Electronic Supplementary Information

for

Upon the α-methylenation of methyl propanoate via catalytic dehydrogenation of methanol

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▪ S-1 General Information

(S-1.1) General materials and methods

All manipulations and reactions were carried out under N_2 gas (dried through a Cr(II)/silica packed glass column) using different techniques including a standard Schlenk, vacuum line and a glove box. Simple base catalysed experiments and deuterium labelling studies reported in section S-3.2 and S-1.3 were performed under aerobic conditions. Solvents were dried and degassed prior to use unless otherwise stated.

$[RuH_2(CO)(PPh_3)_3]$ (**1**), Shvo's catalyst (**2**), $[RuCl(CO)_2(\eta^5\text{-}Ph_5C_5)]$ (**3**), NaOMe, *t*-OBuNa, *t*-OBuK, Cs_2CO_3, DBU, sodium propionate, paraformaldehyde, decane (internal standard), methanol, methanol-d_4, $^{13}CH_3OH$, methyl methacrylate, methyl isobutyrate, *tert*-butyl propanoate, 3-pentanone and propanoic acid were purchase from Sigma-Aldrich. $RuCl_3{\cdot}3H_2O$ and *tert*-butanol were purchased from Alfa Aesar.

Methyl propanoate (supplied by Lucite Int.) was dried, purified and degassed prior to use, following this standard procedure: pre-treatment with Na_2CO_3, stirring over P_2O_5, degassing by three freeze-pump-thaw cycles and final collection by trap-to-trap distillation. *tert*-Butyl propanoate and propanoic acid were dried over Na_2SO_4 and distilled under dinitrogen.

P_2O_5 and $CaCl_2$ were purchased from Fluka. Na_2CO_3 (anhydrous), Na_2SO_4 (anhydrous) and NaOH (pellets) were purchased from Fisher Scientific.

Toluene was dried using a Braun Solvent Purification System. Methanol was dried and degassed by distillation from magnesium under dinitrogen. All gases were purchased from BOC gases.

Unless otherwise mentioned, all other reagents were used without further purification.[1]

$[RuCl_2(PPh_3)_3]$[2] (**7**), $RuH(CO)(OCOEt)(PPh_3)_2]$[3] (**8**), $[Ru(OAc)_2(TriPhos)]$ (**4**) (triphos = $MeC(CH_2PPH_2)_3$)[4], $[RuH_2(CO)(TriPhos)]$[5] (**5**) and $[RhH(CO)(PEt_3)_3]$[6] (**6**) were prepared by published procedures and all observations and NMR data were in accordance with those reported in the literature.

(S-1.2) General Instruments

NMR spectra were recorded on a Bruker Avance II 400 and 300 MHz Spectrometer (^1H NMR at 400 MHz and ^{13}C NMR at 100 MHz and ^1H NMR at 300 MHz and ^{13}C NMR at 75 MHz respectively) at room temperature. ^1H and $^{13}C\{^1H\}$ spectra are referenced to TMS and the residual proton signal of the solvent was used as internal standard. When needed, NMR assignments were performed with the help of 2D (^1H,^1H) COSY experiments.

GC/MS analysis were performed using a Hewlett Packard 6890 series GC system equipped with an Agilent J&W HP-1 column capillary (30.0 m x 248 µm x 0.25 µm nominal). Method: flow rate 0.8 mL min^{-1} (He carrier gas), split ratio 100:1, starting temperature 50 °C (4 min) ramp rate 20 °C min^{-1} to 130 °C (2 min), ramp rate 20 °C min^{-1} to 280 °C (15.50 min). Quantitative analysis, using decane or toluene as an internal standard (IS) were performed using a flame ionisation detector (GC-FID) and qualitative analysis using an HP5973 mass selective detector (GC-MS).

GC-FID integration method details: Initial Area Reject 0; Initial Peak Width 0.038; Shoulder Detection OFF; Initial Threshold 19.

(S-1.3) General Abbreviations

t-BuP	*tert*-butyl propanoate
h	hours
IS	internal standard
MeP	methyl propanoate
MiBu	methyl isobutyrate ((methyl 2-methylpropanoate)
MMA	methyl methacrylate
t	time

▪ S-2 Labelling Experiments

(S-2.1) General procedure for deuterium labelling experiment with MeP, base and methanol-d_4

An autoclave was charged with MeP, a base (K_2CO_3, NaOH or Cs_2CO_3; Table S1) and methanol-d_4 and heated at 170 °C with stirring for 2 h. The autoclave was then cooled to room temperature, vented to the atmosphere and the obtained product mixture analysed by NMR spectroscopy.

Table S1 Conditions for deuterium exchange between methanol-d_4 and MeP.

Experiment	MeP	base	methanol-d_4
a	0.96 mL, 10.0 mmol	K_2CO_3 (0.35 g, 2.53 mmol)	3 mL
b	0.96 mL, 10.0 mmol	NaOH (0.12 g, 2.90 mmol)	3 mL
c	0.96 mL, 10.0 mmol	Cs_2CO_3 (0.82 g, 2.53 mmol)	3 mL

(S-2.2) Time dependent deuterium labelling study with NaP as base

Sodium propanoate (5.48 g, 57.05 mmol) was added to a stainless steel autoclave (**A**) fitted with a magnetic stirring bar. The autoclave was then sealed, purged and connected to a second autoclave (**B**), previously

purged and sealed, via the gas inlet ports by Swagelock tubing. The two autoclaves were isolated from each other by means of valves. Methyl propanoate (10 mL, 103.85 mmol) and methanol-d_4 (28.97 mL, 713.26 ml) were added to autoclave **A** via the injection port. The resulting mixture was heated to 200 °C with stirring and a sample was taken at t = 0 min (at the time the autoclave reached the set temperature), by briefly opening the valves between the autoclaves and allowing a fraction of the vapour phase to condense into autoclave **B** which was immersed in cold water. Similar experiments were carried out with samples being taken at t = 5 min, 10 min and 60 min by the same method. At the end of each experiment the two autoclaves were disconnected, vented to the atmosphere, opened and the two colourless solutions were analysed by NMR spectroscopy. $^{13}C\{^1H\}$ NMR spectra were used to quantify deuterium incorporation.[7]

(S-2.3) Reaction using ^2H or ^{13}C labelled methanol.

The reactions were carried out as described in Table S4, **Entry 18,** using CD_3OD in place of methanol or using a mixture of methanol (3.38 mL, 83.64 mmol) and $^{13}CH_3OH$ (0.4 mL, 9.87 mmol). In the latter case the reaction was scaled-down to 50 %. After the reaction, the crude solutions were analysed by GC-MS. The relative intensities of the signals from the isotopomers from the parent ion and from $[M\text{-}OMe]^{+\cdot}$ integrated over the whole area of the GC peak were used to determine the relative amounts of different isotopomers present. The products expected if methanol is the source of the methylene group are shown in Figure S1 and the actual mass spectra are shown in S-2.4. The observed peak intensities and assignments are in Table S2.

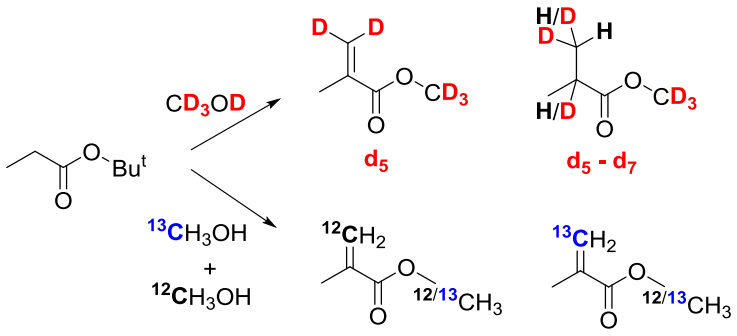

Figure S1 Isotopomers of MeP expected from the methylenation of *t*-BuP in the presence of *t*-BuONa when using labelled methanol if methanol is the source of the methylene group.

Table S2 Intensities of isotopomers of the [M-OMe]$^+$signal in the mass spectra of MMA and MiBu when using CD_3OD or $^{13}CH_3OH$ for the methylenation of *t*-BuP in the presence of *t*-BuONa

		Isotopic mass						
		69	**70**	**71**	**72**	**73**	**74**	**75**
MMA	CH_3OH	147	7					
	$^{13}CH_3OH/CH_3OH$[a]	147	20					
	Assignment	^{12}C 92 %	^{13}C 8 %					
	CD_3OD		43	152	28			
	Assignment		d_1 20 %	d_2 68 %	d_3 12 %[b]			
MiBu	CH_3OH			88	4			
	$^{13}CH_3OH/CH_3OH$[a]			88	12			
	Assignment			^{12}C 92 %	^{13}C 8 %			
	CD_3OD					48	83	40
	Assignment					d_2 29 %	d_3 49 %	d_4 22 %

[a] $^{13}CH_3OH/CH_3OH$ is 1:8.5; [b] some d_3-[M-OMe]$^+$ is observed, suggesting some incorporation of D into the methyl group.

▪ S-3 Catalytic Experiments

(S-3.1) General procedure for base catalysed condensation of MeP and formaldehyde

An autoclave charged with MeP, used as received, (0.96 mL, 10 mmol), a base (K_2CO_3, NaOH or DBU), paraformaldehyde as formaldehyde source and a solvent (toluene or 2-ethylhexanol) was heated to 170 °C for 1-2 h with stirring (Table S3). The autoclave was cooled to room temperature, vented to the atmosphere and the reaction mixture analysed by GC and NMR techniques.

Table S3 Attempted base catalysed formation of MMA from MeP and formaldehyde

Entry	Base	Solvent	Formaldehyde	MMA Yield [%]
1	K_2CO_3 (2.53mmol)	toluene (10.0 mL)	9.7 mmol	< 1
2	K_2CO_3 (2.53 mmol)	2-ethylhexanol (11.72 mL)	15.0 mmol	0
3	K_2CO_3 2.53 mmol	2-ethylhexanol (4.69 mL)	15.0 mmol	0
4	DBU 2.53 mmol	toluene (5.0 mL)	15.0 mmol	< 1
5	DBU 2.53 mmol	2-ethylhexanol (4.69 mL)	15.0 mmol	< 1
6	NaOH 3.0 mmol	2-ethylhexanol (4.69 mL)	15.0 mmol	0

(S-3.2) General procedure for catalytic batch reactions

Catalytic reactions were carried out in a Hastelloy™ autoclave. In a typical experiment the desired amount of the catalyst and all solid compounds were weighed into the autoclave under an inert atmosphere of dinitrogen (glovebox). The autoclave was then sealed and purged with three vacuum/N_2 cycles. At this point all solvents and solutions were added through the injection port. After these operations the autoclave was pressurised with the desired gas or simply resealed. The reactor was then heated to the desired temperature and the reaction mixture was stirred using a magnetic stirrer. After the set reaction time the autoclave was cooled to room temperature, observing a pressure drop, and fully vented prior to opening the autoclave, giving evidence of two phases, solid and liquid. At this stage decane (IS) was added and the reaction mixture vigorously stirred prior to separation of the two phases by filtration. NMR spectroscopy, qualitative GC-MS and quantitative GC-FID spectroscopy were employed to analyse the recovered phases.

(S-3.3) Reaction conditions for catalytic batch reactions reported in Tables 1 and 2 (main paper)

A Hastelloy™ autoclave was fitted with a magnetic stirrer and charged under a dinitrogen atmosphere with the desired catalyst (**1**) (0.124 g, 0.135 mmol), (**7**) (1.129 g, 0.135 mmol) or (**8**) and a base. Toluene (10 mL), MeP (10 mL, 103.85 mmol) or *t*-BuP (15.64 mL, 103.9 mmol) were added together with methanol (7.6 mL, 187.02 mmol) and 2,4-dimethyl-6-tert-butylphenol (Topanol A, 0.01 mL) in order to prevent MMA polymerisation. The autoclave was sealed, pressurised with ethene (6 bar) and heated to 170 °C or 200 °C (Entries 13 and 14) for 1-15 hours. Full details and amounts are given in Table S4.

Table S4 Conditions for methylenation of MeP. The results are in Tables 1 and 2 of the main paper**.**

Entry	Substrate	[Ru]	Base	*t*-BuOH	t [h]
1	MeP	1	NaOMe (1.42 g, 26.3 mmol)	-	1
2	MeP	1	NaOMe (1.42 g, 26.3 mmol)	-	3
3	MeP	1	NaOMe (2.8 g, 51.9 mmol)	-	3
4	MeP	1	NaOMe (5.6 g, 103.85 mmol)	-	3
5	MeP	1	*t*-BuONa (2.6 g, 27.0 mmol)	-	3
6	MeP	1	*t*-BuONa (2.6 g, 27.0 mmol)	-	15
7	MeP	1	*t*-BuONa (4.99 g, 51.9 mmol)	-	3
8	MeP	1[a]	*t*-BuONa (4.99 g, 51.9 mmol)	-	3
9	MeP	1	*t*-BuOK (2.95 g, 26.3 mmol)	-	3
10	MeP	7	*t*-BuONa (2.6 g, 27.0 mmol)	-	3
11	MeP	7	*t*-BuONa (2.6 g, 27.0 mmol)	-	15
12	MeP	1	NaP (2.5 g, 26.3 mmol)	-	15
13[c]	MeP	1	NaP (2.5 g, 26.3 mmol)	-	15
14[b,c]	MeP	8	NaP (2.09 g, 21.8 mmol)	-	15
15	MeP	8	NaOMe (1.42 g, 26.3 mmol)	-	15
16	MeP	1	*t*-BuONa (2.6 g, 27.0 mmol)	8.9 mL, 93.5 mmol	3
17	*t*-BuP	1	NaOMe (1.42 g, 26.3 mmol)	-	3
18	*t*-BuP	1	*t*-BuONa (2.6 g, 27.0 mmol)	-	3
19	*t*-BuP	1	*t*-BuONa (2.6 g, 27.0 mmol)	8.9 mL, 93.5 mmol	3
20	*t*-BuP	1	*t*-BuONa (2.6 g, 27.0 mmol)	17.9 mL, 187.02 mmol	3
21	*t*-BuP	1	*t*-BuONa (2.6 g, 27.0 mmol)	8.9 mL, 93.5 mmol (MeOH: 11.36 mL, 280.5 mmol)	3
22	*t*-BuP	7	*t*-BuONa (2.6 g, 27.0 mmol)	-	3

[a] a stoichiometric amount of xantphos was added; [b] Entry 14: MeP (7 mL, 72.7 mmol), MeOH (2.9 mL, 72.7 mmol) cat. (0.07 g, 0.094 mmol); [c] T = 200 °C

- **S-4 NMR and GC spectra**

(S-4.1) NMR data of Table S1/S-2.1

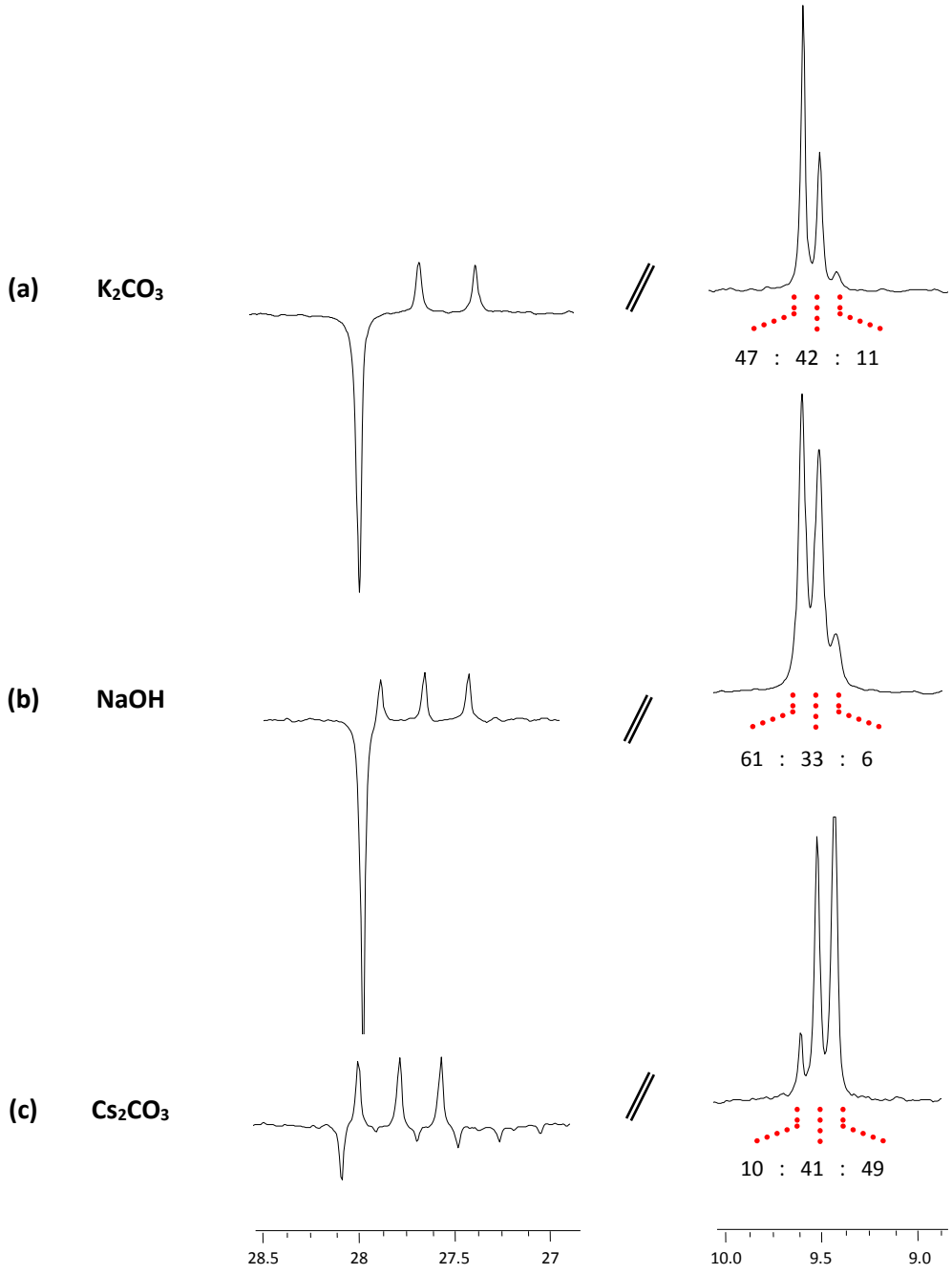

Figure S2 $^{13}C\{^{1}H\}$ DEPT NMR spectra (methanol-d_4): methylene (left) and methyl (right) resonances showing the extent of deuterium incorporation in MeP with **(a)** K_2CO_3, **(b)** NaOH and **(c)** Cs_2CO_3 as base. The ratio of the non- to mono- to bis-deuterated MeP [%] is given below the methyl signals.

S-4.2 NMR data of S-2.2

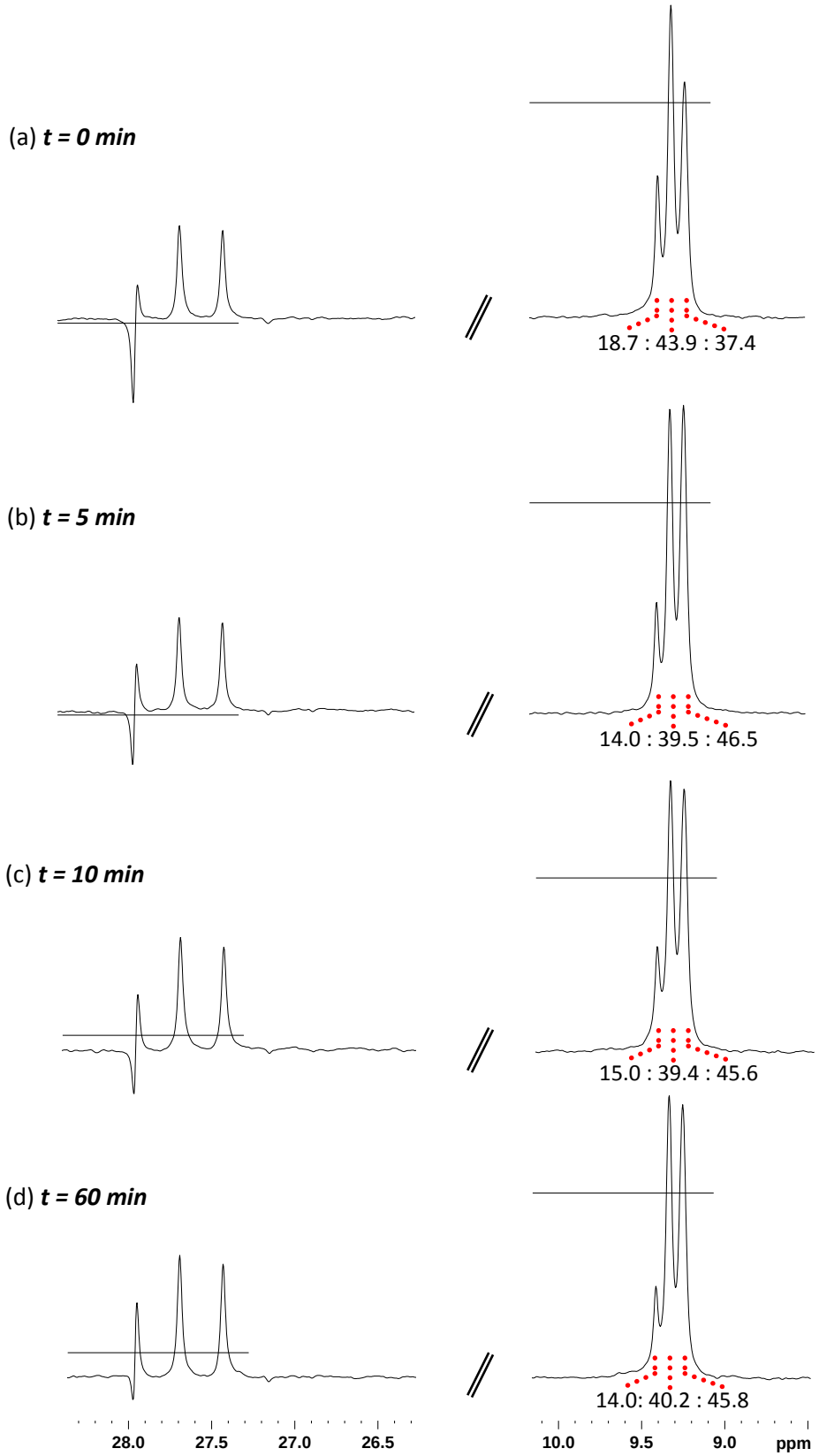

Figure S3 $^{13}C\{^{1}H\}$ DEPT NMR spectra (methanol-d_4): methylene (left) and methyl (right) resonances showing the extent of deuterium incorporation in MeP with NaP as base at time 0 min, 5 min, 10 min and 60 min after the reactor has reached 200 °C. The ratio of the non- to mono- to bis-deuterated MeP [%] is given below the methyl signals. Equilibrium is reached in <5 min after the heating up period.

(S-4.3) Selected GC-MS spectra of table S4/S-3.3

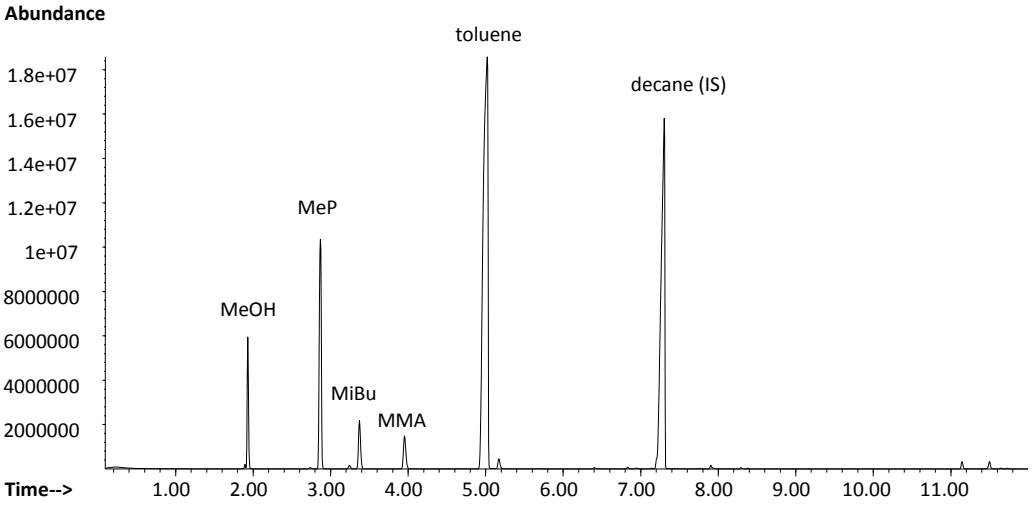

Figure S4 GC-MS of **Entry 2**/Table S4

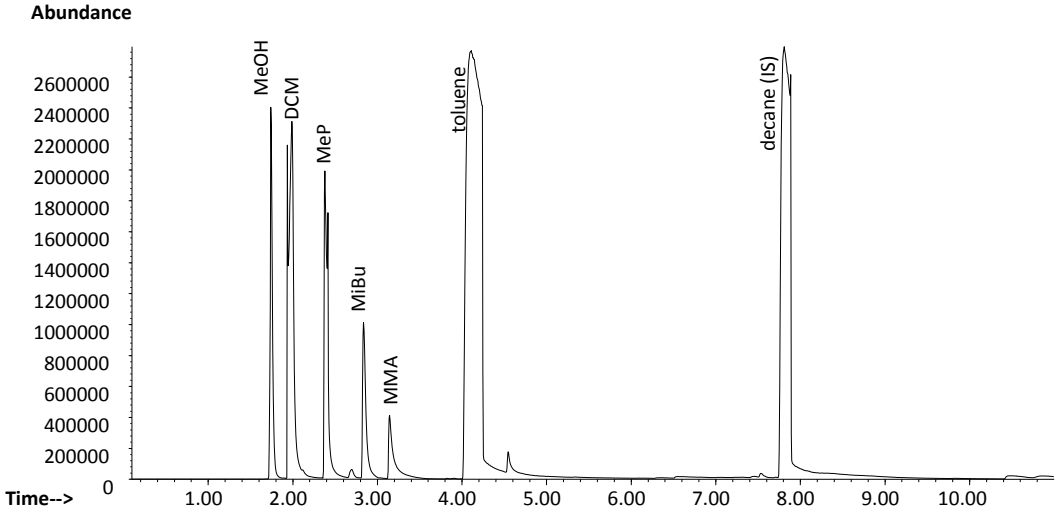

Figure S5 GC-MS **Entry 5**/Table S4

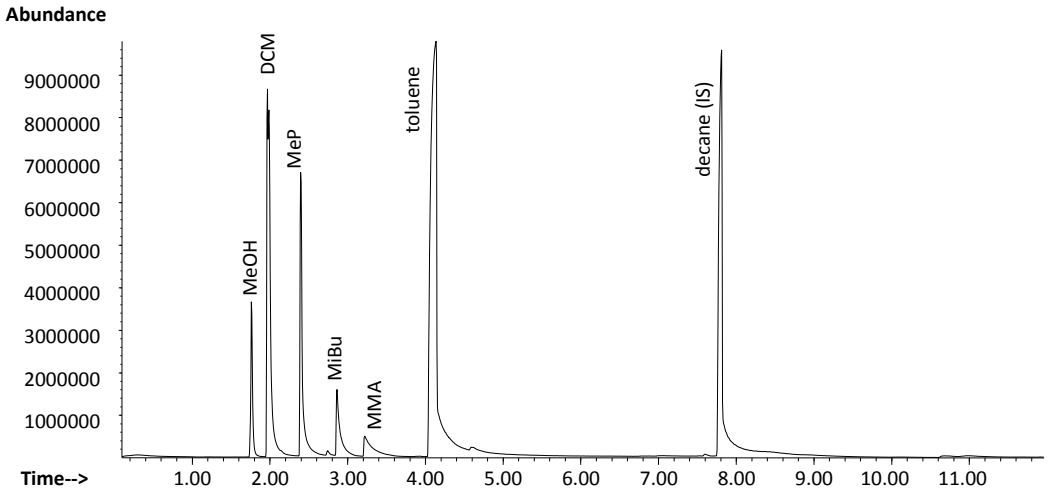

Figure S6 GC-MS **Entry 10**/Table S4

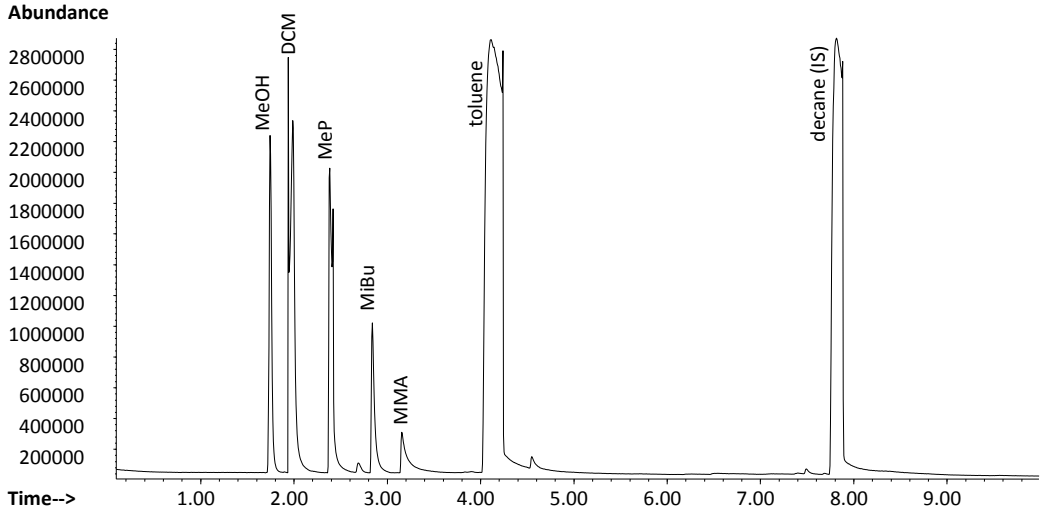

Figure S7 GC-MS **Entry 15**/Table S4

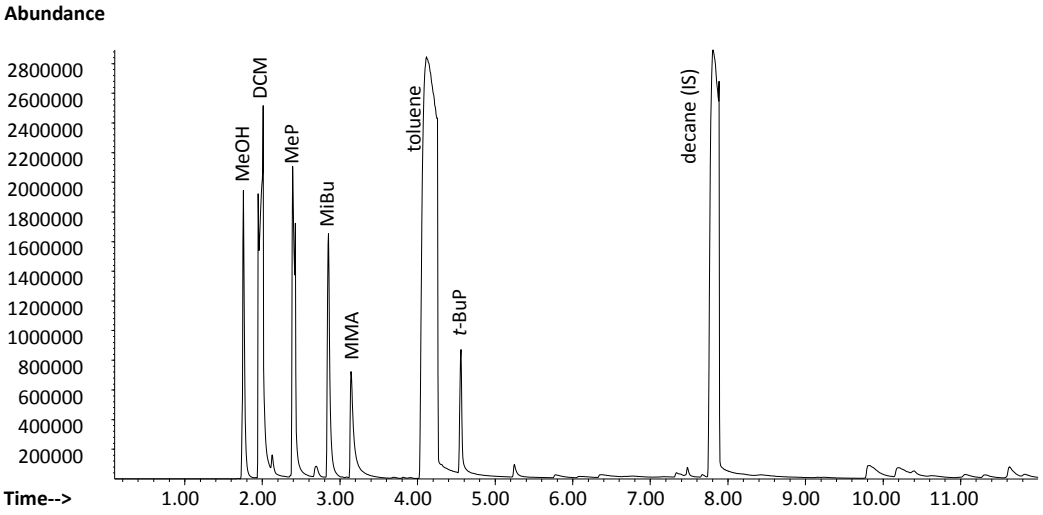

Figure S8 GC-MS **Entry 17**/table S4

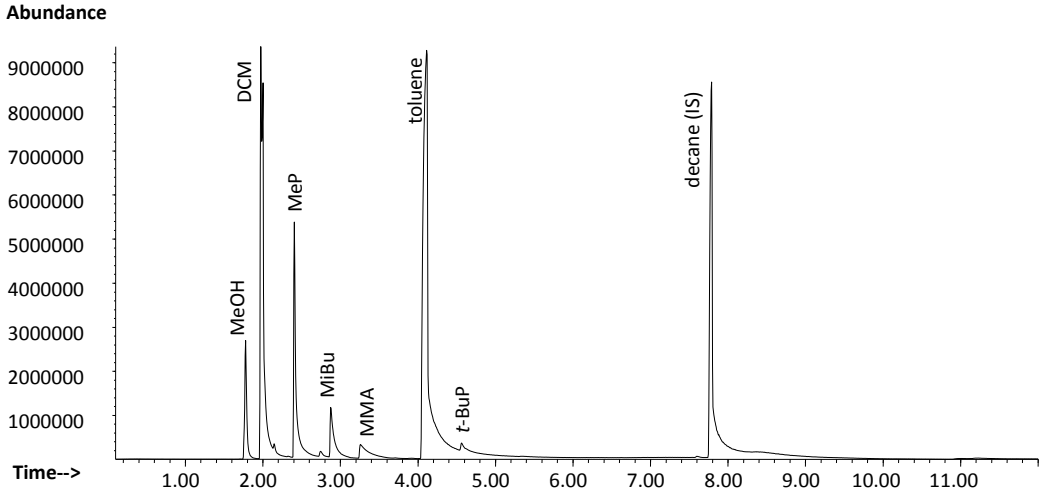

Figure S9 GC-MS **Entry 21**/Table S4

(S-4.4) MiBu and MMA fragmentation pattern using CH_3OH, CD_3OD and $^{13}CH_3OH$ as alkylating agent (reactions reported in S-2.3)

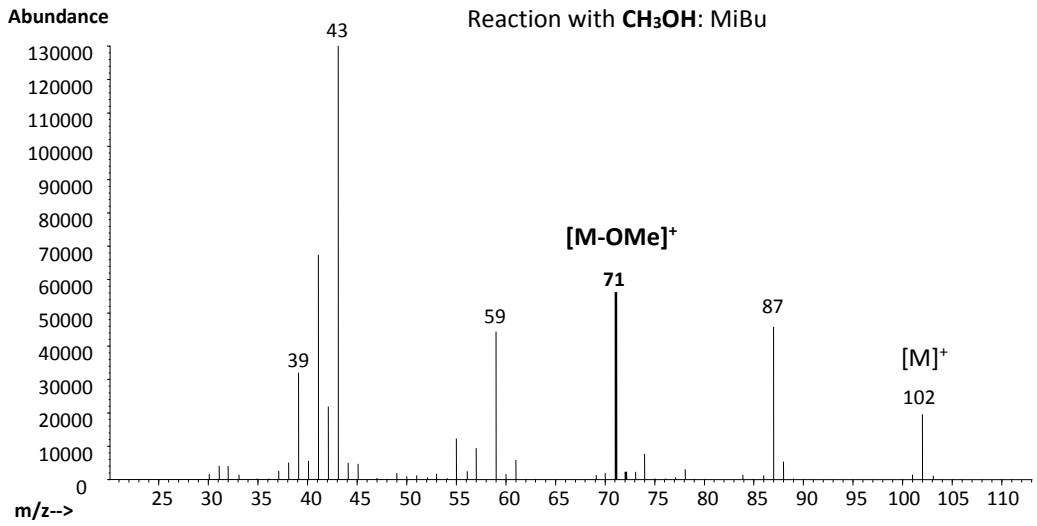

Figure S10 Fragmentation pattern of MiBu when using only CH_3OH.

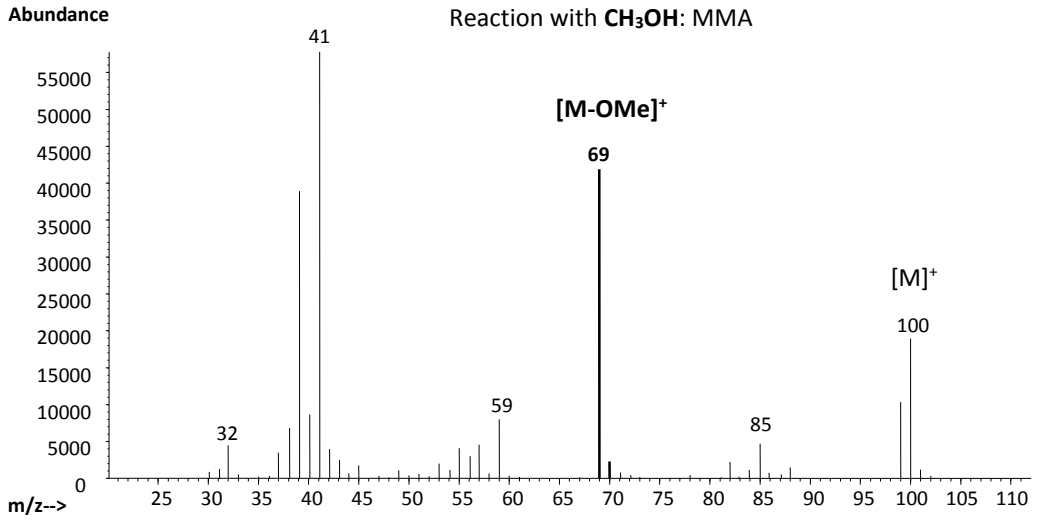

Figure S11 Fragmentation pattern of MMA when using only CH_3OH.

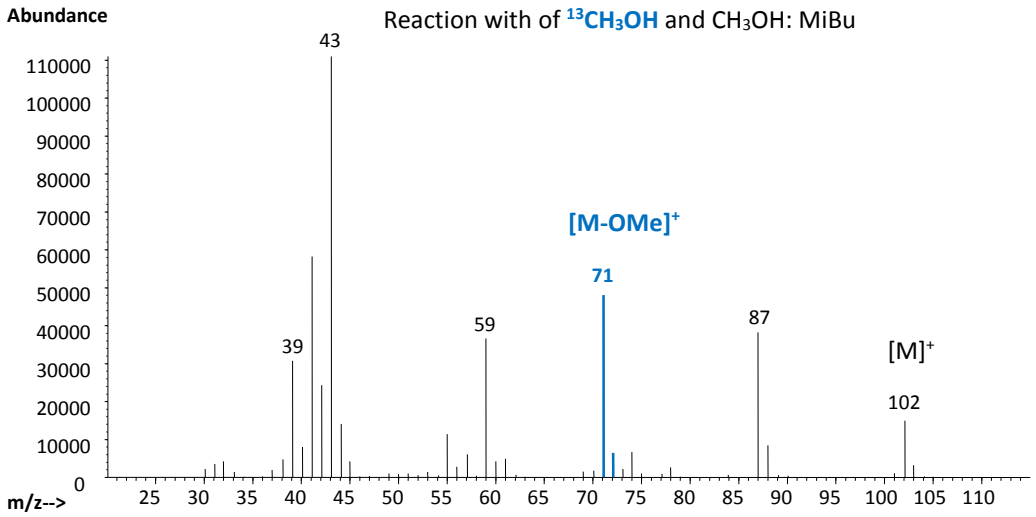

Figure S12 Fragmentation pattern of MiBu when using $^{13}CH_3OH$ and CH_3OH in a 1:8.5 ratio

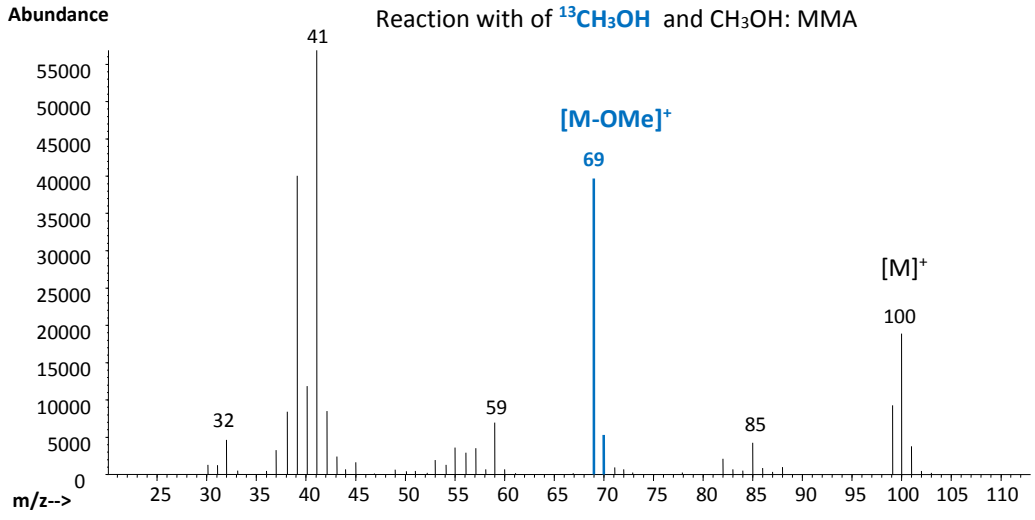

Figure 13 Fragmentation pattern of MMA when using $^{13}CH_3OH$ and CH_3OH in a 1:8.5 ratio

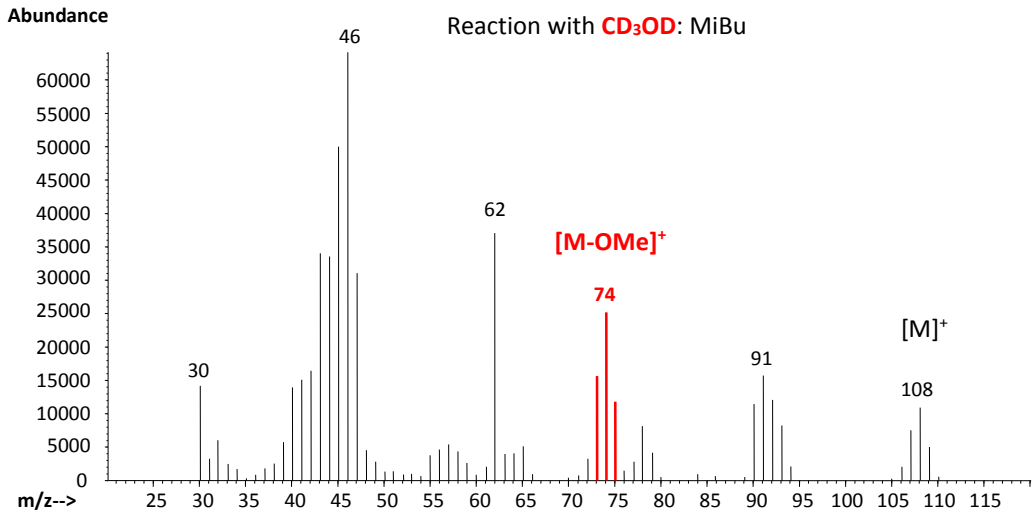

Figure 15 Fragmentation pattern of MiBu when using only CD_3OD.

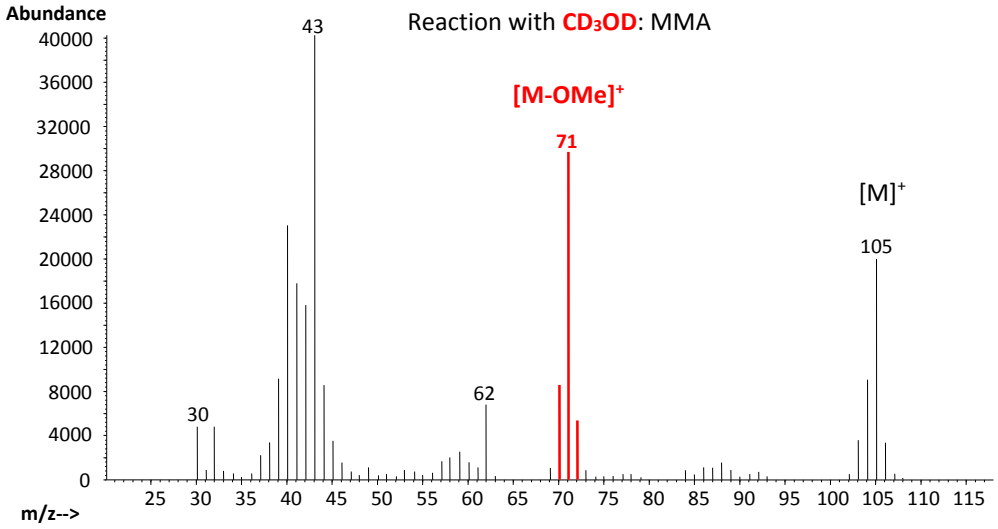

Figure 16 Fragmentation pattern of MMA when using only CD_3OD.

▪ S-5 References

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