Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

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α,β-Unsaturated Acyl Azoliums from N-Heterocyclic Carbene Catalyzed Reactions: Observation and Mechanistic Investigation**

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Supporting Information
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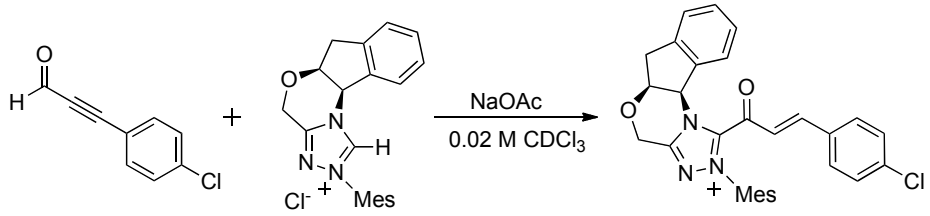
General Method

All reactions utilizing air- or moisture-sensitive reagents were 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. The derivatives of ynals were synthesized according to literature procedure.[1] Other reagents were used without further purification, unless otherwise noted. Reagent grade NaOAc was flame-dried *in vacuo* under N_2 atmosphere before use. For all mechanistic investigations, starting materials, reagents, and solvents were purified by either distillation or sublimation to minimize side products and ensure maximum purity. 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 Bruker Avance II 500 MHz, 125 MHz respectively (University of Pennsylvania) or VARIAN Mercury 300 MHz, 75 MHz (ETH Zurich) or Bruker Avance 400 MHz, 100 MHz respectively (ETH Zurich). HMBC experiment was performed on Bruker Avance III (600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR) by the NMR service of the LOC at the ETHZ. 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. The enolic proton of the products is not usually observed in the proton spectra. Ultraviolet-Visible (UV-VIS) spectra were recorded on a JASCO V570 spectrometer; the wavelength was reported in nanometer (nm). Infrared (IR) spectra were recorded on a JASCO FT:IR-4100 spectrophotometer and reported as wavenumber (cm^{-1}). 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.

(1) (a) S. Serra, C. Fuganti, *Synlett* **2002**, 1661–1664. (b) E. V. Tretyakov, A. V. Tkachev, T. V. Rybalova, Y. V. Gatilov, D. W. Knight, S. F. Vasilevsky, *Tetrahedron* **2000**, *56*, 10075–10080. (c) M. Journet, D. Cai, L. M. DiMichele, R. D. Larsen, *Tetrahedron Lett.* **1998**, *39*, 6427–6428.

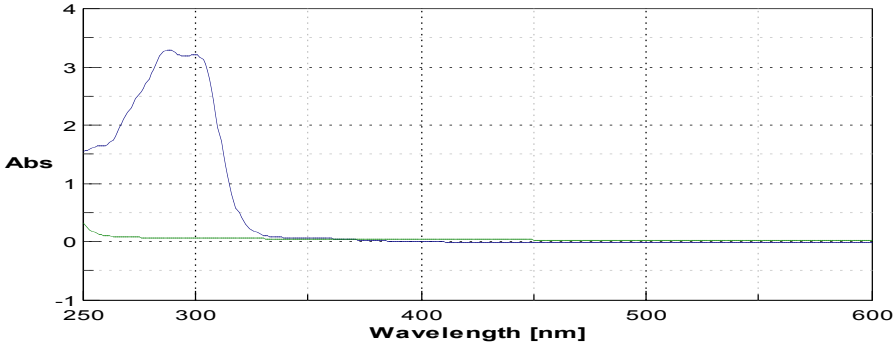
UV-VIS Investigation of Catalytically Generated *α,β*-unsaturated Acyl Azoliums



aldehyde **4** 1.0 equiv | precatalyst **3** 0.5 equiv | acyl azolium **1**

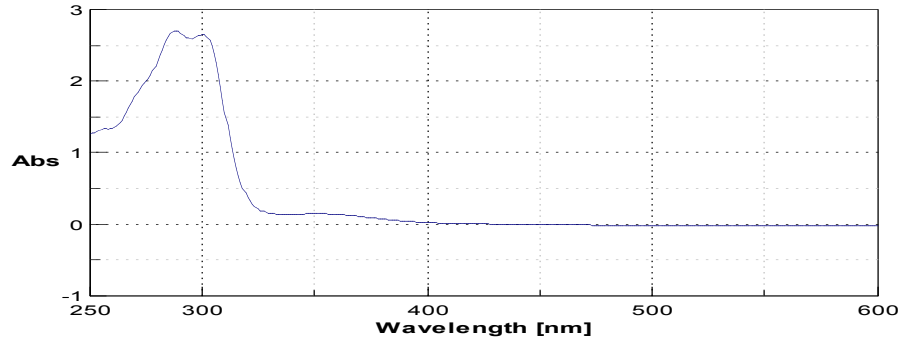
In oven-dried vials with Teflon-coated caps, 3-(4-chlorophenyl) propiolaldehyde (**4**; 0.02 mmol; 1.0 equiv) and (5a*S*,10b*R*)-5a,10b-dihydro-2-(2,4,6-trimethylphenyl)-4*H*,6*H*-indeno[2,1-*b*]-1,2,4-triazolo[4,3-*d*]-1,4-oxazinium chloride monohydrate[2] (**3;** 0.01 mmol; 0.5 equiv) were mixed, along with activated molecular sieves (4Å), and subjected to high vacuum drying for 15 mins. The reaction mixture was dissolved in 0.5 mL $CDCl_3$ (deuterated solvent was selected for the purpose of in conjunction *in-situ* NMR and UV-VIS monitoring), and 3.0 equiv of NaOAc was added to the solution; the color changed from clear-light yellow to deep orange-red. A small amount of sample was subjected UV-VIS spectroscopy (0.3 μL of the original solution in 0.5 mL $CDCl_3$) at 0 (clear), 5 (yellow), 20 (deep red), and 40 (deep red) mins as shown below. The characteristic absorption (λ_{max}) of species **1** was experimentally determined to be 355 nm.

t = 0 min (**4** + **3** with no NaOAc)

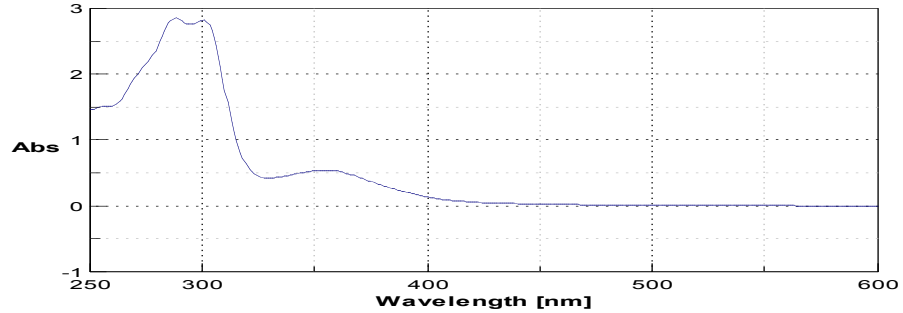


(2) Both (*S,R*) chiral triazolium salt (**3**) and its (*R,S*) enantiomer are commercially available from Sigma-Aldrich (catalog number 683981 and 683973).

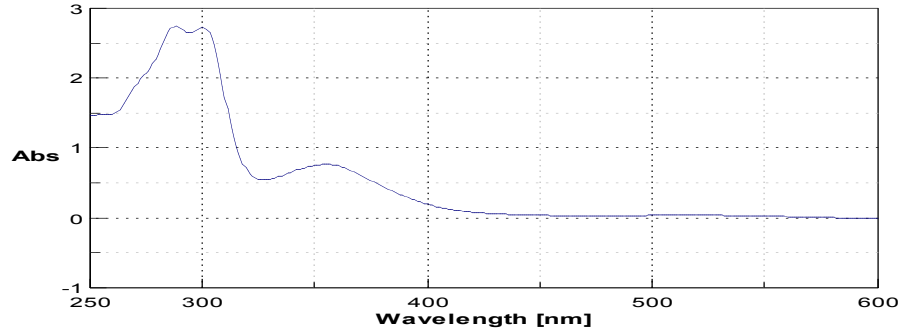
t = 5 mins (after NaOAc added)



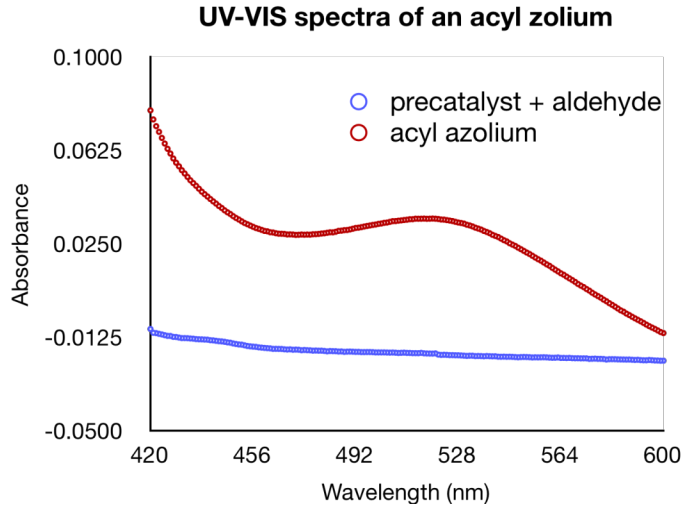
t = 20 mins (after NaOAc added)



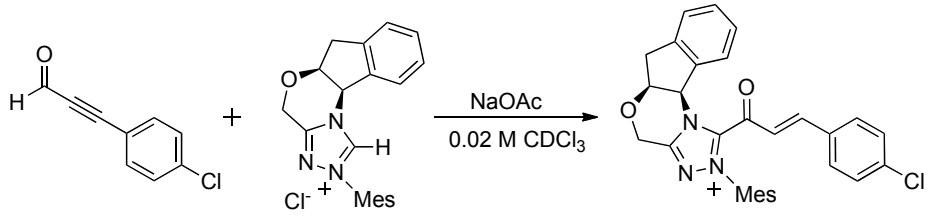
t = 40 mins (after NaOAc added)



t = 40 mins (a zoom in region at 420-600 nm)



An LC/MS Investigation of *α,β*-unsaturated Acyl Azolium



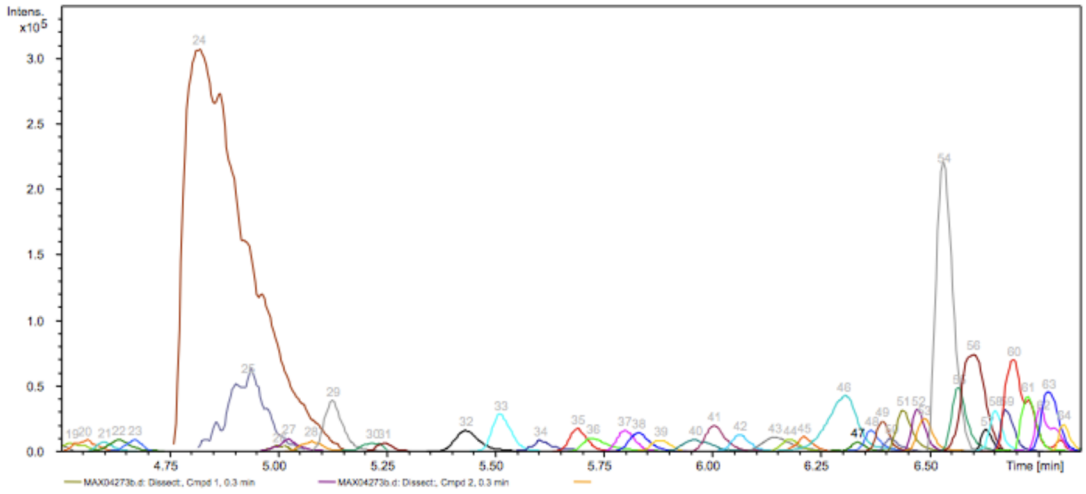
aldehyde **4** 1.0 equiv

precatalyst **3** 0.5 equiv

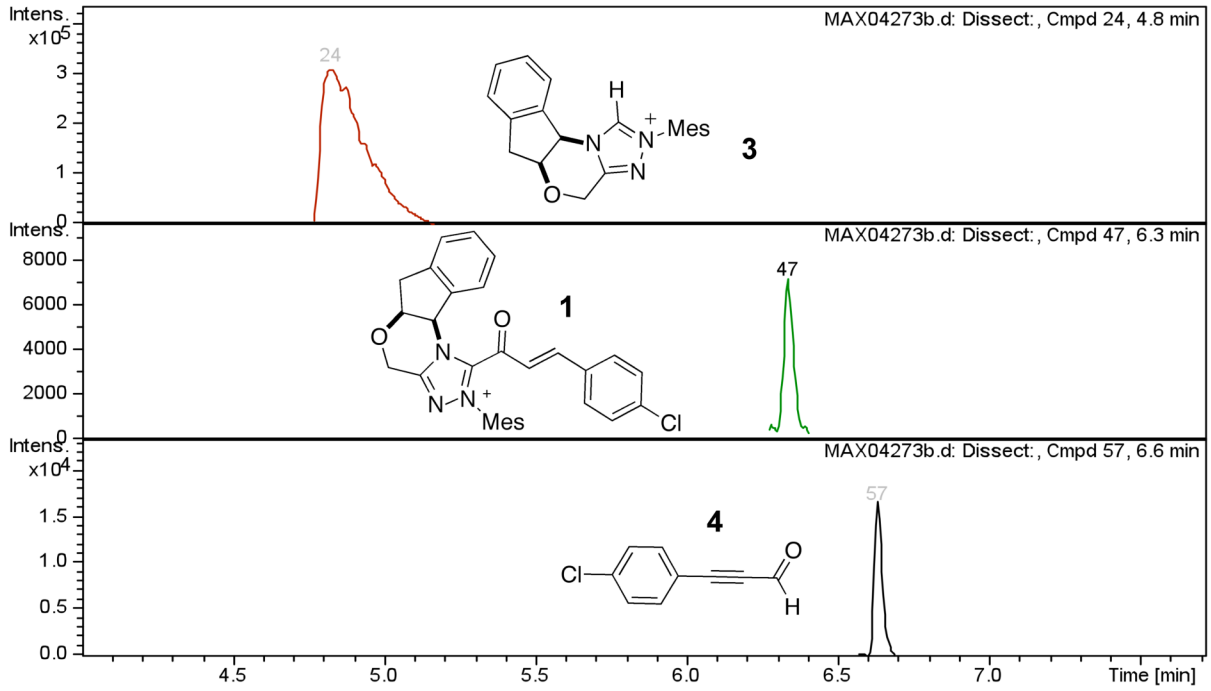
acyl azolium **1**

In oven-dried (overnight) vials with Teflon-coated caps, 3-(4-chlorophenyl) propiolaldehyde (**4**; 0.02 mmol; 1.0 equiv) and **3 (**0.02 mmol; 1.0 equiv) were mixed, along with activated molecular sieves (4Å), and subjected to high vacuum drying for 15 mins. The reaction mixture was dissolved in 0.5 mL $CDCl_3$. The solution was transferred to a dried NMR tube, followed by an addition of 3 equiv of NaOAc. After about 10 mins, the reaction was subjected to ^{1}H NMR (VARIAN Mercury 300 MHz); a new doublet peak at 8.90 ppm, indicative of the corresponding *α,β-unsaturated* acyl azolium, appeared. After ^{1}H NMR confirmation, a small sample was taken out and diluted with acetonitrile. This sample was subjected to liquid chromatography-mass spectrometry (LC-MS) analysis using acetonitrile-water (5-70%) gradient for LC separation and electrospray ionization-TOF for HRMS analysis. The identity and molecular formula of the acyl azolium **1** generated from 3-(4-chlorophenyl) propiolaldehyde was confirmed to be $C_{30}H_{27}ClN_3O_2^+$: m/z = 496.1792 (calculated) and m/z = 496.1793 (experimentally determined). Original and deconvoluted LC and MS spectra are shown below.

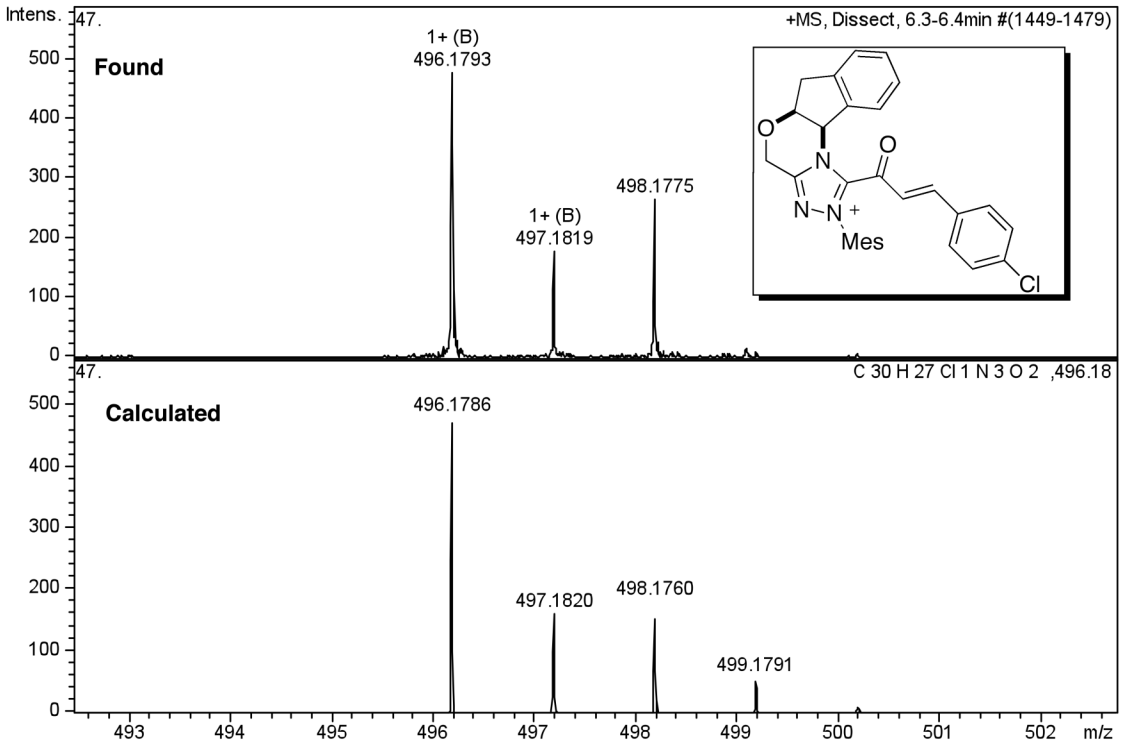
Full Liquid Chromatography Spectra



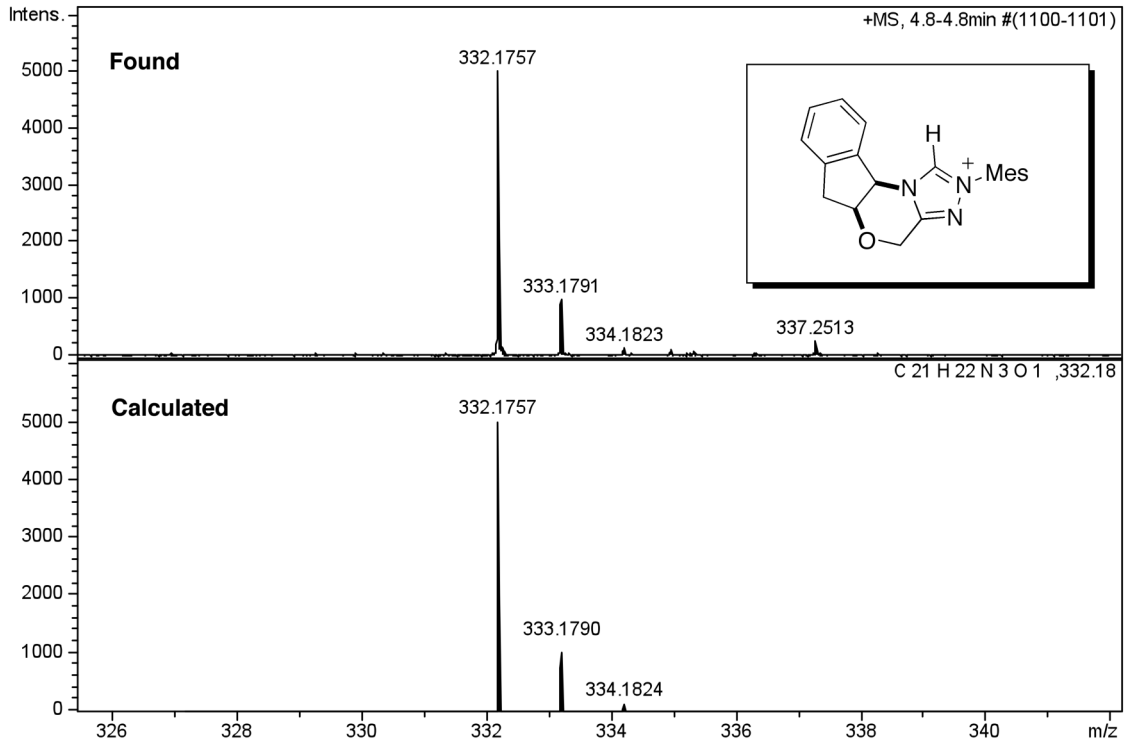
Deconvoluted and Annotated Liquid Chromatography Spectra



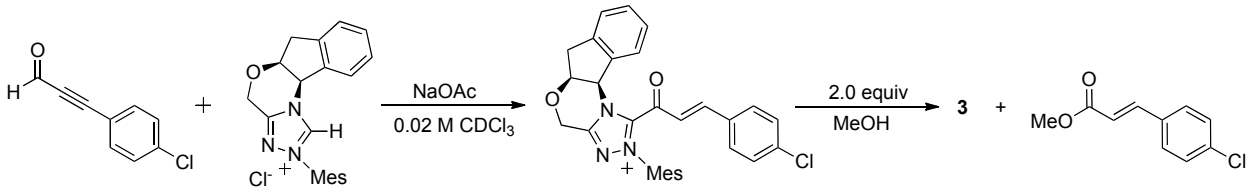
ESI-MS Spectra of the Acyl Azolium (**1**) Generated from 3-(4-Chlorophenyl) Propiolaldehyde



ESI-MS Spectra of the Azolium Precatalyst (**3**)



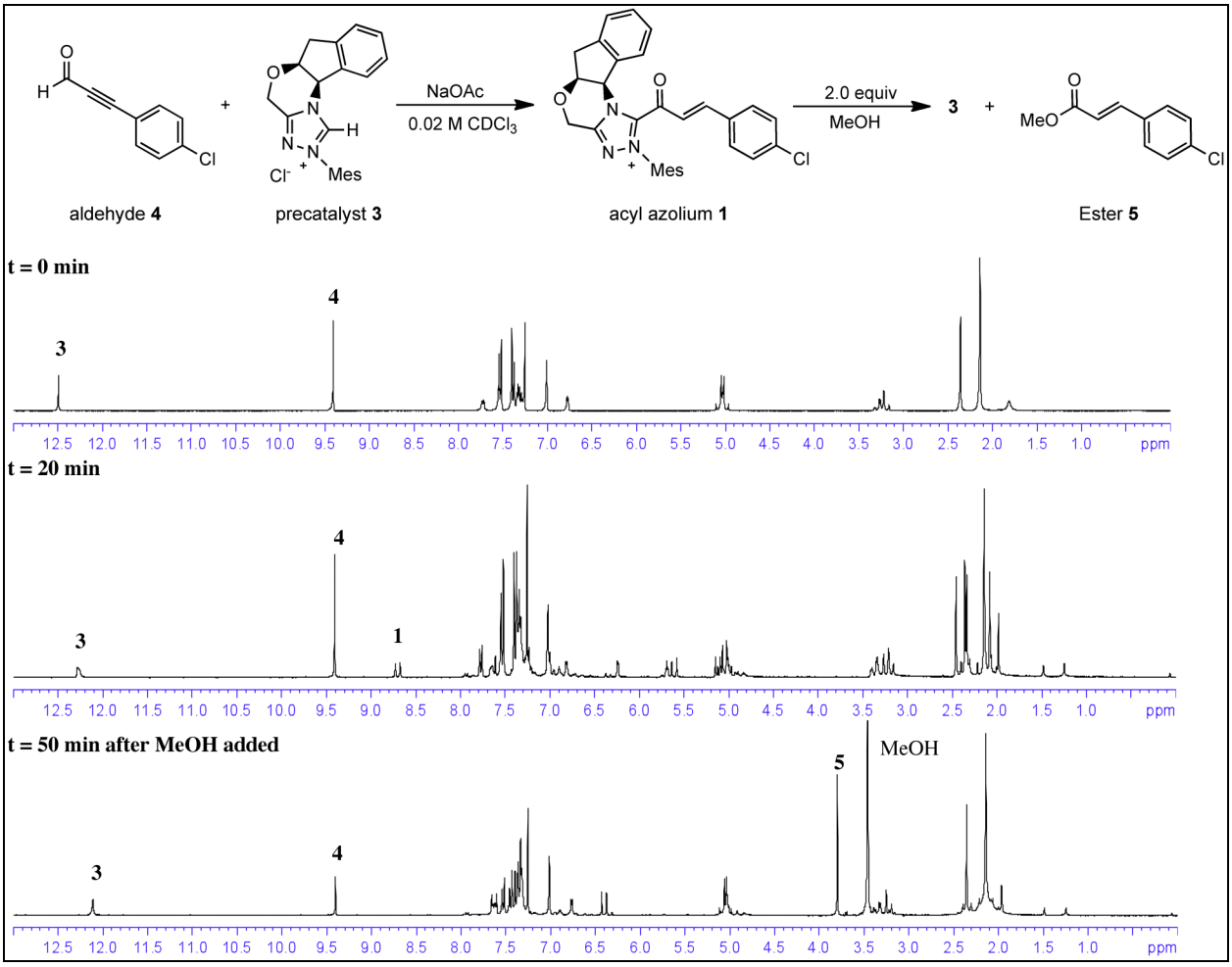
NMR Investigations of Catalytically Generated *α,β*-unsaturated Acyl Azoliums



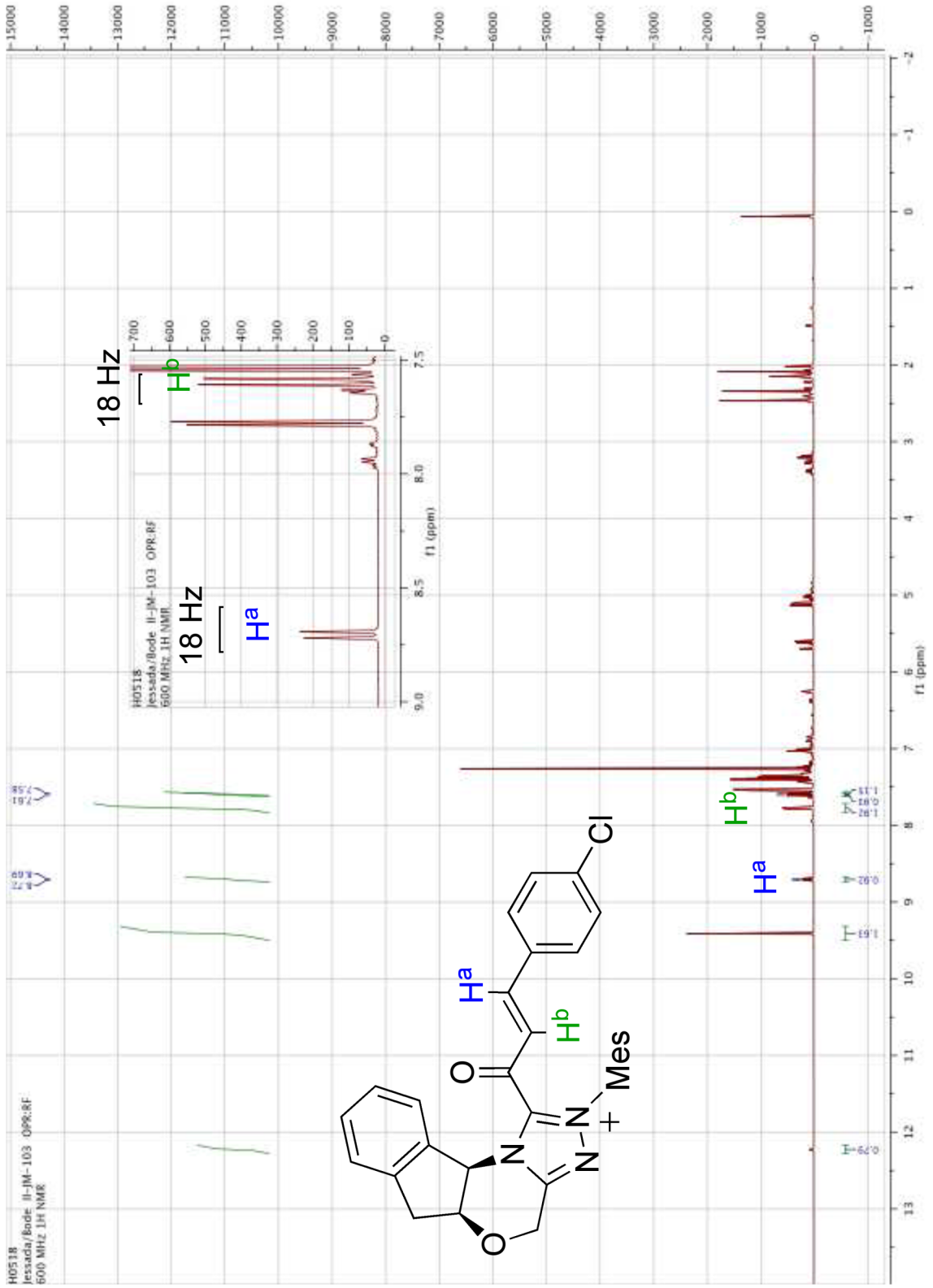
In oven-dried (overnight) vials with Teflon-coated cap, 3-(4-chlorophenyl) propiolaldehyde (**4**; 0.02 mmol; 1.0 equiv) and **3 (**0.01 mmol; 0.5 equiv) were mixed, along with activated molecular sieves (4Å), and subjected to high vacuum drying for 15 mins. The reaction mixture was dissolved in 0.5 mL $CDCl_3$. The solution was transferred to a dried NMR tube, followed by an addition of about 3 equiv of NaOAc. After 10 mins, the reaction was subjected to ^{1}H NMR (VARIAN Mercury 300 MHz); a new doublet peak at 8.87 ppm, indicative of the corresponding *α,β*-unsaturated acyl azolium, appeared. After an additional 30 mins, MeOH (0.02 mmol; 1.0 equiv) was added directly into the NMR tube. The observed acyl azolium

intermediated was converted into the corresponding ester immediately, as indicated in the ^{1}H NMR. In a separate experiment, using the same procedure described previously, the observed acyl azolium was observed (in the mixture with aldehyde **4** and precatalyst **3**) and subjected to COSY, HSQC, and HMBC NMR experiments using a Bruker Avance III (600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR) spectrometer (*vide infra*). In addition, the acyl azolium generated from 3-(4-chlorophenyl) propiolaldehyde was found to be stable up to six hours (ca.) in a sealed NMR tube, but slowly reacted with trace amount of water to become *p*-chlorocinnamic acid after leaving at room temperature for 9 hours in the absence of other nucleophiles.

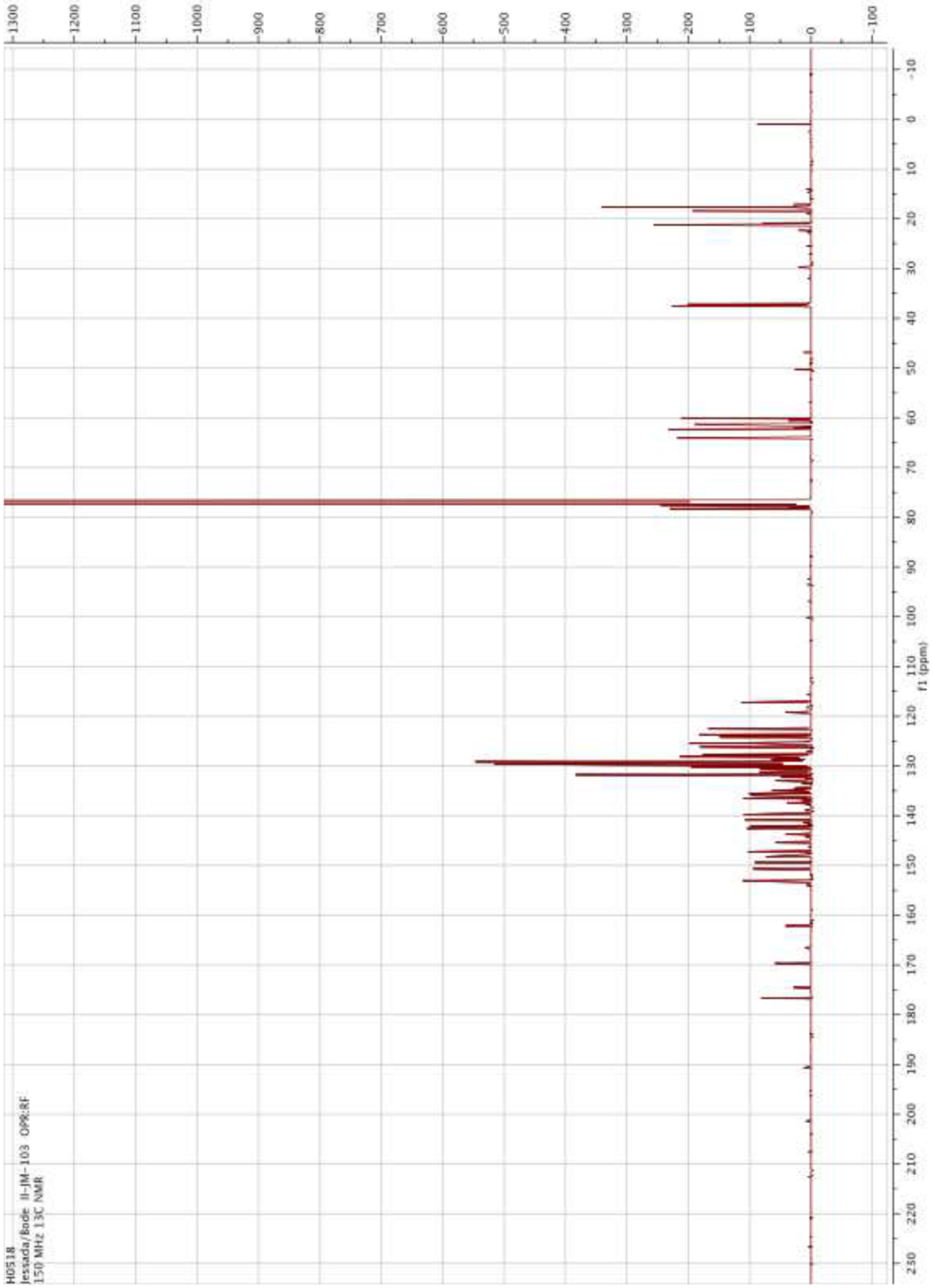
^{1}H NMR Observation:



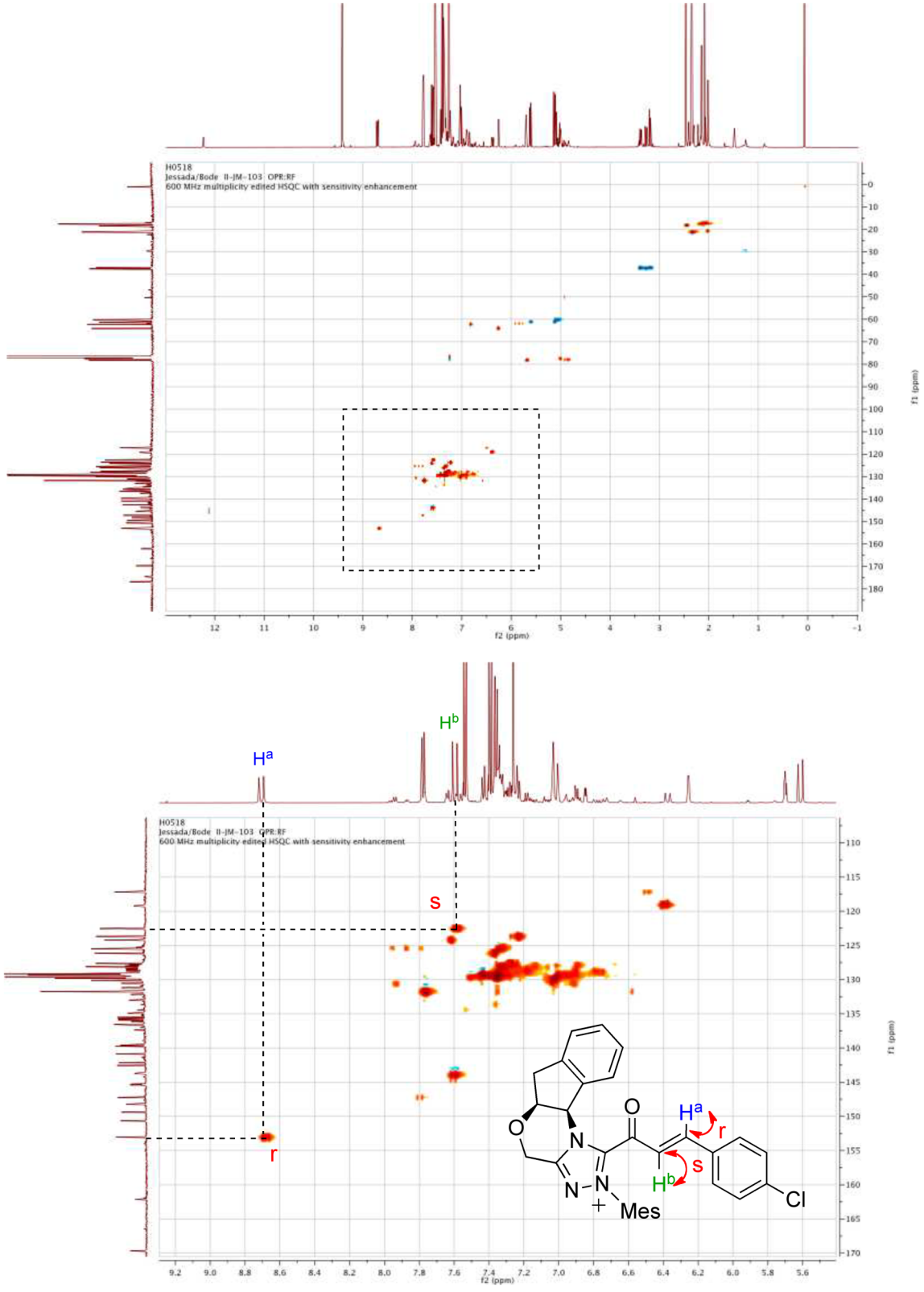
[1]H NMR Spectra for Catalytically Generated *α,β*-unsaturated Acyl Azolium **1**



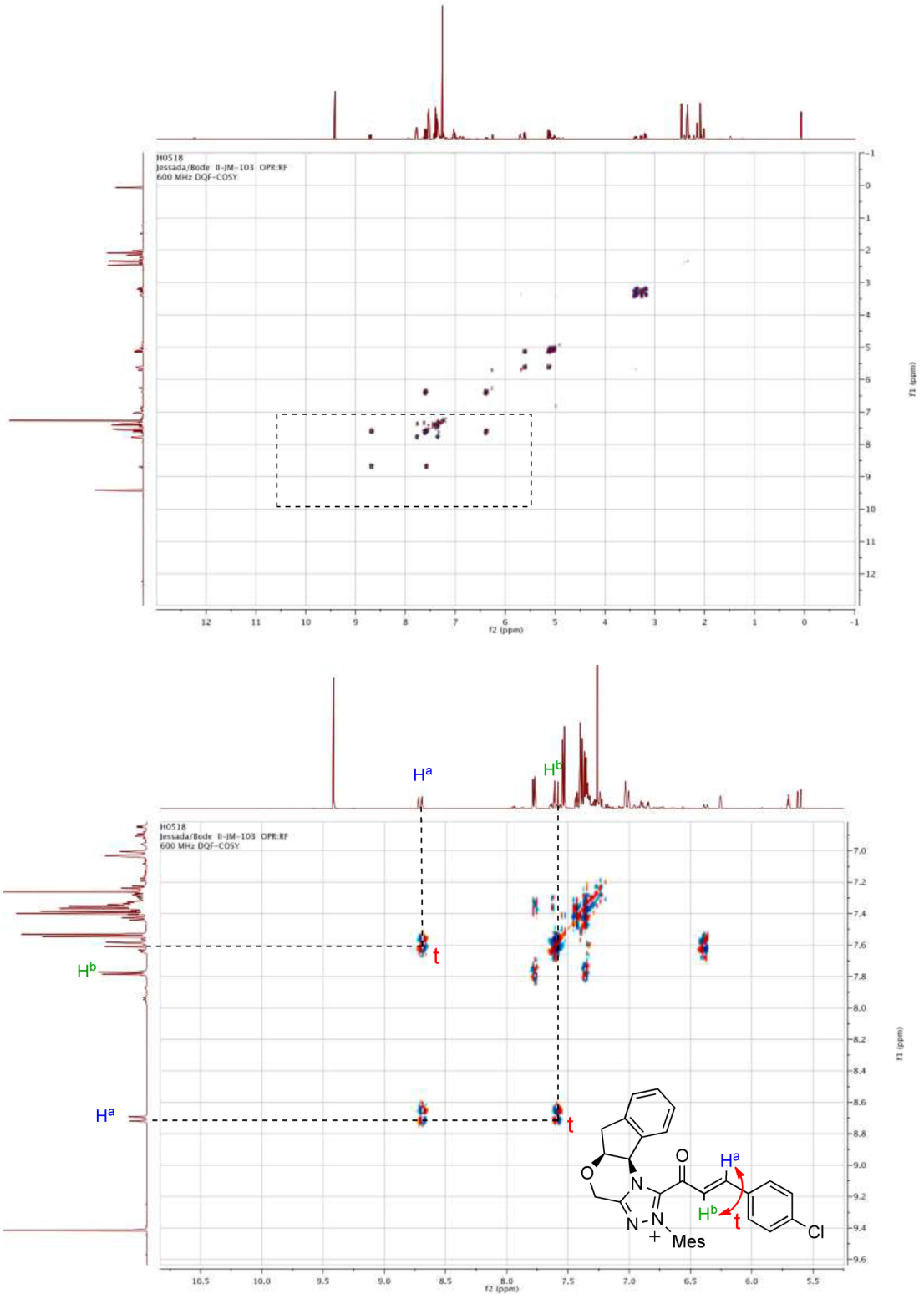
^{13}C NMR Spectra for Catalytically Generated α,β-unsaturated Acyl Azolium **1**



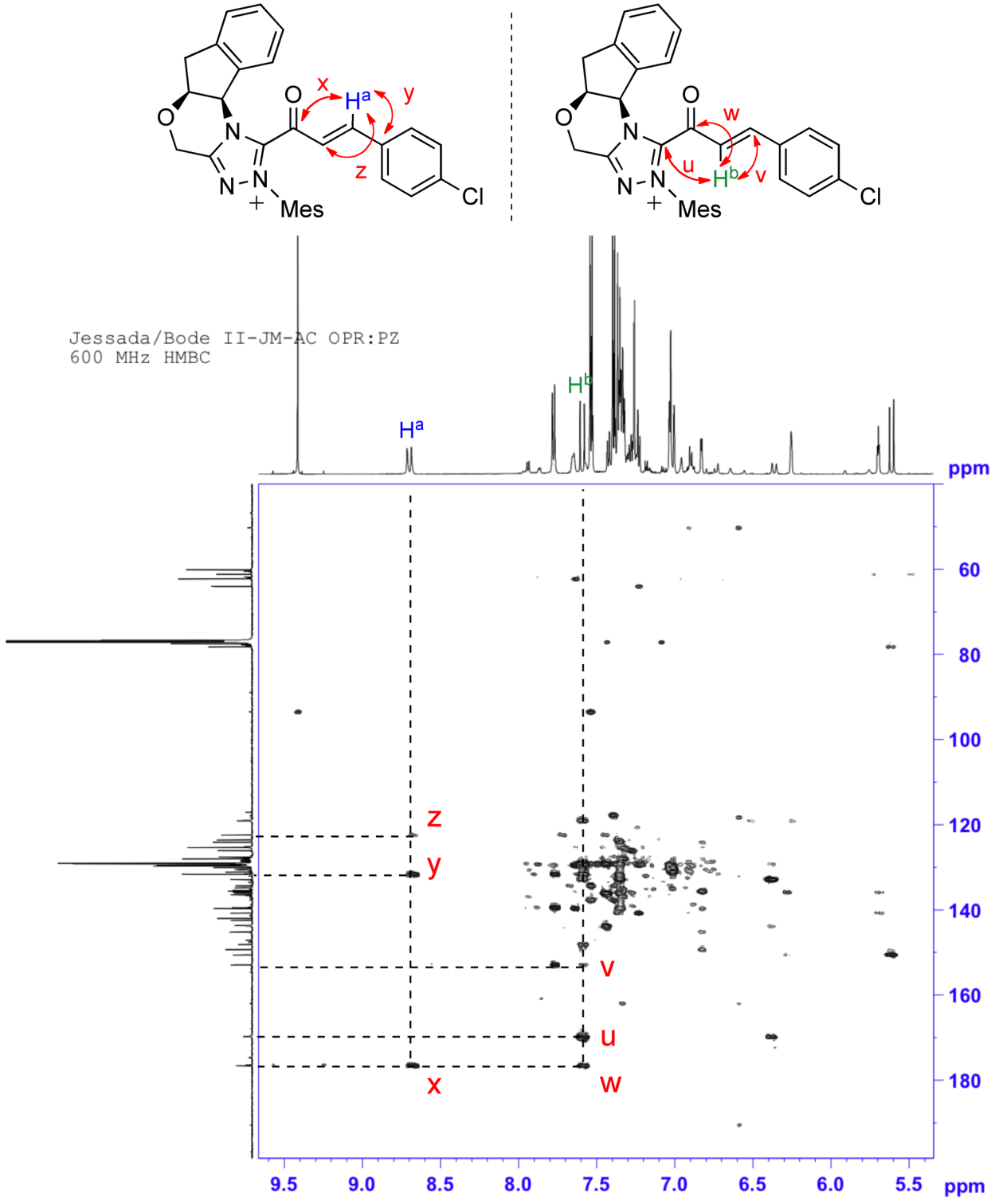
HSQC NMR spectra for Catalytically Generated *α,β*-unsaturated Acyl Azolium **1**



COSY NMR Assignment for Catalytically Generated *α,β*-unsaturated Acyl Azolium **1**

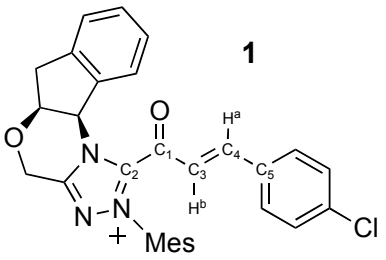


HMBC NMR Assignment for Catalytically Generated *α,β*-unsaturated Acyl Azolium **1**

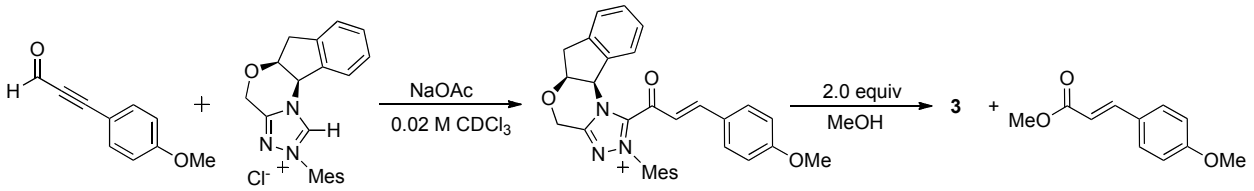


Summary of NMR Characterizations of *α,β*-unsaturated Acyl Azolium **1**

H/C	ppm	Experiment	Correlation
C_1	176.7	*HMBC*	H^a-C_1 (x) & H^b-C_1 (w)
C_2	169.9	*HMBC*	H^b-C_2 (u)
C_3	122.0	*HSQC&HMBC*	H^b-C_3 (s) & H^a-C_3 (z)
C_4	152.9	*HSQC&HMBC*	H^a-C_4 (r) & H^b-C_4 (v)
C_5	131.8	*HMBC*	H^a-C_5 (y)
H^a	8.7 (^1J = 18Hz)	*COSY*	H^a-H^b (t)
H^b	7.6 (^1J = 18Hz)	*COSY*	H^a-H^b (t)



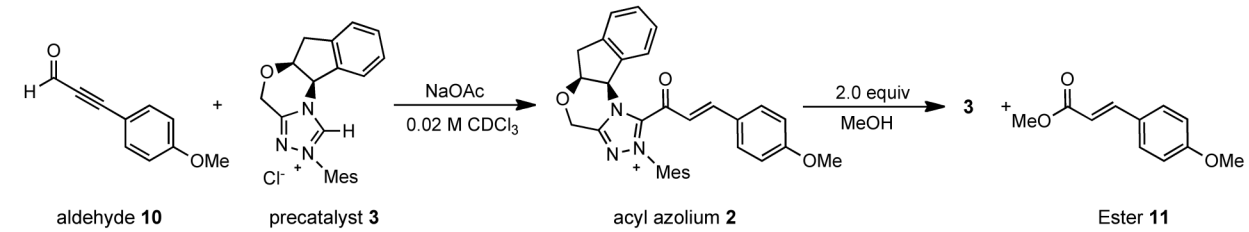
NMR Investigations of Catalytically Generated *α,β*-unsaturated Acyl Azoliums **2**



aldehyde **10** 1.0 equiv | precatalyst **3** 0.5 equiv | acyl azolium **2** | Ester **11**

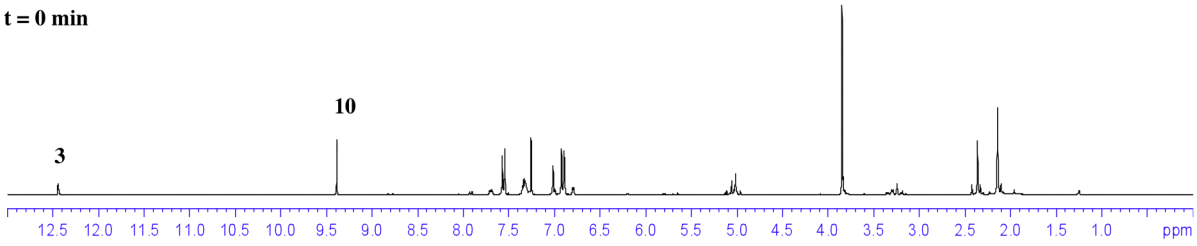
In oven-dried vials with Teflon-coated cap, 3-(4-methoxyphenyl) propiolaldehyde (**10**; 0.02 mmol; 1.0 equiv) and **3** (0.01 mmol; 0.5 equiv) were mixed, along with activated molecular sieves (4Å), and subjected to high vacuum drying for 15 mins. Then, the reaction mixture was dissolved in 0.5 mL $CDCl_3$. The solution was transferred to a dried NMR tube, followed by an addition of about 3 equiv of NaOAc. After about 10 mins, the reaction was subjected to ^{1}H NMR (VARIAN Mercury 300 MHz); a new doublet peak at 8.90 ppm, indicative of the corresponding *α,β-unsaturated* acyl azolium **2**, appeared. After an additional 30 mins, MeOH (0.02 mmol; 1.0 equiv) was added directly into the NMR tube. The observed acyl azolium intermediated was converted into the corresponding expected ester immediately, as indicated in the ^{1}H NMR. In a separate experiment, using the same procedure described previously, the observed acyl azolium was found to be stable up to one hour (ca.) in a sealed NMR tube. Although acyl azolium **2** was obtained in with a higher conversion than **1**, intermediate **2** was more prone to hydrolysis than the *p*-chloro counterpart. After leaving at room temperature for three hours, all of **2** reacted with trace amount of water to become *p*-methoxycinnamic acid.

^{1}H NMR Observation:



aldehyde **10** precatalyst **3** acyl azolium **2** Ester **11**

t = 0 min



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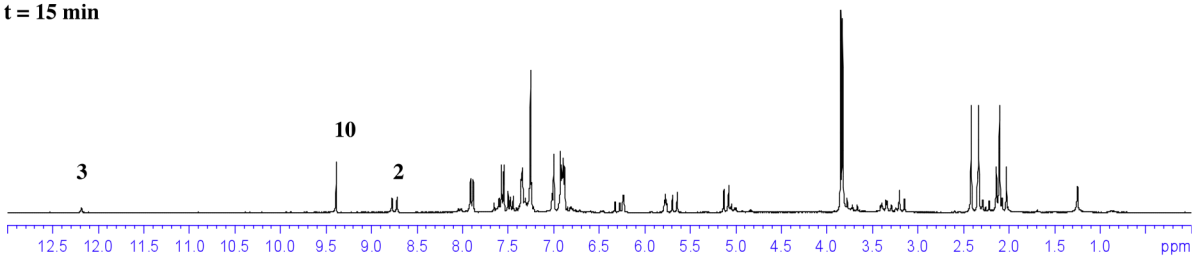
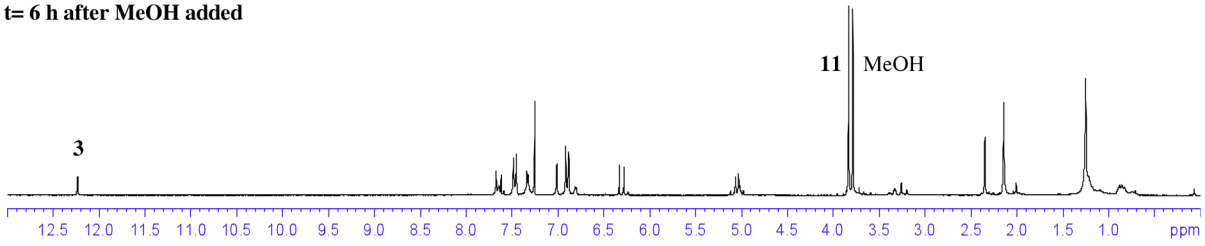
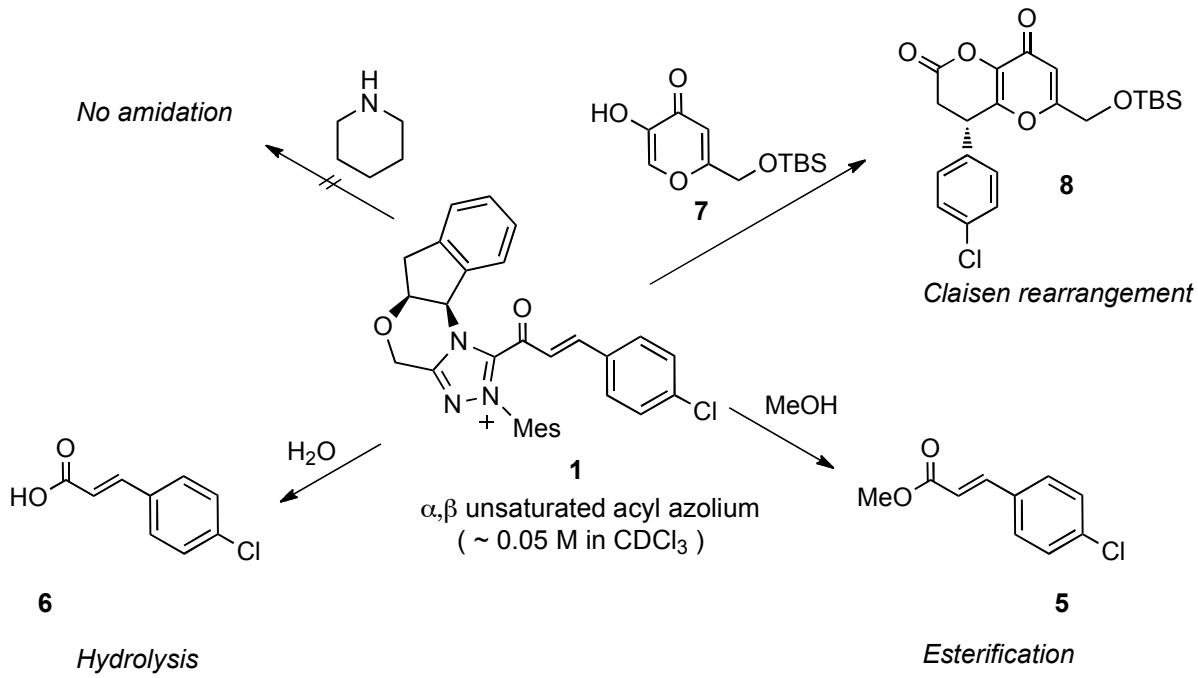


t= 6 h after MeOH added



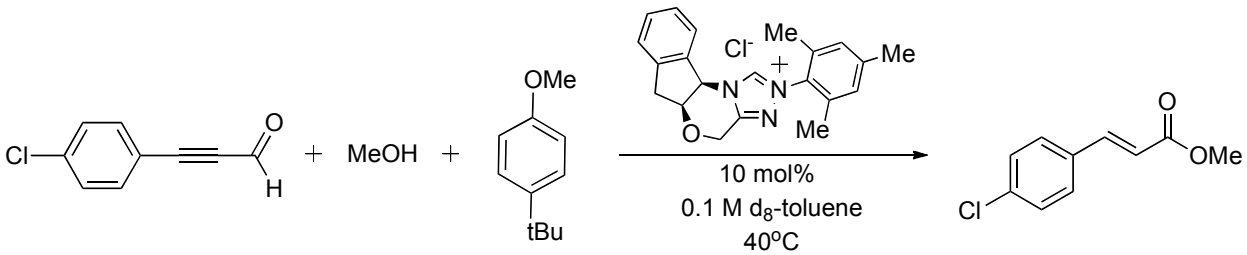
Reactions of an *α,β*-unsaturated Acyl Azolium with Various Nucleophiles



The reactivity of the *α,β*-unsaturated acyl azolium generated in pseudo-stoichiometric fashion was explored. The *α,β*-unsaturated acyl azolium **1** was generated as described in the previous section (*vide supra*) from 3-(4-chlorophenyl) propiolaldehyde (**4**; 0.02 mmol; 1.0 equiv) and **3** (0.02 mmol; 1.0 equiv) with NaOAc (ca. 3 equiv) in $CDCl_3$. After its formation was confirmed by ^1H NMR (with maximum conversion at ca. 30%), the acyl azolium **1** was subjected to an addition of 1.0 equiv of MeOH (in $CDCl_3$ solution), 1.0 equiv of H_2O (in $CDCl_3$ solution), 1.0 equiv of kojic acid derivative **7**, and piperidine, with each nucleophile added separately into four reactions. The acyl azolium **1** reacted instantaneously with water and MeOH to give the acid **6** or the ester **5** products accordingly. The addition of kojic acid derivative **7** afforded the annulation product[3] **8** somewhat more slowly. When **1** was treated with piperidine, only a complex, unidentifiable mixture was obtained. No amidation product was observed, and an attempt to separate this mixture proved unsuccessful due to decomposition.

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

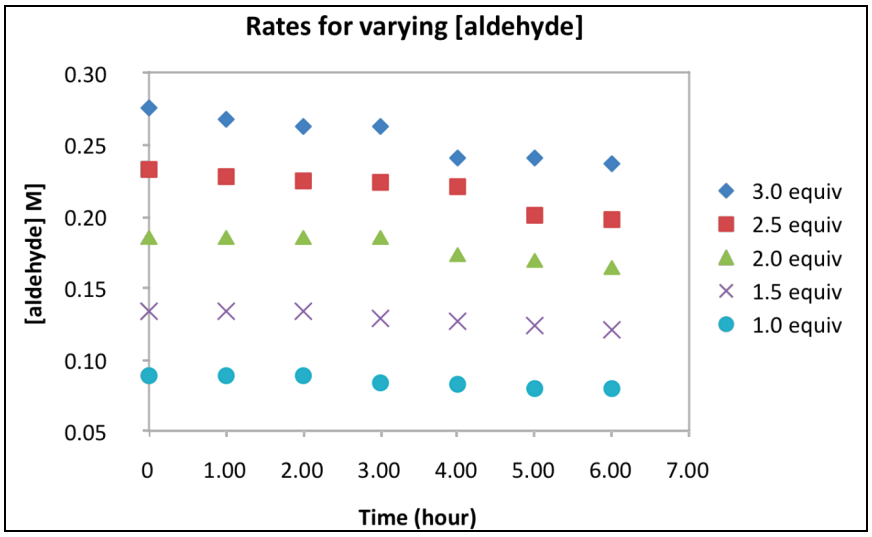
Experimental Rate Orders Measurements

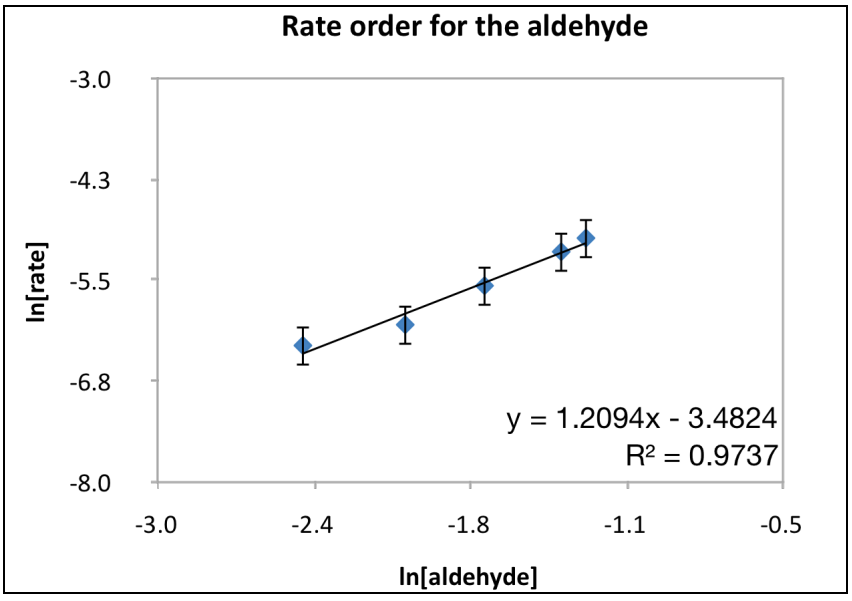


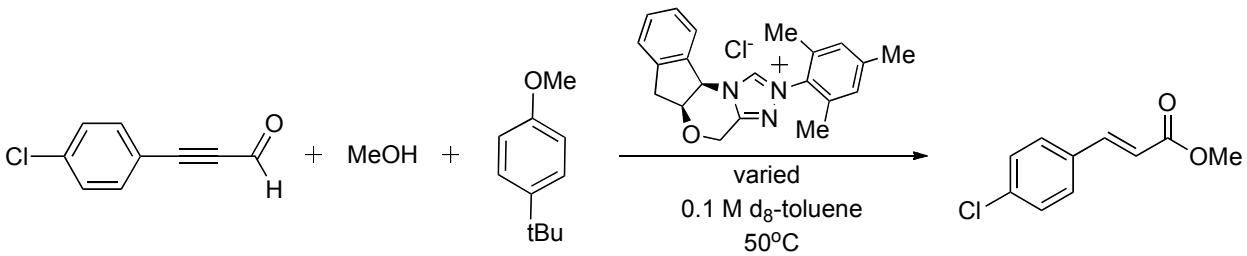
Rate order for aldehyde: A solution of 1-(tert-butyl)-4-methoxybenzene (0.25 mmol; 5.0 equiv as internal standard) and MeOH (0.25 mmol; 5.0 equiv) was prepared using 2.5 mL d_8-toluene (with 10% CD_2Cl_2 to ensure complete solubility). Precatalyst **3** (0.025 mmol; 0.5 equiv) was added to the solution. The final solution was quickly transferred to dried NMR tubes (0.5 mL of the final solution to each tube) containing varied amounts of 3-(4-chlorophenyl) propiolaldehyde **4**: 1.00, 1.50, 2.00, 2.50, and 3.00 equiv. The reactions were performed at 40°C; percentage conversions were measured using ^{1}H NMR (Bruker Avance II 500 MHz) by the disappearance of the ynal, from the integration of the peak at 8.85 ppm (1H)[4] against the internal standard peak at 1.22 ppm (9H). The plots of molar concentration of the ynal versus time (hour) were generated; the rates were determined from the slope of each plot. The rate order was calculated from the plot of ln(rate) against ln(aldehyde concentration) to be 1.29 ($R^2 = 0.97$). Below, the table reports raw data; the plots shows [aldehyde] vs. time, and the ln[rate] vs. ln[aldehyde].

	Aldehyde concentration for the reactions (varying aldehyde equiv).				
Time (h)	3.00 equiv.	2.50 equiv.	2.00 equiv.	1.50 equiv.	1.00 equiv.
0.00	0.2760	0.2330	0.1840	0.1340	0.0890
1.00	0.2680	0.2280	0.1840	0.1340	0.0890
2.00	0.2630	0.2250	0.1840	0.1340	0.0890
3.00	0.2630	0.2240	0.1840	0.1290	0.0840
4.00	0.2410	0.2210	0.1720	0.1270	0.0830
5.00	0.2410	0.2010	0.1680	0.1240	0.0800
6.00	0.2370	0.1980	0.1630	0.1210	0.0800
Rate [M/h]	**-6.89×10^{-3}**	**-5.82×10^{-3}**	**-3.82×10^{-3}**	**-2.36×10^{-3}**	**-1.82×10^{-3}**
R^2	**0.92**	**0.86**	**0.82**	**0.93**	**0.90**

(4) NMR monitoring of the reaction was performed with propiolaldehyde sublimed to pale-yellow solid. We observed very little rate discrepancy (*2.82–7.91% deviation*) between monitoring the aldehyde (RC**H**O), C**H**$_3$OH, or the product (OC**H**$_3$) NMR resonance. The result is reproducible over two separate runs (*1.6–2.62 % deviation)*.



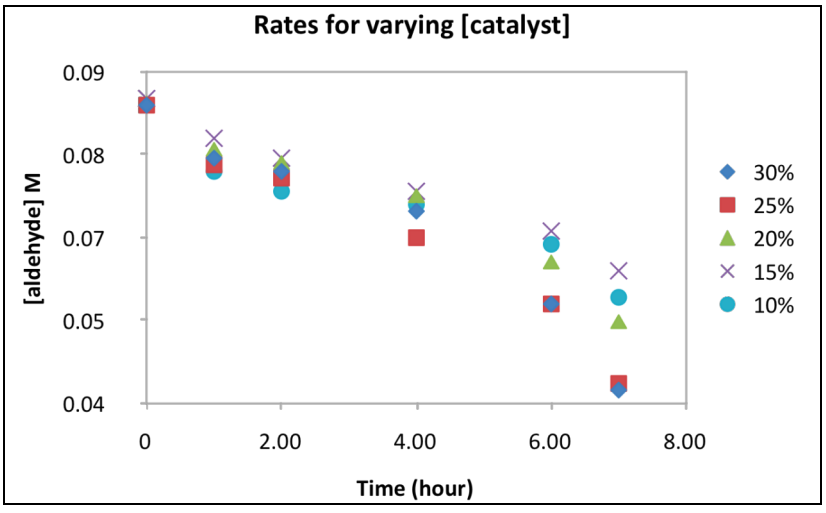


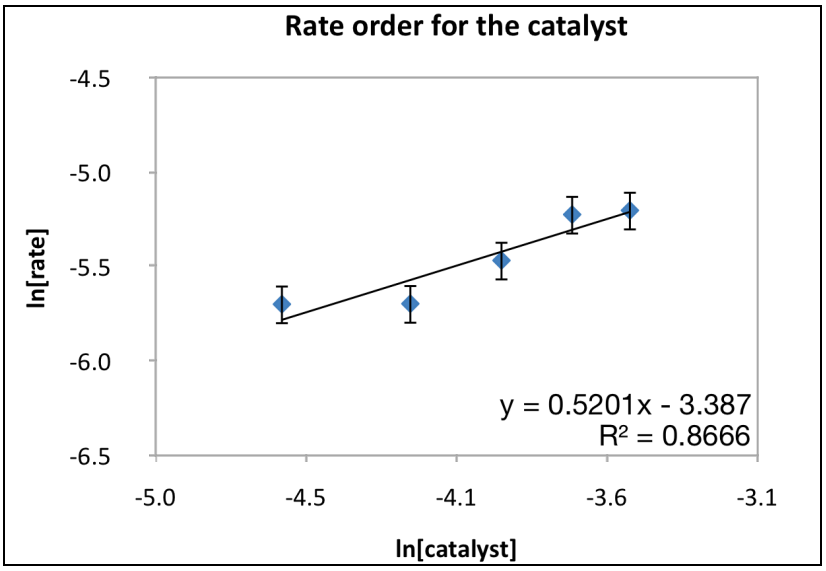


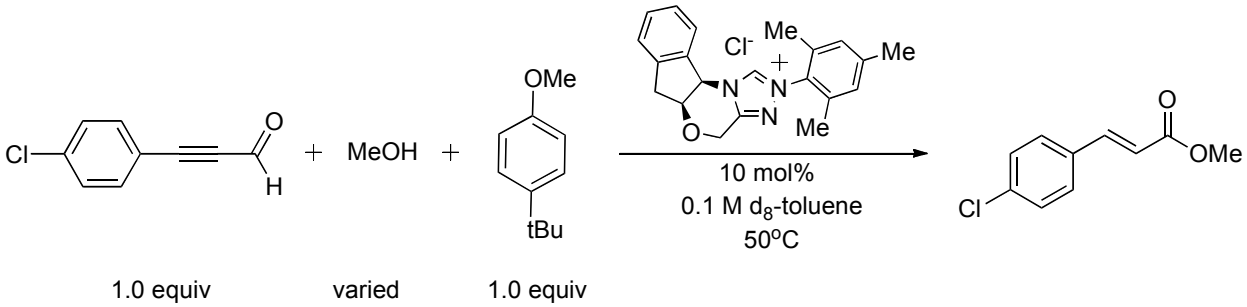
1.0 equiv 1.0 equiv 1.0 equiv

Rate order for the precatalyst: A solution of MeOH (0.25 mmol; 5.0 equiv), 3-(4-chlorophenyl) propiolaldehyde **4** (0.25 mmol; 5.0 equiv), and 1-(tert-butyl)-4-methoxybenzene (0.25 mmol; 5.0 equiv as internal standard) was prepared using 2.5 mL d_8-toluene (with 10% CD_2Cl_2). The final solution was quickly transferred to dried NMR tubes (0.5 mL of the final solution to each tube) containing varied amounts of precatalyst **3**: 0.10, 0.15, 0.20, 0.25, and 0.30 equiv. The reactions were performed at 50°C, the percentage conversions were measured, and the plots were generated as described above. The rate order was calculated from the plot of ln(rate) against ln(precatalyst concentration) to be 0.52 (R^2 = 0.87). Below, the table reports raw data; the plots shows [aldehyde] vs. time, and the ln[rate] vs. ln[precatalyst].

	Aldehyde concentration for the reactions (varying precatalyst concentration)				
Time (h)	30% precat.	25% precat.	20% precat.	15% precat.	10% precat.
0.00	0.0850	0.0850	0.0850	0.0860	0.0850
1.00	0.0770	0.0760	0.0780	0.0800	0.0750
2.00	0.0750	0.0740	0.0760	0.0770	0.0720
4.00	0.0690	0.0650	0.0710	0.0720	0.0700
6.00	0.0550	0.0550	0.0610	0.0660	0.0640
7.00	0.0420	0.0430	0.0520	0.0600	0.0560
Rate [M/h]	**-5.50×10^{-3}**	**-5.38×10^{-3}**	**-4.22×10^{-3}**	**-3.36×10^{-3}**	**-3.35×10^{-3}**
R^2	**0.94**	**0.97**	**0.96**	**0.98**	**0.91**

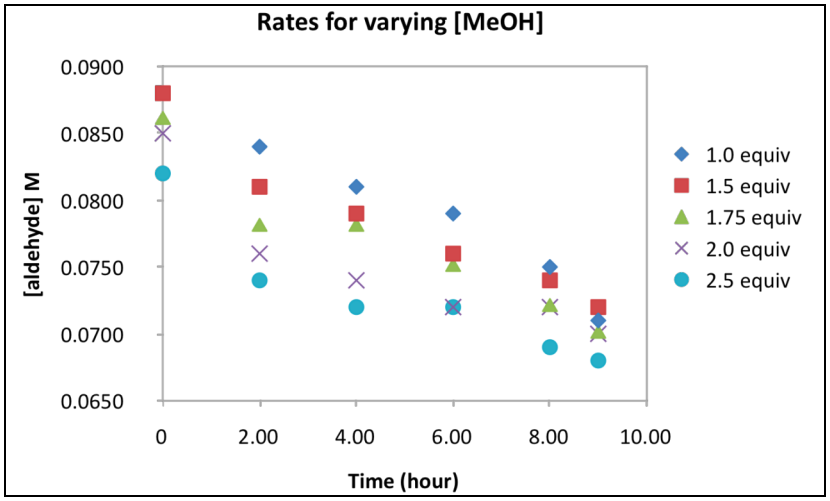


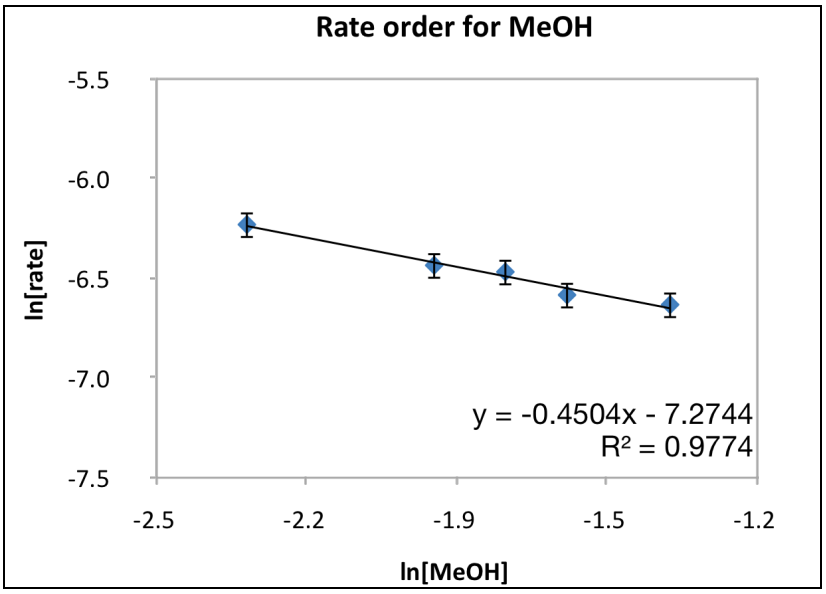




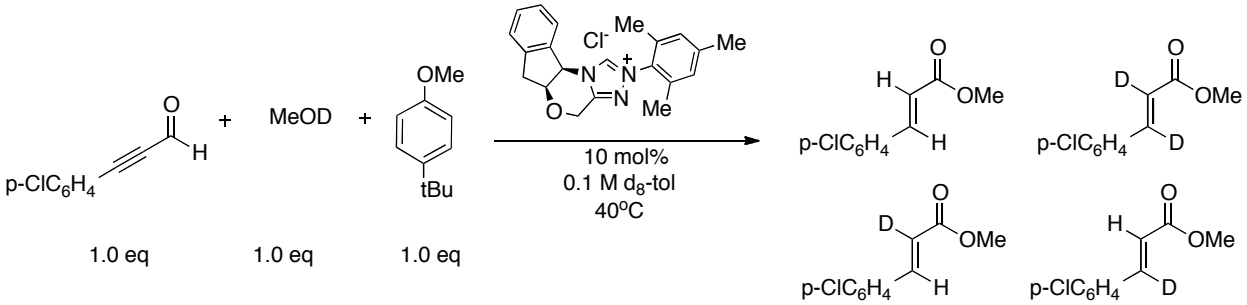
Rate order for MeOH: A solution of the precatalyst (**3,** 0.025 mmol, 0.5 equiv), 1-(tert-butyl)-4-methoxybenzene (0.25 mmol, 5.0 equiv as internal standard), and 3-(4-chlorophenyl) propiolaldehyde (**4**; 0.25 mmol, 5.0 equiv as internal standard) was prepared using d_8-toluene (with 10% CD_2Cl_2). The final solution was then quickly transferred to dried NMR tubes and mixed with varying MeOH the concentration: 1.00, 1.50, 1.75, 2.00, and 2.50 equiv. The reactions were performed at 50°C, the percentage conversions were measured, and the plots were generated as described above. The rate order was calculated from the plot of ln(rate) against ln[MeOH] to be -0.45 ($R^2 = 0.98$). Below, the table reports raw data; the plots shows [aldehyde] vs. time, and the ln[rate] vs. ln[MeOH].

Time (h)	Aldehyde concentration for the reactions (varying MeOH concentration)				
	1.00 equiv	1.50 equiv	1.75 equiv	2.00 equiv	2.50 equiv
0.00	0.0910	0.0880	0.0860	0.0850	0.0820
2.00	0.0840	0.0810	0.0780	0.0760	0.0740
4.00	0.0810	0.0790	0.0780	0.0740	0.0720
6.00	0.0790	0.0760	0.0750	0.0720	0.0720
8.00	0.0750	0.0740	0.0720	0.0720	0.0690
9.00	0.0710	0.0720	0.0700	0.0700	0.0680
Rate [M/h]	**-1.97×10^{-3}**	**-1.61×10^{-3}**	**-1.55×10^{-3}**	**-1.38×10^{-3}**	**-1.32×10^{-3}**
R^2	**0.96**	**0.95**	**0.92**	**0.80**	**0.85**



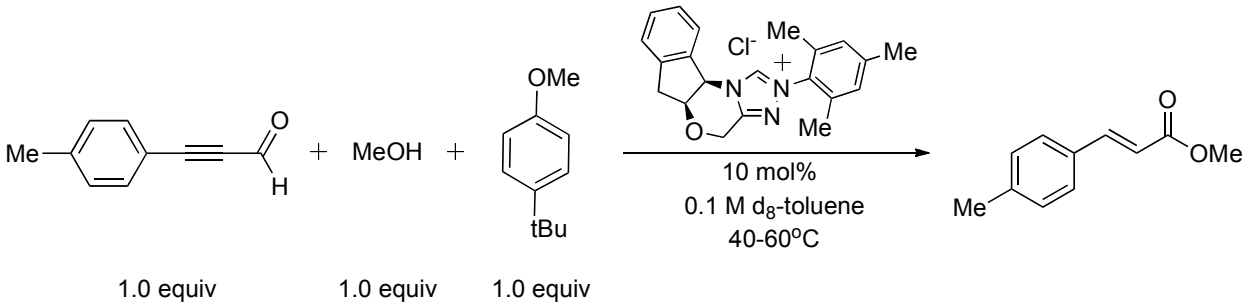


Isotopic Labeling Experiment



A solution of 3-(4-chlorophenyl) propiolaldehyde (0.05 mmol; 1.0 equiv), 1-(tert-butyl)-4-methoxybenzene (0.05 mmol; 1.0 equiv as internal standard), CH_3OD (0.05 mmol; 1.0 equiv), and precatalyst **3** (0.005 mmol; 0.1 equiv) was prepared using 0.5 mL d_8-toluene (with 10% CD_2Cl_2 to ensure complete solubility). The final solution was quickly transferred to a dried NMR tube. The reaction was performed at 40°C overnight. After the reaction completed, the final mixture was analyzed using ^{1}H NMR (Bruker Avance II 500 MHz) based on the doublets integration against the internal standard peak at 1.22 ppm (9H). The final product was a mixture of four esters as a result of deuterium scrambling, which suggested no kinetic isotope effect (KIE). This result excluded protonation as a potential rate-determining step as large kinetic isotope effect has been observed when protonation is rate-limiting.[5]

Activation Parameters Measurement and Analysis

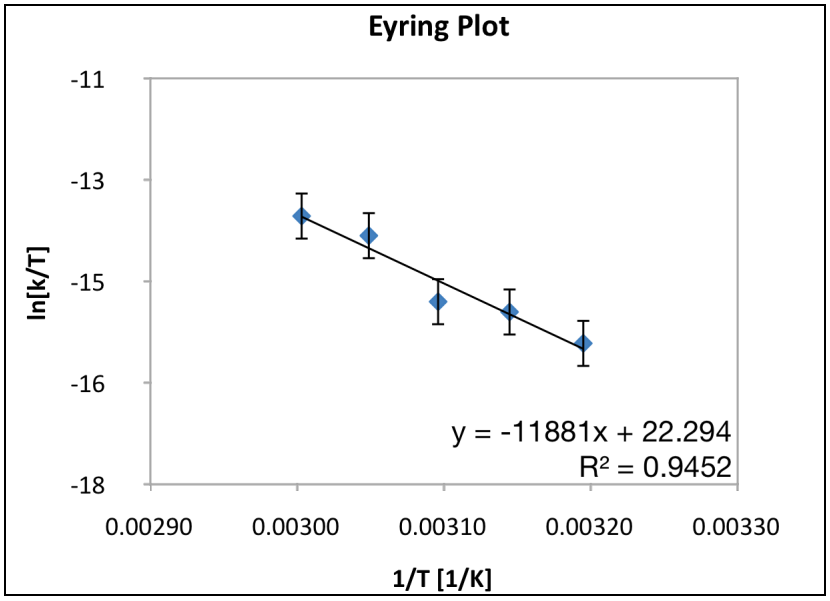


A solution of MeOH (0.25 mmol; 5.0 equiv), 3-(4-methylphenyl)propiolaldehyde (0.25 mmol; 5.0 equiv), and 1-(tert-butyl)-4-methoxybenzene (0.25 mmol; 5.0 equivas internal

(5) For example, see (a) D. S. Noyce, R. M. Pollack, *J. Am. Chem. Soc.* **1969**, *91*, 119–124. (b) K.-Y. Wong, J. P. Richard, J. Gao, *J. Am. Chem. Soc.* **2009**, *131*, 13963–13971.

standard) was prepared using d_8-toluene (with 10% CD_2Cl_2 to ensure complete solubility). When the NMR probe was calibrated at the required temperature, 0.5 mL of the prepared solution was subjected to an addition of **3** (0.005 mmol, 0.1 equiv). The reactions were performed in NMR sealed tubes and placed in the preheated NMR instrument (Bruker Avance II 500 MHz): temperature at 40, 45, 50, 55, and 60°C. Percentage conversions were measured using ^{1}H NMR by the disappearance of the ynal, from the integration of the peak at 8.90 ppm (1H) against the internal standard peak at 1.22 ppm (9H).

The plots of molar concentration of the ynal versus time (hour) were generated; the rates were determined from the slope of each plot. The rate constants (k_{obs}) were calculated from the experimentally determined rate law (1). The plot of ln(k/T) vs 1/T (in K) was then generated (Eyring Plot below). Using the Eyring equation (2), the activation enthalpy ($\Delta H^{\ddagger}$) was calculated from the slope to be +23.60 Kcal/mol, while the entropy of activation ($\Delta S^{\ddagger}$) was calculated from the y-intercept to be -2.91 cal/K.mol.[6] The table below reports raw data; the plot below shows ln(k/T) vs 1/T.



Rate = k_{obs} [ynal]^1 [precatalyst **3**]$^{0.5}$ [MeOH]$^{-0.5}$ (1)

$ln(k/T) = -(\Delta H^{\ddagger}/RT) + (\Delta S^{\ddagger}/R) + ln(k_B/h)$ (2)

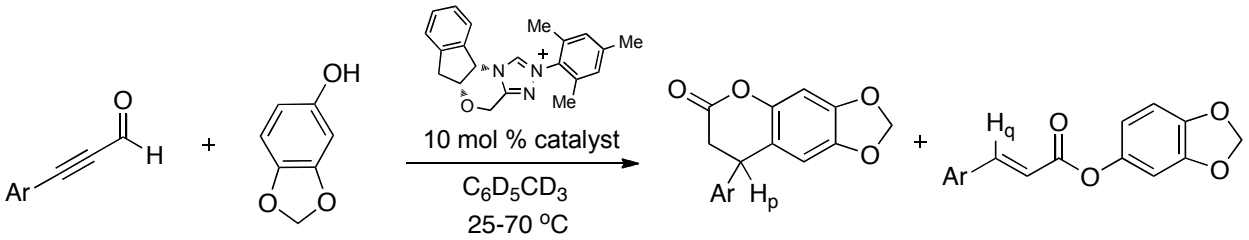
where R = the gas constant; k_B = Boltzmann constant; and h = Planck's constant.

(6) The observed non-integral rate orders may be attributed to an inhibition event. The rationalization of the observed rate law is discussed in the rate law derivation (page S29). From the derivation, the rate law may be refomulated as: rate = k_{obs}[ynal]^1[precatalyst **3**]^1 [MeOH]^0. This reformulation changes the activation entropy for the redox esterification reaction to +3.95 cal/K•mol while the activation enthalpy remains unchanged. In any case, the change in $\Delta S^{\ddagger}$ does not affect the interpretation of the proposed mechanism.

time(sec)	Aldehyde concentration for the reactions (varying temperatures) 333 K	328 K	323 K	318 K	313 K
0	0.0960	0.0911	0.0968	0.0966	0.0968
300	0.0931	0.0899	0.0962	0.0948	0.0955
600	0.0899	0.0869	0.0945	0.0942	0.0950
900	0.0852	0.0836	0.0936	0.0933	0.0948
1200	0.0801	0.0806	0.0933	0.0925	0.0941
1500	0.0751	0.0768	0.0918	0.0918	0.0938
1800	0.0693	0.0724	0.0906	0.0908	0.0933
2100	0.0646	0.0690	0.0896	0.0900	0.0926
2400	0.0581	0.0644	0.0883	0.0893	0.0921
2700	0.0531	0.0618	0.0869	0.0877	0.0919
Rate [M/sec]	**-1.64×10^{-5}**	**-1.15×10^{-5}**	**-3.62×10^{-6}**	**-2.99×10^{-6}**	**-1.71×10^{-6}**
R^2	**0.99**	**0.99**	**0.99**	**0.99**	**0.98**
k_{obs} [sec^{-1}]	**5.18×10^{-4}**	**3.64×10^{-4}**	**1.15×10^{-4}**	**9.45×10^{-5}**	**5.41×10^{-5}**

ln(k/T)	1/T (K^{-1})	Constants		Parameters	
-13.37	3.003×10^{-3}	R(cal/Kmol)	1.986	slope	-11881.10
-13.71	3.049×10^{-3}	k_B (m^2kg s^{-2} K^{-1})	1.38×10^{-23}	R^2	0.95
-14.85	3.096×10^{-3}	h (m^2 kg s^{-1})	6.63×10^{-34}	y-intercept	22.29
-15.03	3.145×10^{-3}	$\Delta H^{\ddagger}$ = +23.60 (Kcal/mol)			
-15.57	3.195×10^{-3}	$\Delta S^{\ddagger}$ = -2.91 (cal/mol.K)			

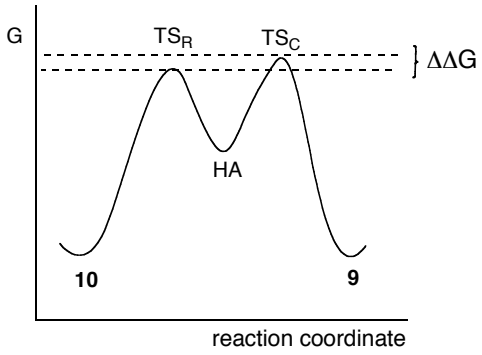
Differential Activation Parameters Measurement and Analysis



1.0 equiv 1.0 equiv **Ar = p-OMeC_6H_4** Claisen **9** Redox **10**

A solution of MeOH (0.25 mmol; 5.0 equiv), 3-(4-methylphenyl)propiolaldehyde (0.25 mmol; 5.0 equiv), 1-(tert-butyl)-4-methoxybenzene (0.25 mmol; 5.0 equivas internal standard), and (5a*R*,10b*S*)-5a,10b-dihydro-2-(2,4,6-trimethylphenyl)-4*H*,6*H*-indeno[2,1-*b*]-1,2,4-triazolo [4,3-*d*]-1,4-oxazinium chloride monohydrate (0.025 mmol, 0.5 equiv) was prepared using d_8-toluene (with 10% CD_2Cl_2 to ensure complete solubility). Five 0.5 mL portions of the final solution were placed in five NMR sealed tubes and placed in oil bath at various temperature: 25,

35, 45, 60, and 70°C. The relative percentage product ratio between the Claisen product **9**[7] and redox product **10** (see below for characterization data) was analyzed based on ^{1}H NMR (VARIAN Mercury 300 MHz at ETHZ) integration of the internal standard peak at 1.22 ppm (9H) against an indicative proton peak of H_p of **9** at 4.75 ppm and an indicative unsaturated proton peak of H_p of **10** at 7.86-7.91 ppm (^1J = 15 Hz). The relative rate constants (k_{rel}) at each temperature were calculated from the ratio of **10**/**9** (see Equation 3) for all five temperatures. The plot of ln(k_{rel}) vs 1/T (in K) was generated (Eyring method[8]). Using the Eyring equation (below), the difference in the activation enthalpy between the Claisen and the redox pathways ($\Delta\Delta H^{\ddagger}$) was calculated from the slope to be +7.61 Kcal/mol, while the differential entropy of activation ($\Delta\Delta S^{\ddagger}$) was calculated from the y-intercept to be 26.62 cal/K.mol (see detailed data below).

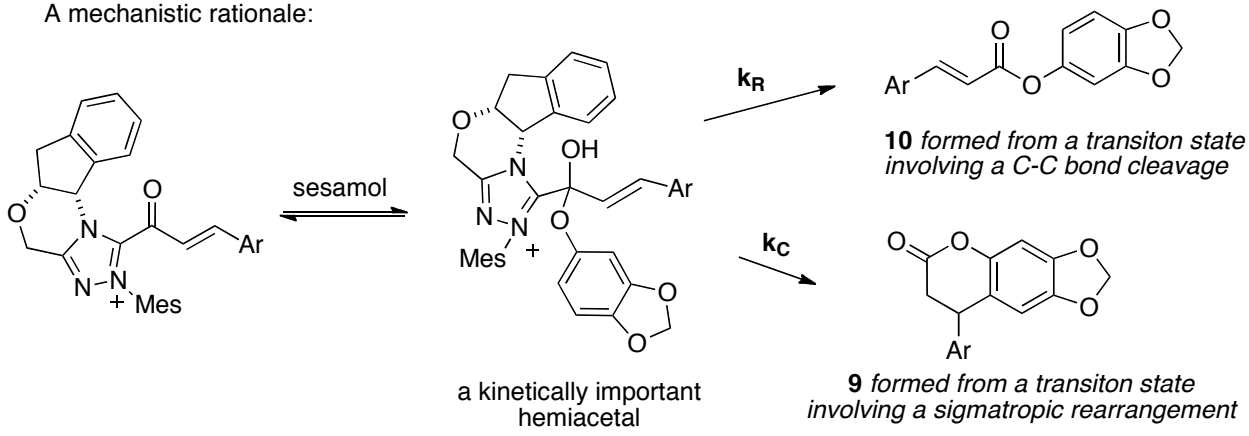


$$\ln\frac{\kappa_S k_R}{\kappa_R k_C} = \frac{-\Delta\Delta H^{\ddagger}}{RT} + \frac{\Delta\Delta S^{\ddagger}}{R} \qquad (\Delta\Delta G^{\ddagger} = \Delta\Delta H^{\ddagger} - T\Delta\Delta S^{\ddagger})$$

(κ = transmission coefficient ~ 1)

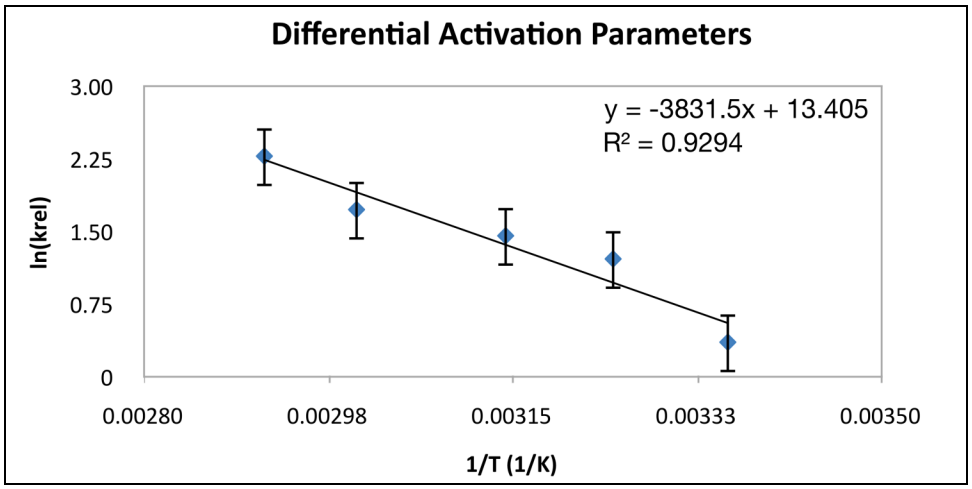
$$k_{rel} = \frac{k_R}{k_C} = \frac{\%\ \mathbf{10}}{\%\ \mathbf{9}} \qquad (3)$$

A mechanistic rationale:



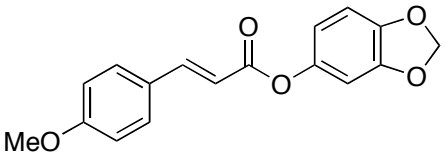
(7) NMR characterizations of compound **9** (both in d_8-toluene and in $CDCl_3$) were in good agreement with the reported values in literature: a) C. Jia, D. Piao, T. Kitamura, Y. Fujiwara, *J. Org. Chem*. **2000**, *65*, 7516–7522; b) S. Aoki, C. Amamoto, J. Oyamada, T. Kitamura, *Tetrahedron* **2005**, *61*, 9291–9297.

(8) For a similar approach to the measurements of the difference in the activation parameters between two competing pathways, see M. Nigam, M. S. Platz, B. M. Showalter, J. P. Toscano, R. Johnson, S. C. Abbot, M. M. Kirchhoff, *J. Am. Chem. Soc.* **1998**, *120*, 8055–8059.



T (K)	T (K)	% **9**	% **10**	k_{rel} **(10/9)**	$\Delta\Delta G^{\ddagger}$ **kcal/mol**
25	298.15	14	20	1.429	**-0.33**
35	308.15	16	54	3.375	**-0.59**
45	318.15	14	60	4.286	**-0.86**
60	333.15	13	73	5.615	**-1.26**
70	343.15	8	78	9.750	**-1.53**
$\ln(k_{rel})$	1/T (K^{-1})	slope	*-3831.52*	y intercept	13.41
0.36	$3.354x10^{-3}$	R^2	*0.93*	$\Delta\Delta S^{\ddagger}$ = *(y intercept x R)*	
1.22	$3.245x10^{-3}$	*R(cal/Kmol)*	*1.986*	$\Delta\Delta$**S**‡	**+26.62**
1.46	$3.143x10^{-3}$	$\Delta\Delta H^{\ddagger}$ = *(-slope x R)*		**cal/mol.K**	
1.73	$3.002x10^{-3}$	$\Delta\Delta$**H**‡	**+7.61**		
2.28	$2.914x10^{-3}$	**(kcal/mol)**			

Characterization of Compound **10**[9]

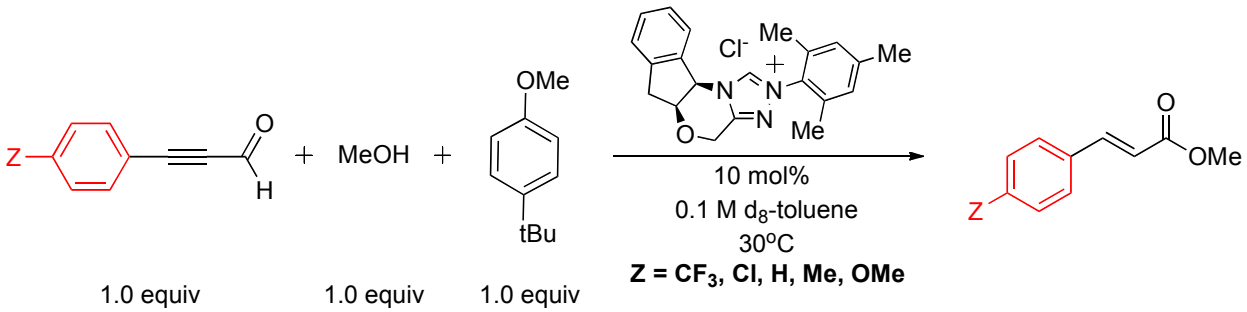


(*E*)-benzo[*d*][1,3]dioxol-5-yl 3-(4-methoxyphenyl)acrylate. ^{1}H NMR (Bruker 400 MHz at ETHZ, $CDCl_3$) δ 7.85–7.81 (d, 16Hz, 1H), 7.79-7.76 (m, 2H), 6.97–6.95 (m, 2H), 6.83–6.81 (m, 1H), 6.71 (s, 1H), 6.63–6.61 (m, 1H), 6.51–6.47 (d, 16Hz, 1H), 6.02 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.04, 161.76, 148.00, 146.31 (2C), 145.27 (2C), 145.23, 130.04 (2C), 126.92, 114.51–114.45 (2C), 114.03, 107.99, 103.90, 101.67, 55.42; IR (thin film)

(9) Compound **10** (CAS: 26790-32-6) was originally reported in C. Jia, D. Piao, J. Oyamada, W. Lu, T. Kitamura, Y. Fujiwara, *Science* **2000**, *287*, 1992–1995, but no spectroscopic information was given.

ν 1718.26, 1604.48, 1489.74, 1251.58, 1150.33, 1093.44, 1030.77, 990.27, 926.63, 842.74, 821.53, 780.07 cm^{-1}; HRMS (ESI) $[M+H]^+$ calcd. for $C_{17}H_{15}O_5$, 299.0914 found, 299.0906.

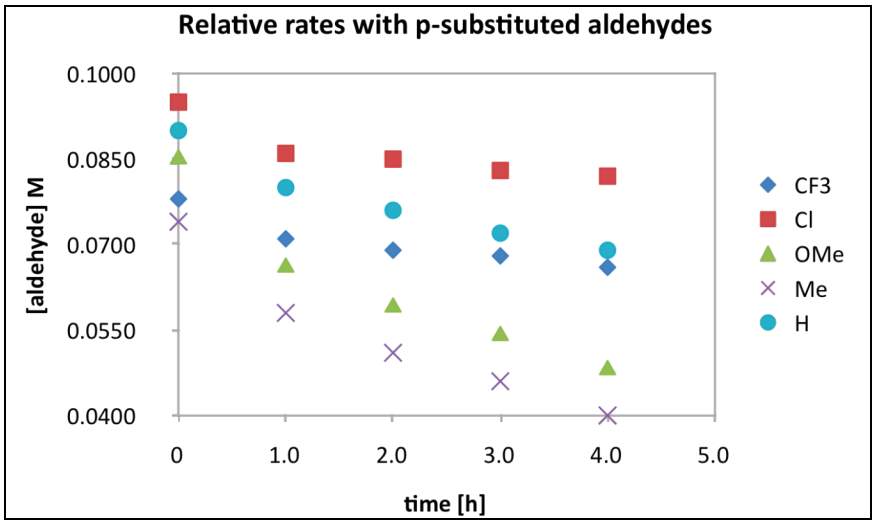
Linear Free-Energy Relationship (Hammett) Study: *p*-Substituted Ynal

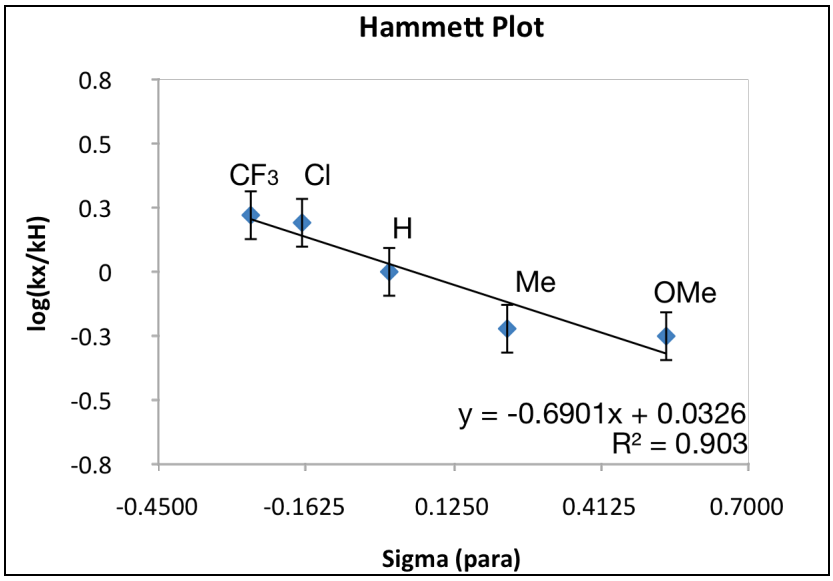


A solution of MeOH (0.25 mmol; 5.0 equiv), 1-(tert-butyl)-4-methoxybenzene (0.25 mmol; 5.0 equiv as internal standard), **3** (0.025 mmol; 0.5 equiv) was prepared using d_8-toluene (with 10% CD_2Cl_2 to ensure complete solubility). The final solution was quickly transferred to pre-dried NMR tubes containing various 3-(*para*-substituted-phenyl) propiolaldehyde: CF_3, Cl, H, Me, and OMe. The reactions were performed at 30°C; percentage conversions were measured using ^1H NMR (Bruker Avance II 500 MHz) by the disappearance of the ynal from integration of the peak at 8-9 ppm (1H) against the internal standard peak at 1.22 ppm (9H). The plots of molar concentration of the ynal versus time (hour) were generated; the rates were determined from the slope of each plot. The rate constants (k_{obs}) were calculated from the experimentally determined rate law (1). The plot of $\log(k_X/k_H)$ vs σ_p[10] (Hammett Plot) was then generated. The ρ value was determined from the slope of the Hammett Plot to be -0.69 ($R^2 = 0.90$).

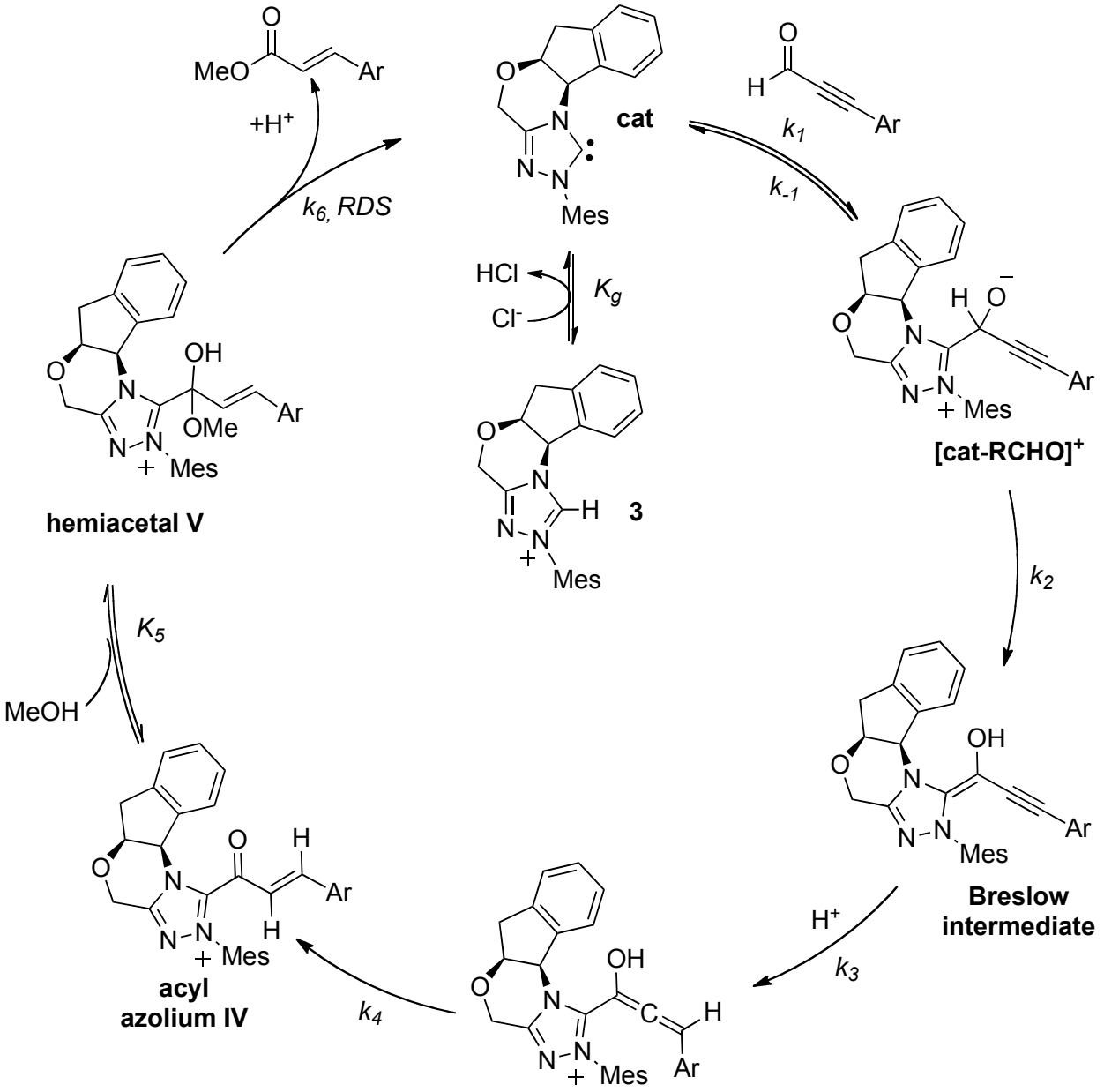
	Aldehyde concentration for the reactions (varying the *para*-subtitution)				
time(h)	**CF_3**	**Cl**	**OMe**	**Me**	**H**
0	0.0780	0.091	0.085	0.074	0.09
1	0.0710	0.086	0.066	0.058	0.08
2	0.0690	0.085	0.059	0.051	0.076
3	0.0680	0.084	0.054	0.046	0.072
4	0.0660	0.084	0.048	0.04	0.069
Rate [M/h]	-2.70×10^{-3}	-2.90×10^{-3}	-8.60×10^{-3}	-8.00×10^{-3}	-5.00×10^{-3}
R^2	0.86	0.79	0.91	0.93	0.94
k_{obs}	8.54×10^{-2}	9.17×10^{-2}	2.72×10^{-1}	2.53×10^{-1}	1.58×10^{-1}
$\log(k_X/k_H)$	-0.268	-0.237	0.236	0.204	0.000
σ_p	0.54	0.23	-0.27	-0.17	0

(10) C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195.


Relative rates with p-substituted aldehydes
0.1000
0.0850
0.0700
0.0550
0.0400
[aldehyde] M
0
1.0
2.0
3.0
4.0
5.0
time [h]
CF3
Cl
OMe
Me
H


Hammett Plot
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
log(kx/kH)
CF3
Cl
H
Me
OMe
y = -0.6901x + 0.0326
R² = 0.903
-0.4500
-0.1625
0.1250
0.4125
0.7000
Sigma (para)

Derivation of rate law for redox esterification



The unimolecular collapse of the hemiacetal intermediate is proposed to be the rate-determining step. Assuming steps 1-4 are either reversible or fast and irreversible, that is $[\text{cat} - \text{RCHO}^+] \approx$ [acyl azolium IV], the overall rate is defined as:

$$\frac{d[P]}{dt} = k_6[hemiacetal]$$

The equilibrium constant (K_g) for the generation of the active catalyst is defined as:

$$K_g = \frac{[cat][HX]}{[precat^+][X^-]} \quad \text{or} \quad [precat^+] = \frac{1}{K_g}\frac{[cat][HX]}{[X^-]} \qquad \text{eq 1.}$$

The overall catalyst concentration is defined as:

$$[cat]_0 = [cat] + [precat^+] + [cat - RCHO^+] \qquad \text{eq 2.}$$

Substitute eq. 1 into eq. 2 to obtain:

$$[cat]_0 = [cat] + \frac{1}{K_g}\frac{[cat][HX]}{[X^-]} + [cat - RCHO^+] \quad \text{or} \quad (1 + \frac{1}{K_g}\frac{[HX]}{[X^-]})[cat] = [cat]_0 - [cat - RCHO^+]$$

$$[cat] = \frac{[cat]_0 - [cat - RCHO^+]}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}} \qquad \text{eq 3.}$$

The rate of the catalyst-aldehyde complex can be expressed by:

$$\frac{d[cat - RCHO^+]}{dt} = k_1[cat][RCHO] - k_{-1}[cat - RCHO^+] - k_2[cat - RCHO^+] \qquad \text{eq 4.}$$

Assumption 1: The concentration of catalyst-aldehyde complex does not change over time (steady state approximation); thus,

$$\frac{d[cat - RCHO^+]}{dt} = k_1[cat][RCHO] - k_{-1}[cat - RCHO^+] - k_2[cat - RCHO^+] = 0 \qquad \text{eq 5.}$$

Substitute eq. 3 into eq. 5 to obtain:

$$k_1\frac{[cat]_0 - [cat - RCHO^+]}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}}[RCHO] - k_{-1}[cat - RCHO^+] - k_2[cat - RCHO^+] = 0$$

$$\frac{k_1}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}}[cat]_0[RCHO] = (k_{-1} + k_2 + \frac{k_1}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}}[RCHO])[cat - RCHO^+]$$

$$[cat - RCHO^+] = \frac{\frac{k_1}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}}[cat]_0[RCHO]}{k_{-1} + k_2 + \frac{k_1}{1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}}[RCHO]}$$

$$[cat - RCHO^+] = \frac{[cat]_0[RCHO]}{[RCHO] + \frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[HX]}{[X^-]})} \quad \text{eq 6.}$$

Assuming that the collapse of the hemiacetal intermediate is the rate-determining step; thus,

$$\frac{d[P]}{dt} = k_6[hemiacetal] \quad \text{eq 7.}$$

The equilibrium between the acyl azolium IV and the kinetically important hemiacetal V can be written as:

$$K_5 = \frac{[hemiacetal]}{[acyl\ azolium][MeOH]} \quad \text{eq 8.}$$

Rearranging eq. 8 as:

$$[hemiacetal] = K_5[MeOH][acyl\ azolium] \quad \text{eq 9.}$$

Substituted eq. 9 into the rate equation 7, the rate law may be expressed as:

$$\frac{d[P]}{dt} = k_6K_5[acyl\ azolium][MeOH] = (k_6K_5[MeOH])[acyl\ azolium] \quad \text{eq 10.}$$

Assumption 2*:* At any given time in the catalytic cycle, [acyl azolium IV] << [MeOH] (small K_5). This implies that [MeOH] is essentially constant and is pseudo 0^{th} order, eq. 10 may be rewritten as:

$$\frac{d[P]}{dt} = k'[acyl\ azolium] \qquad \text{where } k' = k_6K_5[\text{MeOH}] \quad \text{eq 11.}$$

Assumption 3: Since we have shown the importance of the acyl azolium in the catalytic cycle and the steps prior its formation are not rate-limiting (*vide supra*), [*acyl azolium*] can be approximated by $[\text{cat} - \text{RCHO}^+] \approx$; eq. 11 may be rewritten as:

$$\frac{d[P]}{dt} = k' \frac{[cat]_0[RCHO]}{[RCHO] + \frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[HX]}{[X^-]})} \quad \text{eq 12.}$$

Assumption 4*:* Since in the absence of base we observed a significant amount of the precatalyst in the presence of ynal, we maintain that the binding between RCHO and the active catalyst (cat) is small (that is $k_1 << k_{-1}$ and k_2), the term $\frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[HX]}{[X^-]}) >>$ [RCHO]. Consequently eq. 12 may be approximated by eq 13.

$$\frac{d[P]}{dt} = k' \frac{[cat]_0[RCHO]}{\frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[HX]}{[X^-]})} \quad \text{eq 13.}$$

However, if MeOH is considered as a general acid, eq. 1 for K_g may be modified as:

$$K_g = \frac{[cat][MeOH]}{[precat^+][MeO^-]} \text{ or } [precat^+] = \frac{1}{K_g}\frac{[cat][MeOH]}{[MeO^-]} \quad \text{eq 14.}$$

Following eq. 14, eq. 13 may be rewritten as:

$$\frac{d[P]}{dt} = k' \frac{[cat]_0[RCHO]}{\frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[MeOH]}{[MeO^-]})} \quad \text{eq 15.}$$

From eq. 16, the overall rate constant ($k_{overall}$) is shown to be:

$$k_{overall} = \frac{k'}{\frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[MeOH]}{[MeO^-]})} = \frac{k_6 K_5 [MeOH]}{\frac{k_{-1} + k_2}{k_1}(1 + \frac{1}{K_g}\frac{[MeOH]}{[MeO^-]})} \quad \text{eq 16.}$$

The overall rate law is finally expressed as:

$$\frac{d[P]}{dt} = k_{overall}[cat]_0^{1}[RCHO]^{1}[MeOH]^{0} \quad \text{eq 17.}$$

The complicated relationships between active catalyst generation (from the triazolium precatalyst and a general base, either MeO^- or Cl^-) and the catalyst inhibition (from the protic nucleophilic MeOH) gave rise to the experimentally-determined partial rate orders:

$$\frac{d[P]}{dt} = k_{obs}[precatalyst\ 3]^{0.5}[RCHO]^{1}[MeOH]^{-0.5} \quad \text{eq 18.}$$