Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Mukaiyama aldol reaction catalyzed by (benz)imidazolium-based halogen bond donors

*Revannath L. Sutar, Nikita Erochok and Stefan M. Huber**

Contents

1. General Remarks

All reagents and chemicals were obtained from *ABCR, Alfa Aesar, Carbolution, Merck, ChemPur, TCI and Sigma-Aldrich* and were used without further purification. Unless otherwise stated, all solvents used were of technical grade and were purified by distillation prior to use. Anhydrous solvents (DCM, ether and THF) were taken from *MBRAUN* (type: *MB SPS-800*) solvent drying system which were pre-dried by passing through an ALOX column followed by storing over 4 Å molecular sieve, and distillation. Thin layer chromatography was performed on *Merck TLC aluminum sheets* (silical gel 60, F254) and compounds were detected by fluorescence visualization under UV lamp (λ = 254 nm), iodine stain or using charring agents. Column chromatography was performed on silica gel (grain size 0.04-0.063 cm, *Macherey-Nagel Si60*). *Hamilton*® syringes were used for the addition of liquid reactants and solutions. All deuterated solvents were stored over the activated molecular sieves. NMR spectra were recorded on *AV-250, AV-300 and AV-400* instruments from *Bruker*. Multiplicities are given as s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), dd (doublet of doublet), m (multiplet) etc., and the coupling constants (*J*) are given in *Hz*.

The reactants **1**, and **12** were obtained from the commercial sources and were used without further purification. Commercially obtained benzaldehyde (**2**) was purified by distillation and was stored under argon at 4 °C. The catalysts **4**,[1a] **5**,[1a] **6**,[1b] **7**,[2] **8**,[1b] **9a,b**,[3] **9c**,[1b] **10a**,[3] **10b**,[1b] **11**[1b] were prepared according to the reported procedures and their spectral data was found in good agreement with the reported ones in the respective papers. Aldol products **3**,[4a] **13**,[4b] **15**[4c] were confirmed by comparing the ^{1}H NMR spectrums with the reported ones and found to be in good agreement.

2. Catalysis of Mukaiyama aldol reaction

2.1. General Procedure

The catalyst was weighed in an oven dried GC vial and was dissolved in anhydrous $CDCl_3$ (0.25 mL). An oven dried NMR tube was charged with this solution under argon atmosphere. $CDCl_3$ (0.25 mL) was again added to the above vial and the traces of catalyst leftovers were completely transferred to the above NMR tube. Mesitylene (1 µl) followed by benzaldehyde (10.2 µl, 0.1 mmol) was added to it under argon. ^{1}H NMR was recorded to determine the accurate equivalence of mesitylene. Enolate **2** (30 µl, 0.15 mmol) was added to it and ^{1}H NMR was quickly recorded. Further progress of the reaction was measured by ^{1}H NMR at regular intervals based on the progress after the first measurement. Conversions were determined based on the consumption of aldehyde through the measurement of integration of proton 'a' relative to that of the aromatic protons of mesitylene.

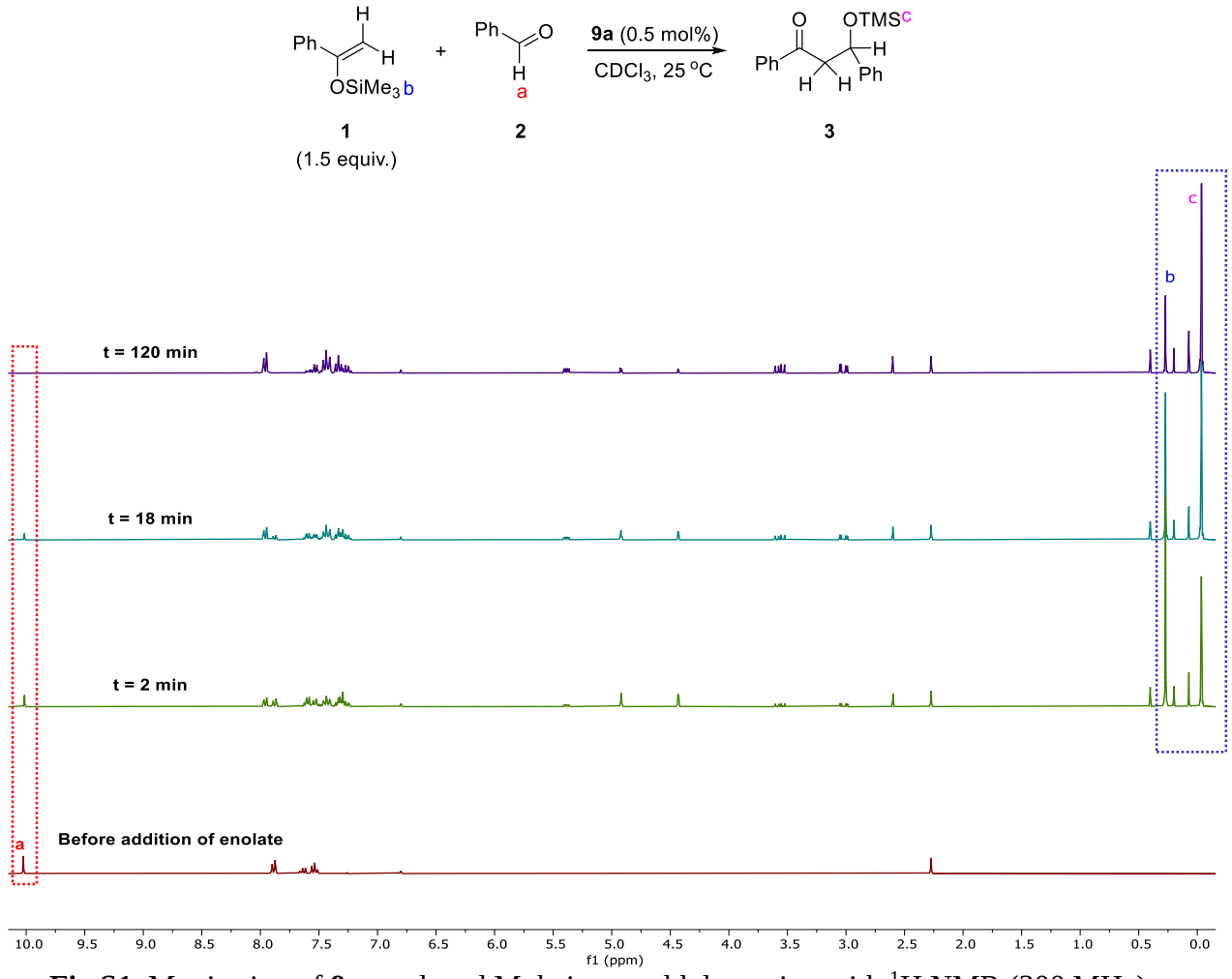


Fig S1. Monitoring of **9a** catalyzed Mukaiyama aldol reaction with ^{1}H NMR (300 MHz).

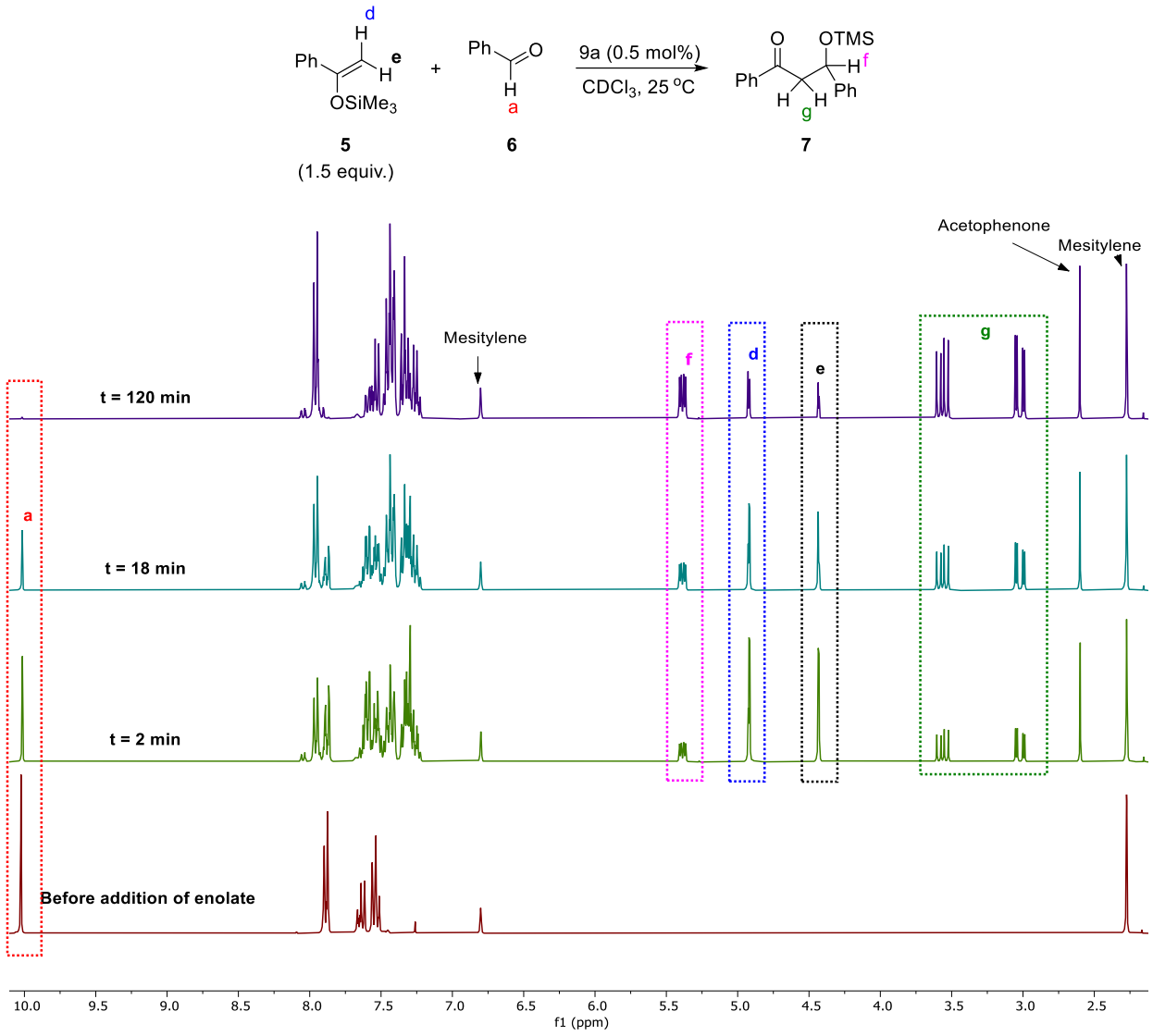


Fig S2. Zoomed spectra of **9a** catalyzed Mukaiyama aldol reaction at different time intervals.

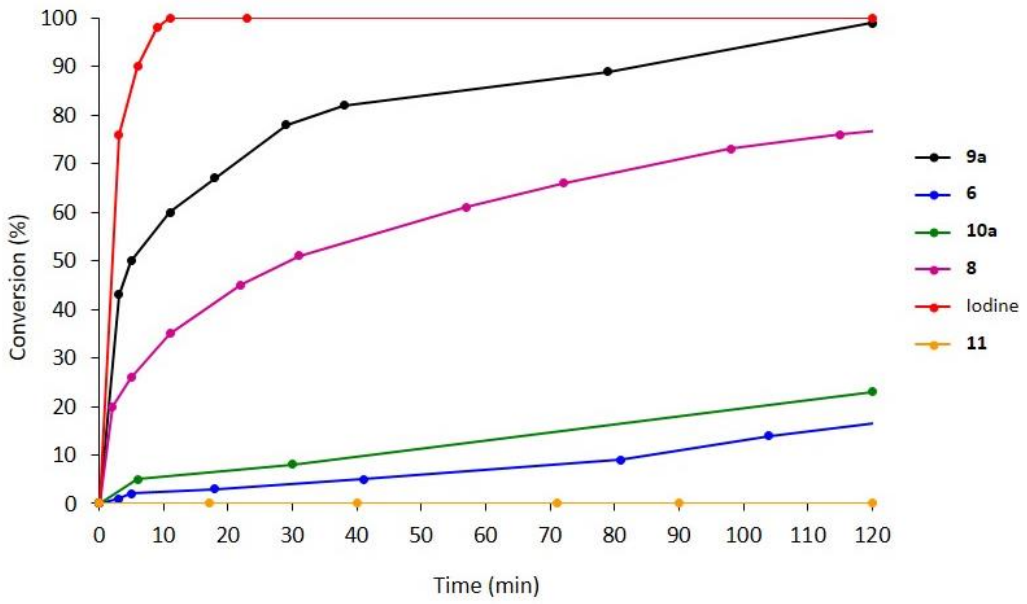


Figure S3. Full kinetics of Mukaiyama aldol reaction at 0.5 mol% catalyst loading.

2.2. Repeated addition experiments

Following the general catalysis procedure mentioned above, an oven NMR tube was charged with catalyst (0.5 mol%), benzaldehyde (10.2 µl, 0.1 mmol), mesitylene (1 µl) and $CDCl_3$ (0.5 mL) under argon. ^{1}H NMR was recorded and accurate equivalence of mesitylene was determined. Enolate **2** (20 µl, 0.1 mmol) was added and ^{1}H NMR was immediately recorded. Further progress of the reaction was measured by ^{1}H NMR at regular intervals. After complete consumption of TMS-enolate **2**, based on the unreacted benzaldehyde (~8%), another portion of benzaldehyde (9.4 µl) was added to make its net quantity to 0.1 mmol. It was confirmed by ^{1}H NMR through comparison of its equivalence with respect to mesitylene measured during the first cycle. TMS-enolate **2**, (20 µl, 0.1 mmol) was added and the progress of reaction was monitored for second cycle. After complete consumption of **2**, same procedure was repeated for the third cycle. During each cycle, conversions were determined based on the consumption of aldehyde obtained by the measurement of integration of proton 'a' relative to that of the aromatic protons of mesitylene.

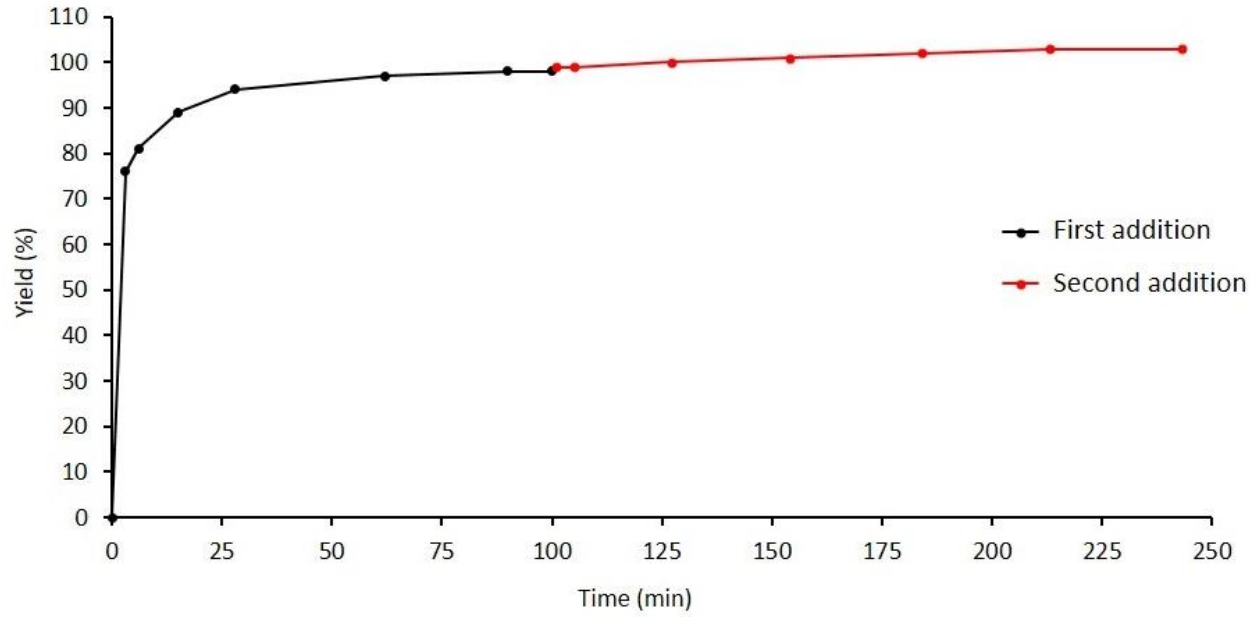


Figure S4. Kinetics of the repeated-addition experiment between **1** (0.1 mmol, 1.0 equiv.) and **2** (0.1 mmol, 1.0 equiv.) with iodine (0.5 mol%) as the catalyst at 0.2M initial concentration and mesitylene as the internal standard.

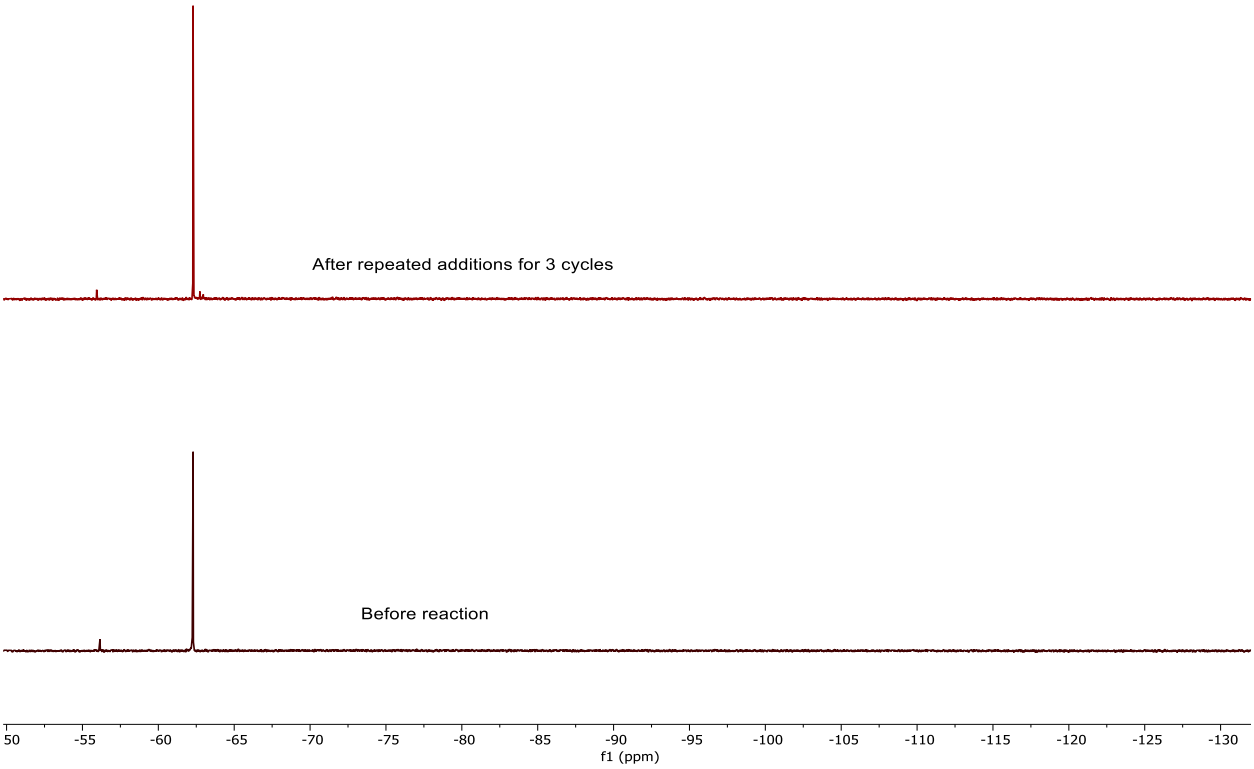


Figure S5. Stability of **9a** after repeated addition for three cycles ^{19}F NMR (235 MHz, $CDCl_3$).

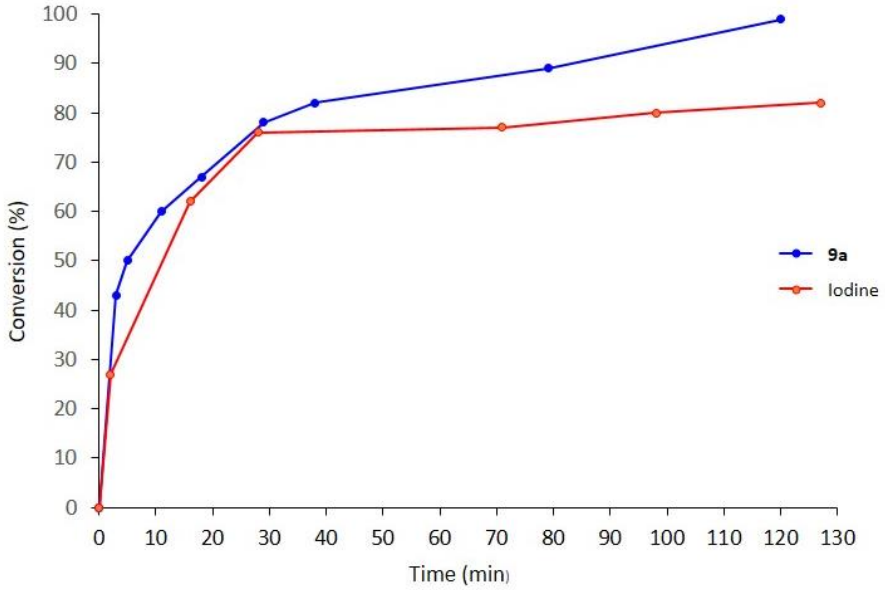


Figure S6. Kinetics of Mukaiyama aldol reaction between **1** (0.15 mmol, 1.5 equiv.) and **2** (0.1 mmol, 1.0 equiv.) catalyzed by **9a** (0.5 mol%) and iodine (0.3 mol%) using mesitylene as internal standard.

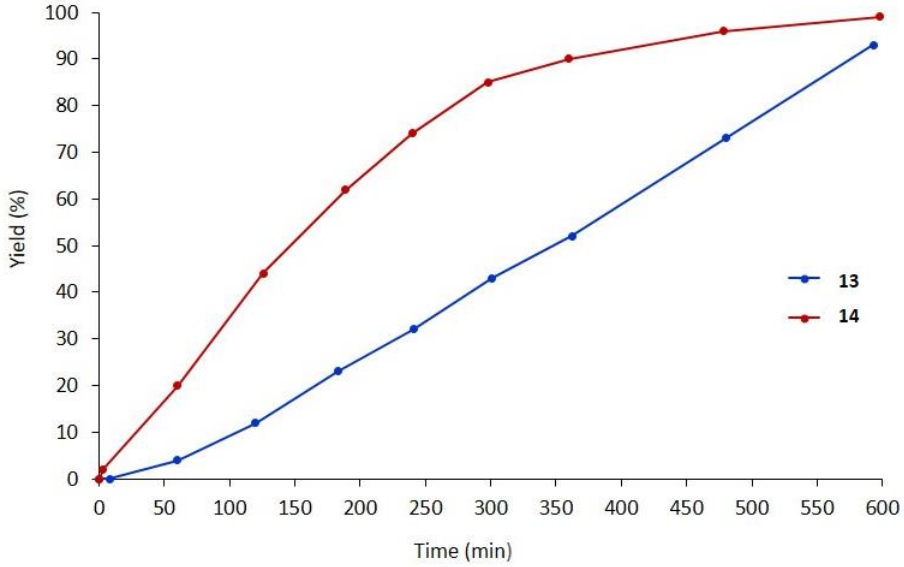


Figure S7. Kinetics of Mukaiyama aldol reaction of **1** (0.15 mmol, 1.5 equiv.) with ketones **12** and **15** 0.1 mmol, 1 equiv.) catalyzed by **9a** (5 mol%) using mesitylene as internal standard. Error of around 6% was noted in the yields of **14** based on its formation during the reaction of **12** to **13**.

2.3. Determination of k_{rel}

Relative reaction rate (k_{rel}) were derived from the kinetic plots of the reaction. The conversions after 6 min of the reaction were used to determine the conversion/time slopes of each plot. By considering the conversion/time slope of *syn*/*anti*-**10a** as reference (k_{rel} = 1), k_{rel} values of all other experiments were determined.

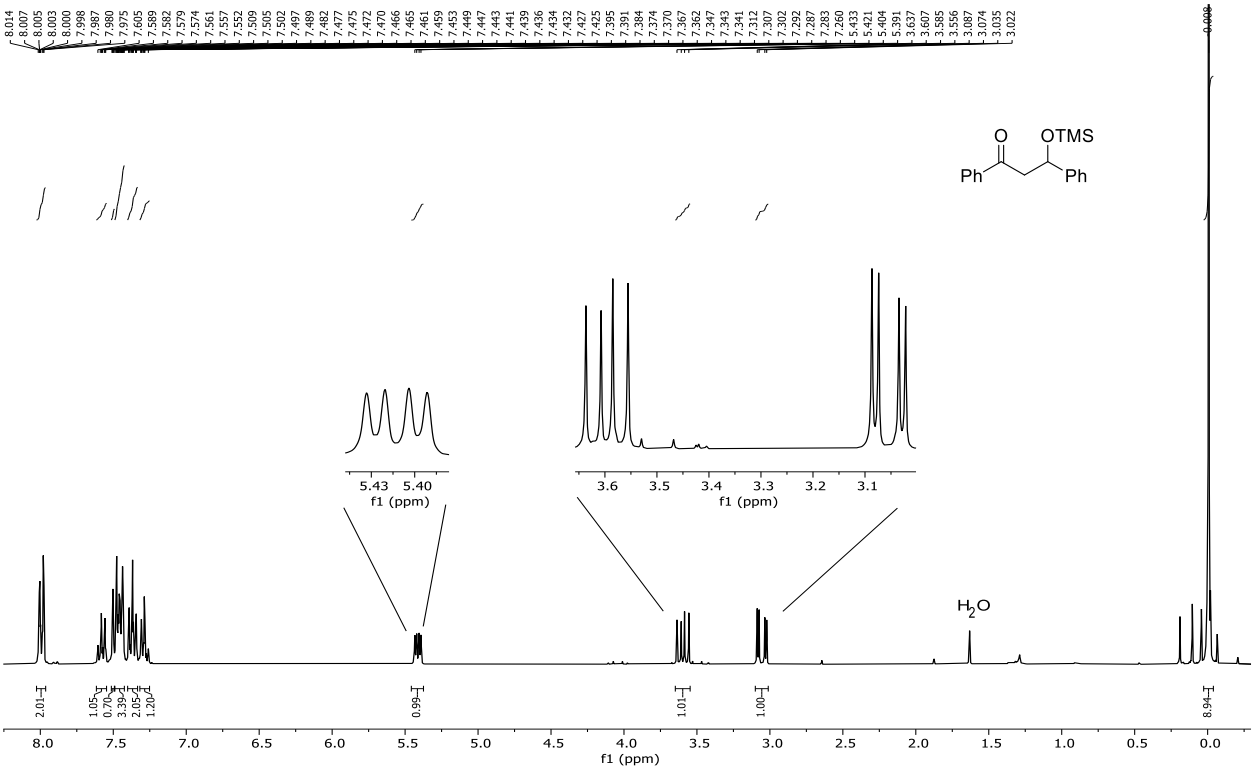
2.4. Determination of turnover numbers (TON) and turnover frequency (TOF) of catalysts

Turn over number (TON) and turn over frequency (TOF) are determined for the conversion at 3-6 min. for all reactions.

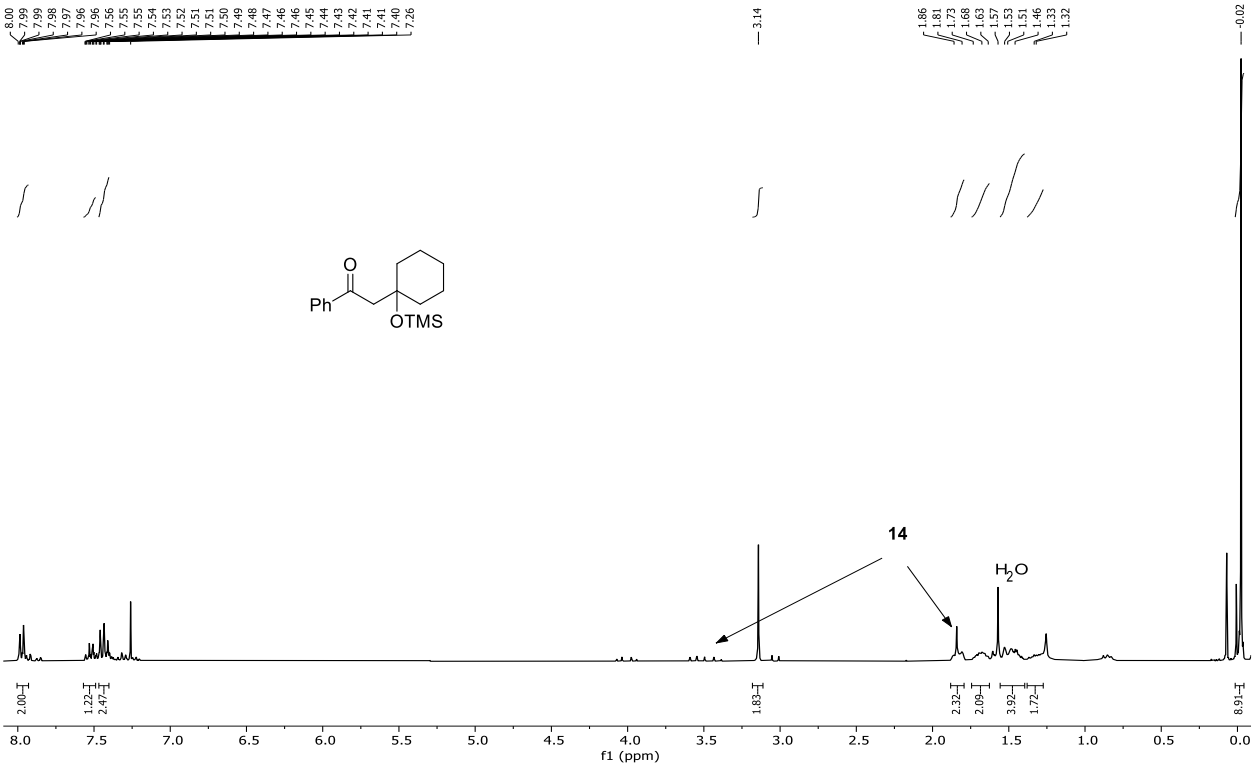
No	**Catalyst**	**TON**	**TOF** (s^{-1})
1	**4**	1.2	0.0028
2	**5**	0.4	0.001
3	**6**	4	0.013
4	**7**	0.6	0.002
5	**8**	52	0.173
6	**9a**	100	0.333
7	*syn/anti*-**10a**	10	0.028
8	iodine	152	0.835

3. NMR spectra

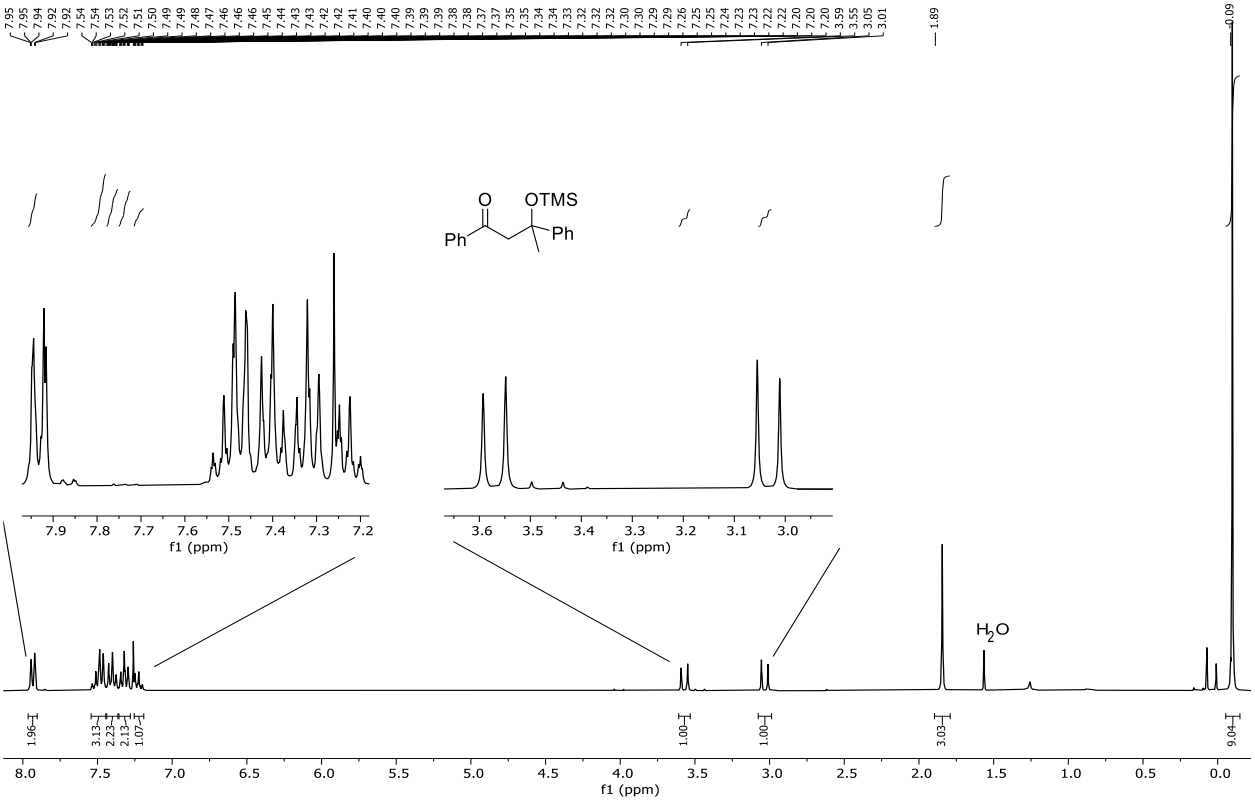
^{1}H NMR spectra of 3



^{1}H NMR spectra of 13



^{1}H NMR spectra of 14



4. DFT calculations

4.1 Coordinates and energies of transition state

Energy (ht) = -3138.405394
Gibbs free energy (ht) = -3138.498745

C	-2.82231900	-0.59028200	0.49638700
O	-1.64087000	-0.15526400	0.76150700
C	3.31838700	0.28787500	0.30263900
C	3.68431400	0.70225700	3.05470400
C	3.48294800	-0.78394200	1.18389500
C	3.23702800	1.56524800	0.85685600
C	3.43321700	1.77299500	2.21526700
C	3.67839400	-0.58447200	2.53972300
H	3.36794800	2.78142500	2.60326000
H	3.80846600	-1.44425400	3.18435300
C	1.64285500	2.99442100	-0.36629800
N	1.68668200	4.12592300	-1.06565100
H	3.84107500	0.86464900	4.11198300
C	2.99774900	4.59911400	-1.09115800
N	2.88638500	2.70596600	0.06896300
N	3.39463200	-2.13556800	0.71745700
C	2.23990100	-2.82508900	0.57496800
N	2.52963400	-4.07841200	0.23742900
C	3.91443800	-4.22900000	0.17196100
C	3.76602100	3.69510000	-0.36677400
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I	0.37512800	-1.93978000	0.80012600
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C	-4.06535800	-2.38480500	-0.70677600
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H	5.39974000	6.75523700	-1.95425400
H	2.96183500	6.43209100	-2.24602500

4.2 Coordinates and energies of starting materials complex

Energy (ht) = -3138.422602
Gibbs free energy (ht) = -3138.519709

C	-2.56233000	-1.78655800	0.36746000
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C	5.32425000	-1.94307900	-0.01481500
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C	7.62427600	-1.97575200	-0.49285500
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F	2.23707200	-0.25258600	-1.54484300
F	2.70580600	1.83952900	-1.65103800
C	3.91530600	6.03082300	0.06637300
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H	0.77887300	6.77353000	-1.07852300

5. References

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