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Dehydrohalogenation of isomeric 2- and 3-bromomethyl substituted 2,3-dihydrooxazolo[3,2-*a*]pyridines

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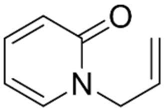
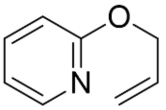
^{1}H and ^{13}C NMR spectra were acquired on a Agilent 400-MR spectrometer (360 and 90 MHz, respectively) with TMS as internal standard. Mass spectra were recorded on an AB Sciex TripleTOF 5600+ MS system with a DuoSprayTM ion source in electrospray ionization mode. Elemental analysis was performed on an Elementar vario MICRO cube CHN-analyzer. Melting points were determined on an Electrothermal IA910 melting point apparatus. Monitoring of the reaction progress was done by TLC on Silufol UV-254 plates, with chloroform as eluent; visualization under UV light (at 254 and 365 nm) or Ehrlich's reagent. Chromatographic purification was done on Merck silica gel (particle size 40–63 μ). Solvents were purified by routine methods. Images of NMR and mass spectra are given in Figures S1-S18.


2a

1-Prop-2-en-1-ylpyridine-2(1*H*)-one (2a) was obtained either by reaction of allyl bromide and 2-methoxypiridine in the presence of NaI [S1] (yield 21%) or by analogous allylation of Na salt of pyridine-2-one [S2] (yield 74%). Colorless oil.

^{1}H NMR spectra ($CDCl_3$): 4.48 - 4.60 (m, 2H, $N\underline{CH_2}CH{=}CH_2$); 5.16 (dd, J=17.1, 1.2 Hz, 1H, $NCH_2CH{=}\underline{CH_2}$); 5.20 - 5.27 (m, 1H, $NCH_2CH{=}\underline{CH_2}$); 5.87 - 5.98 (m, 1 H, $NCH_2\underline{CH}{=}CH_2$); 6.12 - 6.21 (m, 1 H); 6.55 (dd J=8.9, 1.8 Hz, 1H); 7.2 (d, J=6.6 Hz, 1H); 7.27 - 7.3 (m, 1H).

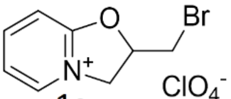
^{13}C NMR spectra ($CDCl_3$): 50.0; 105.4; 117.2; 119.6; 133.5; 138.8; 139.9; 162.3.


2b

2-(Prop-2-en-1-yloxy)pyridine (2b) was obtained with the yield 82% by heating of 2-clhoropyridine and sodium allylate (4 h) according to ref. [S3]. Colorless oil.

^{1}H NMR spectra ($CDCl_3$): 4.84 (dt, J=5.4, 1.4 Hz, 2 H, $O\underline{CH_2}CH{=}CH_2$); 5.25 (dd, J=10.5, 1.3 Hz, 1H, $CH_2CH{=}\underline{CH_2}$); 5.40 (dd, J=17.3, 1.6 Hz, 1H, $CH_2CH{=}\underline{CH_2}$); 6.10 (m, 1H, $OCH_2\underline{CH}{=}CH_2$); 6.77 (d, J=8.4 Hz, 1H); 6.86 (m, 1H); 7.57 (m, 1H); 8.11 - 8.19 (m, 1H).

Hydroperchlorate **2b**·$HClO_4$, mp 50-52 °C (from EtOH); X-ray is shown on Fig. S19.


1a

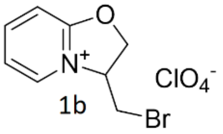
2-Bromomethyl-2,3-dihydro[1,3]oxazolo[3,2-*a*]pyridinium perchlorate (1a). To the cooled solution of allyl derivative **2a** in CCl_4 slowly added the solution of equimolar amount of Br_2 in CCl_4. After 24 h the precipitated bromide was filtered, dissolved in hot EtOH and equimolar amount of 72% $HClO_4$ was added. The mixture was slowly cooled, precipitated salts **1a** were filtered, dried in vacuo and recrystallized from EtOH. Yield 54%, white crystals, mp 185-188 °C [S4].

^{1}H NMR spectra (DMSO-d_6): 4.00 - 4.10 (m, 2H); 4.72 (dd, J=12.8, 7.3 Hz, 1H); 5.07 (dd, J=12.8, 9.8 Hz, 1H); 5.71 (td, J=2.8, 1.7 Hz, 1H); 7.61 (t, J=6.9 Hz, 1H); 7.72 (d, J=8.8 Hz, 1H); 8.42 - 8.51 (m, 1H); 8.71 (d, J=6.2 Hz, 1H). See Fig. 3.

^{13}C NMR spectra (DMSO-d_6): 32.9; 54.2; 81.9; 110.0; 119.3; 138.3; 148.7; 159.5.

HRMS: calculated 215.0666; C_8H_9BrNO; found 213.9865 + 215.9839 (M^+).

X-ray is shown on Fig. S20.



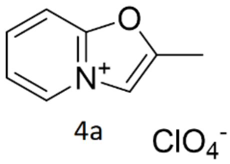
3-Bromomethyl-2,3-dihydro[1,3]oxazolo[3,2-a]pyridinium perchlorate (1b). To the cooled solution of allyl derivative **2b** in CCl_4 slowly added the solution of equimolar amount of Br_2 in CCl_4. After 24 h the precipitated bromide was filtered, dissolved in hot EtOH and equimolar amount of 72% $HClO_4$ was added. The mixture was slowly cooled, precipitated salts **1b** were filtered, dried in vacuo and recrystallized from EtOH. Yield 42%, white crystals, mp 94-95 °C.

^{1}H NMR spectra (DMSO-d_6): 4.22 (ddd, J=51.0, 11.7, 3.3 Hz, 2H); 4.92 (dd, J=9.6, 5.5 Hz, 1H); 5.20 (t, J=9.7 Hz, 1H); 5.73 - 5.82 (m, 2H); 7.64 - 7.70 (m, 1H); 7.72 (d, J=8.8 Hz, 1H); 8.51 (ddd, J=8.8, 7.3, 1.5 Hz, 2H); 8.81 (d, J=6.46 Hz, 2H). See Fig. 6.

^{13}C NMR spectra (DMSO-d_6): 34.63; 62.4; 74.8; 110.7; 120.2; 137.0; 149.6; 160.7.

HRMS: calculated 215.0666; C_8H_9BrNO; found 213.9866 + 215.9839 (M^+).

X-ray shown on Fig. S21.

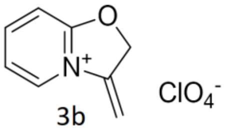


2-Methyl[1,3]oxazolo[3,2-*a*]pyridin-4-ium perchlorate (4a) was obtained by boiling **1a** in excess of absolute Et_3N for 5 hours. Unreacted Et_3N was evaporated to dryness, yield 95%, mp 126-127 °C.[53] Lit 127-128 °C.[6]

^{1}H NMR spectra (DMSO-d_6): 2.64 (s, 3H); 7.89 (t, *J*=7.0 Hz, 1H); 8.34 - 8.48 (m, 2H); 8.53 (s, 1H); 9.10 (d, *J*=6.6 Hz, 1H).

^{13}C NMR spectra (DMSO-*d*$_6$): 11.2; 111.3; 113.3; 119.1; 121.1; 131.9; 140.8; 153.3.

HRMS: calculated 134.1547; C_8H_8NO; found 134.0601 (M^+).

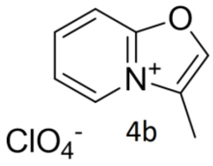


3-Methylidene-2,3-dihydro[1,3]oxazolo[3,2-*a*]pyridin-4-ium perchlorate (3b) was obtained by boiling **1b** in excess of absolute Et_3N for 5 hours. Unreacted Et_3N was evaporated to dryness, yield 97%, mp 181-182 °C.

^{1}H NMR spectra (DMSO-d_6): 5.57 - 5.63 (m, 1H); 5.67 (t, *J*=2.9 Hz, 2H); 6.22 - 6.27 (m, 1H); 7.66 (m, 1H); 7.79 (d, *J*=9.0 Hz, 1H); 8.52 (m, 1H); 9.17 (d, *J*=6.7 Hz, 1 H). See Fig.11.

^{13}C NMR spectra (DMSO-*d*$_6$): 73.6; 98.9; 111.7; 119.2; 131.8; 138.2; 149.7; 161.8.
HRMS: calculated 134.1547 C_8H_8NO; found 134.0600 (M^+).

X-ray is shown on Fig. S22.

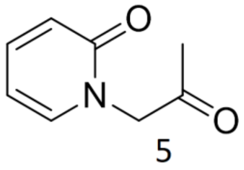


3-Methyl[1,3]oxazolo[3,2-*a*]pyridin-4-ium perchlorate (4b). Compound **3b** (40 mg, 0.17 mmol) and triflic acid (0.5 ml) were placed in the NMR tube with an internal capillary filled with D_2O. After that, ^{1}H and ^{13}C spectra were registered immediately, after 1 hour and overnight (Figure S18). Attempts to remove the solvent under reduced pressure caused resinification.

^{1}H NMR spectra (D_2O): 2.60 (s, 3H); 7.85 (m, 1H); 7.99 - 8.09 (m, 2H); 8.39 (m, 1H); 8.55 (d, *J*=6.5 Hz, 1H). See Fig. 14.

^{13}C NMR spectra (D_2O): 5.2; 111.4; 121.3; 126.3; 128.3; 138.6; 141.3; 153.6.

HRMS: calculated 134.1547; C_8H_8NO; found 134.0599 (M^+).

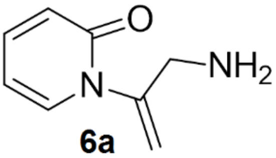


1-(2-Oxopropyl)pyridin-2(1*H*)-one (5). Compound **1a** (1 equiv.) was dissolved in water, and K_2CO_3 (2 equiv.) was added. The mixture was boiled for 3 hours. After cooling the product was extracted by chloroform, and the solvent was removed on a rotary evaporator giving to oily product.

^{1}H NMR spectra ($CDCl_3$): 2.24 (s, 3H) 4.68 (s, 2H) 6.15 - 6.21 (m, 1H) 6.54 (d, J=9.19 Hz, 1H) 7.13 (dd, J=6.85, 1.96 Hz, 1H) 7.31 - 7.39 (m, 1H). See Fig. 16.

^{13}C NMR spectra ($CDCl_3$): 27.44; 57.81; 106.01; 120.65; 137.95; 140.15; 162.15; 200.83.

HRMS: calculated 151.1626; $C_8H_9NO_2$; found 152.0708 (MH^+)

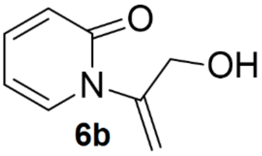

6a

1-[1-(Aminomethyl)ethenyl]pyridin-2(1*H*)-one (6a) was obtained by passing gaseous ammonia through an ethanol solution of structure **3b**. The process was monitored by TLC. After the reaction was complete, the solvent was removed in vacuo. Yield 85%, mp 124-126 °C.

^{1}H NMR spectra (DMSO-d_6): 4.21 (s, 2H); 5.70 (s, 1H); 5.88 (s, 1H); 6.92 (t, J=6.43 Hz, 1H); 7.12 (d, *J*=8.8 Hz, 1H); 7.84 (d, *J*=6.4 Hz, 1H); 7.91 (d, *J*=7.9 Hz, 1H).

^{13}C NMR spectra (DMSO-d_6): 60.2; 112.2; 114.4; 119.4; 139.8; 143.0; 145.1; 153.4.

HRMS: calculated 150.1778; $C_8H_{10}N_2O$; found 151.0867 (MH^+).


6b

1-[1-(hydroxymethyl)ethenyl]pyridin-2(1*H*)-one (6b). Salt **3b** (1 equiv.) was dissolved in water, and K_2CO_3 (2 equiv.) was added. The mixture was boiled for 3 hours. After cooling the product was extracted by chloroform, and the solvent was removed on a rotary evaporator. A colorless thick liquid was obtained. Yield 72%.

Another method of synthesizing: substance **3b** was dissolved in water, after which K_2CO_3 (2 equiv.) was added. The mixture was boiled for 3 hours, after which the product was extracted with chloroform, which was removed on a rotary evaporator. Yield 81%.

^{1}H NMR spectra ($CDCl_3$): 4.29 (s, 2H); 4.71 (br. s., 1 H); 5.24 (s, 1H); 5.54 (s, 1H); 6.22 (m, *J*=6.6 Hz, 1H); 6.51 (d, *J*=9.0 Hz, 1H); 7.25 (d, J=7.04 Hz, 1H); 7.34 - 7.40 (m, 1H).

^{13}C NMR spectra ($CDCl_3$): 62.6; 106.6; 114.9; 120.8; 138.1; 140.7; 150.3; 162.7.

HRMS: calculated 151.1626; $C_8H_9NO_2$; found 152.0708 (MH^+).

References

S1. W. R. Bowman, C. F. Bridge, *Synth. Comm.* 1999, **22**, 4051. https://doi.org/10.1080/00397919908085926

S2. J. G. Sosnicki, L. Struk, T. Idzik, G. Maciejewska, *Tetrahedron*, 2014, **45**, 8624. https://doi.org/10.1016/j.tet.2014.09.043

S3. B. I. Mikhent'ev, E. I. Fedorov, A. I. Kucherova, V. P. Potapova, *Russ. J. Gen. Chem.* 1959, **29**, 1844.

S4. Only bromide (mp 178 °C) is described: D. G. Kim, Alalikina N. P, E. I. Sogrina, *Russ. J. Org. Chem.* 1985, **9**, 2022.

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S6. C. K Bradsher, M. Zinn, *J. Heterocycl. Chem.* 1967, **4**, 66. https://doi.org/10.1002/jhet.5570040111

NMR spectra

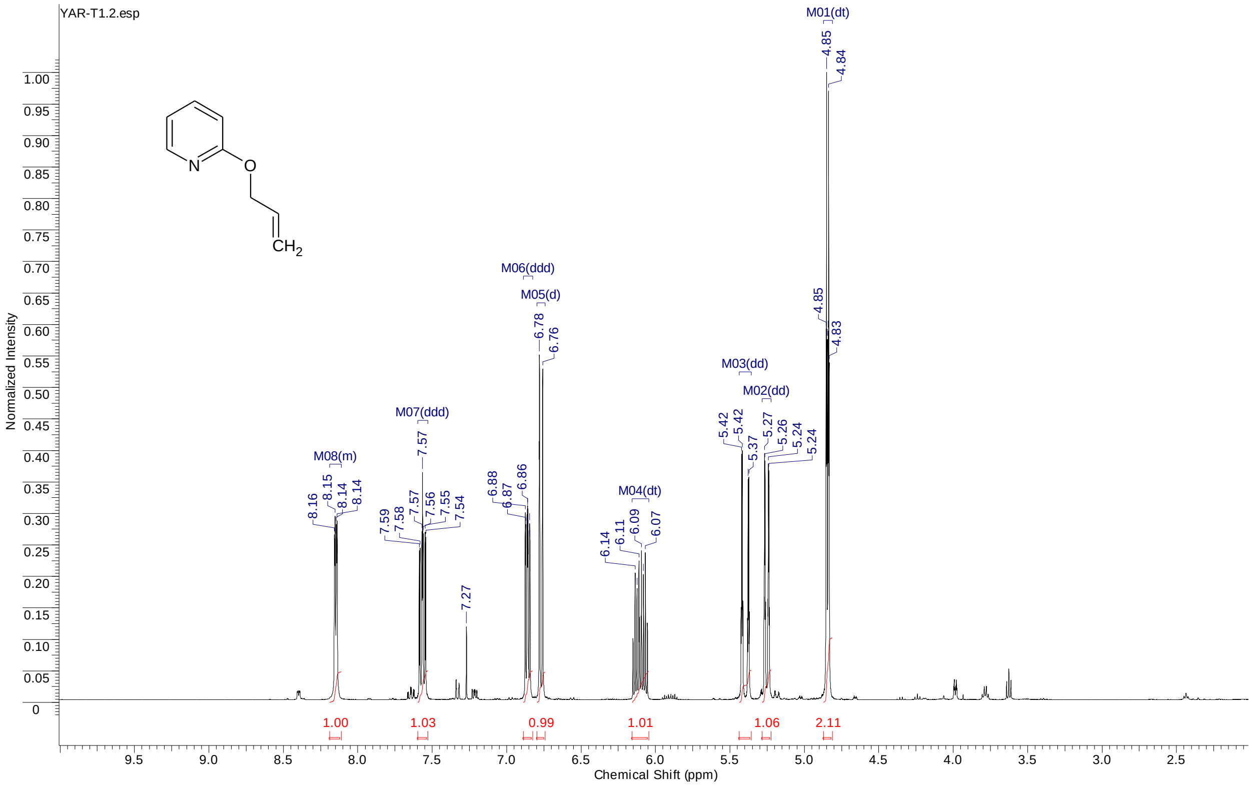

Figure S1. ^{1}H NMR spectra of compound 2b

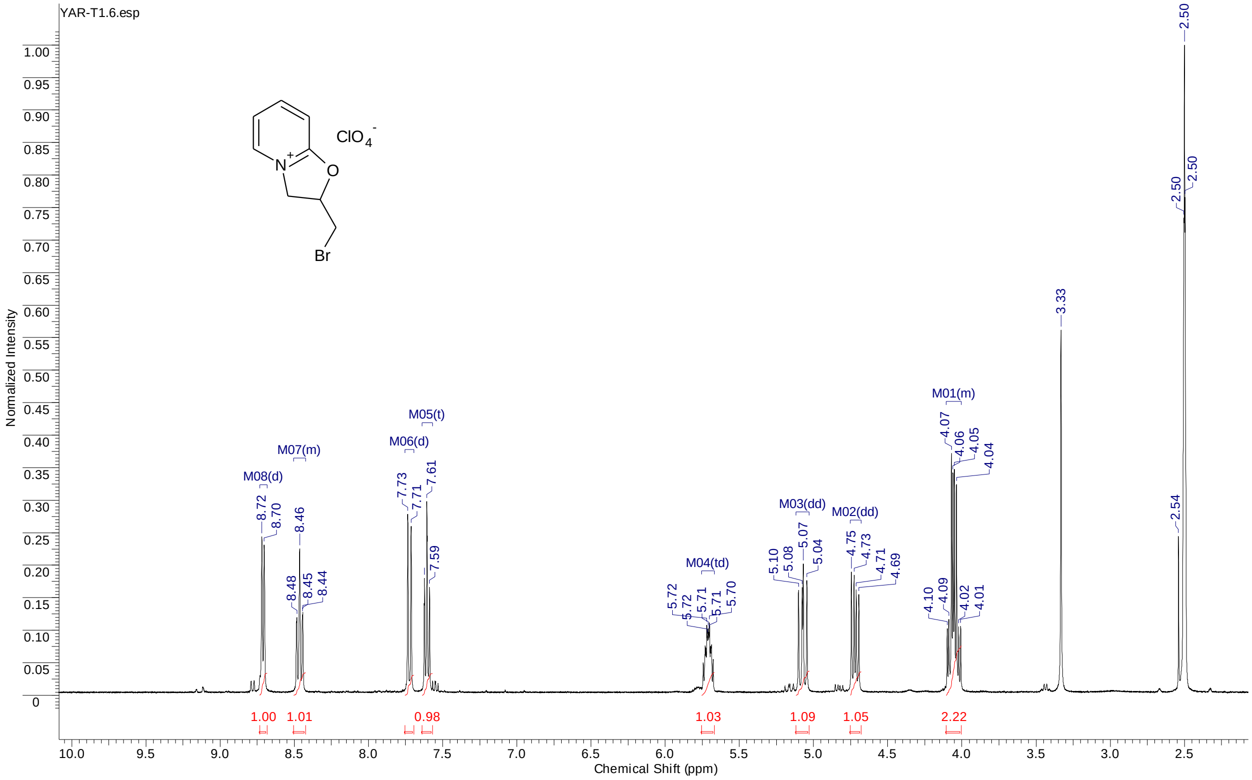

Figure S2. ^{1}H NMR spectra of compound 1a

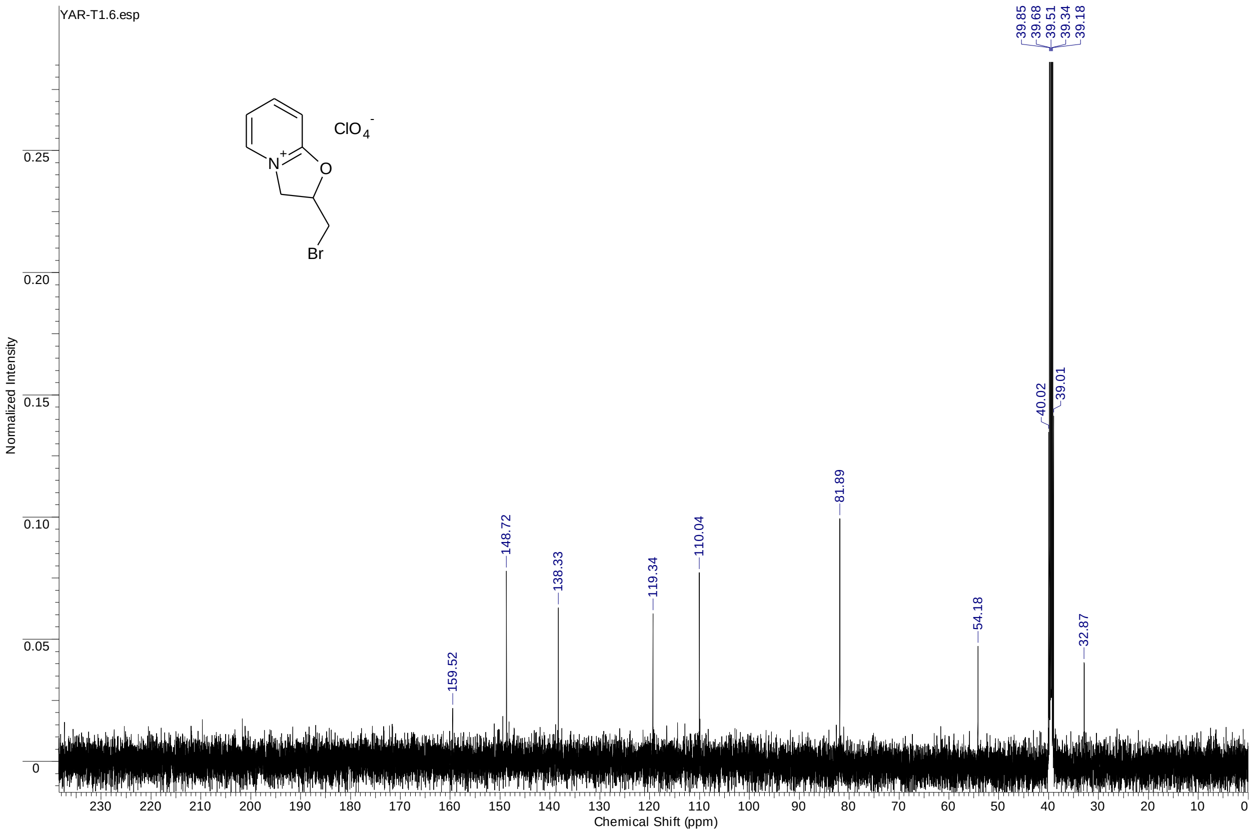

Figure S3. ^{13}C NMR spectra of compound 1a

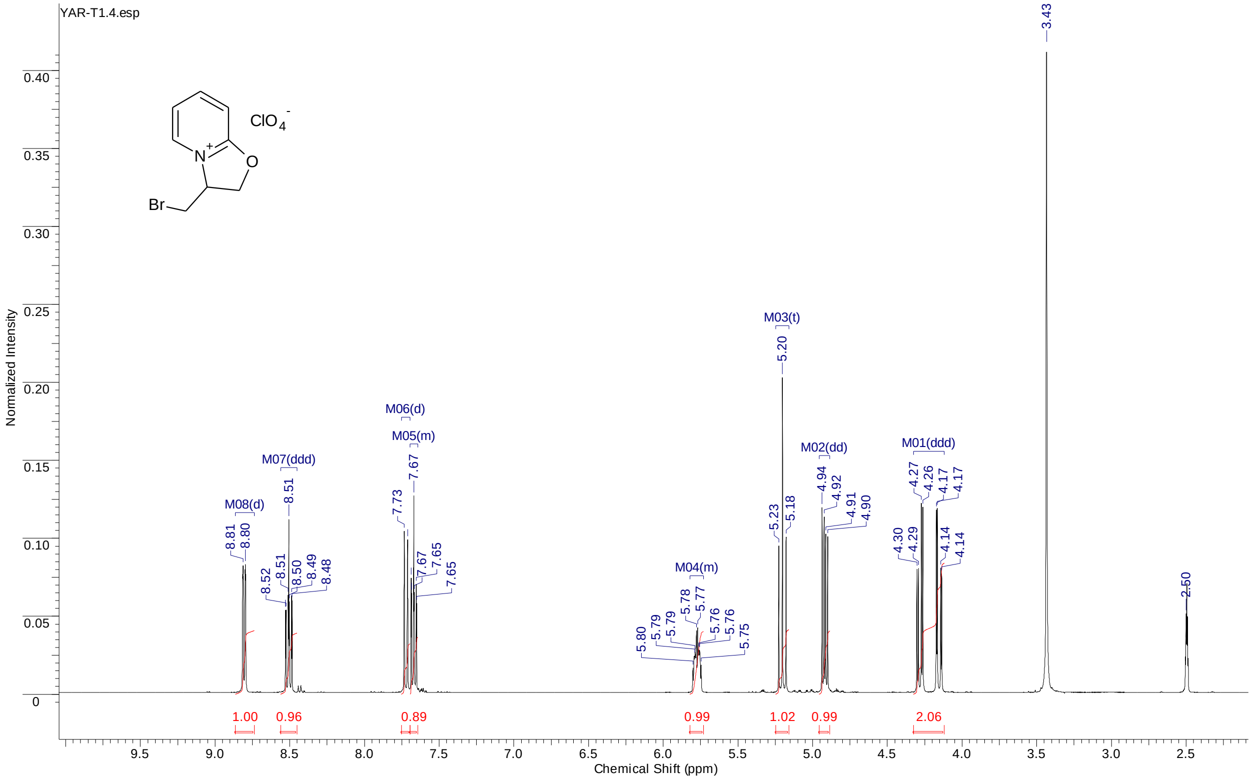

Figure S4. ^{1}H NMR spectra of compound 1b

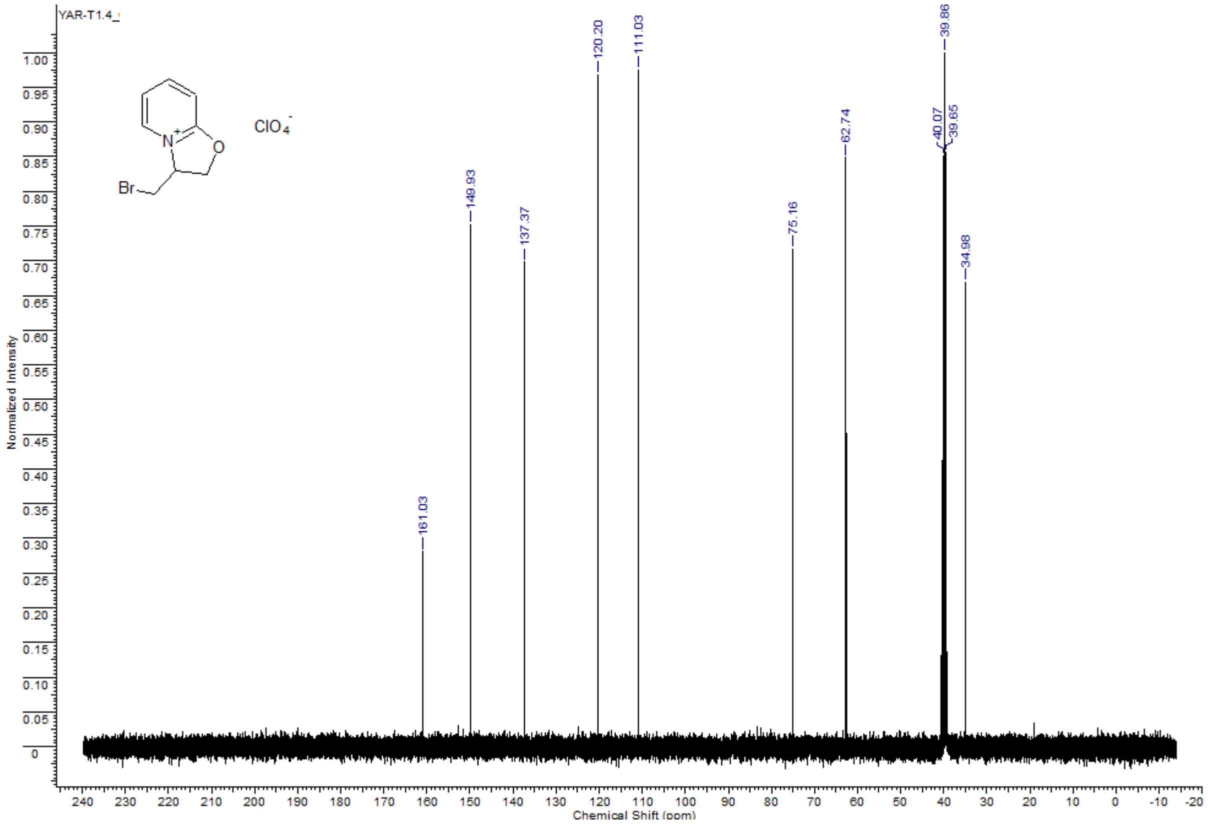

Figure S5. ^{1}H NMR spectra of compound 1b

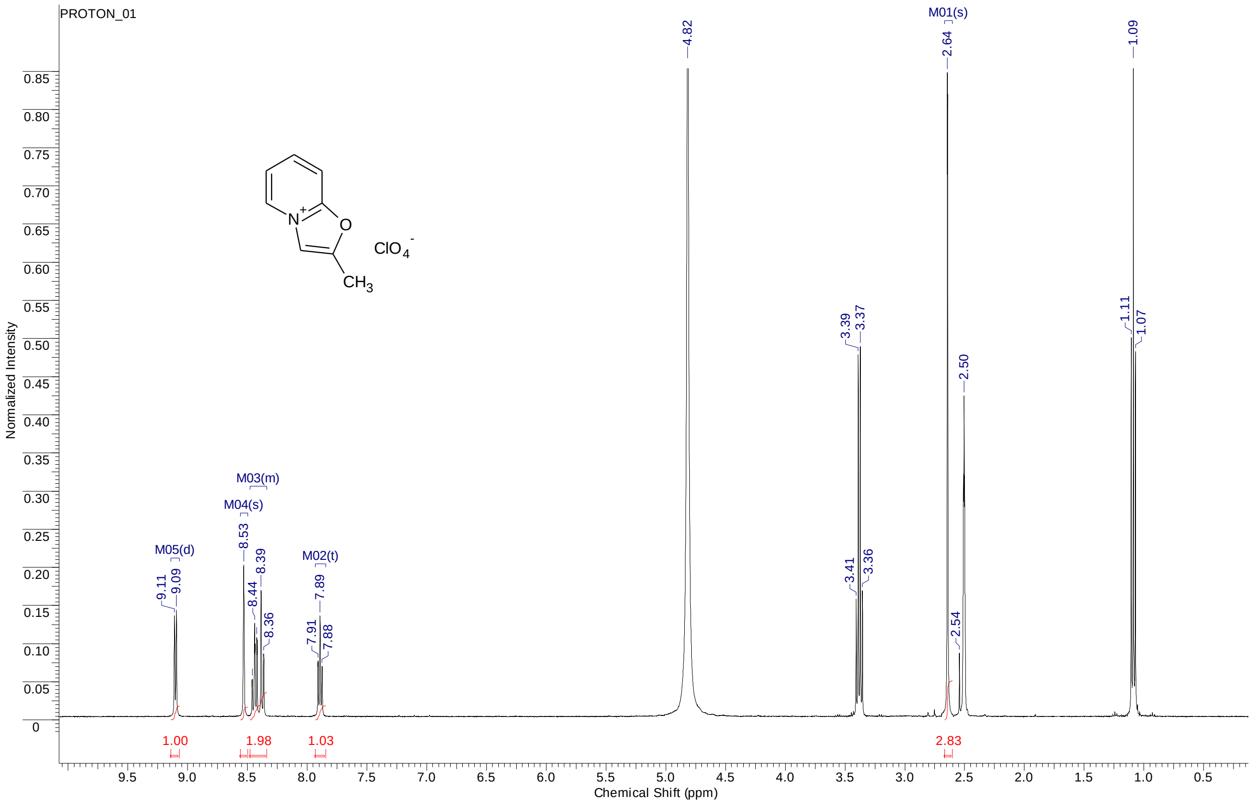

Figure S6. ^{1}H NMR spectra of compound 4a

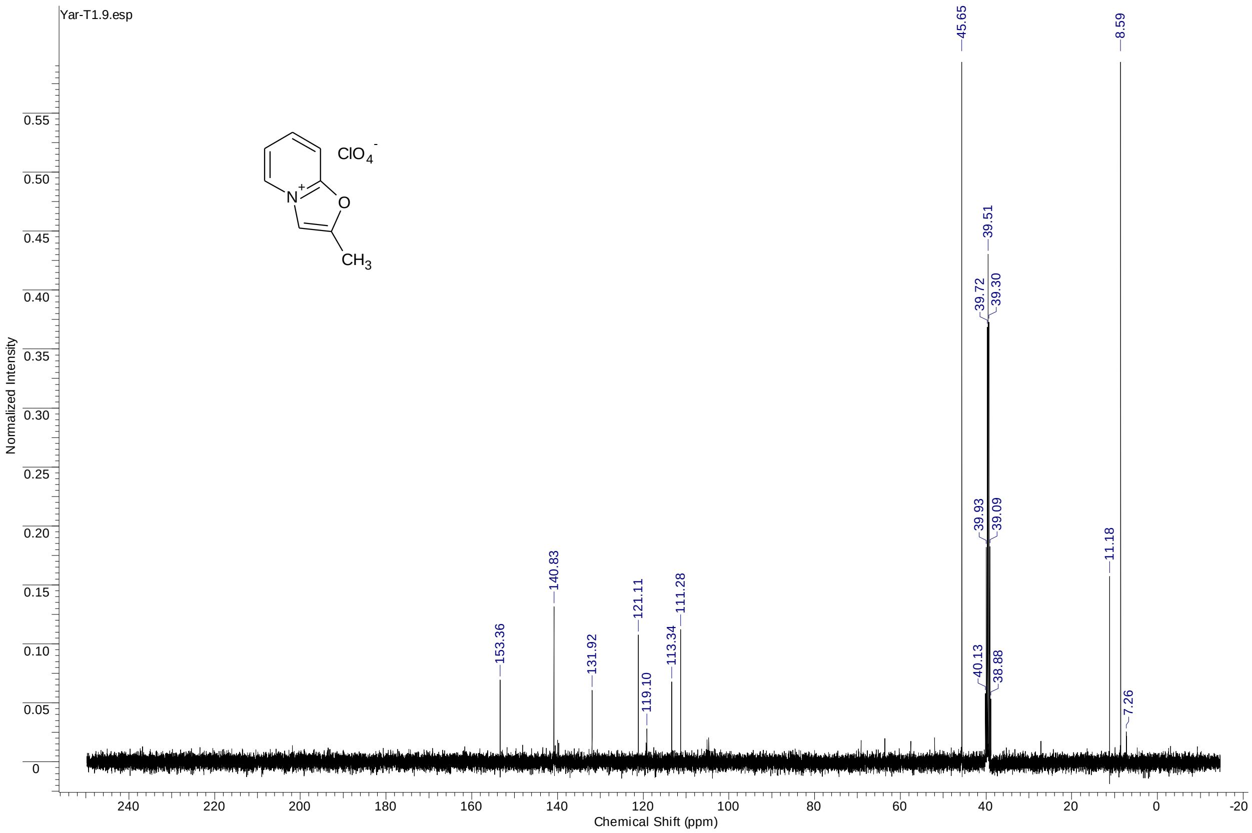

Figure S7. ^{13}C NMR spectra of compound 4a

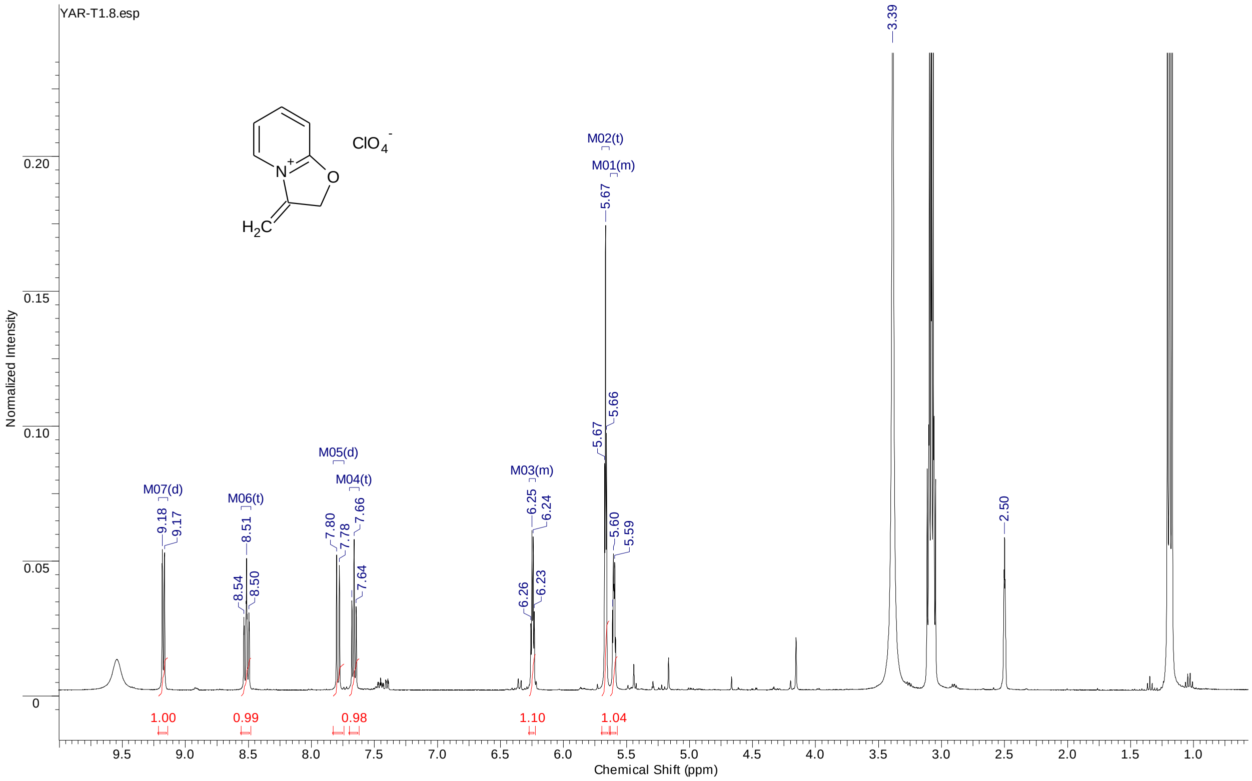

Figure S8. ^{1}H NMR spectra of compound 3b

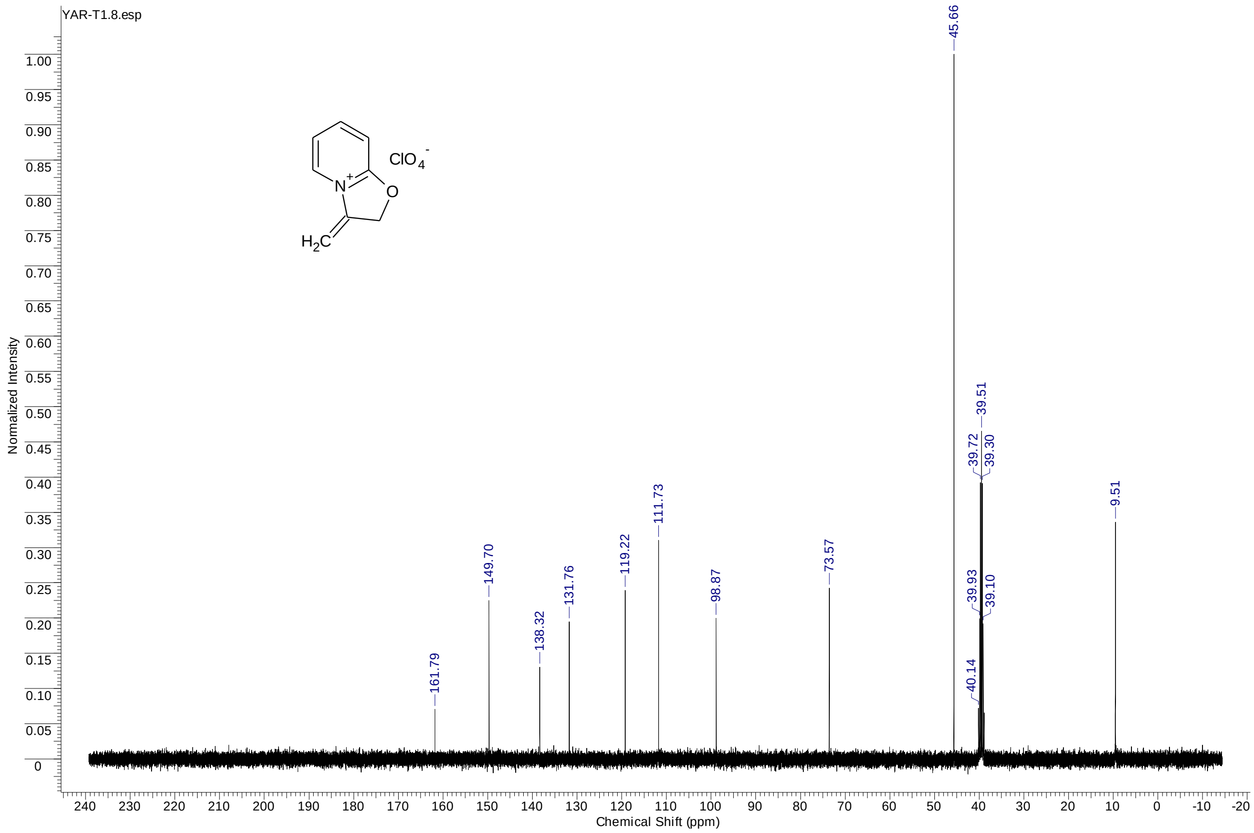

Figure S9. ^{13}C NMR spectra of compound 3b

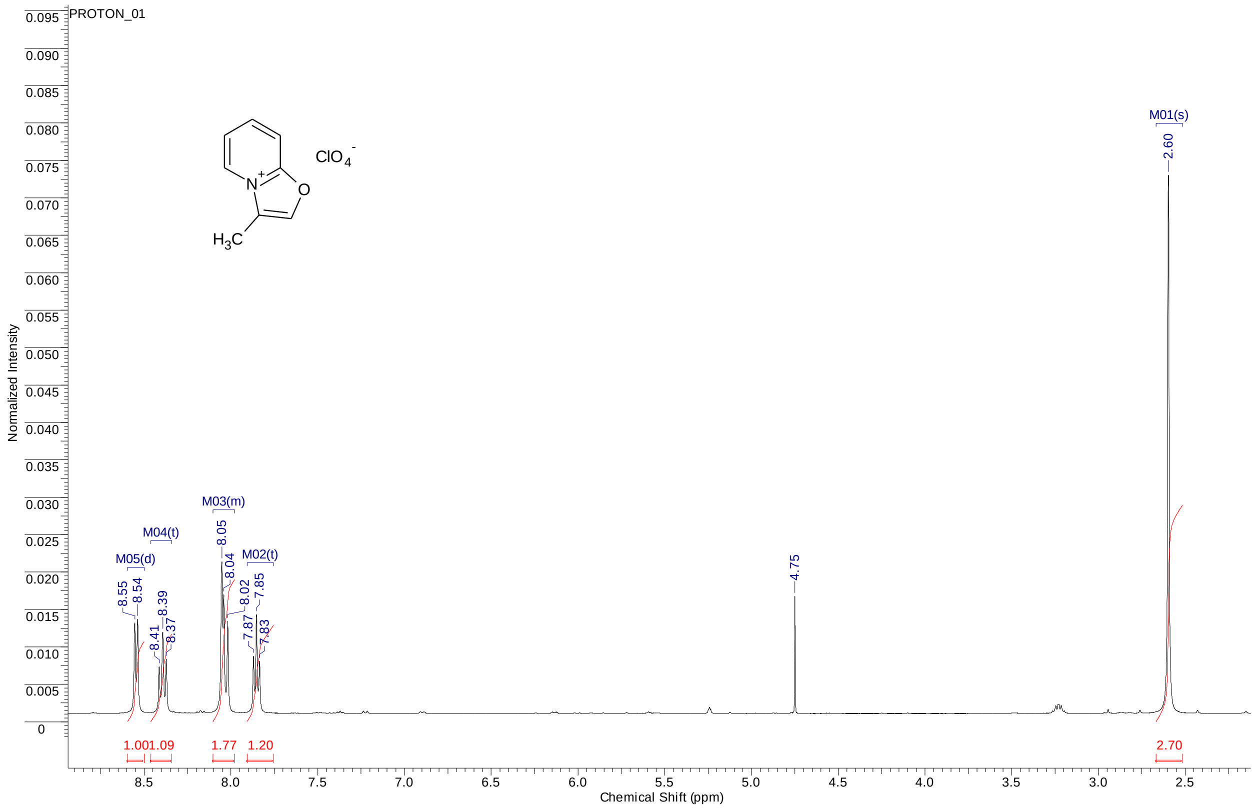

Figure S10. ^{1}H NMR spectra of compound 4b

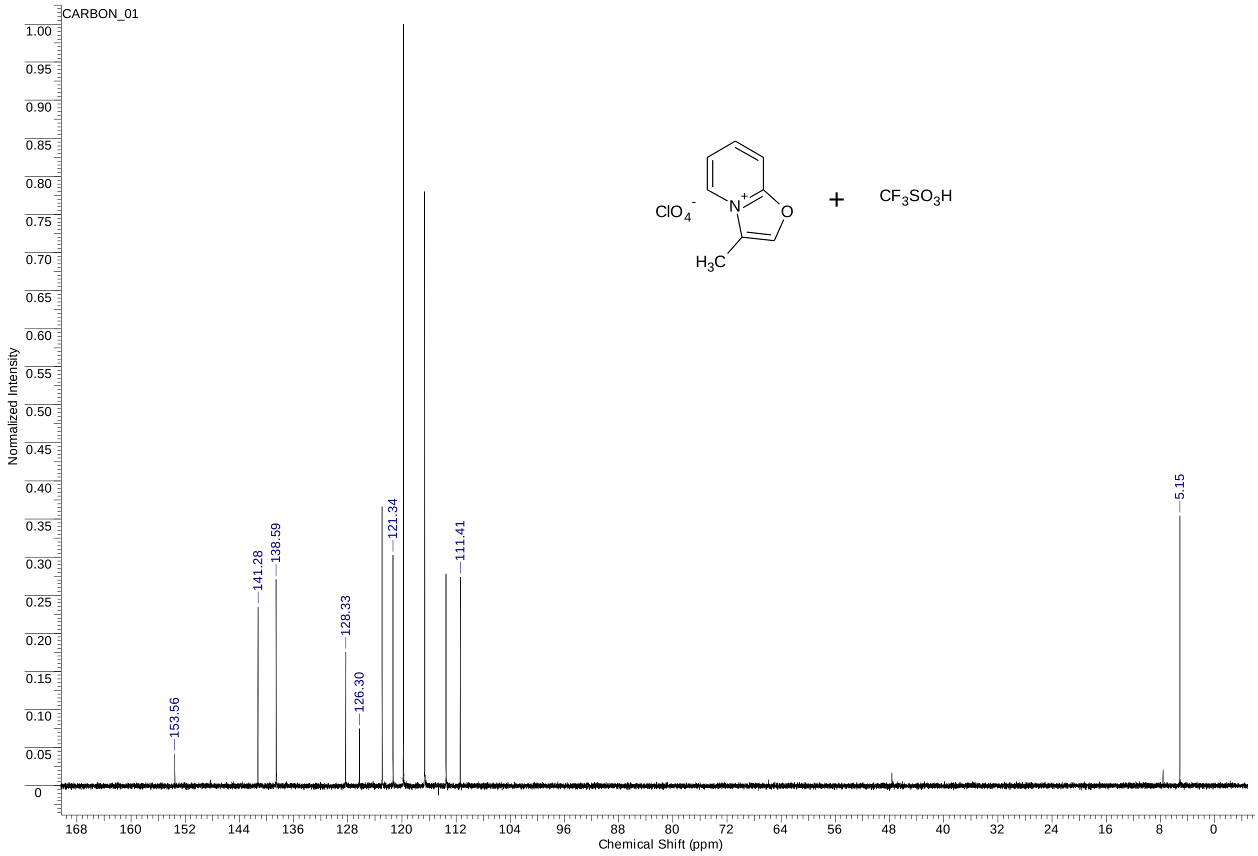

Figure S11. ^{13}C NMR spectra of compound 4b

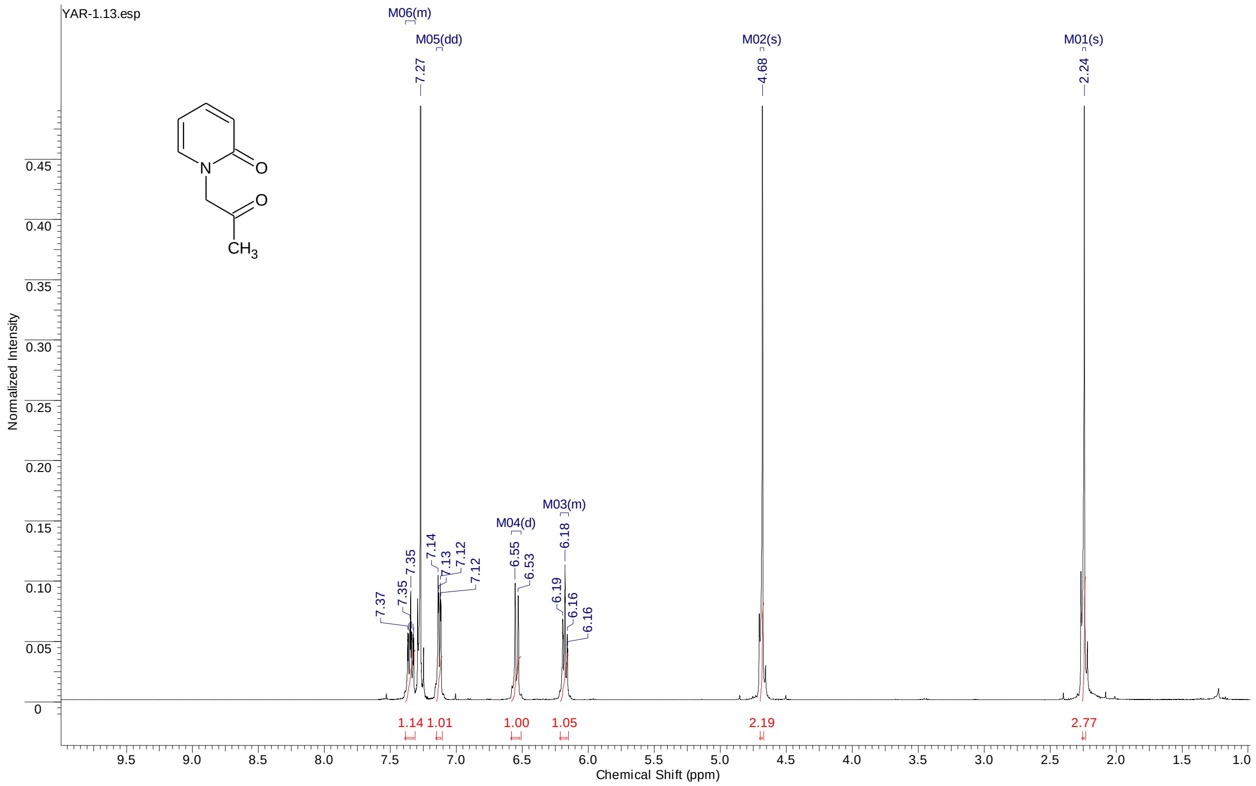

Figure S12. ^{1}H NMR spectra of compound 5

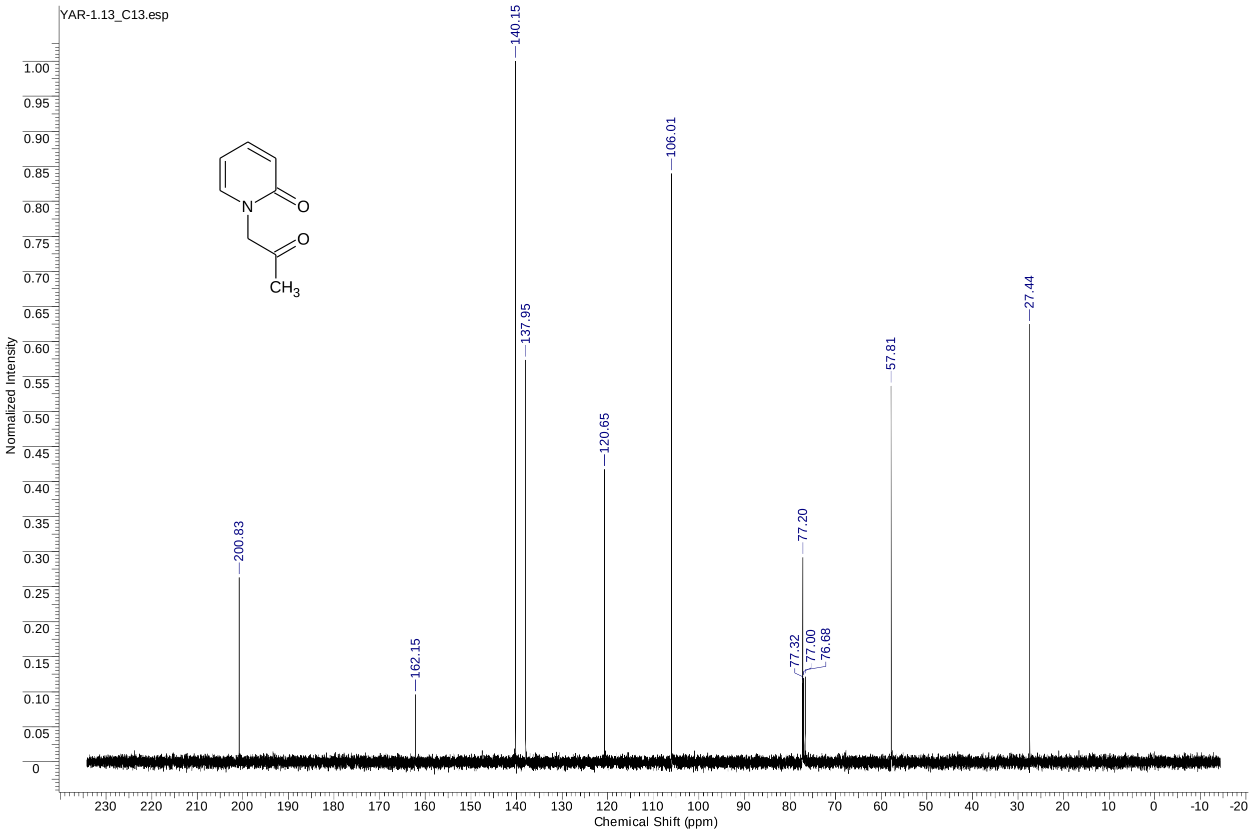

Figure S13. ^{13}C NMR spectra of compound 5

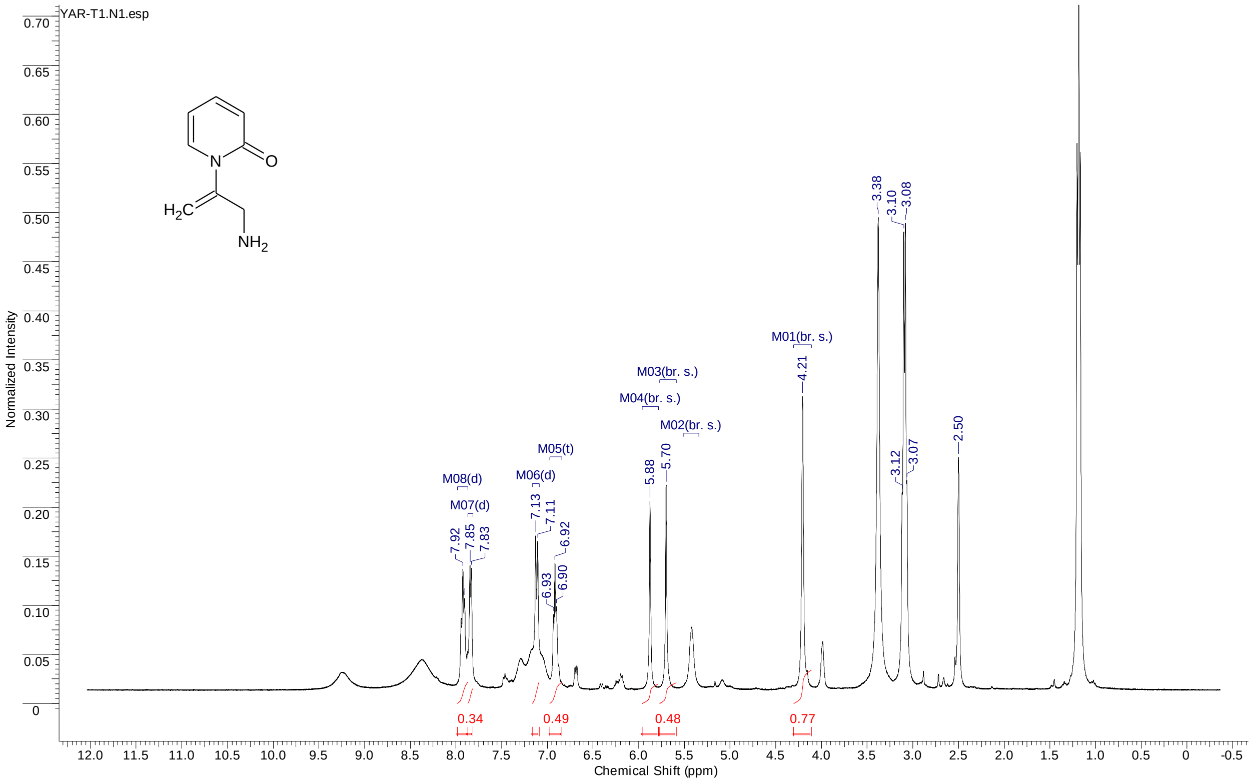

Figure S14. ^{1}H NMR spectra of compound 6a

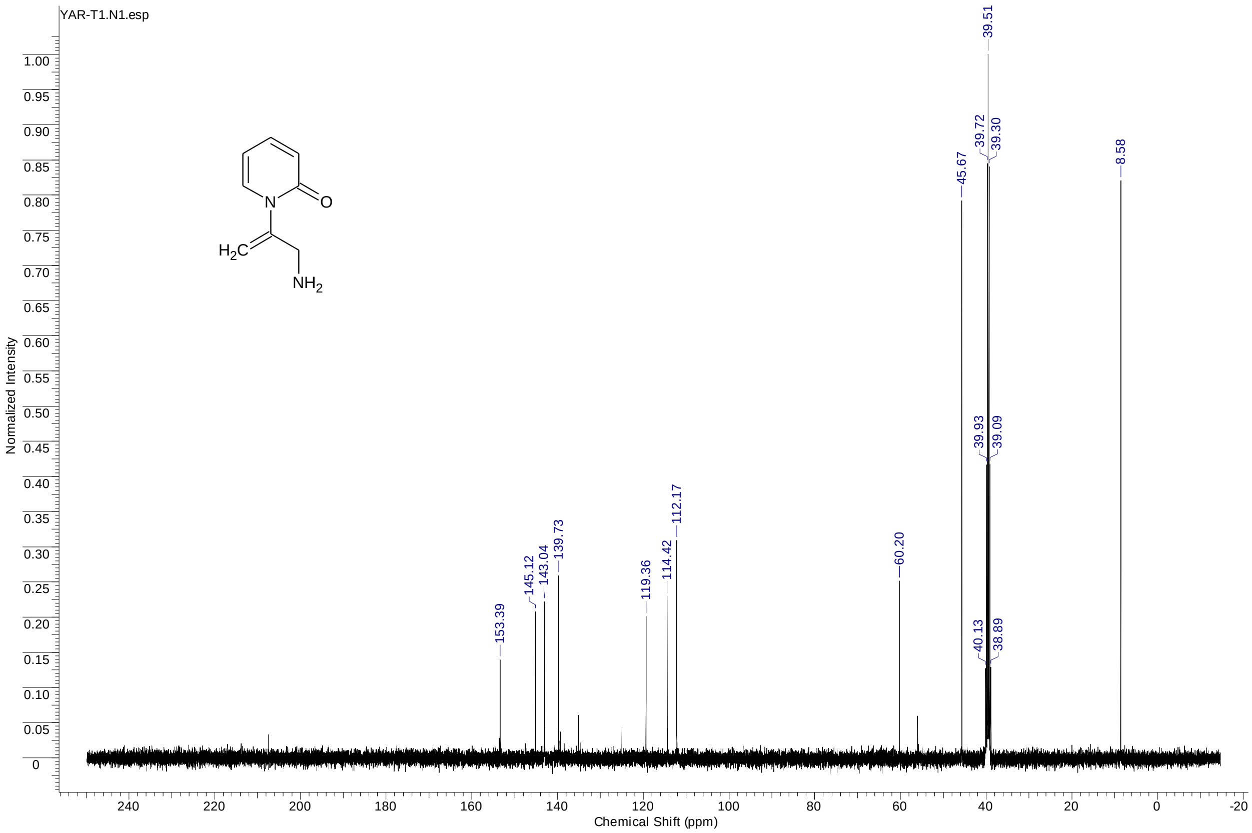

Figure S15. ^{13}C NMR spectra of compound 6a

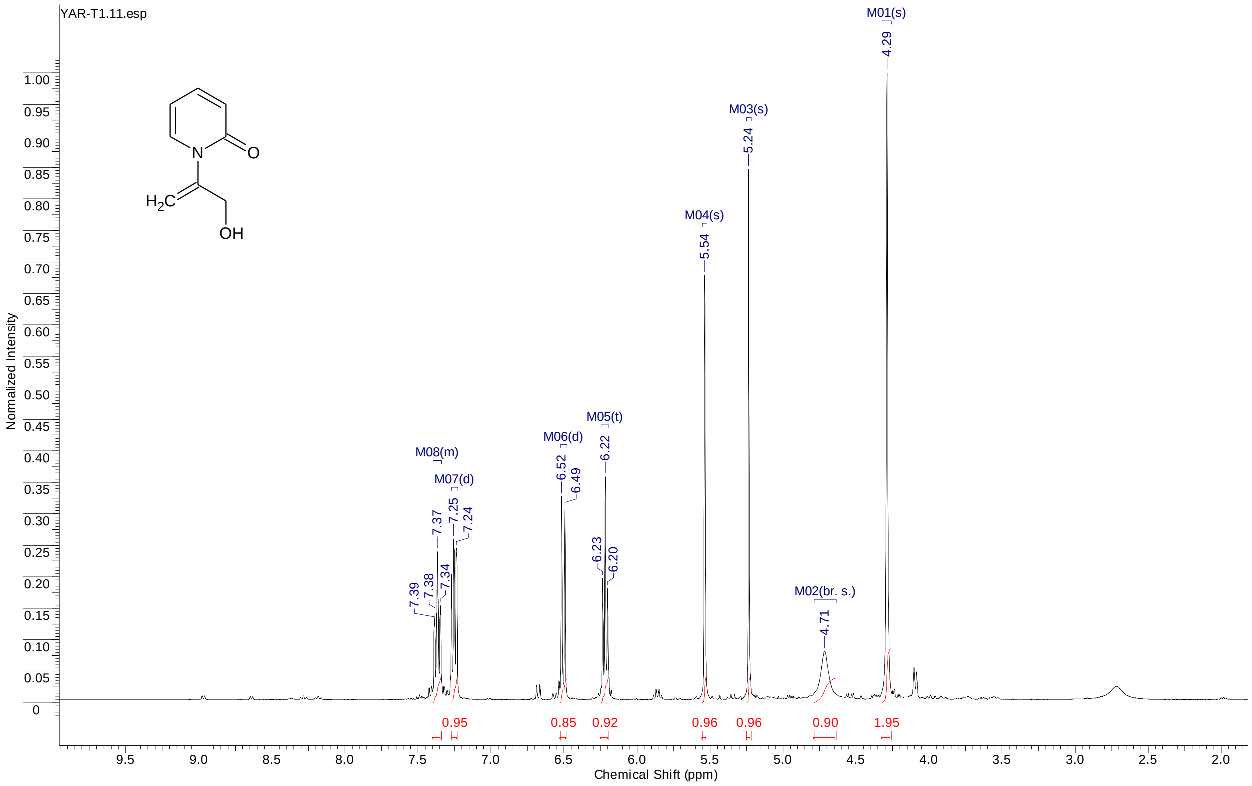

Figure S16. ^{1}H NMR spectra of compound 6b

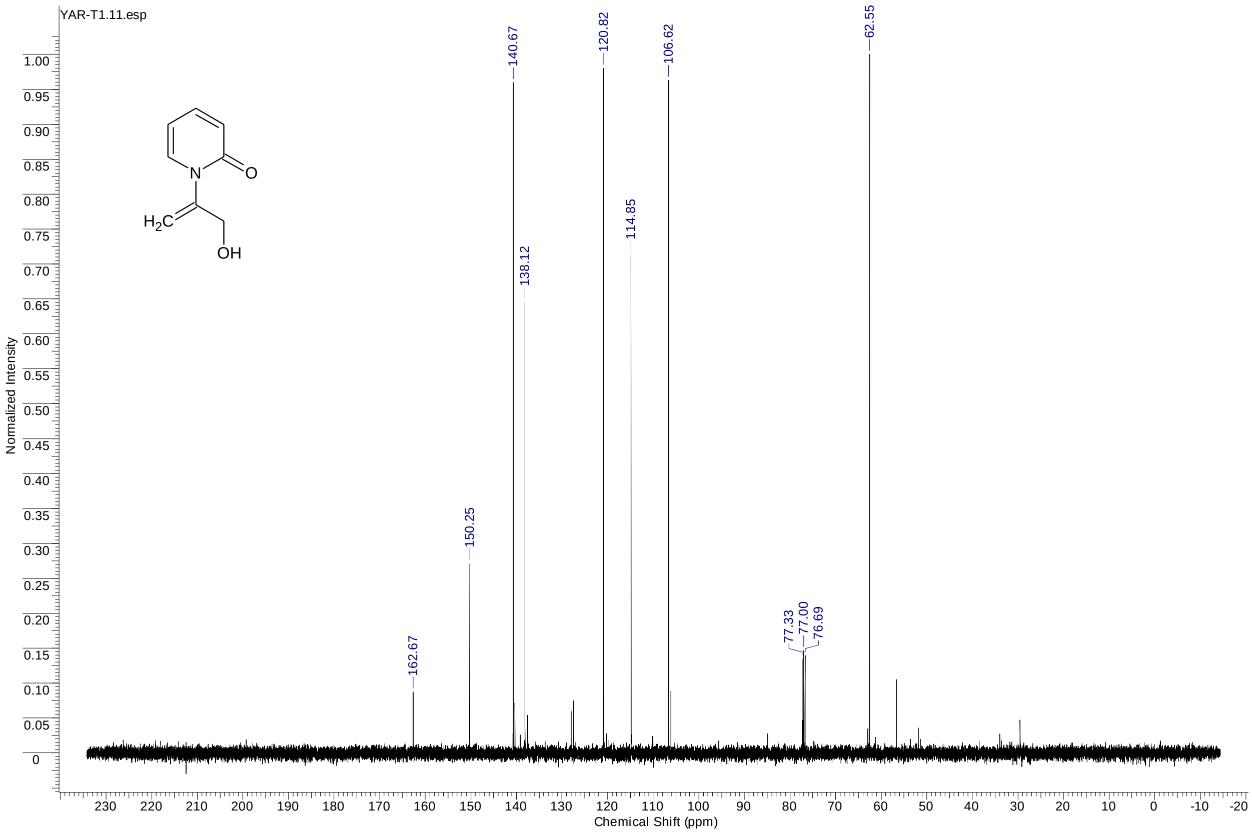

Figure S17. ^{13}C NMR spectra of compound 6b

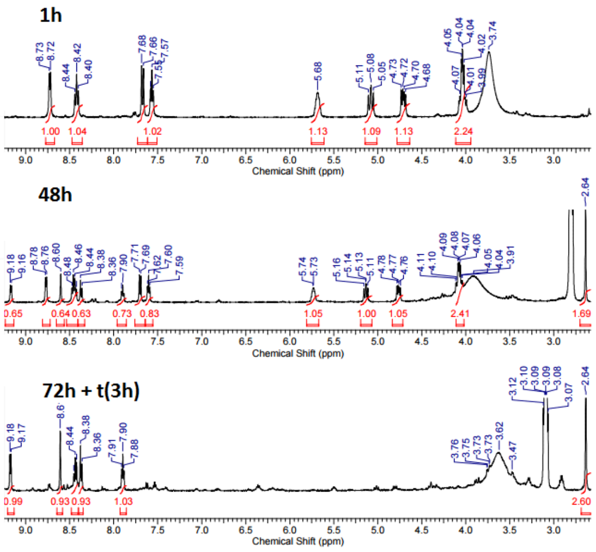

Figure S18. Changes in the ^{1}H NMR spectra of **1a** and Et_3N immediately after mixing (top), after 2 days (middle), and after 3 days with 3 hours of heating (bottom).

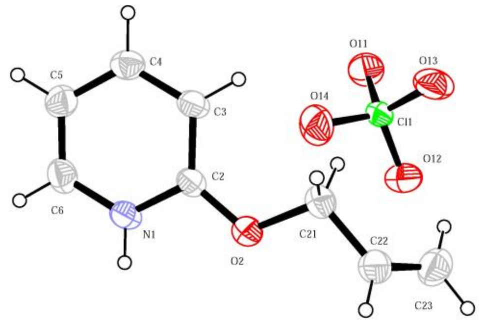

Figure S19. X-ray diffraction of **2b**

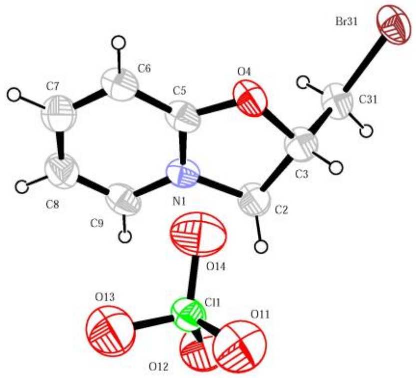

Figure S20. X-ray diffraction of **1a**

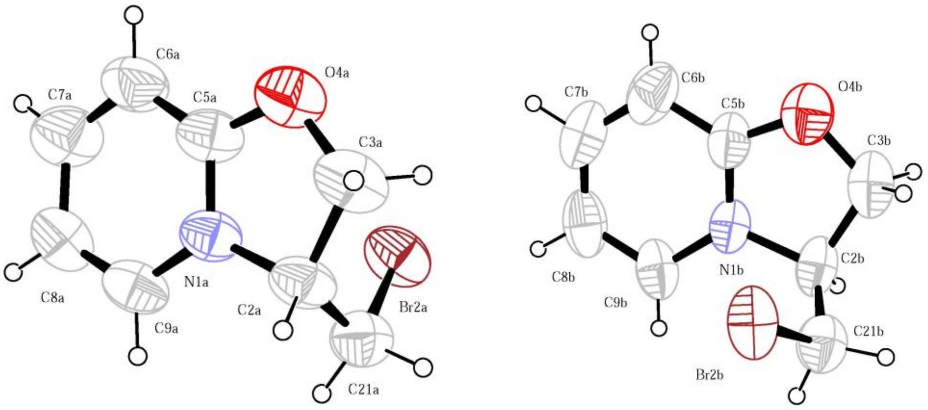

Figure S21. X-ray diffraction of **1b** (perchlorate anion not shown)

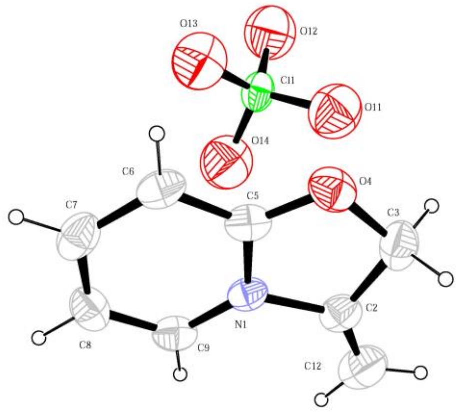

Figure S22. X-ray diffraction of **3b**