Electronic Supplementary Information

Catalytic etherification of hydroxyl compounds to methyl ethers with 1,2-dimethoxyethane

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1. Materials

All chemicals employed here were commercially available with analytical grade purity or better unless otherwise specified. Isosorbide (98%) was available from Wuhan DKY Technology Co., Ltd. (China). 1,2-dimethoxyethane (DMET, 99.5%) from Aladdin Reagent Inc. (China) was stored over 3 Å molecular sieves until used. 2-Methoxyethanol (≥99.8%), diethylene glycol monomethyl ether (≥99.5%), diglyme (≥99.5%), and triglyme (≥99%) were also obtained from Aladdin Reagent Inc. Dimethyl isosorbide (98%), naphthalene (≥99%) and mesitylene (≥98%) were supplied by Alfa-aesar Chemical Co., Ltd. Isomannide (99%) was purchased from HWRK Chemical Engineering Co., Ltd. (China). *n*-Butanol (≥99.5%) and *n*-hexanol (≥98%) were obtained from Tianjin Kermiou Chemical Reagent Co., Ltd. and corresponding methyl ethers (*n*-butyl methyl ether, >99.0%, *n*-hexyl methyl ether, >98.0%) were from TCI. Because the authentic samples for isosorbide monomethyl ethers and isoidide are not commercially available, pure 2-*O*-monomethyl isosorbide and 5-*O*-monomethyl isosorbide were achieved in our lab using silica-gel column chromatography to separate the reaction mixtures (see Experimental section in the main text) and isoidide were achieved according to the previously reported procedure.[1]

All catalysts here were of analytical grade. Sulfuric acid (98%) from local suppliers was used without any pretreatment. 12-Tungstophosphoric acid ($H_3PW_{12}O_{40}$, Sigma-Aldrich Co., Llc.) and 12-tungstosilicic acid ($H_4SiW_{12}O_{40}$, Aladdin Reagent Inc.) were dried at 130 °C for 2 h under air flow to remove physisorbed water. Then, six moles of hydrate water were attributed to each mole of $H_3PW_{12}O_{40}$ or $H_4SiW_{12}O_{40}$ by thermogravimetric analysis. Amberlyst-15 (ion exchange capacity: 4.7 mmol g^{-1}, Romn and Hass) and Nafion-H (NR-50, ion exchange capacity: 0.8 mmol g^{-1}, Alfa-aesa) were used as received, while Amberlyst-70 (ion exchange capacity: 2.55 mmol g^{-1}, Romn and Hass) was dried at 105 ^{o}C for 10 h to remove large amounts of water prior to use.

2. Experimental Procedure and Quantification

2.1 Experimental Procedure

General procedure for the etherification of alcohol with DMET (Table 1): Alcohol (2 mmol), DMET (43 mmol) and $H_3PW_{12}O_{40}$ (0.026 mmol) were loaded into a 20 mL stainless steel autoclave reactor provided with a manometer, automatic temperature controller and a magnetic stirring bar. Subsequently, the sealed reactor was heated to 150 ^{o}C with stirring (900 rpm) for 60 min under autogenous pressure. After reaction, the autoclave was cooled down to room temperature.

General procedure for the reaction of isosorbide with etherification agent (Fig. 4): Isosorbide (2 mmol), etherification agent (4.5 mL) and $H_3PW_{12}O_{40}$ (0.026 mmol) were loaded into a 20 mL stainless steel autoclave reactor provided with a manometer, automatic temperature controller and a magnetic stirring bar. Subsequently, the sealed reactor was heated to 150 ^{o}C with stirring (900 rpm) for 60 min under autogenous pressure. After reaction, the autoclave was cooled down to room temperature.

Recyclability of $H_3PW_{12}O_{40}$ for the reaction of isosorbide with DMET: Isosorbide (2 mmol) was reacted with DMET (43 mmol) using $H_3PW_{12}O_{40}$ (0.026 mmol) as catalyst at 150 ^{o}C with stirring (900 rpm) for 60 min. At the end of the reaction, with the addition of hexane, the reaction mixtures were separated into two layers after centrifugation. The transparent upper layer (cyclohexane and DMET as solvents) was withdrawn for quantitative analysis. The bottom layer containing $H_3PW_{12}O_{40}$ was washed with the mixture of DMET/hexane (1/1, v/v) three times, centrifuged and dried at 130 °C. The recovered solid was added to the new substrates directly for the next run.

2.2 Quantification

A HP-INNOWAX capillary column (30 m × 0.32 mm × 0.25 μm) was employed to separate the reaction mixtures under the following oven temperature program with splitless injection mode.

$$50\ ^{\circ}\mathrm{C} \xrightarrow{40\ ^{\circ}\mathrm{C/min}} 120\ ^{\circ}\mathrm{C} \xrightarrow{15\ ^{\circ}\mathrm{C/min}} 250\ ^{\circ}\mathrm{C} \xrightarrow{5\ \mathrm{min}} 250\ ^{\circ}\mathrm{C}$$

The catalytic results were exhibited here either in terms of conversion or in terms of yields towards desired methyl ethers, were expressed in mol% and determined by GC internal standard method using naphthalene as internal standard. All results were calculated based on the initial amount of isohexide (isosorbide, isomannide and isoidie).

In the case of the etherification of either isomannide or isoidide, the quantification of the monoether, diether and starting diol were determined by assuming the same FID response factors as monomethyl isosorbide, dimethyl isosorbide and isosorbide, respectively, due to their corresponding isomeric relationships. With respect of the quantification of isosorbide-derived byproducts containing other substituents, the monoether and diether byproducts were determined by assuming the same FID response factors as monomethyl isosorbide and dimethyl isosorbide, respectively.

The conversion of isohexides and the yields of corresponding mono- and diether products, expressed as mol%, were determined as below.

$$\text{Isohexide conversion (mol\%)} = \left(1 - \frac{\text{moles of unreacted isohexide}}{\text{moles of initial isohexide}}\right) \times 100\%$$

$$\text{Monoether yield (mol\%)} = \left(\frac{\text{moles of formed monoether}}{\text{moles of initial isohexide}}\right) \times 100\%$$

$$\text{Diether yield (mol\%)} = \left(\frac{\text{moles of formed diether}}{\text{moles of initial isohexide}}\right) \times 100\%$$

When *n*-butanol or *n*-hexanol was employed as staring reagent, GC analysis of products was performed on a DB-5 capillary column (30 m × 0.53 mm × 0.5 μm) under the following oven temperature program with split injection model.

$$50\ ^{\circ}\text{C} \xrightarrow{2\ \text{min}} 50\ ^{\circ}\text{C} \xrightarrow{10\ ^{\circ}\text{C/min}} 220\ ^{\circ}\text{C}$$

The catalytic results are shown here as conversion of alcohols (*n*-butanol and *n*-hexanol) and yields of methyl ethers, expressed as mol%, and calculated by GC internal standard method using mesitylene as internal standard. All results were calculated based on the initial amount of alcohol. The conversion of alcohol and the yields of corresponding methyl ether, expressed as mol%, were determined as below.

$$\text{Alcohol conversion (mol\%)} = \left(1 - \frac{\text{moles of unreacted alcohol}}{\text{moles of initial alcohol}}\right) \times 100\%$$

$$\text{Methyl ether yield (mol\%)} = \left(\frac{\text{moles of formed methyl ether}}{\text{moles of initial alcohol}}\right) \times 100\%$$

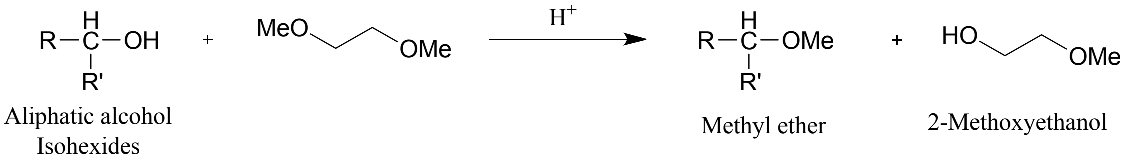
3. Catalytic Results for Etherification of Isosorbide with Different Reagents

Table S1 Reaction of isosorbide with different etherification agents[a]

Entry	Etherification agent	Isosorbide conversion (%)	GC Yield (%)	
			Methyl ethers	Other ethers
1	Methanol	1	1	–
2	Methyl *tert*-butyl ether	17	10	5[b]
3	*n*-Butyl methyl ether	43	27	11[c]
4	1,2-Dimethoxyethane	87	76	3[d]

[a] Reaction conditions: Isosorbide (2 mmol), $H_3PW_{12}O_{40}$ (0.026 mmol), etherification agent (4.5 mL), 150 °C, 60min. Data given by GC internal standard method. [b] Isosorbide-derived ethers containing *tert*-butyl substituent. [c] Isosorbide-derived ethers containing *n*-butyl substituent. [d] Isosorbide-derived ethers containing methoxyethyl substituent.

4. Possible Reaction Pathway for the Etherification of Hydroxyl Groups with DMET



Scheme S1. Possible reaction pathway for etherificaton of hydroxyl group with DMET.

5. Recyclability of $H_3PW_{12}O_{40}$

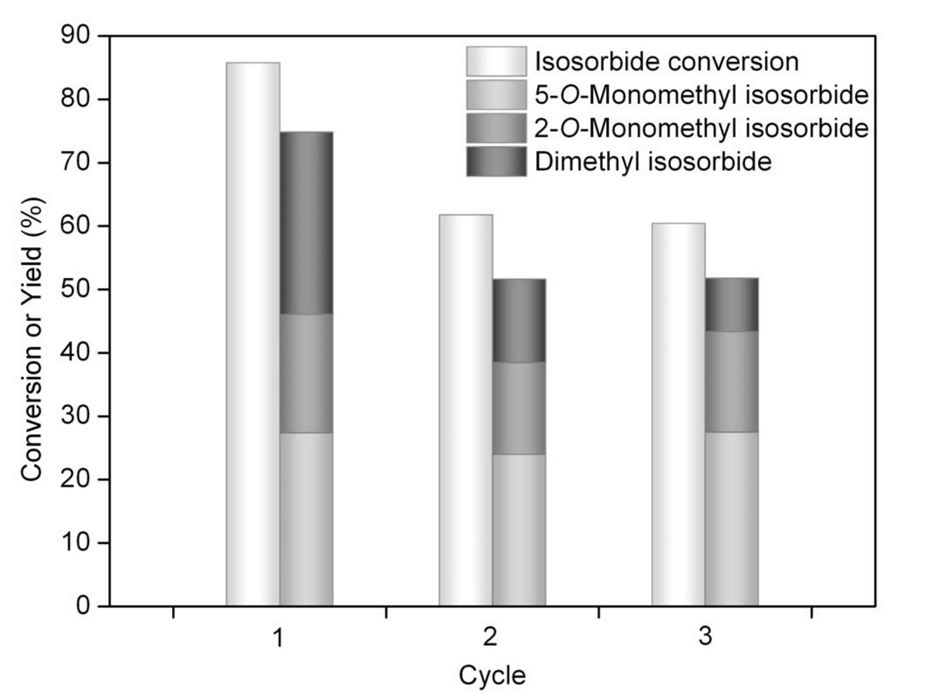


Figure S1. Recycling study of $H_3PW_{12}O_{40}$ for the etherification of isosorbide with DMET. Reaction conditions: Isosorbide (2 mmol), $H_3PW_{12}O_{40}$ (0.026 mmol), DMET (43 mmol), 150 °C for 60 min.

6. Typical GC Trace

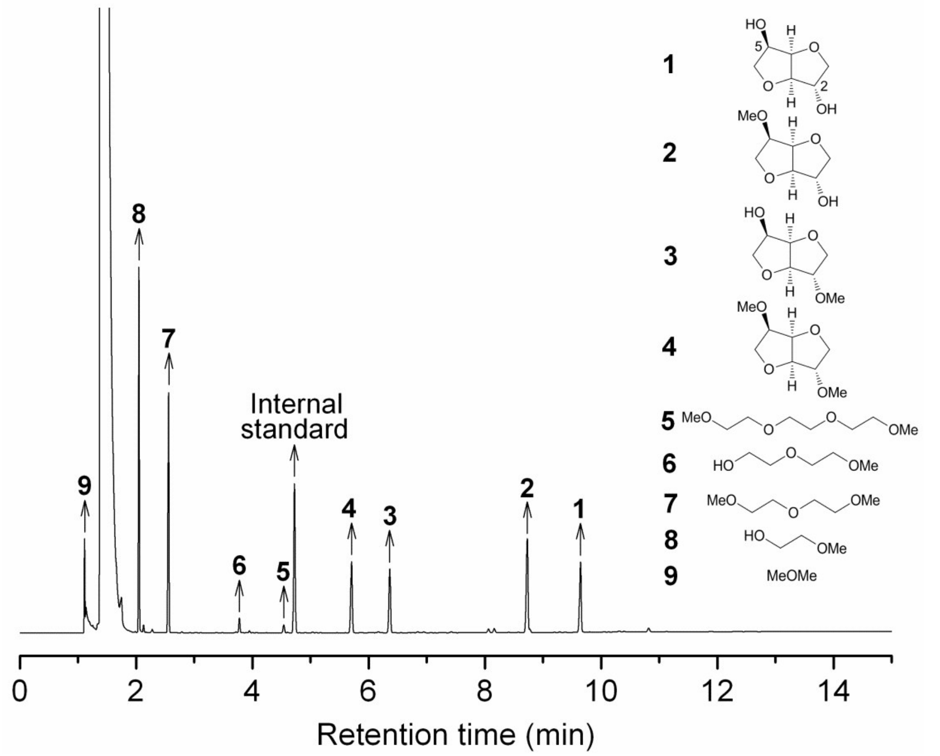


Figure S2. Typical GC trace for the reaction of isosorbide with 1,2-dimethoxyethane catalyzed by $H_3PW_{12}O_{40}$ at 30 min of reaction time.

7. Identification of Major Byproducts for the Etherification of Isosorbide with 1,2-Dimethoxyethane by GC-MS Analysis

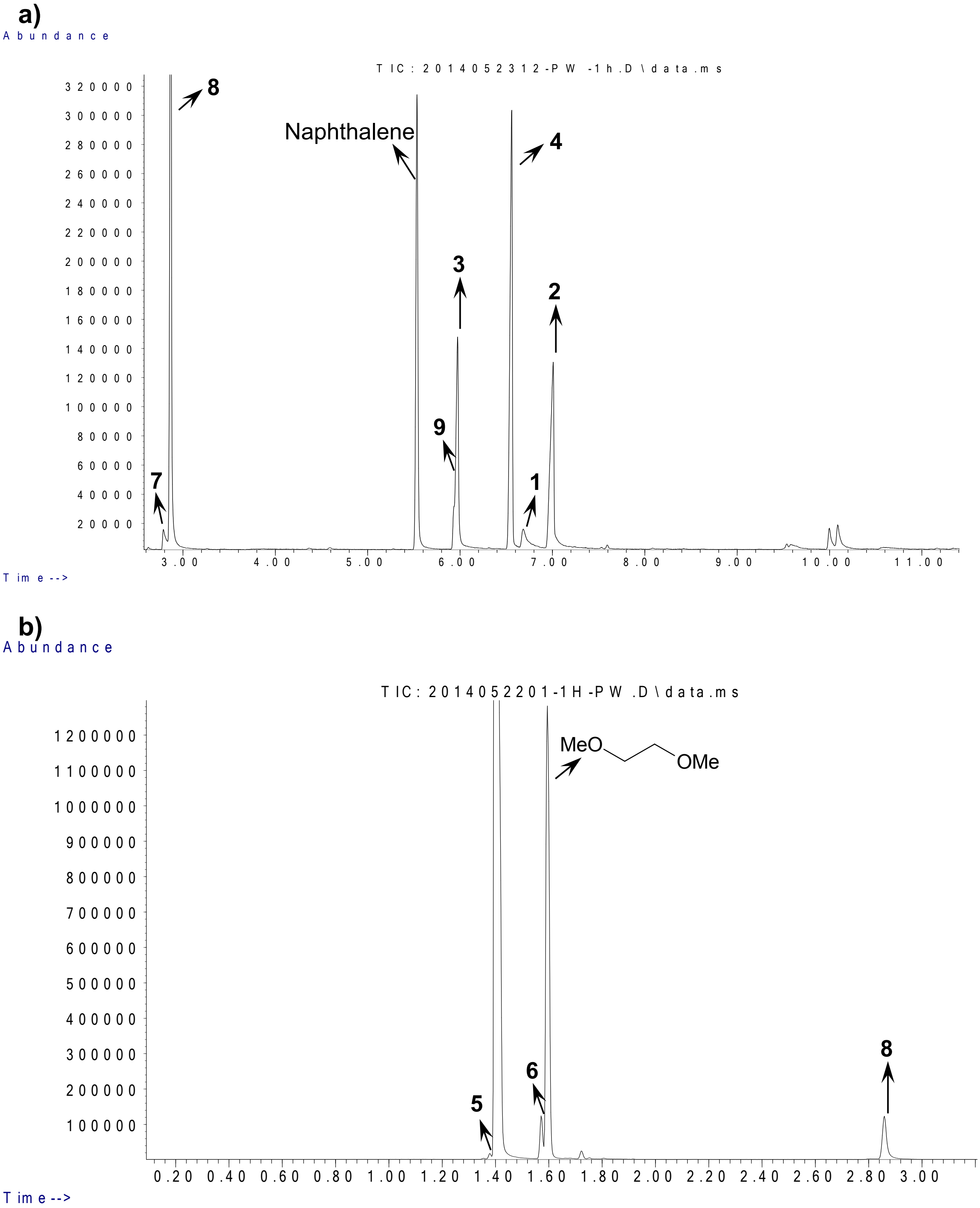


Figure S3. Typical total ion chromatogram (TIC) spectra a) and b) for the etherification of isosorbide with 1,2-dimethoxyethane in the presence of $H_3PW_{12}O_{40}$. Peaks assignment of the etherification reaction mixture: 1: isosorbide, 2: 5-*O*-monomethyl isosorbide, 3: 2-*O*-monomethyl isosorbide, 4: dimethyl isosorbide, 5: dimethyl ether, 6: 2-methoxyethanol, 7: diethylene glycol monomethyl ether, 8: diglyme, 9: triglyme.

The major ether products of isosorbide: dimethyl isosorbide, 2-*O*-monomethyl isosorbide, 5-*O*-monomethyl isosorbide.

The byproducts: 2-methoxyethanol, dimethyl ether, diglyme, diethylene glycol monomethyl ether, triglyme.

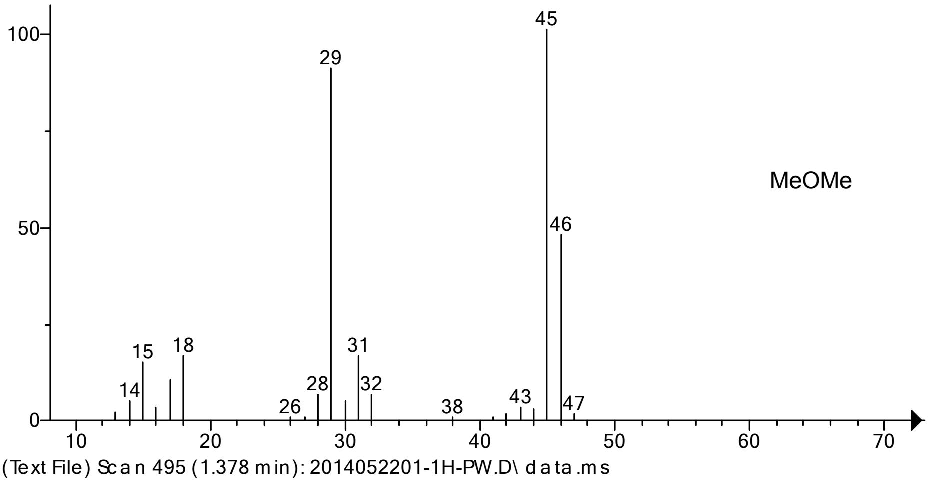


Figure S4. Mass spectrum of dimethyl ether. MS (70 eV): *m/z* 46 (M^+, 48%), 45 (100), 31 (16), 29 (90).

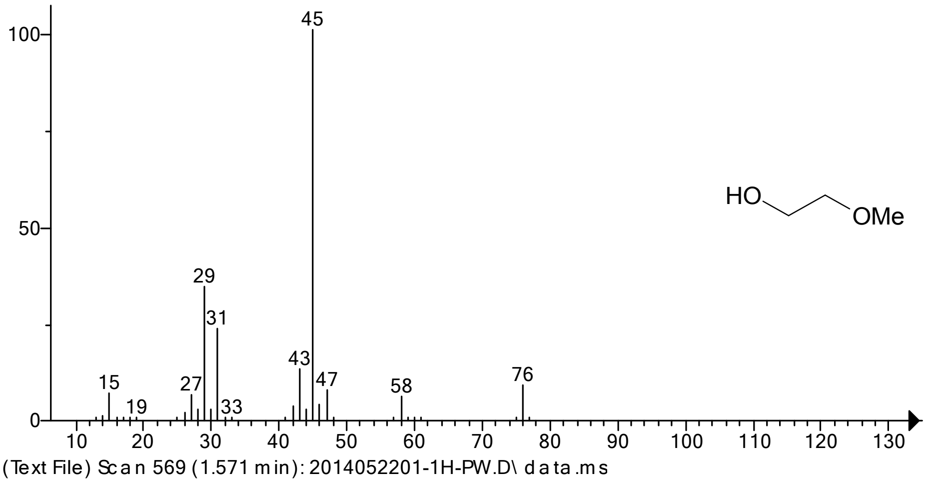


Figure S5. Mass spectrum of 2-methoxyethanol. MS (70 eV): *m/z* 76 (M^+, 9%), 58 (6), 45(100), 31 (23), 29 (34).

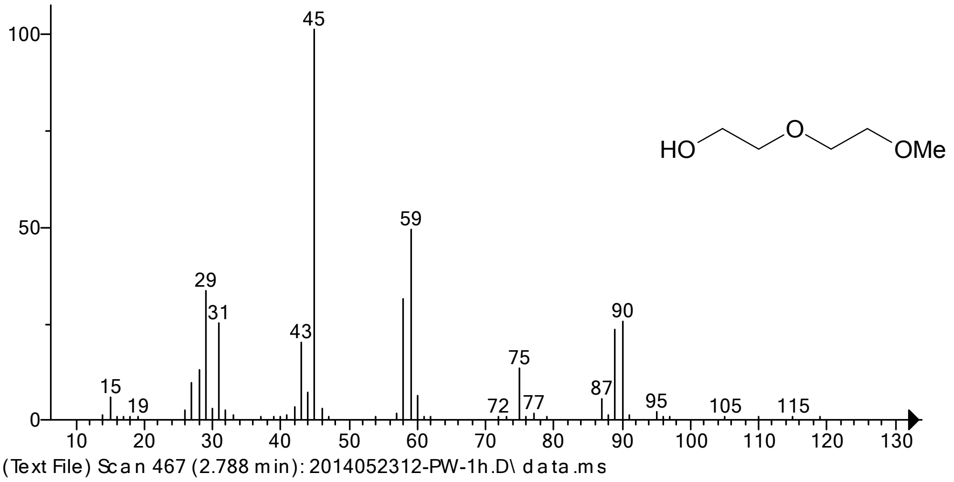


Figure S6. Mass spectrum of diethylene glycol monomethyl ether. MS (70 eV): *m/z* 120 (M^+, 0), 90 (25), 75 (13), 59 (49), 45 (100), 29 (33).

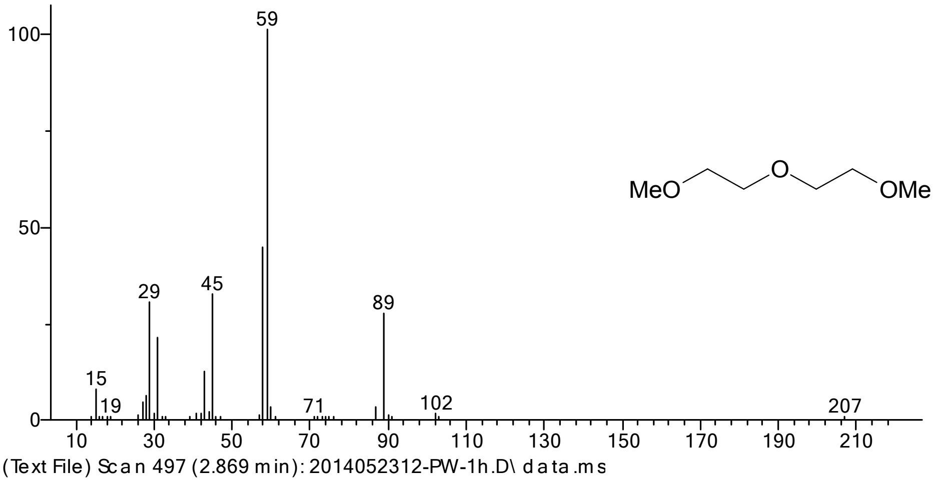


Figure S7. Mass spectrum of diglyme. MS (70 eV): *m/z* 134 (M^+, 0), 102 (1), 89 (27) 59 (100), 45 (32), 29 (30).

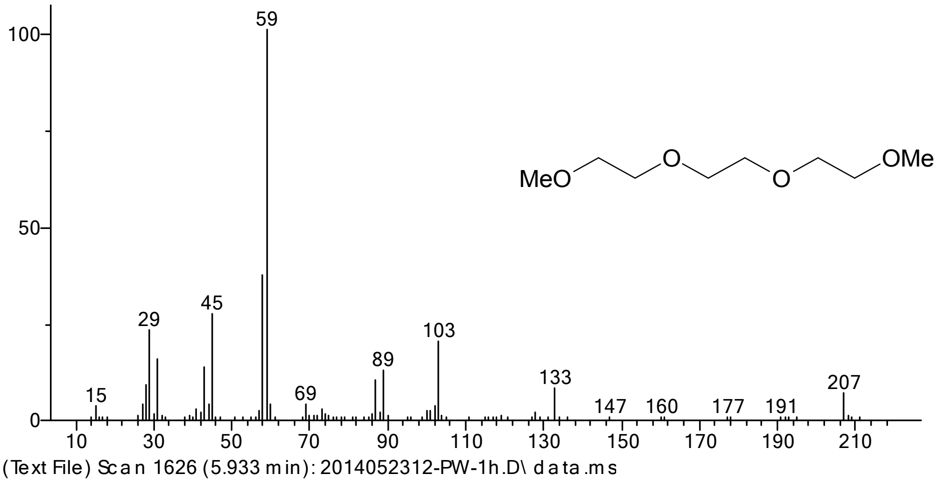


Figure S8. Mass spectrum of triglyme. MS (70 eV): *m/z* 178 (M^+, 0), 133 (10), 103 (20), 89 (10) 59 (100), 45 (30), 29 (20).

8. NMR and MS Traces

8.1 NMR Traces

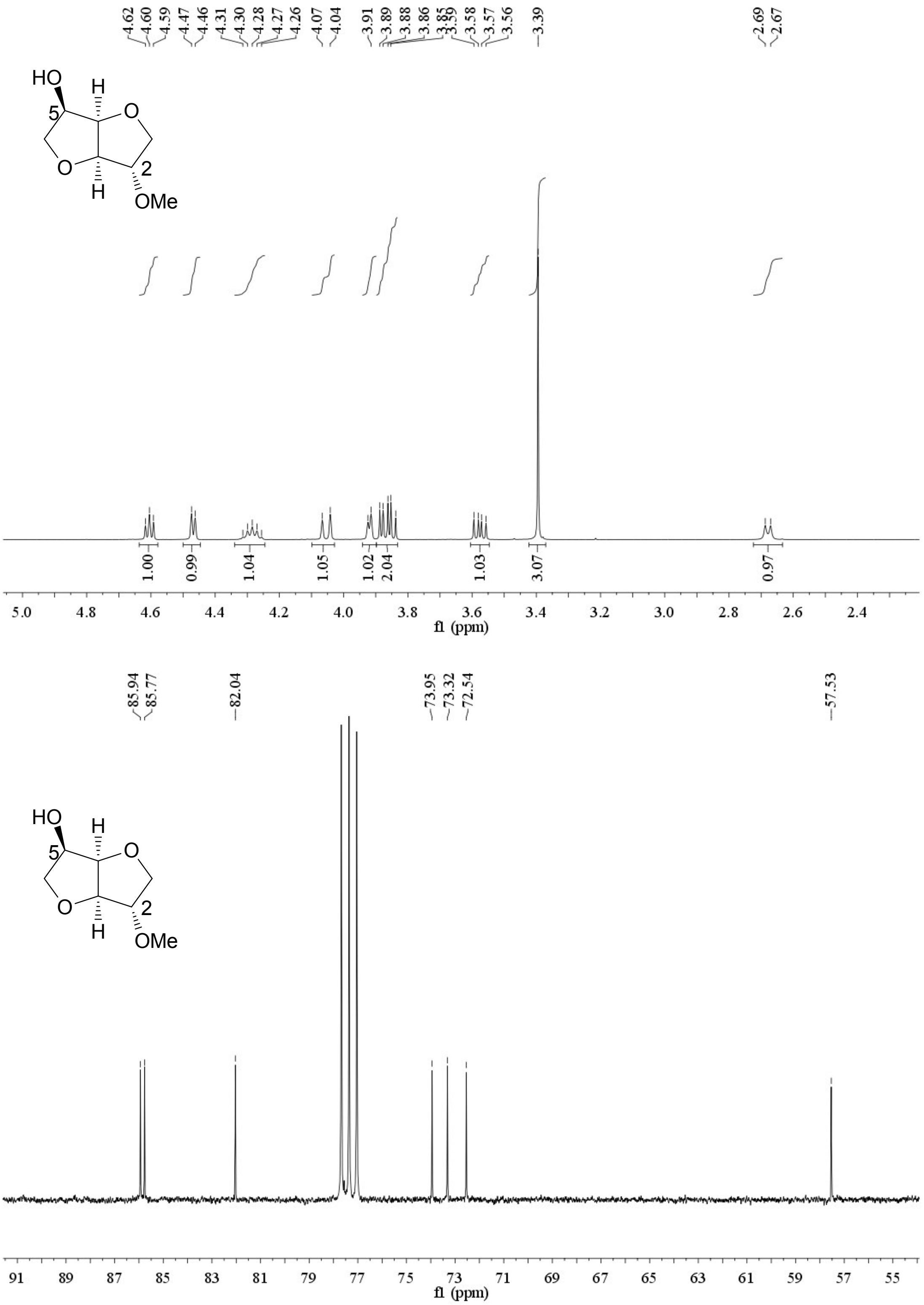


Figure S9. ^1H and ^{13}C NMR spectra of 2-*O*-monomethyl isosorbide in $CDCl_3$ at room temperature.

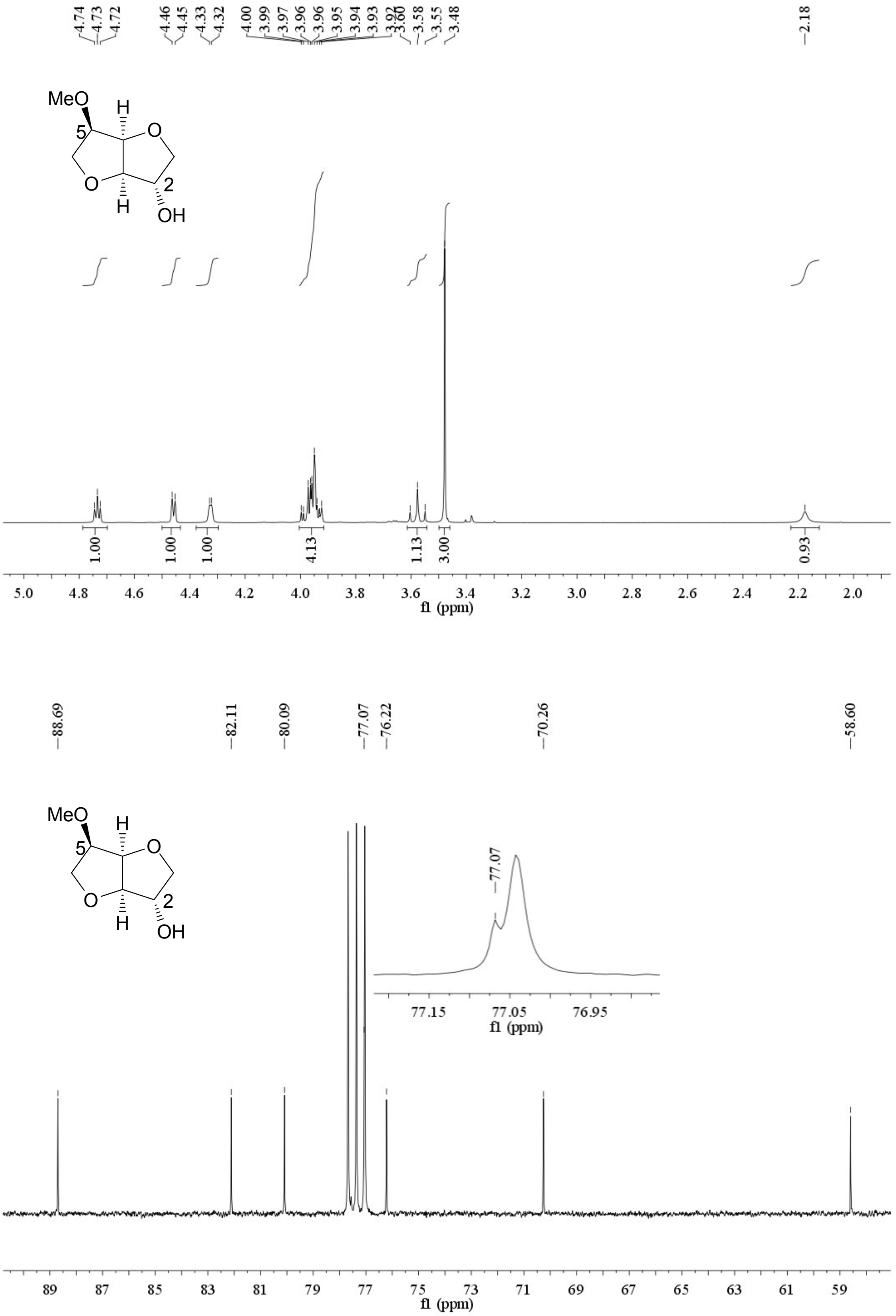


Figure S10. ^{1}H and ^{13}C NMR spectra of 5-*O*-monomethyl isosorbide in $CDCl_3$ at room temperature.

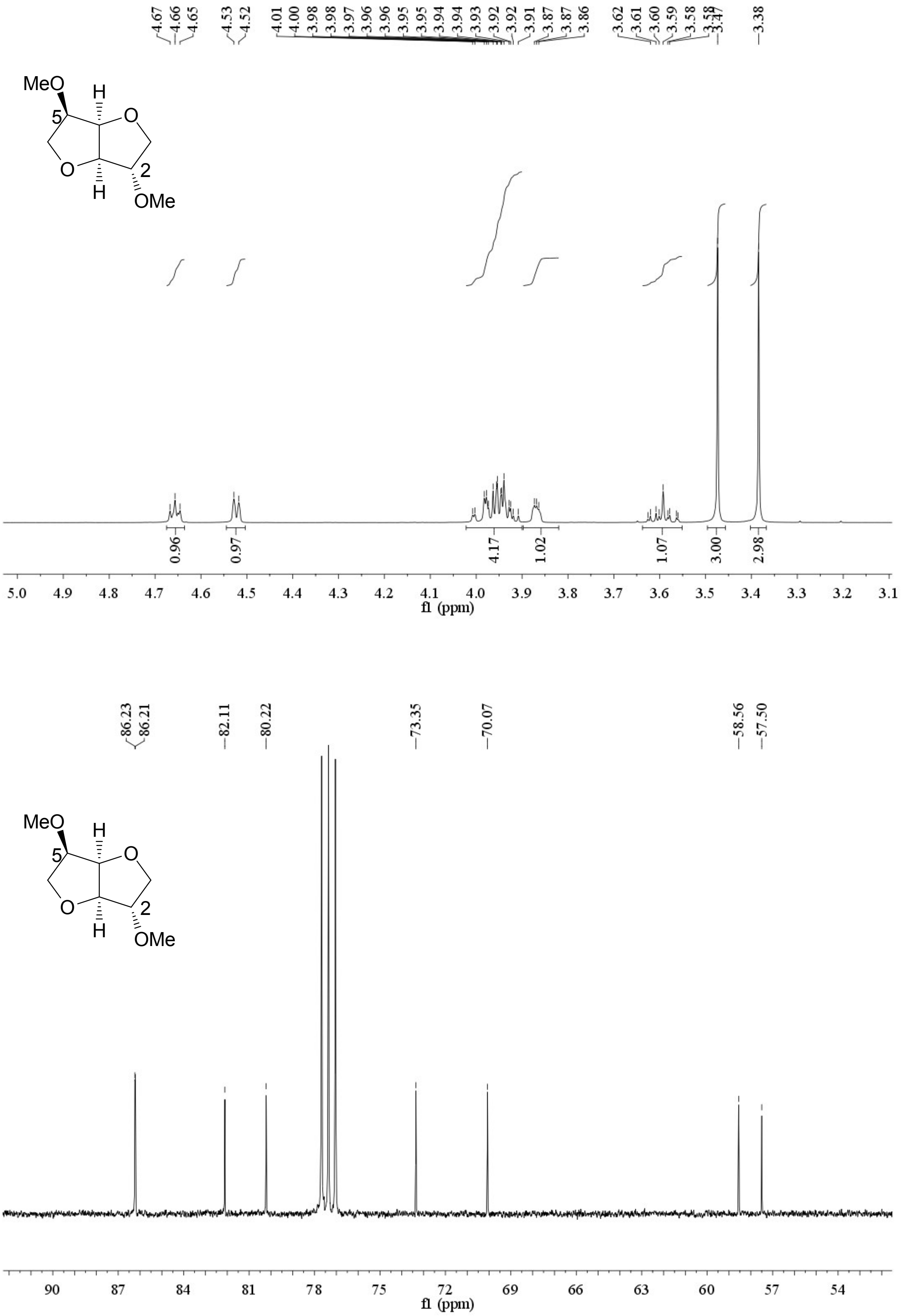


Figure S11. ^1H and ^{13}C NMR spectra of dimethyl isosorbide in $CDCl_3$ at room temperature.

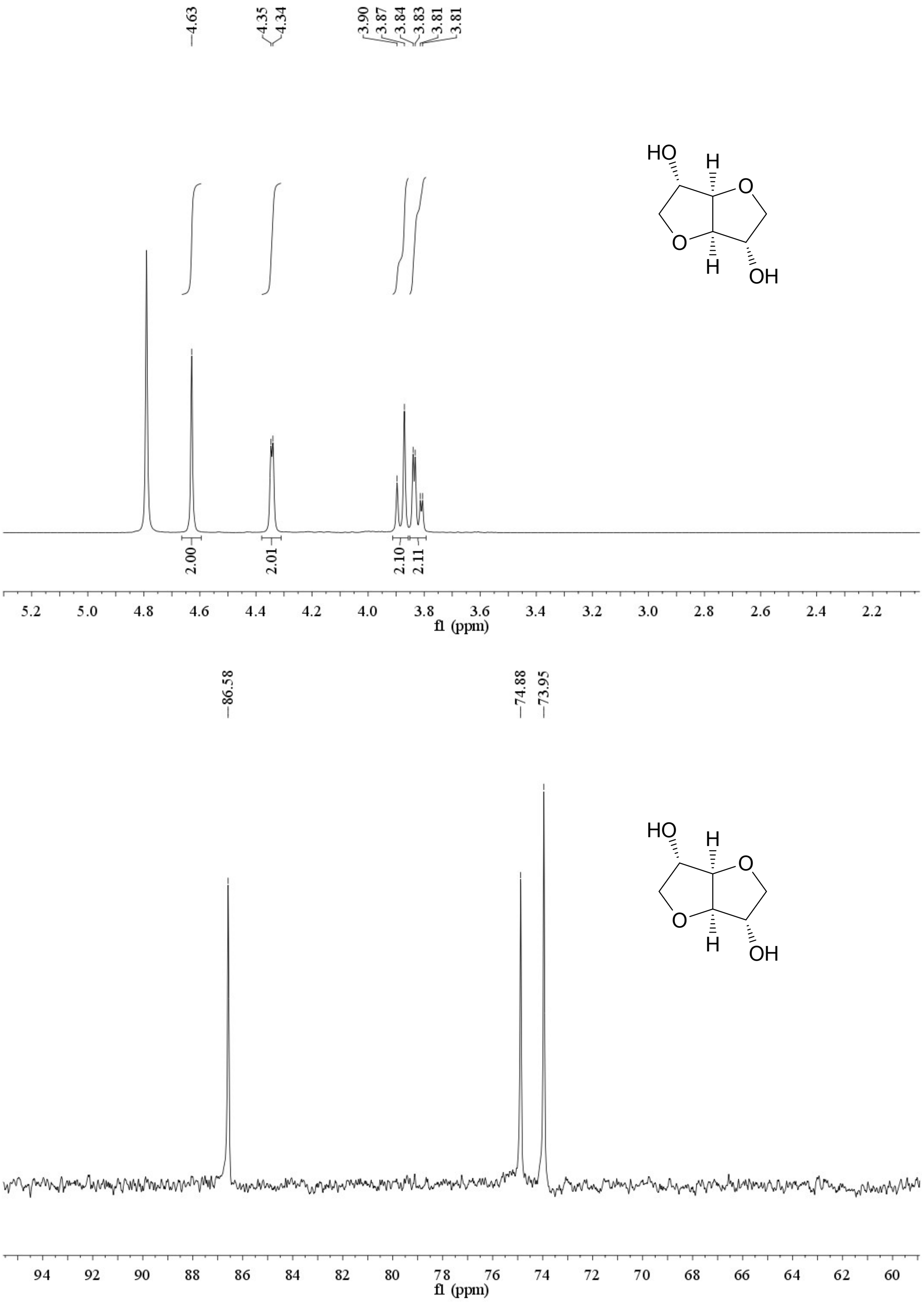


Figure S12. ^{1}H and ^{13}C NMR spectra of isoidide in D_2O at room temperature.

8.2 MS Traces

Etherification of isosorbide with DMET catalyzed by $H_3PW_{12}O_{40}$

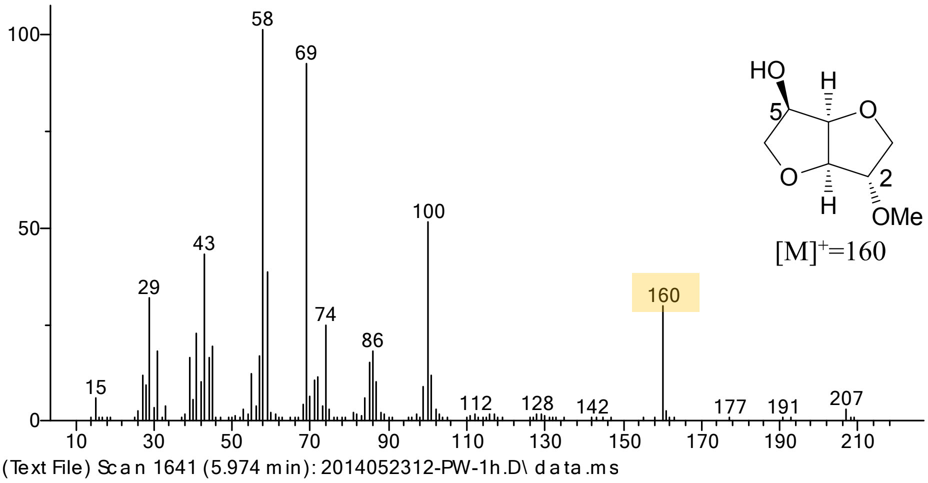


Figure S13. Mass spectrum of 2-*O*-monomethyl isosorbide.

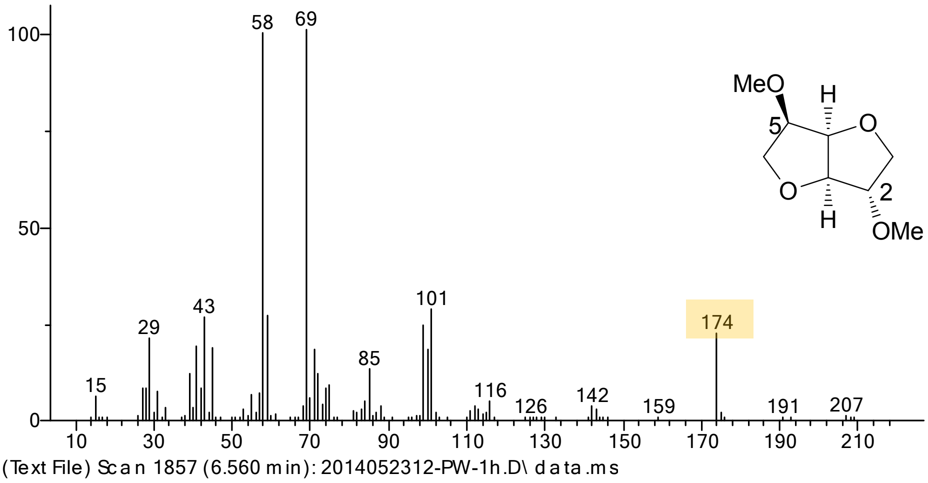


Figure S14. Mass spectrum of dimethyl isosorbide.

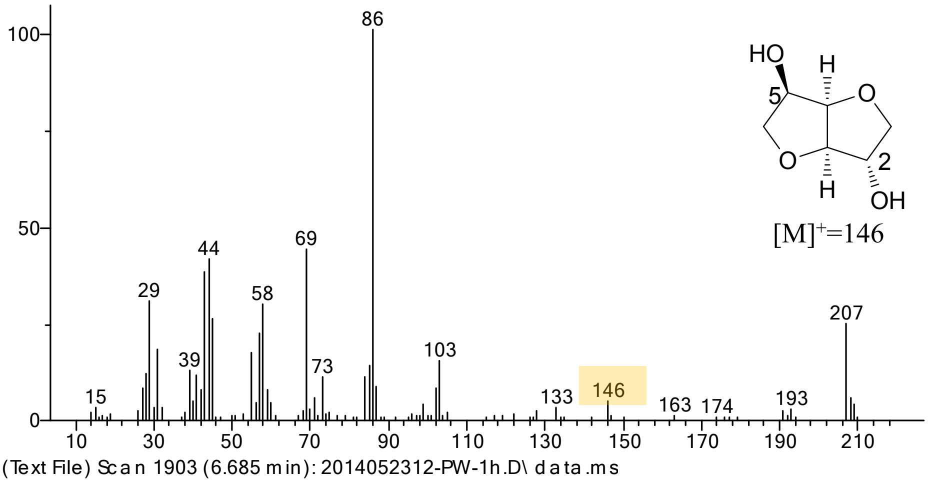
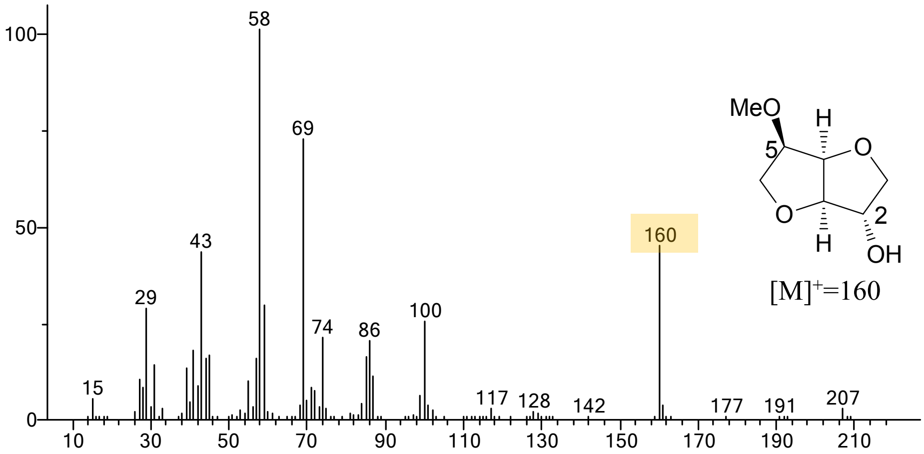
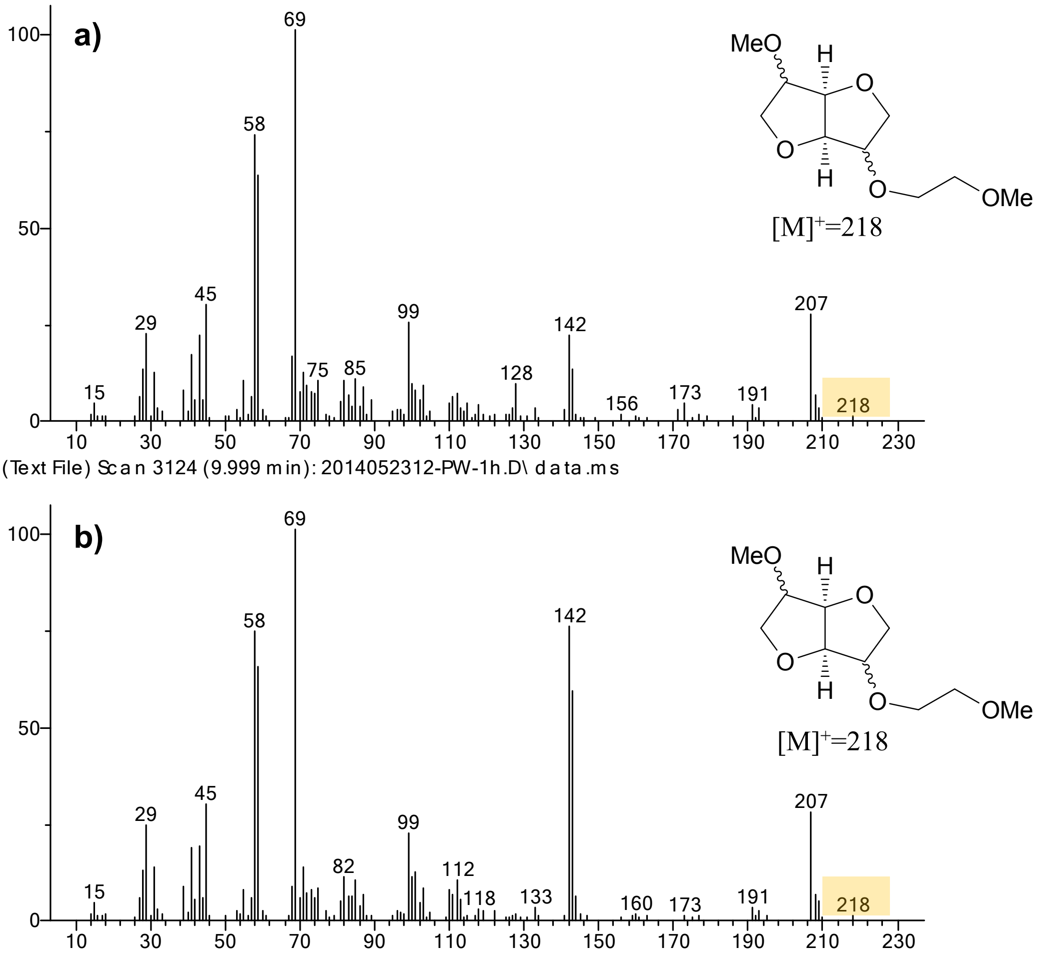


Figure S15. Mass spectrum of isosorbide.



(Text File) Scan 2022 (7.008 min): 2014052312-PW-1h.D\ data.ms

Figure S16. Mass spectrum of 5-*O*-monomethyl isosorbide.



(Text File) Scan 3124 (9.999 min): 2014052312-PW-1h.D\ data.ms

(Text File) Scan 3159 (10.094 min): 2014052312-PW-1h.D\ data.ms

Figure S17. Mass spectra of isosorbide etherified byproducts with the methoxyethyl substituent (a) and (b).

Isosorbide-derived byproducts from the etherification of isosorbide with n-butyl methyl ether catalyzed by $H_3PW_{12}O_{40}$

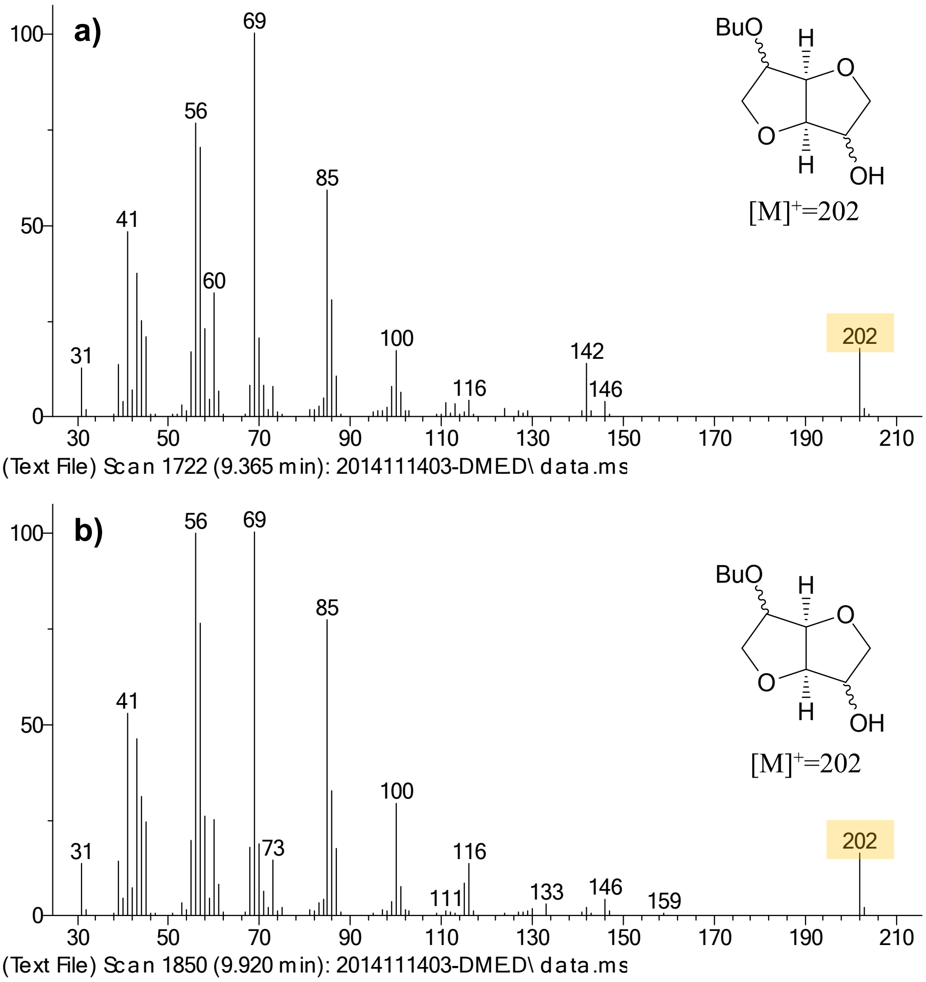
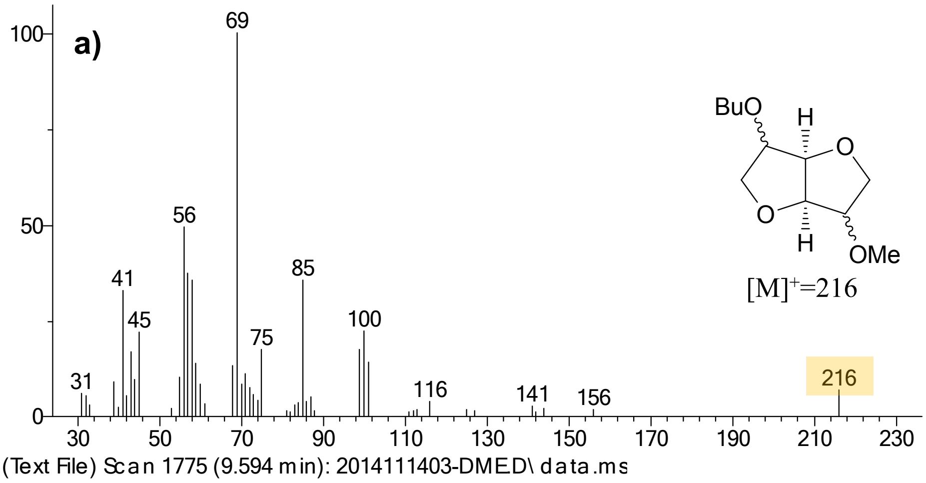


Figure S18. Mass spectra of isosorbide monoether byproducts with *n*-butyl group (a) and (b).



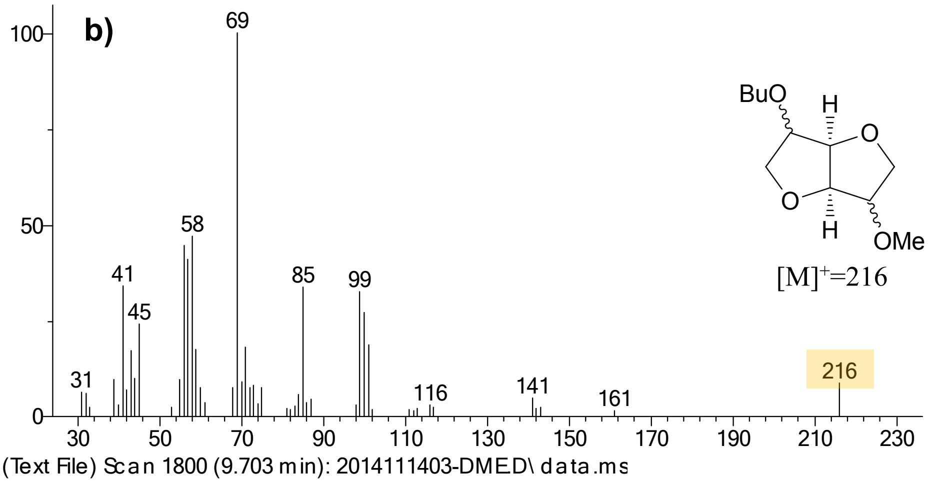


Figure S19. Mass spectra of isosorbide diether byproducts with *n*-butyl group (a) and (b).

Isosorbide-derived byproducts from the etherification of isosorbide with methyl tert-butyl ether catalyzed by $H_3PW_{12}O_{40}$

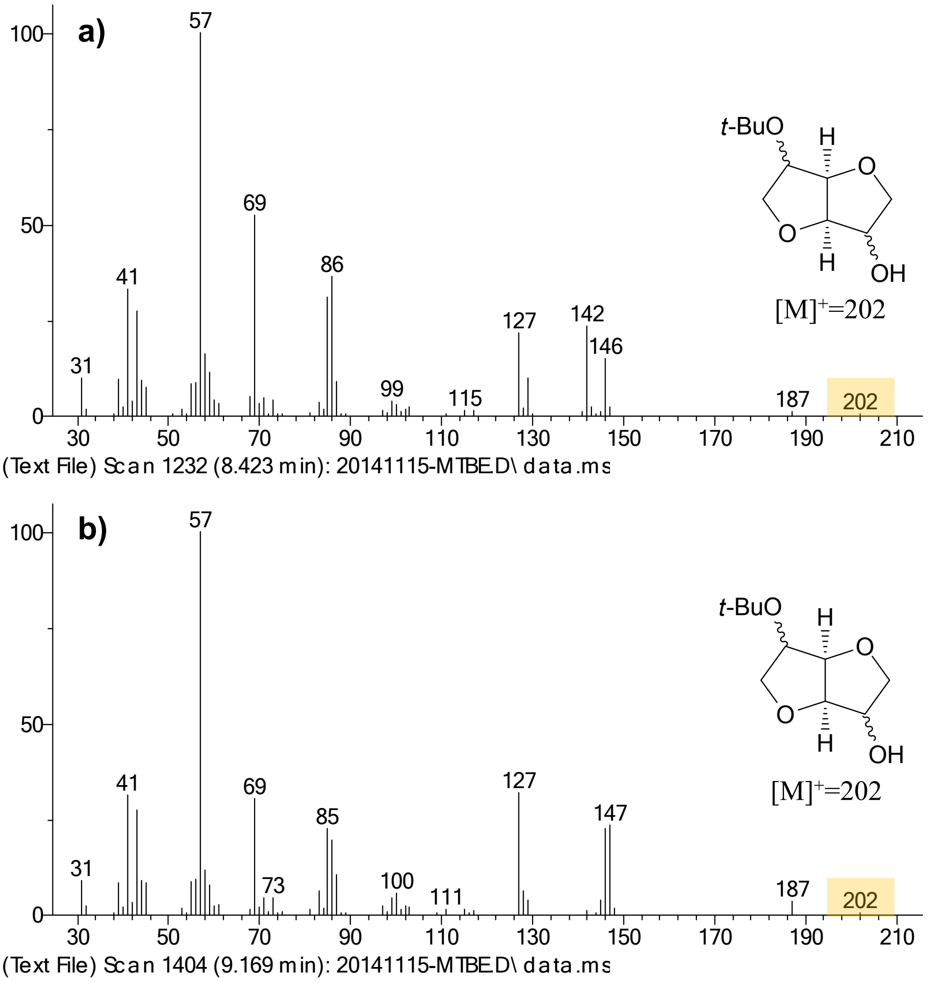


Figure S20. Mass spectra of isosorbide monoether byproducts with *tert*-butyl group (a) and (b).

Etherification of isomannide with DMET catalyzed by $H_3PW_{12}O_{40}$

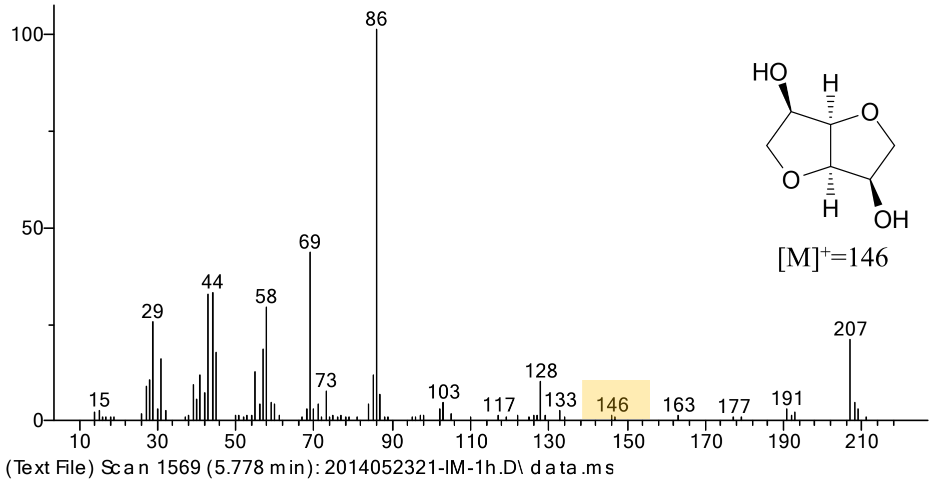


Figure S21. Mass spectrum of isomannide.

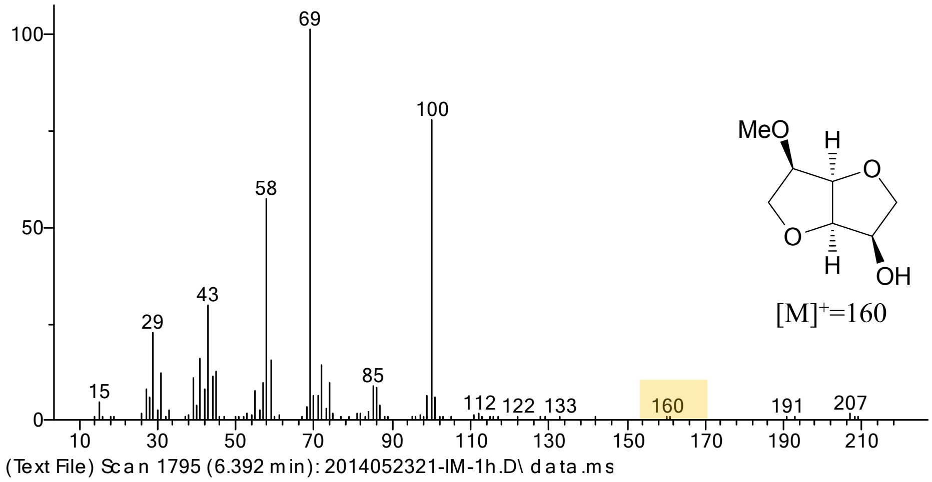


Figure S22. Mass spectrum of monomethyl isomannide.

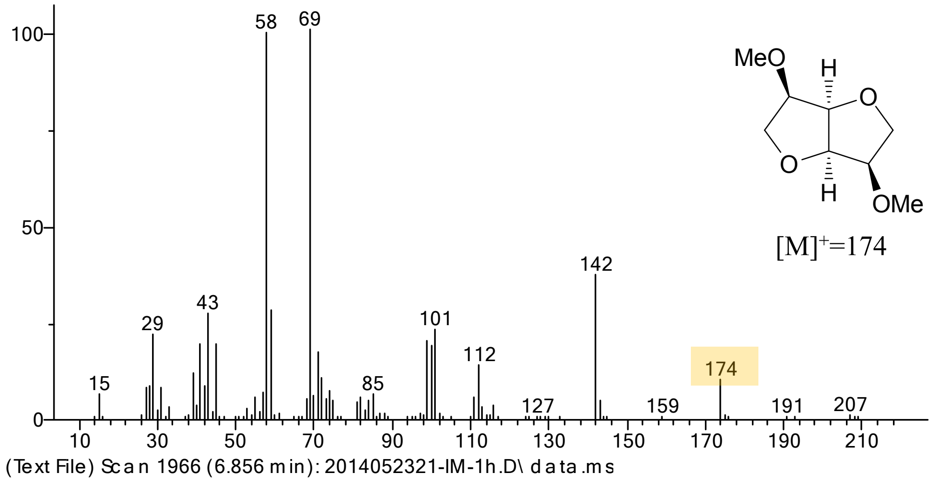


Figure S23. Mass spectrum of dimethyl isomannide.

Etherification of isoidide with DMET catalyzed by $H_3PW_{12}O_{40}$

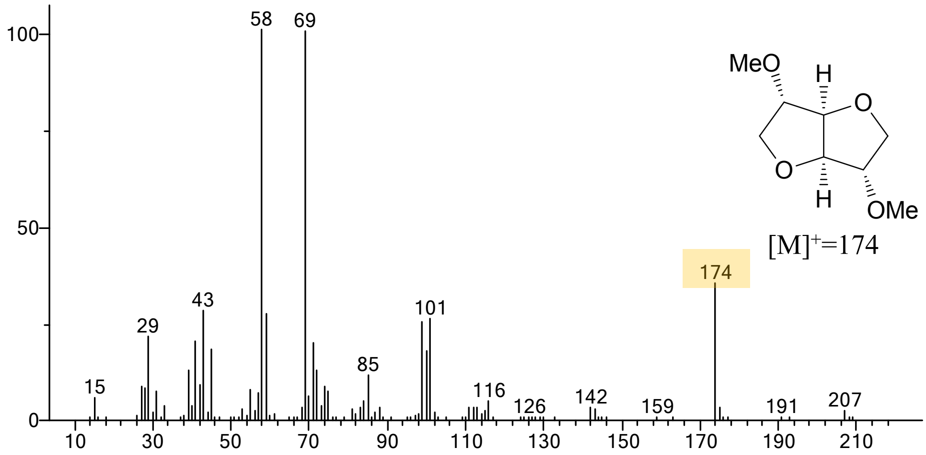


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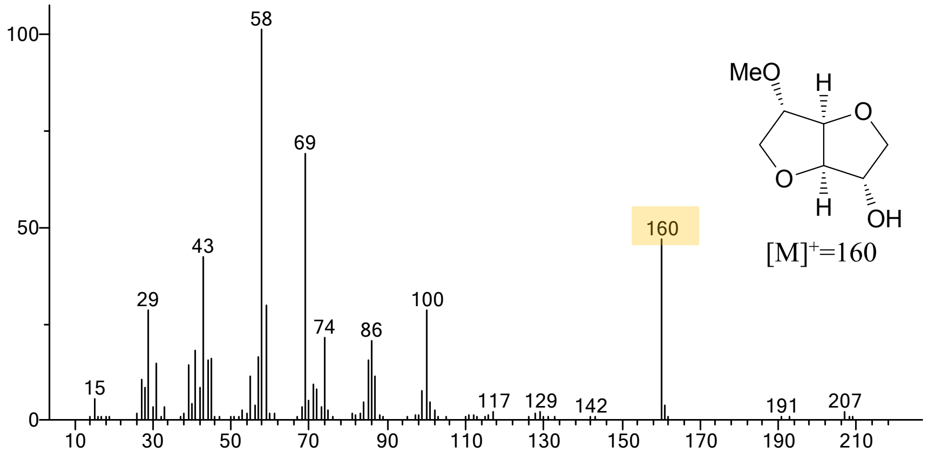
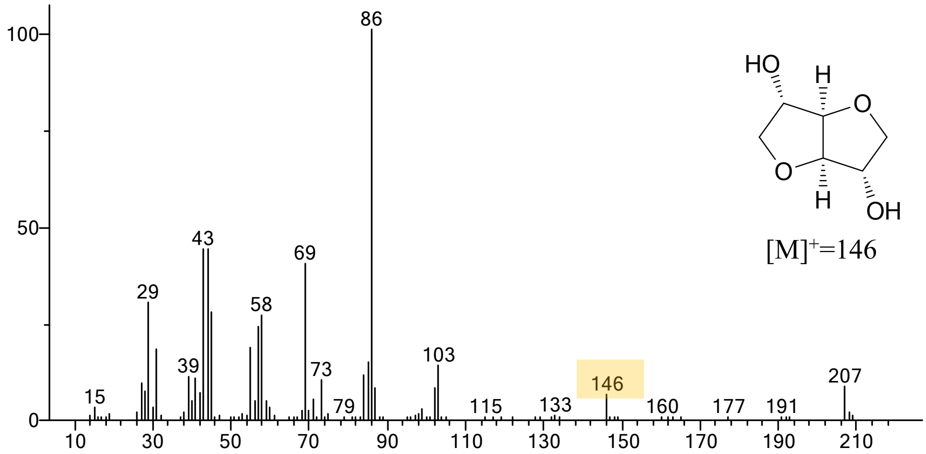
Figure S24. Mass spectrum of dimethyl isoidide.



(Text File) Scan 1949 (6.810 min): 2014052331-II-1h.D\ data.ms

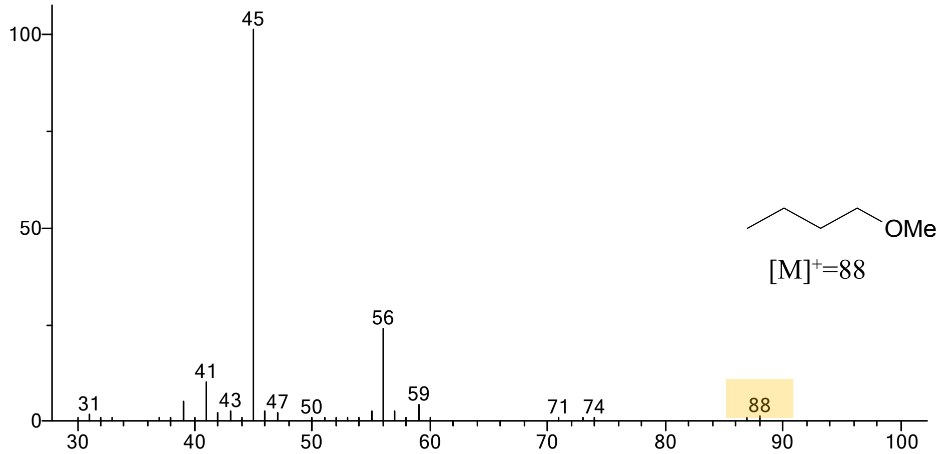
Figure S25. Mass spectrum of monomethyl isoidide.



(Text File) Scan 2205 (7.505 min): 2014052331-II-1h.D\ data.ms

Figure S26. Mass spectrum of isoidide.

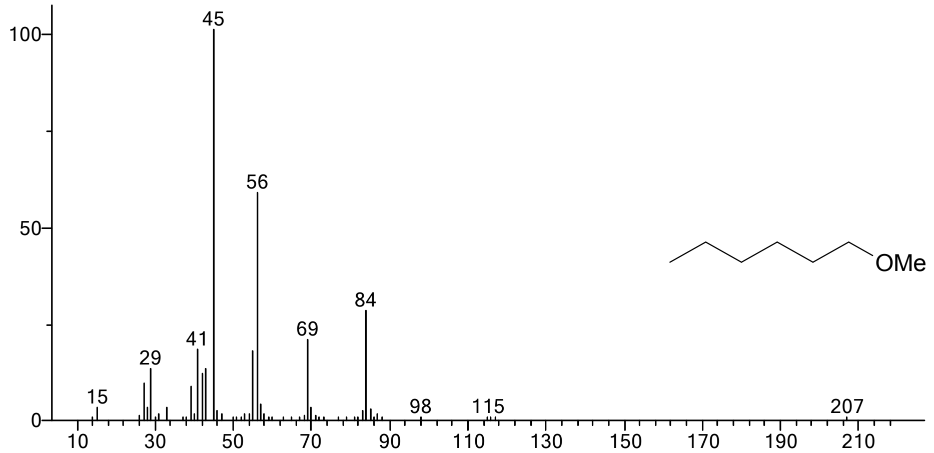
Etherification of n-butanol with DMET catalyzed by $H_3PW_{12}O_{40}$



(Text File) Scan 395 (1.796 min): 2014053001-n-butanol.D\ data.ms

Figure S27. Mass spectrum of *n*-butyl methyl ether.

Etherification of n-hexanol with DMET catalyzed by $H_3PW_{12}O_{40}$



(Text File) Scan 217 (2.109 min): 2014052351-hexanol.D\ data.ms

Figure S28. Mass spectrum of *n*-hexyl methyl ether.

9. Additional Reference

1 J. Le Nôtre, J. van Haveren and D. S. van Es, *ChemSusChem*, 2013, **6**, 693.