

Electronic Supplementary Information

**Trends of intramolecular hydrogen bonding in substituted
alcohols: A deeper investigation**

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Experimental Details

Preparation of 3-ethoxypropan-1-ol (3). 5 g of propane-1,3-diol (**1**) (66 mmol) and 60 mL of dry THF were placed in a 125 mL two-neck round-bottomed flask, fitted with a calcium chloride protected reflux condenser, a dropping funnel, and a magnetic stirrer. 1.6 g (67 mmol) of sodium hydride was added and the reaction mixture was stirred in an ice bath at 0° C for 1 h. Next, 10.4 g (67 mmol) of ethyl iodide in 15 mL of dry THF was gradually added. The ice bath was removed and stirring was continued for another 1 h, under reflux. The solution was cooled to 20° C and water was gradually added to the reaction flask. The organic layer was separated with diethyl ether, dried over MgSO₄ and filtered, and the solvent was evaporated. The crude product was purified by column chromatography, using 3:1 hexane:ethyl acetate as eluent and 230-400 mesh silica gel providing 2.05g of **3** (41% yield).

¹H NMR (600 MHz, CD₃CN): δ (ppm) 3.55 (td, 6.19 Hz, 5.42 2H); 3.47 (t, 6.31 Hz, 2H); 3.43 (q, 7.03 Hz, 2H); 2.65 (t, 5.42 Hz, 1H); 1.69 (quint, 6.27 Hz, 2 H); 1.13 (t, 7.03 Hz, 3 H). ¹³C NMR (150 MHz, CD₃CN): δ (ppm) 68.75; 66.79; 60.40; 33.67; 15.63 (Fig. S1).

Preparation of 3-isopropoxypropan-1-ol (4). The compound was obtained via the same procedure described for **3**, replacing ethyl iodide by isopropyl iodide and yielding 400 mg (8%) of **4**.

¹H NMR (600 MHz, CDCl₃): δ (ppm) 3.77 (t, 5.52 Hz, 2 H); 3.62 (t, 5.73 Hz, 2 H); 3.58 (sept, 6.10 Hz, 1 H); 1.81 (quint, 5.59 Hz, 2 H); 1.16 (d, 6.12 Hz, 6H). ¹³C NMR (150 MHz, CDCl₃): δ (ppm) 72.02; 67.81; 62.64; 32.15; 22.05 (Fig. S3).

Preparation of 3-*tert*-butoxypropan-1-ol (5). 6 g of **1** (78.8 mmol), 9 mL of *tert*-butyl chloride (81.4 mmol) and 12 mL of pyridine were placed in a two-neck 125 mL round-bottom flask, fitted with reflux condenser, and a magnetic stirrer. The mixture was stirred overnight under reflux. Water was added to the reaction flask after. The organic layer was separated with diethyl ether, dried over MgSO₄, filtered and the solvent was evaporated. The crude product was purified by column chromatography, using 3:1 hexane:ethyl acetate as eluent and 230-400 mesh silica gel providing 720 mg of **5** (12% of yield).

¹H NMR (600 MHz, CDCl₃): δ (ppm) 3.76 (dd, 5.40 Hz, 2 H); 3.58 (dd, 5.64 Hz, 2 H); 1.79 (quint, 5.52 Hz, 2 H); 1.20 (s, 9 H). ¹³C NMR (150 MHz, CDCl₃): δ (ppm) 73.49; 63.14; 61.90; 32.45; 27.62(Fig. S3).

Preparation of 3-methylbutane-1,3-diol (8). 5 g of 3-methylbut-3-en-1-ol (58 mmol) and 50 mL of concentrated hydrochloric acid were placed in a 125 mL two-neck round-bottom flask, fitted with a reflux condenser, and a magnetic stirrer. The reaction mixture was stirred for 2 hours. After, water was added to the reaction flask. The organic layer was separated with diethyl ether, dried over MgSO₄ and filtered, and the solvent was evaporated. The crude product was purified by column chromatography, using 3:1 hexane:ethyl acetate as eluent and 230-400 mesh silica gel providing 2.35 g (47% yield).

¹H NMR (600 MHz, CDCl₃): δ (ppm) 3.89 (t, 5.70 Hz, 2 H); 1.74 (t, 5.67 Hz, 2 H); 1.29 (s, 6 H). ¹³C NMR (150 MHz, CDCl₃): δ (ppm) 72.17; 60.33; 43.57; 29.84. (Fig. S3).

Preparation of 3-methyl-3-methoxybutan-1-ol (9). The compound was obtained via the same procedure described for **8**. However, it was added 5 mL of methanol to the reaction mixture yielding 2 g (40%) of **9**.

¹H NMR (600 MHz, CDCl₃): δ (ppm) 3.78 (t, 5.82 Hz, 2 H); 3.29 (s, 3 H); 1.75 (t, 5.82 Hz, 2 H); 1.22 (s, 6 H). **¹³C NMR** (150 MHz, CDCl₃): δ (ppm) 76.41; 59.90; 49.30; 42.48; 24.67. (Fig. S3).

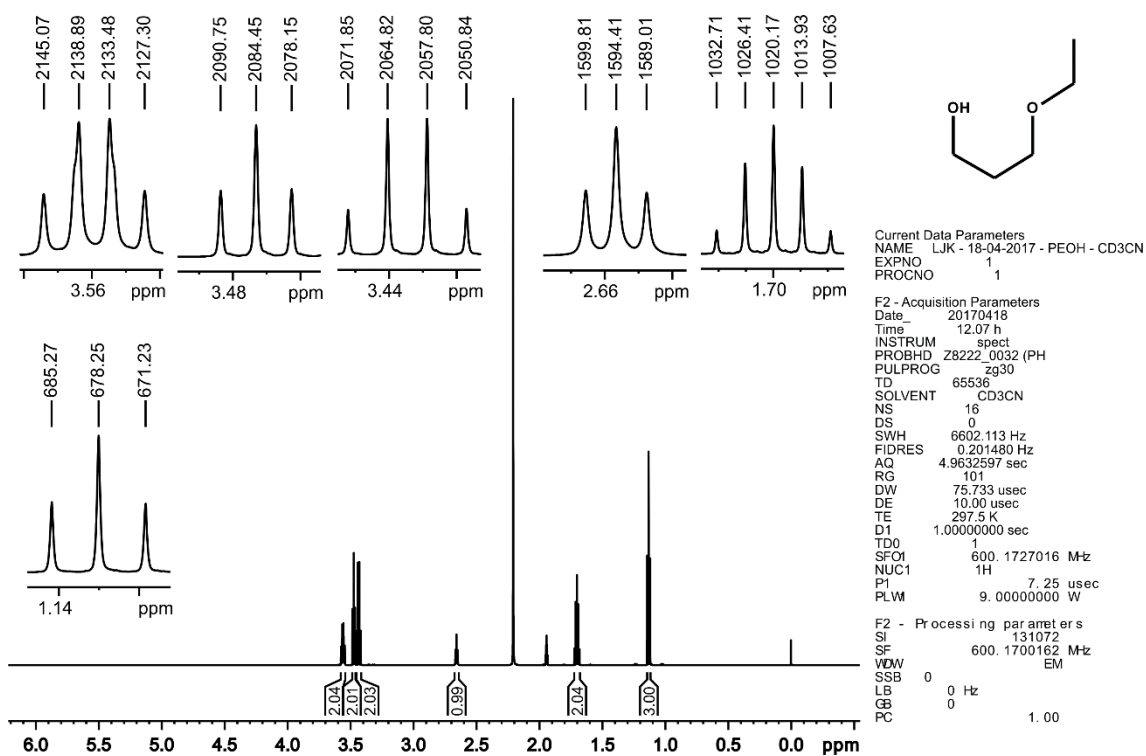


Fig. S1. ^1H NMR spectrum of 3-ethoxypropan-1-ol in CD_3CN acquired at 600 MHz for ^1H .

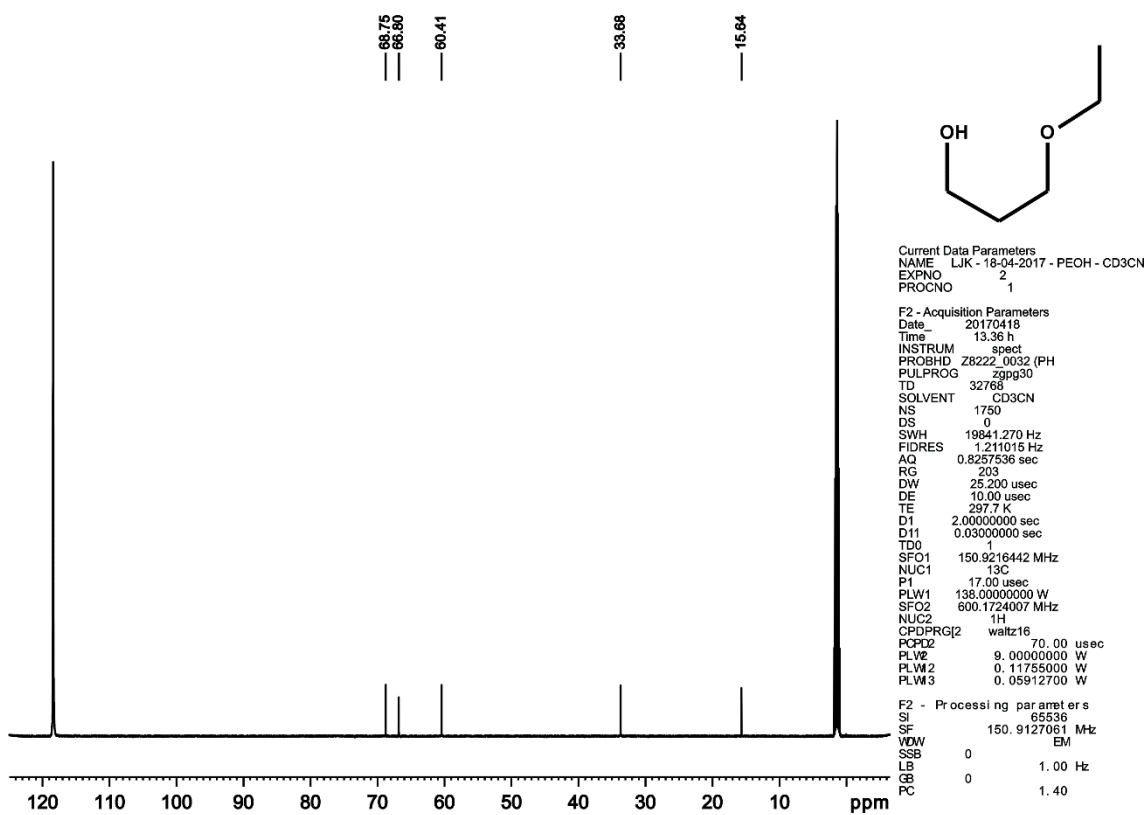


Fig. S2. ^{13}C NMR spectrum of 3-ethoxypropan-1-ol in CD_3CN acquired at 150 MHz for ^{13}C .

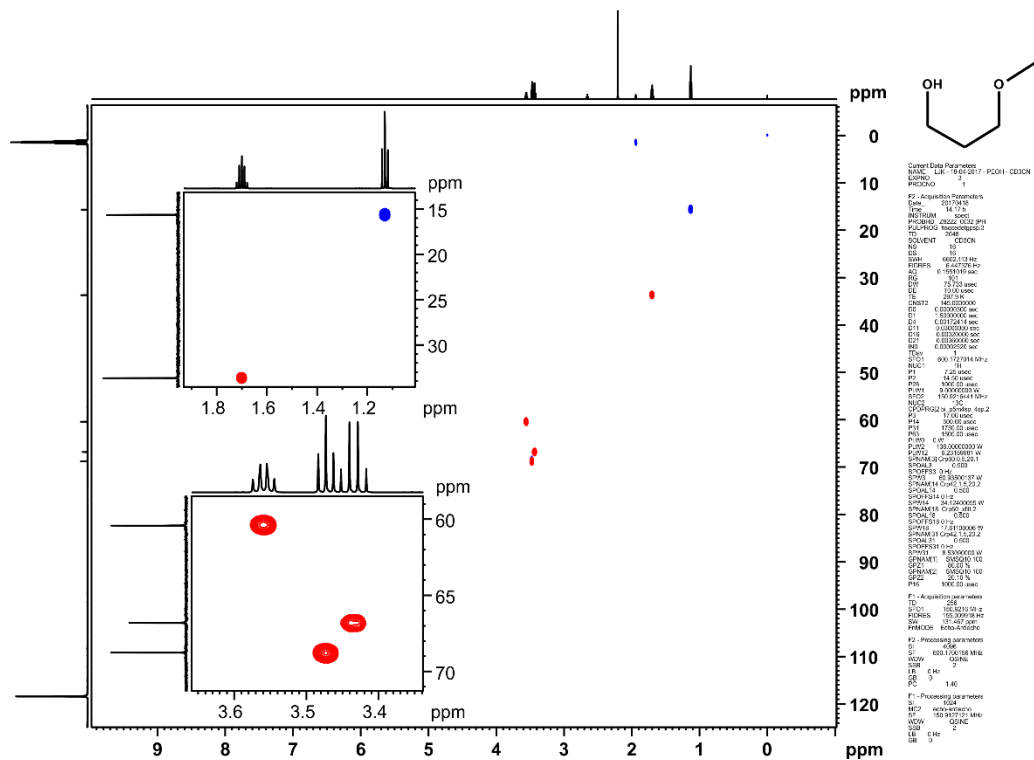


Fig. S3. HSQC contour plot of 3-ethoxypropan-1-ol in CD₃CN (red cross peaks represent CH₂ and blue cross peaks represent CH or CH₃).

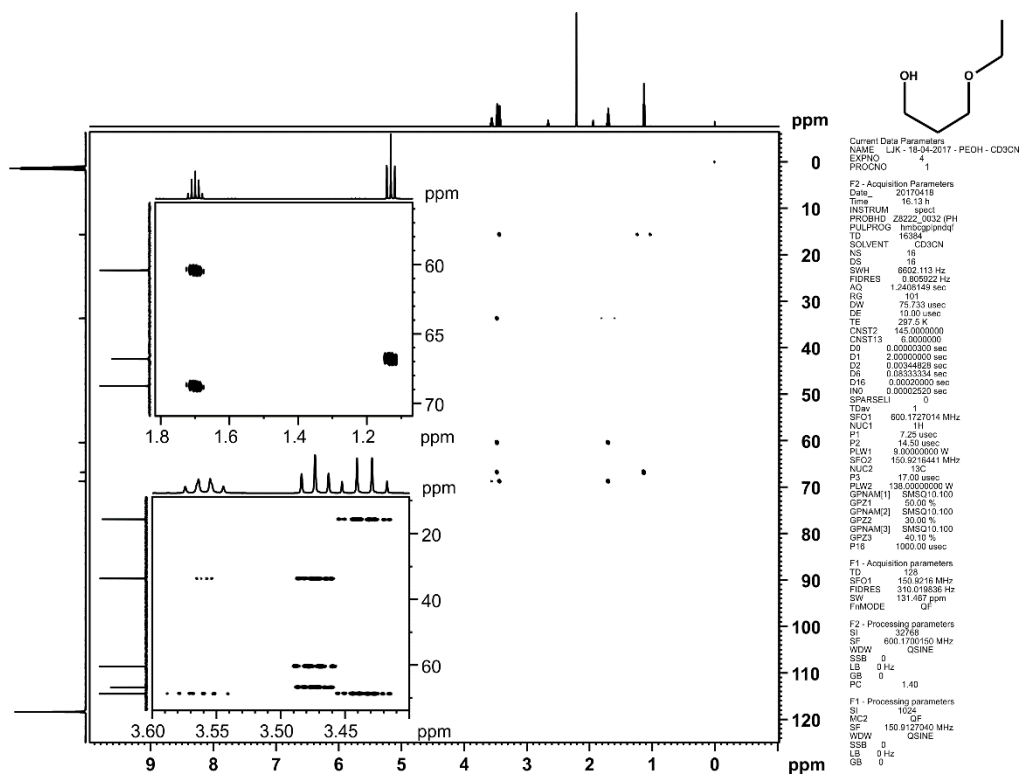


Fig. S4. HMBC contour plot of 3-ethoxypropan-1-ol in CD₃CN.

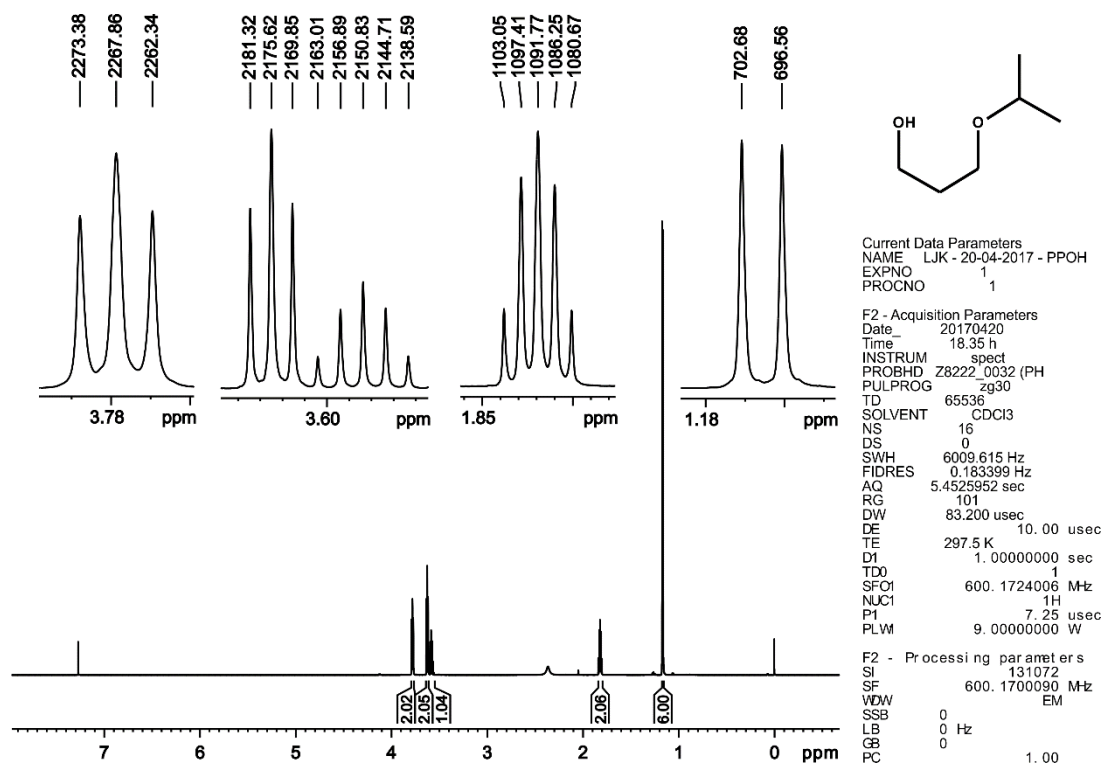


Fig. S5. ^1H NMR spectrum of 3-isopropoxypropan-1-ol in CDCl_3 acquired at 600 MHz for ^1H .

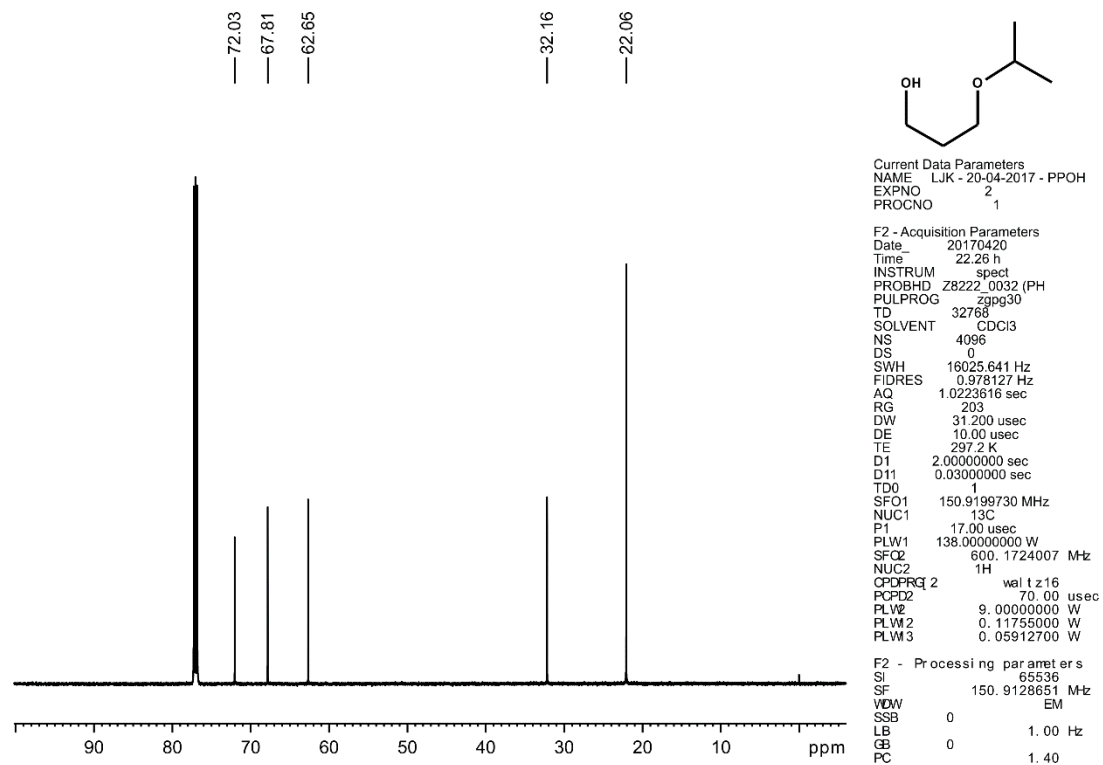


Fig. S6. ^{13}C NMR spectrum of 3-isopropoxypropan-1-ol in CDCl_3 acquired at 150 MHz for ^{13}C .

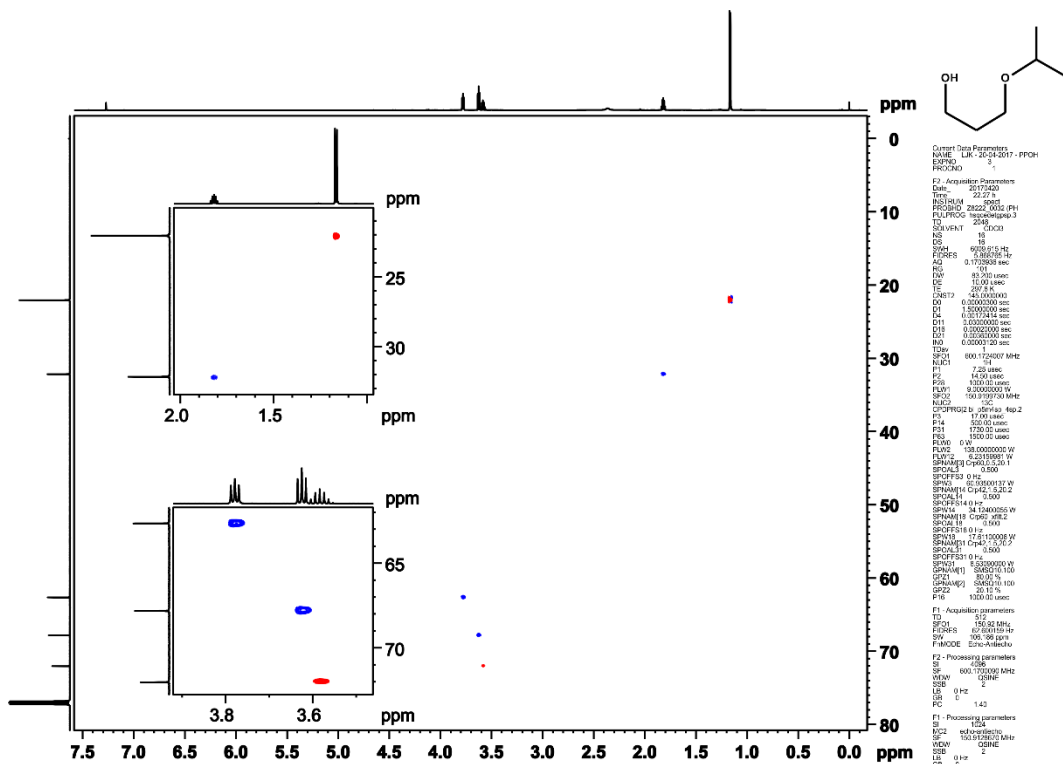


Fig. S7. HSQC contour plot of 3-isopropoxypropan-1-ol in CDCl_3 (red cross peaks represent CH_2 and blue cross peaks represent CH or CH_3).

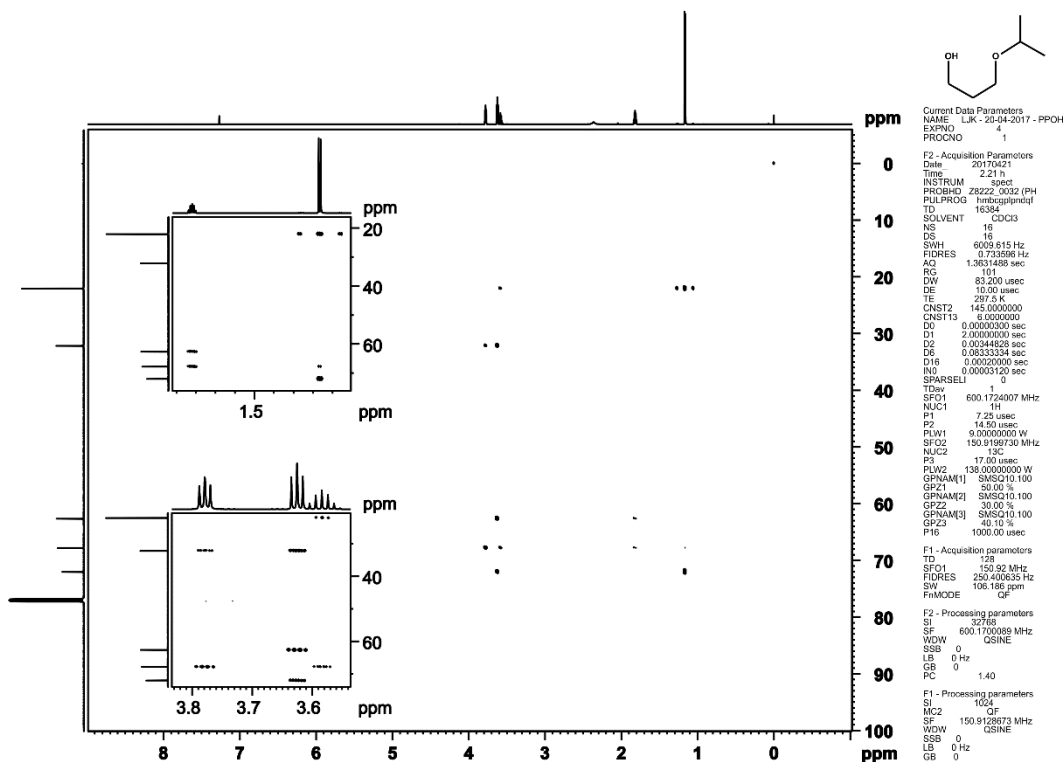


Fig. S8. HMBC contour plot of 3-isopropoxypropan-1-ol in CDCl_3 .

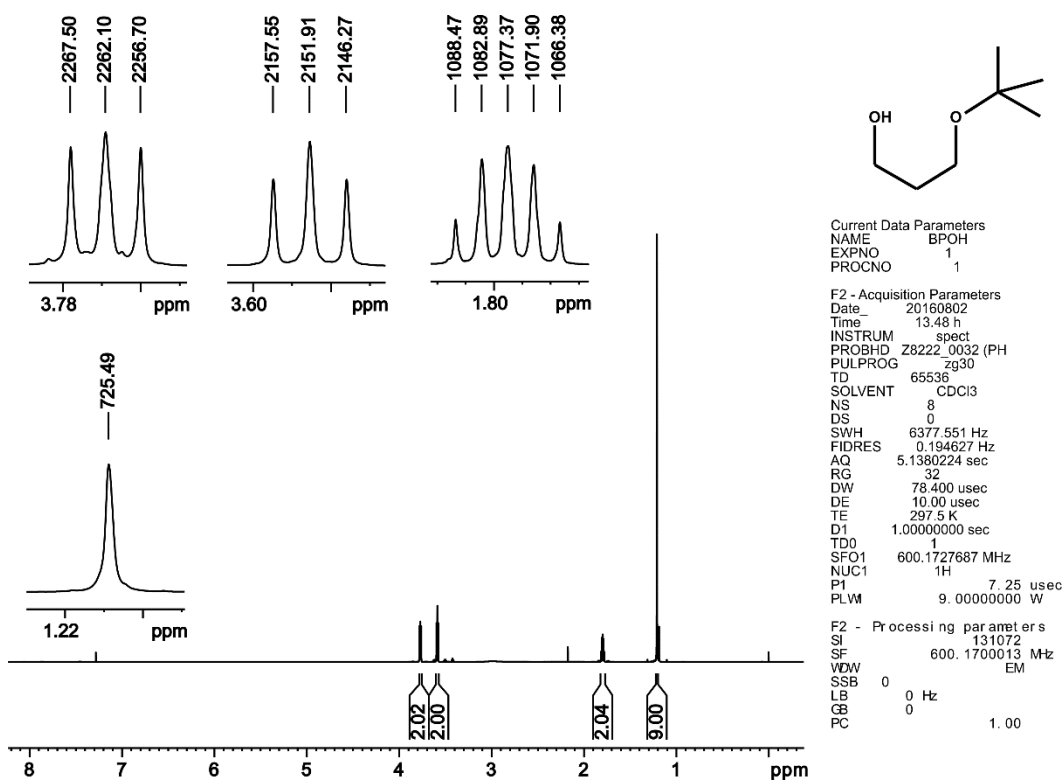


Fig. S9. ^1H NMR spectrum of 3-*tert*-butoxypropan-1-ol in CDCl_3 acquired at 600 MHz for ^1H .

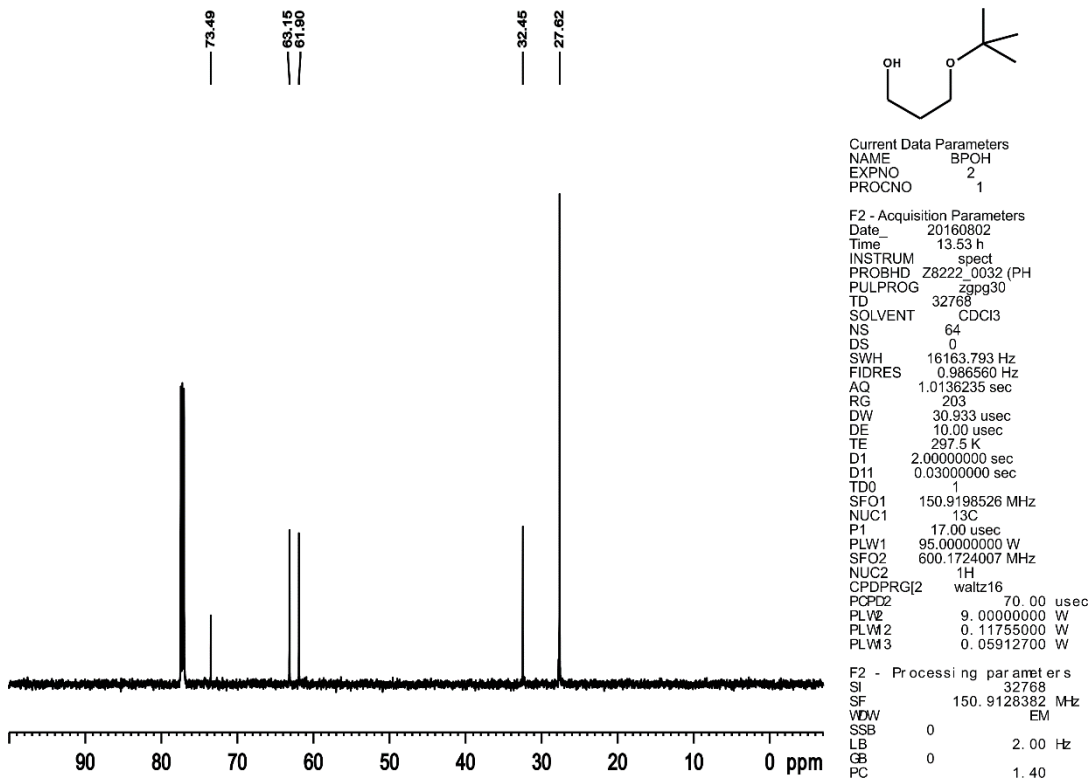


Fig. S10. ^{13}C NMR spectrum of 3-*tert*-butoxypropan-1-ol in CDCl_3 acquired at 150 MHz for ^{13}C .

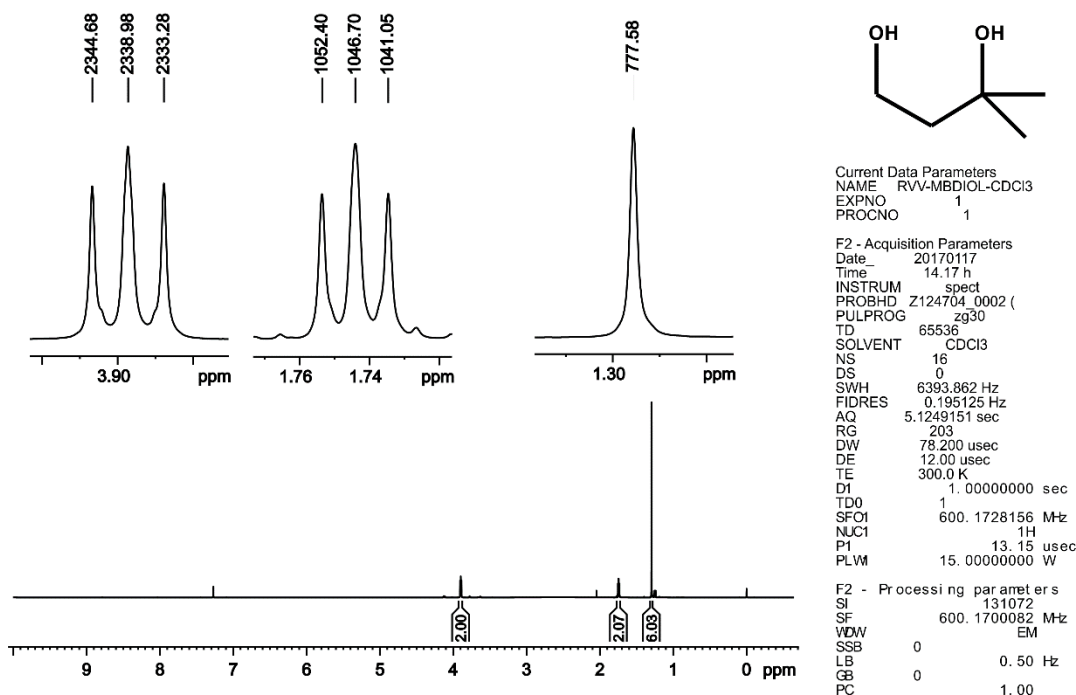


Fig. S13. ^1H NMR spectrum of 3-methylbutane-1,3-diol in CDCl_3 acquired at 600 MHz for ^1H .

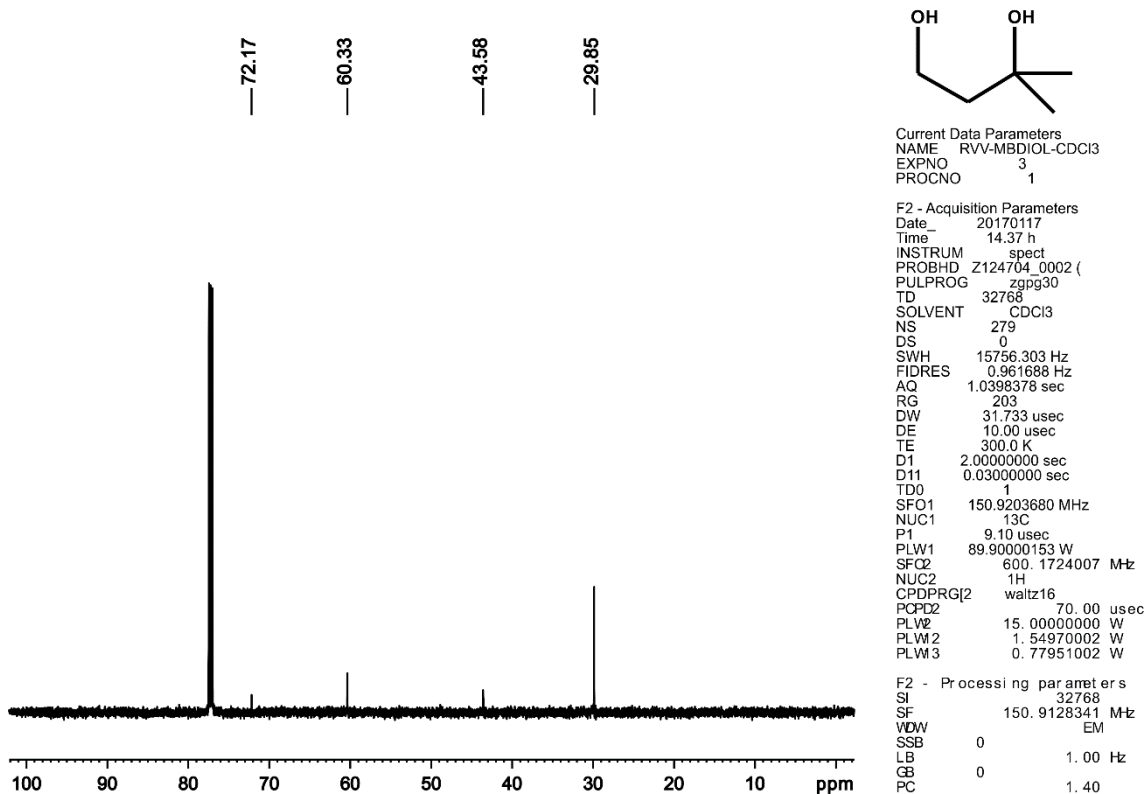


Fig. S14. ^{13}C NMR spectrum of 3-methylbutane-1,3-diol in CDCl_3 acquired at 150 MHz for ^{13}C .

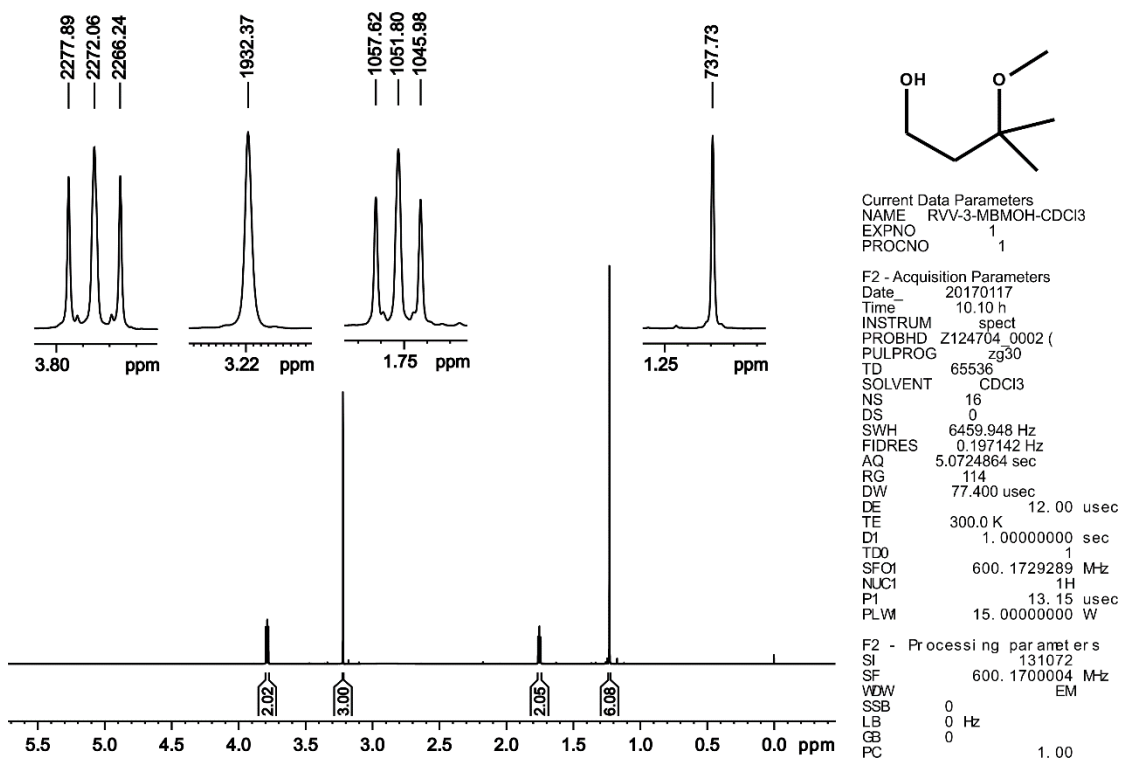


Fig. S15. ^1H NMR spectrum of 3-methyl-3-methoxybutan-1-ol in CDCl_3 acquired at 600 MHz for ^1H .

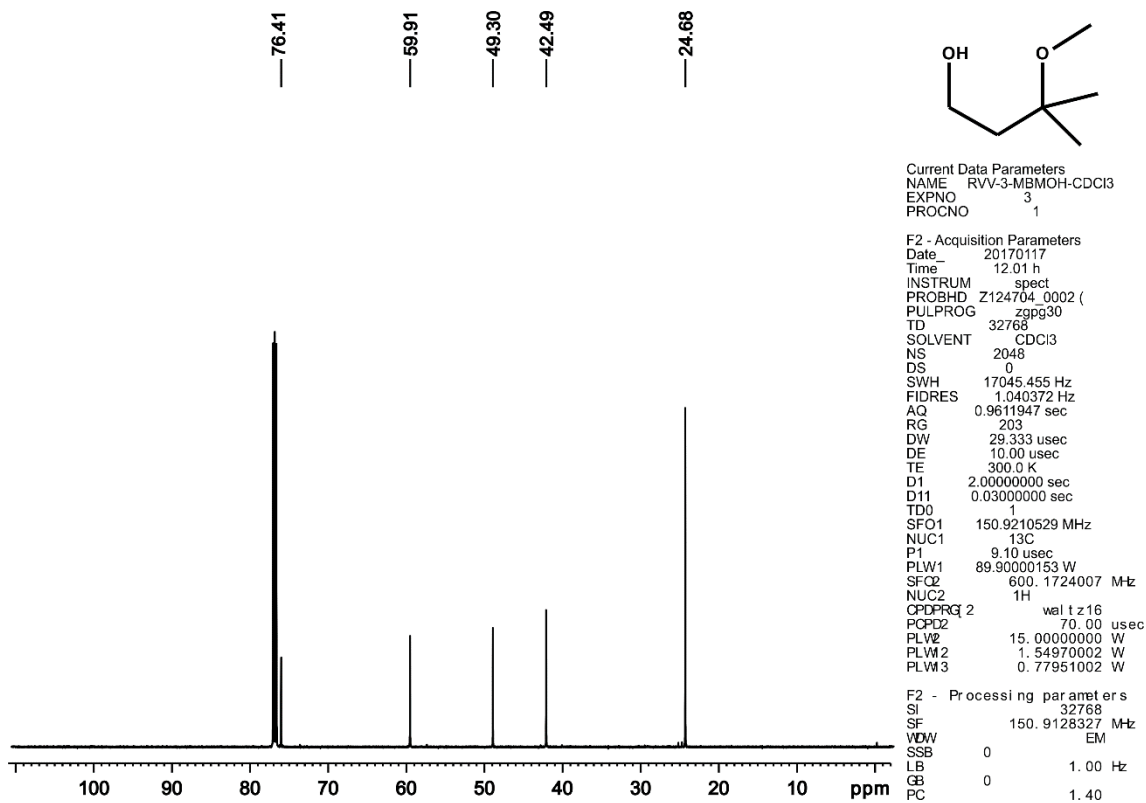


Fig. S16. ^{13}C NMR spectrum of 3-methyl-3-methoxybutan-1-ol in CDCl_3 acquired at 150 MHz for ^{13}C .

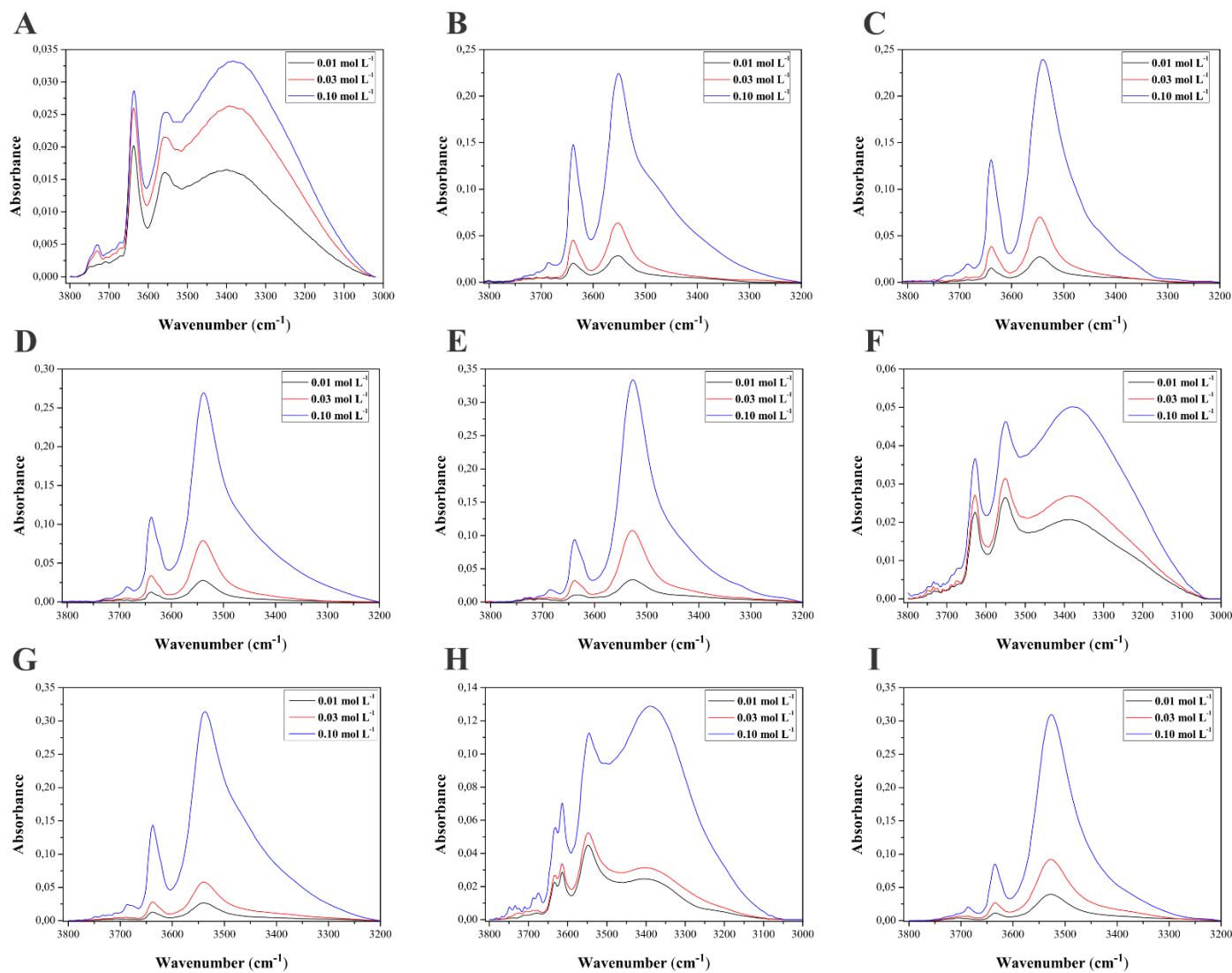


Fig. S17. Infrared spectra of **1** (A), **2** (B), **3** (C), **4** (D), **5** (E), **6** (F), **7** (G), **8** (H), and **9** (I) in CCl_4 solution: 0.01, 0.03, and 0.10 mol L^{-1} .

Table S1. Relative Gibbs energy (ΔG^a) and thermal population (P)^b for the most stable conformers of compounds **1-5** at 298 K.

1			2			3			4			5		
Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b
1a ^c	0,00	43	2a ^c	0,00	61	3a ^c	0,00	54	4a ^c	0,00	66	5a ^c	0,00	77
1b ^c	0,40	22	2b	0,99	11	3b	1,11	8	4b	1,15	10	5b ^c	0,79	20
1c	0,67	14	2c	1,39	6	3c ^c	1,11	8	4c	1,37	7	5c	1,74	3
1d	1,33	5	2d ^c	1,54	5	3d ^c	1,25	6	4d	1,64	4			
1e	1,34	4	2e	1,60	4	3e ^c	1,43	5	4e	1,81	3			
1f	1,47	4	2f	1,62	4	3f	1,46	5	4f ^c	1,88	3			
1g	1,49	3	2g	1,71	3	3g	1,68	3	4g	1,92	3			
1h	1,61	3	2h	1,75	3	3h	1,69	3	4h	1,94	3			
1i	1,62	3	2i	1,81	3	3i	1,79	3	4i	1,96	2			
						3j	1,82	3						
						3k	1,90	2						

^a In kcal mol⁻¹. ^b In %. ^c Conformers hydrogen-bonded.

Table S2. Relative Gibbs energy (ΔG)^a and thermal population (P)^b for the most stable conformers of compounds **6-9** at 298 K.

6			7			8			9		
Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b	Conformer	ΔG^a	P^b
6a ^c	0,00	29	7a ^c	0,00	57	8a ^c	0,00	47	9a ^c	0,00	90
6b ^c	0,16	22	7b ^c	0,93	12	8b ^c	0,51	20	9b ^c	1,37	9
6c ^c	0,50	12	7c	0,99	11	8c ^c	0,55	19	9c	2,44	1
6d ^c	0,51	12	7d ^c	1,25	7	8d ^c	0,78	13			
6e	1,09	5	7e	1,49	5	8e	2,08	1			
6f ^c	1,09	5	7f	1,76	3						
6g ^c	1,54	2	7g	1,79	3						
6h ^c	1,57	2	7h	1,88	2						
6i ^c	1,64	2									
6j ^c	1,65	2									
6k	1,66	2									
6l ^c	1,78	1									
6m ^c	1,80	1									
6n ^c	1,83	1									
6o	1,92	1									

^a In kcal mol⁻¹. ^b In %. ^c Conformers hydrogen-bonded.

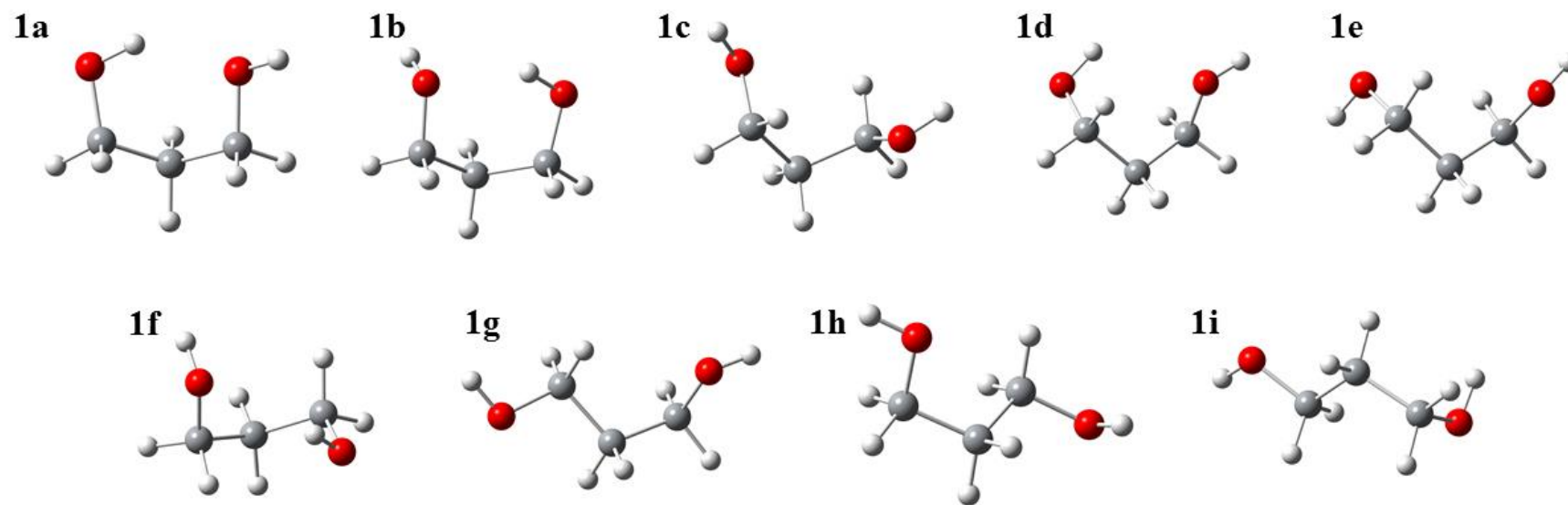


Fig. S18. Stable conformers for compound 1.

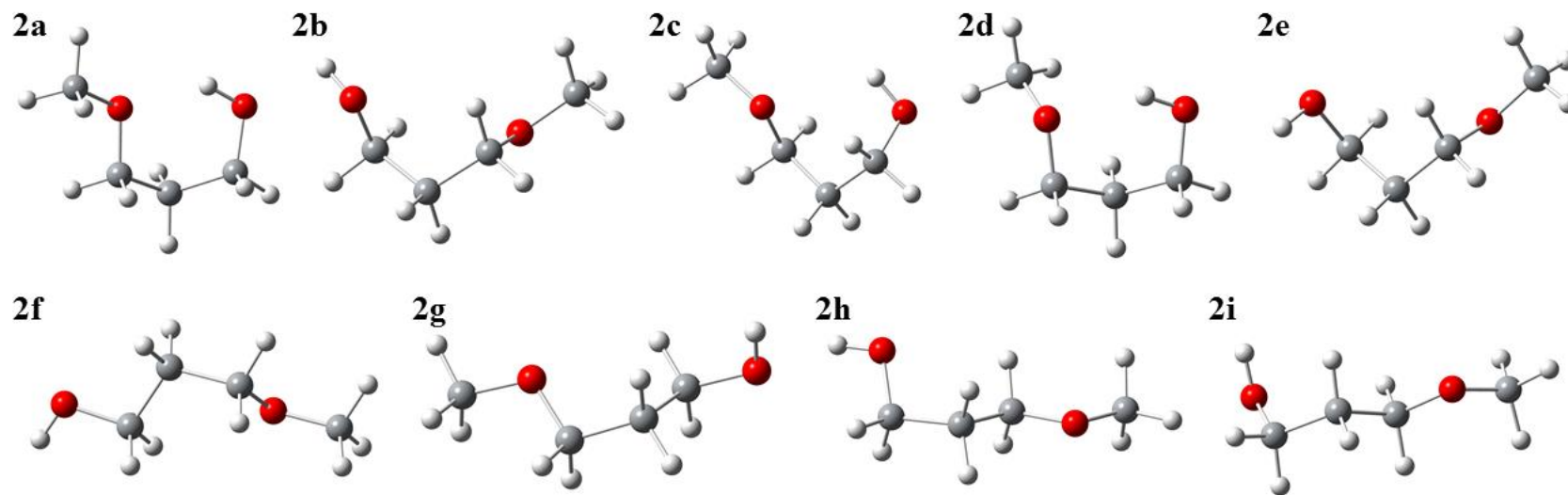


Fig. S19. Stable conformers for compound 2.

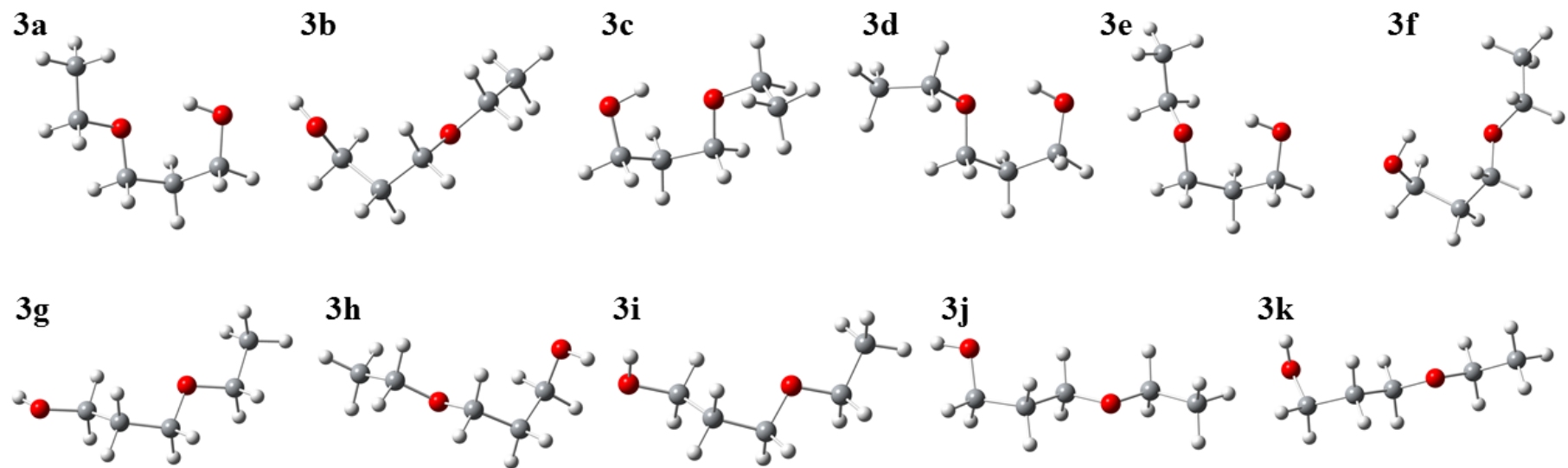


Fig. S20. Stable conformers for compound 3.

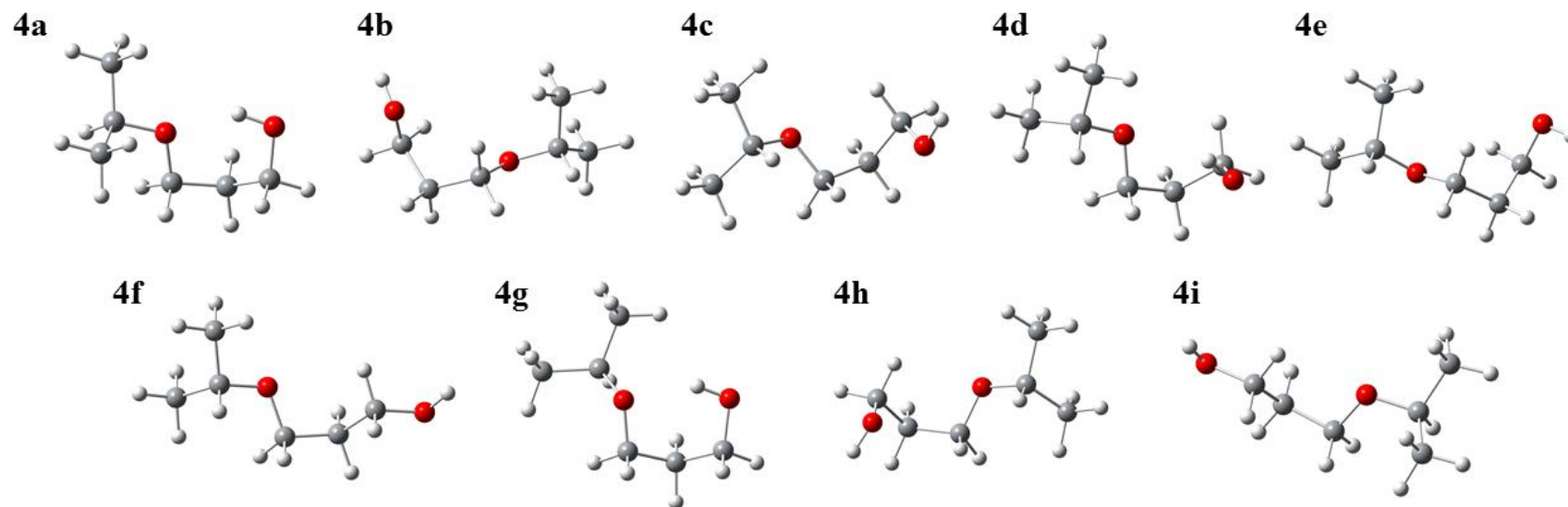


Fig. S21. Stable conformers for compound 4.

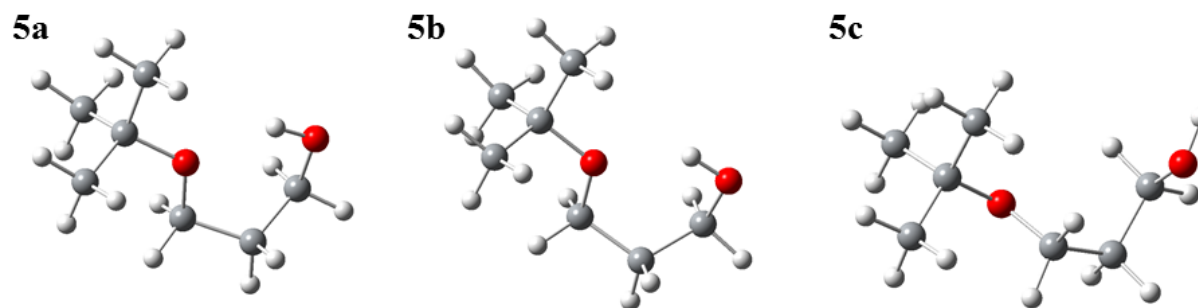


Fig. S22. Stable conformers for compound 5.

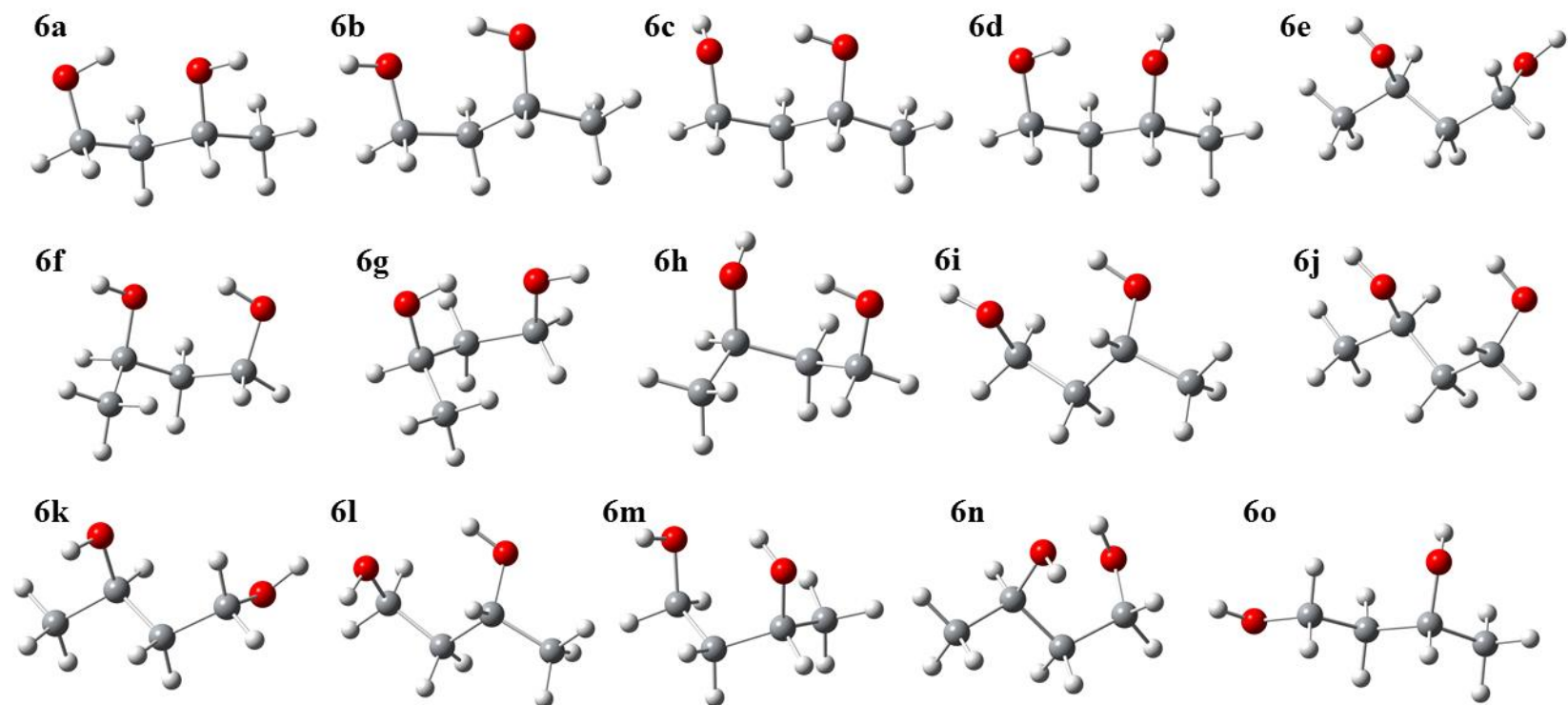


Fig. S23. Stable conformers for compound **6**.

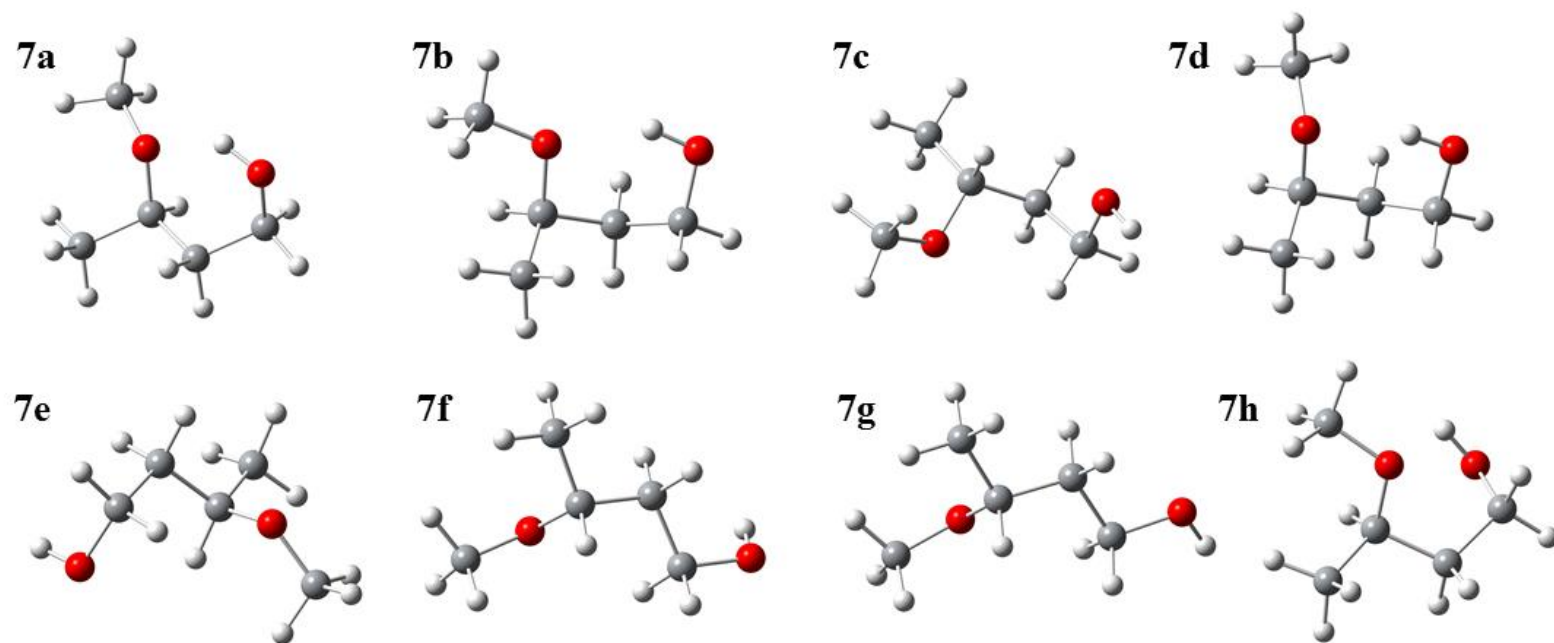


Fig. S24. Stable conformers for compound 7.

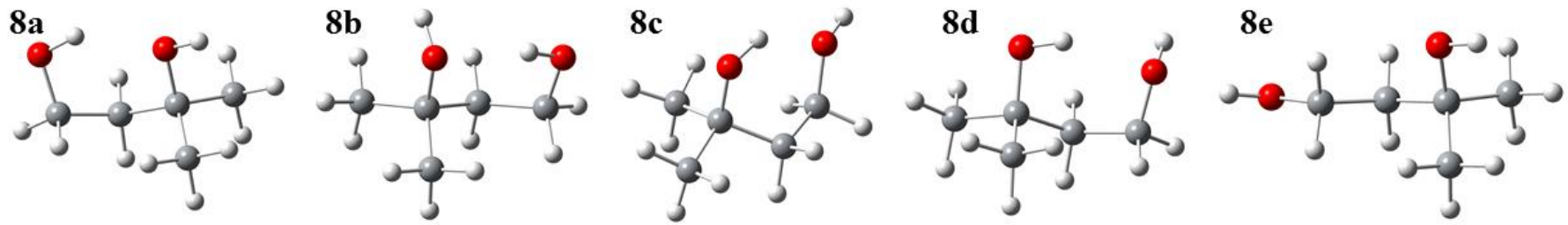


Fig. S25. Stable conformers for compound 8.

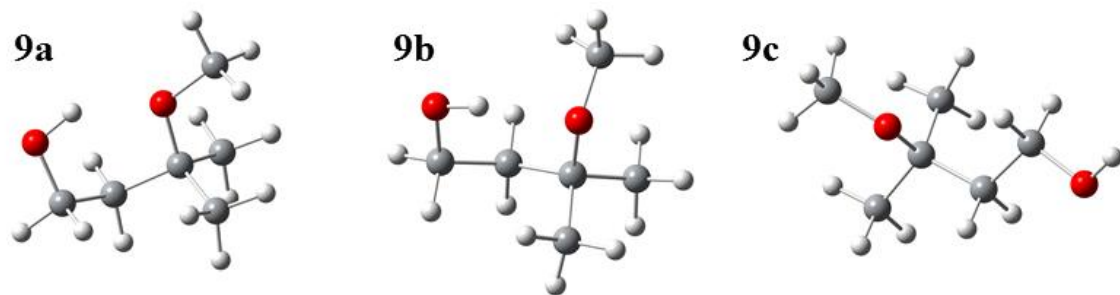


Fig. S26. Stable conformers for compound 9.

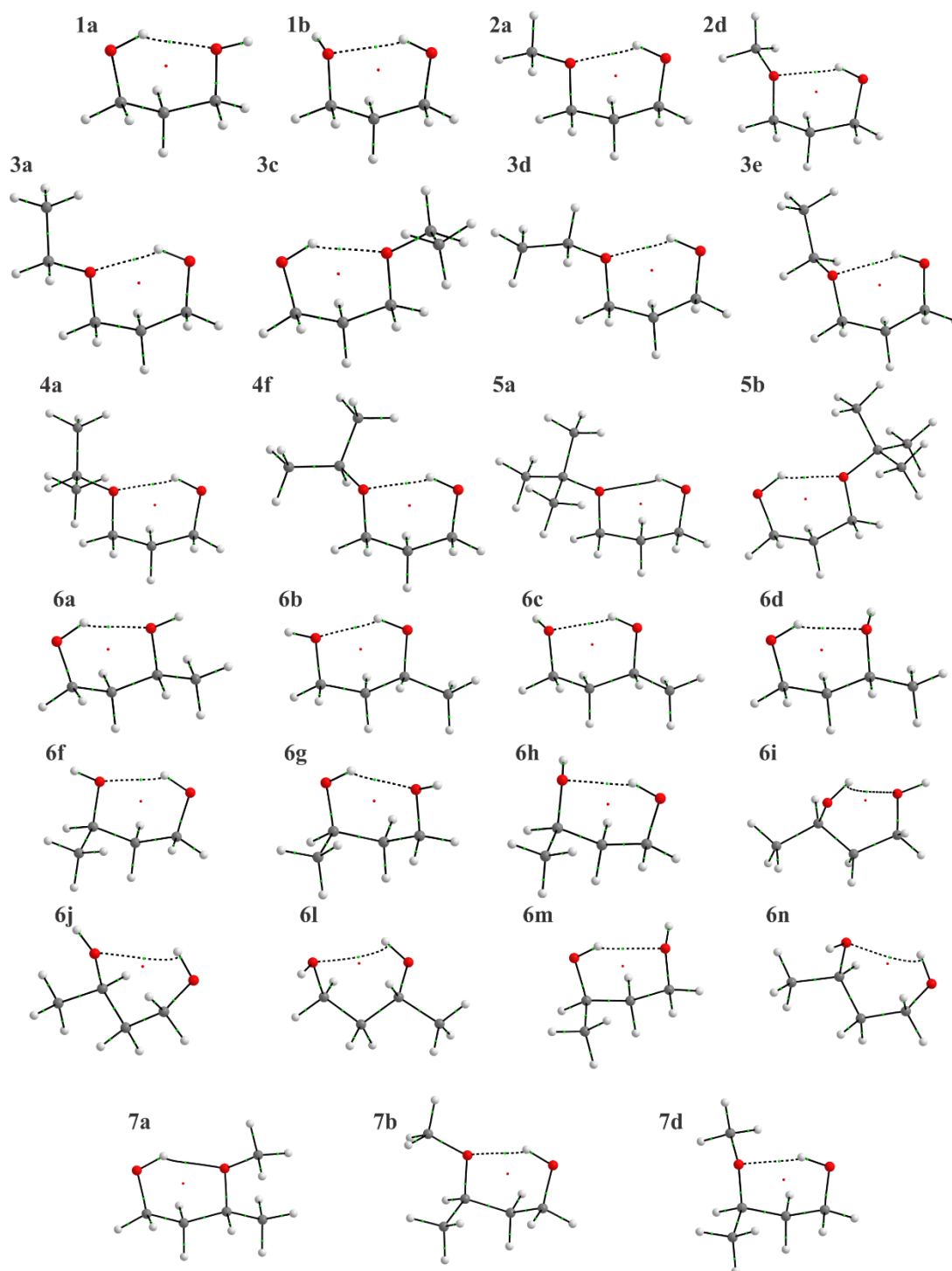


Fig. S27. QAIM molecular graphs for hydrogen-bonded conformers of compounds **1-7**. BCPs and RCPs are shown as green and red circles, respectively, and BPs are indicated by dotted lines.

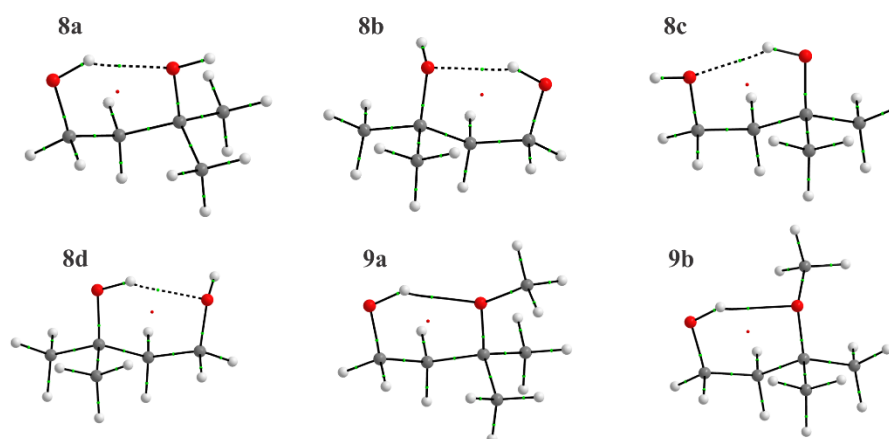


Fig. S28. QTAIM molecular graphs for hydrogen-bonded conformers of compounds **8-9**. BCPs and RCPs are shown as green and red circles, respectively, and BPs are indicated by dotted lines.

Table S3. QTAIM topological parameters obtained for hydrogen-bonded conformers at the hydrogen bond BCP and atomic properties of atoms H and O donor of IAHB calculated at the LC- ω PBE/6-311+G(d,p) level of theory.

Conformer	1a	1b	2a	2d	3a	3c	3d	3e	4a	4f	5a
$\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0226	0.0219	0.0232	0.0229	0.0234	0.0238	0.0242	0.0237	0.0240	0.0247	0.0251
$\nabla^2\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0879	0.0763	0.0889	0.0802	0.0896	0.0913	0.0914	0.0831	0.0920	0.0874	0.0950
$\Delta R_{\text{H}}^{\text{a}}$	0.8211	0.8174	0.8341	0.7984	0.8394	0.8488	0.8527	0.8205	0.8534	0.8503	0.8831
$\Delta R_{\text{O}}^{\text{a}}$	0.9524	0.2128	1.0158	0.0573	1.1087	0.0675	0.0672	0.0594	1.1311	0.0627	1.1594
$\Delta q(\text{H})^{\text{a}}$	-0.0391	-0.0321	-0.0387	-0.0321	-0.0391	-0.0402	-0.0397	-0.0331	-0.0403	-0.0369	-0.0419
$\Delta E(\text{H})^{\text{a}}$	-0.0214	-0.0204	-0.0232	-0.0202	-0.0238	-0.0243	-0.0240	-0.0211	-0.0247	-0.0234	-0.0257
$\Delta M(\text{H})^{\text{a}}$	0.0193	0.0233	0.0290	0.0243	0.0490	0.0298	0.0298	0.0251	0.0299	0.0277	0.0313
$\Delta V(\text{H})^{\text{a}}$	6.6710	5.8705	6.8043	6.1267	6.7692	7.0153	7.0103	6.0664	6.9115	7.0276	6.9504
Conformer	5b	6a	6b	6c	6d	6f	6g	6h	6i	6j	6l
$\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0248	0.0236	0.0242	0.0238	0.0236	0.0236	0.0225	0.0228	0.0116	0.0112	0.0215
$\nabla^2\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0950	0.0921	0.0942	0.0841	0.0828	0.0925	0.0888	0.0801	0.0440	0.0430	0.0748
$\Delta R_{\text{H}}^{\text{a}}$	0.8775	0.8369	0.8810	0.8477	0.8115	0.8416	0.8426	0.7999	0.2068	0.0846	0.1341
$\Delta R_{\text{O}}^{\text{a}}$	0.0702	0.9720	0.9804	0.0602	0.9206	0.9736	0.9577	0.9062	0.6191	0.6049	0.6064
$\Delta q(\text{H})^{\text{a}}$	-0.0423	-0.0408	-0.0447	-0.0380	-0.0380	-0.0447	-0.0414	-0.0370	-0.0150	-0.0093	-0.0200
$\Delta E(\text{H})^{\text{a}}$	-0.0257	-0.0243	-0.0245	-0.0226	-0.0220	-0.0246	-0.0237	-0.0217	-0.0084	-0.0075	-0.0114
$\Delta M(\text{H})^{\text{a}}$	0.0314	0.0298	0.0335	0.0285	0.0252	0.0302	0.0309	0.0242	0.0115	0.0015	0.0143
$\Delta V(\text{H})^{\text{a}}$	7.0063	6.8653	7.6202	6.9355	6.2954	6.9516	7.1185	6.1707	2.7679	1.8257	3.0796

^aIn a.u.

Table S3. QTAIM topological parameters obtained for hydrogen-bonded conformers at the hydrogen bond BCP and atomic properties of atoms H and O donor of IAHB calculated at the LC- ω PBE/6-311+G(d,p) level of theory.

Conformer	6m	6n	7a	7b	7d	8a	8b	8c	8d	9a	9b
$\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0215	0.0114	0.0252	0.0246	0.0241	0.0245	0.0248	0.0238	0.0230	0.0268	0.0255
$\nabla^2\rho(\mathbf{r})_{\text{BCP}}^{\text{a}}$	0.0748	0.0440	0.0947	0.0961	0.0850	0.0965	0.0873	0.0940	0.0805	0.1023	0.0894
$\Delta\mathbf{R}_{\text{H}}^{\text{a}}$	0.7766	0.0588	0.9241	0.9291	0.8900	0.9276	0.8934	0.8632	0.8073	0.9123	0.8658
$\Delta\mathbf{R}_{\text{O}}^{\text{a}}$	0.8793	0.6098	1.0447	1.0600	0.9975	0.9954	0.9411	0.9814	0.9100	1.0984	1.0382
$\Delta\mathbf{q}(\text{H})^{\text{a}}$	-0.0091	-0.0204	-0.0405	-0.0429	-0.0349	-0.0449	-0.0390	-0.0461	-0.0364	-0.0463	-0.0379
$\Delta\mathbf{E}(\text{H})^{\text{a}}$	-0.0053	-0.0109	-0.0243	-0.0255	-0.0219	-0.0266	-0.0247	-0.0246	-0.0206	-0.0276	-0.0238
$\Delta\mathbf{M}(\text{H})^{\text{a}}$	0.0046	0.0118	0.0301	0.0317	0.0259	0.0320	0.0277	0.0356	0.0279	0.0337	0.0279
$\Delta\mathbf{V}(\text{H})^{\text{a}}$	0.5579	2.5620	7.1139	7.3610	6.5675	7.2424	6.8292	7.8671	6.8307	7.7308	7.0041

^a In a.u.

Table S4. Energy (ϵ_i) and s-character of LP₁O orbital, atomic charge on the oxygen atom (q_O), second-order perturbation energy of $\sigma_{CH} \rightarrow \sigma_{CO}^*$ interaction, and bond angle between C-O-R atoms for prototype molecules that support the results obtained for the second group of compounds.

Compound	ϵ_i (LP ₁ O) ^a	s-character ^b	q_O ^a	$\sigma_{CH} \rightarrow \sigma_{CO}^*$ ^c	\angle C-O-R
Methoxymethane	-0,591	42	-0,583	-	112,2
Methoxyethane	-0,590	42	-0,594	6,94	112,5
2-methoxypropane	-0,581	41	-0,603	14,41	114,6
2-methoxy-2-methylpropane	-0,568	39	-0,616	22,72	117,4

^a In au. ^b In %. ^c In kcal mol⁻¹.