

entry	solvent	d.r.[a]	yield of **16** [%]	yield of **17**[a] [%]	conversion of **15**[a] [%]
1	DMF	n.d.	n.d.	n.d.	58
2	DCM	n.d.	n.d.	< 5	36
3	toluene	n.d.	n.d.	n.d.	27
4	MeCN	n.d.	n.d.	n.d.	25
5	THF	n.d.	n.d.	n.d.	23
6	$MeNO_2$	n.d.	n.d.	< 5	48
7	*i*PrOH	n.d.	n.d.	n.d.	54
8	MeOH	n.d.	n.d.	n.d.	61
9	PFTB	n.d.	< 5	25	77
10	TFE	n.d.	< 5	27	89
11	HFIP	84:16	19	41	> 99

[a]determined from the ^{1}H-NMR spectra of the crude mixture.



The corresponding solvent mixture (1.00 mL, 0.1 M) was cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the chlorinating reagent **19** (33.9 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S5. Screening of HFIP/TFE mixtures as solvent and the influence of water addition on the chlorocyclization of geranyl acetate (**15**).

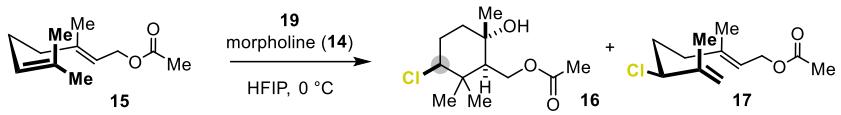
entry	HFIP [mL]	TFE [mL]	H_2O [mL]	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	1.00	-	-	84:16	19	41
2	0.75	0.25	-	86:14	10	28
3	0.50	0.50	-	87:13	6	35
4	0.25	0.75	-	89:11	5	38
5	-	1.00	-	n.d.	< 5	27
6	1.00	-	5 eq	83:17	19	26
7	0.33	0.33	0.33	92:8	6	34
8	0.75	0.25	-	84:16	18	29
9	0.50	0.50	-	86:14	14	33
10	0.25	0.75	-	85:15	9	36
11	-	1.00	-	n.d.	< 5	27

[a]determined from the ^{1}H-NMR spectra of the crude mixture.

Table S6. Screening of different HFIP/DCM mixtures as solvent.

entry	HFIP [mL]	DCM [mL]	d.r.[a]	yield of **14**[a] [%]	yield of **15**[a] [%]
1	1.00	-	84 : 16	19	41
2	0.75	0.25	84 : 16	18	29
3	0.50	0.50	86 : 14	14	33
4	0.25	0.75	85 : 15	9	36
5	-	1.00	n.d.	0	4

[a]determined from the ^{1}H-NMR spectra from the crude mixture.

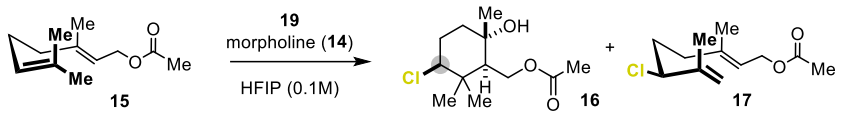


Varying volumes of HFIP were cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the chlorinating reagent **19** (33.9 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S7. Optimization of the concentration in the chlorocyclization of **15**.

entry	concentration	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	0.50 M	84:16	10	31
2	0.10 M	84:16	19	41
3	0.02 M	85:15	20	16
4	0.01 M	81:19	10	< 5

[a]determined from the ^{1}H-NMR spectra of the crude mixture.

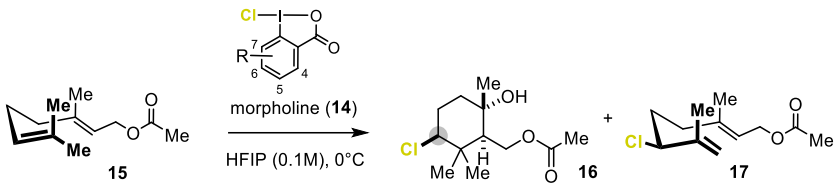


HFIP (1.00 mL, 0.1M) was brought to the corresponding temperature before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the chlorinating reagent **19** (33.9 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at the given temperature. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S8. Screening of different temperatures in the chlorocyclization of geranyl acetate (**15**).

entry	temperature	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	-15 °C[b]	84:16	18	20
2	0 °C	84:16	19	41
3	rt	84:16	16	23
4	35 °C	92:8	12	12

[a]determined from the ^{1}H-NMR spectra of the crude mixture with internal standard; [b]mixture solidified.

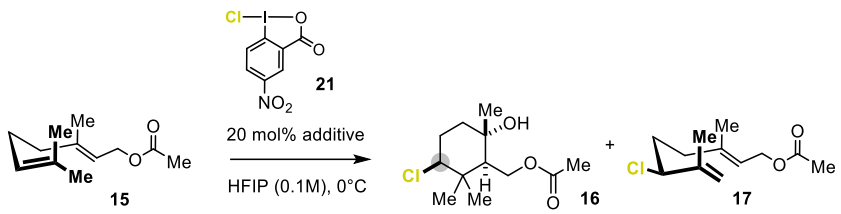


HFIP was cooled to 0 °C before adding the morpholine-HFIP salt (59.3 mg, 140 µmol, 1.4 eq) and the corresponding λ^3-hypervalent iodane reagent (120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S9. Screening of differently substituted λ^3-hypervalent iodane reagents in the chlorocyclization of geranyl acetat (**15**).

entry	R	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	5-H (**19**)	84:16	20	23
2	6-NO_2[b] (**S6**)	84:16	12	29
3	5-NO_2 (**21**)	83:17	23	19
4	6-OMe (**S7**)	83:17	21	24
5	5-CF_3[b] (**S8**)	86:14	17	18
6	5-Me (**S9**)	84:16	20	23
7	6-Cl (**S10**)	85:15	19	21
8	5-Cl (**S11**)	84:16	20	19
9	4-Cl (**S12**)	83:17	19	20

[a]determined from ^{1}H-NMR spectra of the crude mixture. [b]low solubility of the reagent was observed.

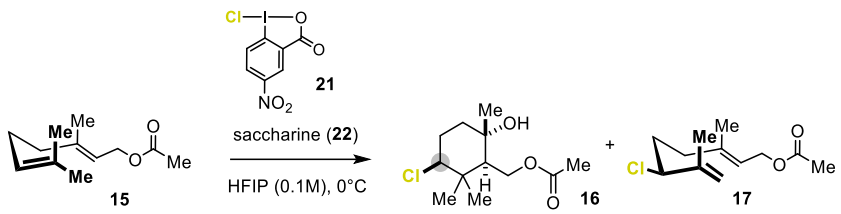


HFIP (1.00 mL, 0.1M) was cooled to 0 °C before adding the additive (20 µmol, 0.2 eq) and the 4-NO_2 chlorinating reagent **21** (39.3 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S10. Screening of different acidic additives in the chlorocyclization of geranyl acetate (**15**).

entry	additive	pK_a	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	triflic acid	-14.7[1]	n.d.	decomp.	decomp.
2	*p*-toluenesulfonic acid	-2.80[2]	83:17	25	10
3	trifluoroacetic acid	-0.25[3]	83:17	26	12
4	TFA	0.65[3]	86:14	27	12
5	saccharin (**22**)	1.60[4]	83:17	30	14
6	benzoic acid	4.20[3]	83:17	25	11
7	acetic acid	4.76[3]	83:17	25	12
8	cyanuric acid	6.88[5]	84:16	21	24

[a]determined from the ^{1}H-NMR spectra of the crude mixture.



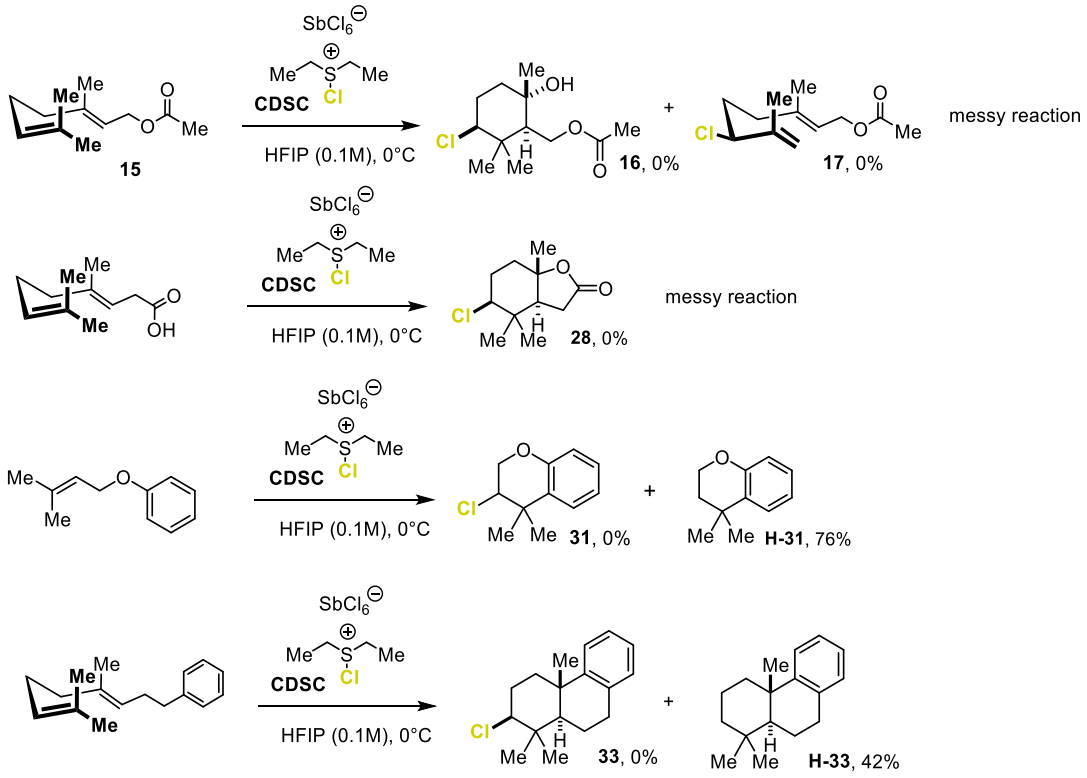
HFIP (1.00 mL, 0.1M) was cooled to 0 °C before adding saccharine (**22**) and the 4-NO_2 chlorinating reagent **21** (39.3 mg, 120 µmol, 1.2 eq). The reaction mixture was stirred for 20 min at 0 °C. Then geranyl acetate (**15**, 19.6 mg, 100 µmol, 1.0 eq) was added and the reaction mixture was stirred for another 20 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and stirring was continued for another 10 min before pouring it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

Table S11. Chlorocyclization of geranyl acetate (**15**) with varying amounts of saccharine (**22**).

entry	eq of **22**	d.r.[a]	yield of **16**[a] [%]	yield of **17**[a] [%]
1	0.05	83:17	26	11
2	0.10	83:17	26	11
3	0.20	83:17	30	14
4	0.60	83:17	26	12
5	1.00	83:17	24	10
6	1.40	84:16	26	11
7	2.00	82:18	23	11

[a]determined from the ^{1}H-NMR spectra of the crude mixture.

3. Chlorocyclizations of different substrates using CDSC in HFIP



Scheme S1. Chlorocyclizations of different substrates using CDSC in HFIP.

HFIP (1.00 mL, 0.1M) was cooled to 0 °C before adding the substrate (100 µmol, 1.0 eq) and CDSC (110 µmol, 1.1 eq). The reaction mixture was stirred for 10 min at 0 °C. A freshly prepared aq. 10% (w/w) Na_2SO_3-solution (2 mL) was added and then poured it into DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layers were washed with brine (1 × 15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude reaction mixture was subjected to ^{1}H-NMR analysis using an internal standard.

In all cases, no chlorine-containing product was formed. CDSC readily decomposed upon addition of HFIP according to ^{1}H-NMR investigations.

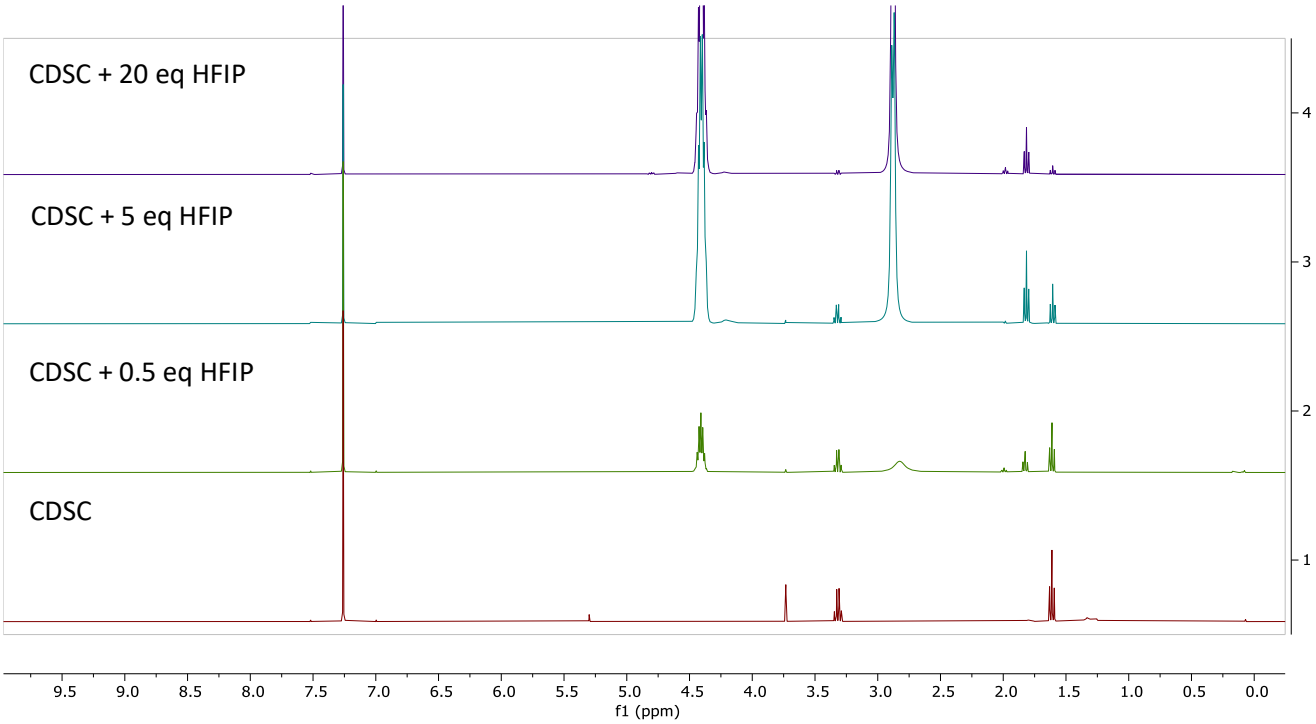


Figure S1. ^{1}H-NMR study of 0.1M CDSC with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 500 MHz.

The observed terpene cyclization upon protonation for prenylphenylether and homogeranylbenzene substrates was facilitated by the high acidity of the CDSC-HFIP mixture (pH 0), leading to **H-31** (76% yield) and **H-33** (42% yield) as the major products.

4. NMR Investigations on the Interactions of HFIP with λ³-Iodane 19

11 mL of a stock solution of hypervalent iodane **19** (0.1M, 300 mg, 1.06 mmol) in $CDCl_3$ was prepared. 15 NMR samples with a volume of 550 µL each were prepared with varying amount of HFIP (0 → 24 eq). The samples were analyzed by ^{1}H-, ^{13}C- and ^{19}F-NMR spectroscopy.

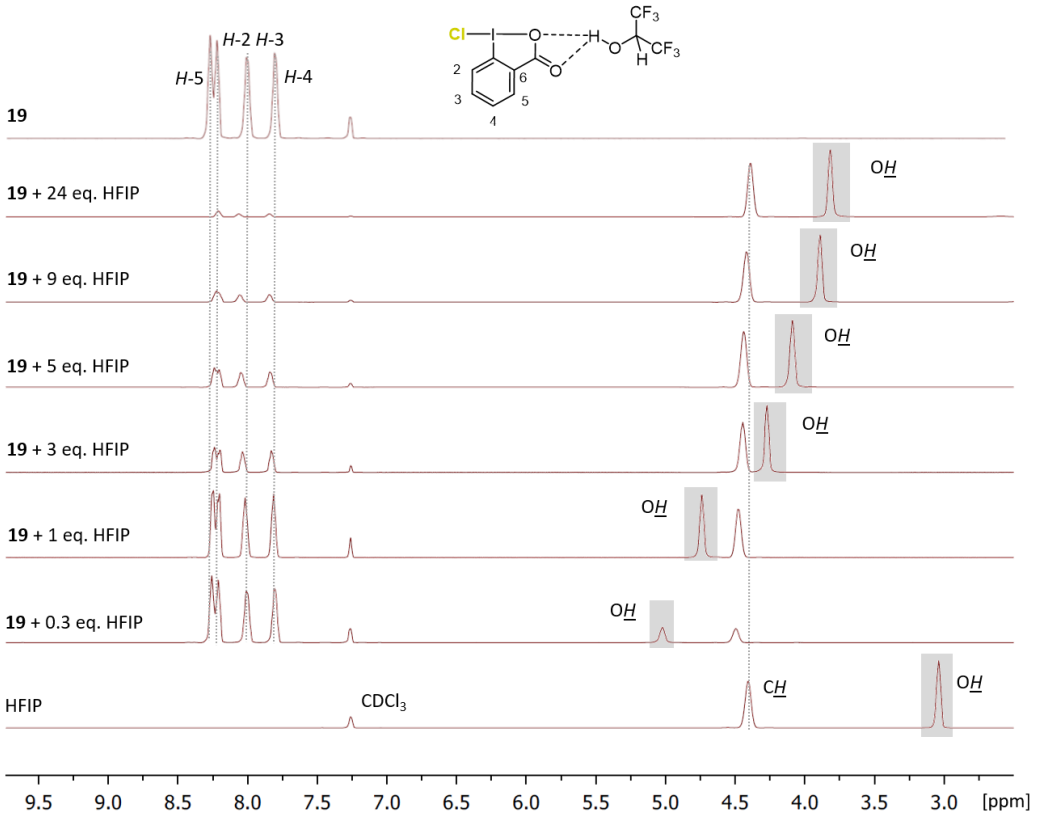


Figure S2. ^{1}H-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 500 MHz.

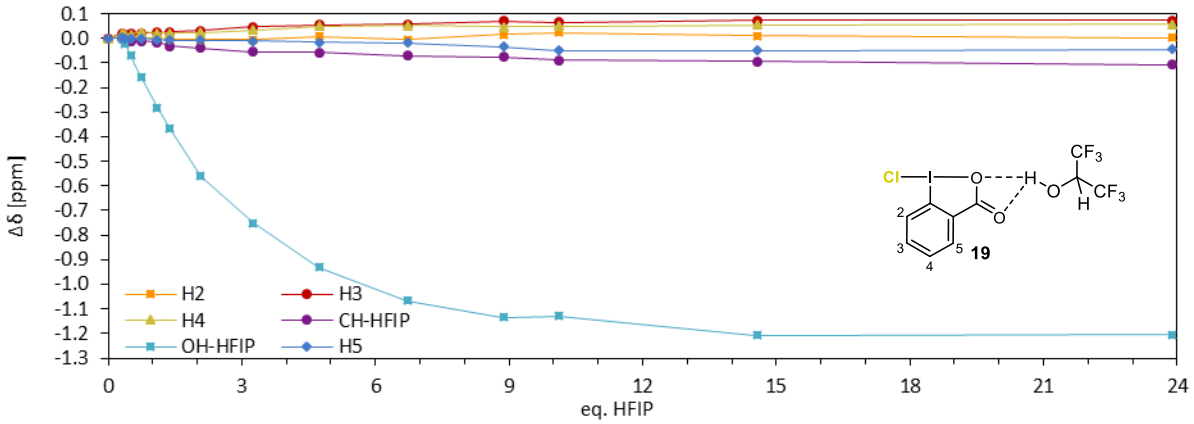


Figure S32. Titration curves of iodane **19** (0.1M in $CDCl_3$) and HFIP determined by ^{1}H-NMR spectroscopy.

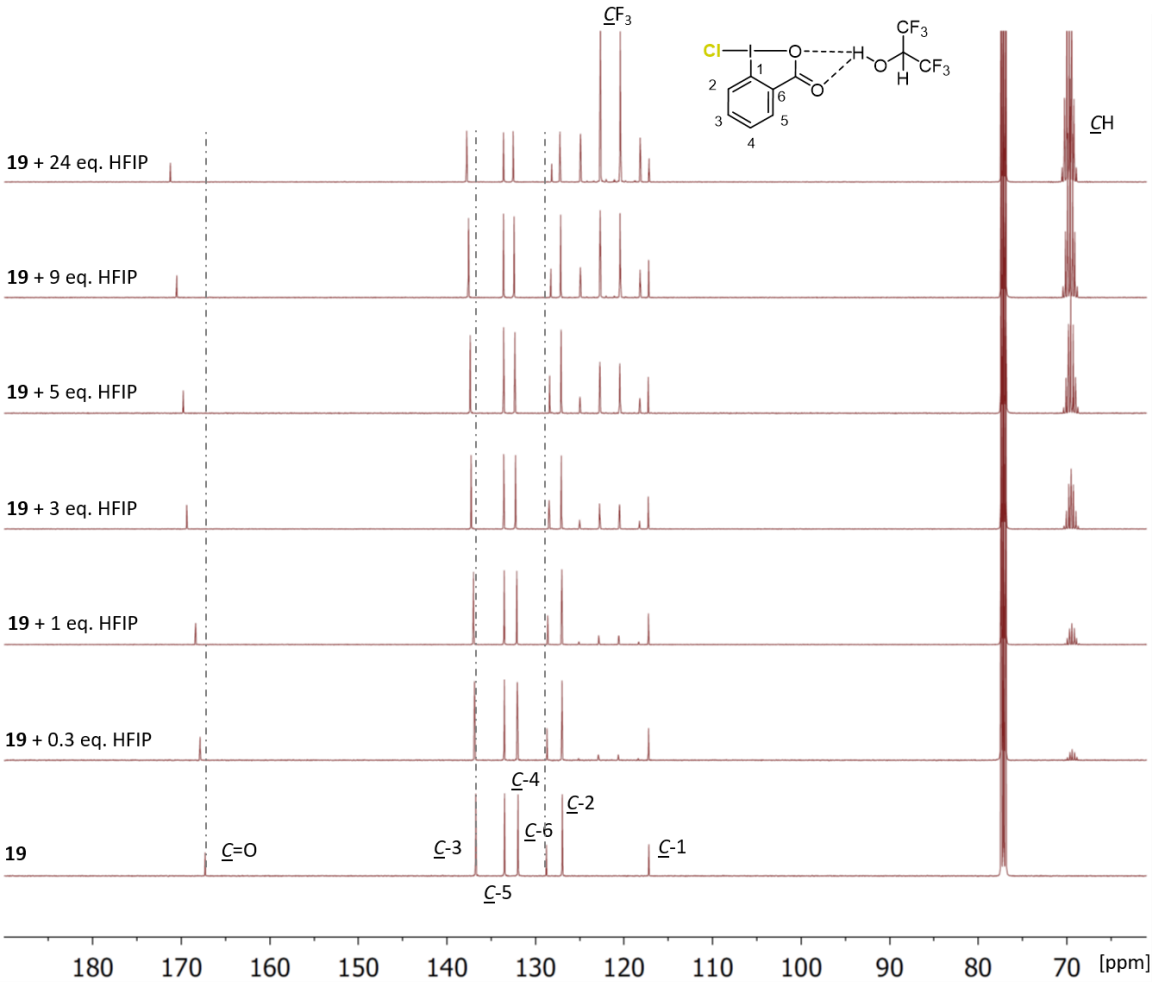


Figure S4. ^{13}C-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 126 MHz.

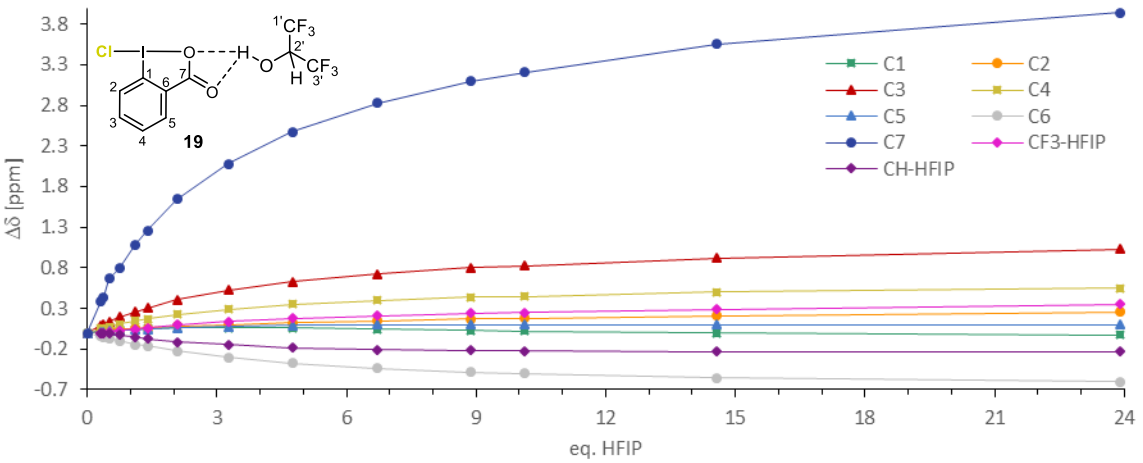


Figure S5. Changes on the chemical shift of specific carbon atoms upon addition of HFIP.

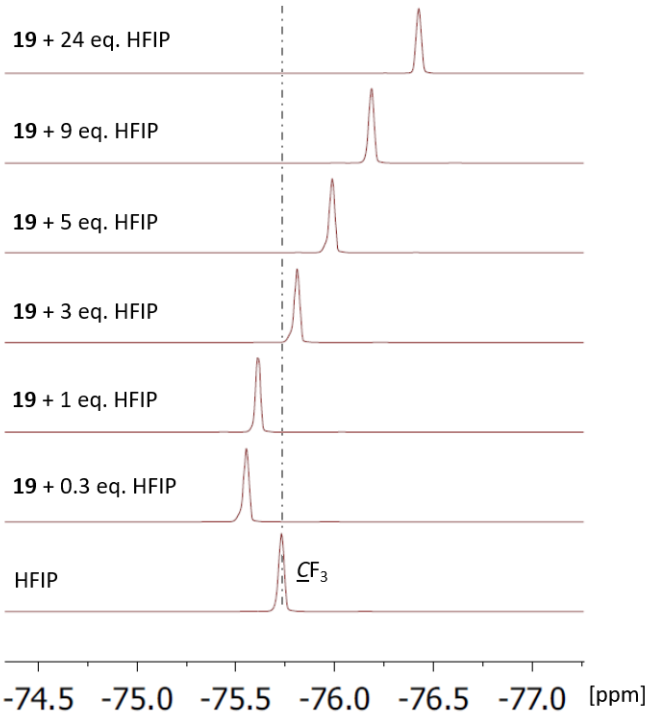


Figure S6. ^{19}F-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 471 MHz.

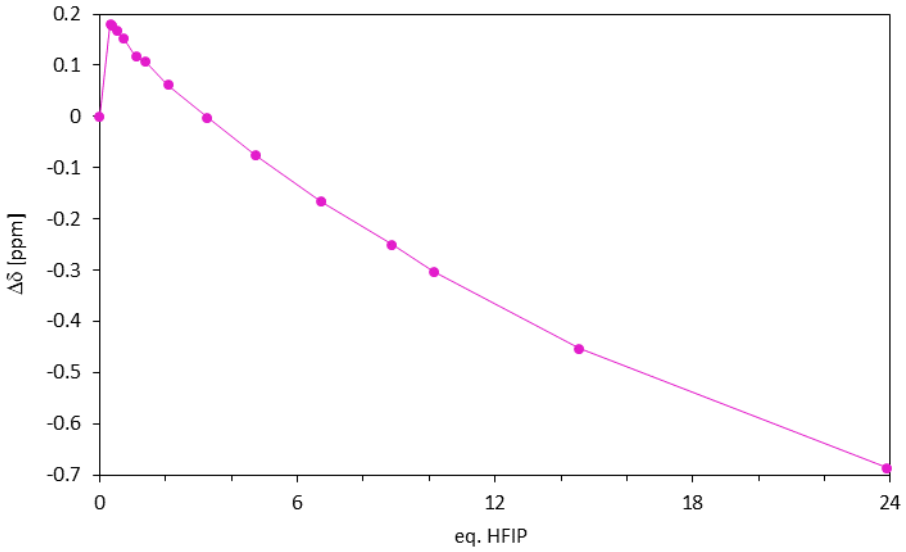


Figure S7. Alterations on the chemical shift of of the CF_3 group in HFIP upon addition of HFIP to a 0.1M iodane **19** solution in $CDCl_3$.

5. Job's Plot Analysis of the Interaction of Iodane 19 and HFIP

A 0.1 M λ^3-iodane **19** stock solution was prepared by mixing 6.0 mL of $CDCl_3$ with iodane **19** (167 mg, 0.59 mmol). A 0.1 M HFIP-stock solution was prepared by mixing 6.0 mL $CDCl_3$ and HFIP (62.1 µL, 99.1 mg, 0.59 mmol). 11 NMR samples with a volume of 600 µL each were prepared with the following iodane/HFIP-ratios: 1:0, 1:9, 1:4, 3:7, 2:3, 1:1, 3:2, 7:3, 4:1, 9:1 and 0:1. The samples were analyzed by ^{1}H NMR with respect to the chemical shift of the hydroxyl proton of HFIP.

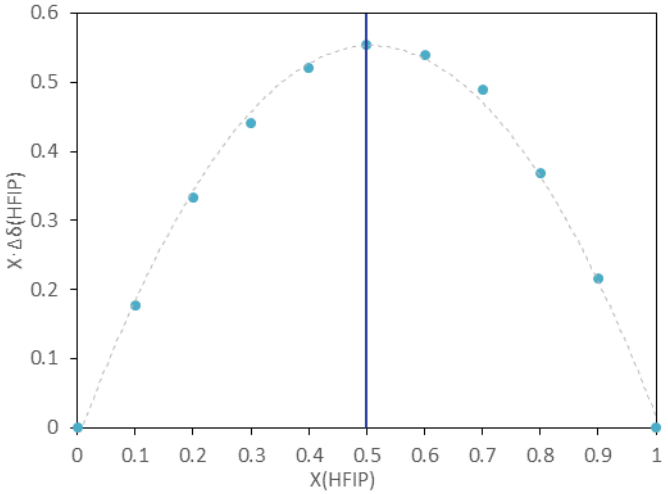


Figure S8. *Job's* plot on the complex formation of **19** and HFIP.

6. NMR Investigations on the Interaction of Saccharin (22) with Chlorobenziodoxolone 19 in HFIP

A 0.12 M HFIP-stock solution was prepared by mixing 7.46 mL of $CDCl_3$ with 1.34 mL HFIP (2.14 g, 1.06 mmol). 550 µL of this stock solution was mixed with saccharin (**22**, 10.0 mg, 54.2 µmol) in a NMR tube. 10 further NMR samples were prepared by mixing 550 µL of HFIP stock solution with iodane **19** (15.0 mg, 53.1 µmol) and the following equivalents of saccharin (**22**): 0, 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.5, 1.0, 1.5 and 3.0. The samples were analyzed by ^{1}H-, ^{13}C- and ^{29}F-NMR spectroscopy.

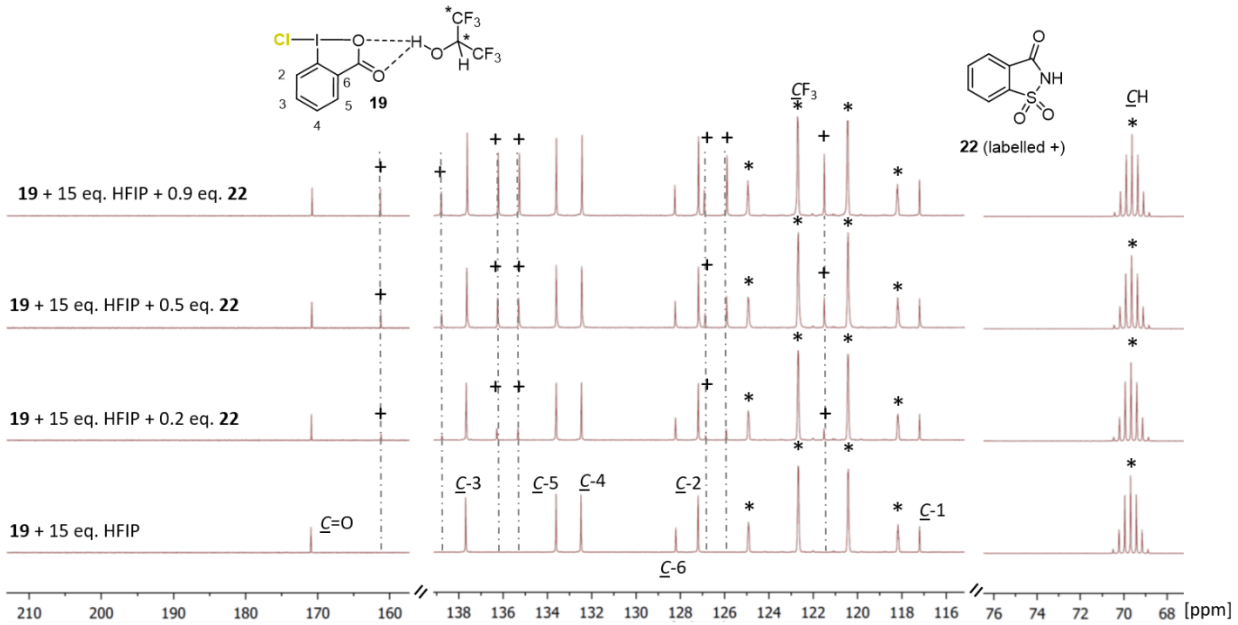


Figure S9. ^{13}C-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 126 MHz (+ correspond to the signals resonating from **22**; * correspond to the signals resonating from HFIP).

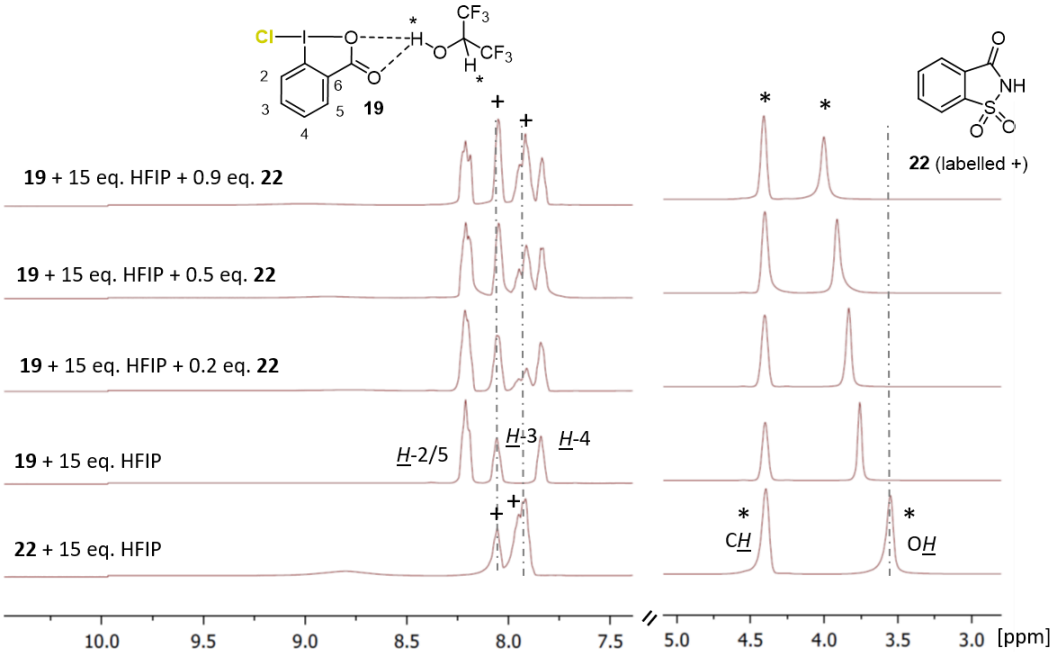


Figure S10. ^{1}H-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded with 500 MHz MHz (+ correspond to the signals resonating from **22**; * correspond to the signals resonating from HFIP).

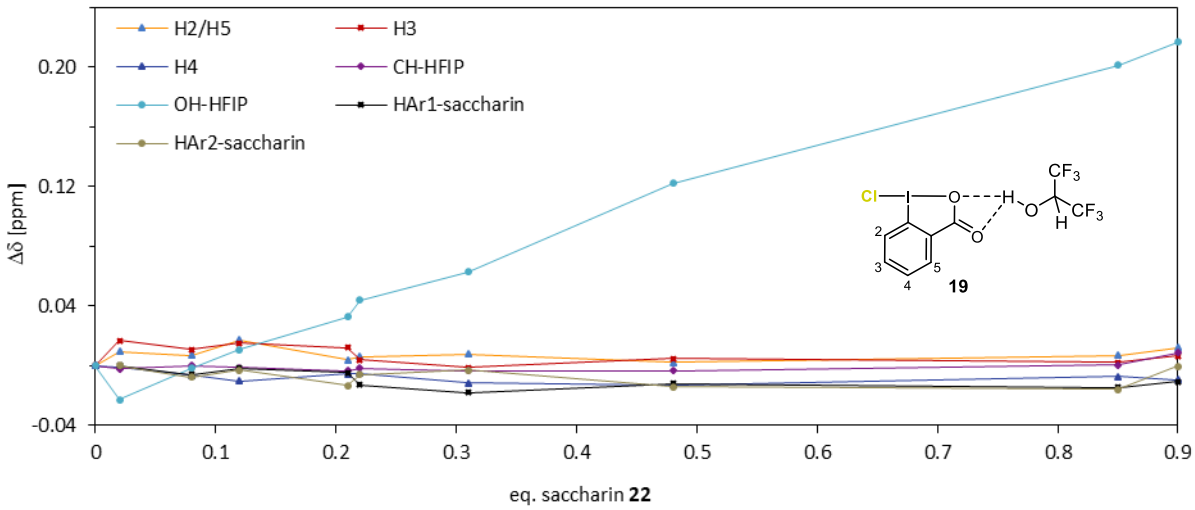


Figure S11. Alterations on the ^{1}H-NMR signals of **19**, **22** and HFIP upon addition of several equivalents of **22** to 0.1M solution of **19** in an HFIP/$CDCl_3$ (15:85) mixture.

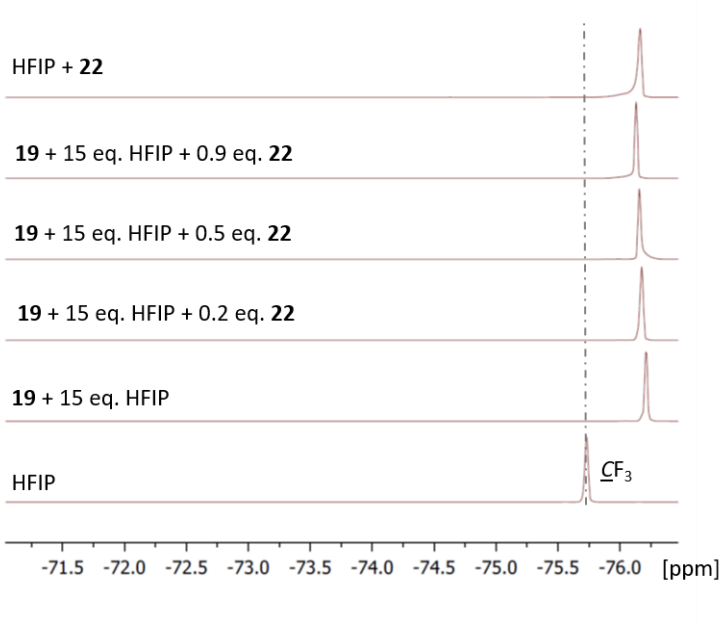


Figure S12. ^{1}H-NMR study of 0.1M iodane **19** with increasing amounts of HFIP in $CDCl_3$ (0.55 mL) at 300 K, recorded at 471 MHz**.**

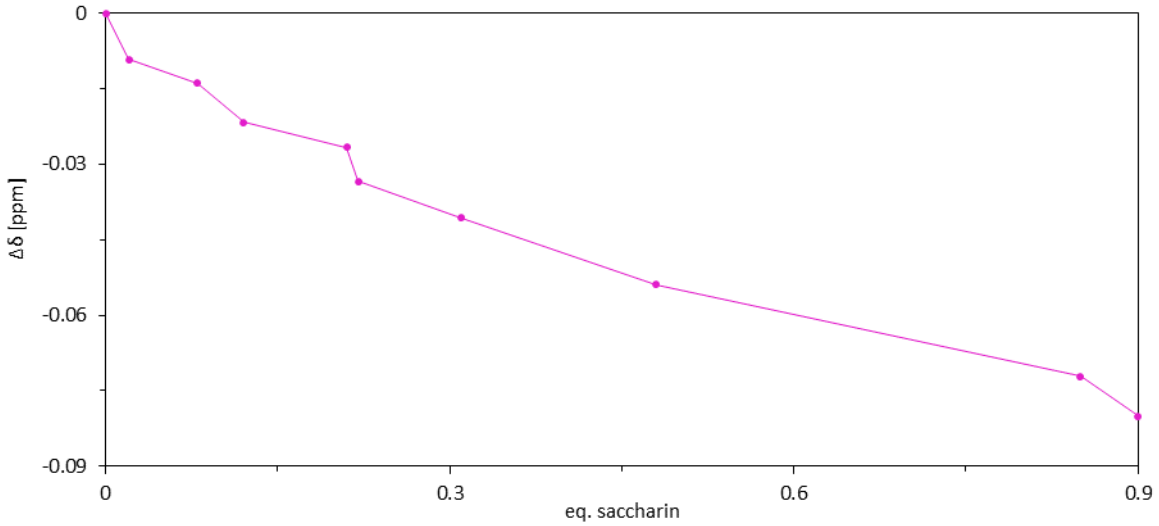
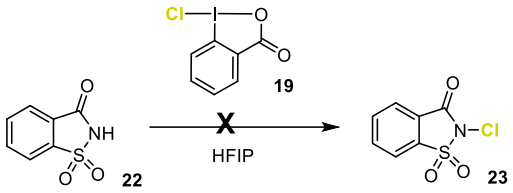


Figure S13. Changes in the chemical shift of of the CF_3 group in HFIP upon addition of several equivalents of **22** to 0.1M solution of **19** in an HFIP/$CDCl_3$ (15:85) mixture.

In all these titration experiments, no signals of chloro saccharine (**23**) were observed, which excludes formation of **23** under the given reaction conditions and thus **23** as the actual chlorinating reagent in the chlorocyclization.

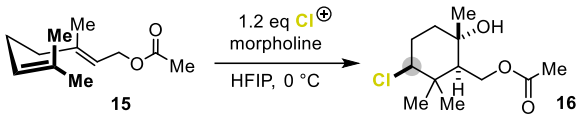


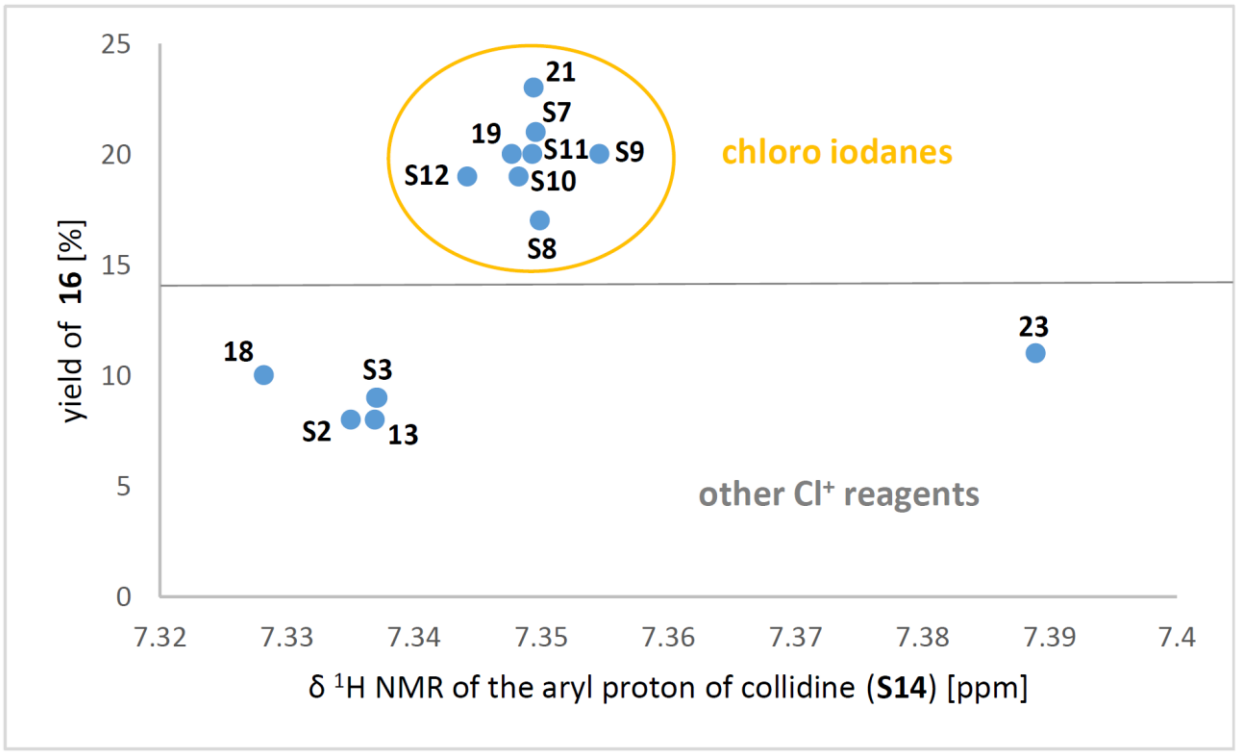
Scheme S2. Putative transformation of saccharine (**22**) to *N*-chlorosaccharin **23** by iodane **19**.

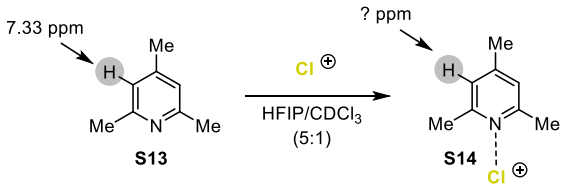
7. Comparison of the Chlorination Abilities (*HalA*) of Chloro Iodanes 19, 21, S6 – S12 in HFIP

In order to investigate the halogenating ability of the chloro iodanes **19**, **21**, **S6** – **S12** in comparison with other chlorinating agents, a HFIP stock solution was prepared by mixing 5.0 mL HFIP with 50 mL $CDCl_3$. For

sample preparation, collidine (**S13**, 50.0 µmol, 1.0 eq) was mixed with 50.0 µmol (1.0 eq) halogen source in 0.5 mL HFIP stock solution in an NMR tube. A ^{1}H-NMR spectrum was recorded (Figure S13).[6]







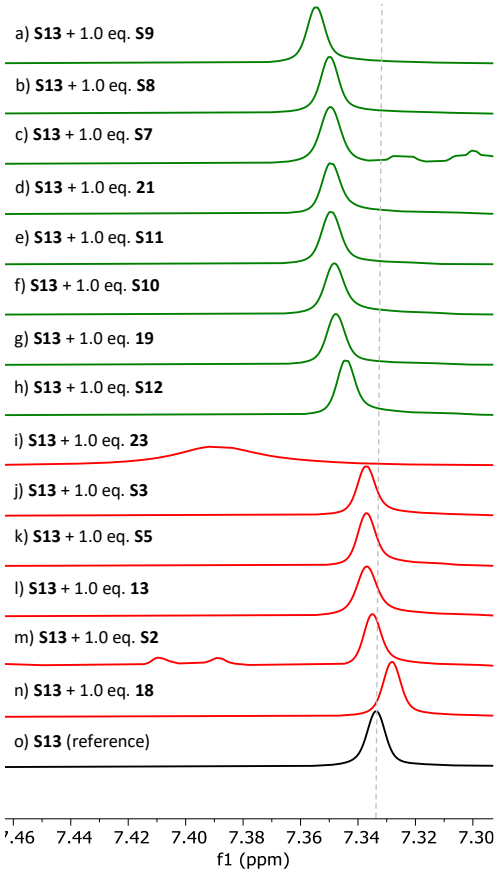


Figure S14. ^{1}H NMR study of chlorinating reagents (0.1 M, 1.0 eq.) with 1.0 eq 2,4,6-collidine (**S13**) in HFIP/$CDCl_3$ 5:1, recorded at 300K at 400 MHz.

8. Time Course of the Methyl Jamonate (40) Conversion

HFIP (0.1 M, 2 mL) was cooled to 0 °C before adding saccharin (**22**, 7.3 mg, 0.20 eq) and iodane **21** (78.6 mg, 0.24 mmol, 1.20 eq). Then methyl jasmonate (**41**, 44.9 mg, 0.2 mmol, 1.00 eq) together with the internal standard mesitylen (13.0 mg, 0.11 mmol, 0.54 eq) were added and the reaction mixture was stirred for 2 h at 0 °C. During this time periode aliquots of 15 µL were taken every 15 min. The reaction was stopped by immediately adding freshly prepared aq. 10% (w/w) Na_2SO_3-solution. The organic layer was analyzed by GC-MS and ^{1}H-NMR.

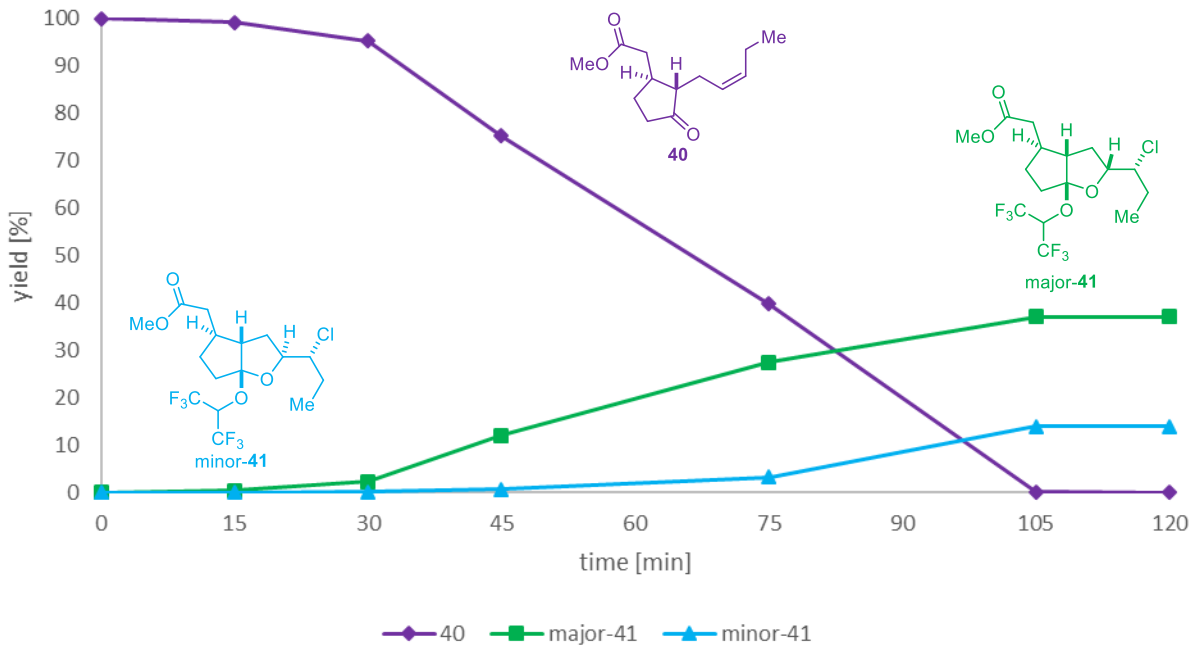
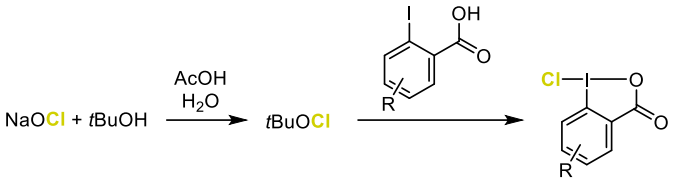


Figure S15. Time course of the formation of the major and minor isomer of **41**.

9. Experimental Procedures

9.1 General Procedure for the Synthesis of Hypervalent Iodanes 19, 21, S6 – S12 (GP1)



Following a literature procedure,[7] NaOCl (11-15wt% in H_2O, 25.0 mL, 30.0 g, 48.4 mmol, 1.0 eq.) was added to 25.0 mL water at 0 °C. Acetic acid (3.60 mL, 3.78 g, 60.1 mmol, 1.3 eq.) was mixed with *tert*-butanol (5.56 mL, 4.31 g, 58.1 mmol, 1.2 eq.) and the mixture was slowly added to NaOCl in water at 0 °C. The reaction was stirred for 5 min under light exclusion and then poured into a 10wt% solution of Na_2CO_3 in water (5 mL). The aq. phase was discarded and the yellow organic phase was washed once with water (10 mL). The obtained yellow oil was dried over $CaCl_2$ and the *t*BuOCl solution was used directly in the next step.

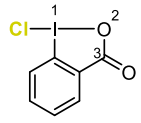
Following a literature procedure,[8] the corresponding iodobenzoic acid (1 mmol, 1 eq.) was dissolved in a mixture of DCM and *tert*-butanol (9:1, 3.5 mL). At 0 °C *t*BuOCl (0.13 mL, 119 mg, 1.1 mmol, 1.1 eq.) was added in one portion under light exclusion. The mixture was stirred for 20 min in the dark and the produced solid was filtered, washed with cold DCM and dried under reduced pressure yielding hypervalent iodane reagents **19**, **21**, **S6** – **S12**.

9.2 General Procedure for the Chlorocyclization of Polyenes (GP2)

HFIP (0.1 M, 2 mL) was cooled to 0 °C before adding saccharin (7.3 mg, 0.04 mmol, 0.2 eq) and iodane **21** (78.6 mg, 0.24 mmol, 1.2 eq). Then the corresponding starting material (1.0 eq) was added and the reaction mixture was stirred at 0 °C. Freshly prepared aq. 10% (w/w) Na_2SO_3-solution (5 mL) was added and the mixture was stirred for another 10 min before pouring it into DCM (5 mL). The aq. layer was extracted with DCM (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography using silica gel.

10.Analytical Data of Hypervalent Iodanes

1-Chloro-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (19), prepared from 2-iodobenzoic acid (248 mg, 1.00 mmol) following general procedure GP1 yielded **19** as a slightly yellow solid (189 mg, 0.67 mmol, 67%)

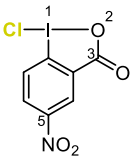


19

m.p. = 181 °C (DCM, decomposition); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.5, 1.7 Hz, 1H, H_{Ar}), 8.21 (dd, *J* = 8.5, 0.8 Hz, 1H, H_{Ar}), 7.99 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H, H_{Ar}), 7.79 (td, *J* = 7.3, 0.9 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.3, 136.8, 133.5, 132.0, 128.8, 127.0, 117.2 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3433, 1671, 1438, 1285, 1241, 1120, 743 cm^{-1}; **HRMS** (ESI+) calcd. for $C_7H_5IO_2$ $[M\text{-}Cl+H]^+$ 247.9329, found 247.9331.

The analytical data obtained were in agreement with those reported in the literature.[8]

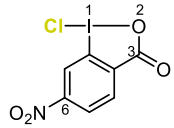
1-Chloro-5-nitro-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (21), prepared from 2-iodo-5-nitrobenzoic acid (293 mg, 1.00 mmol) following the general procedure GP1 yielded **21** as a slightly yellow solid (320 mg, 0.98 mmol, 98%)



21

m.p. = 231 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 8.39 (d, *J* = 2.8 Hz, 1H, H_{Ar}), 8.28 (d, *J* = 8.6 Hz, 1H, H_{Ar}), 8.00 (dd, *J* = 8.6, 2.8 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 166.3, 147.3, 142.5, 137.9, 126.2, 124.2, 103.9 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3430, 3092, 1692, 1658, 1350, 1274, 1145, 735 cm^{-1}; **MS** (EI, 70 eV) = 329/327 (1/3) $[M]^+$, 293 (100) $[M\text{-}Cl+H]^+$, 283 (11), 276 (17), 254 (32), 237 (11); **HRMS** (EI) calcd. for $C_7H_3ClIO_4$ [M] 326.8790, found 326.8783.

1-Chloro-6-nitro-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S6), prepared from 2-iodo-4-nitrobenzoic acid (293 mg, 1.00 mmol) following the following general procedure GP1 yielded **S6** as a slightly yellow solid (317 mg, 0.97 mmol, 97%).

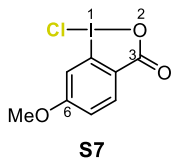


S6

m.p. = 188 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 9.02 (d, *J* = 1.9 Hz, 1H, H_{Ar}), 8.61 (dd, *J* = 8.3, 1.9 Hz, 1H, H_{Ar}), 8.37 (d, *J* = 8.2 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 167.4, 148.3, 143.4, 134.4, 130.2, 123.1, 94.07 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3431, 3090, 1686, 1660, 1531, 1346, 1284, 1139, 822, 732 cm^{-1}; **MS** (EI, 70 eV) = 329/327

(0.6/2) $[M]^+$, 293 (100) $[M\text{-}Cl+H]^+$, 283 (5), 276 (14), 247 (12), 237 (7); **HRMS** (EI) calcd. for $C_7H_3ClIO_4$ $[M]^+$ 326.8790, found 326.8811.

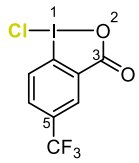
1-Chloro-6-methoxy-1λ³-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S7), prepared from 2-iodo-6-methoxybenzoic acid (278 mg, 1.00 mmol) following the general procedure GP1 yielded **S7** as a slightly yellow solid (268 mg, 0.86 mmol, 86%).



S7

m.p. = 178 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 7.78 (d, *J* = 8.8 Hz, 1H, H_{Ar}), 7.52 (d, *J* = 2.5 Hz, 1H, H_{Ar}), 7.04 (dd, *J* = 8.7, 2.6 Hz, 1H, H_{Ar}), 3.80 (s, 3H, OMe) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 166.8, 161.4, 132.2, 127.1, 126.2, 113.7, 96.08, 55.74 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3434, 1660, 1485, 1265, 1023, 770 cm^{-1}; **MS** (ESI+) m/z (%) 331 (44), 317 , 315/313 (1.5/4) $[M+H]^+$, 300 (17) $[M\text{-}Cl+Na]^+$, 295 (42), 278 (100) $[M\text{-}Cl+H]^+$, 261 (75); **HRMS** (ESI+) calcd. for $C_8H_7ClIO_3$ $[M+H]^+$ 312.9123, found 312.9115.

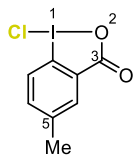
1-Chloro-5-(trifluoromethyl)-1λ³-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S8), prepared from 2-iodo-5-(trifluoromethyl)benzoic acid (316 mg, 1.00 mmol) following the general procedure GP1 yielded **S8** as a slightly yellow solid (252 mg, 0.72 mmol, 72%).



S8

m.p. = 202 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 8.23 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.97 (d, *J* = 2.3 Hz, 1H, H_{Ar}), 7.58 (d, *J* = 8.2 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 167.0, 141.9, 138.1, 128.8 (q, *J* = 33 Hz; signal overlapps with the adjacent signal), 128.4 (q, *J* = 3.3 Hz), 126.1 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 272.3 Hz), 99.97 ppm; **^{19}F NMR** (377 MHz, DMSO) δ -61.66; **IR** (KBr) $\tilde{\nu}_{max}$ = 3430, 1693, 1677, 1330, 1257, 1240, 1139, 703 cm^{-1}; **MS** (EI, 70 eV) = 352/350 (2/5) $[M]^+$, 316 (59) $[M\text{-}Cl+H]^+$, 308/306 (22/69), 299 (46), 271 (37), 209/207 (3/9), 181/179 (19/51), 144 (100); **HRMS** (ESI+) calcd. for $C_8H_4F_3ClIO_2$ $[M+H]^+$ 350.8891, found 350.8891.

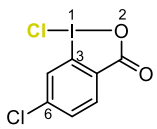
1-Chloro-5-methyl-1λ³-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S9), prepared from 2-iodo-5-methylbenzoic acid (262 mg, 1.00 mmol) following the general procedure GP1 yielded **S9** as a slightly yellow solid (253 mg, 0.85 mmol, 85%).



S9

m.p. = 199 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 7.83 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.53 (d, *J* = 2.2, 1H, H_{Ar}), 7.11 – 7.02 (m, 1H, H_{Ar}), 2.28 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 168.0, 140.3, 137.9, 136.6, 133.3, 130.7, 90.04, 20.25 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3431, 1685, 1661, 1455, 1283, 1247, 1198, 1116, 776 cm^{-1}; **MS** (ESI+) m/z (%) = 579 (10), 301 (23), 284 (6) $[M\text{-}Cl+Na]^+$, 262 (100) $[M\text{-}Cl+H]^+$, 245 (56); **HRMS** (ESI+) calcd. for $C_8H_7IO_2$ $[M\text{-}Cl+H]^+$ 261.9485, found 261.9485.

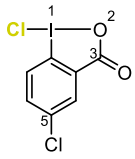
1,6-Dichloro-1λ³-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S10), prepared from 4-chloro-2-iodobenzoic acid (283 mg, 1.00 mmol) following the general procedure GP1 yielded **S10** as a slightly yellow solid (285 mg, 0.90 mmol, 90%).



S10

m.p. = 222 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 8.07 (d, *J* = 2.1 Hz, 1H, H_{Ar}), 7.73 (d, *J* = 8.3 Hz, 1H, H_{Ar}), 7.56 (dd, *J* = 8.4, 2.1 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 167.2, 139.5, 136.2, 135.4, 131.3, 128.2, 95.41 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3435, 3085, 1693, 1661, 1582, 1450, 1380, 1267, 1127, 561 cm^{-1}; **MS** (EI, 70 eV) = 318/316 (7/11) $[M]^+$, 284/282 (14/48) $[M\text{-}Cl+H]^+$, 274/272 (20/34), 267/265 (13/39), 254 (40), 239/237 (10/28), 112/110 (6/18), 69 (100); **HRMS** (EI) calcd. for $C_7H_3Cl_2IO_2$ $[M]^+$ 315.8549, found 315.8551.

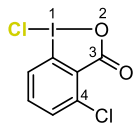
1,5-Dichloro-1λ³-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S11), prepared from 5-chloro-2-iodobenzoic acid (283 mg, 1.00 mmol) following the general procedure GP1 yielded **S11** as a slightly yellow solid (307 mg, 0.97 mmol, 97%).



S11

m.p. = 230 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 7.97 (d, *J* = 8.5 Hz, 1H, H_{Ar}), 7.72 (d, *J* = 2.6 Hz, 1H, H_{Ar}), 7.32 (dd, *J* = 8.4, 2.6 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 166.8, 142.1, 138.7, 133.2, 132.2, 129.5, 92.20 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3431, 3059, 1665, 1399, 1260, 1136, 866, 777 cm^{-1}; **MS** (EI, 70 eV) = 318/316 (19/28) $[M]^+$, 274/272 (40/65), 267/265 (10/32), 254 (65), 239/237 (32/100), 112/110 (24/73), 75 (36); **HRMS** (EI) calcd. for $C_7H_3Cl_2IO_2$ $[M]^+$ 315.8549, found 315.8540.

1,4-Dichloro-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (S12), prepared from 2-chloro-6-iodobenzoic acid (283 mg, 1.00 mmol) following the general procedure GP1 yielded **S12** as a slightly yellow solid (231 mg, 0.73 mmol, 73%).



S12

m.p. = 215 °C (DCM, decomposition); **^{1}H NMR** (400 MHz, DMSO) δ 7.84 (dd, *J* = 7.9, 1.0 Hz, 1H, H_{Ar}), 7.55 (dd, *J* = 8.1, 1.0 Hz, 1H, H_{Ar}), 7.18 (t, *J* = 8.0 Hz, 1H, H_{Ar}) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 167.5, 137.4, 133.7, 131.7, 128.9, 128.9, 92.92 ppm; **IR** (KBr) $\tilde{\nu}_{max}$ = 3432, 1702, 1547, 1433, 1223, 1035, 791 cm^{-1}; **MS** (ESI+) m/z (%) = 595/593 (16/25), 319/317 (12/17) $[M+H]^+$, 306/304 (2/6) $[M-Cl+Na]^+$, 301/299 (14/42) $[M-Cl+NH_4]^+$, 284/282 (21/58) $[M-Cl+H]^+$, 267/265 (32/100); **HRMS** (ESI+) calcd. for $C_7H_4ClIO_2$ $[M+H]^+$ 316.8628, found 316.8621.

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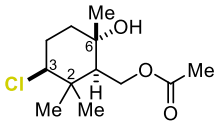
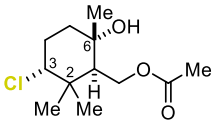
3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl acetate (16), prepared from **15** (39.3 mg, 200 µmol) following general procedure GP2 yielded **16** as a 83:17 mixture of separable diastereomers;



major-16

major diastereomer: colorless oil (12.5 mg, 50.1 µmol, 25%); **TLC:** R_f = 0.15 (silica gel, pentane/EtOAc 70:30) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.42 (dd, *J* = 11.9, 5.3 Hz, 1H, CH_2), 4.32 (dd, *J* = 11.9, 5.0 Hz, 1H, CH_2), 3.78 (dd, *J* = 12.1, 4.1 Hz, 1H, CHCl), 2.50 (bs, 1H, OH), 2.07 (s, 3H, $OCCH_3$), 2.05 – 2.00 (m, 1H, CH_2), 1.93 – 1.85 (m, 1H, CH), 1.84 – 1.77 (m, 1H, CH_2), 1.68 (t, *J* = 5.1 Hz, 1H), 1.65 – 1.56 (m, 1H, CH_2), 1.24 (d, *J* = 0.9 Hz, 3H, CH_3), 1.17 (s, 3H, CH_3), 0.96 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.2, 71.87, 70.72, 63.26, 55.80, 41.83, 40.04, 30.90, 29.11, 24.01, 21.33, 16.38 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3449, 1734, 1367, 1238, 1029, 915 cm^{-1}.

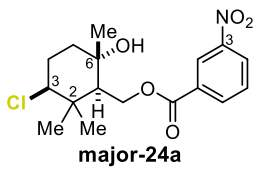


minor-16

minor diastereomer: colorless oil (2.49 mg, 10.2 µmol, 5%); **TLC:** R_f = 0.21 (silica gel, pentane/EtOAc 80:20) [CAM]; characteristic signals: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.37 (dd, *J* = 11.9, 5.0 Hz, 1H, CH_2), 4.26 (dd, *J* = 11.8, 5.2 Hz, 1H, CH_2), 4.01 – 3.97 (m, 1H, CHCl), 2.06 (s, 3H, $OCCH_3$), 2.06 – 2.04 (m, 3H, CH_2), 1.69 – 1.66 (m, 1H, CH_2), 1.27 – 1.24 (m, 1H, CH), 1.23 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.05 (s, 3H, CH_3) ppm; characteristic signals: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 72.19, 70.41, 62.84, 39.46, 36.27, 29.82, 29.48, 28.63, 25.38, 23.80, 21.34 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3456, 1735, 1367, 1231, 1027, 960 cm^{-1}.

The analytical data obtained were in agreement with those reported in the literature.[9]

3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl 3-nitrobenzoate (24a), prepared from *(E)*-3,7-dimethylocta-2,6-dien-1-yl 3-nitrobenzoate (60.7 mg, 200 µmol) following general procedure GP2 yielded **24a** as a 81:19 mixture of separable diastereomers;

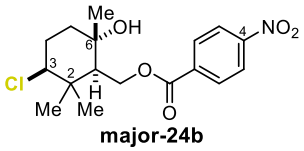


major-24a

major diastereomer: colorless solid (18.7 mg, 52.6 µmol, 26%); **m.p.** = 117 °C ($CDCl_3$); **TLC:** R_f = 0.36 (silica gel, pentane/EtOAc 67:33) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.87 - 8.79 (m, 1H, H_{Ar}), 8.44 (dd, *J* = 2.3, 1.1 Hz, 1H, H_{Ar}), 8.34 (dt, *J* = 7.8, 1.4 Hz, 1H, H_{Ar}), 7.66 (t, *J* = 8.0 Hz, 1H, H_{Ar}), 4.82 (dd, *J* = 11.9, 3.6 Hz, 1H, CH_2), 4.55 (dd, *J* = 11.9, 5.7 Hz, 1H, CH_2), 3.82 (dd, *J* = 11.9, 4.2 Hz, 1H, CHCl), 2.15 - 2.05 (m, 1H, CH_2), 1.99 - 1.90 (m, 1H, CH_2), 1.90 - 1.81 (m, 2H, CH, CH_2), 1.69 - 1.57 (m, 1H, CH_2), 1.29 (d, *J* = 0.9 Hz, 3H, CH_3), 1.25 (s, 3H,

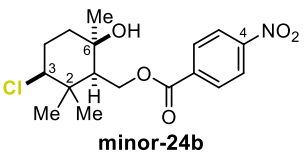
CH_3), 1.05 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.8, 148.5, 135.3, 132.0, 129.9, 127.7, 124.7, 71.85, 70.38, 64.29, 56.31, 42.30, 40.31, 31.00, 29.35, 24.09, 16.64 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3453, 1717, 1528, 1349, 1297, 1260, 1134, 1068, 920 cm^{-1}; **HRMS** (ESI-) calcd. for $C_{18}H_{23}ClNO_7$ $[M+FA-H]^-$ 400.1169, found 400.1170. *characteristic signals for the minor diastereomer*: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.81 (dd, *J* = 12.6, 3.8 Hz, 1H, CHCl), 1.34 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.14 (s, 3H, CH_3) ppm; the minor diastereomer could not be separated from side products.

3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl 4-nitrobenzoate (24b), prepared from (*E*)-3,7-dimethylocta-2,6-dien-1-yl 4-nitrobenzoate (60.7 mg, 200 µmol) following general procedure GP2 yielded **24b** as a 80:20 mixture of separable diastereomers;



major-24b

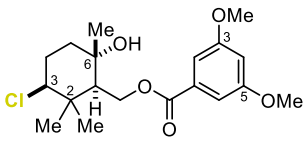
major diastereomer: colorless solid (17.8 mg, 50 µmol, 25%); **m.p.** = 149 °C ($CDCl_3$); **TLC:** R_f = 0.41 (silica gel, pentane/EtOAc 80:20) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.34 - 8.23 (m, 2H, H_{Ar}), 8.24 - 8.12 (m, 2H, H_{Ar}), 4.81 (dd, *J* = 11.9, 3.7 Hz, 1H, CH_2), 4.54 (dd, *J* = 11.9, 5.7 Hz, 1H, CH_2), 3.81 (dd, *J* = 11.9, 4.1 Hz, 1H, CHCl), 2.16 - 2.01 (m, 2H, OH, CH_2), 1.96 - 1.78 (m, 3H, CH, CH_2), 1.71 - 1.54 (m, 1H, CH_2), 1.29 (d, *J* = 0.9 Hz, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.05 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.9, 150.8, 135.6, 130.8, 123.8, 71.84, 70.37, 64.31, 56.26, 42.24, 40.27, 30.96, 29.36, 24.12, 16.61 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3556, 1717, 1516, 1343, 1279, 1252, 1235, 1156, 1105, 720 cm^{-1}; **MS** (ESI-) m/z (%) = 402/400 (30/100) $[M+FA-H]^-$, 392/390 (3/4) $[M+Cl]^-$; **HRMS** (ESI-) calcd. for $C_{18}H_{23}ClNO_7$ $[M+FA-H]^-$ 400.1169, found 400.1171.



minor-24b

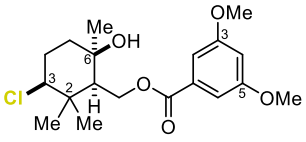
minor diastereomer: colorless solid (4.3 mg, 12.0 µmol, 6%); **m.p.** = 128 °C ($CDCl_3$); **TLC:** R_f = 0.31 (silica gel, pentane/EtOAc 67:33) [CAM]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 – 8.28 (m, 2H, H_{Ar}), 8.20 – 8.16 (m, 2H, H_{Ar}), 4.73 – 4.66 (m, 2H, CH_2), 3.80 (dd, *J* = 12.6, 3.8 Hz, 1H, CHCl), 2.26 (tdd, *J* = 13.6, 12.6, 3.9 Hz, 1H, CH_2), 1.93 (dq, *J* = 13.4, 3.7 Hz, 1H, CH_2), 1.75 (dt, *J* = 14.3, 3.5 Hz, 1H, CH_2), 1.64 (td, *J* = 14.0, 4.1 Hz, 1H, CH_2), 1.53 (dd, *J* = 5.1, 3.0 Hz, 1H, CH), 1.33 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.14 (s, 3H, CH_3) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.6, 150.7, 135.7, 130.8, 123.8, 71.54, 71.39, 64.45, 53.79, 41.19, 40.07, 31.07, 29.04, 28.64, 16.38 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3513, 1704, 1526, 1348, 1289, 1264, 1124, 1106, 873, 717 cm^{-1}; **MS** (ESI-) m/z (%) = 402/400 (30/100) $[M+FA-H]^-$; **HRMS** (ESI-) calcd. for $C_{18}H_{23}ClNO_7$ $[M+FA-H]^-$ 400.1169, found 400.1170.

3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl 3,5-dimethoxybenzoate (24c), prepared from *(E)*-3,7-dimethylocta-2,6-dien-1-yl 3,5-dimethoxybenzoate (63.7 mg, 200 µmol) following general procedure GP2 yielded **24c** as a 71:29 mixture of separable diastereomers;



major-24c

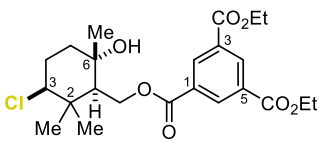
major diastereomer: co less oil (25.8 mg, 69.6 µmol, 35%); **TLC:** R_f = 0.38 (silica gel, pentane/EtOAc 67:33) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.14 (d, *J* = 2.4 Hz, 2H, H_{Ar}), 6.65 (t, *J* = 2.4 Hz, 1H, H_{Ar}), 4.73 (dd, *J* = 12.0, 4.2 Hz, 1H, CH_2), 4.49 (dd, *J* = 11.9, 5.6 Hz, 1H, CH_2), 3.82 (s, 6H, 2xOMe), 3.81 - 3.75 (m, 1H, CHCl), 2.46 (bs, 1H, OH), 2.14 - 2.00 (m, 1H, CH_2), 1.97 - 1.88 (m, 1H, CH_2), 1.88 - 1.78 (m, 2H, CH, CH_2), 1.69 - 1.54 (m, 1H, CH_2), 1.28 (d, *J* = 0.9 Hz, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.04 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.6, 160.9, 132.0, 107.3, 105.9, 71.81, 70.69, 63.66, 56.21, 55.72, 42.08, 40.21, 30.98, 29.33, 24.09, 16.52 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 2936, 1592, 1457, 1417, 1319, 1246, 1135, 822 cm^{-1}; **MS** (ESI-) m/z (%) = 485/483 (0.7/2) $[M+TFA-H]^-$, 417/415 (30/100) $[M+FA-H]^-$; **HRMS** (ESI-) calcd. for $C_{20}H_{28}ClO_7$ $[M+FA-H]^-$ 415.1529, found 415.1530.



minor-24c

minor diastereomer: colorless oil (10.6 mg, 28.6 µmol, 14%); **TLC:** R_f = 0.21 (silica gel, pentane/EtOAc 80:20) [CAM]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 2.4 Hz, 2H, H_{Ar}), 6.65 (t, *J* = 2.4 Hz, 1H, H_{Ar}), 4.63 (d, *J* = 4.0 Hz, 2H, CH_2), 3.82 (s, 6H, 2xOMe), 3.80 (dd, *J* = 12.2, 3.5 Hz, 1H, CHCl), 2.32 – 2.22 (m, 1H, CH_2), 1.92 (dq, *J* = 13.3, 3.7 Hz, 1H, CH_2), 1.80 – 1.71 (m, 2H, CH, CH_2), 1.60 (td, *J* = 14.0, 4.0 Hz, 1H, CH_2), 1.32 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.16 (s, 3H, CH_3) ppm; **^{13}C NMR** (126 Hz, $CDCl_3$) δ 166.2, 160.9, 132.1, 107.3, 105.7, 71.67, 63.62, 53.60, 41.10, 40.11, 31.00, 29.15, 28.64, 16.50 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3522, 1715, 1595, 1457, 1349, 1304, 1229, 1205, 1155, 1048, 767 cm^{-1}; **MS** (ESI-) m/z (%) = 619/617 (21/31), 417/415 (10/32) $[M+FA-H]^-$; **HRMS** (ESI-) calcd. for $C_{20}H_{28}ClNO_7$ $[M+FA-H]^-$ 415.1529, found 415.1531.

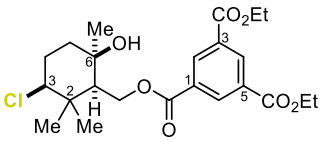
3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl) 3,5-diethyl benzene-1,3,5-tricarboxylate (24d), prepared from *(E)*-1-(3,7-dimethylocta-2,6-dien-1-yl) 3,5-diethyl benzene-1,3,5-tricarboxylate (80.5 mg, 200 µmol) following general procedure GP2 yielded **24d** as a 69:31 mixture of separable diastereomers;



major-24d

major diastereomer: colorless oil (13.7 mg, 30.1 µmol, 15%); **TLC:** R_f = 0.55 (silica gel, pentane/EtOAc 67:33) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.96 – 8.84 (m, 1H, H_{Ar}), 8.81 (d, *J* = 1.7 Hz, 2H, H_{Ar}), 4.83 (dd, *J* = 11.9, 3.5 Hz, 1H, CH_2), 4.53 (dd, *J* = 11.9, 5.8 Hz, 1H, CH_2), 4.44 (q, *J* = 7.1 Hz, 4H, 2xethyl-CH_2),

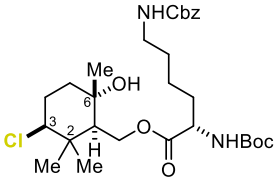
3.82 (dd, *J* = 12.0, 4.1 Hz, 1H, CHCl), 2.15 – 2.02 (m, 1H, CH_2), 1.98 – 1.89 (m, 1H, CH_2), 1.89 – 1.80 (m, 2H, CH, CH_2), 1.71 – 1.59 (m, 1H, CH_2), 1.43 (t, *J* = 7.1 Hz, 6H, 2xethyl-CH_3), 1.29 (d, *J* = 0.8 Hz, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.05 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.4, 165.1 (2C), 134.8, 134.5 (2C), 131.8 (2C), 131.2, 71.80, 70.50, 63.99, 61.90 (2C), 56.36, 41.78, 40.34, 31.03, 29.32, 24.04, 16.94, 14.44 (2C) ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3517, 1723, 1022, 913, 733 cm^{-1}; **MS** (ESI+) m/z (%) = 495/493 (23/64) $[M+K]^+$, 479/477 (13/44) $[M+Na]^+$, 455/453 (20/58) $[M+H]^+$, 439/437 (34/100) $[M-H_2O+H]^+$, 267 (60), 173/171 (13/41); **HRMS** (ESI-) calcd. for $C_{24}H_{32}ClO_9$ $[M+FA-H]^-$ 499.1740, found 499.1741.



minor-24d

minor diastereomer: colorless oil (3.8 mg, 8.35 µmol, 4%); **TLC:** R_f = 0.38 (silica gel, pentane/EtOAc 80:20) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.88-8.84 (m, 1H, H_{Ar}), 8.82 (d, *J* = 1.7 Hz, 2H, H_{Ar}), 4.69 (d, *J* = 4.1 Hz, 2H, CH_2), 4.44 (q, *J* = 7.1 Hz, 4H, 2xethyl-CH_2), 3.81 (dd, *J* = 12.5, 3.8 Hz, 1H, CHCl), 2.26 (qd, *J* = 13.2, 4.1 Hz, 1H, CH_2), 1.93 (dq, *J* = 13.2, 3.8 Hz, 1H, CH_2), 1.86 – 1.79 (m, 1H, CH), 1.75 (dt, *J* = 14.2, 3.6 Hz, 1H, CH_2), 1.66 (dd, *J* = 13.7, 4.0 Hz, 1H, CH_2), 1.43 (t, *J* = 7.1 Hz, 6H, 2xethyl-CH_3), 1.34 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.15 (s, 3H, CH_3) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.1, 165.0 (2C), 134.7, 134.5 (2C), 131.7 (2C), 131.3, 71.54, 71.52, 64.15, 61.92 (2C), 53.74, 41.18, 40.05, 31.04, 29.09, 28.60, 16.37, 14.44 (2C) ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3530, 1724, 1235, 1095, 1022, 931, 739 cm^{-1}; **MS** (ESI+) m/z (%) = 479/477 (37/100) $[M+Na]^+$, 455/453 (6/18) $[M+H]^+$, 439/437 (7/24) $[M-H_2O+H]^+$, 267 (26), 173/171 (5/17); **HRMS** (ESI-) calcd. for $C_{24}H_{32}ClO_9$ $[M+FA-H]^-$ 499.1740, found 499.1742.

3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl *N*^{6}-((benzyloxy)carbo-nyl)-*N*^{2}-(*tert*-butoxycarbo-nyl)lysinate (25), prepared from (*E*)-3,7-dimethylocta-2,6-dien-1-yl *N*^{6}-((benzyloxy)carbonyl)-*N*^{2}-(*tert*-butoxycarbonyl)-*L*-lysinate (103 mg, 200 µmol) following general procedure GP2 yielded **25** as a colorless oil (13.9 mg, 24.4 µmol, 12%, d.r. > 95:5)

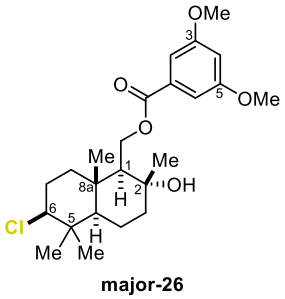


25

TLC: R_f = 0.38 (silica gel, *n*-hexane/EtOAc 67:33); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42 - 7.26 (m, 5H, Cbz), 5.09 (s, 3H, CH_2Cbz, NH), 4.98 - 4.81 (m, 1H, NH), 4.49 (dd, *J* = 11.7, 4.30 Hz 1H, CH_2), 4.40 - 4.18 (m, 2H, CH, CH_2), 3.74 (dt, *J* = 11.9, 4.4 Hz, 1H, CHCl), 3.27 - 3.10 (m, 2H, CH_2), 2.02 (dt, *J* = 14.0, 4.1 Hz, 1H, CH), 1.94 - 1.74 (m, 3H, CH_2), 1.74 - 1.59 (m, 3H, CH_2), 1.59 - 1.46 (m, 3H, CH_2), 1.43 (d, *J* = 0.9 Hz, 9H, Boc), 1.39 - 1.30 (m, 2H), 1.29 - 1.21 (m, 3H, CH_3), 1.18 - 1.10 (m, 3H, CH_3), 0.94 (d, *J* = 1.8 Hz, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.7, 155.5, 136.7 (d, *J* = 2.6 Hz), 128.7, 128.7, 128.3, 128.3, 128.2, 80.27, 71.69 (d, *J* = 5.8 Hz), 70.61, 66.88, 64.02, 55.99 (d, *J* = 25.9 Hz), 41.91 (d, *J* = 10.5 Hz), 40.61, 40.11

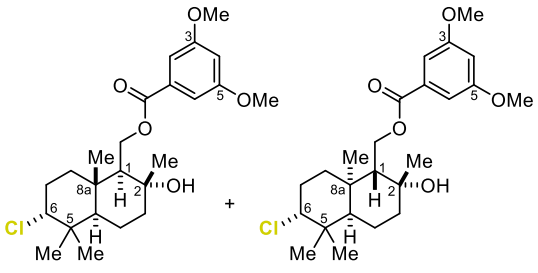
(d, *J* = 10.2 Hz), 32.20, 30.96 (d, *J* = 9.0 Hz), 29.53, 29.17, 28.47, 23.92, 22.42, 16.49 (d, *J* = 2.8 Hz) ppm; **IR** (film) $\tilde{\nu}_{max}$ = 3349, 2920, 1693, 1249, 1161, 731, 697 cm^{-1}; **MS** (ESI+) m/z (%) = 593/591 (37/100) $[M+Na]^+$, 471/469 (13/36) $[M\text{-}Boc+H]^+$, 453/451 (13/38) $[M\text{-}Boc\text{-}H_2O+H]^+$; **HRMS** (ESI-) calcd. for $C_{30}H_{46}ClN_2O_9$ $[M+FA\text{-}H]^-$ 613.2892, found 613.2893.

6-Chloro-2-hydroxy-2,5,5,8a-tetramethyldecahydronaphthalen-1-yl)methyl 3,5-dimethoxybenzoate (26), prepared from (2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl 3,5-dimethoxybenzoate (77.3 mg, 200 µmol) following general procedure GP2 yielded **26** as a 45:33:22 mixture of separable diastereomers;



major-26

colorless oil (14.7 mg, 33.5 µmol, 17%); **TLC:** R_f = 0.19 (silica gel, pentane/EtOAc 88:12) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 2.4 Hz, 2H, H_{Ar}), 6.64 (t, *J* = 2.3 Hz, 2H, H_{Ar}), 4.68 (dd, *J* = 11.9, 3.2 Hz, 1H, CH_2), 4.37 (dd, *J* = 11.9, 6.2 Hz, 1H, CH_2), 3.82 (s, 6H, 2xOCH_3), 3.74 (dd, *J* = 12.1, 4.7 Hz, 1H, CHCl), 2.05 - 1.97 (m, 1H, CH_2), 1.99 - 1.89 (m, 2H, CH_2), 1.88 - 1.77 (m, 2H, CH_2), 1.62 (td, *J* = 5.3, 4.4, 2.2 Hz, 2H, CH, CH_2), 1.54 - 1.43 (m, 1H, CH_2), 1.37 - 1.28 (m, 1H, CH_2), 1.21 (d, *J* = 0.9 Hz, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.09 - 1.01 (m, 1H, CH), 0.97 (s, 3H, CH_3), 0.90 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 160.9, 132.1, 107.4, 105.7, 72.44, 72.22, 62.76, 60.14, 56.26, 55.72, 44.16, 40.00, 39.87, 38.14, 29.45, 29.42, 24.60, 21.31, 16.86, 15.96 ppm; **IR** (film) $\tilde{\nu}_{max}$ = 3446, 2942, 1715, 1596, 1458, 1157, 757 cm^{-1}; **MS** (ESI+) m/z (%) = 901/900 (40/51) $[2M+Na]^+$, 463/461 (35/100) $[M+Na]^+$; **HRMS** (ESI+) calcd. for $C_{24}H_{35}ClNaO_5$ $[M+Na]^+$ 461.2065, found 461.2066.

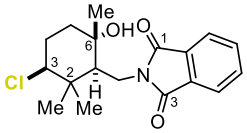


minor1-26 **minor2-26**

colorless oil (17.9 mg, 40.7 µmol, 20%); **TLC:** R_f = 0.29 (silica gel, pentane/EtOAc 88:12) [CAM]; *minor diastereomers*: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.17 (d, *J* = 2.4 Hz, 1H, H_{Ar}), 7.15 (d, *J* = 2.4 Hz, 1H, H_{Ar}), 6.65 (d, *J* = 2.4 Hz, 2x 1H, H_{Ar}), 4.70 (dd, *J* = 11.9, 3.3 Hz, 1H, CH_2), 4.64 (dd, *J* = 5.2, 3.3 Hz, 2H, CH_2), 4.42 (dd, *J* = 11.8, 6.2 Hz, 1H, CH_2), 4.09 - 4.00 (m, 2x 1H, CHCl), 3.82 (d, *J* = 1.8 Hz, 2x 6H, 2xOCH_3), 2.36 - 2.19 (m, 2x 1H, CH_2), 2.08 - 1.90 (m, 2x 1H, CH_2), 1.88 - 1.71 (m, 3H, 2x CH_2), 1.71 - 1.42 (m, 3H, CH, CH_2), 1.35 (s, 3H, CH_3), 1.31 (m, 2H, CH_2), 1.29 (s, 3H, CH_3), 1.25 (m, 1H, CH), 1.22 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.97 (s, 3H, CH_3), 0.96 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 166.5, 160.9, 160.8, 132.3, 132.1, 107.3, 107.2, 106.1, 105.9, 72.44, 72.37, 72.00, 69.09, 64.26, 62.87, 59.94, 57.52, 55.73, 55.71, 52.94, 48.05, 44.23, 42.58, 39.41, 39.25, 38.30, 38.08, 33.27, 33.33, 31.21, 31.08, 29.86, 28.17, 27.04, 25.07, 24.66, 24.31,

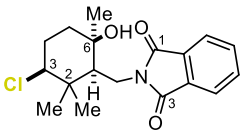
22.96, 22.34, 20.02, 16.51 ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ , **IR** (film) $\tilde{\nu}_{max}$ = 3492, 2937, 1716, 1597, 1206, 1157, 1050, 768 cm^{-1}; **MS** (ESI+) m/z (%) = 463/461 (15/41) $[M+Na]^+$, 423/421 (36/100) $[M-H_2O+H]^+$, 241/239 (28/85), 203 (45); **HRMS** (ESI+) calcd. for $C_{24}H_{35}ClNaO_5$ $[M+Na]^+$ 461.2065, found 461.2068.

3-Chloro-6-hydroxy-2,2,6-trimethylcyclohexyl)methyl)isoindoline-1,3-dione (27), prepared from (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindoline-1,3-dione (56.7 mg, 200 µmol) following general procedure GP2 yielded **27** as a 81:19 mixture of separable diastereomers;



major-27

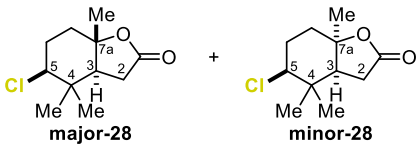
major diastereomer: colorless solid (22.9 mg, 68.2 µmol, 34%); **m.p.** = 127 °C ($CDCl_3$); **TLC:** R_f = 0.30 (silica gel, pentane/EtOAc 67:33) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.86 - 7.77 (m, 2H, H_{Ar}), 7.74 - 7.65 (m, 2H, H_{Ar}), 3.93 (d, *J* = 5.1 Hz, 2H, CH_2), 3.75 (dd, *J* = 12.0, 4.3 Hz, 1H, CHCl), 2.60 (bs, 1H, OH), 2.09 - 1.98 (m, 1H, CH_2), 1.93 (t, *J* = 5.1 Hz, 1H, CH_2), 1.90 - 1.77 (m, 2H, CH_2), 1.61 - 1.45 (m, 1H, CH), 1.35 (d, *J* = 0.9 Hz, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.03 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.2 (2C), 134.2 (2C), 132.1 (2C), 123.4 (2C), 72.27, 70.79, 55.10, 42.58, 40.77, 36.11, 31.17, 28.71, 23.02, 16.04 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3468, 1767, 1695, 1408, 1394, 1379, 962, 916, 723, 712 cm^{-1}; **MS** (ESI+) m/z (%) = 392/390 (17/43) $[M+MeOH+H]^+$, 320/318 (26/80) $[M-H_2O+H]^+$, 282 (100), 160 (79); **HRMS** (ESI-) calcd. for $C_{19}H_{23}ClNO_5$ $[M+FA-H]^-$ 380.1270, found 380.1272.



minor-27

minor diastereomer: colorless solid (5.40 mg, 16.1 µmol, 8%); **m.p.** = 106 °C ($CDCl_3$); **TLC:** R_f = 0.21 (silica gel, pentane/EtOAc 80:20) [CAM]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H, H_{Ar}), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H, H_{Ar}), 3.98 - 3.95 (m, 1H, CHCl), 3.93 (dd, *J* = 14.5, 4.95 Hz, 1H, CH_2), 3.86 (dd, *J* = 14.5, 5.72 Hz, 1H, CH_2), 2.62 (bs, 1H, OH), 2.39 (t, *J* = 5.3 Hz, 1H, CH_2), 2.12 - 2.06 (m, 2H, CH_2), 1.94 - 1.88 (m, 1H, CH_2), 1.68 - 1.63 (m, 1H, CH), 1.32 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.12 (s, 3H, CH_3) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.1, 134.2, 132.1, 123.4, 72.55, 70.92, 48.74, 40.14, 36.65, 35.12, 30.04, 28.79, 23.30, 22.36 ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3439, 1763, 1690, 1439, 1394, 1365, 1191, 1085, 914, 719, 709 cm^{-1}; **MS** (ESI+) m/z (%) = 360/358 (33/100) $[M+Na]^+$, 322 (40) $[M-HCl+Na]^+$; **HRMS** (ESI+) calcd. for $C_{18}H_{22}ClNNaO_3$ $[M+Na]^+$ 358.1180, found 358.1175.

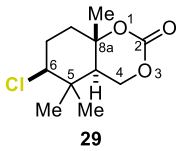
5-Chloro-4,4,7a-trimethylhexahydrobenzofuran-2(*3H*)-one (28), prepared from homogeranylic acid (36.5 mg, 200 µmol) following general procedure GP2 yielded **28** as a 86:14 mixture of inseparable diastereomers;



colorless solid (29.0 mg, 134 µmol, 67%); **TLC:** R_f = 0.29 (silica gel, pentane/EtOAc 88:12) [CAM]; *major diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.77 (dd, *J* = 12.1, 4.7 Hz, 1H, CHCl), 2.51 (dd, *J* = 16.3, 14.5 Hz, 1H, CH_2), 2.37 (dd, *J* = 16.3, 6.7 Hz, 1H, CH_2), 2.28 - 2.20 (m, 1H, CH_2), 2.04 (dt, *J* = 12.0, 3.4 Hz, 1H, CH_2), 1.99 (dd, *J* = 14.5, 6.7 Hz, 1H, CH), 1.94 - 1.85 (m, 1H, CH_2), 1.85 - 1.75 (m, 1H, CH_2), 1.37 (d, *J* = 1.0 Hz, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.98 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 175.6, 84.70, 68.81, 54.92, 38.55, 37.61, 31.40, 29.93, 29.07, 20.58, 15.81 ppm; *minor diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.77 (dd, *J* = 12.1, 4.7 Hz, 1H, CHCl), 2.63 - 2.54 (m, 1H, CH_2), 2.37 (dd, *J* = 16.3, 6.7 Hz, 1H, CH_2), 2.04 (dt, *J* = 12.0, 3.4 Hz, 1H, CH_2), 1.99 (dd, *J* = 14.5, 6.7 Hz, 1H, CH), 1.94 - 1.85 (m, 1H, CH_2), 1.85 - 1.75 (m, 1H, CH_2), 1.54 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.07 (s, 3H, CH_3) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 175.0, 84.69, 65.71, 52.00, 37.34, 33.73, 32.78, 28.79, 27.32, 26.91, 24.11 ppm; *mixture*: **IR** (film) $\tilde{\nu}_{max}$ = 3445, 1606, 1574, 1394, 1316, 1130 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{11}H_{17}ClNaO_2$ $[M+Na]^+$ 239.0809, found 239.0802.

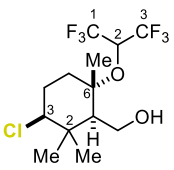
The analytical data obtained were in agreement with those reported in the literature.[9]

6-Chloro-5,5,8a-trimethylhexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (29), prepared from *(E)*-3,7-dimethylocta-2,6-dien-1-yl *tert*-butylcarbamate (50.7 mg, 200 µmol) following general procedure GP2 yielded **29** as a colorless solid (8.37 mg, 36.0 µmol, 18%, d.r. > 95:5);



m.p. = 103°C ($CDCl_3$); **TLC:** R_f = 0.38 (silica gel, *n*-hexane/EtOAc 50:50); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.49 (dd, *J* = 10.8, 5.80 Hz, 1H, CH_2), 4.43 (dd, *J* = 12.7, 10.8 Hz, 1H, CH_2) 3.80 (dd, *J* = 12.2, 4.2 Hz, 1H, CHCl), 2.18 (dq, *J* = 13.8, 3.8 Hz, 1Hz, CH_2), 2.07 - 1.98 (m, 2H, CH_2), 1.89 (tdd, *J* = 13.9, 12.1, 3.3 Hz, 1H, CH), 1.82 - 1.73 (m, 1H, CH_2), 1.52 (d, *J* = 0.9 Hz, 3H, CH_3), 1.16 (s, 3H, CH_3), 0.97 (s, 3H, CH_3) ppm; **^{13}C NMR** (76 MHz, $CDCl_3$) δ 148.5, 80.78, 68.60, 67.32, 47.66, 38.46, 38.30, 30.07, 20.96, 15.95 ppm; **IR** (film) $\tilde{\nu}_{max}$ = 3349, 1708, 1266, 1214, 1078, 743 cm^{-1}; **MS** (ESI+) m/z (%) = 257/255 (5/17) $[M+Na]^+$; **HRMS** (ESI+) calcd. for $C_{11}H_{17}ClNaO_3$ $[M+Na]^+$ 255.0758, found 255.0757.

3-Chloro-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2,2,6-trimethylcyclohexyl)methanol (30), prepared from geraniol (30.9 mg, 200 µmol) following general procedure GP2 yielded **30** as a colorless solid (20.7 mg, 58.0 µmol, 29%, d.r. > 95:5);

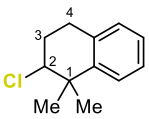


30

m.p. = 100 – 101 °C (EtOAc); **TLC:** R_f = 0.63 (silica gel, n-hexane/EtOAc 80:20); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.35 (hept, *J* = 5.7 Hz, 1H, $(CF_3)_2CH$), 3.98 (ddd, *J* = 12.1, 6.3, 1.4 Hz, 1H, CHCl), 3.83 – 3.73 (m, 2H, CH_2), 2.22 (br d, *J* = 9.0 Hz, 1H, CH_2), 2.18 – 2.10 (m, 1H, CH_2), 1.89 – 1.69 (m, 4H, 2xCH_2, OH), 1.38 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 0.90 (s, 3H, CH_3) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 124.8 – 118.1 (m, 2C), 85.64, 69.64, 68.57 (hept, *J* = 32.3 Hz) 61.13, 58.50, 40.13, 37.33, 30.38, 29.38, 19.18 (t, *J* = 2.6 Hz), 16.96 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -72.61 – -72.88 (m, 2x CF_3) ppm; **IR** (ATR) $\tilde{\nu}_{max}$ = 3541, 2964, 1397, 1276, 1229, 1187, 1102, 909, 687 cm^{-1}.

The analytical data obtained were in agreement with those reported in the literature.[10]

2-Chloro-1,1-dimethyl-1,2,3,4-tetrahydronaphthalene (31), prepared from (3-methylbut-2-en-1-yl)benzene (32.1 mg, 200 µmol) following general procedure GP2 yielded **31** as a colorless oil (30.4 mg, 156 µmol, 78%);

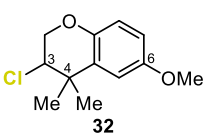


31

TLC: R_f = 0.50 (silica gel, pentane) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.8, 1.4 Hz, 1H, H_{Ar}), 7.23 – 7.17 (m, 1H, H_{Ar}), 7.14 (td, *J* = 7.3, 1.4 Hz, 1H, H_{Ar}), 7.09 – 7.05 (m, 1H, H_{Ar}), 4.24 (dd, *J* = 9.4, 3.2 Hz, 1H, CHCl), 3.06 (dt, *J* = 17.2, 5.9 Hz, 1H, CH_2), 2.97 – 2.86 (m, 1H, CH_2), 2.38 – 2.29 (m, 1H, CH_2), 2.28 – 2.19 (m, 1H, CH_2), 1.46 (s, 3H, CH_3), 1.42 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.6, 133.8, 128.9, 126.9, 126.4, 126.1, 69.36, 39.95, 29.84, 28.97, 28.33, 27.00 ppm.

The analytical data obtained were in agreement with those reported in the literature.[10]

3-chloro-6-methoxy-4,4-dimethylchromane (32), prepared from 1-methoxy-4-((3-methylbut-2-en-1-yl)oxy)benzene (38.5 mg, 200 µmol) following general procedure GP2 yielded **32** as a colorless oil (34.5 mg, 152 µmol, 76%);

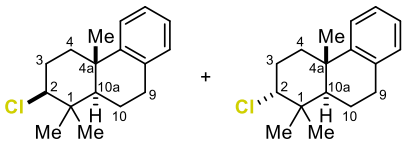


32

TLC: R_f = 0.74 (silica gel, pentane/EtOAc 95:5) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.17 (m, 2H, H_{Ar}), 7.07 (dd, *J* = 2.86, 0.78 Hz, 1H, H_{Ar}), 4.61 (dd, *J* = 8.7, 5.6 Hz, 1H, CHCl), 4.24 (s, 3H, OCH_3), 3.74 (dd, *J* = 16.9, 5.6 Hz, 1H, CH_2), 3.53 (ddt, *J* = 17.0,

8.7, 0.9 Hz, 1H, CH_2), 1.96 (s, 3H, CH_3), 1.85 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.7, 146.6, 119.9, 118.0, 114.3, 113.5, 76.72, 60.28, 55.81, 33.63, 26.14, 20.86 ppm; **IR** (film) $\tilde{\nu}_{max}$ 2920, 1715, 1416, 1333, 1222, 1129 cm^{-1}; **MS** (EI, 70 eV) = 195 (31) $[M\text{-}CH_3O]^+$, 197 (28), 212 (100), 69 (69); **HRMS** (EI, 70 eV) calcd. for $C_{12}H_{15}ClO_2$ $[M]^+$ 226.0755, found 226.0764.

2-Chloro-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (33), prepared from homogeranyl benzene (46.1 mg, 200 µmol) following general procedure GP2 yielded **33** as a 79:21 mixture of inseparable diastereomers;

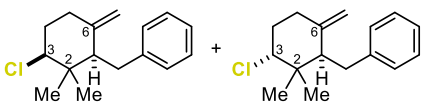


major-33 **minor-33**

colorless oil (24.3 mg, 92.5 µmol, 46%); **TLC:** R_f = 0.29 (silica gel, pentane) [CAM]; *major diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.01 (m, 4H, H_{Ar}), 3.81 (dd, *J* = 12.0, 4.7 Hz, 1H, CHCl), 3.03 – 2.81 (m, 2H, CH_2), 2.36 (dt, *J* = 13.4, 3.7 Hz, 1H, CH_2), 2.24 – 2.05 (m, 2H, CH_2), 2.04 – 1.74 (m, 3H, CH, CH_2), 1.65 – 1.52 (m, 2H, CH_2), 1.42 (dd, *J* = 12.1, 2.3 Hz, 1H, CH_2), 1.24 (d, *J* = 0.8 Hz, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.02 (s, 3H, CH_3) ppm; *minor diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.01 (m, 5H, H_{Ar}), 4.13 (t, *J* = 3.0 Hz, 1H, CHCl), 3.03 – 2.81 (m, 2H, CH_2), 2.36 (dt, *J* = 13.4, 3.7 Hz, 1H, CH_2), 2.24 – 2.05 (m, 2H, CH_2), 2.04 – 1.74 (m, 3H, CH, CH_2), 1.65 – 1.52 (m, 2H, CH_2), 1.42 (dd, *J* = 12.1, 2.3 Hz, 1H, CH_2), 1.22 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.09 (s, 3H, CH_3) ppm; **HRMS** (EI, 70 eV) calcd. for $C_{17}H_{23}Cl$ $[M]^+$ 262.1483, found 262.1475.

The analytical data obtained were in agreement with those reported in the literature.[10]

3-Chloro-2,2-dimethyl-6-methylenecyclohexyl)methyl)benzene (34), prepared from geranyl benzene (42.9 mg, 200 µmol) following general procedure GP2 yielded **34** as a 81:19 mixture of inseparable diastereomers;

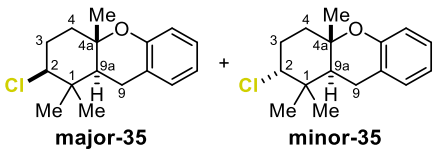


major-34 **minor-34**

colorless oil (9.01 mg, 36.2 µmol, 18%); **TLC:** R_f = 0.23 (silica gel, pentane) [CAM]; *major diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 - 7.22 (m, 2H, H_{Ar}), 7.16 (m, 3H, H_{Ar}), 4.86 (br, 1H, CH_2), 4.64 (br, 1H, CH_2), 3.99 (dd, *J* = 10.9, 4.3 Hz, 1H, CHCl), 3.02 (dd, *J* = 15.0, 2.7 Hz, 1H, CH_2), 2.84 (dd, *J* = 15.0, 10.7 Hz, 1H, CH_2), 2.38 (dt, *J* = 13.1, 4.2 Hz, 1H, CH), 2.26 (ddt, *J* = 10.7, 2.8, 1.4 Hz, 1H, CH_2), 2.14 (m, 1H, CH_2), 2.10 - 2.00 (m, 1H, CH_2), 1.96 - 1.84 (m, 1H, CH, CH_2), 1.25 (s, 3H, CH_3), 0.96 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.3, 141.9, 128.7, 128.3, 125.8, 110.9, 71.15, 53.77, 42.02, 35.33, 34.54, 32.58,

27.60, 16.33 ppm; *minor diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 - 7.22 (m, 1H, H_{Ar}), 7.16 (dd, *J* = 7.7, 2.3 Hz, 2H, H_{Ar}), 7.08 (dd, *J* = 6.9, 1.8 Hz, 2H, H_{Ar}), 4.64 (br, 1H, CH_2), 4.27 (br, 1H, CH_2), 4.21 (dd, *J* = 10.7, 4.3 Hz, 1H, CHCl), 2.96 (dd, *J* = 13.6, 3.6 Hz, 1H, CH_2), 2.60 (dd, *J* = 13.6, 11.7 Hz, 1H, CH_2), 2.38 (dt, *J* = 13.1, 4.2 Hz, 1H, CH), 2.26 (ddt, *J* = 10.7, 2.8, 1.4 Hz, 1H, CH_2), 2.14 (m, 1H, CH_2), 2.10 - 2.00 (m, 1H, CH_2), 1.96 - 1.84 (m, 1H, CH_2), 1.18 (s, 3H, CH_3), 1.06 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.0, 141.2, 128.9, 128.2, 125.9, 112.5, 68.03, 40.15, 33.63, 32.08, 31.11, 29.51, 22.85, 14.27 ppm; *mixture:* **IR** (film) $\tilde{\nu}_{max}$ = 2926, 1650, 1455, 1216, 758, 698 cm^{-1}; **MS** (EI, 70 eV) = 250/248 (5:16) $[M]^+$, 212 (4) $[M\text{-}HCl]^+$, 121 (40), 91 (78), 69 (100); **HRMS** (EI, 70 eV) calcd. for $C_{16}H_{21}Cl$ $[M]^+$ 248.1332, found 248.1336.

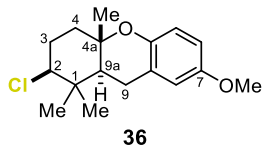
2-Chloro-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene (35), prepared from (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)phenol (46.1 mg, 200 µmol) following general procedure GP2 yielded **35** as a 73:27 mixture of inseparable diastereomers;



colorless oil (25.6 mg, 96.7 µmol, 48%); **TLC:** R_f = 0.59 (silica gel, pentane/EtOAc 95:5) [CAM]; *major diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 - 7.02 (m, 2H, H_{Ar}), 6.89 - 6.73 (m, 2H, H_{Ar}), 3.85 (dd, *J* = 12.1, 4.0 Hz, 1H, CHCl), 2.80 - 2.62 (m, 2H, CH_2), 2.19 - 2.09 (m, 1H, CH_2), 2.09 - 2.00 (m, 1H, CH_2), 1.99 - 1.90 (m, 1H, CH), 1.84 - 1.70 (m, 2H, CH_2), 1.24 (d, *J* = 0.9 Hz, 3H, CH_3), 1.17 (s, 3H, CH_3), 0.99 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.9, 129.7, 127.5, 121.8, 120.2, 117.2, 75.89, 70.87, 48.46, 39.68, 39.49, 30.50, 28.49, 24.15, 20.00, 15.63 ppm; *minor diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 - 7.02 (m, 2H, H_{Ar}), 6.89 - 6.73 (m, 2H, H_{Ar}), 4.07 (t, *J* = 2.9 Hz, 1H, CHCl), 2.80 - 2.62 (m, 2H, CH_2), 2.19 - 2.09 (m, 1H, CH_2), 2.09 - 2.00 (m, 1H, CH_2), 1.99 - 1.90 (m, 1H, CH), 1.84 - 1.70 (m, 2H, CH_2), 1.25 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.06 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.2, 129.8, 127.5, 122.3, 120.0, 117.3, 76.49, 70.35, 41.37, 38.68, 33.16, 29.65, 28.31, 22.86, 22.04, 20.42 ppm; *mixture*: **MS** (EI, 70 eV) = 264/266 (3:1) (6/18) $[M]^+$, 169 (22), 107 (54), 69 (100); **HRMS** (EI, 70 eV) calcd. for $C_{16}H_{21}ClO$ $[M]^+$ 264.1275, found 264.1269.

The analytical data obtained were in agreement with those reported in the literature.[10]

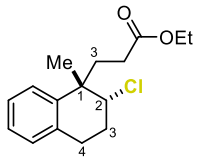
2-Chloro-7-methoxy-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene (36), prepared from (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-5-methoxyphenol (52.1 mg, 200 µmol) following general procedure GP2 yielded **36** as a colorless oil (17.7 mg, 60.0 µmol, 30%, d.r. > 95:5);



36

TLC: R_f = 0.60 (silica gel, pentane/EtOAc 95:5) [CAM]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 6.70 - 6.66 (m, 2H, H_{Ar}), 6.62 (br, 1H, H_{Ar}), 3.85 (dd, *J* = 12.0, 4.1 Hz, 1H, CHCl), 3.75 (s, 3H, OCH_3), 2.81 - 2.60 (m, 2H, CH_2), 2.21 - 2.06 (m, 1H, CH), 2.07 - 1.86 (m, 2H, CH_2), 1.84 - 1.69 (m, 2H, CH_2), 1.21 (d, *J* = 1.0 Hz, 3H, CH_3), 1.16 (s, 3H, CH_3), 0.98 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.3, 146.9, 122.4, 117.7, 114.2, 113.6, 75.58, 70.90, 55.85, 48.50, 39.65, 39.45, 30.51, 28.47, 24.51, 19.86, 15.57 ppm; **IR** (film) $\tilde{\nu}_{max}$ = 2951, 1497, 1228, 1148, 1042, 808 cm^{-1}; ; **MS** (EI, 70 eV) = 296/294 (12/37) $[M]^+$, 137 (100), 121 (18), 69 (15); **HRMS** (EI, 70 eV) calcd. for $C_{17}H_{23}ClO_2$ $[M]^+$ 294.1381, found 294.1384.

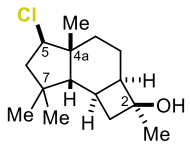
Ethyl 3-(2-chloro-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)propanoate (37), prepared from ethyl *(E)*-4-methyl-7-phenylhept-4-enoate (49.3 mg, 200 µmol) following general procedure GP2 yielded **37** as a colorless oil (27.7 mg, 98.7 µmol, 49%, d.r. > 95:5);



37

TLC: R_f = 0.51 (silica gel, pentane/EtOAc 90:10) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 - 7.26 (m, 1H, H_{Ar}), 7.20 - 7.15 (m, 1H, H_{Ar}), 7.12 (td, *J* = 7.3, 1.5 Hz, 1H, H_{Ar}), 7.08 - 7.02 (m, 1H, H_{Ar}), 4.29 (dd, *J* = 9.6, 4.2 Hz, 1H, CHCl), 4.06 (qd, *J* = 7.2, 1.5 Hz, 2H, CH_2), 3.02 - 2.85 (m, 2H, CH_2), 2.35 - 2.15 (m, 5H, 3xCH_2), 2.09 - 1.95 (m, 1H, CH_2), 1.38 (s, 3H, CH_3), 1.22 (t, *J* = 7.2 Hz, 3H, CH_3) ppm; **^{13}C NMR** (76 MHz, $CDCl_3$) δ 173.5, 141.0, 135.0, 129.2, 126.8, 126.6, 126.4, 64.84, 60.56, 42.97, 33.96, 29.63, 29.08, 28.94, 26.38, 14.31 ppm; **IR** (film) $\tilde{\nu}_{max}$ = 2977, 1734, 1446, 1182, 763 cm^{-1}; **MS** (ESI+) m/z (%) = 305/303 (8/24) $[M+Na]^+$, 267 (100) $[M-HCl+Na]^+$, 247/245 (3/11); **HRMS** (ESI+) calcd. for $C_{16}H_{21}ClNaO_2$ $[M+Na]^+$ 303.1122, found 303.1124.

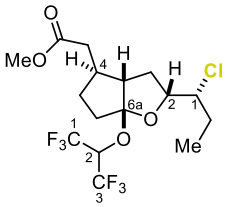
5-Chloro-2,4a,7,7-tetramethyldecahydro-1*H*-cyclobuta[*e*]inden-2-ol (39), prepared from **38** (40.9 mg, 200 µmol) following general procedure GP2 yielded **39** as a lightgreen oil (12.8 mg, 50.0 µmol, 25%, *d.r.* > 95:5);



39

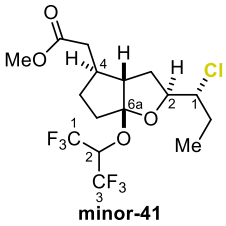
TLC: R_f = 0.47 (silica gel, pentane) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.15 (dd, *J* = 12.1, 6.0 Hz, 1H, CHCl), 2.38 - 2.30 (m, 2H, CH_2), 2.30 - 2.21 (m, 2H, 2xCH), 1.97 - 1.92 (m, 1H, CH_2), 1.88 (d, *J* = 5.9 Hz, 1H, CH_2), 1.84 - 1.81 (m, 1H, CH_2), 1.77 (s, 3H, CH_3), 1.68 (dd, *J* = 3.2, 2.0 Hz, 1H, CH_2), 1.65 (dt, *J* = 3.8, 1.1 Hz, 1H, CH_2), 1.52 (d, *J* = 3.9 Hz, 1H, CH_2), 1.43 (d, *J* = 0.9 Hz, 1H, CH), 1.12 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 0.80 (s, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 67.89, 66.39, 55.26, 49.06, 45.09, 44.99, 42.10, 38.88, 32.64, 30.80, 29.74, 29.62, 26.72, 24.00, 21.01 ppm; **IR** (film) $\tilde{\nu}_{max}$ = 2958, 2927, 1466, 1380, 1216, 758 cm^{-1}; **MS** (EI, 70 eV) = 241/239 (3/8) $[M\text{-}OH]^+$, 200/198 (19/57), 133/131 (13/50), 164 (68), 119 (63), 95 (61), 69 (100); **HRMS** (EI, 70 eV) calcd. for $C_{15}H_{24}Cl$ $[M\text{-}OH]^+$ 239.1561, found 239.1561.

Methyl 2-(2-(1-chloropropyl)-6a-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)hexahydro-2*H*-cyclopenta[*b*]furan-4-yl)acetate (41), prepared from **40** (44.9 mg, 200 µmol) following general procedure GP2 yielded **41** as a 73:27 mixture of separable diastereomers;



major-41

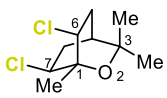
major diastereomer: colorless oil (31.6 mg, 74.0 µmol, 37%); **TLC:** R_f = 0.38 (silica gel, pentane/EtOAc 90:10) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.54 (hept, *J* = 12.1, 6.1 Hz, 1H, $CHCF_3$), 4.33 (ddd, *J* = 10.1, 5.9, 4.4 Hz, 1H, CH), 3.79 (dt, *J* = 8.8, 4.3 Hz, 1H, CHCl), 3.68 (s, 3H, OCH_3), 2.49 - 2.44 (m, 1H, CH), 2.41 (dd, *J* = 7.7, 6.7 Hz, 2H, CH_2), 2.38 - 2.30 (m, 1H, CH_2), 2.25 - 2.16 (m, 1H, CH), 2.10 - 1.97 (m, 2H, CH_2), 1.97 - 1.88 (m, 1H, CH_2), 1.84 - 1.73 (m, 2H, CH_2), 1.72 - 1.65 (m, 1H, CH_2), 1.62 - 1.55 (m, 1H, CH_2), 1.06 (t, *J* = 7.3 Hz, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0, 123.2 (q, *J* = 283.2 Hz), 123.2, 84.33, 70.56 (p, *J* = 32.8 Hz), 65.48, 55.94, 51.75, 42.05, 38.75, 36.21, 33.94 (q, *J* = 2.2 Hz), 30.94, 28.21, 11.39 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -72.90 (dqd, *J* = 160.2, 10.0, 5.8 Hz) ppm; **IR** (film) $\tilde{\nu}_{max}$ = 2954, 1736, 1288, 1221, 1193, 1100, 760 cm^{-1}; **MS** (ESI+) m/z (%) = 451/449 (14/42) $[M+Na]^+$, 413 (37) $[M\text{-}HCl+H]^+$, 283/281 (32/100) $[M\text{-}HFIP+H]^+$; **HRMS** (ESI+) calcd. for $C_{16}H_{21}F_6ClNaO_4$ $[M+Na]^+$ 449.0925, found 449.0920.



minor-41

minor diastereomer: colorless oil (12.0 mg, 28.1 µmol, 14%); **TLC:** R_f = 0.32 (silica gel, pentane/EtOAc 90:10) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.91 (hept, *J* = 6.0 Hz, 1H, $CHCF_3$), 4.25 (dt, *J* = 10.6, 5.9 Hz, 1H, CH), 3.79 (ddd, *J* = 9.2, 6.3, 3.8 Hz, 1H, CHCl), 3.68 (s, 3H, OCH_3), 2.52 - 2.37 (m, 2H, CH_2), 2.34 (t, *J* = 7.5 Hz, 1H, CH), 2.18 - 2.07 (m, 2H, CH, CH_2), 2.06 - 1.93 (m, 3H, CH_2), 1.92 - 1.86 (m, 1H, CH_2), 1.82 (ddq, *J* = 11.1, 7.3, 3.6 Hz, 1H, CH_2), 1.70 (dqd, *J* = 14.4, 7.3, 1.8 Hz, 1H, CH_2), 1.54 - 1.44 (m, 1H, CH_2), 1.08 (t, *J* = 7.3 Hz, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.9, 120.95, 84.94, 69.49 (p, *J* = 32.6 Hz), 66.38, 55.23, 51.81, 40.14, 39.65, 36.49, 33.55, 30.69, 28.29, 11.05 ppm (significant signals); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -72.76 - -73.08 (m) ppm; **IR** (film) $\tilde{\nu}_{max}$ = 2957, 1738, 1288, 1258, 1224, 1191, 1100, 688 cm^{-1}; **MS** (ESI+) m/z (%) = 451/449 (2/6) $[M+Na]^+$, 413 (15) $[M-HCl+H]^+$, 299/297 (9/26) $[M-HFIP+K]^+$; **HRMS** (ESI+) calcd. for $C_{16}H_{21}F_6ClNaO_4$ $[M+Na]^+$ 449.0925, found 449.0922.

6,7-Dichloro-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane (43), prepared from **42** (30.9 mg, 200 µmol) following general procedure GP2 using 2.4 eq of reagent **21** yielded **43** as a colorless oil (17.9 mg, 80.0 µmol, 40%, d.r. > 95:5);

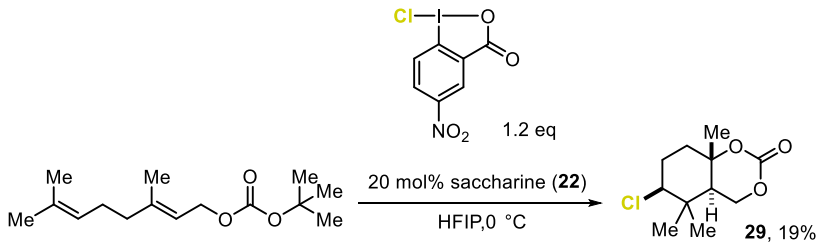


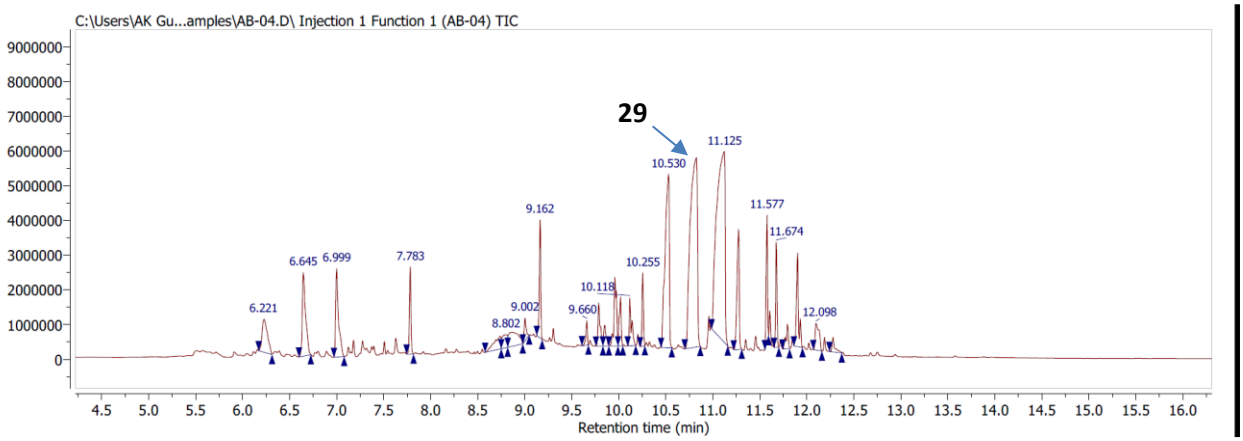
43

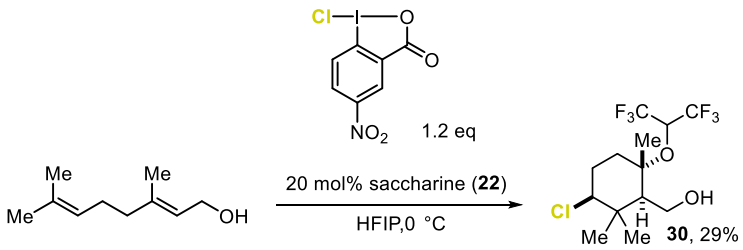
TLC: R_f = 0.49 (silica gel, pentane/EtOAc 90:10) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.17 – 3.99 (m, 2H, 2xCH), 2.88 – 2.77 (m, 2H, CH_2), 2.01 (dddd, *J* = 12.9, 6.2, 2.3, 0.9 Hz, 2H, CH_2), 1.74 (tt, *J* = 4.2, 2.3 Hz, 1H, CH), 1.43 (s, 3H, CH_3), 1.25 (s, 6H, 2xCH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 75.55, 75.08, 57.13, 36.16, 35.72, 29.85, 28.51, 23.27 ppm.

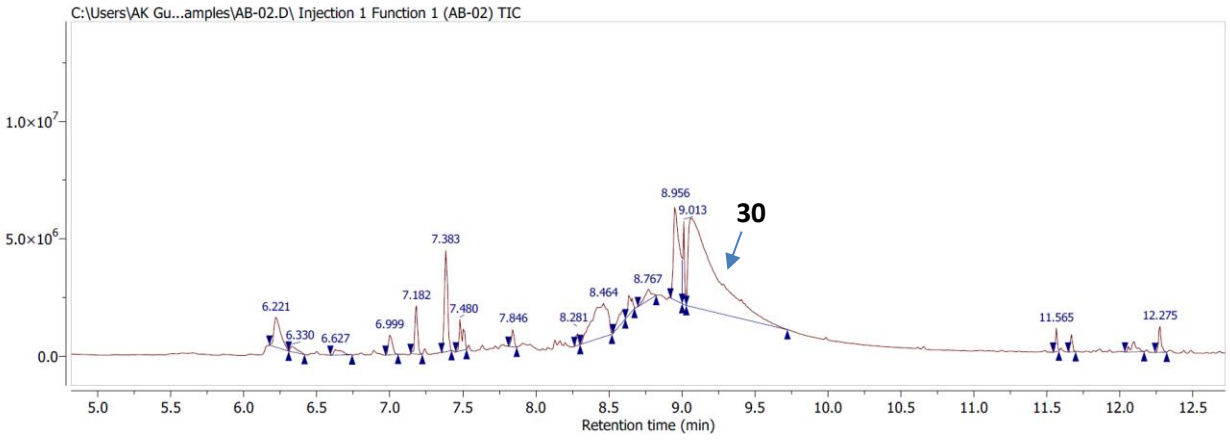
The analytical data obtained were in agreement with those reported in the literature.[11]

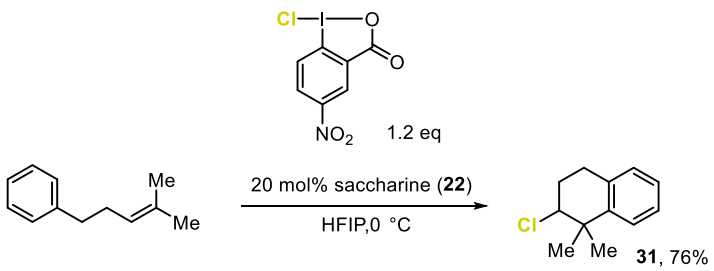
12. Crude Reaction Mixtures (GC-MS) for the Synthesis of Compounds 29-31, 34, and 36

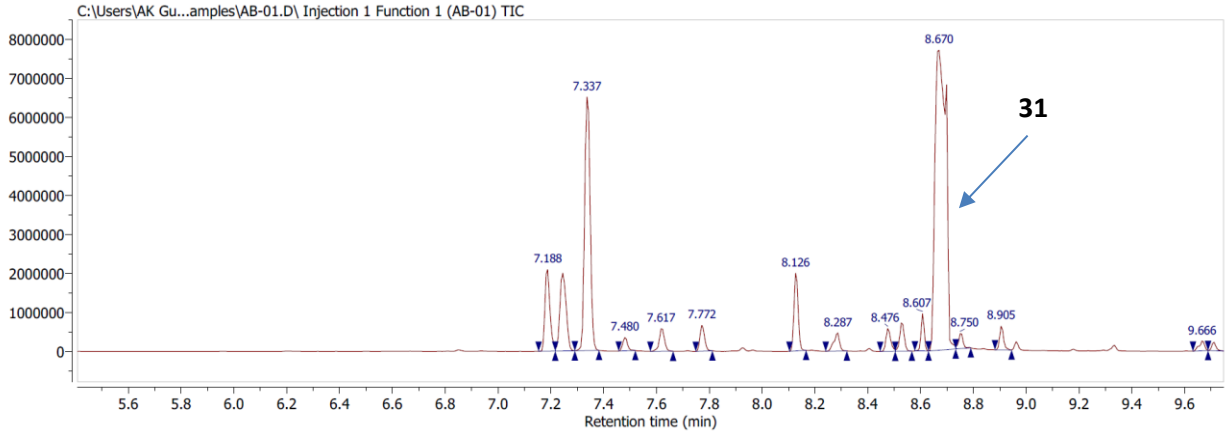


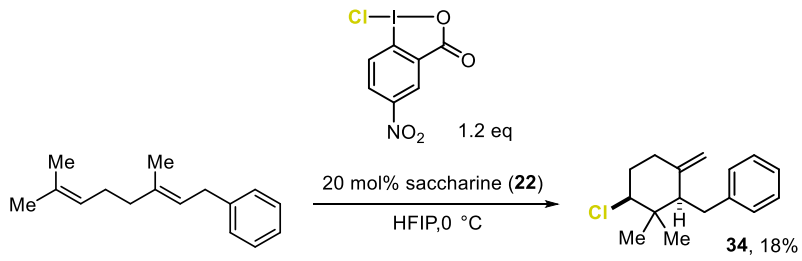


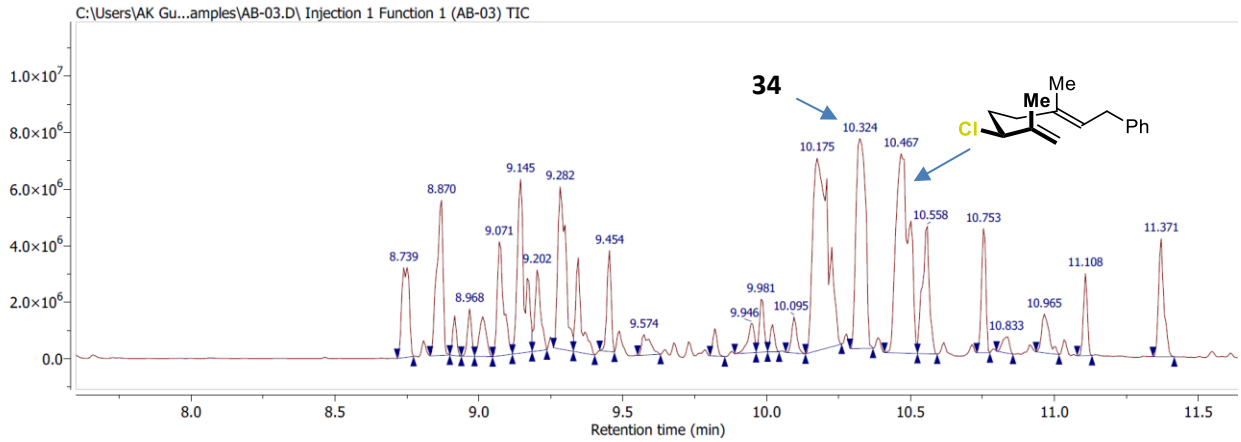


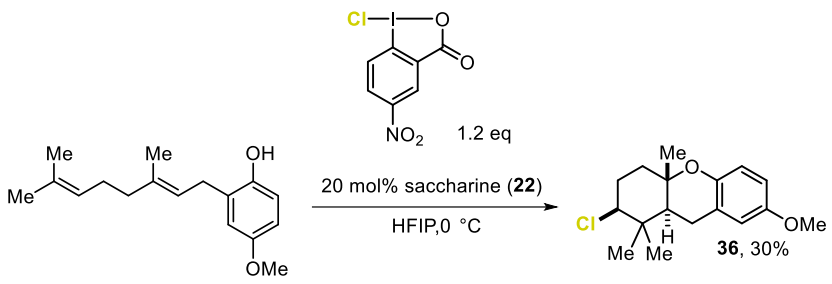


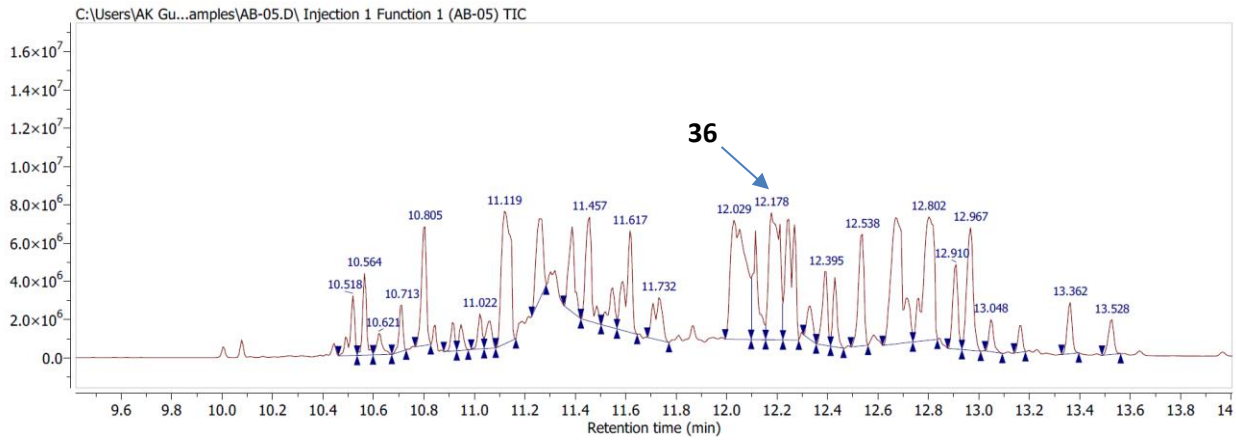

Cl
I
O
O
NO2
1.2 eq
Me
Me
20 mol% saccharine (22)
HFIP,0 °C
Cl
Me
Me
31, 76%


C:\Users\AK Gu...amples\AB-01.D\ Injection 1 Function 1 (AB-01) TIC
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
8.670
7.337
31
7.188
8.126
7.480
7.617
7.772
8.287
8.476
8.607
8.750
8.905
9.666
5.6
5.8
6.0
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
7.8
8.0
8.2
8.4
8.6
8.8
9.0
9.2
9.4
9.6
Retention time (min)


Cl
I
O
O
NO2
1.2 eq
Me
Me
Me
20 mol% saccharine (22)
HFIP,0 °C
Cl
H
Me
Me
34, 18%


C:\Users\AK Gu...amples\AB-03.D\ Injection 1 Function 1 (AB-03) TIC
1.0×10^7
8.0×10^6
6.0×10^6
4.0×10^6
2.0×10^6
0.0
34
Me
Me
Cl
Ph
10.324
10.175
10.467
9.145
9.282
8.870
10.558
10.753
11.371
9.071
9.454
8.739
9.202
11.108
9.981
8.968
10.095
9.946
10.965
9.574
10.833
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
Retention time (min)





13. References

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