SUPPORTING INFORMATION ACCOMPANYING

The effect of the *N*-mesityl group in NHC-catalyzed reactions

Jessada Mahatthananchai and Jeffrey W. Bode*

Laboratory for Organic Chemistry, Department of Chemistry and Applied Biosciences,
Swiss Federal Institute of Technology (ETH) Zurich,
Wolfgang-Pauli-Strasse 10, 8093 Zurich, Switzerland

Corresponding Author Email Address:
bode@org.chem.ethz.ch

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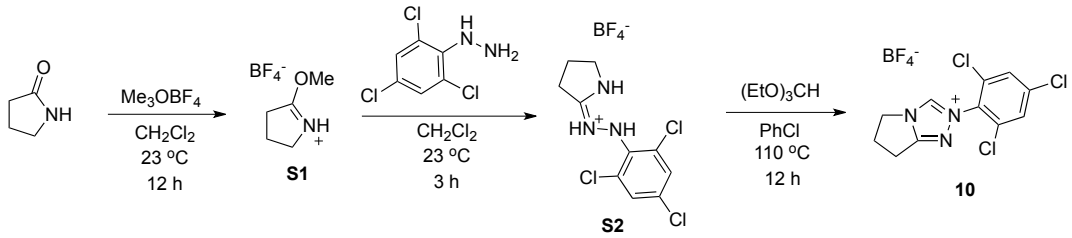
General methods

All reactions were generally performed in dried glassware under an atmosphere of dry N_2. Dichloromethane (CH_2Cl_2) was distilled over CaH_2; EtOH was distilled over Na. THF and toluene were dried by passage over activated alumina under an Ar atmosphere. All other reagents were used without further purification, unless otherwise noted. Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) and were visualized by fluorescence quenching under UV light or by staining with phosphomolybdic acid. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck Kieselgel 60 PF_{254} (Art 7747). Flash column chromatography was performed on E. Merck Silica Gel 60 (230–400 Mesh) using a forced flow of 0.5–1.0 bar. ^{1}H NMR and ^{13}C NMR were measured on VARIAN Mercury 300 MHz, 75 MHz or Bruker Avance 400 MHz, 100 MHz respectively. Chemical shifts are expressed in parts per million (ppm) downfield from residual solvent peaks, and coupling constants are reported in Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded using a JASCO FT:IR-4100 spectrophotometer and reported as wavenumber (cm^{-1}). Gas-chromatography/mass spectrometry was preformed using an Agilent 7820A (GC, 70 eV) coupled with an Agilent 5975 MSD Series (MS) system. Liquid-chromatography/mass spectrometry was preformed using a Dionex UltiMate3000 RSLC (LC) coupled with a Surveyor MSQ Plus (MS). High-resolution mass spectrometric measurements were performed by the mass spectrometry service of the LOC at the ETHZ on Agilent 1200 (LC) and Bruker maXis for ESI-Q-TOF. High Performance Liquid Chromatography was performed using pumps and UV-VIS detector manufactured by JASCO: Daicel Chiralpak AD-H Column (4.6 × 250 mm) with 9:1 hexanes:*i*PrOH as eluent, flow rate of 1.0 mL/min, and detection wavelength at 220 nm.

Synthesis and characterization of triazolium salt precatalysts in this study

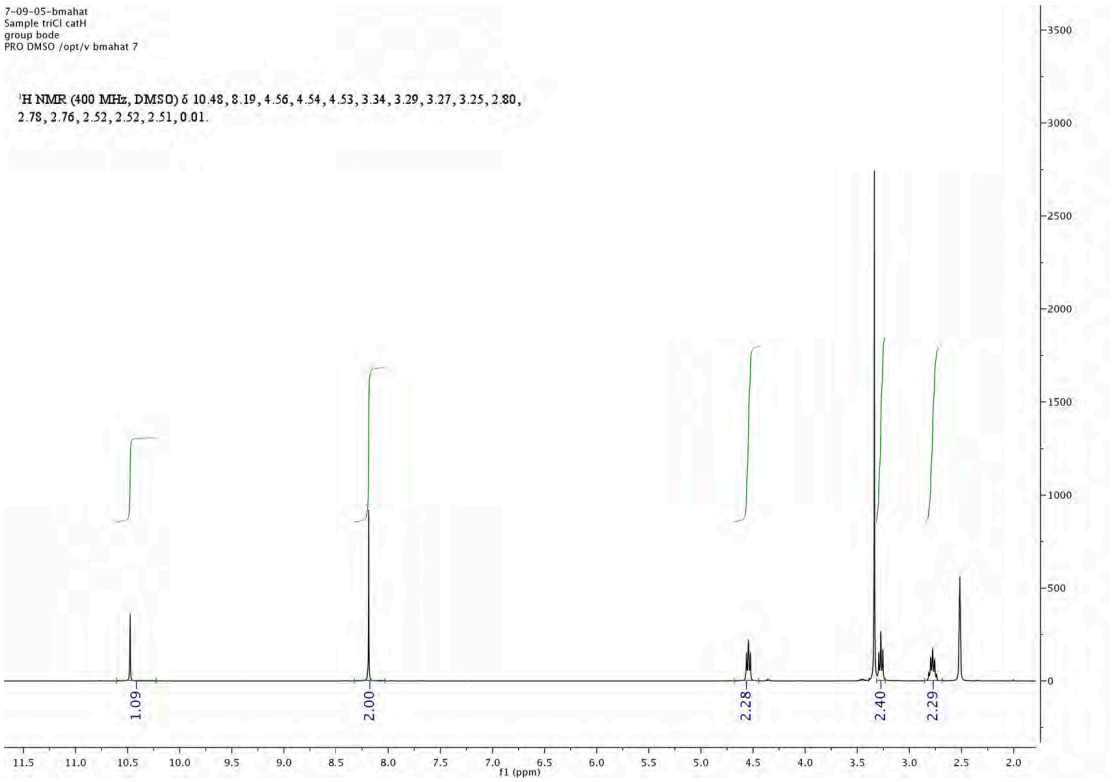
2-(2,4,6-trichlorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium (**10** BF_4^-)

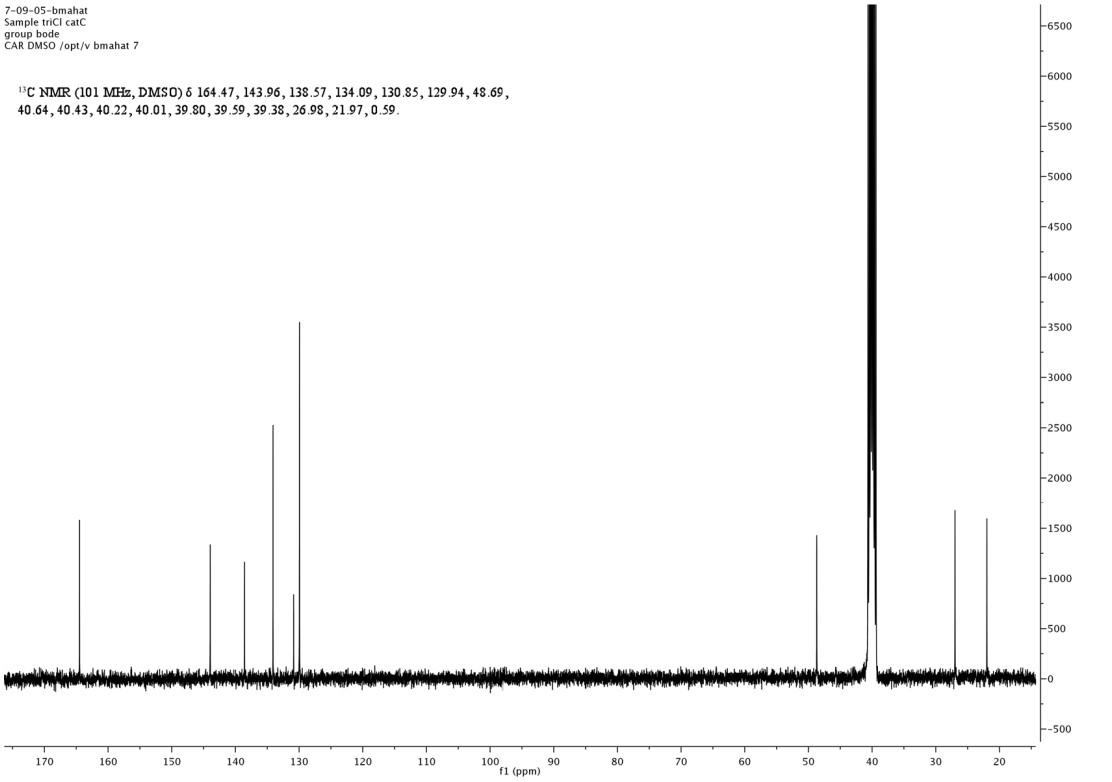


The synthesis of *N*-2,4,6-trichloro triazolium salt **10** was slightly modified from a procedure reported by Rovis.[1] In a dried round bottom flask, 1.09 g (12.8 mmol; 1 equiv) of pyrrolidin-2-one was dissolved in 60 mL CH_2Cl_2 (0.2 M), followed by an addition of 1.89 g of Me_3OBF_4 (12.8 mmol; 1 equiv). The reaction was allowed to stir overnight (ca. 12 hours). GC/MS was used to monitor the reaction and identify the methyl ether product **S1**.[2] Without further purification, 2.10 g (10.0 mmol; 0.78 equiv) of (2,4,6-trichlorophenyl)hydrazine (commercially available from TCI) was added to the solution of **S1** in CH_2Cl_2. This reaction was allowed to stir at room temperature for 3 hours (monitor by LC/MS). The mixture was concentrated *in vacuo*, and the desired 1-(pyrrolidin-2-ylidene)-2-(2,4,6-trichlorophenyl)hydrazin-1-ium[3] (**S2**) was obtained as white solid after recrystallization in $CHCl_3$. The obtained intermediate **S2** was dissolved in a mixture of 5 mL of $(EtO)_3CH$, 5 mL chlorobenzene, and 1 mL MeOH. This solution was heated under N_2 overnight (ca. 12 hours) at 110°C (monitor by LC/MS). After cooling down, three portions of toluene was added to precipitate the desired triazolium salt as yellow solid, which was recrystallized first in THF and then in EtOH to afford white crystalline solid of **10** in 45% yield: ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.48 (s, 1H), 8.19 (s, 2H), 4.56-4.53 (m, 2H), 3.29-3.25 (m, 2H), 2.80-2.76 (m, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 164.47, 143.96, 138.57, 134.09, 130.85, 129.94, 48.69, 26.98, 21.97. HRMS (ESI) $[M]^+$ calcd. for $C_{11}H_9Cl_3N_3^+$, 287.9858 found, 287.9857.

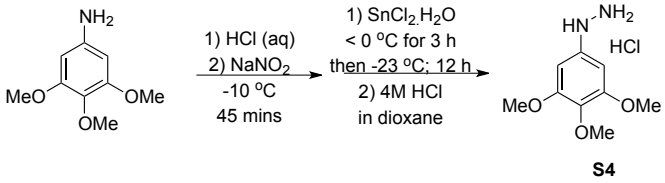
(1)M. S. Kerr, J. Read de Alaniz and T. Rovis, *J. Org. Chem.,* 2005, **70**, 5725–5728.
(2) ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.80 (s, 3H), 3.66 (t, 2H), 2.47-2.44 (t, 2H), 2.05-2.00 (m, 2H). GC/MS (EI) = 99 $[M-H]^+$, 84, 69, 56 (100%). Spectroscopic data matched those reported in the literature: C. Dinesh, M. Clive, S. Hosahalli, S. Ramesh, P. Chetan and M. Henrik, Heterocyclic Compounds as MEK Inhibitors. U.S. Patent US2009/275606 A1, April 21 2008.
(3) **S2**: ^{1}H NMR (acetone-d_6, 400 MHz): δ 9.52 (b, 1H), 8.03 (s, 1H), 7.69 (s, 1H), 7.59 (s, 2H), 3.98-3.95 (m, 2H), 3.14-3.10 (m, 2H), 2.46-2.41 (m, 2H). ^{13}C NMR (acetone-d_6, 100 MHz): δ 171.09, 137.18, 130.09, 129.09, 128.17, 78.32, 47.89, 20.92. HRMS (ESI) $[M]^+$ calcd. for $C_{10}H_{11}Cl_3N_3^+$, 278.0013 found, 278.0015.

^{1}H and ^{13}C NMR of **10**





1-(3,4,5-trimethoxyphenyl)hydrazin-1-ium chloride **S4**.

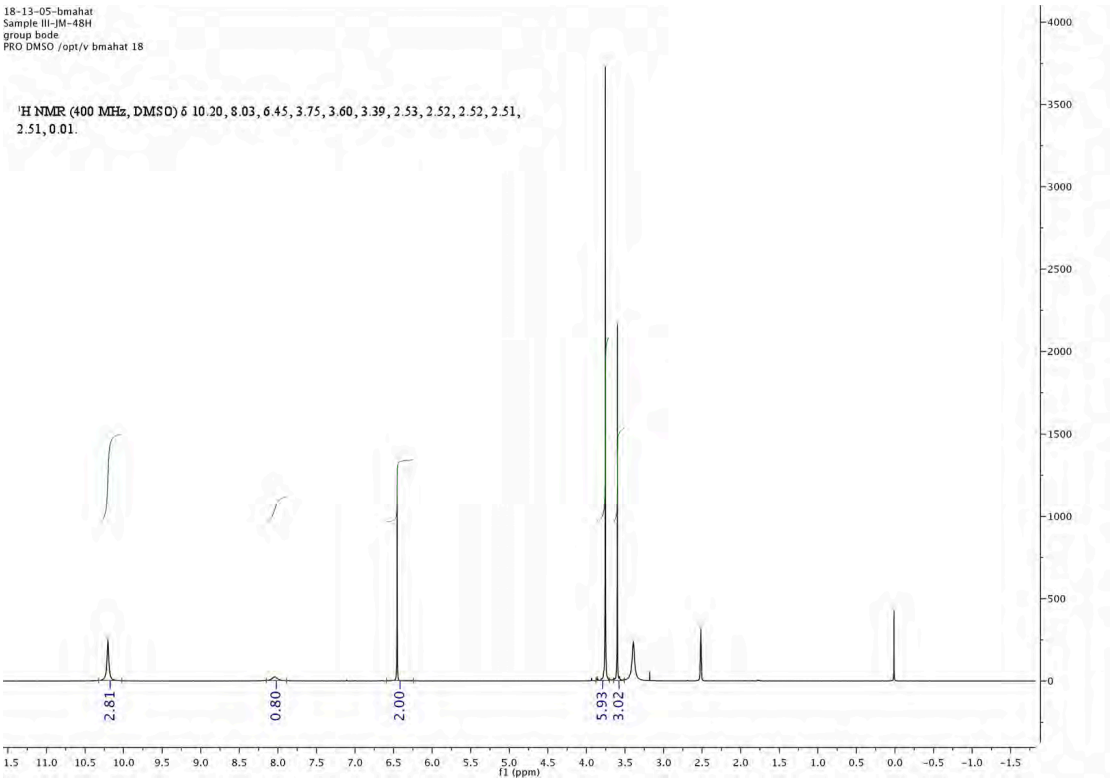


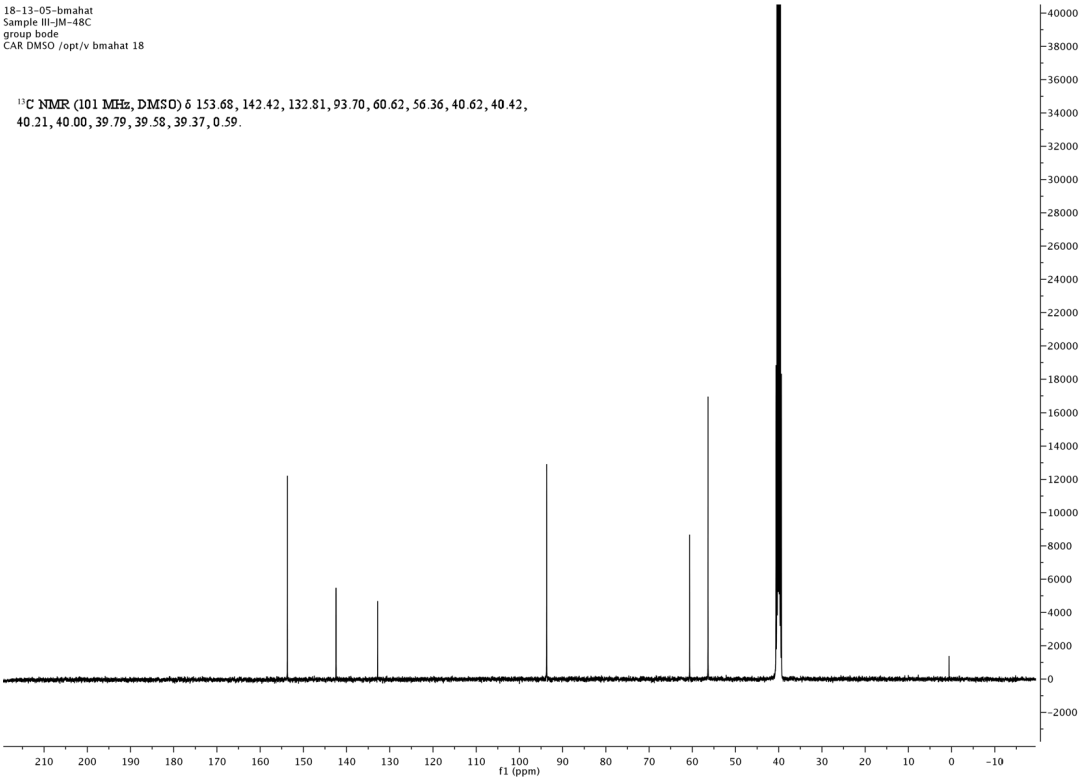
S4

The synthesis of (3,4,5-trimethoxyphenyl)hydrazin-1-ium chloride **S4** followed the procedure described by Bode.[4] A 200 mL three-necked flask was charged with a solution of 3.0 mL concentrated HCl (aq) and 6.0 mL H_2O, followed by a portion-wise addition of 2.0 g of 3,4,5-trimethoxyaniline (commercially available from Acros) over five minutes. A freshly prepared solution of $NaNO_2$ (0.8 g in 2 mL H_2O) was added dropwise via syringe over 30 mins. The greenish yellow reaction mixture was vigorously stirred for another 30 mins while maintaining the temperature below 0°C. A slurry solution of 6.0 g $SnCl_2.H_2O$ in 3.0 mL H_2O and 3.0 mL concentrated HCl (aq) was added via an additional funnel over three hours (maintaining the temperature below 0°C). The temperature was allowed to rise to room temperature overnight. It should be noted that vigorous stirring is extremely important since a lot of foam was produced. The crude reaction mixture was neutralized with NaOH (monitor pH until neutral). This caused Sn salt to precipitate; it was then filtered off. The remaining mixture was extracted with 1:1 CH_2Cl_2:H_2O several times. The organic layer was dried and concentrated to thick oil (GC/MS indicated the desired product in free base form was obtained: $[M]^+$ = 198.0). This oil was dissolved in 20 mL CH_2Cl_2 and 20 mL Et_2O, followed by dropwise addition of 3.0 mL 4N HCl in dioxane to afford the crude purple solid of the hydrazine HCl salt, which was then recrystallized several times in 2-propanol:MeOH mixture to afford pale pink solid of **4** in 0.9 g (30% overall yield): ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.20 (br, 1H), 8.03 (s, 3H), 6.45 (s, 2H), 3.75 (s, 6H), 3.60 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 153.68, 142.42, 132.81, 93.70, 60.62, 56.36. HRMS (ESI) $[M]^+$ calcd. for $C_9H_{15}N_2O_3^+$, 199.1074 found, 199.1077.

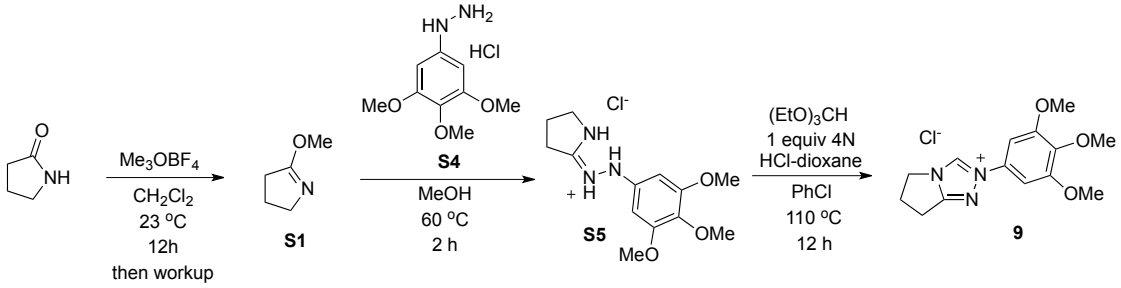
(4) J.R. Struble and J. W. Bode, *Org. Synth.*, 2010, **87**, 362–376.

^{1}H and ^{13}C NMR of **S4**





2-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium (**9** Cl^-)

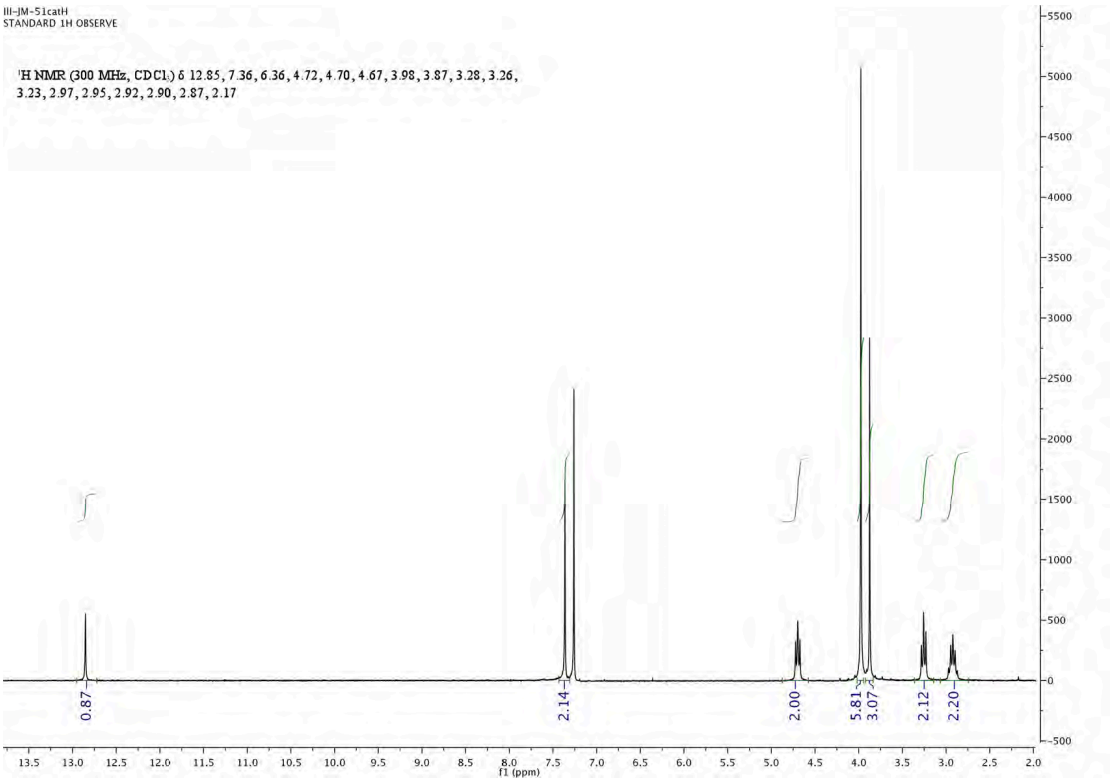


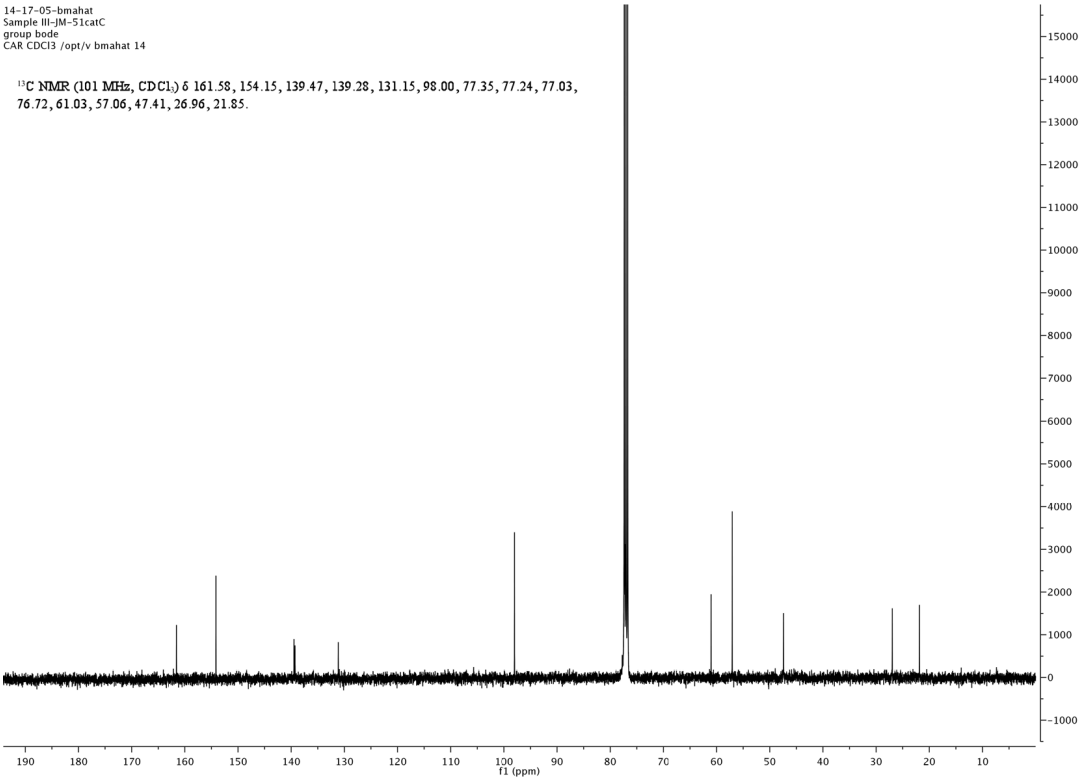
The synthesis of *N*-3,4,5-trimethoxy triazolium salt **9** was slightly modified from a procedure reported by Bode.[4] In a dried round bottom flask, 0.52 g (4.40 mmol; 1 equiv) of pyrrolidin-2-one was dissolved in 60 mL CH_2Cl_2 (0.2 M), followed by an addition of 0.65 g of Me_3OBF_4 (4.84 mmol; 1.1 equiv). The reaction was allowed to stir overnight (ca. 12 hours), worked up with sat. $NaHCO_3$ solution and extracted thrice in CH_2Cl_2 to afford the desired methyl ether **S1**[2] in quantitative yield. This product was then dissolved in 15.0 mL MeOH (0.15 M) and mixed with 0.98 g (1.00 equiv) of 3,4,5-trimethoxy hydrazine HCl **S4**; the solution was allowed to stir at 60°C for 2 hours. The mixture was concentrated *in vacuo* to afford orange solid, which was recrystallized once in a mixture of 2-propanol and CH_2Cl_2 to afford the desired 1-(pyrrolidin-2-ylidene)-2-(3,4,5-trimethoxyphenyl)hydrazin-1-ium chloride (**S5**)[5] in 0.98 g (85% yield).

The obtained intermediate **S5** was dissolved in a mixture of 5.4 mL of $(EtO)_3CH$ (10.0 equiv), 3.0 mL chlorobenzene (10.0 equiv), and 0.75 mL 4N solution of HCl in dioxane (1.0 equiv). This solution was heated under N_2 overnight (ca. 12 hours) at 110°C (monitor by LC/MS). After cooling, three portions of toluene was added to precipitate the desired triazolium salt as black solid, which was recrystallized five times in a mixture of 2-propanol and acetone to afford white powder of the triazolium salt **9** in 0.5 g (50% yield): ^{1}H NMR ($CDCl_3$, 300 MHZ): 12.85 (s, 1H), 7.36 (s, 2H), 4.72-4.67 (m, 2H), 3.97 (s, 6H), 3.87 (s, 3H), 3.28-3.23 (m, 2H), 2.94-2.90 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHZ): δ 161.58, 154.15, 139.47, 139.28, 131.15, 98.00, 61.03, 57.06, 47.41, 26.96, 21.85. HRMS (ESI) $[M]^+$ calcd. for $C_{14}H_{18}N_3O_3^+$, 276.1341 found, 276.1343.

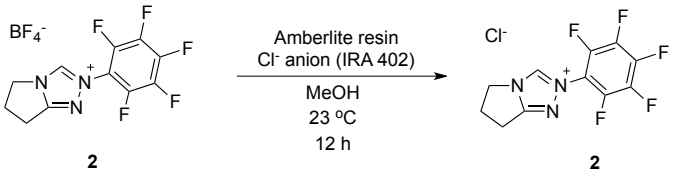
(5) **S5**: ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.42 (br, 1H), 10.02 (br, 1H), 8.48 (br, 1H), 6.16 (s, 2H), 3.61 (s, 6H), 3.58-3.56 (overlapping m & s, 5H), 3.02-2.98 (m, 2H), 2.19 (m, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 170.81, 153.95, 143.16, 132.43, 91.99, 91.44, 60.68, 56.44, 47.43, 29.04, 21.11. HRMS (ESI) $[M]^+$ calcd. for $C_{13}H_{20}N_3O_3^+$, 266.1499 found, 266.1492.

^{1}H and ^{13}C NMR of **9**





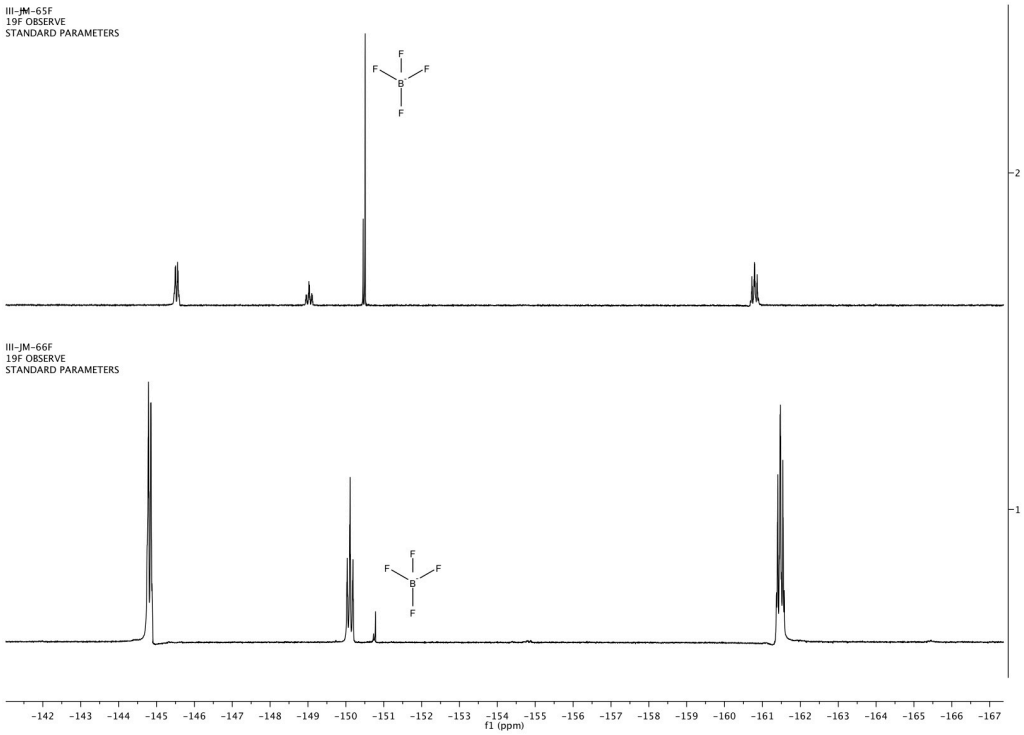
Counter-ion exchange from BF_4^- to Cl^- salt of 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium **2**.



2 **2**

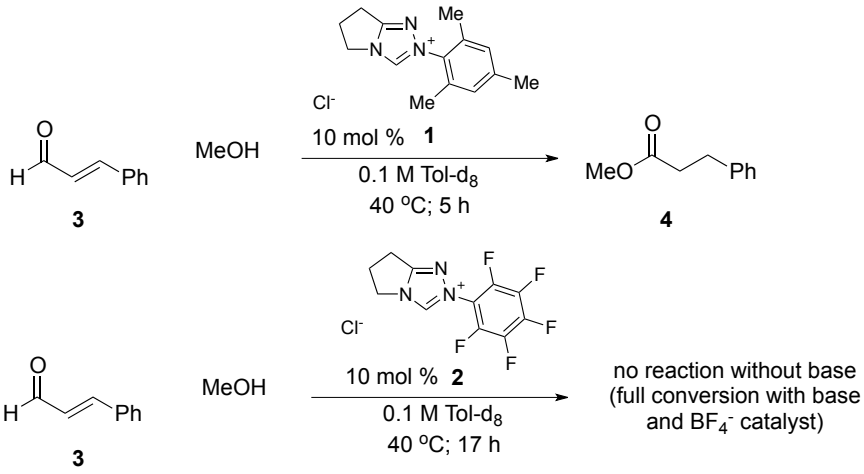
In a dried flask, 50.0 mg of the BF_4^- salt of 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium (**2**) and 0.5 g of Fluka Amberlite ion-exchange resin IRA 402 (Cl^-) were dissolved in 2.0 mL MeOH and allowed to stir at room temperature overnight (ca. 12 hours). Filtration and washing with CH_2Cl_2 afforded the desired Cl^- salt of 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium (**2**) in 12.0 mg (28% yield). With the exception of the chemical shift of the C-2 H in ^{1}H NMR (acetone-d_6) from 10.26 ppm (BF_4^- salt) to 12.41 ppm (Cl^- salt), other spectroscopic data were identical to those reported by Rovis.[1] ^{19}F NMR spectra was measured on the Cl^- salt and compared against BF_4^- salt (spectra below clearly showed almost complete disappearance of BF_4^-.

^{19}F NMR spectra of authentic **2** BF_4^- salt



^{19}F NMR spectra of anion-exchanged **2** Cl^- salt

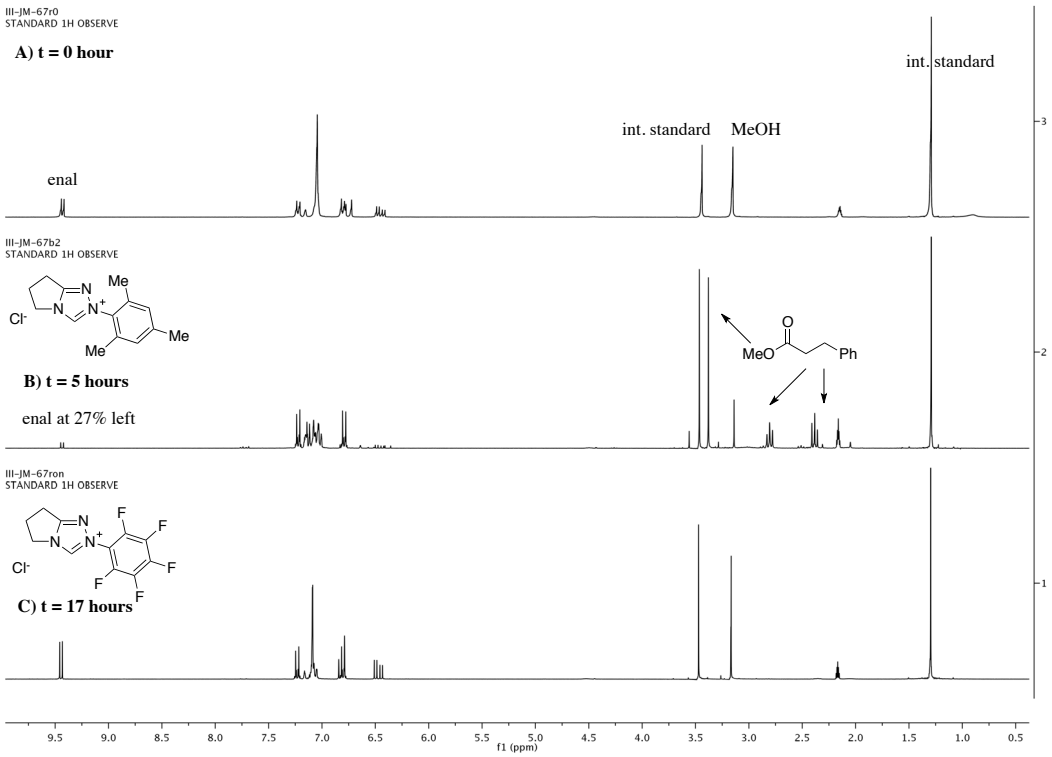
Redox esterification of cinnamaldehyde in the absence of external base



A solution of cinnamaldehyde (13.2 mg, 0.1 mmol, 1.0 equiv) and 1-(tert-butyl)-4-methoxybenzene (16.4 mg, 0.1 mmol, 1.0 equiv as internal standard), and 5.0 µL MeOH (0.1 mmol, 1.0 equiv) was prepared using 1.0 mL Tol-d_8 (with 10% CD_2Cl_2 to ensure solubility). This solution was transferred equally (0.5 mL) to two NMR tubes: one charged with 10 mol% of 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium chloride[6] **1** and another with 10 mol% 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium chloride **2** (prepared as described above). ^{1}H NMR spectra of the two reactions were recorded (A) before and (B and C) after heating at 40°C in an oil bath (see spectra comparison below). The percentage conversions were measured by the disappearance of the enal, from the integration of the peak at 9.45 ppm (d, 1H) against the internal standard peak at 1.22 ppm (9H). At 5 hours, the reaction with *N*-mesityl triazolium salt proceeded to 73% conversion while the *N*-C_6F_5 triazolium salt showed no conversion (even after 17 hours). The identity of the isolated ester product **4** was confirmed by ^{1}H NMR and GC/MS[7]: ^{1}H NMR ($CDCl_3$, 300 MHz): 7.30-7.19 (m, 5H), 3.68 (s, 3H), 2.98-2.93 (m, 2H), 2.67-2.61 (m, 2H). GC/MS (EI): 164 (M^+), 104 (100%), 90.9, 77.0.

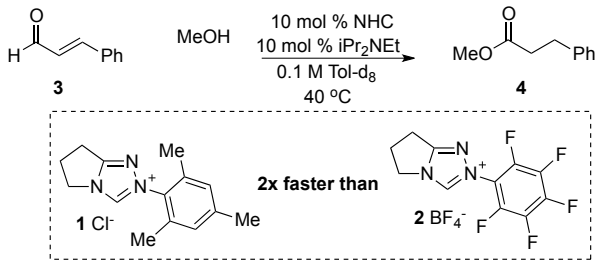
(6) (a) S. S. Sohn and J. W. Bode, *Org. Lett.,* 2005, **7**, 3873–3876. (b) The analogous ClO_4^- triazolium salt is commercially available from BioBlocks Inc. (catalog number BC003-4).
(7) Spectroscopic data compared well with the literature values: ^{1}H NMR with S. S. Sohn and J. W. Bode, *Org. Lett.,* 2005, **7**, 3873–3876. and GC/MS with X.-F. Wu and C. Darcel. *Eur, J. Org. Chem.,* 2009, **8**, 1144–1147.

^{1}H NMR comparison of the reactions with two catalysts in Tol-d_8



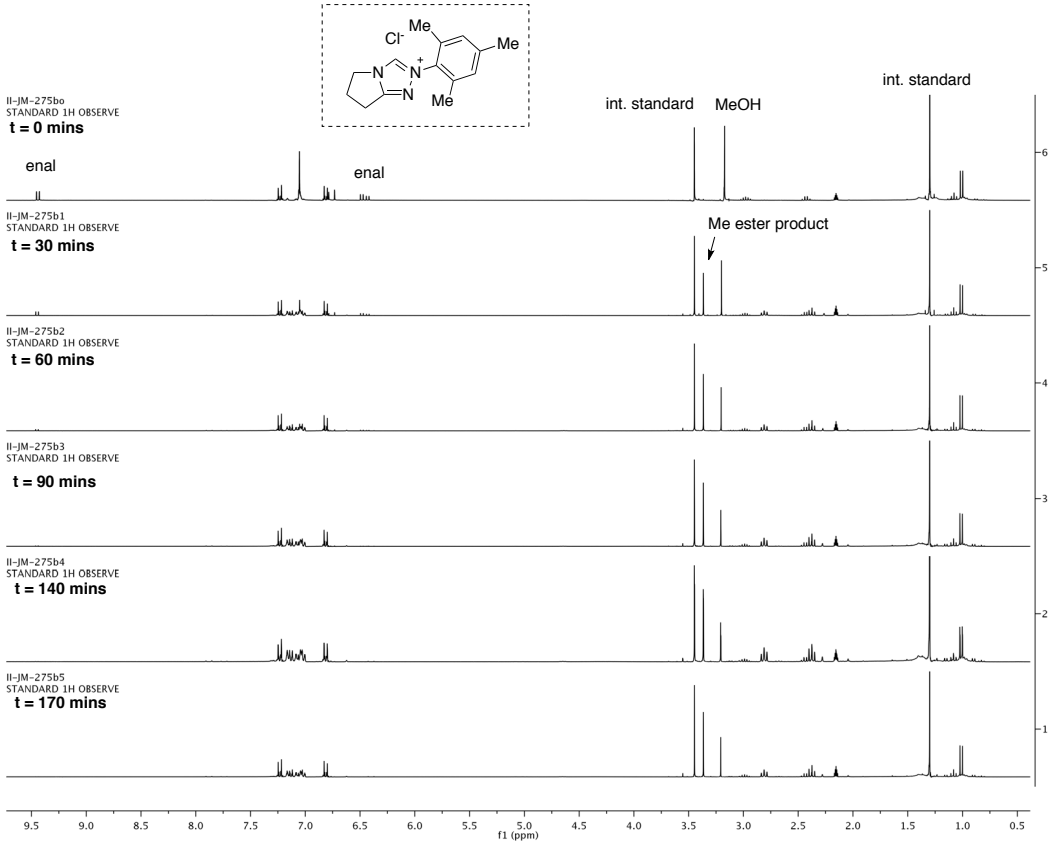
Redox esterifications of enal and α-chloroaldehyde

A) Enal comparison

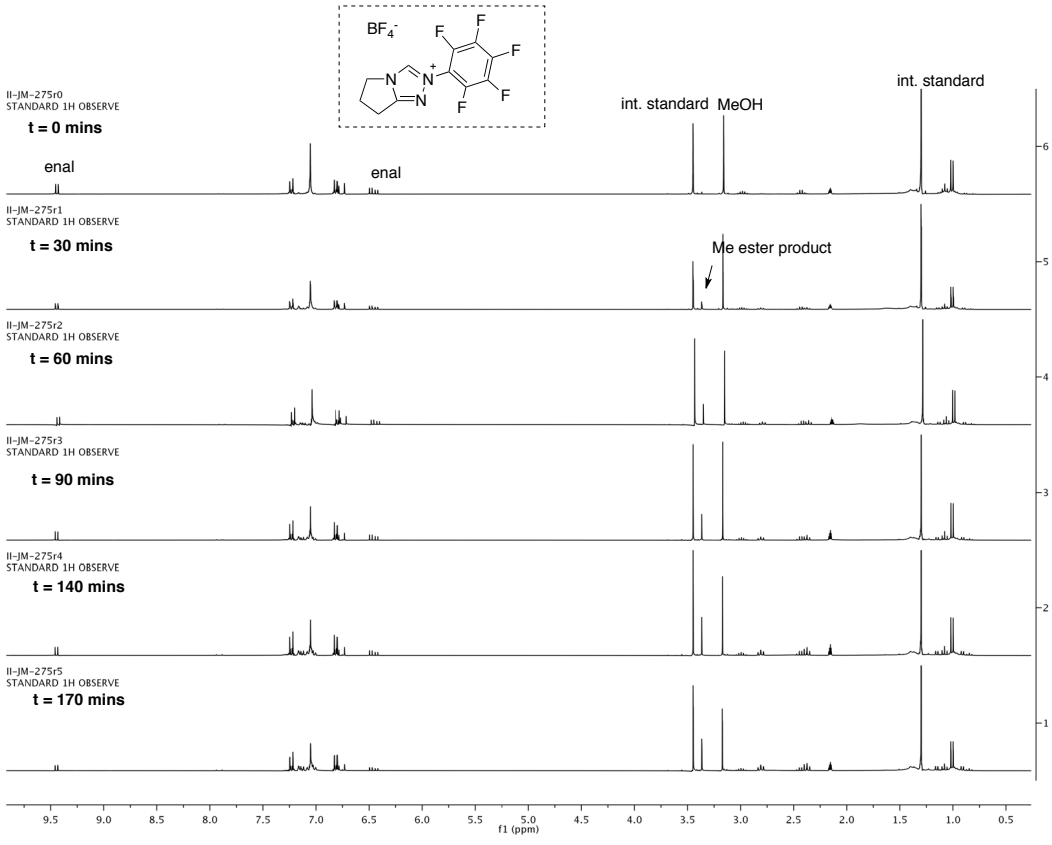


The reaction was prepared according to the procedure describe previously with two exception: 1) 10 mol% of 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium tetrafluoroborate[1] **2** was used in one case while 10 mol% of 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium chloride **1** was used in another, and 2) 10 mol% of *i*Pr_2NEt was added to both reaction. The rate was measured by the disappearance of MeOH and the formation of the product **4**[7] via integrations of the peak at 3.20 ppm (MeOH) and 3.38 (Me ester) against the internal standard peak at 1.29 ppm (9H). The rate plots are shown below.

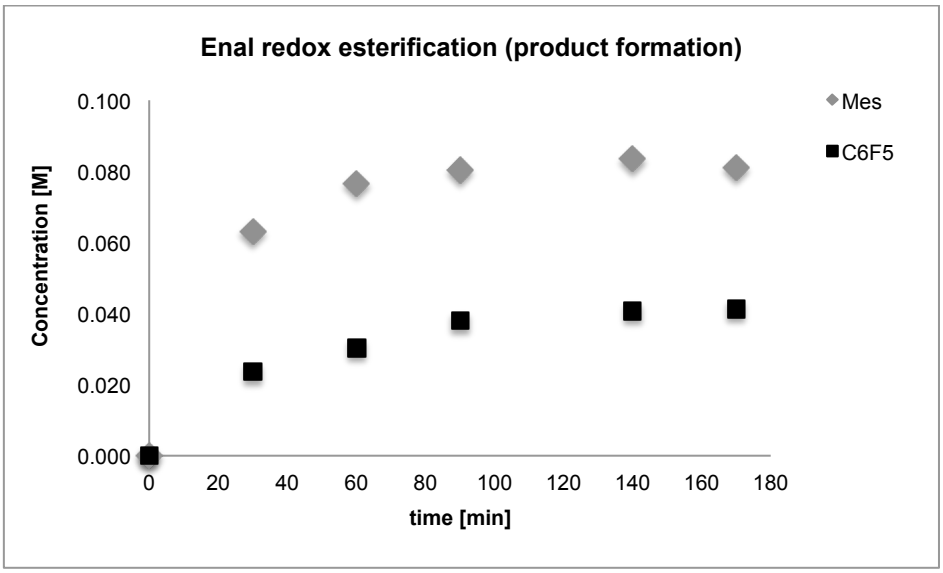
*^{1}H NMR recorded over 170 minutes for the reaction with catalyst **1**.*

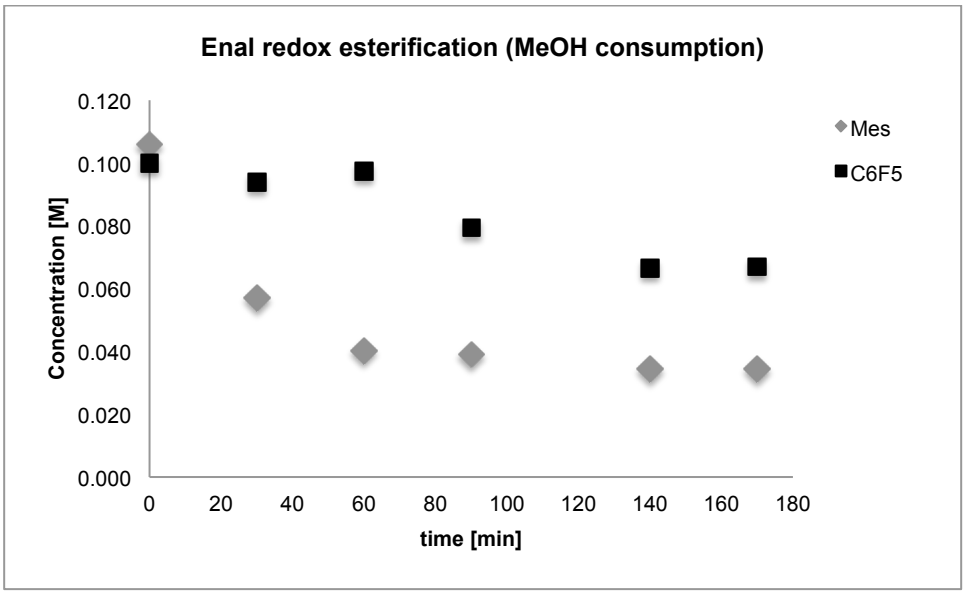


*^{1}H NMR recorded over 170 minutes for the reaction with catalyst **2**.*

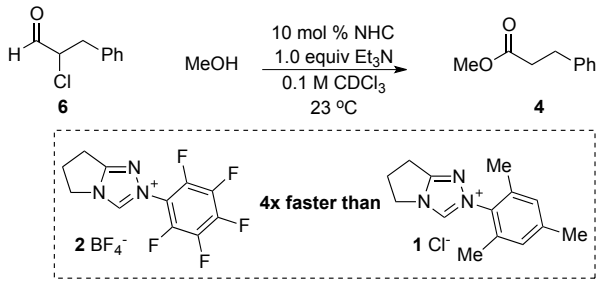


Plots of rate comparison:



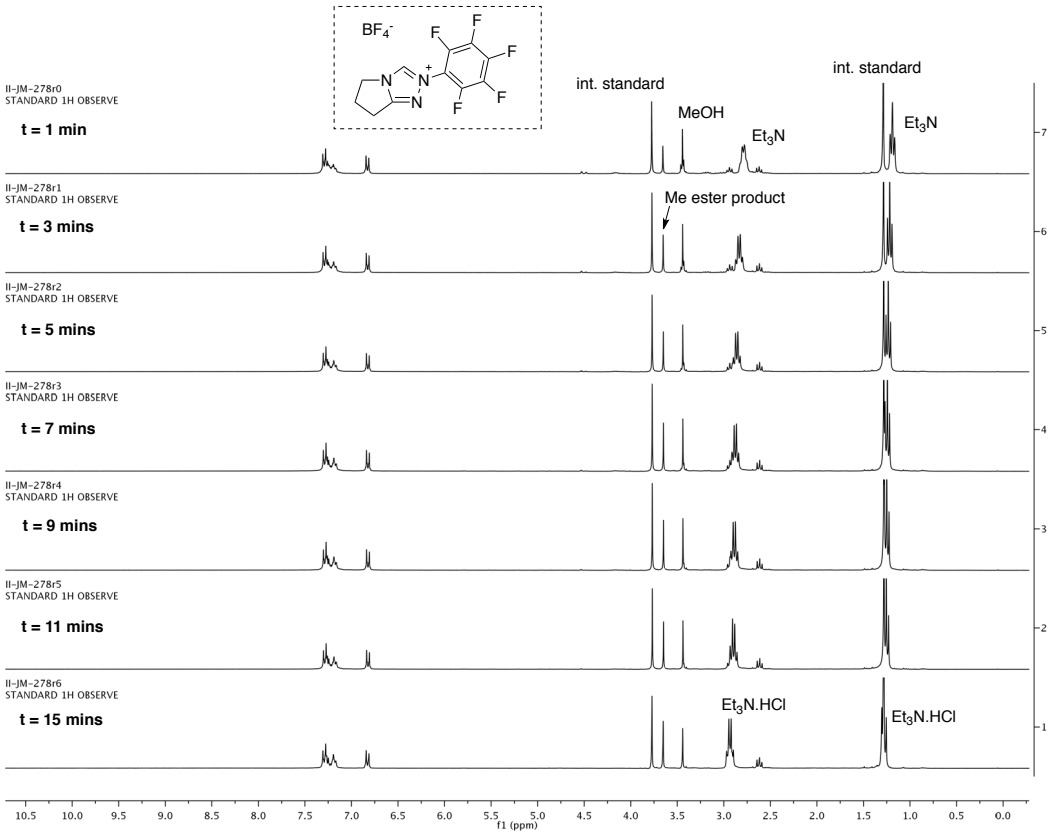


B) α-chloroaldehyde comparison



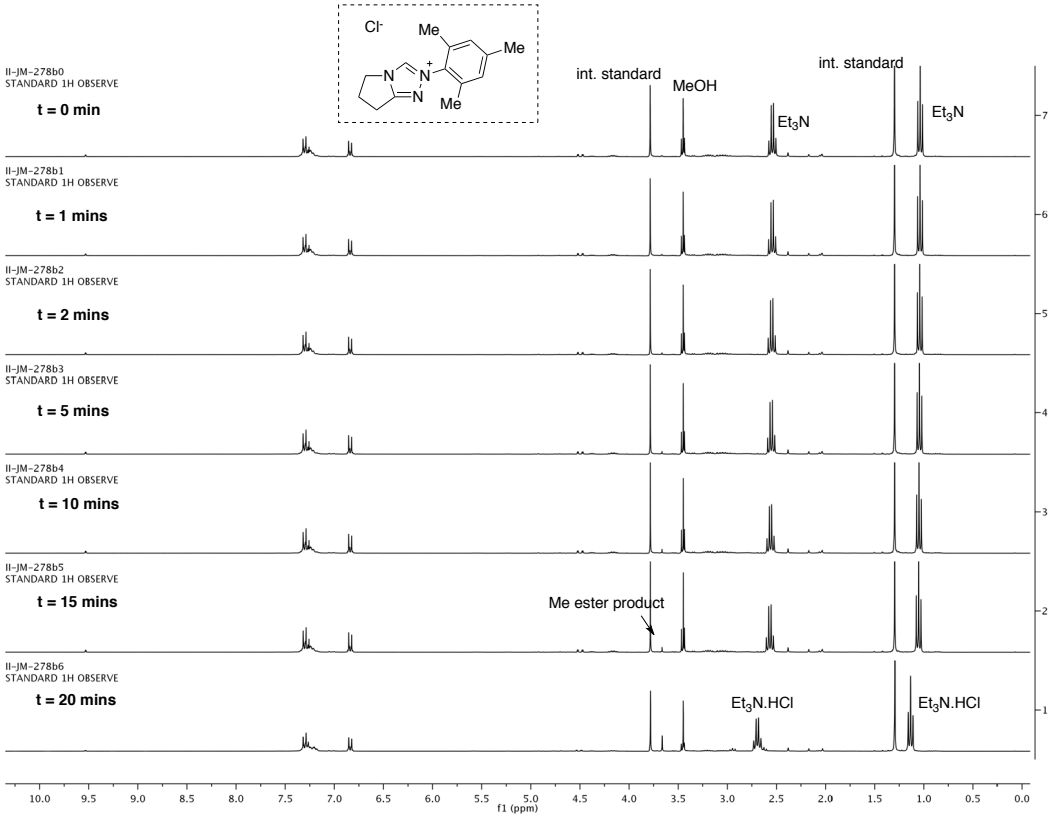
A solution of 2-chloro-3-phenylpropanal[8] **6** (17.0 mg, 0.1 mmol, 1.0 equiv) and 1-(tert-butyl)-4-methoxybenzene (16.4 mg, 0.1 mmol, 1.0 equiv as internal standard), 5.0 μL MeOH (0.1 mmol, 1.0 equiv), and 20.0 μL Et_3N was prepared using 1.0 mL $CDCl_3$. Then this solution was transferred equally (0.5 mL) to two NMR tubes: one charged with 10 mol% of 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium chloride **1** and another with 10 mol% of 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium BF_4^- **2**. ^1H NMR spectra of the two reactions were recorded over 15 minutes while the reaction was allowed to run at room temperature (see spectra comparison below). The rate was measured by the formation of the ester product **4** [7] via integrations of the peak at 3.69 (Me ester) against the internal standard peak at 1.29 ppm (9H). The rate plots are shown below.

*^1H NMR recorded over 15 minutes for the reaction with catalyst **2**.*

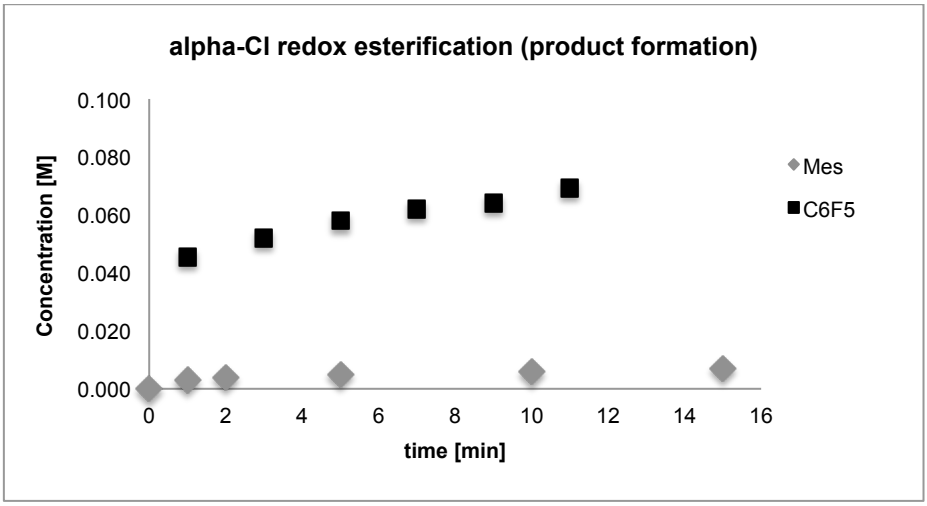


(8) Prepared according to a procedure described in M. He, B. J. Beahm and J. W. Bode, *Org. Lett.,* 2008, **10**, 3817–3820.

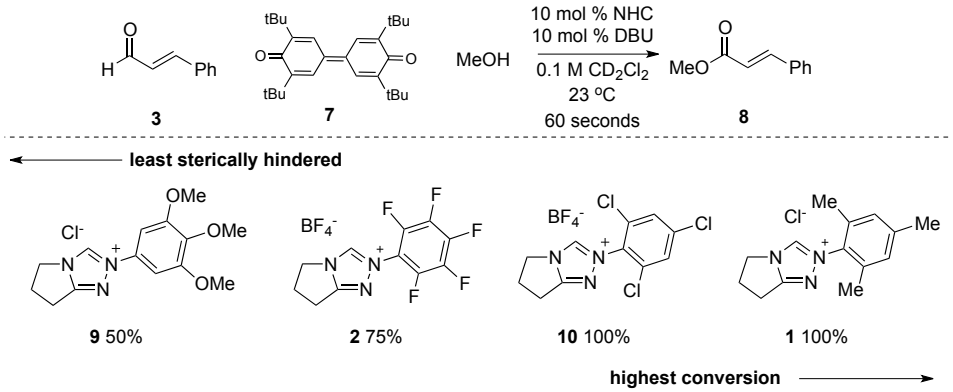
*^{1}H NMR recorded over 15 minutes for the reaction with catalyst **1**.*



A plot of rate comparison:

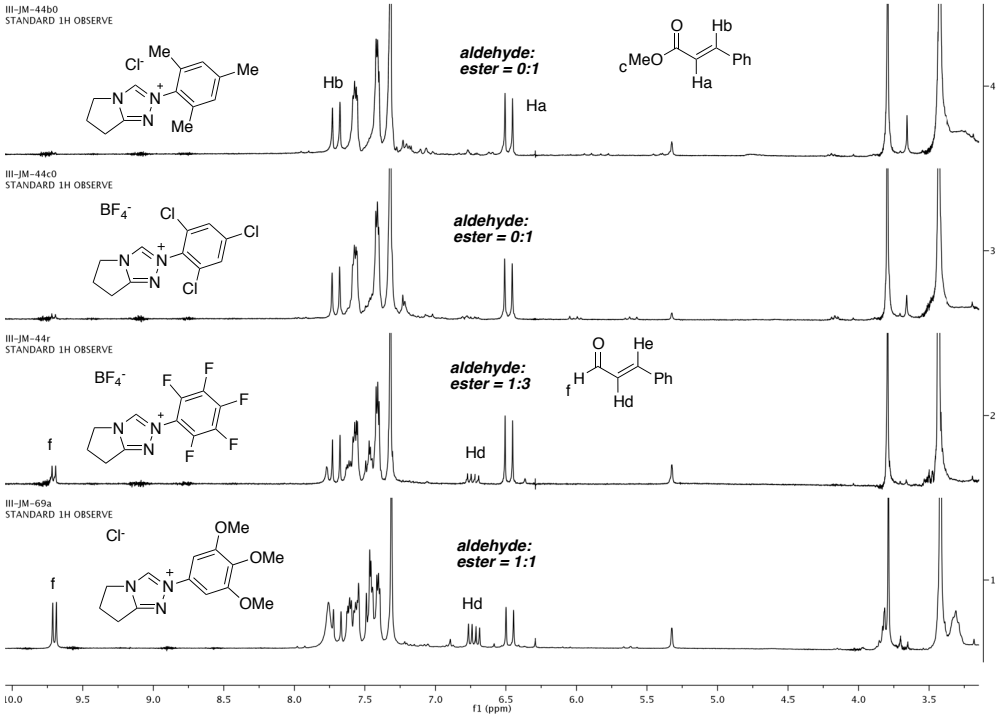


Oxidative esterification of enal comparison

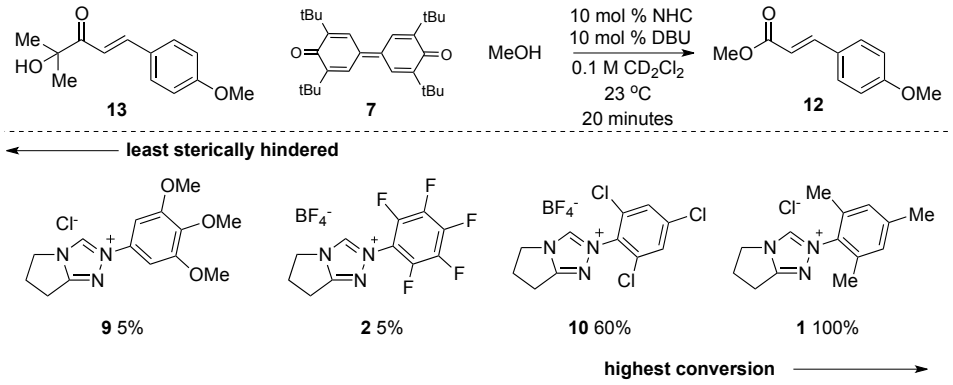


A solution of cinnamaldehyde (26.4 mg, 0.2 mmol, 1.0 equiv), 30.0 μL MeOH (0.6 mmol, 3.0 equiv), diquinone oxidant **7**[9] (80.0 mg, 0.2 mmol, 1.0 equiv), and 10 mol% 1,8-diazabicycloundec-7-ene (DBU) was prepared using 2.0 mL CD_2Cl_2. Then this solution was transferred equally (0.5 mL) to four NMR tubes charged with triazolium salt precatalyst **9**, **2**, **10**, and **1** respectively. ^{1}H NMR spectra of all four reactions were recorded after the reaction was allowed to run at room temperature for 60 seconds (upon shimming). Percentage conversions were measured by the integration of enal peak at 6.77-6.69 ppm (dd, 1H) against the product peak at 6.50-6.45 (d, ^1J = 15 Hz, 1H) ppm (see ^{1}H NMR spectra of unpurified mixture below for comparison). Percent conversions are calculated to be 100%, 100%, 75%, and 50% for **9**, **2**, **10**, and **1** respectively. The identity of the ester product **8** was confirmed by GC/MS[10] (EI): 162 (50%, M^+), 131 (100%, M^+-OMe), 103 (M^+- CO_2Me), 77 (Ph).

(9) Prepared according to M. S. Kharasch and B. S. Joshi, *J. Org. Chem.,* 1957, **22**, 1439–1443. ***Emphatically***, the oxidant must be pure and free of trace amount of hydroxide base (used in the preparation) in order to obtain consistent result.
(10) Spectroscopic data matched identically with the literature value in R. Lerebours and C. J. Wolf, *J. Am. Chem. Soc.,* 2006, **128**, 13052–13053.



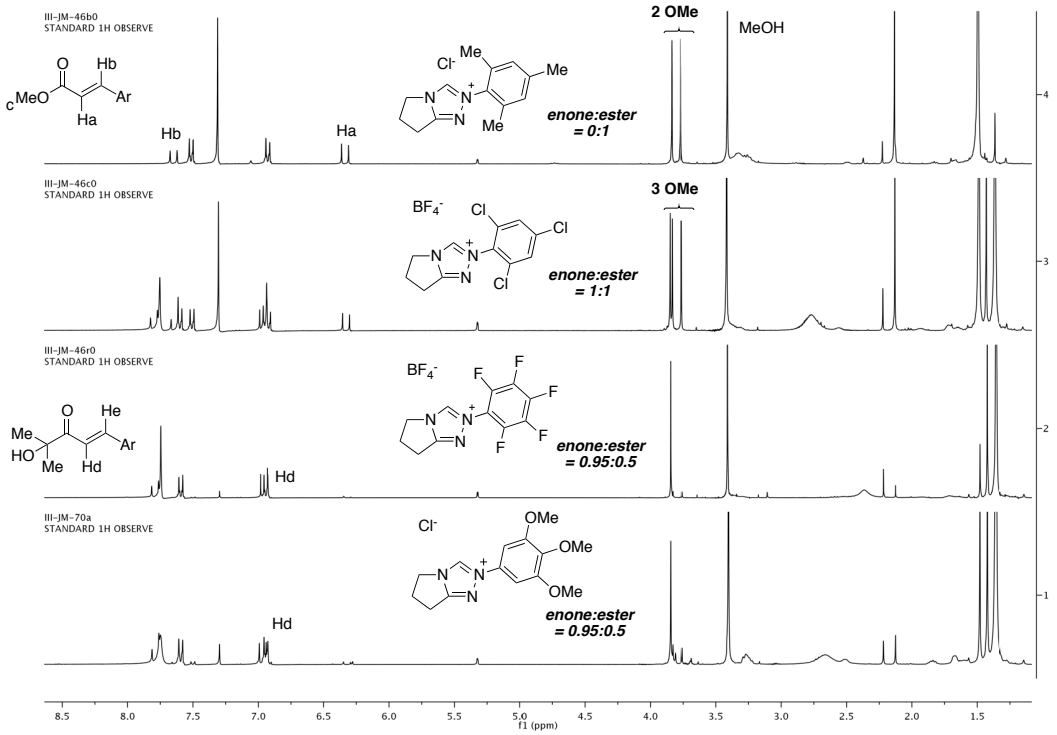
Oxidative esterification of α-hydroxyenone comparison



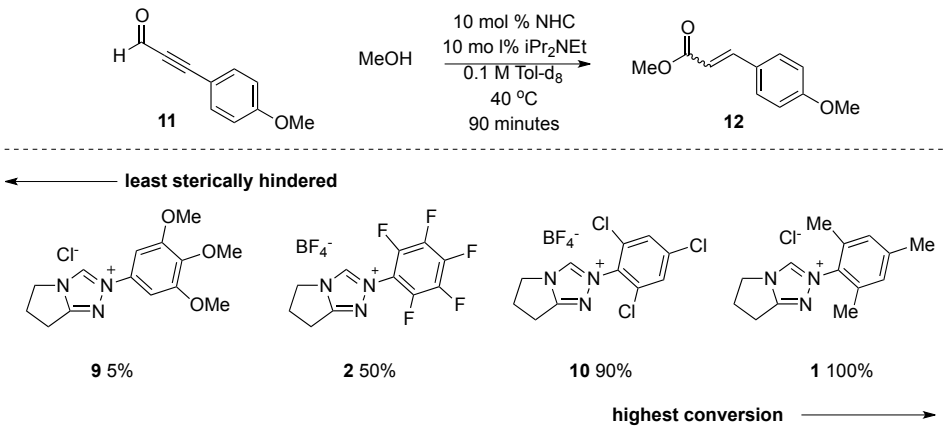
A solution of (*E*)-4-hydroxy-1-(4-methoxyphenyl)-4-methylpent-1-en-3-one [11] (**13**, 44.0 mg, 0.2 mmol, 1.0 equiv), 30.0 µL MeOH (0.6 mmol, 3.0 equiv), diquinone oxidant **7** (80.0 mg, 0.2 mmol, 1.0 equiv), and 10 mol% 1,8-diazabicycloundec-7-ene (DBU) was prepared using 2.0 mL CD_2Cl_2. This solution was transferred equally (0.5 mL) to four NMR tubes charged with triazolium salt precatalyst **9**, **2**, **10**, and **1** respectively. ^{1}H NMR spectra of all four reactions were recorded after the reaction was allowed to run at room temperature for 20 minutes. Percentage conversions were measured by the integration of the enone peak at 6.95 ppm against the product peak at 6.33 ppm (see ^{1}H NMR spectra of unpurified mixture

(11) P.-C. Chiang, M. Rommel and J. W. Bode, *J. Am. Chem. Soc.,* 2009, **131**, 8714–8718.

comparison). Percent conversions are calculated to be 100%, 50%, ~5%, and ~5% for **1**, **10**, **2**, and **9** respectively (the reactions with **2** and **9** did proceed to full conversion over 12 hours). The identity of the ester product **12** was confirmed by ^{1}H NMR and GC/MS[12]: ^{1}H NMR (CD_2Cl_2, 300 MHz): 7.67-7.62 (d, ^{1}J = 15 Hz, 1H), 7.53-7.51 (m, 2H), 6.94-6.92 (m, 2H), 6.36- 6.31 (d, ^{1}J = 15 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H). GC/MS (EI): 192 (M^{+}, 75%), 162, 161 (100%), 134, 133, 118, 90, 89, 63.

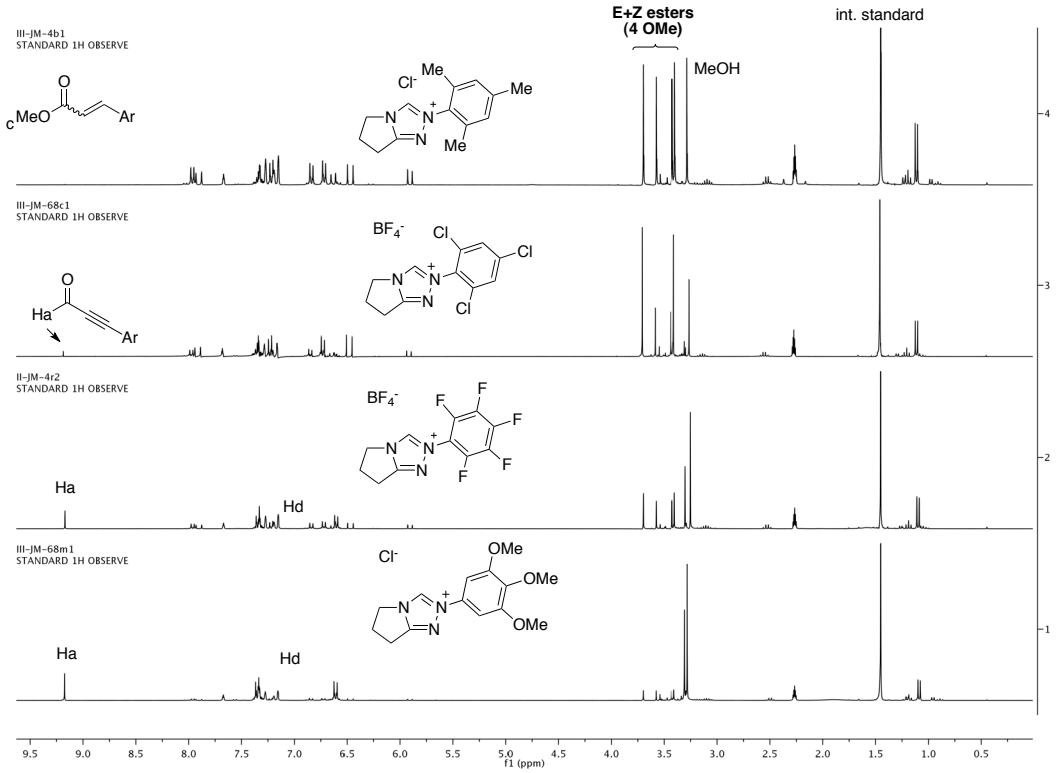


Redox esterification of ynal comparison



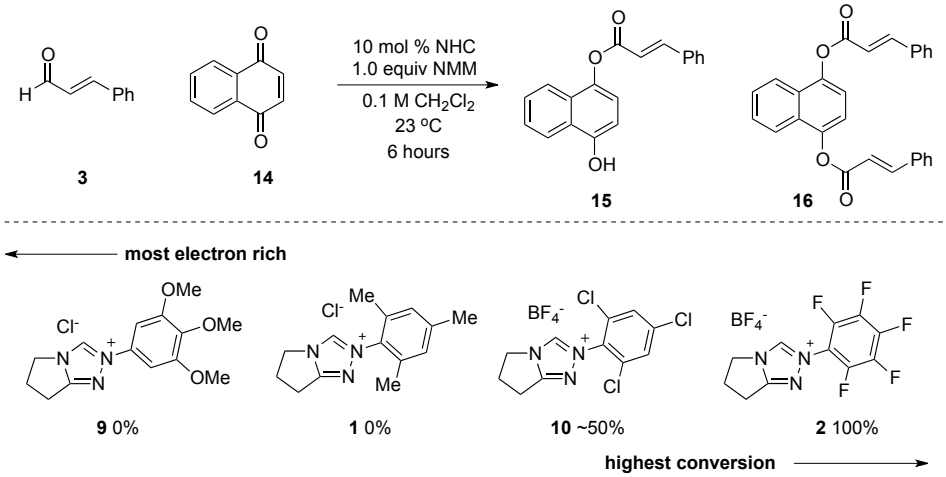
(12) Spectroscopic data compared well with the literature value in P. S. van Heerden, B. C. B. Bezuidenhoudt and D. Ferreira, *Tetrahedron,* 1996, **52**, 12313–12322.

A solution of 3-(4-methoxyphenyl)propiolaldehyde **11** (32.0 mg, 0.2 mmol, 1.0 equiv), 10.0 μL MeOH (0.2 mmol, 1.0 equiv), 1,3-di-tert-butylbenzene (0.1 mmol, 0.5 equiv as internal standard), and 10 mol% *i*Pr_2NEt was prepared using 2.0 mL tol-d_8 (with 10% CD_2Cl_2 to ensure solubility). This solution was transferred equally (0.5 mL) to four NMR tubes charged with triazolium salts **9**, **2**, **10**, and **1**. ^{1}H NMR spectra of all four reactions were recorded after the reactions were allowed to run at 40°C for 90 minutes. Percentage conversions were measured by the integration of the ynal peak at 9.18 ppm against an internal standard at 1.45 ppm (see ^{1}H NMR spectra comparison of unpurified mixtures). Percent conversions[13] are calculated to be 100%, ~90%, 50%, and ~5% for **9**, **2**, **10**, and **1** respectively.

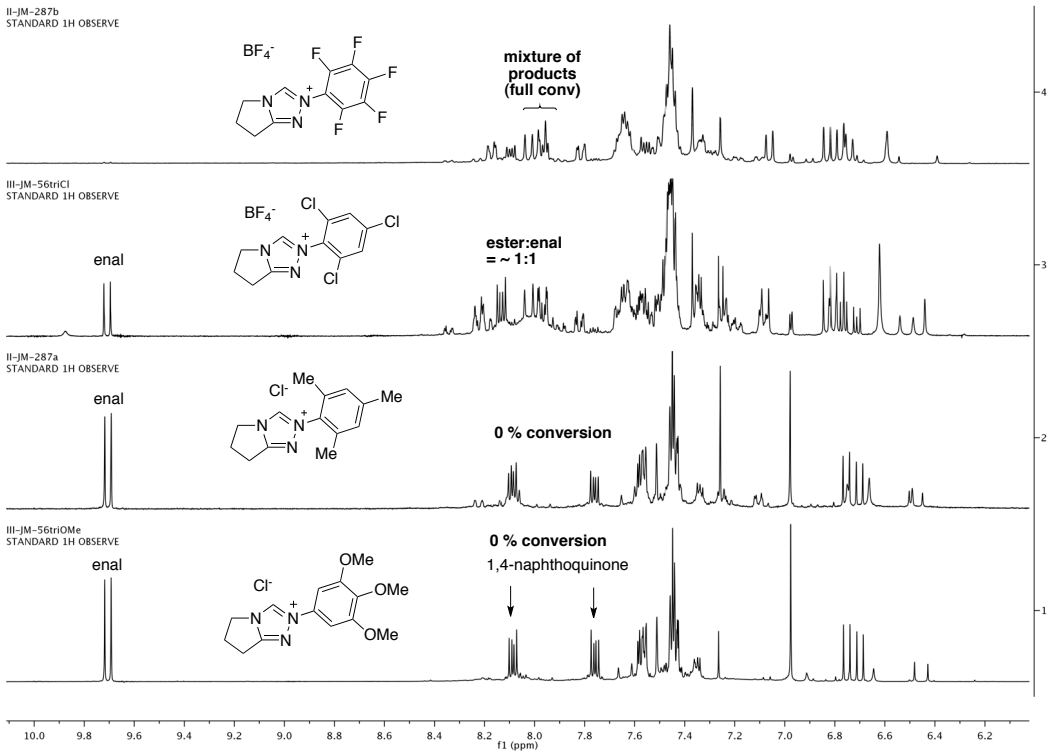


(13) Both *E* and *Z* esters were formed and detected in GC/MS: R_t = 13.4 and 12.8 mins (M^+ = 192.1).

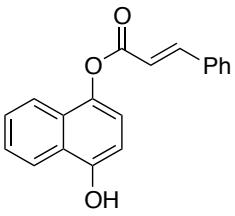
Oxidative esterification of enal by hydride transfer comparison



A solution of (*E*)-cinnamaldehyde (56.0 mg, 0.4 mmol, 1.0 equiv), 1,4-naphthoquinone **14** (63.2 mg, 0.4 mmol, 1.0 equiv), and *N*-methylmorpholine (NMM, 40.0 µL, 1.0 equiv) was prepared using 4.0 mL CH_2Cl_2. This solution was transferred equally (0.5 mL) to four dried vials containing triazolium salts **9**, **1**, **10**, and **2** respectively. ^{1}H NMR spectra of all four reactions were recorded for the concentrated, unpurified mixtures after stirring at 40°C for 6 hours. Both mono and diacylated products were obtained (in 1:1 ratio) in quantitative conversion for catalyst **2**, in ~50% for **10**, and 0% for **1** and **9** (see ^{1}H NMR spectra below for comparison). The products **15** and **16** were isolated by preparative TLC in 3:2 hexanes: EtOAc.

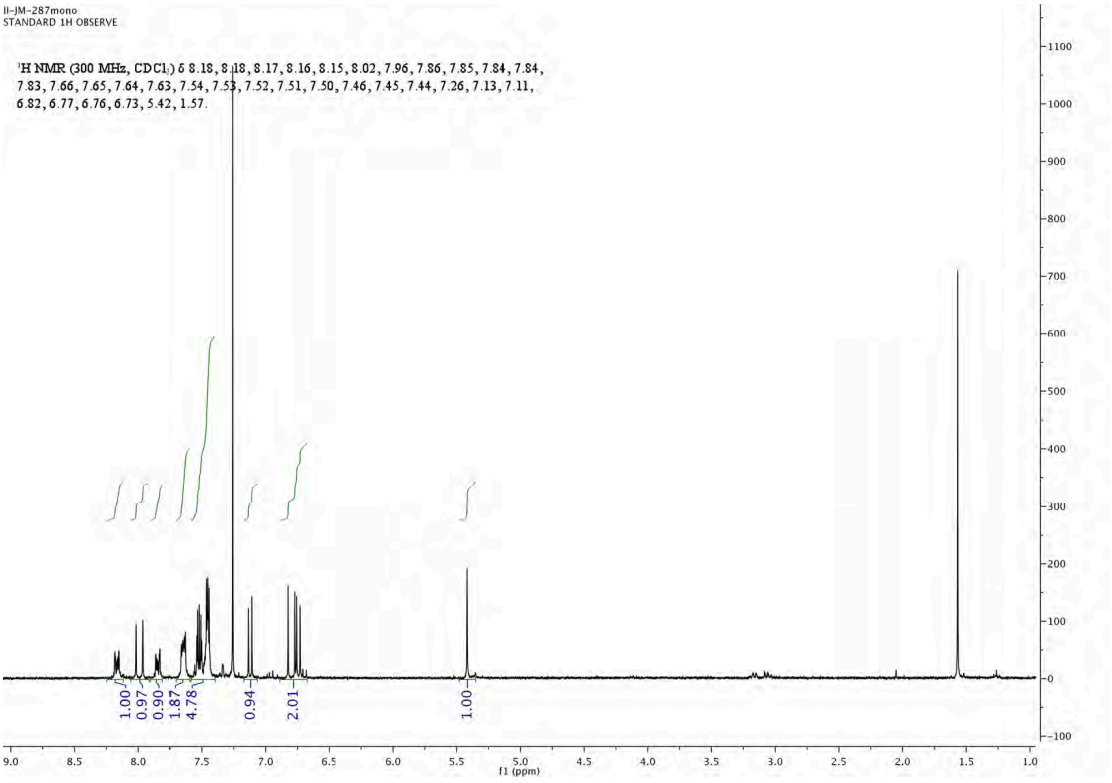


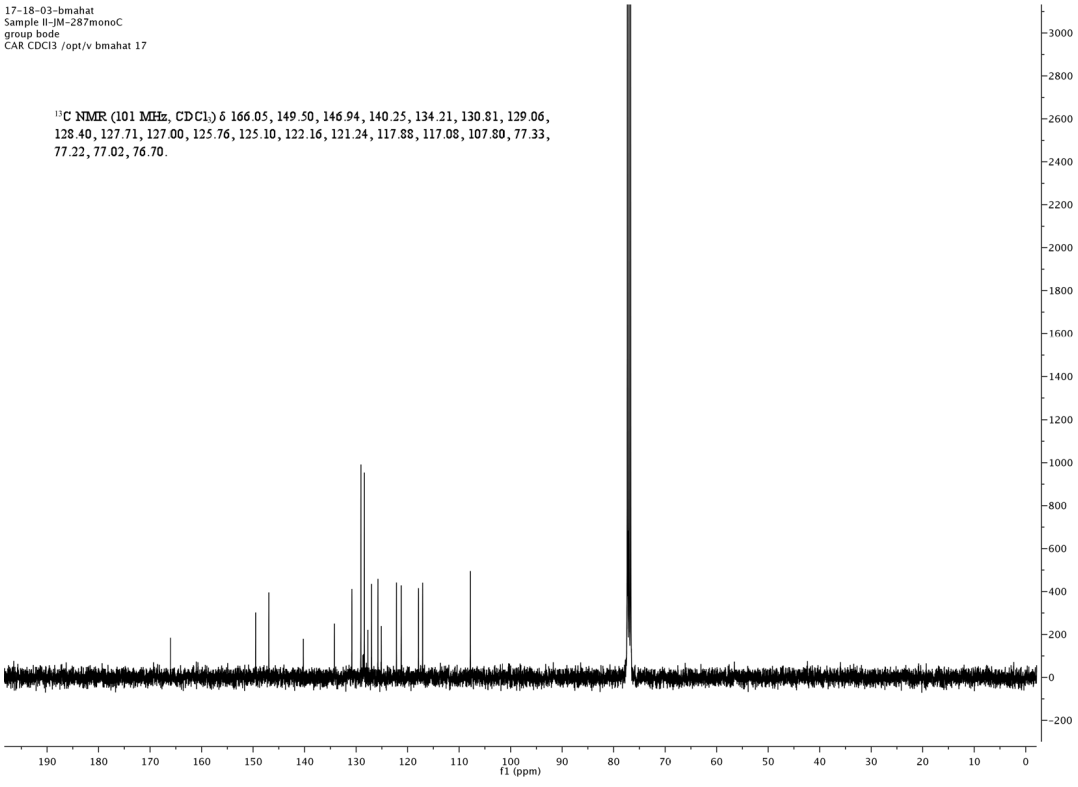
Characterization data of both the monoacylated and diacylated products 15 and 16

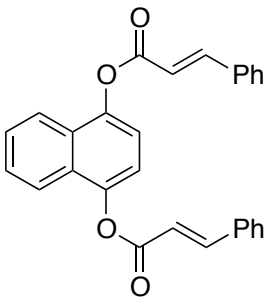


4-hydroxynaphthalen-1-yl cinnamate (15). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1H NMR (300 MHz, $CDCl_3$) δ 8.18-8.15 (m, 1H), 8.02-7.96 (d, ^{1}J = 16 Hz, 1H), 7.86-7.83 (m, 1H), 7.66-7.63 (m, 2H), 7.54-7.44 (m, 5H), 7.13-7.11 (d, ^{1}J = 6 Hz, 1H), 6.82-6.76 (d, ^{1}J = 16 Hz, 1H), 6.77-6.73 (d, ^{1}J =12 Hz, 1H) , 5.42 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.05, 149.50, 146.94, 140.25, 134.21, 130.81, 129.06, 128.40, 127.71, 127.00, 125.76, 125.10, 122.16, 121.24, 117.88, 117.08, 107.80. IR (thin film) v 3401, 1703, 1631, 1548, 1386, 1352, 1331, 1260, 1239, 1201, 1146, 1063 cm^{-1}; HRMS (ESI) $[M+H]^{+}$ calcd. for $C_{19}H_{15}O_3$, 291.1013 found, 291.1016.

^{1}H and ^{13}C NMR of 4-hydroxynaphthalen-1-yl cinnamate **15**

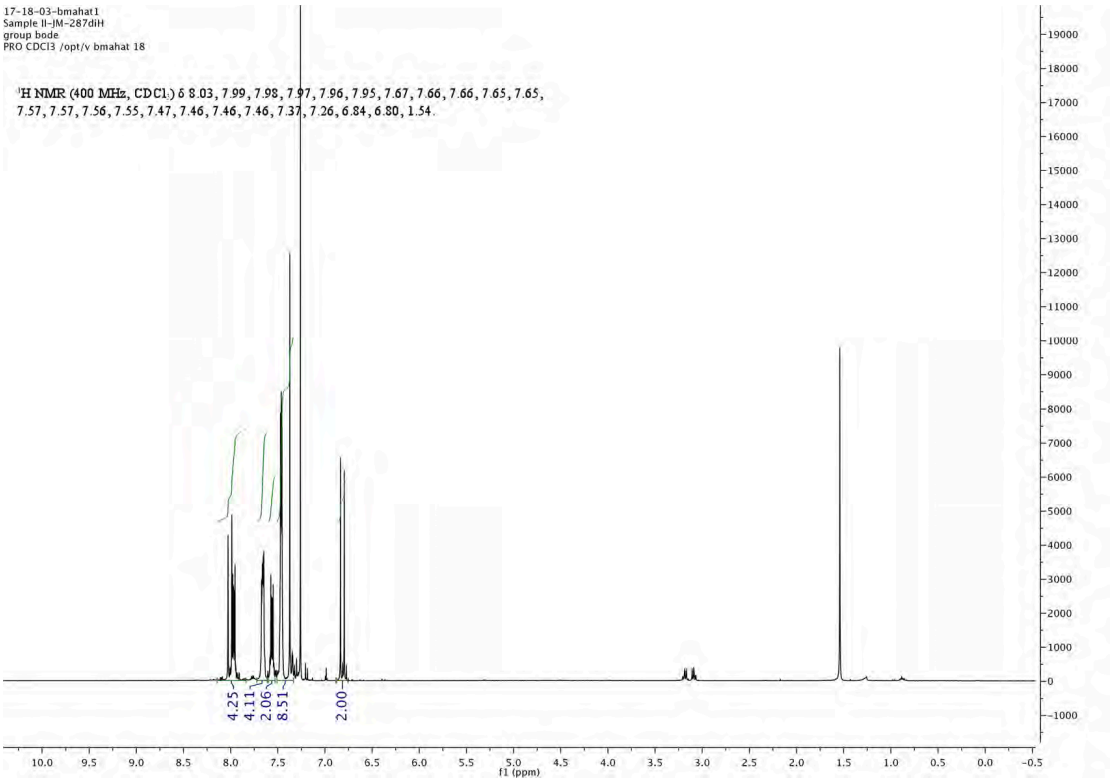


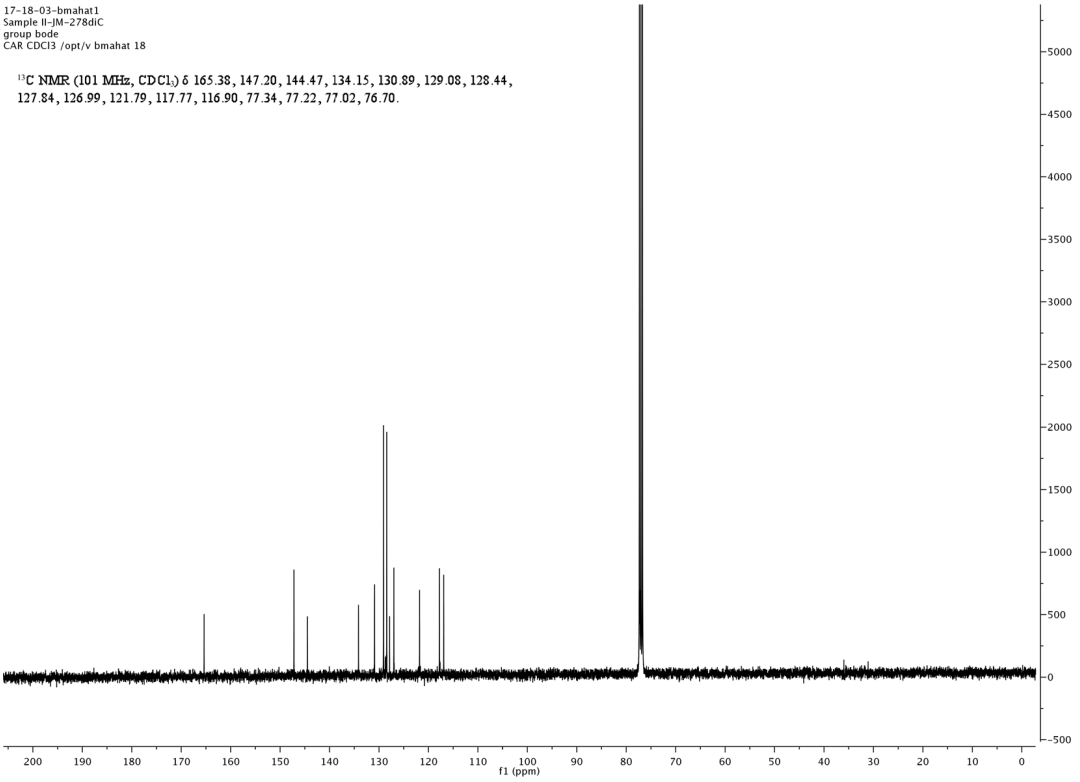




(2*E*,2'*E*)-naphthalene-1,4-diyl bis(3-phenylacrylate) (16). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1H NMR (400 MHz, $CDCl_3$) δ 8.03-7.95 (m, 4H), 7.67-7.65 (m, 4H), 7.57-7.55 (m, 2H), 7.47- 7.37 (m, 8H), 6.84-6.80 (d, ^{1}J = 16 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.38, 147.20, 144.47, 134.15, 130.89, 129.08, 128.44, 127.84, 126.99, 121.79, 117.77, 116.90, 77.34, 77.22, 77.02, 76.70. IR (thin film) v 1733, 1634, 1600, 1577, 1329, 1308, 1262, 1244, 1215, 1201, 1131, 1060 cm^{1}; HRMS (ESI) $[M+H]^+$ calcd. for $C_{28}H_{21}O_4$, 421.1429 found, 421.1434.

^{1}H and ^{13}C NMR of (2*E*,2'*E*)-naphthalene-1,4-diyl bis(3-phenylacrylate) **16**

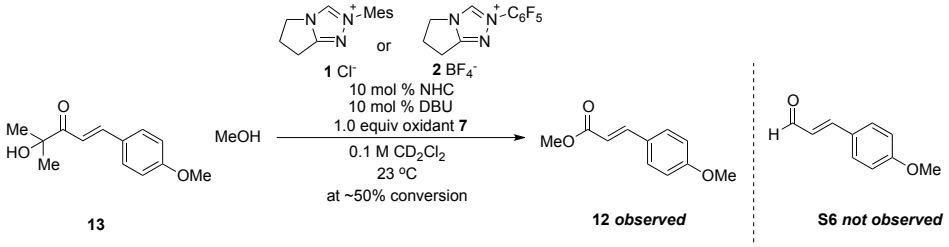




Additional mechanistic probes

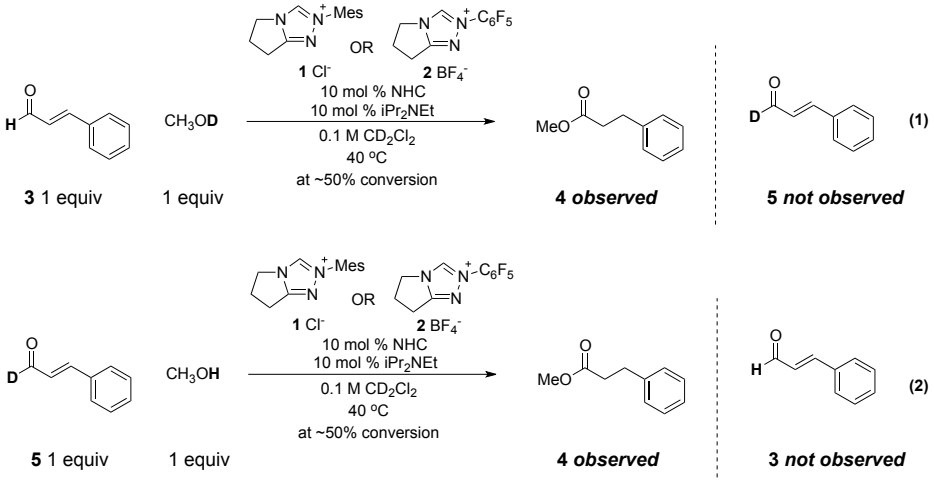
A) Evidence for the irreversibility of the Breslow intermediate

AA) No aldehyde formation observed when α-hydroxyenone was used:

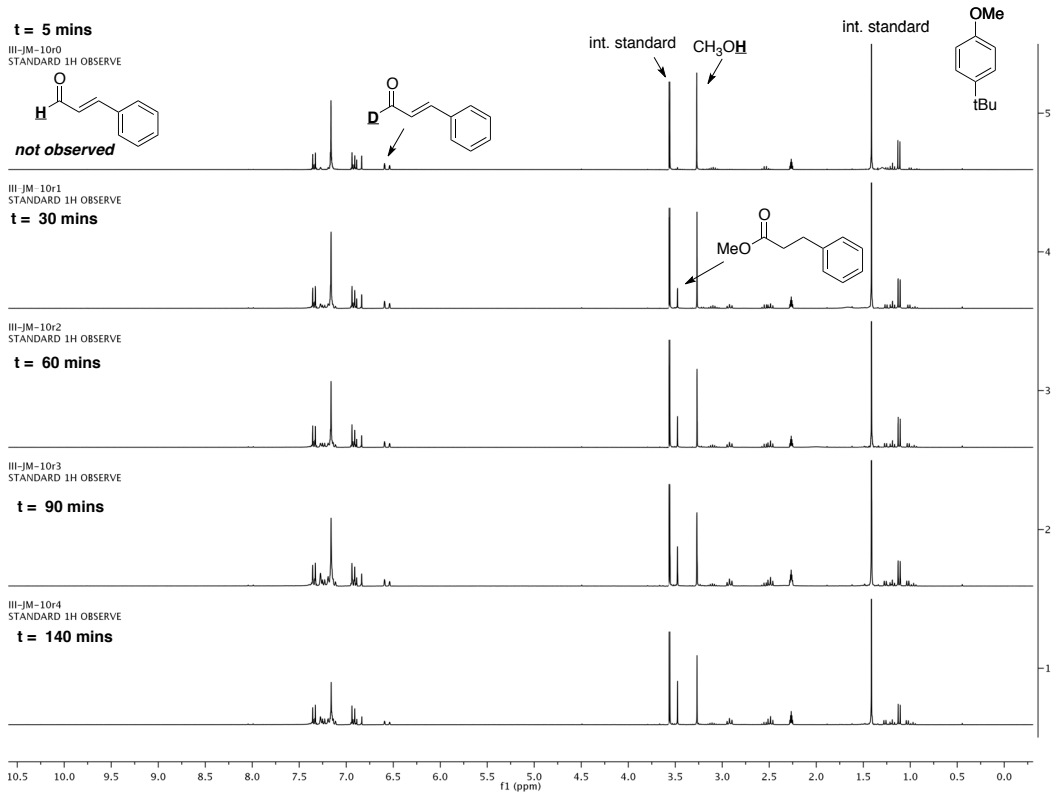


13 | **12** *observed* | **S6** *not observed*

AB) No aldehyde H-D exchange during redox esterification:

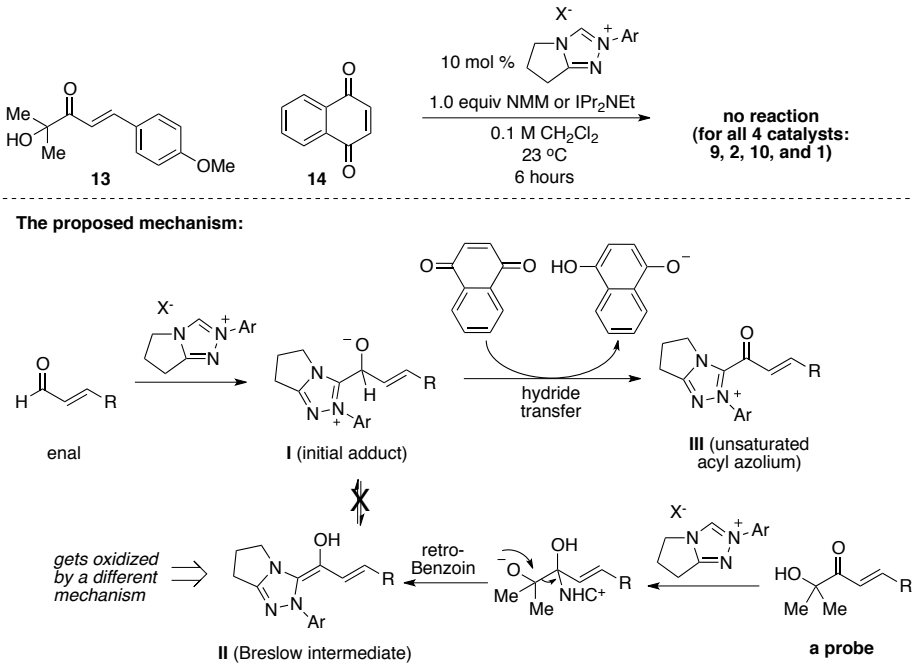


^{1}H NMR of a representative reaction ***(2)*** *with N-C_6F_5 catalyst* **2**

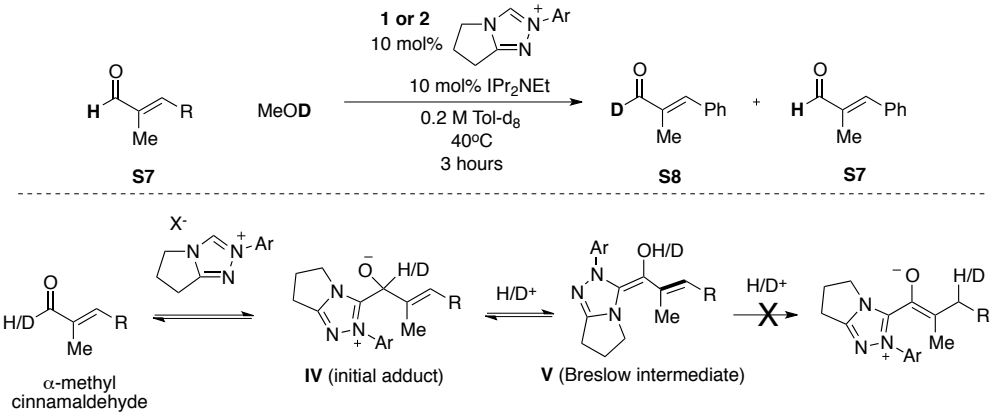


B) An additional evidence for hydride transfer mechanism.

As an addition confirmation of the proposed hydride transfer mechanism by Csáky,[14] (*E*)-4-hydroxy-1-(4-methoxyphenyl)-4-methylpent-1-en-3-one **13** was used in place of enal with 1,4-naphthoquinone **14** as the stoichiometric oxidant with all 4 triazolium salts used in this study. We obtained no reaction (starting material recovery) for all four reactions. This showed that the mechanism of oxidation by 1,4-napthoquinone **14** (hydride transfer) must be different than that with diquinone oxidant **7** (electron-transfer oxidation).[15] With α-hydroxyenone, the Breslow intermediate **II** is generated directly, does not revert back to the initial adduct **I** (*vide supra*), and therefore no hydride donor was generated (below).

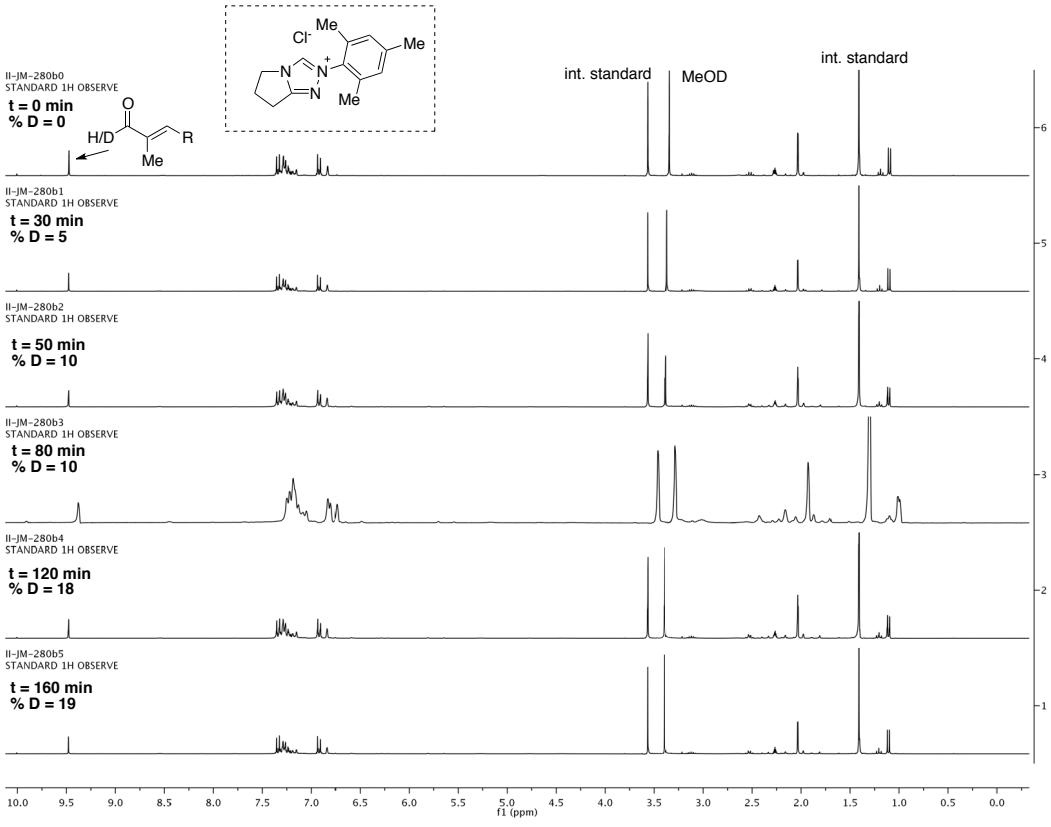


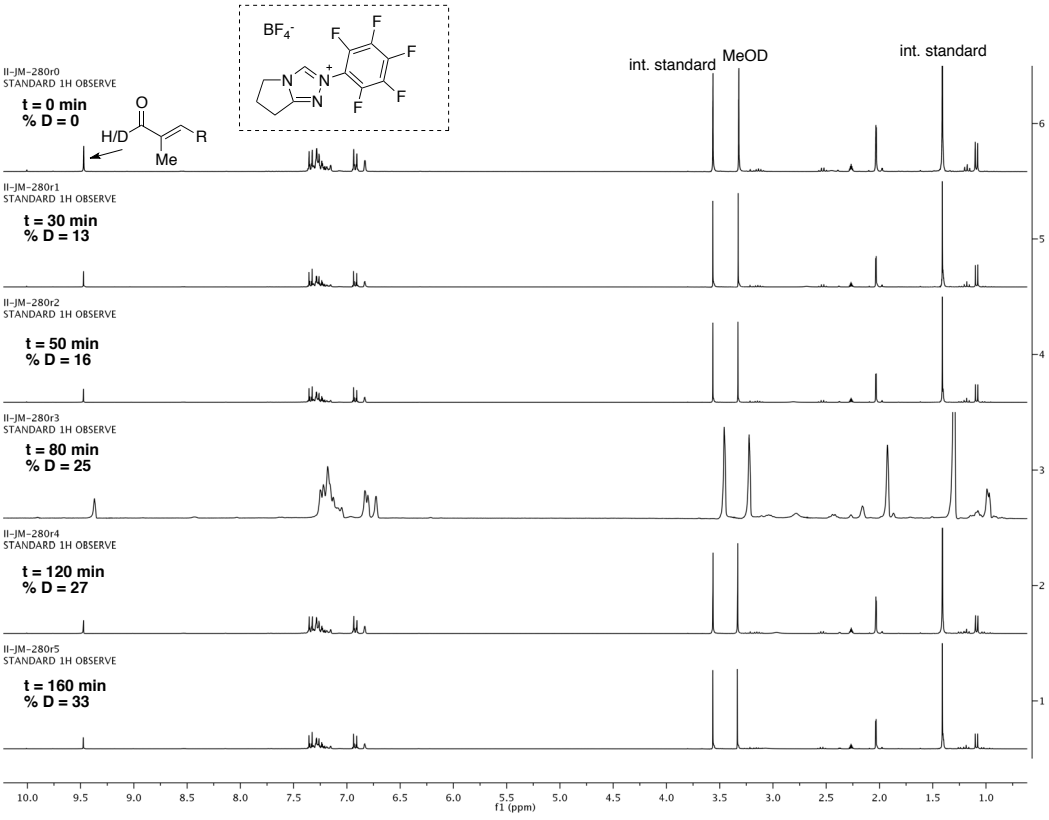
C) The Breslow intermediate from α-methyl cinnamaldehyde is reversible

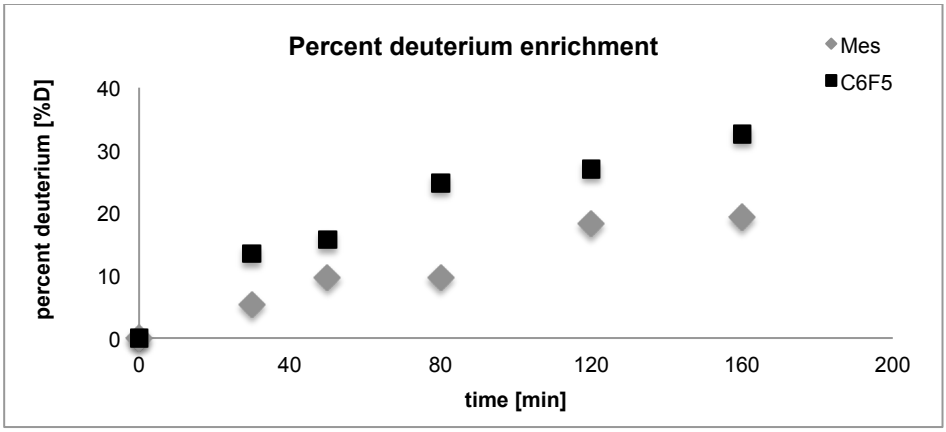


(14)M. T. Molina, C. Navarro, A. Moreno and A. G. Csaky, *J. Org. Chem.,* 2009, **74**, 9573-9575.
(15) (a) S. De Sarkar, S. Grimme and A. Studer, *J. Am. Chem. Soc.,* 2010, **132**, 1190–1191. (b) S. De Sarkar and A. Studer, *Org. Lett.,* 2010, **12**, 1992–1995.

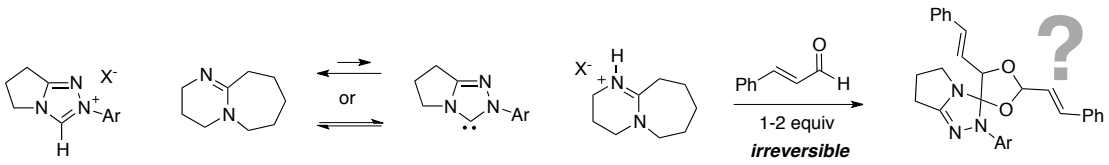
A solution of α-methyl cinnamaldehyde **S7** (14.6 mg, 0.1 mmol, 1.0 equiv) and 1-(tert-butyl)-4-methoxybenzene (16.4 mg, 0.1 mmol, 1.0 equiv as internal standard), and 5.0 µL MeOD (0.1 mmol, 1.0 equiv) was prepared using 0.5 mL tol-d_8 (with 10% CD_2Cl_2 to ensure solubility). This solution was transferred (0.5 mL) to an NMR tubes charged with 10 mol% of 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium chloride **1** or with 10 mol% 2-(perfluorophenyl)-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium BF_4^- **2**. The NMR tubes were heated at 40°C in an oil bath, and ^{1}H NMR was used to minor both reactions periodically over 3 hours. The rate of H/D exchange was measured by the disappearance of the aldehyde singlet at 9.50 ppm (1H) against an internal standard peak (9H) at 1.29 ppm (see plots below). The *N*-C_6F_5 catalyst is more reversible by 1.5 time than the *N*-mesityl counterpart.







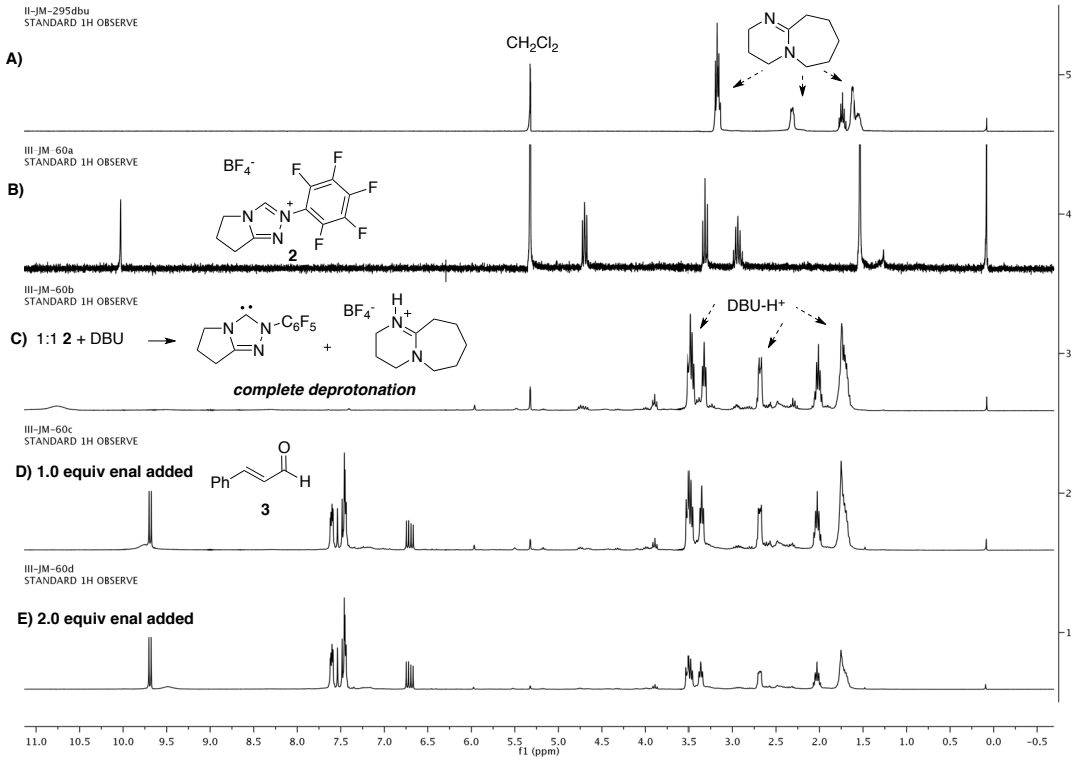
Extent of deprotonation of triazolium salts and enal titration experiments



A general procedure: In an NMR tube charged with triazolium salt (either **9**, **2**, **10**, or **1**; 0.05 mmol, 1 equiv) and 0.5 mL (0.1 M) CD_2Cl_2, 7.5 μL (0.05 mmol, 1.0 equiv) of DBU was added. The mixture was shaken, and ^1H NMR was recorded (frame C). For triazolium salt **2**

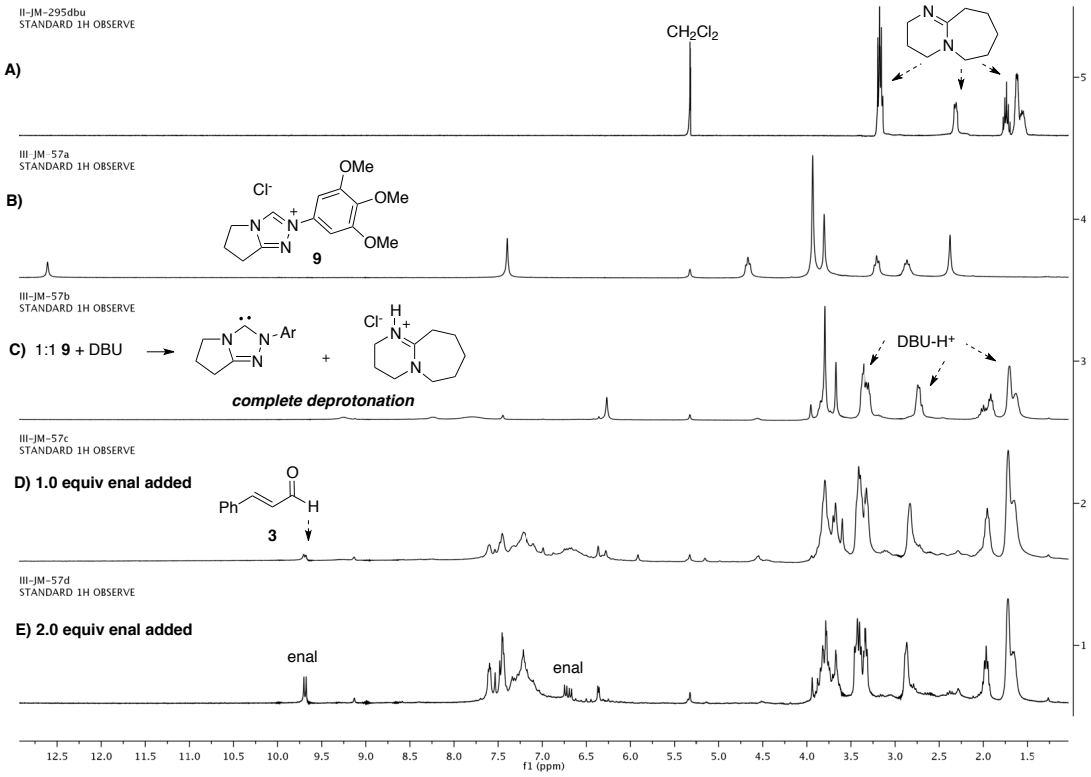
and **9**, apparent shift of DBU signals indicated complete (if not near) protonation of DBU and hence implies deprotonation of azolium salts. On the contrary, **10** and **1** seemed to be partially deprotonated (not significant shift for DBU peaks). To this mixture, 3.3 μL (0.05 mmol, 1.0 equiv) of cinnamaldehyde was added in, and ^{1}H NMR was recorded (frame D). After about 5 minutes, an additional 3.3 μL (0.05 mmol, 1.0 equiv) of cinnamaldehyde was added in; ^{1}H NMR was recorded again (frame E). For *N*-C_6F_5 catalyst **2**, no change was observed in the ^{1}H NMR spectra as cinnamaldehyde was titrated in. While DBU was protonated, the *N*-3,4,5-trimethoxy catalyst **9** formed some adduct[16] (based on rapid consumption of enal), which is irreversible[17] and unidentifiable. As for catalysts **10** and **1**, DBU became more protonated while cinnamaldehyde was titrated in, which also formed similar catalyst-dead-end adduct. These ^{1}H NMR spectra were compared against one with only DBU in CD_2Cl_2 (frame A) and another with just triazolium salt in CD_2Cl_2 (frame B).

*^{1}H NMR spectra of the extent of deprotonation of **2** and titration with enal **3***

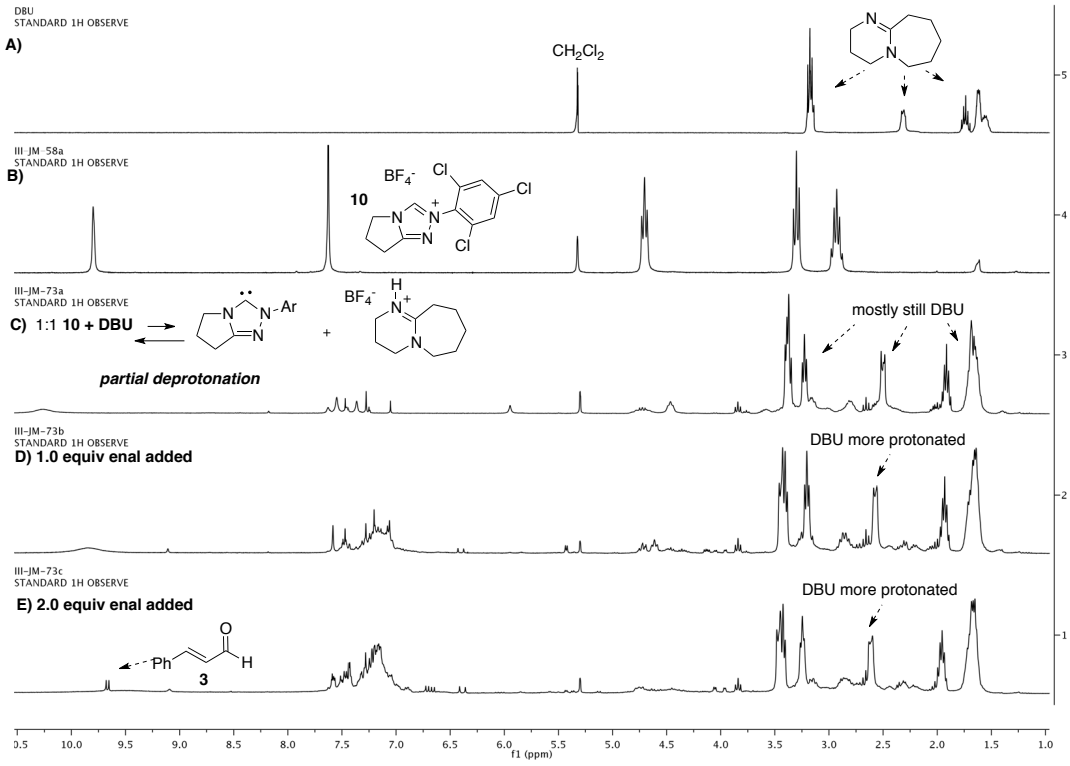


(16) In the absence of other suitable reaction partner, enal seemed to form a complex adduct with NHC catalysts, possibly such as that demonstrated in A. Berkessel, S. Elfert, K. Etzenbach-Effers and J. H. Teles, *Angew. Chem., Int. Ed.,* 2010, **49**, 7120–7124.
(17) For example, adding MeOH to any of these complex mixture did not afford redox esterification product. Adding diquinone oxidant **7** and MeOH – a reaction demonstrated to be very rapid – also did not afford any oxidative esterification product.

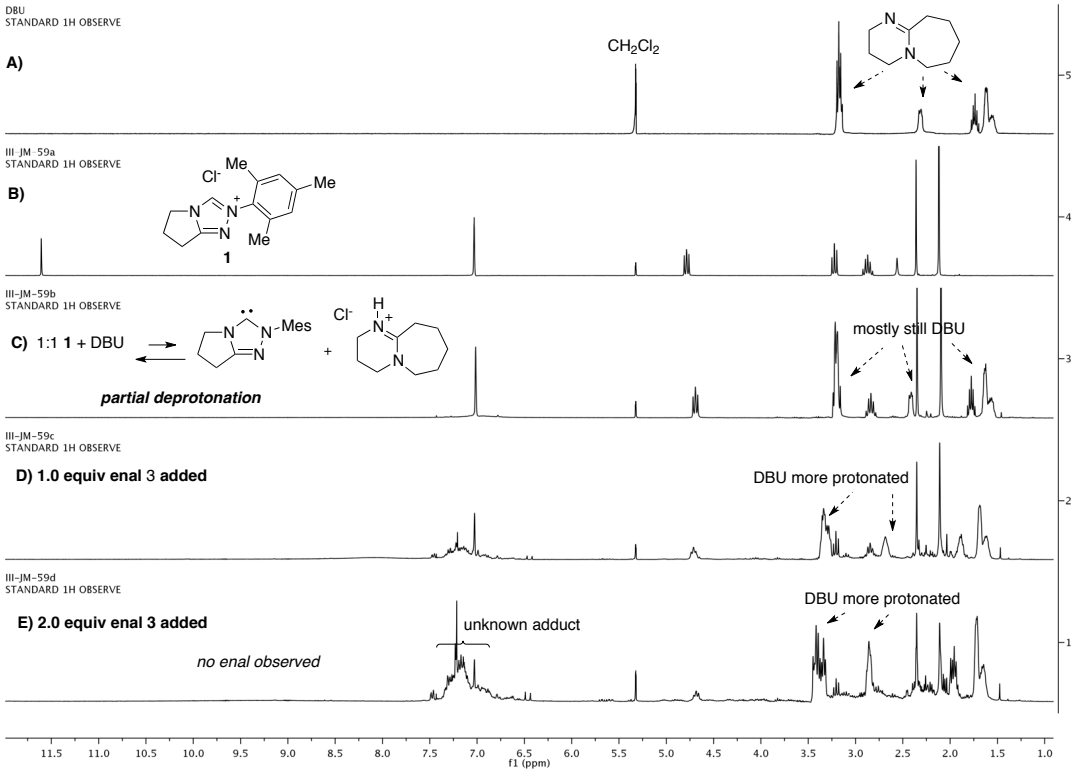
*^{1}H NMR spectra of the extent of deprotonation of **9** and titration with enal **3***



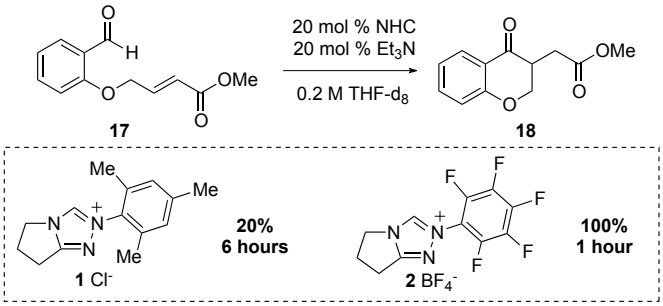
*^{1}H NMR spectra of the extent of deprotonation of **10** and titration with enal **3***



*^{1}H NMR spectra of the extent of deprotonation of **1** and titration with enal **3***

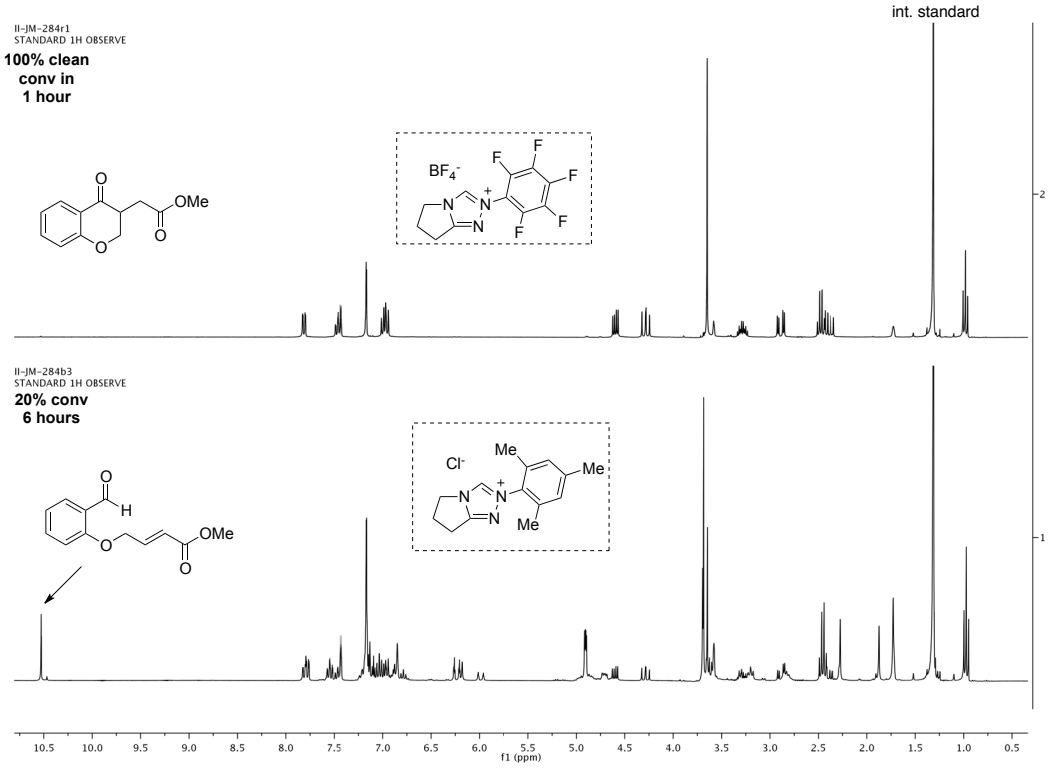


Intramolecular Stetter reaction comparison

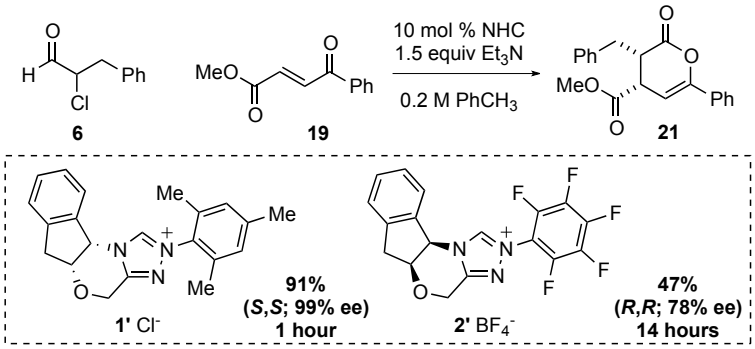


A solution of (*E*)-methyl 4-(2-formylphenoxy)but-2-enoate **17** (52.8 mg, 0.4 mmol, 1.0 equiv), triethylamine (7.0 μL, 20.0 mol%), and 1,3-di-tert-butylbenzene (0.1 mmol, 0.5 equiv as internal standard) was prepared using 1.2 mL THF-d_8. This solution was transferred equally (0.6 mL) to two NMR tubes containing triazolium salts **1** and **2** respectively. The reactions were carried out at room temperature, and ^{1}H NMR spectra of both reactions were recorded for the unpurified reaction mixture at 1 and 6 hours. The reaction with *N*-C_6F_5 catalyst is more rapid and completed within 1 hour while that with the *N*-mesityl catalyst proceeded more slowly (20% at 6 hours). ^{1}H NMR spectra below compared the result. The

identity of methyl 2-(4-oxochroman-3-yl)acetate[18] **18** was confirmed by ^{1}H NMR and GC/MS: ^{1}H NMR (300 MHz, THF-d_8): δ 7.83-7.80 (m, 1H), 7.46- 7.43 (1H), 7.17 (s, 1H), 7.01-6.94 (m, 1H), 4.62-4.57 (m, 1H), 4.32-4.24 (t, 1H), 3.65 (s, 3H), 3.32-3.28 (m, 1H), 2.92-2.85 (m, 1H), 2.51-2.43 (m, 1H). GC/MS (EI): 220 (M^+), 207, 189, 147 (100%), 120, 92, 97.



Hetero Diels-Alder reaction comparison

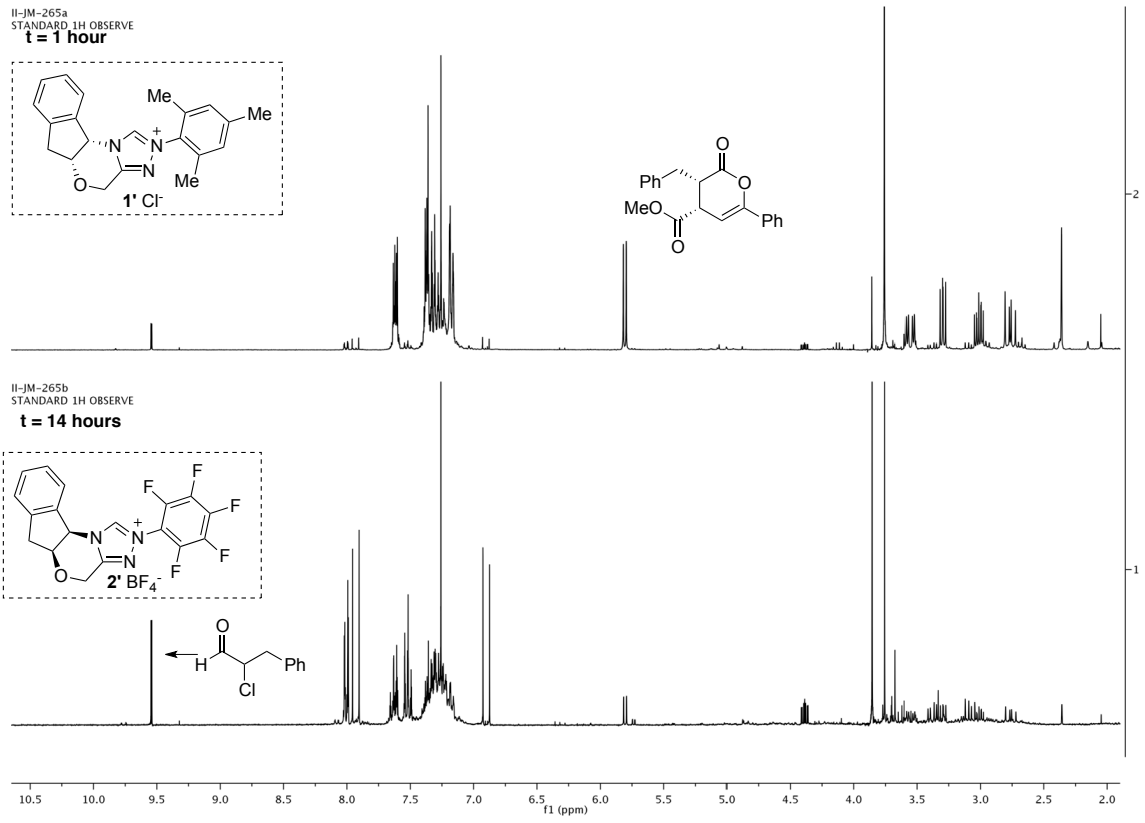


A solution of 2-chloro-3-phenylpropanal **6** (26.0 mg, 0.4 mmol, 1.0 equiv), triethylamine (20.0 μL, 3.0 equiv), and (*E*)-methyl 4-oxo-4-phenylbut-2-enoate **19** (20.0 mg,

(18) Spectroscopic data compared well with the literature value in J. R. de Alaniz, M. S. Kerr, J. L. Moore and T. Rovis, *J. Org. Chem.,* 2008, **73**, 2033–2040.

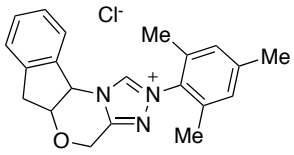
0.4 mmol, 1.0 equiv) was prepared using 0.5 mL $PhCH_3$. This solution was transferred equally to two vials containing chiral triazolium salts **7'**[1] and **9'**[4] respectively. The reactions were carried out at room temperature, and ^{1}H NMR spectra of both reactions were recorded for the unpurified reaction mixtures at 1 and 18 hours. The reaction with *N*-mesityl catalyst is more rapid and completed within 1 hour while that with the *N*-C_6F_5 catalyst proceeded more slowly (47% at 14 hours). The products were isolated by preparative TLC using 10:1 hexanes: EtOAc. ^{1}H NMR spectra below compared the result. HPLC analysis showed that both the *N*-mesityl and the *N*-C_6F_5 catalyst have the same sense of asymmetric induction, despite a different degree of enantioselectivity. The identity of the product **21**[19] was confirmed by ^{1}H NMR and GC/MS: ^{1}H (300 MHz, $CDCl_3$): δ 7.63-7.60 (m, 2H), 7.38-7.16 (m, 8H), 5.82-5.79 (d, ^1J = 9 Hz), 3.76 (s, 3H), 3.58-3.52 (dd, ^1J = 16.5 Hz, ^2J = 6 Hz), 3.32-3.27 (m, 1H), 3.01-2.80 (m, 1H), 2.75-2.72 (m, 1H). GC/MS (EI): 322.1 (M^+), 262.0, 231.0, 199.0, 131.0, 105.0, 91.0 (100%), 77.

^{1}H NMR spectra comparison

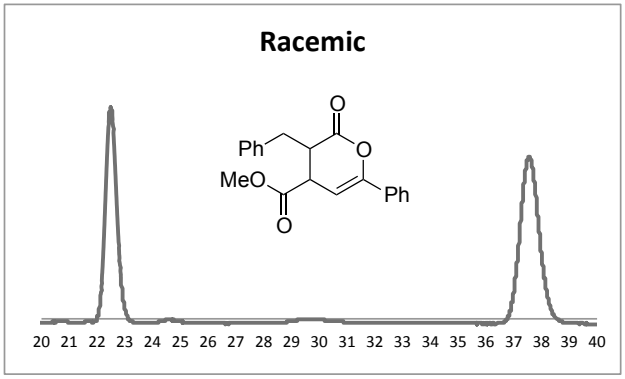


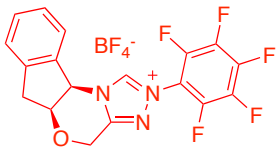
(19) Spectroscopic data compared well with the literature value in M. He, J. R. Struble and J. W. Bode, *J. Am. Chem. Soc.,* 2006, **128**, 8418–8420.

Prepared with catalyst: **HPLC trace:**

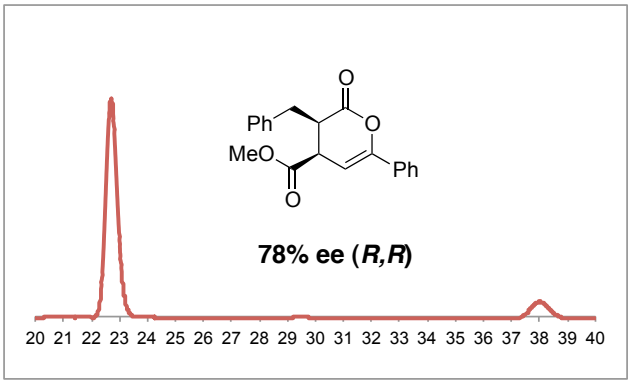


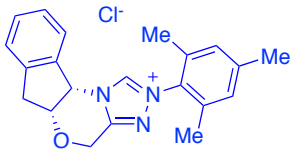
racemic mixture



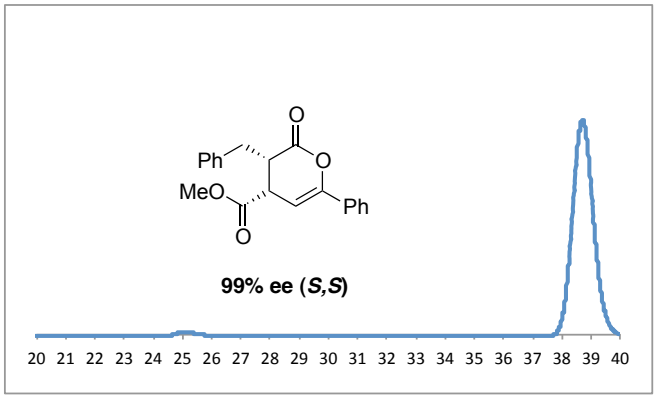


2'

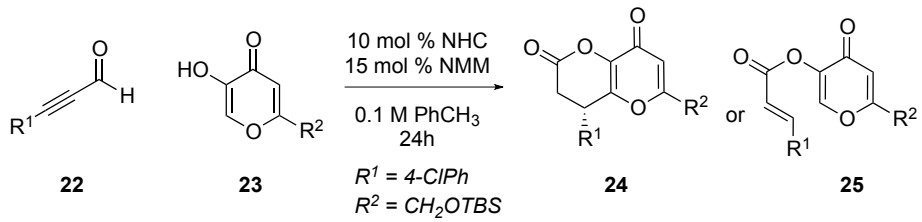




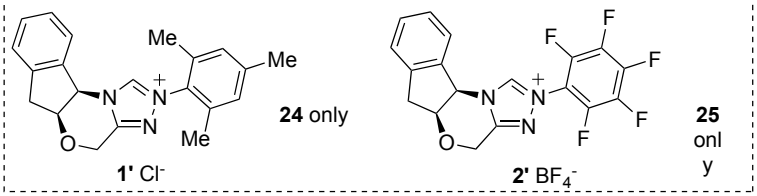
1'



Claisen vs. esterification reaction comparison



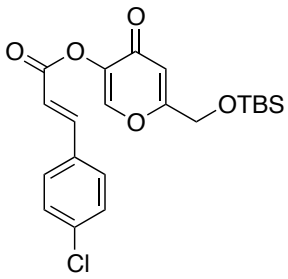
22 **23** **24** **25**



1' Cl^- **2'** BF_4^-

Into an oven dried 4.0 mL vial, 2-((*tert*-butyldimethylsilyloxy)methyl)-5-hydroxy-4H-pyran-4-one **23** (25.6 mg, 0.10 mmol, 1.0 equiv), (*R,S*) triazolium precatalyst (**1'** or **2'**; 0.10 equiv), and *N*-methylmorpholine (NMM; 0.15 equiv), were added, followed by 1.0 mL toluene (0.1 M) and 3-(4-chlorophenyl)propiolaldehyde **22** (16.4 mg, 0.10 mmol, 1.0 equiv). The flask was sealed with a polyethylene cap. The resulting solution was heated to 40°C and stirred for 24 hours before it was concentrated. The reaction with chiral *N*-mesityl catalyst **9'** afforded the desired Coates-Claisen annulation product **24** as described previously.[20] The reaction with the chiral *N*-C_6F_5 catalyst **2'** afforded the desired ester product **25** as the sole product, which was isolated as white solid preparative TLC (3:1 hexanes:EtOAc) as the sole product in 60% yield.

Characterization data



(*E*)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-oxo-4*H*-pyran-3-yl-3-(4-chlorophenyl)acrylate 25. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.87–7.83 (d, 1H, ^1J = 16 Hz), 7.53–7.85 (m, 2H), 7.42–7.40 (m, 2H), 6.64–6.60 (d, 1H, ^1J = 16 Hz), 6.63 (s, 1H), 4.53 (s, 2H), 0.96 (s, 9H); 0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.83, 167.91, 163.57, 147.47, 146.41, 141.02, 136.93, 132.47, 129.58, 129.33, 61.08, 25.74, 18.27, -5.47. IR (thin film) v 3106, 2928, 2859, 2359, 1732, 1659, 1635, 1460, 1204, 1146, 1109, 838, 779 cm^{-1}; HRMS (ESI) $[M+H]^+$ calcd. for $C_{21}H_{26}ClO_5Si$, 421.1233 found, 421.1241.

(20) J. Kaeobamrung, J. Mahatthananchai, P. Zheng and J. W. Bode, *J. Am. Chem. Soc.,* 2010, **132**, 8810–8812.

^{1}H and ^{13}C NMR of ester **25**