# Oxazoline amino acid bioconjugates: One-pot synthesis and analysis of supramolecular interactions

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## Supplementary materials

## 1. Compounds overview, syntheses schemes and spectroscopic characterization data

Chart S1. Bis-amino acids **2**, mixed derivatives **3** and bis-amino alcohols **4** derived from isophthalic (**m**) and terephthalic (**p**) acid synthesized in this paper, using achiral amino alcohols and chiral amino acids.

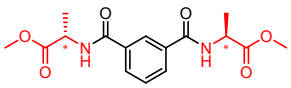
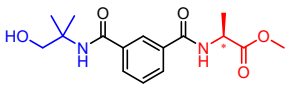
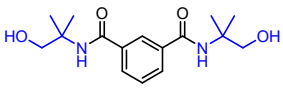
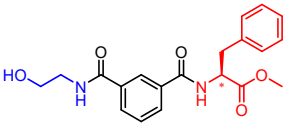
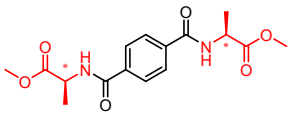
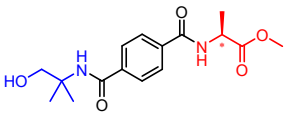
| | **2** | **3** | 4 |
|---|---|---|---|
| **m1** |  **$2_{m1}$** |  **$3_{m1}$** |  **$4_{m1}$** |
| **m2** | not isolated |  **$3_{m2}$** | not isolated |
| **p1** |  **$2_{p}$** |  **$3_{p}$** | not isolated |

Chart S2. Mixed derivatives **3** and bis-amino alcohols **4** derived from isophthalic (**m**) acid synthesized in this paper, using chiral amino alcohols and chiral amino acids.

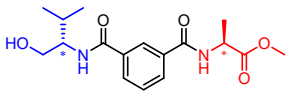
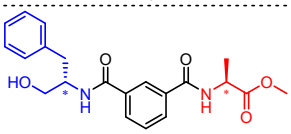
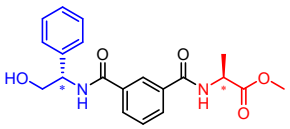
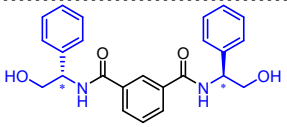
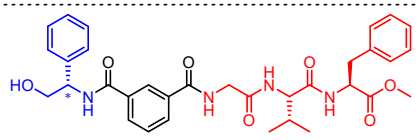
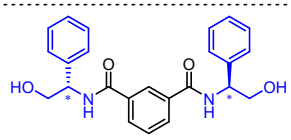
| | **2** | **3** | 4 |
|---|---|---|---|
| **m3** | not isolated |  **$3_{m3}$** | not isolated |
| **m4** | not isolated |  **$3_{m4}$** | not isolated |
| **m5** | not isolated |  **$3_{m5}$** |  **$4_{m5}$** |
| **m6** | not isolated |  **$3_{m6}$** |  **$4_{m5}$** |

Chart S3. Bis-amino acids **2**, mixed derivatives **3** and bis-amino alcohols **4** derived from 1,4-naphthalic ($\mathbf{n_1}$), 1,5-naphthalic ($\mathbf{n_3}$), 2,6-naphthalic ($\mathbf{n_4}$), 2,7-naphthalic ($\mathbf{n_5}$) or 9,10-anthracene ($\mathbf{a_1}$) diacids, using achiral amino alcohols, achiral ($\mathbf{n_2}$) and chiral amino acids synthesized in this paper.

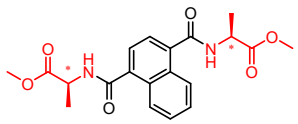
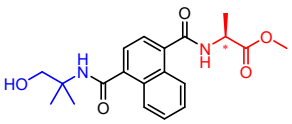
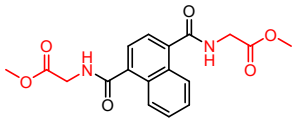
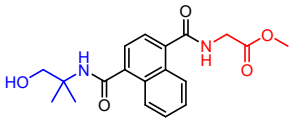
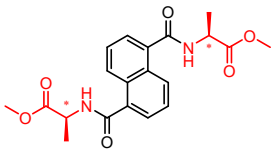
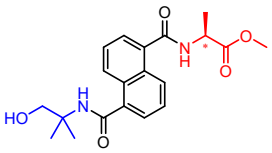
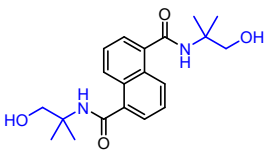
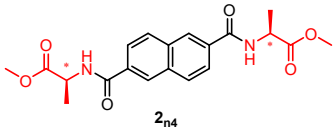
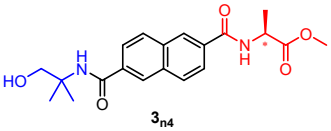
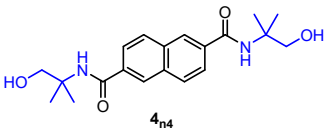
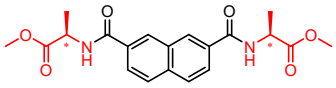
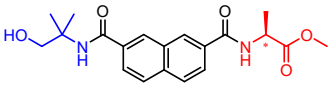
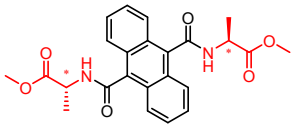
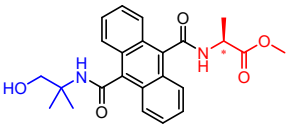
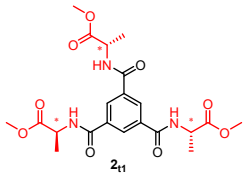
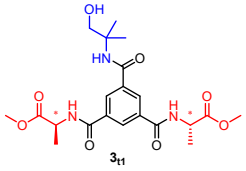
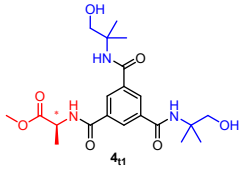
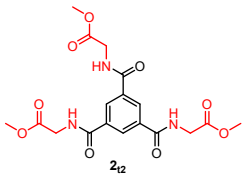
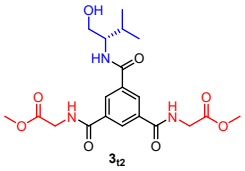
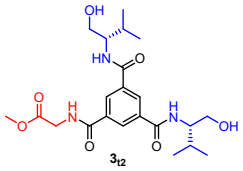
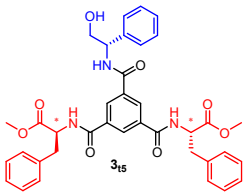
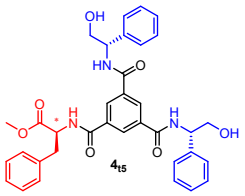
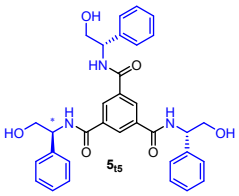
| | **2** | **3** | 4 |
|---|---|---|---|
| **n1** |  $\mathbf{2_{n1}}$ |  $\mathbf{3_{n1}}$ | not isolated |
| **n2** |  $\mathbf{2_{n2}}$ |  $\mathbf{3_{n2}}$ | not isolated |
| **n3** |  $\mathbf{2_{n3}}$ |  $\mathbf{3_{n3}}$ |  $\mathbf{4_{n3}}$ |
| **n4** |  $\mathbf{2_{n4}}$ |  $\mathbf{3_{n4}}$ |  $\mathbf{4_{n4}}$ |
| **n5** |  $\mathbf{2_{n5}}$ |  $\mathbf{3_{n5}}$ | not isolated |
| **a1** |  $\mathbf{2_a}$ |  $\mathbf{3_a}$ | not isolated |

Chart S4. Tris-amino acids **2**, mixed derivatives **3**, bis-amino alcohols **4** and tris-amino alcohols derived from trimesic acid (**t**), using achiral and chiral amino alcohols, as well as achiral and chiral amino acids synthesized in this paper.

| | **2** | **3** | 4 | 5 |
|---|---|---|---|---|
| **t1** |  $\mathbf{2}_{t1}$ |  $\mathbf{3}_{t1}$ |  $\mathbf{4}_{t1}$ | not isolated |
| **t2** |  $\mathbf{2}_{t2}$ |  $\mathbf{3}_{t2}$ |  $\mathbf{3}_{t2}$ | not isolated |
| **t5** | not isolated |  $\mathbf{3}_{t5}$ |  $\mathbf{4}_{t5}$ |  $\mathbf{5}_{t5}$ |

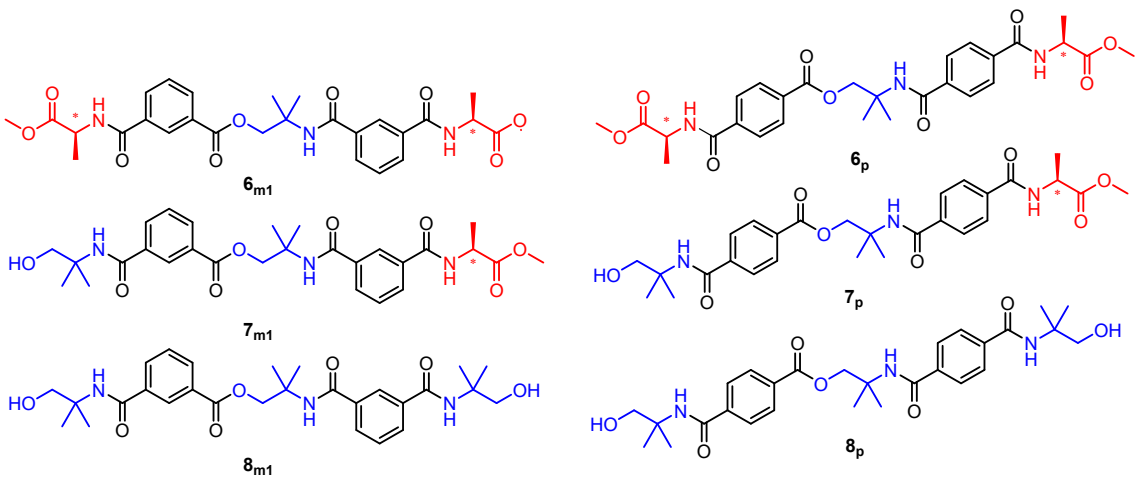
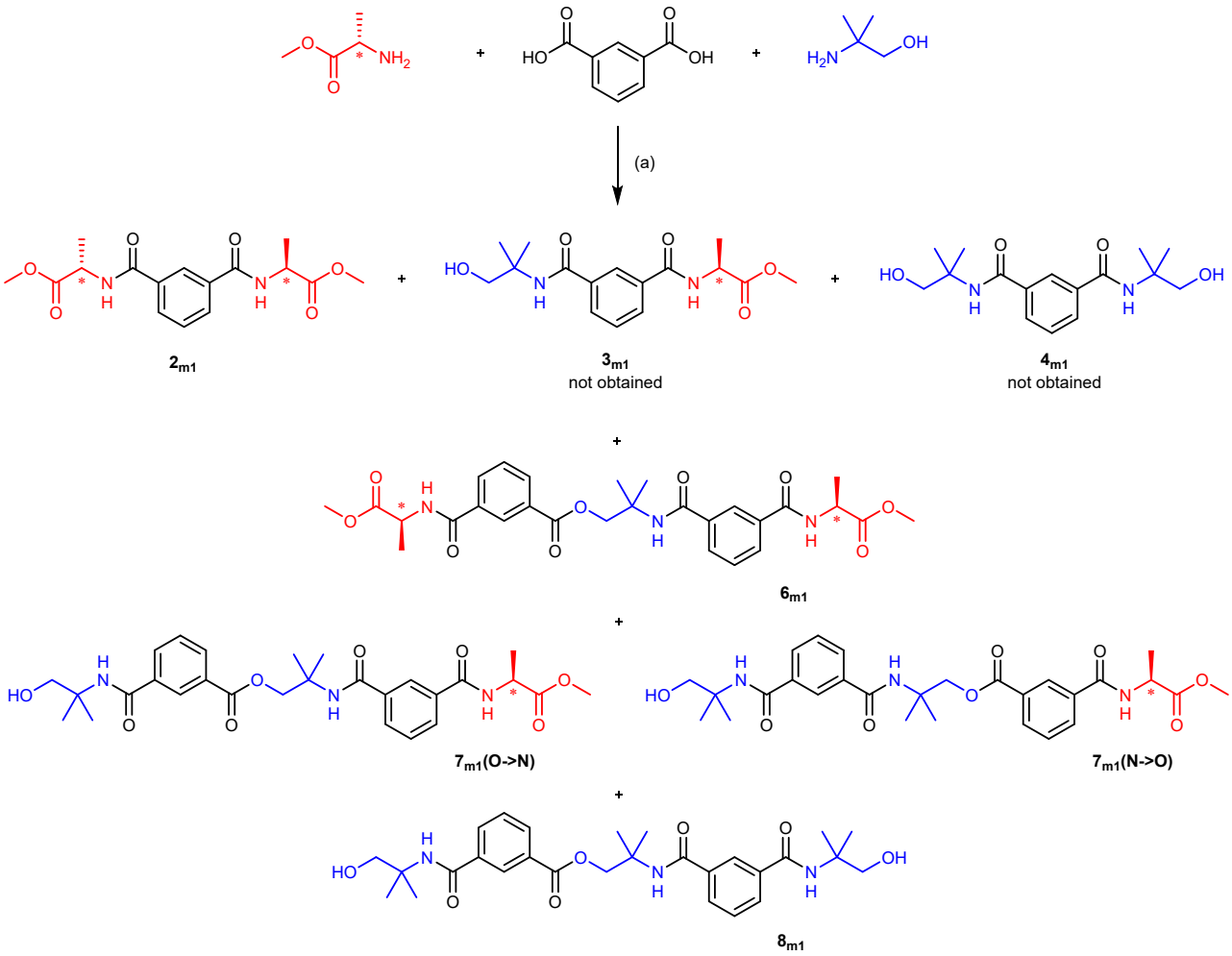
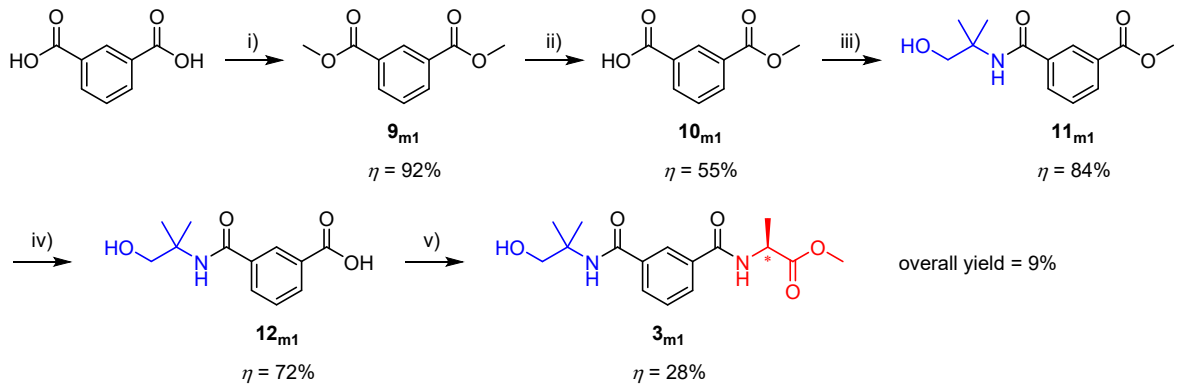


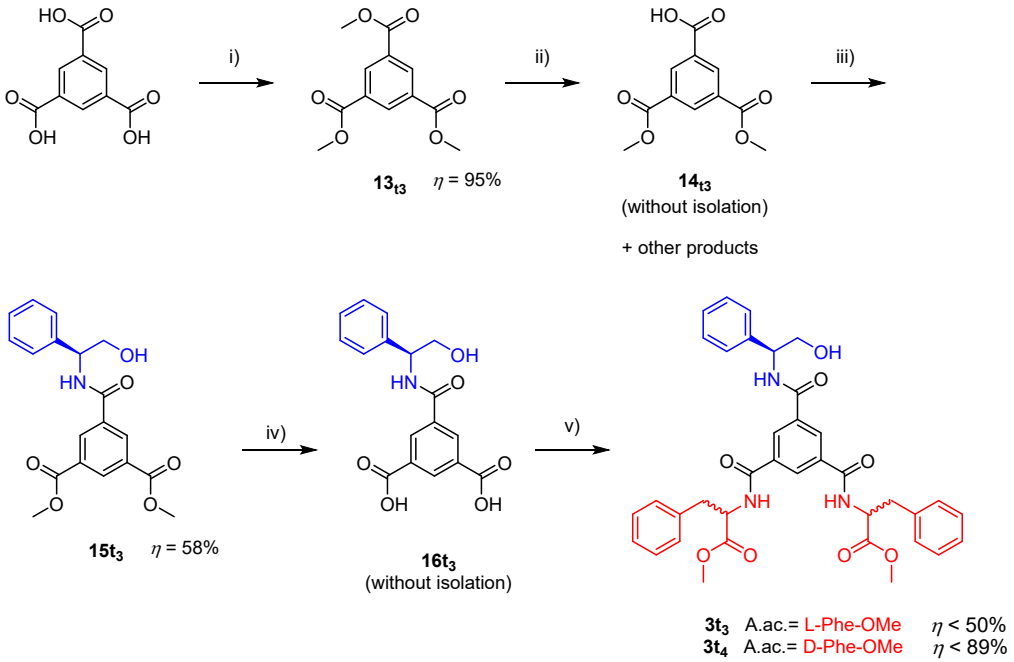

Chart S5. Ester-amide byproducts obtained in reaction 1 and 7 (tables 1 and 2 respectively).



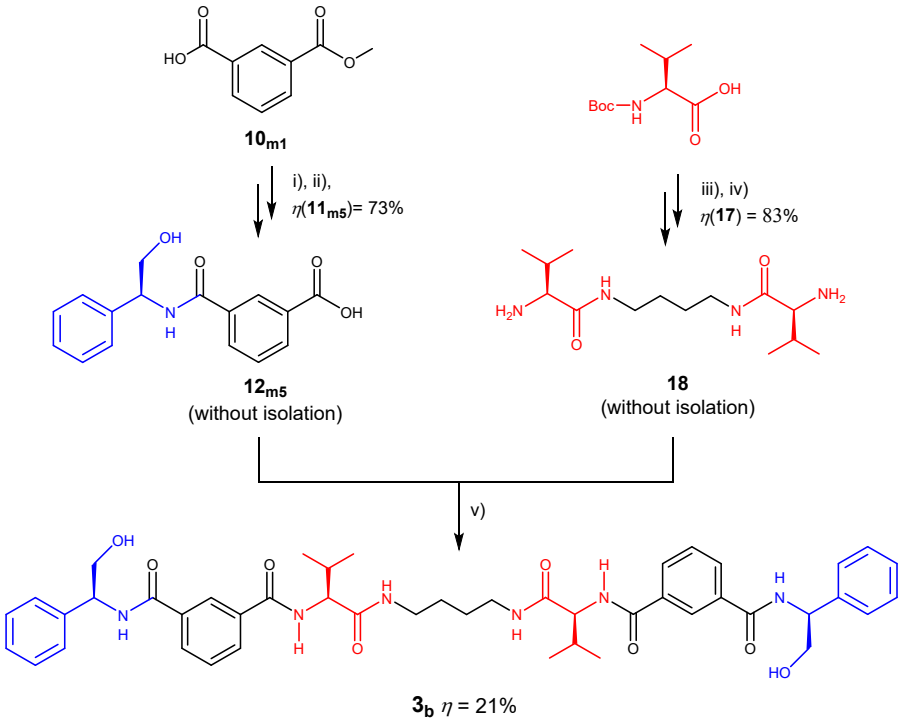

Scheme S1. Reaction conditions (a). TBTU/HOBt, DIPEA, DCM, 2 days (Table 1, reaction 1).




Scheme S2. Reaction conditions. i) $H_2SO_4$ (conc.), MeOH, 75 °C, stirring overnight; ii) MeOH : $H_2O$ (2 : 1), NaOH, microwave, 50 W, 150 °C, 20 min, HCl (conc.); iii) AMP, HATU, DIPEA, DCM, 1 day; iv) MeOH:$H_2O$ (2:1), NaOH, microwave, 50 W, 150 °C, 20 min, HCl (conc.); v) H-Ala-OMe, HATU, DIPEA, DCM, 1 day.




Scheme S3. Reaction conditions. i) $H_2SO_4$ (conc.), MeOH, 75 °C, stirring overnight; ii) MeOH : $H_2O$ (2 : 1), NaOH, microwave, 50 W, 150 °C, 20 min, HCl (conc.); iii) (S)-(+)-phenylglycinol, HATU, DIPEA, DCM, 1 day; iv) MeOH:$H_2O$ (2:1), NaOH, microwave, 50 W, 150 °C, 20 min, HCl (conc.); v) $H_2N$-L-Ala-OMe, HATU, DIPEA, DCM, 1 day.




Scheme S4. Reaction conditions. i) Phg#, TBTU/HOBt, DIPEA, DCM, 1 day; ii) MeOH:$H_2O$ (2:1), NaOH, microwave, 50 W, 150 °C, 20 min, HCl (conc.); iii) Boc-Val-OH, 1,4-diaminobutane, TBTU/HOBt, DIPEA, DCM, 1 day; iv) TFA : DCM = 1 : 1, 2h, r.t., DIPEA; v) HATU, DIPEA, DCM, 1 day.

## 1.1. Spectroscopic characterization of compounds **2-15**

**Ala-*m*$C_6H_4$-Ala ($2_{m1}$).** Reactions 1, 4 and 5. $M_r(C_{16}H_{20}N_2O_6)$ = 336.13. ESI-MS (*m*/*z*): 337.3 ($M + H^+$), 673.6 ($2M + H^+$). Crystals suitable for single-crystal x-ray diffraction obtained from dichloromethane/water mixture after one month. $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.22 (s, 1H), 7.95 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 7.0 Hz, 2H), 4.82 (quin., *J* = 7.2 Hz, 2H), 3.80 (s, 6H), 1.54 (d, *J* = 7.2 Hz, 6H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm: 172.88, 165.24, 133.20, 129.57, 128.06, 124.42, 51.75, 47.76, 17.33.

**Ala-*m*$C_6H_4$-AMP ($3_{m1}$).** Reactions 3, 4 and 5. $M_r(C_{16}H_{20}N_2O_6)$ = 322.15. ESI-MS (*m*/*z*): 323.1 ($M + H^+$), 645.2 ($2M + H^+$), 667.2 ($2M + Na^+$). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.11 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.04 (d, *J* = 7.1 Hz, 1H), 6.38 (s, 1H), 4.80 (quin., *J* = 7.2 Hz, 1H), 4.48 (t, *J* = 6.2 Hz, 1H), 3.81 (s, 3H), 3.76 – 3.67 (m, 2H), 1.53 (d, *J* = 7.2 Hz, 3H), 1.43 (s, 5H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm: 174.11, 167.64, 166.15, 135.54, 133.75, 130.55, 130.07, 129.01, 125.34, 70.31, 56.76, 52.84, 48.79, 24.63, 24.59, 18.22.

**AMP-*m*$C_6H_4$-AMP ($4_{m1}$).** Reaction 6. $^1$H NMR (600 MHz, DMSO) *δ*/ppm: 8.46 – 8.41 (m, 1H), 7.89 (dd, *J* = 7.5, 1.6 Hz, 3H), 7.29 (t, *J* = 7.5 Hz, 2H), 3.34 (s, 4H), 1.15 (s, 13H). $^{13}$C NMR (151 MHz, DMSO) δ/ppm: 170.24, 137.45, 130.39, 130.05, 126.56, 67.43, 53.58, 23.19. ESI-MS spectrum was recorded, but the results suggested there was a problem with recording this compound.

**Ala-*m*$C_6H_4$-AMP-*m*$C_6H_4$-Ala ($6_{m1}$).** Reaction 1. $M_r(C_{40}H_{46}N_4O_{12})$ = 555.22. ESI-MS (*m*/*z*): 556.4 ($M + H^+$), 1111.9 ($2M + H^+$). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.45 (s, 1H), 8.19 – 8.08 (m, 2H), 8.03 – 7.96 (m, 1H), 7.90 – 7.80 (m, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.07 – 6.96 (m, 2H), 6.64 (s, 1H), 4.82 – 4.71 (m, 2H), 4.57 (s, 2H), 3.76 (t, *J* = 5.0 Hz, 6H), 1.58 (d, *J* = 3.3 Hz, 6H), 1.52 – 1.46 (m, 6H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm: 173.70, 173.66, 166.56, 166.28, 166.24, 165.91, 132.75, 132.14, 130.3, 130.33, 130.15, 129.09, 129.08, 128.31, 125.37, 70.44, 54.63, 52.73, 48.75, 48.73, 24.32, 24.27, 18.43.

**AMP-*m*$C_6H_4$-AMP-*m*$C_6H_4$-Ala ($7_{m1}$).** Reaction 1. $M_r(C_{28}H_{35}N_3O_8)$ = 541.24. ESI-MS (*m*/*z*): 542.4 ($M + H^+$), 1105.9 ($2M + Na^+$). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.48 (s, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.07 (s, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.90 – 7.86 (m, 2H), 7.56 – 7.47 (m, 2H), 6.93 (d, J = 7.2 Hz, 1H), 6.66 (s, 1H), 6.38 (s, 1H), 4.79 (quin., J = 7.2 Hz, 1H), 4.58 (s, 2H), 3.79 (s, 3H), 3.70 (s, 2H), 1.61 – 1.59 (m, 6H).

**AMP-*m*$C_6H_4$-AMP-*m*$C_6H_4$-AMP ($8_{m1}$).** Reaction 1.
$M_r(C_{28}H_{37}N_3O_7)$ = 527.26. ESI-MS (*m*/*z*): 528.4 ($M + H^+$), 1077.9 ($2M + Na^+$). $^1$H NMR (600 MHz, $CDCl_3$) *δ*/ppm: 8.33 (s, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.60 (d, *J* = 2.2 Hz, 2H), 4.68 (s, 2H), 4.53 (s, 2H), 3.66 – 3.60 (m, 4H), 1.55 (s, 6H), 1.39 – 1.36 (m, *J* = 4.0 Hz, 12H).

**Ala-*p*$C_6H_4$-Ala ($2_p$).** Reaction 7. $M_r(C_{16}H_{20}N_2O_6)$ = 336.13. ESI-MS (*m*/*z*): 337.1 ($M + H^+$, 55%) $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 7.86 (s, 4H), 6.87 (d, *J* = 7.1 Hz, 2H), 4.80 (quin., *J* = 7.2 Hz, 2H), 3.80 (s, 6H), 1.54 (d, *J* = 7.2 Hz, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) δ/ppm: 174.71, 169.18, 138.04, 128.70, 52.82, 50.17, 38.88, 17.19.

**AMP-*p*$C_6H_4$-Ala ($3_p$).** Reaction 7. $M_r(C_{16}H_{20}N_2O_6)$ = 322.15. ESI-MS (*m*/*z*) obtained from $\mathbf{3_{p1}}$ and $\mathbf{7_{p1}}$ mixture: 323.1 ($M + H^+$, 33%), 345.1 ($M + Na^+$, 78%), 667.3 ($2M+Na^+$ 32%). $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm obtained from $\mathbf{3_{p1}}$ and $\mathbf{7_{p1}}$ mixture: 7.95 – 7.60 (m, 4H), 6.83 (d, 1H), 6.29 (s, 1H), 4.80 (quin., 1H), 4.34 (s, 1H), 3.81 (s, 3H), 3.71 (s, 2H), 1.54 (d, 3H), 1.44 (s, 6H). $^{13}$C NMR (75 MHz, $CD_3OD$) δ/ppm obtained

from $\mathbf{3_{p1}}$ and $\mathbf{7_{p1}}$ mixture: 174.72, 169.20, 166.91, 137.56, 134.07, 130.62, 128.77, 128.61, 128.52, 70.11, 55.17, 52.82, 50.17, 24.63, 17.19.

**AMP-*p*$C_6H_4$-AMP-*p*$C_6H_4$-Ala ($\mathbf{7_p}$).** Reaction 7. $M_r(C_{28}H_{35}N_3O_8)$ = 541.24. ESI-MS (*m*/*z*) obtained from **3p** and **6p** mixture: 564.2 ($M + Na^+$), 1105.5 ($2M + Na^+$, 5%). $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm obtained from $\mathbf{3_{p1}}$ and $\mathbf{7_{p1}}$ mixture: 8.13 – 8.00 (m, 2H), 7.95 – 7.60 (m, 6H), 6.83 (s, 1H), 6.53 (d, 1H), 6.29 (s, 1H), 4.80 (quin., 1H), 4.59 (s, 2H), 4.34 (s, 1H), 3.81 (s, 3H), 3.71 (s, 2H), 1.60 (s, 6H), 1.54 (d, 3H), 1.44 (s, 6H).

**ETA-*m*$C_6H_4$-Phe ($\mathbf{3_{m2}}$)**. Reaction 8. $^1$H NMR (600 MHz, $CDCl_3$) *δ*/ppm: 8.09 (t, *J* = 1.9 Hz, 1H), 7.91 (ddd, *J* = 7.7, 1.8, 1.1 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.34 – 7.24 (m, 3H) 7.20 – 7.12 (m, 2H), 6.92 (d, *J* = 7.3 Hz, 2H), 5.07 (dt, *J* = 7.6, 6.0 Hz, 1H), 3.84 (dd, *J* = 5.9, 2.7 Hz, 2H), 3.79 (s, 3H), 3.67 – 3.59 (m, 2H), 3.49 (t, *J* = 1.9 Hz, 2H), 3.26 (ddd, *J* = 54.3, 13.9, 6.0 Hz, 2H), 2.87 (s, 1H).$^{13}$C NMR (151 MHz, $CD_3OD$) *δ*/ppm: 173.55, 169.61, 169.41, 138.43, 136.19, 135.64, 131.43, 131.29, 130.22, 129.81, 129.54, 127.90, 127.46, 61.55, 55.96, 52.79, 43.63, 38.18.

**Val$^{\#}$-*m*$C_6H_4$-Ala ($\mathbf{3_{m3}}$)**. Reaction 9. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.15 (d, *J* = 1.9 Hz, 1H), 7.83 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 1H), 4.80 (s, 1H), 4.09 – 3.94 (m, 1H), 3.81 (s, 5H), 2.96 (t, *J* = 5.6 Hz, 1H), 2.00 (dt, *J* = 13.8, 7.0 Hz, 1H), 1.55 (d, *J* = 7.2 Hz, 3H), 1.02 (dd, *J* = 6.8, 4.5 Hz, 6H).

**Phe$^{\#}$-*m*$C_6H_4$-Ala ($\mathbf{3_{m4}}$)**. Reaction 10. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.07 (t, *J* = 1.8 Hz, 1H), 7.78 (ddt, *J* = 26.5, 7.8, 1.4 Hz, 2H), 7.46 – 7.19 (m, 5H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 4.81 (t, *J* = 7.3 Hz, 1H), 4.42 (dd, *J* = 11.0, 5.9 Hz, 1H), 3.89 – 3.64 (m, 5H), 3.08 – 2.95 (m, 2H), 1.54 (d, *J* = 7.2 Hz, 3H).

**Phg$^{\#}$-*m*$C_6H_4$-Ala ($\mathbf{3_{m5}}$)**. Reaction 11. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.18 (s, 1H), 7.80 (d, *J* = 6.3 Hz, 2H), 7.56 – 7.21 (m, 8H), 5.35 (s, 1H), 4.82 (s, 1H), 4.01 (s, 2H), 3.82 (s, 3H), 3.36 (t, *J* = 6.3 Hz, 1H).

**(Phg$^{\#}$)$_2$-*m*$C_6H_4$ ($\mathbf{4_{m5}}$)**. Reaction 11. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.03 (s, 1H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.48 – 7.11 (m, 12H), 6.85 (t, *J* = 7.7 Hz, 1H), 5.30 (q, *J* = 4.6 Hz, 2H), 4.44 (s, 2H), 3.96 (d, *J* = 19.7 Hz, 4H).

**Phe$^{\#}$-*m*$C_6H_4$-Gly-Val-Phe-OMe ($\mathbf{3_{m6}}$)**. Reaction 12. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.22 (s, 1H), 7.84 (dt, *J* = 26.5, 7.9 Hz, 2H), 7.53 (s, 1H), 7.47 – 7.11 (m, 5H), 7.07 (d, *J* = 7.0 Hz, 2H), 6.79 (s, 1H), 5.32 (d, *J* = 13.5 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.30 (t, *J* = 7.3 Hz, 1H), 4.22 – 3.83 (m, 5H), 3.65 (s, 3H), 3.01 (d, *J* = 7.6 Hz, 2H), 2.07 (q, *J* = 6.8 Hz, 1H), 0.97 – 0.79 (m, 6H).

**Ala-1,4-Nph-Ala ($\mathbf{2_{n1}}$).** Reaction 13. $M_r(C_{20}H_{22}N_2O_6)$ = 386.15. ESI-MS (*m*/*z*): 387.2 ($M + H^+$, 50%), 409.0 ($M + Na^+$, 39%), 773.3 ($2M + H^+$, 78%), 795.1 ($2M + Na^+$, 49%). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.31 (dd, *J* = 6.5, 3.3 Hz, 2H), 7.62 – 7.53 (m, 4H), 6.62 (d, *J* = 7.4 Hz, 2H), 4.89 (quin., *J* = 7.2 Hz, 2H), 3.82 (s, 6H), 1.58 (d, *J* = 7.2 Hz, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) δ/ppm: 174.67, 171.86, 137.48, 131.64, 128.35, 126.79, 125.27, 52.87, 50.14, 17.09.

**AMP-1,4-Nph-Ala ($\mathbf{3_{n1}}$).** Reaction 13. $M_r(C_{20}H_{24}N_2O_5)$ = 372.14. ESI-MS (*m*/*z*): 373.2 ($M + H^+$), 395.1 ($M + Na^+$, 22%), 745.3 ($2M + H^+$, 83%), 767.2 ($2M + Na^+$, 26%). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.31 – 8.23 (m, 1H), 8.18 – 8.11 (m, 1H), 7.59 – 7.52 (m, 2H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 7.1 Hz, 1H), 6.68 (d, *J* = 7.4 Hz, 1H), 6.28 (s, 1H), 4.86 (quin., *J* = 7.2 Hz, 1H), 4.51 (s, 1H), 3.81 (d, *J* = 9.0 Hz, 3H), 3.74 (s, 2H), 1.56 (d, *J* = 6.8 Hz, 3H), 1.45 (s, 6H). $^{13}$C NMR (75 MHz, $CD_3OD$) δ/ppm: 174.68, 172.01, 171.89, 138.96, 136.94, 131.64, 131.50, 128.26, 128.23, 126.80, 126.63, 125.41, 124.85, 68.94, 57.16, 52.86, 49.85, 24.13, 17.11.

**Gly-1,4-Nph-Gly ($2_{n2}$)**. Reaction 14. $M_r(C_{18}H_{18}N_2O_6)$ = 358.12. ESI-MS (*m*/*z*): 359.1 (M + $H^+$, 40%), 717.1 (2M + $H^+$, 22%). $^1$H NMR (300 MHz, $CD_3CN$) δ/ppm: 8.38 – 8.26 (m, 2H), 7.69 – 7.59 (m, 4H), 7.39 – 7.26 (m, 2H), 4.16 (d, *J* = 6.0 Hz, 4H), 3.77 (s, 6H). $^{13}$C NMR (151 MHz, CD3OD) δ/ppm: 172.37, 171.72, 137.54, 131.62, 128.45, 126.84, 125.30, 52.74, 42.30.

**AMP-1,4-Nph-Gly ($3_{n2}$)**. Reaction 14. $M_r(C_{19}H_{22}N2O_5)$ = 358.15. ESI-MS (*m*/*z*): 359.1 (M + $H^+$), 717.1 (2M + $H^+$). $^1$H NMR (600 MHz, $CD_3CN$) δ 8.35 – 8.28 (m, 1H), 8.24 – 8.18 (m, 1H), 7.64 – 7.60 (m, 3H), 7.57 (d, *J* = 7.1 Hz, 1H), 7.31 (s, 1H), 6.78 (s, 1H), 4.15 (d, *J* = 6.0 Hz, 2H), 3.97 (t, *J* = 6.1 Hz, 1H), 3.76 (s, 3H), 3.67 (d, *J* = 6.1 Hz, 2H), 1.40 (s, 6H). $^{13}$C NMR (75 MHz, DMSO) δ/ppm: 170.37, 168.88, 168.34, 138.00, 135.20, 129.82, 129.77, 126.79, 125.66, 124.15, 123.59, 67.18, 55.30, 51.87, 41.11, 23.64.

**Ala-1,5-Nph-Ala ($2_{n3}$).** Reaction 15. $M_r(C_{20}H_{22}N_2O_6)$ = 386.15. ESI-MS (*m*/*z*): 387.2 (M + $H^+$, 24%), 773.3 (2M + $H^+$, 7%). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm:8.47 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 6.9 Hz, 2H), 7.55 (dd, *J* = 8.4, 7.1 Hz, 2H), 6.55 (d, *J* = 7.3 Hz, 2H), 4.95 – 4.86 (m, 2H), 3.83 (s, 6H), 1.60 – 1.57 (m, 6H). $^{13}$C NMR (151 MHz, DMSO) δ/ppm: 173.14, 168.58, 134.53, 129.85, 127.31, 125.65, 125.51, 51.99, 48.24, 16.60.

**AMP-1,5-Nph-Ala ($3_{n3}$).** Reaction 15. $M_r(C_{20}H_{24}N_2O_5)$ = 372.17. ESI-MS (*m*/*z*): 373.1 (M + $H^+$), 745.2 (2M + $H^+$). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm:8.42 (d, *J* = 8.6 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.69 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.59 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.56 – 7.47 (m, 2H), 6.59 (d, *J* = 7.4 Hz, 1H), 6.11 (s, 1H), 4.89 (quin., *J* = 7.3 Hz, 1H), 4.59 (s, 1H), 3.82 (s, 3H), 3.77 (d, *J* = 3.9 Hz, 2H), 1.58 (d, *J* = 7.2 Hz, 3H), 1.47 (s, 6H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm:172.50, 169.55, 167.97, 134.03, 133.17, 129.44, 129.26, 127.09, 127.06, 125.03, 124.97, 124.80, 124.36, 69.64, 56.15, 51.76, 47.73, 23.79, 17.46.

**AMP-1,5-Nph-AMP ($4_{n3}$).** Reaction 15. $M_r(C_{20}H_{26}N_2O_4)$ = 358.19. ESI-MS (*m*/*z*): 359.1 (M + $H^+$, 59 %), 717.2 (2M + $H^+$, 31 %), $^1$H NMR (600 MHz, DMSO) δ/ppm: 8.19 – 8.16 (m, 2H), 7.87 (s, 2H), 7.56 – 7.53 (m, 2H), 4.91 (s, 2H), 3.60 – 3.55 (m, 4H), 1.37 (s, 12H). $^{13}$C NMR (75 MHz, DMSO) δ/ppm: 168.72, 136.35, 129.80, 126.63, 125.51, 124.89, 67.32, 55.25, 23.65.

**Ala-2,6-Nph-Ala ($2_{n4}$).** Reaction 16. $M_r(C_{20}H_{22}N_2O_6)$ = 386.15. ESI-MS (*m*/*z*): 387.1 (M + $H^+$, 42%), 773.1 (2M + $H^+$, 11%).a $^1$H NMR (600 MHz, $CD_3OD$) δ/ppm: 8.47 (s, 2H), 8.13 – 8.04 (m, 2H), 8.03 – 7.94 (m, 2H), 4.75 – 4.61 (m, 2H), 3.77 (s, 6H), 1.55 (d, J = 7.3 Hz, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) δ/ppm: 174.85, 169.79, 135.46, 134.23, 130.48, 128.82, 125.99, 52.83, 50.27, 17.26.

**AMP-2,6-Nph-Ala ($3_{n4}$).** Reaction 16. $M_r(C_{20}H_{24}N_2O_5)$ = 372.42. ESI-MS (*m*/*z*): 373.1 (M + $H^+$). $^1$H NMR (600 M Hz, $CD_3OD$) δ/ppm: 8.45 (s, 1H), 8.37 (s, 1H), 8.05 (t, J = 8.3 Hz, 2H), 7.98 – 7.95 (m, J = 8.5, 1.7 Hz, 1H), 7.93 – 7.89 (m, J = 8.5, 1.7 Hz, 1H), 4.72 – 4.64 (m, 1H), 3.77 (s, 3H), 3.75 (s, 2H), 1.55 (d, J = 7.3 Hz, 3H), 1.46 (s, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) δ/ppm:174.86, 170.29, 169.83, 136.06, 135.47, 135.17, 133.95, 130.37, 130.32, 128.78, 128.36, 126.09, 125.86, 69.19, 56.91, 52.83, 50.26, 24.09, 17.26.

**AMP-2,6-Nph-AMP ($4_{n4}$).** Reaction 16. $M_r(C_{20}H_{26}N_2O_4)$ = 358.19. ESI-MS (*m*/*z*): 359.1 (M + $H^+$), $^1$H NMR (600 MHz, $CD_3OD$) δ/ppm: 8.35 (s, 2H), 8.03 (s, 2H), 7.90 (s, 2H), 3.75 (s, 4H), 1.45 (s, 12H). $^{13}$C NMR (75 MHz, DMSO) δ/ppm:166.23, 134.11, 132.84, 128.38, 126.78, 124.91, 67.18, 54.93, 23.38.

**Ala-2,7-Nph-Ala ($2_{n5}$).** Reaction 17. $M_r(C_{20}H_{22}N_2O_6)$ = 386.15. ESI-MS (*m*/*z*): 387.1 (M + $H^+$), 773.2 (2M + $H^+$). Crystals suitable for single-crystal x-ray diffraction were obtained from solution in NMR tube after several months. $^1$H NMR (600 MHz, $CDCl_3$)

δ/ppm: 8.39 – 8.29 (m, 2H), 7.94 – 7.89 (m, 2H), 7.88 – 7.82 (m, 2H), 7.05 (d, *J* = 7.2 Hz, 2H), 4.88 (quin., *J* = 7.2 Hz, 2H), 3.83 (s, 6H), 1.59 (d, *J* = 7.2 Hz, 6H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm:174.00, 136.16, 132.04, 131.70, 128.54, 128.28, 125.72, 52.80, 48.80, 18.61.

**AMP-2,7-Nph-Ala ($3_{n5}$).** Reaction 17. $M_r(C_{20}H_{24}N_2O_5)$ = 372.42. ESI-MS (*m/z*): 373.1 ($M + H^+$), 745.2 ($2M + H^+$, 85%). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.31 (s, 1H), 8.15 (s, 1H), 7.90 – 7.70 (m, 4H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.59 (s, 1H), 4.89 (quin., *J* = 7.2 Hz, 1H), 4.62 (t, *J* = 6.2 Hz, 1H), 3.84 (s, 3H), 3.76 (d, *J* = 6.0 Hz, 2H), 1.59 (d, *J* = 7.2 Hz, 3H), 1.50 (s, 6H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ/ppm: 174.33, 168.45, 167.08, 135.78, 133.20, 131.39, 131.22, 128.33, 128.06, 128.00, 127.80, 125.91, 125.42, 70.80, 56.72, 52.86, 48.82, 24.57, 24.56, 18.29.

**Ala-9,10-Anth-Ala ($2_{a1}$).** Reaction 18. $Mr(C_{24}H_{24}N_2O_6)$ = 436.16. ESI-MS (*m/z*): 437.1 ($M + H^+$, 18%), 873.3 ($2M + H^+$, 26%). $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 8.43 – 7.87 (m, 4H), 7.60 – 7.49 (m, 4H), 6.55 (d, *J* = 7.4 Hz, 2H), 5.06 (quin., 2H), 3.86 (s, 6H), 1.65 (d, *J* = 7.2 Hz, 6H). $^{13}$C NMR (75 MHz, $CD_3OD$) δ/ppm: 174.63, 129.17, 128.70, 127.70, 126.90, 126.44, 52.90, 50.30, 17.00.

**AMP-9,10-Anth-Ala ($3_{a1}$).** Reaction 18. $Mr(C_{24}H_{26}N_2O_5)$ = 422.18. ESI-MS (*m/z*): 423.1 ($M + H^+$), 845.3 ($2M + H^+$). $^1$H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.38 – 8.04 (m, 4H), 7.59 – 7.55 (m, 4H), 6.54 (s, 1H), 6.08 (s, 1H), 5.06 (quin., *J* = 7.2 Hz, 1H), 4.56 (s, 1H), 3.91 (d, *J* = 6.1 Hz, 2H), 3.86 (s, 3H), 1.65 (d, *J* = 7.2 Hz, 3H), 1.53 (s, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) δ/ppm: 174.63, 171.96, 171.70, 135.63, 134.02, 129.21, 128.79, 128.61, 128.56, 127.81 – 127.48 (4C), 127.02, 126.64, 126.44, 126.36, 68.94, 57.60, 52.89, 50.29, 24.24, 16.99.

**1,3,5-$C_6H_3$-(Ala-OMe)$_3$ ($2_{t1}$)**. Reaction 19. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.39 (s, 3H), 7.51 (d, *J* = 7.0 Hz, 3H), 4.60 (quin., *J* = 7.2 Hz, 3H), 3.71 (s, 9H), 1.48 (d, *J* = 7.3 Hz, 9H).

**AMP-1,3,5-$C_6H_3$-(Ala-OMe)$_2$ ($3_{t1}$)**. Reaction 19. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.37 (t, *J* = 1.7 Hz, 1H), 8.32 (d, *J* = 1.7 Hz, 2H), 7.50 (d, *J* = 6.8 Hz, 2H), 6.87 (s, 1H), 4.60 (quin., *J* = 7.2 Hz, 2H), 3.71 (s, 6H), 3.62 (s, 2H), 1.48 (d, *J* = 7.3 Hz, 6H), 1.38 (s, 6H). $^{13}$C NMR (151 MHz, $CD_3OD$) *δ*/ppm: 174.70, 168.94, 168.55, 137.97, 135.91, 130.34, 130.11, 68.88, 57.01, 52.85, 50.26, 24.05, 17.23.

**(AMP)$_2$-1,3,5-$C_6H_3$-Ala-OMe ($4_{t1}$)**. Reaction 19. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.30 (s, 2H), 8.25 (s, 1H), 7.49 (s, 1H), 6.86 (s, 2H), 4.59 (quin., *J* = 7.3 Hz, 1H), 3.87 (t, *J* = 6.2 Hz, 2H), 3.70 (s, 3H), 3.62 (d, *J* = 6.2 Hz, 4H), 1.48 (d, *J* = 7.3 Hz, 3H), 1.38 (s, 12H).

**1,3,5-$C_6H_3$-(Gly-OMe)$_3$ ($2_{t2}$)**. Reaction 20. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.40 (s, 3H), 7.64 (s, 3H), 4.11 (d, *J* = 5.9 Hz, 6H), 3.72 (s, 9H).

**Val$^{\#}$-1,3,5-$C_6H_3$-(Gly-OMe)$_2$ ($3_{t2}$)**. Reaction 20. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.37 (s, 3H), 7.66 (s, 2H), 7.05 (d, *J* = 9.1 Hz, 1H), 4.11 (d, *J* = 5.9 Hz, 4H), 3.99 – 3.83 (m, 1H), 3.72 (s, 6H), 3.64 (dt, *J* = 9.7, 4.1 Hz, 2H), 0.97 (dd, *J* = 7.8, 6.8 Hz, 6H).

**(Val$^{\#}$)$_2$-1,3,5-$C_6H_3$-Gly-OMe ($4_{t2}$)**. Reaction 20. $^1$H NMR (300 MHz, $CD_3CN$) *δ*/ppm: 8.37 (s, 3H), 7.71-7.49 (m, 1H), 7.03 (d, *J* = 9.0 Hz, 2H), 4.11 (d, *J* = 5.9 Hz, 2H), 4.02 – 3.82 (m, 2H), 3.72 (s, 3H), 3.69 – 3.60 (m, 4H), 2.97 (t, *J* = 6.0 Hz, 2H), 0.98 (dd, *J* = 8.1, 6.8 Hz, 12H).

**Phg$^{\#}$-1,3,5-$C_6H_3$-(Phe-OMe)$_2$ ($3_{t5}$)**. Reaction 21. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.16 (s, 1H), 8.02 (s, 0H), 7.58 (dd, *J* = 25.6, 7.9 Hz, 3H), 7.48 – 7.14 (m, 15H), 5.40 – 5.31 (m, 1H), 5.13 – 5.00 (m, 2H), 4.07 – 3.92 (m, 1H), 3.81 (s, 3H), 3.33 – 3.12 (m, 2H).

**(Phg$^{\#}$)$_2$-1,3,5-$C_6H_3$-Phe-OMe ($4_{t5}$)**. Reaction 21. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$/ppm: 8.09 (s, 1H), 8.00 (s, 2H), 7.71 (d, $J$ = 7.7 Hz, 3H), 7.48 – 7.06 (m, 15H), 5.36 (q, $J$ = 6.9, 5.3 Hz, 2H), 5.05 (q, $J$ = 7.2 Hz, 1H), 4.55 – 4.40 (m, 2H), 4.14 – 3.99 (m, 2H), 3.85-3.75 (m, 5H), 3.33 – 3.10 (m, 2H).

**(Phg$^{\#}$)$_3$-1,3,5-$C_6H_3$ ($5_{t5}$)**. Reaction 21. $^1$H NMR (300 MHz, $CD_3OD$) $\delta$/ppm: 8.49 (s, 2H), 8.36 (s, 1H), 7.51 – 7.18 (m, 15H), 5.23 (t, $J$ = 6.6 Hz, 3H), 3.87 (d, $J$ = 6.8 Hz, 6H).

**Linear reaction sequence 1**

**Dimethyl isophthalate ($9_{m1}$)**. Isophthalic acid (1 666.1 mg, 10 mmol) was dissolved in MeOH (100mL) and 2 mL of conc. $H_2SO_4$ was added to the solution. The reaction mixture was refluxed at 75˚C with continuous stirring overnight. MeOH was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (100 mL) and washed with water (100 mL), $NaHCO_3$ (sat. aq, 100 mL), water (100 mL), dried over $Na_2SO_4$, filtered and evaporated under reduced pressure to yield the crude white product. No further purification was required. Yield: 1 792.8 mg (9.23 mmol, 92%), white powder. $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 8.69 (t, J = 1.5 Hz, 1H), 8.23 (dd, J = 7.8, 1.7 Hz, 2H), 7.53 (t, J = 7.8 Hz, 1H), 3.95 (s, 6H).

**HOOC-*m*$C_6H_4$-COOMe ($10_{m1}$)**. Dimethyl isophthalate ($9_{m1}$) (1 791.8 mg, 9.23 mmol) was dissolved in MeOH (20 mL) by using an ultrasonic bath. Aqueous solution of NaOH (368.0 mg, 9.23 mmol in 10 mL of distilled water) was added to the mixture and the reaction mixture heated in a CEM Microwave Reactor for 20 min (150 W, 50 ˚C). To the aqueous residue HCl (284 µL conc., 9.23 mmol in 10 mL of distilled water) was added, and the white precipitate extracted with ethyl acetate (3 x 40 mL). Combined organic extracts were washed with citric acid (10% aq, 100 mL), NaCl (sat. aq. 100 mL), dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. Chromatography: 38 g of silica gel, 3% MeOH in DCM. Yield: 912.2 mg (5.06 mmol, 55%), white powder. $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 8.81 – 8.74 (m, 1H), 8.34 – 8.26 (m, 2H), 7.59 (t, $J$ = 7.8 Hz, 1H), 3.97 (s, 3H).

**AMP-*m*$C_6H_4$-COOMe ($11_{m1}$).** HOOC-*m*$C_6H_4$-COOMe (**$10_{m1}$**) (360.3 mg, 2.0 mmol), HATU (836.5 mg, 2.2 mmol), DIPEA (1. 360 mL, 8.0 mmol), AMP (222.9 mg, 2.5 mmol). NMR spectrum showed significant content of tetramethyl urea (mass ratio *w*(product) = 84 %). The compound was used without further purification. Yield: 421,5 mg (as calculated from NMR spectrum, 1.68 mmol, 84%), colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 8.33 (s, 1H), 8.17 (d, $J$ = 7.8 Hz, 1H), 8.00 (d, $J$ = 7.8 Hz, 1H), 7.54 (t, $J$ = 7.8 Hz, 1H), 6.23 (s, 1H), 3.95 (s, 3H), 3.72 (s, 2H), 1.44 (s, 7H).

**AMP-*m*$C_6H_4$-COOH ($12_{m1}$).** AMP-*m*$C_6H_4$-COOMe (**$11_{m1}$**) (421.5 mg, 1.68 mmol) was dissolved in MeOH (20 mL) by using an ultrasonic bath. Aqueous solution of NaOH (80.0 mg, 2.00 mmol in 10 mL of distilled water) was added to the mixture and the reaction mixture heated in a CEM Microwave Reactor for 20 min (150 W, 50 ˚C). To the aqueous residue HCl (62 µL conc., 2.0 mmol in 10 mL of distilled water) was added, and the white precipitate extracted with ethyl acetate (3 x 40 mL). Combined organic extracts were washed with citric acid (10% aq, 100 mL), NaCl (sat. aq. 100 mL), dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. NMR spectrum showed significant content of tetramethyl urea and water (mass ratio *w*(product) = 72 %). The compound was used without further purification. Yield: 387.0 mg (as calculated from NMR spectrum, 1.63 mmol, 97%) $^1$H NMR (300 MHz, $CD_3OD$) δ 8.43 (s, 1H), 8.17 (d, $J$ = 7.8 Hz, 1H), 8.00 (d, $J$ = 7.9 Hz, 1H), 7.57 (t, $J$ = 7.8 Hz, 1H), 3.73 (s, 2H), 1.44 (s, 6H).

**AMP-*m*$C_6H_4$-Ala ($3_{m1}$).** AMP-*m*$C_6H_4$-COOH (**$11_{m1}$**) (387.0 mg, 1.63 mmol), HATU (762.47 mg, 2.0 mmol), DIPEA (1. 360 mL, 8.0 mmol), AMP (222.9 mg, 2.5 mmol)

Chromatography: 30 g of silica gel, 3% MeOH in DCM. Yield: 147.3 mg (0.46 mmol, 28%; overall yield: 9%), colorless oil. Recorded spectra were analogous to the previously obtained spectra of the $\mathbf{3_{m1}}$ compound.

**Linear reaction sequence 2**

**1,3,5-$C_6H_3$-$(COOMe)_3$ ($\mathbf{13_{t3}}$)**. Trimesic acid (1 441.7 mg, 6.9 mmol) was dissolved in MeOH (100mL) and 2 mL of conc. $H_2SO_4$ was added to the solution. The reaction mixture was refluxed at 75˚C with continuous stirring overnight. MeOH was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (100 mL) and washed with water (100 mL), $NaHCO_3$ (sat. aq, 100 mL), water (100 mL), dried over $Na_2SO_4$, filtered and evaporated under reduced pressure to yield the crude white product. No further purification was required. Yield: 1 638.1 mg (6.5 mmol, 95%), white solid. $^1$H NMR (300 MHz, $CDCl_3$) δ/ppm: 8.86 (s, 3H), 3.98 (s, 9H).$^{13}$C NMR (151 MHz, $CD_3OD$) *δ*/ppm: 164.65, 133.21, 130.72, 51.27.

**HOOC-1,3,5-$C_6H_3$-$(COOMe)_2$ ($\mathbf{14_{t3}}$)**. 1,3,5-$C_6H_3$-$(COOMe)_3$ (**$\mathbf{13_{t3}}$**) (1 638.1 mg, 6.5 mmol) was dissolved in MeOH (20 mL) by using an ultrasonic bath. Aqueous solution of NaOH (259.9 mg, 6.5 mmol in 10 mL of distilled water) was added to the mixture and the reaction mixture heated in a CEM Microwave Reactor for 20 min (150 W, 50 ˚C). To the aqueous residue HCl (546 µL conc., 6.50 mmol in 10 mL of distilled water) was added, and the white precipitate extracted with ethyl acetate (3 x 40 mL). Combined organic extracts were washed with citric acid (10% aq, 100 mL), NaCl (sat. aq. 100 mL), dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The obtained mixture could not be purified by chromatography, therefore, it was used without purification in the next step. Yield: 945.0 mg (<4.0 mmol, <51%), white powder.

**Phg$^{\#}$-1,3,5-$C_6H_3$-$(COOMe)_2$ ($\mathbf{15_{t3}}$).** HOOC-1,3,5-$C_6H_3$-$(COOMe)_2$ (**$\mathbf{14_{t3}}$**) (571.5 mg, 2.4 mmol), HATU (912.6 mg, 2.4 mmol), DIPEA (1.666 mL, 9.6 mmol), Phg$^{\#}$ (329.2 mg, 2.4 mmol). Chromatography: 30 g of silica gel, 3% MeOH in DCM. Yield: 497.1 mg (1.39 mmol, 58%), white solid. $^1$H NMR (300 MHz, $CDCl_3$) *δ*/ppm: 8.79 (t, J = 1.7 Hz, 1H), 8.65 (d, J = 1.6 Hz, 2H), 7.39 (d, J = 4.3 Hz, 5H), 7.09 (d, J = 7.3 Hz, 1H), 5.32 (dt, J = 7.2, 4.8 Hz, 1H), 4.04 (t, J = 5.4 Hz, 2H), 3.97 (s, 6H), 2.47 (t, J = 6.1 Hz, 1H).

**Phg$^{\#}$-1,3,5-$C_6H_3$-$(Phe\text{-}OMe)_2$ ($\mathbf{3_{t3}}$).** Phg$^{\#}$-1,3,5-$C_6H_3$-$(COOMe)_2$ (**$\mathbf{15_{t3}}$**) (556.5 mg, 1.6 mmol) was dissolved in MeOH (20 mL) by using an ultrasonic bath. Aqueous solution of NaOH 200.0 mg, 5.0 mmol in 10 mL of distilled water) was added to the mixture and the reaction mixture heated in a CEM Microwave Reactor for 20 min (150 W, 50 ˚C). To the aqueous residue HCl (422 µL conc., 5.0 mmol in 10 mL of distilled water) was added gradually until neutralization was achieved. Water was evaporated from the mixture and the solid suspended in the DCM. The suspension was used in the next step without further processing. HATU (1 901.2 mg, 5.0 mmol), DIPEA (2.318 mL, 12.4 mmol), Phe-OMe·HCl (1 078.4 mg, 5 mmol) Chromatography: 50 g of silica gel, 2% MeOH in DCM. Yield: 505.8 mg (0.78 mmol, 50%; overall yield: 28%), white solid. $^1$H NMR spectrum of compound **$\mathbf{3_{t3}}$** corresponds to $^1$H NMR of compound **$\mathbf{3_{t5}}$**, however high amounts of contaminant TMU and other unidentified compounds are present ($^1$H and $^{13}$C NMR spectra in the supplement).

**Phg$^{\#}$-1,3,5-$C_6H_3$-$(D\text{-}Phe\text{-}OMe)_2$ ($\mathbf{3_{t4}}$).** Phg$^{\#}$-1,3,5-$C_6H_3$-$(COOMe)_2$ (**$\mathbf{15_{t3}}$**) (504.0 mg, 1.4 mmol) was dissolved in MeOH (20 mL) by using an ultrasonic bath. Aqueous solution of NaOH 200.0 mg, 5.0 mmol in 10 mL of distilled water) was added to the mixture and the reaction mixture heated in a CEM Microwave Reactor for 20 min (150 W, 50 ˚C). To the aqueous residue HCl (422 µL conc., 5.0 mmol in 10 mL of distilled water) was added gradually until neutralization was achieved. Water was evaporated from the mixture and the solid suspended in the DMF. The suspension was used in the next step without further processing. COMU (2 141.3 mg, 5.0 mmol), TEA (1.868 mL, 13.4 mmol), D-Phe-OMe·HCl (1 078.4 mg, 5 mmol) Chromatography: 60 g of silica gel, 3% MeOH in DCM. Yield: 819.3 mg (<1.3 mmol, <89%; overall yield: 50%), white

solid. $^{1}$H NMR spectrum of compound $\mathbf{3_{t4}}$ showed high amounts of unidentified contaminants which could not be purified by additional chromatography, therefore the compound was used in the next step as is ($^{1}$H and $^{13}$C NMR spectra in the supplement).

**One-pot products** within the same series do not have the same limiting reactant. To avoid discrepancies, all yields presented in the paper were calculated with the aromatic acid **P** as the limiting reactant (Obt. $\eta$). In Table S1 maximum yields (Max $\eta$) for all one-pot products for 100% of the mass of the isopthalic acid are presented (intermediates whose limiting reactant is not the aromatic acid **P** have this maximum yield value lower than 100%).

Table S1. Obtained yield values as calculated with the mass of the aromatic acid **P** as the limiting reactant.

| Reaction | Compound | Obt. $\eta$ / % | Max. $\eta$ /% |
|---|---|---|---|
| 1 | $\mathbf{2_{m1}}$ | 1 | 100 |
| | $\mathbf{6_{m1}}$ | 8 | 100 |
| | $\mathbf{7_{m1}}$ | 4 | 100 |
| | $\mathbf{8_{m1}}$ | 2 | 100 |
| 3 | $\mathbf{3_{m1}}$ | 17 | 100 |
| 4 | $\mathbf{2_{m1}}$ | 25 | 50 |
| | $\mathbf{3_{m1}}$ | 13 | 100 |
| 5 | $\mathbf{2_{m1}}$ | 20 | 50 |
| | $\mathbf{3_{m1}}$ | 15 | 100 |
| 6 | $\mathbf{4_{m1}}$ | 27 | 100 |
| 7 | $\mathbf{2_{p1}}$ | 7 | 50 |
| | $\mathbf{3_{p1}}$ | <13 | 100 |
| 8 | $\mathbf{3_{m2}}$ | 22 | 100 |
| 9 | $\mathbf{3_{m3}}$ | 16 | 100 |
| 10 | $\mathbf{3_{m4}}$ | 26 | 100 |
| 11 | $\mathbf{3_{m5}}$ | 13 | 100 |
| | $\mathbf{5_{m5}}$ | 3 | 50 |
| 12 | $\mathbf{3_{m6}}$ | <52 | 100 |
| 13 | $\mathbf{2_{n1}}$ | 8 | 50 |
| | $\mathbf{3_{n1}}$ | 36 | 100 |
| 13 | $\mathbf{2_{n1}}$ | 8 | 50 |
| | $\mathbf{3_{n1}}$ | 36 | 100 |
| 14 | $\mathbf{2_{n2}}$ | 17 | 50 |
| | $\mathbf{3_{n2}}$ | 18 | 100 |
| 15 | $\mathbf{2_{n3}}$ | 31 | 50 |
| | $\mathbf{3_{n3}}$ | 15 | 100 |
| | $\mathbf{4_{n3}}$ | 17 | 50 |
| 16 | $\mathbf{2_{n4}}$ | 5 | 50 |
| | $\mathbf{3_{n4}}$ | 33 | 100 |
| | $\mathbf{4_{n4}}$ | 38 | 50 |
| 17 | $\mathbf{2_{n5}}$ | 18 | 50 |
| | $\mathbf{3_{n5}}$ | 23 | 100 |
| 18 | $\mathbf{2_{a1}}$ | 19 | 50 |
| | $\mathbf{3_{a1}}$ | 16 | 100 |
| 19 | $\mathbf{2_{t1}}$ | 6 | 18 |
| | $\mathbf{3_{t1}}$ | 27 | 75 |
| | $\mathbf{4_{t1}}$ | 10 | 77 |
| 20 | $\mathbf{2_{t2}}$ | 2 | 50 |
| | $\mathbf{3_{t2}}$ | 16 | 76 |
| | $\mathbf{4_{t2}}$ | 6 | 75 |
| 21 | $\mathbf{3_{t5}}$ | 5 | 29 |
| | $\mathbf{4_{t5}}$ | 26 | 52 |
| | $\mathbf{5_{t5}}$ | 5 | 38 |

Table S2. Isolated yields of oxazoline compounds **1**.

| Compound | yield / % | Compound | yield / % | Compound | yield / % |
|---|---|---|---|---|---|
| $\mathbf{1_{m1}}$ | 57 | $\mathbf{1_{n1}}$ | 42 | $\mathbf{1_{t1}}$ | 86 |
| $\mathbf{1_{p}}$* | 22 | $\mathbf{1_{n2}}$ | 35 | $\mathbf{1_{t2}}$ | 13 |
| $\mathbf{1_{m2}}$ | 68 | $\mathbf{1_{n3}}$ | 42 | $\mathbf{1_{t3}}$ | 38 |
| $\mathbf{1_{m3}}$ | 54 | $\mathbf{1_{n4}}$ | 43 | $\mathbf{1_{t4}}$* | 24 |
| $\mathbf{1_{m4}}$ | 67 | $\mathbf{1_{n5}}$ | 14 | $\mathbf{1_{t5}}$* | 33 |
| $\mathbf{1_{m5}}$ | 36 | $\mathbf{1_{a}}$ | 87 | $\mathbf{1_{t6}}$ | 10 |
| $\mathbf{1_{m6}}$* | <47 | | | $\mathbf{1_{b}}$ | 34 |

*not chromatographically purified in the previous step(s).

## 2. NMR spectra.

Table S3. NMR shifts of amide peaks of derivatives **2** and oxazolines **1** at c ~ 6 mM.

| Compound | Solvent | $\delta$(N-H) /ppm |
|---|---|---|
| $\mathbf{2_{m1}}$ | $CHCl_3$ | 6.88 |
| $\mathbf{1_{m1}}$ | $CHCl_3$ | 6.77 |
| | DCM | 6.76 |
| | MeCN | 7.40 |
| | DMSO | 9.02 |
| $\mathbf{1_{p}}$ | $CHCl_3$ | 6.76 |
| $\mathbf{1_{m2}}$ | $CHCl_3$ | 6.63 |
| $\mathbf{1_{m3}}$ | $CHCl_3$ | 6.80 |
| $\mathbf{1_{m4}}$ | $CHCl_3$ | 6.80 |
| $\mathbf{1_{m5}}$ | $CHCl_3$ | 6.85 |
| $\mathbf{4_{m5}}$ | $CHCl_3$ | 6.85 |
| $\mathbf{1_{m6}}$ | $CHCl_3$ | 7.28 (Gly)<br>6.65 (Val)<br>6.48 (Phe) |
| $\mathbf{2_{n1}}$ | $CHCl_3$ | 6.57 |
| $\mathbf{1_{n1}}$ | $CHCl_3$ | 6.53 |
| $\mathbf{2_{n2}}$ | $CHCl_3$ | 6.94 |
| $\mathbf{1_{n2}}$ | $CHCl_3$ | 6.55 |
| $\mathbf{2_{n3}}$ | $CHCl_3$ | 7.03 |
| $\mathbf{1_{n3}}$ | $CHCl_3$ | 6.89 |
| $\mathbf{2_{n4}}$ | $CHCl_3$ | 6.55 |
| $\mathbf{1_{n4}}$ | $CHCl_3$ | 6.56 |
| $\mathbf{2_{n5}}$ | $CHCl_3$ | 7.05 |
| $\mathbf{1_{n5}}$ | $CHCl_3$ | 6.88 |
| $\mathbf{2_{a}}$ | $CHCl_3$ | 6.55 |
| $\mathbf{1_{a}}$ | $CHCl_3$ | 6.51 |
| $\mathbf{2_{t1}}$ | MeCN | 7.51 |
| $\mathbf{1_{t1}}$ | $CHCl_3$ | 6.95 |
| $\mathbf{2_{t2}}$ | MeCN | 7.64 |
| $\mathbf{1_{t2}}$ | MeCN | 7.93, 7.62 |
| $\mathbf{1_{t3}}$ | CHCl3 | 6.74 |
| $\mathbf{1_{t4}}$ | MeCN | 7.50 |
| $\mathbf{1_{t5}}$ | $CHCl_3$ | 6.70 |

NMR spectra of selected ligands (namely $\mathbf{1_{m1}}$, $\mathbf{1_p}$ $\mathbf{1_{m5}}$, $\mathbf{1_{m6}}$, $\mathbf{1_{n4}}$, $\mathbf{1_{t1}}$ and $\mathbf{1_{t5}}$) were recorded in $CDCl_3$ and DMSO (both at $c$ = 6 mM, and additionally at $c$ = 60 mM in $CDCl_3$), and respective hydrogen bond acidity values ($A_{NMR}$) calculated from the equation:

$$A_{NMR} = 0.0065 + 0.133\Delta\delta_{DMSO\text{-}CDCl3}.$$

$A_{NMR}$ values which are greater than 0.15 indicate no significant hydrogen bonding with the amide protons in these solutions occurs.

Table S4. Hydrogen bond acidity values ($A_{NMR}$) and $\Delta\delta_{conc.\text{-}dil}$ of amide peaks of selected ligands.

| | $\delta$(N-H)/ppm | | | | | |
|---|---|---|---|---|---|---|
| comp. | DMSO | $CDCl_3$ | $\Delta\delta_{DMSO\text{-}CDCl3}$* | $A_{NMR}$ | $CDCl_3$ (konc.) | $\Delta\delta_{conc.\text{-}dil.}$ |
| $\mathbf{1_{m1}}$ | 9.02 | 6.80 | 2.22 | 0.30 | 6.85 | 0.05 |
| $\mathbf{1_p}$ | 8.94 | 6.75 | 2.19 | 0.30 | 6.78 | 0.03 |
| $\mathbf{1_{m5}}$ | 9.04 | 6.79 | 2.25 | 0.31 | 6.87 | 0.08 |
| | 8.95(Gly) | 7.28 (Gly) | 1.67 (Gly) | 0.23 | 7.82 (Gly) | 0.54 (Gly) |
| $\mathbf{1_{m6}}$ | 7.81 (Val) | 6.65 (Val) | 1.16 (Val) | 0.16 | 7.03 (Val) | 0.38 (Val) |
| | 8.48 (Phe) | 6.48 (Phe) | 2.00 (Phe) | 0.27 | 7.01 (Phe) | 0.53 (Phe) |
| $\mathbf{1_{n4}}$ | 9.01 | 6.88 | 2.13 | 0.29 | 6.94 | 0.06 |
| $\mathbf{1_{t1}}$ | 9.20 | 6.95 | 2,25 | 0,31 | 7.31 | 0.36 |
| $\mathbf{1_{t5}}$ | 9.35 | 6.70 | 2.65 | 0.36 | 6.78 | 0.08 |

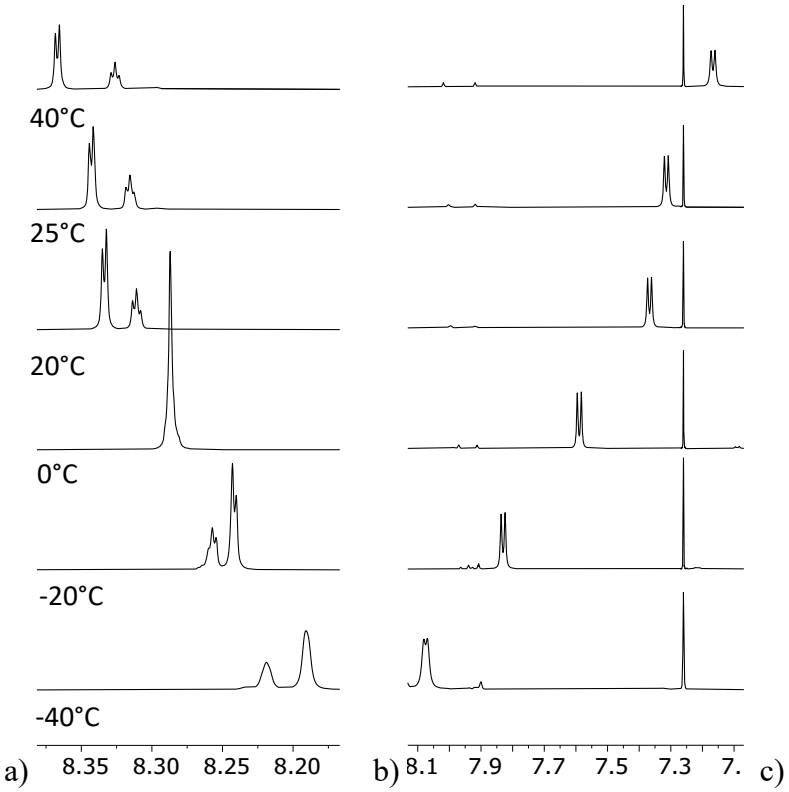
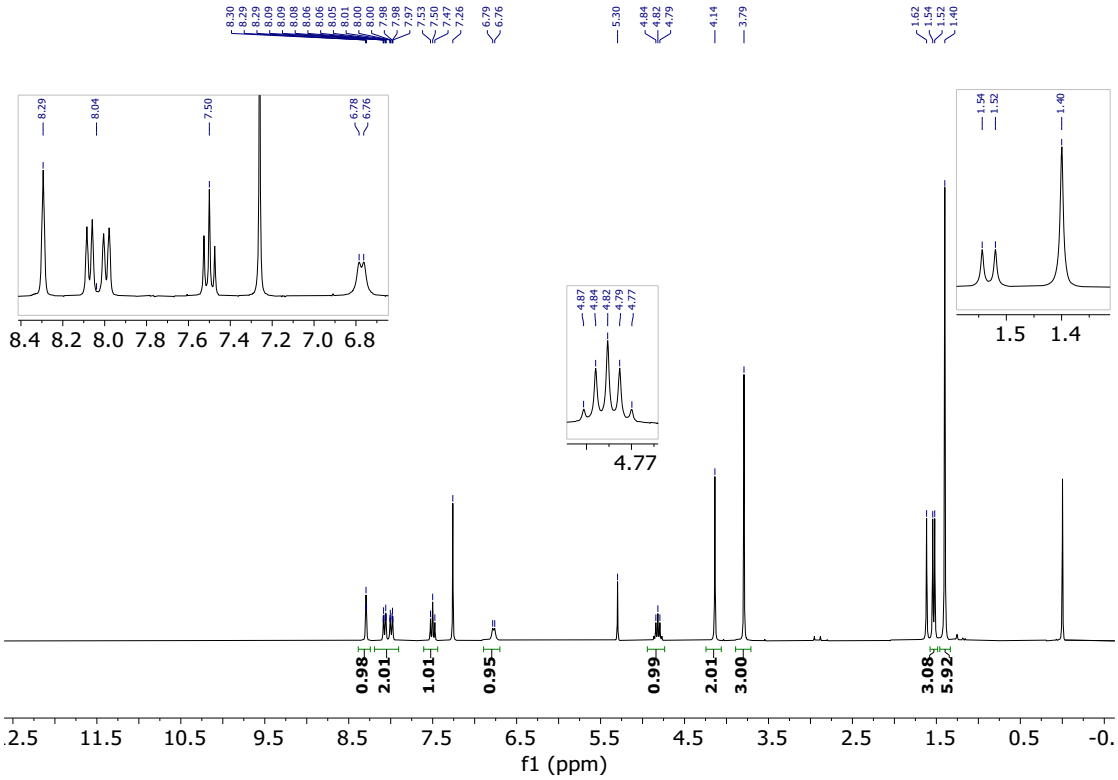


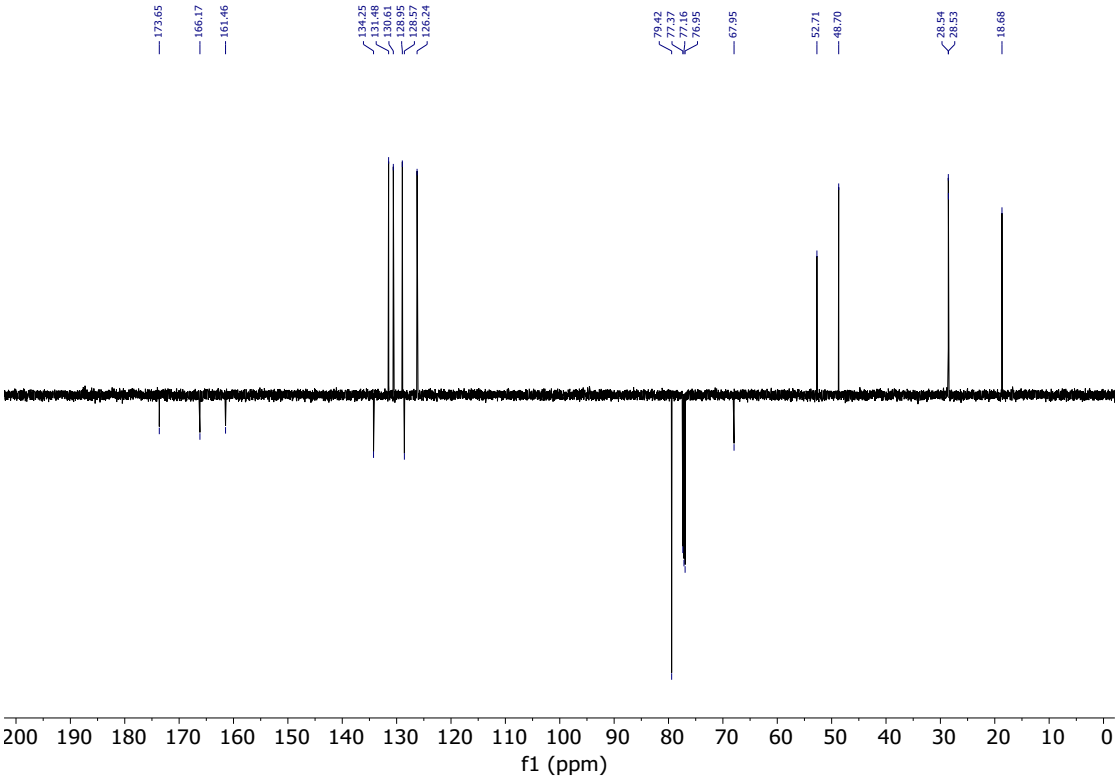

Figure S1. Temperature dependent $^{1}$H NMR spectra of oxazoline $\mathbf{1_{t1}}$: a) aromatic region, b) amide region, c) aliphatic region.

## 2.1. Oxazolines

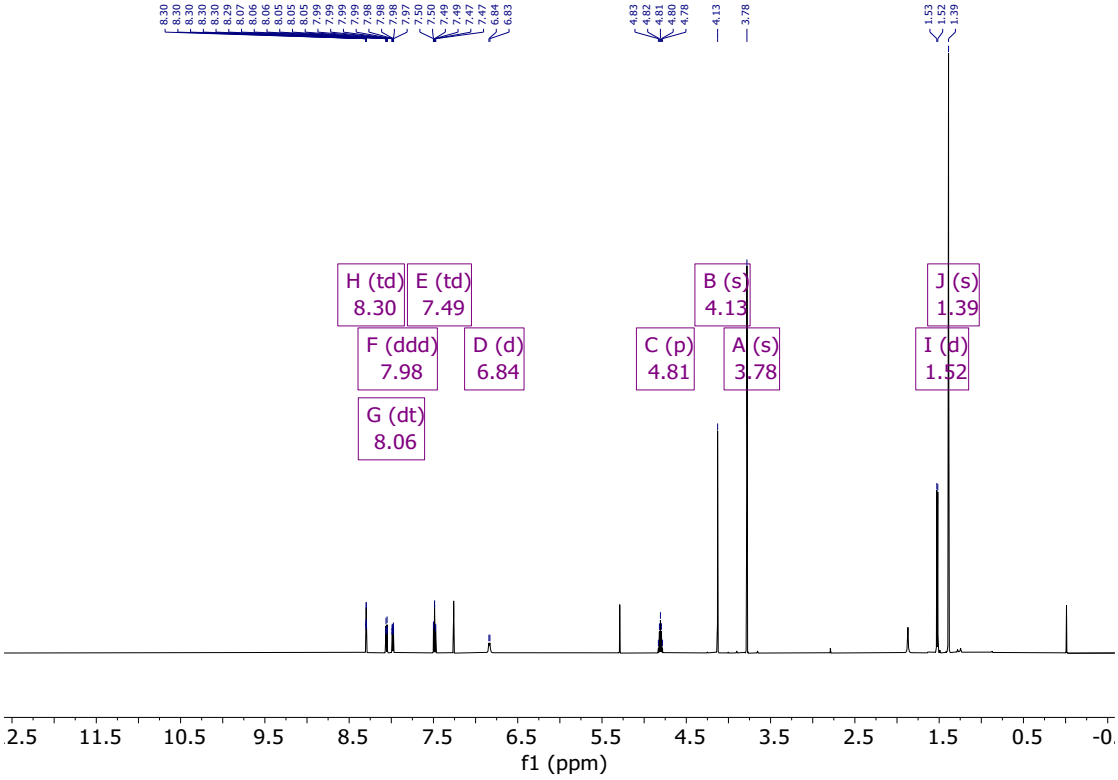
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m1}}$, $c$ = 6 mM.



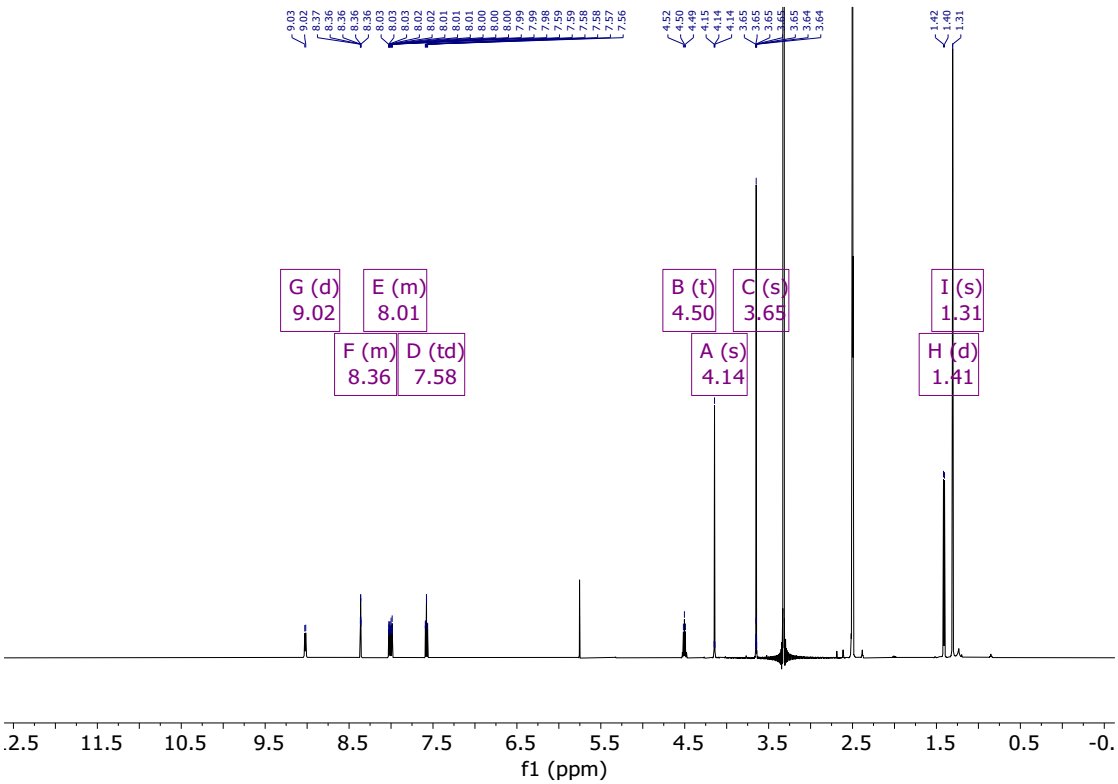

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{m1}}$.



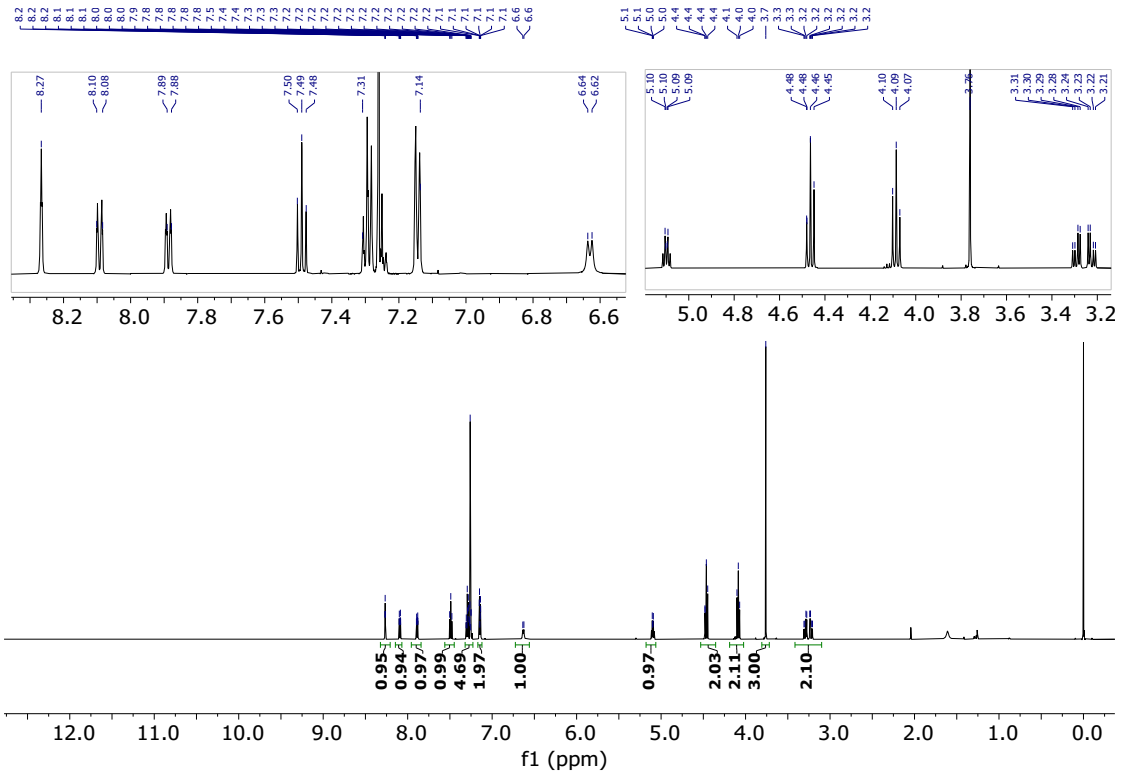
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m1}}$, $c$ = 60 mM.



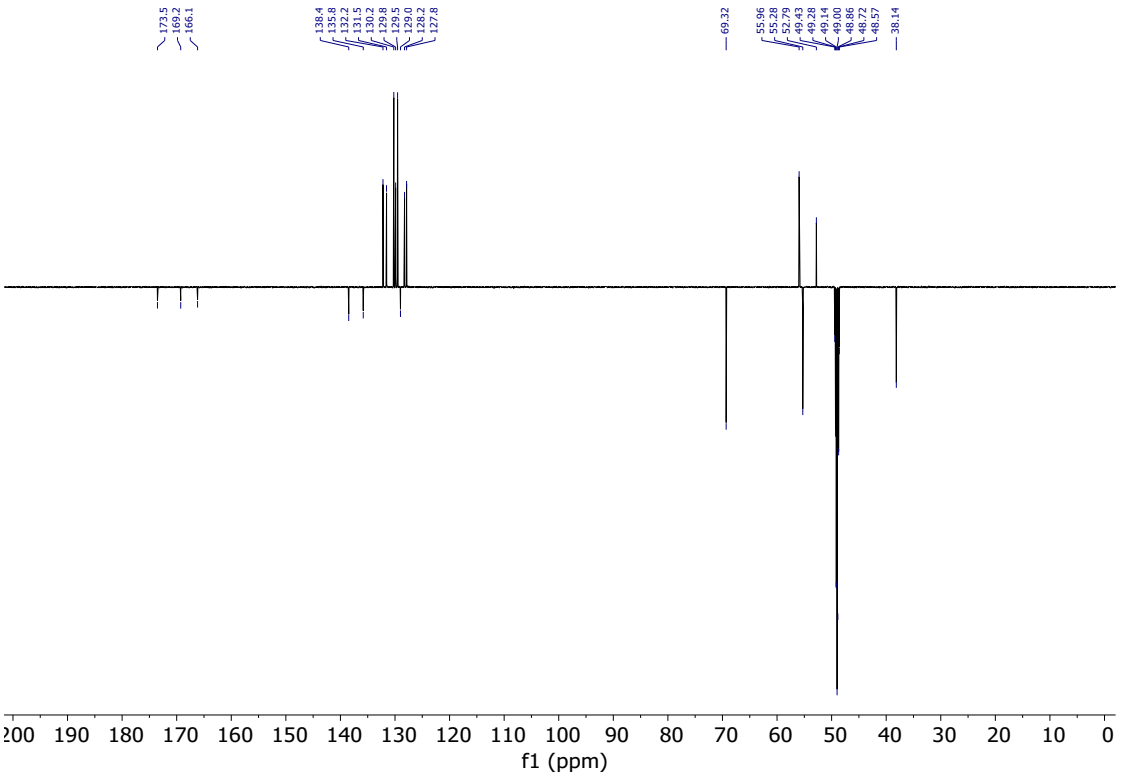

$^1$H NMR (600 MHz, DMSO) of $\mathbf{1_{m1}}$, $c$ = 6 mM.



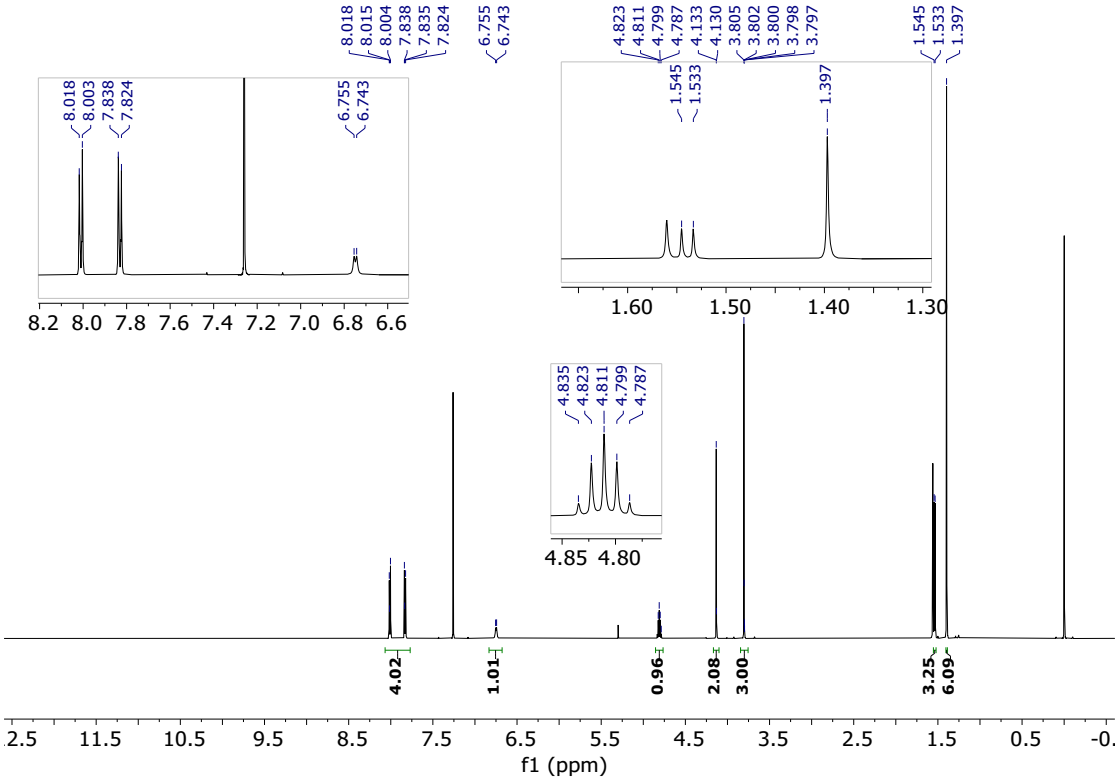
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m2}}$.



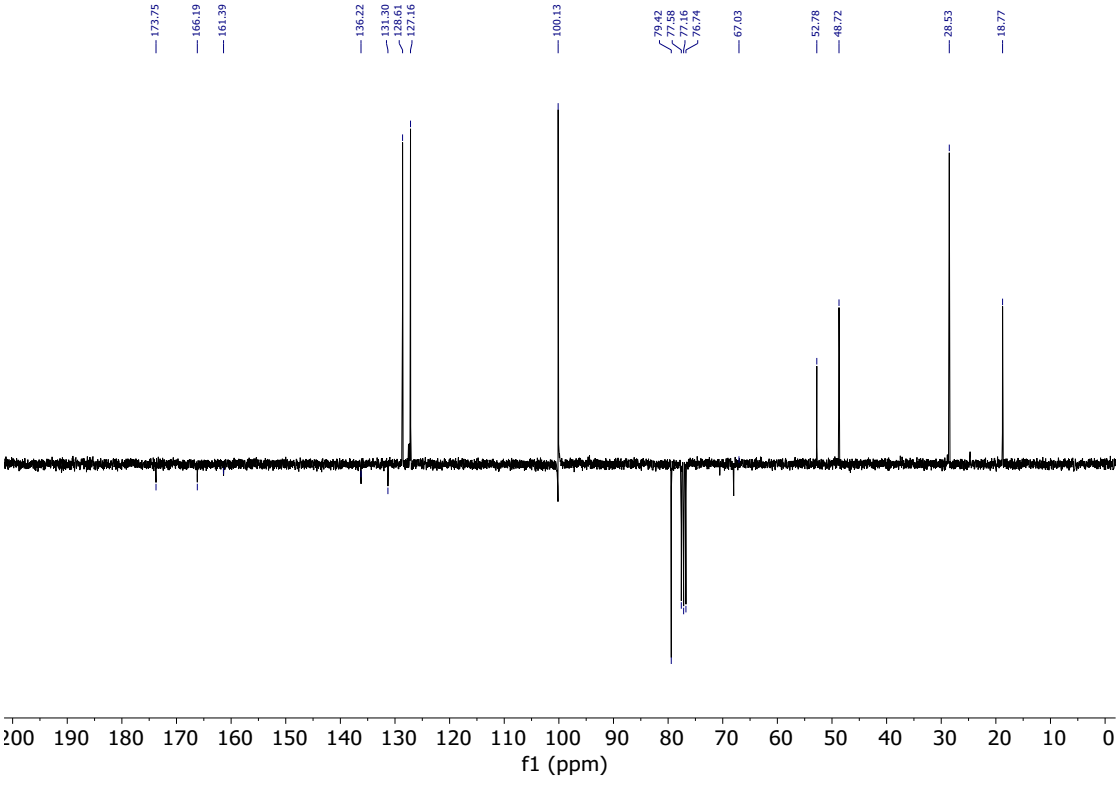

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{m2}}$.



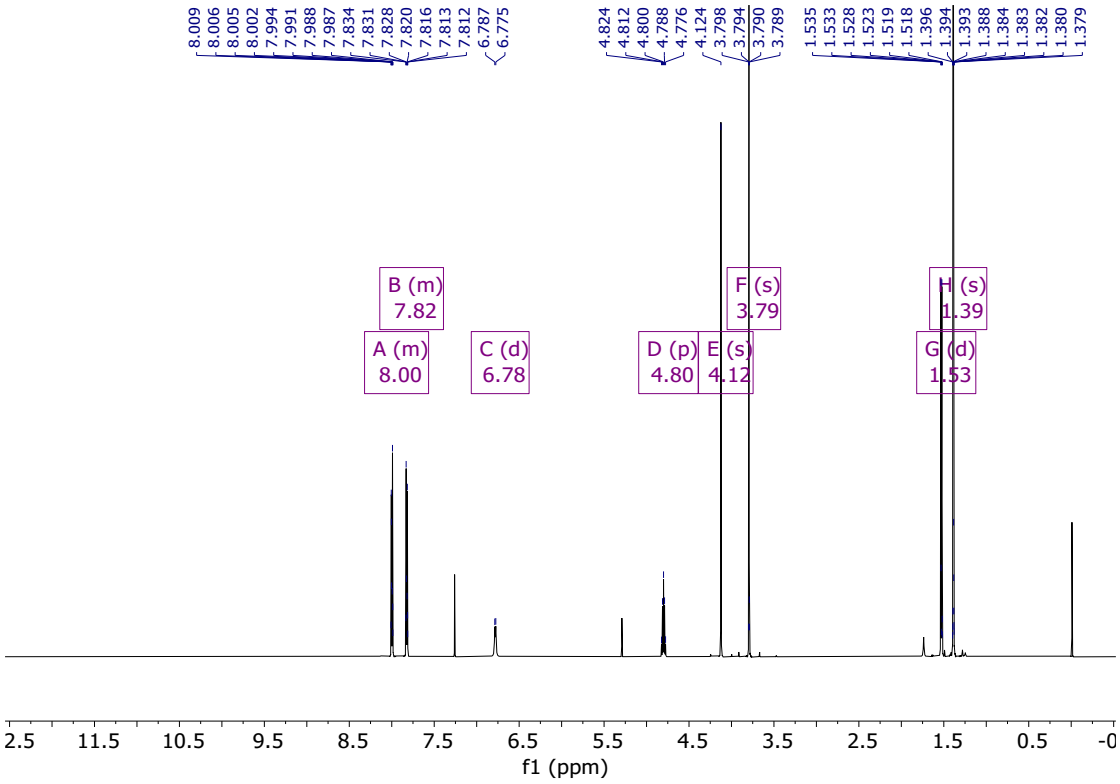
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_p}$, $c$ = 6 mM.



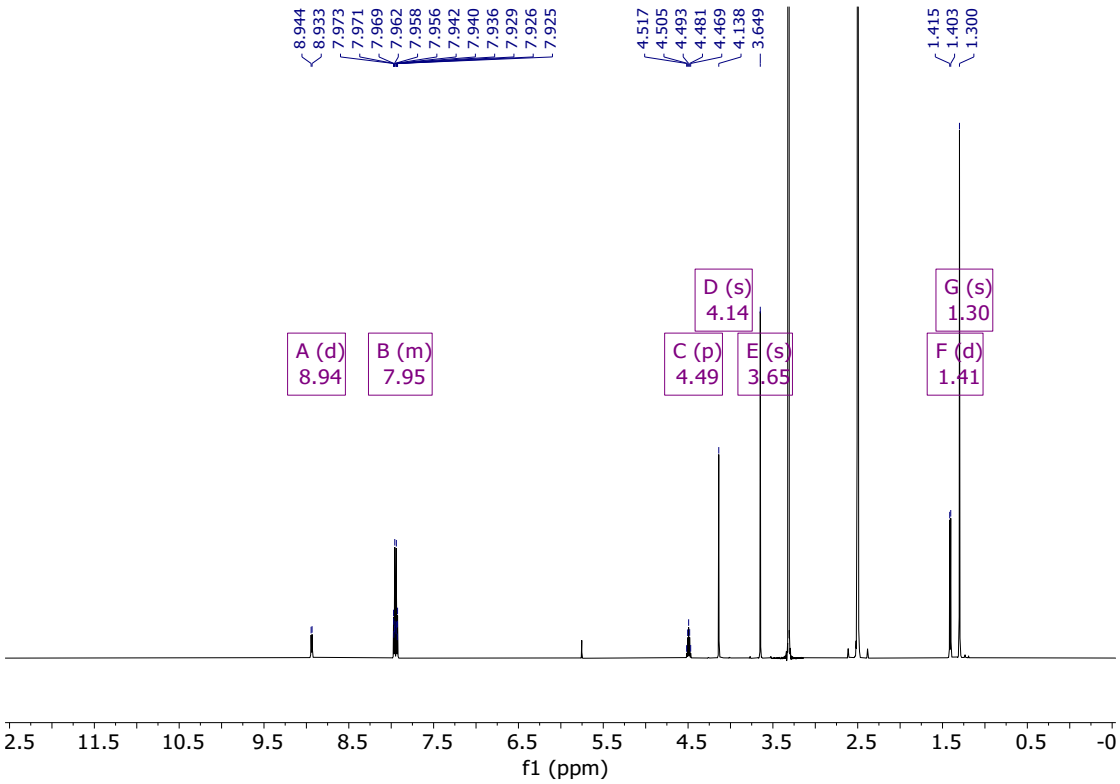

$^{13}$C NMR (75 MHz, $CDCl_3$) of $\mathbf{1_p}$.



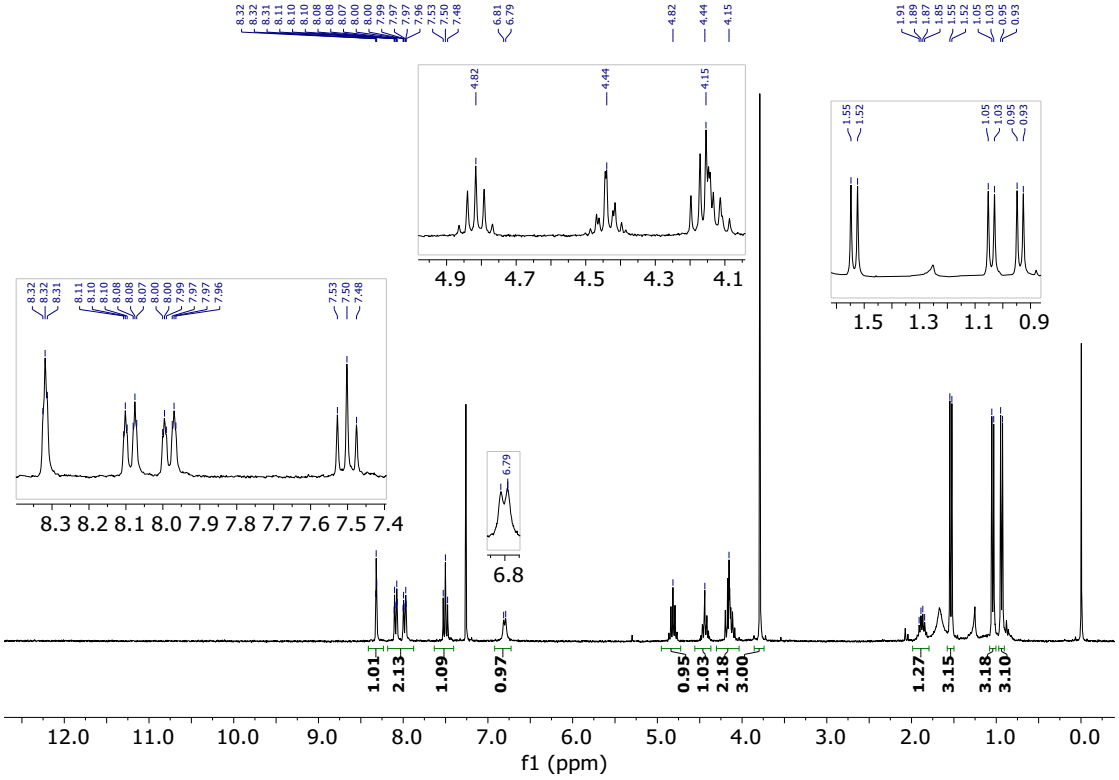
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_p}$, $c$ = 60 mM.



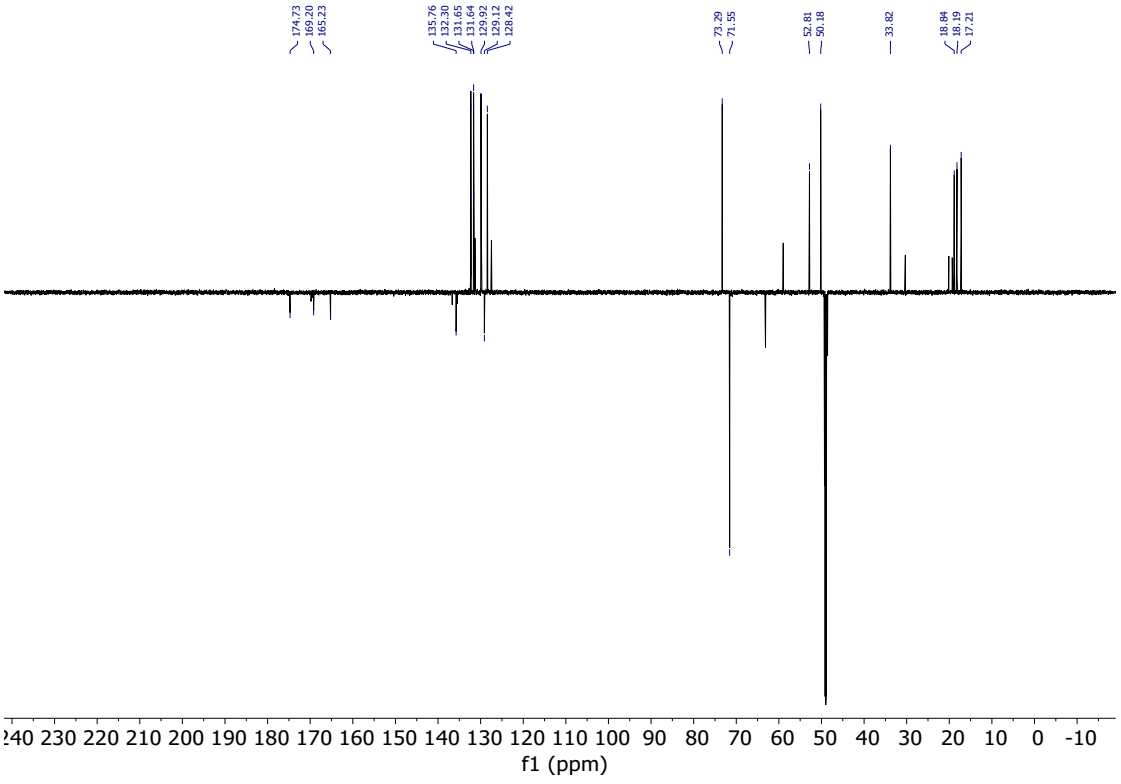

$^1$H NMR (600 MHz, DMSO) of $\mathbf{1_p}$, $c$ = 6 mM.



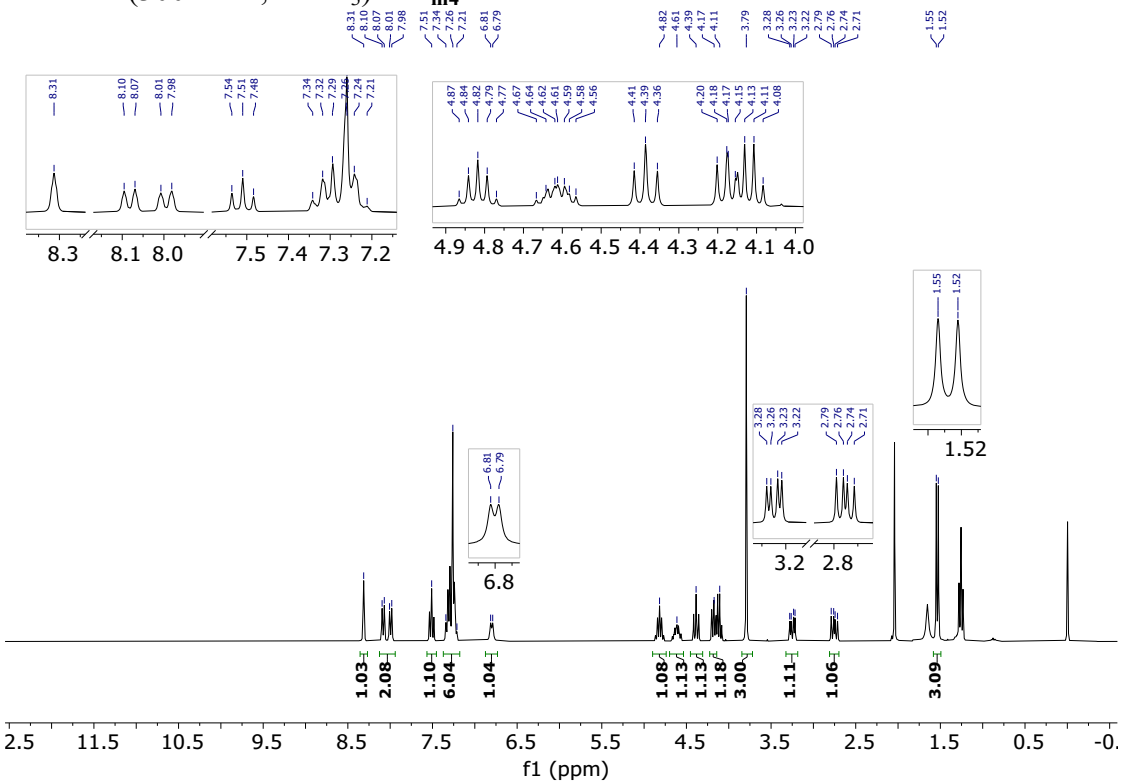
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{m3}}$.



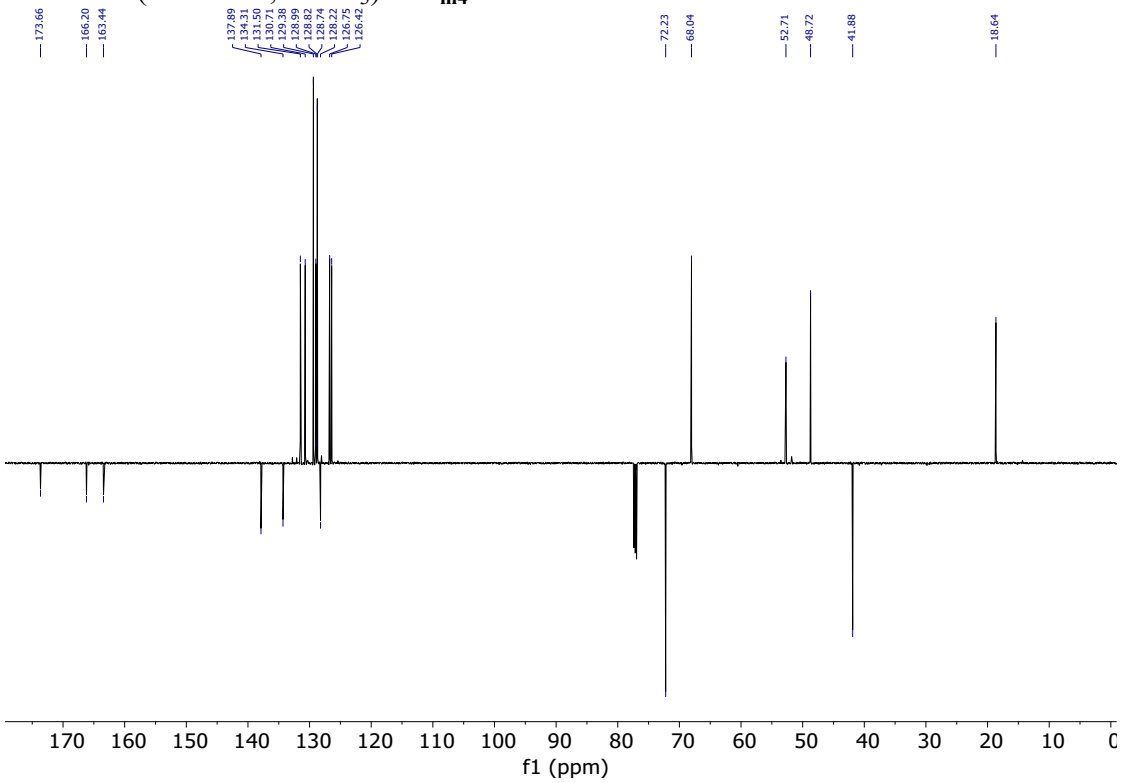

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{m3}}$.



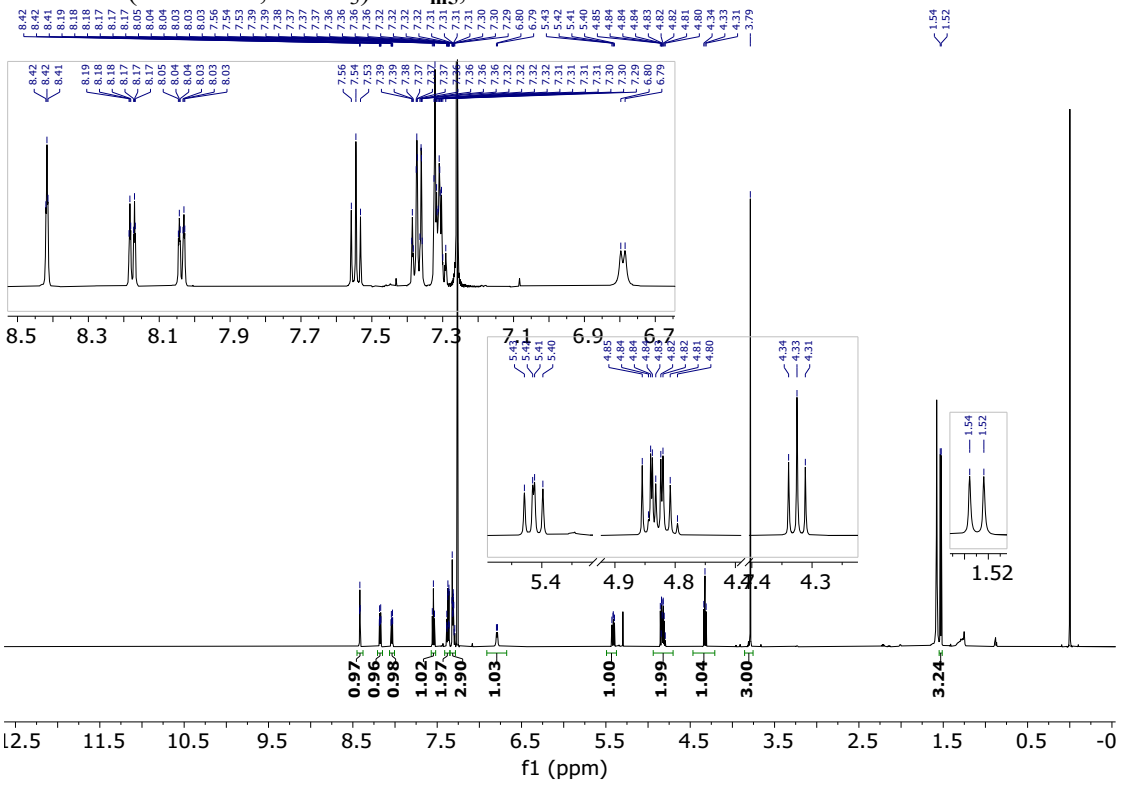
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{m4}}$.



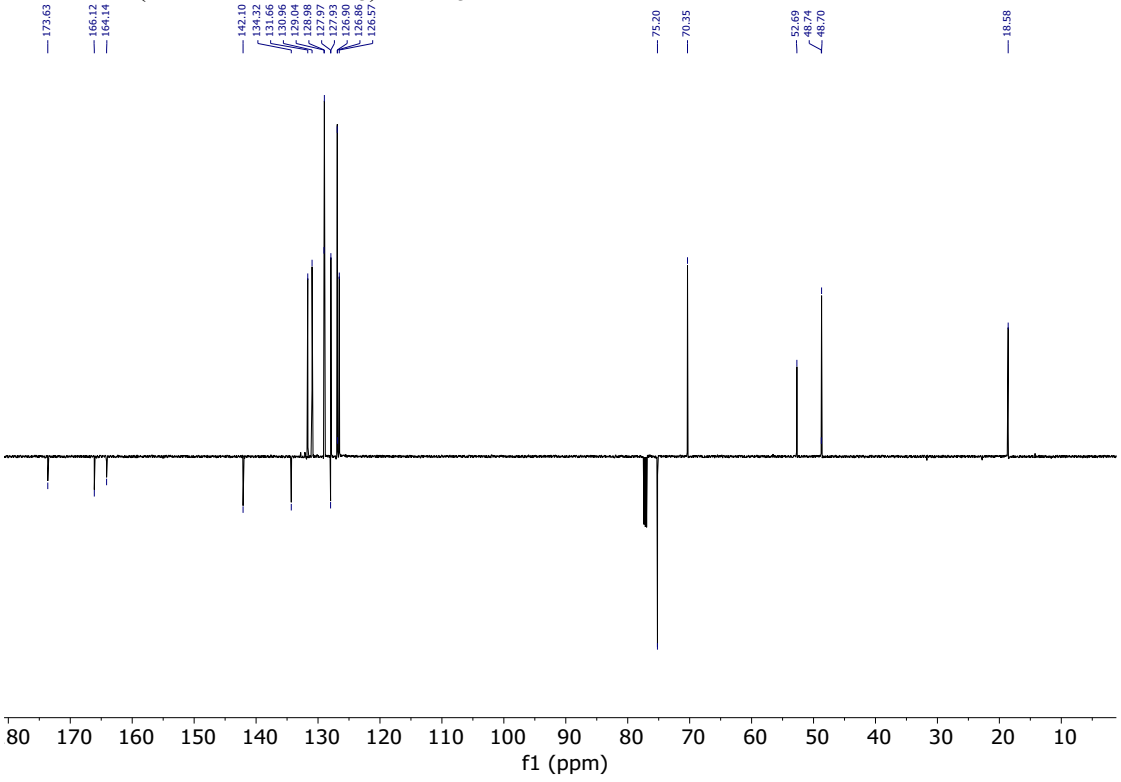

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{m4}}$.



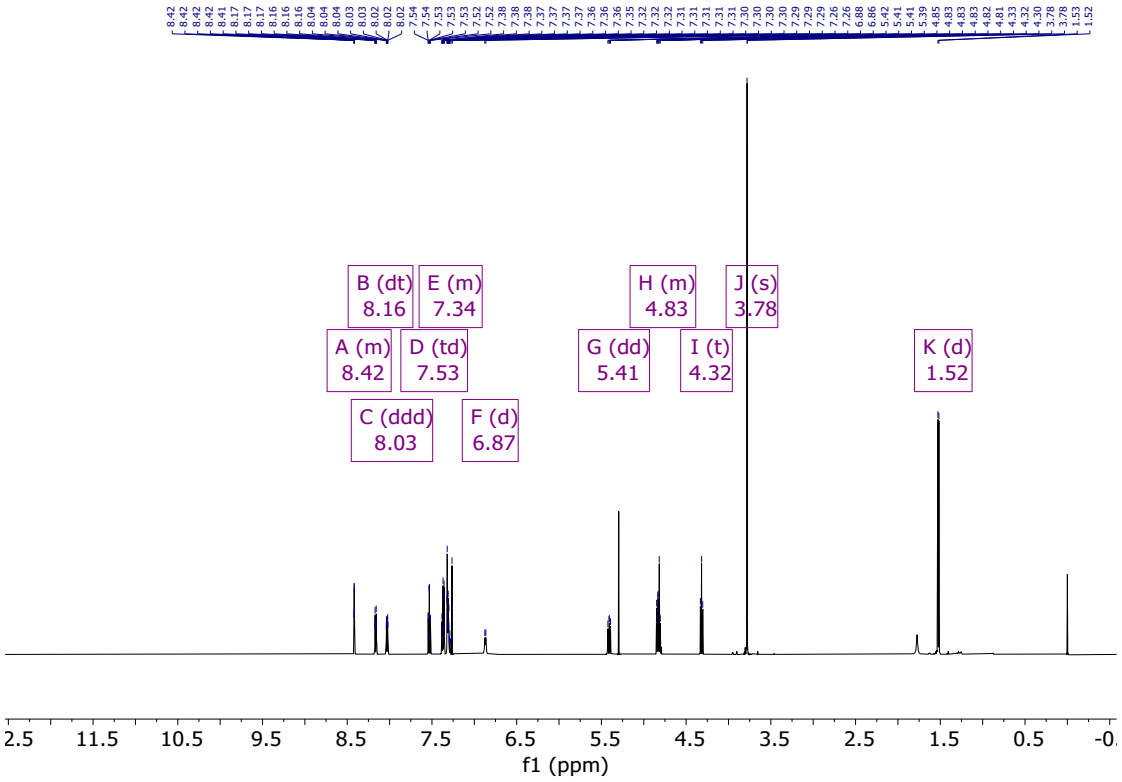
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m5}}$, $c$ = 6 mM.



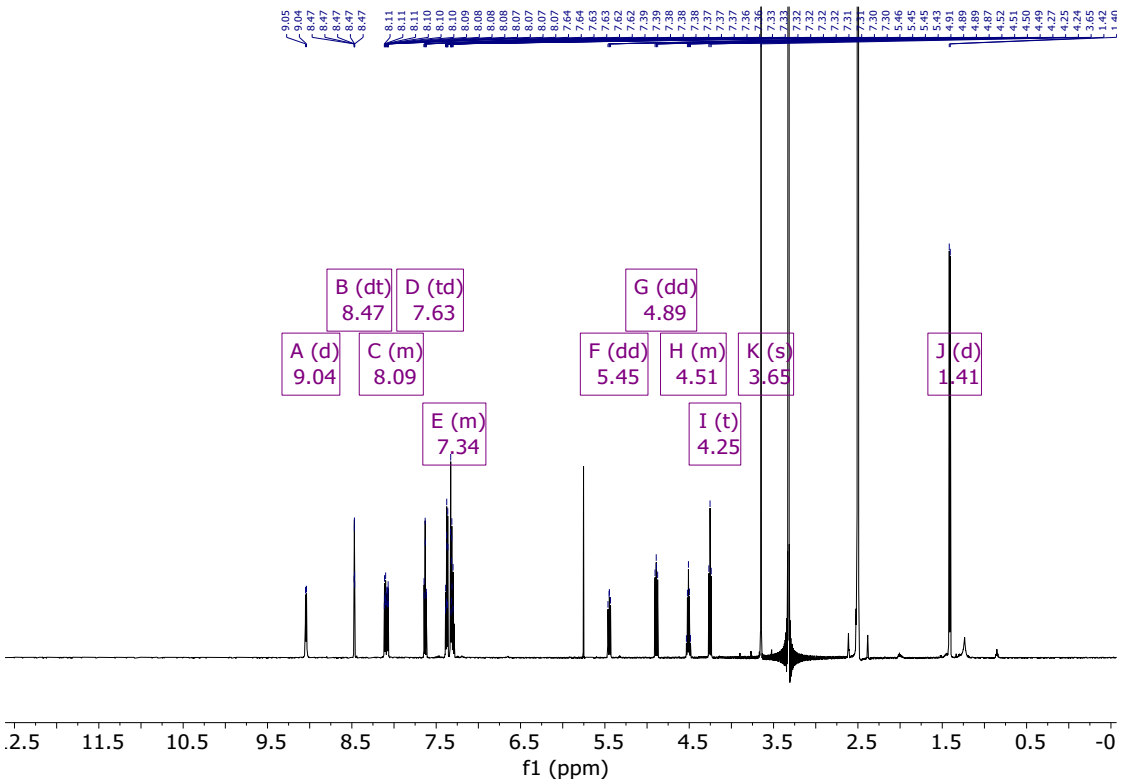

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{m5}}$.



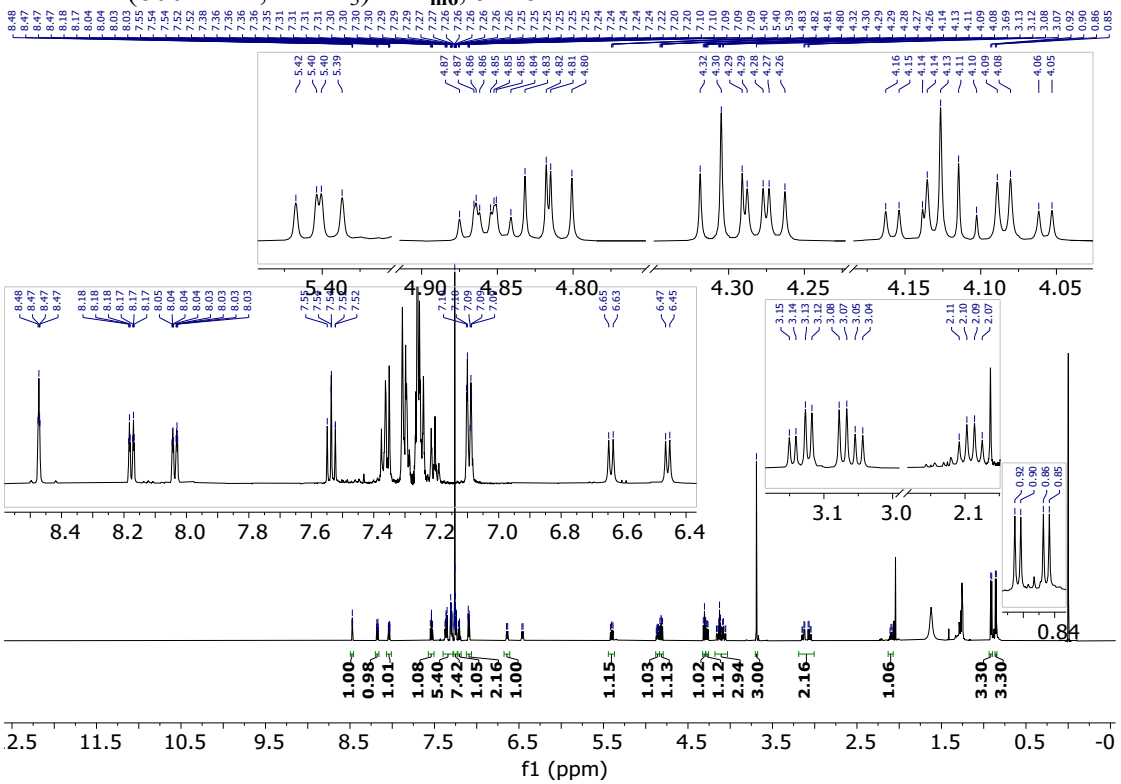
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m5}}$, $c$ = 60 mM.



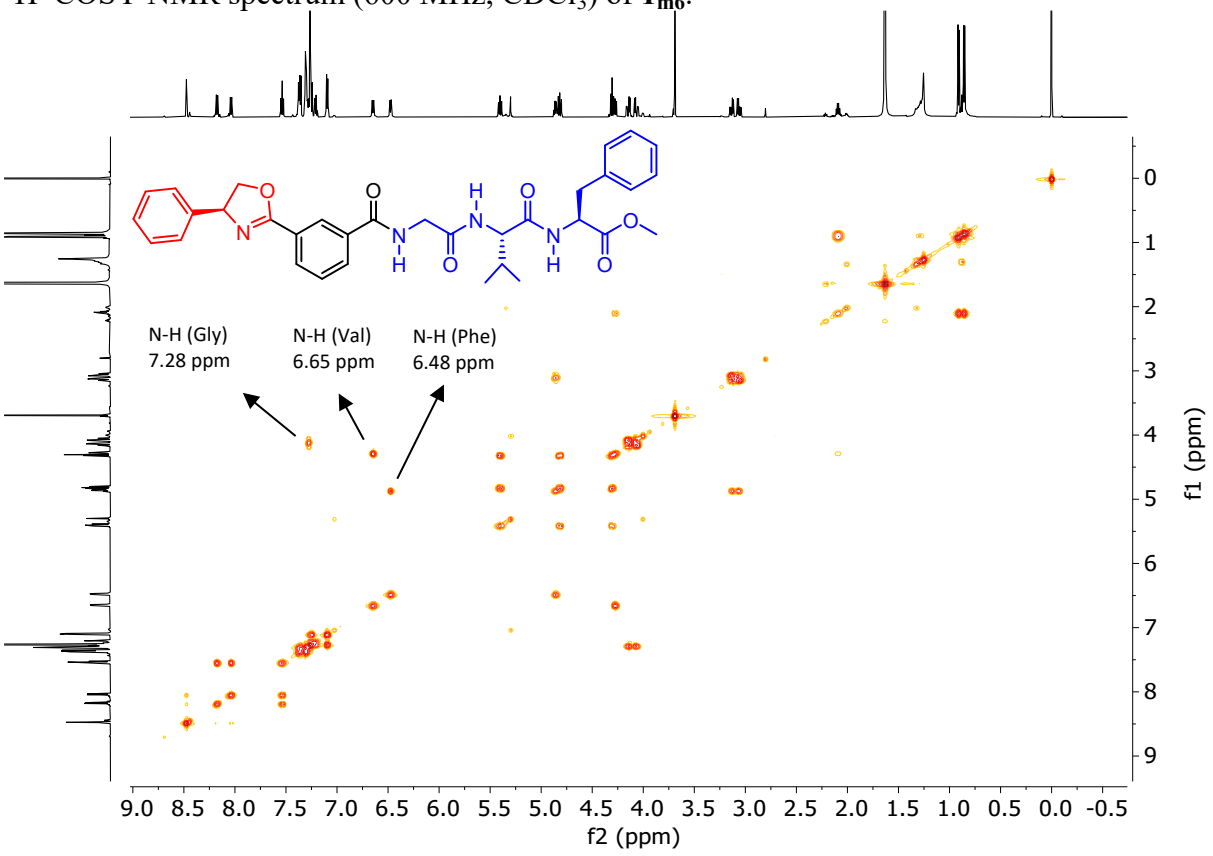

$^1$H NMR (600 MHz, DMSO) of $\mathbf{1_{m5}}$, $c$ = 6 mM.



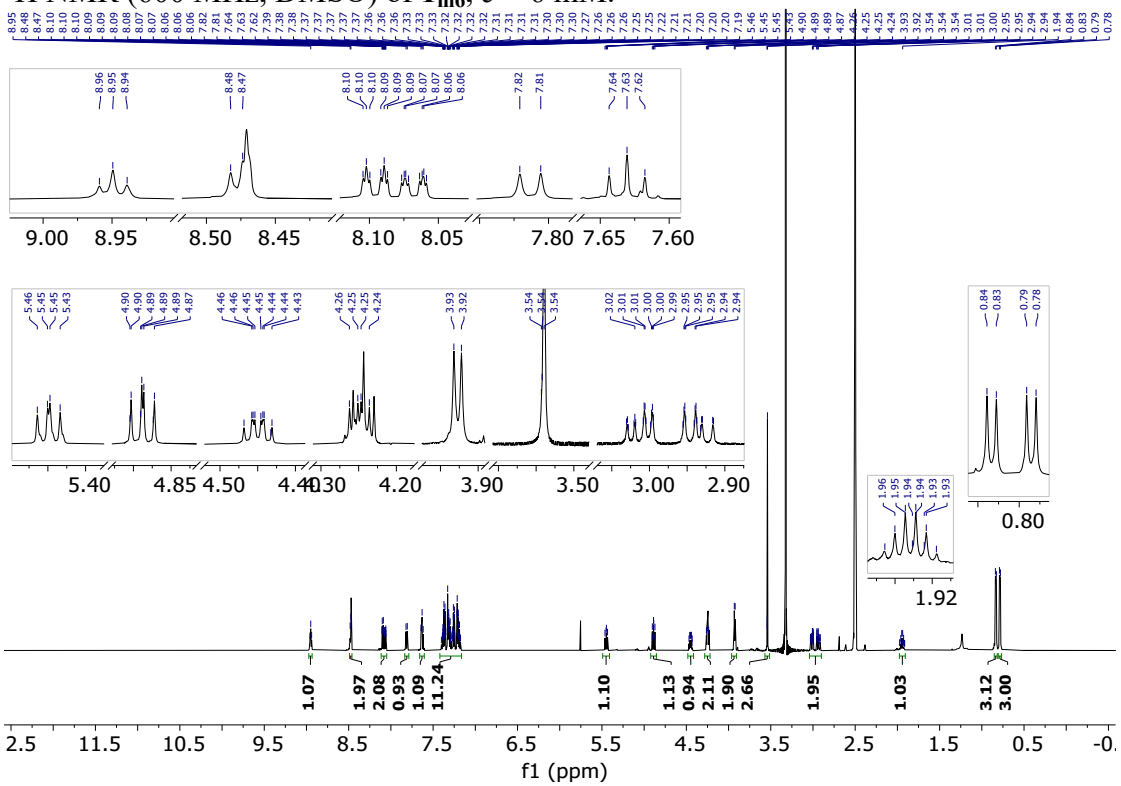
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{m6}}$, $c$ = 6 mM.



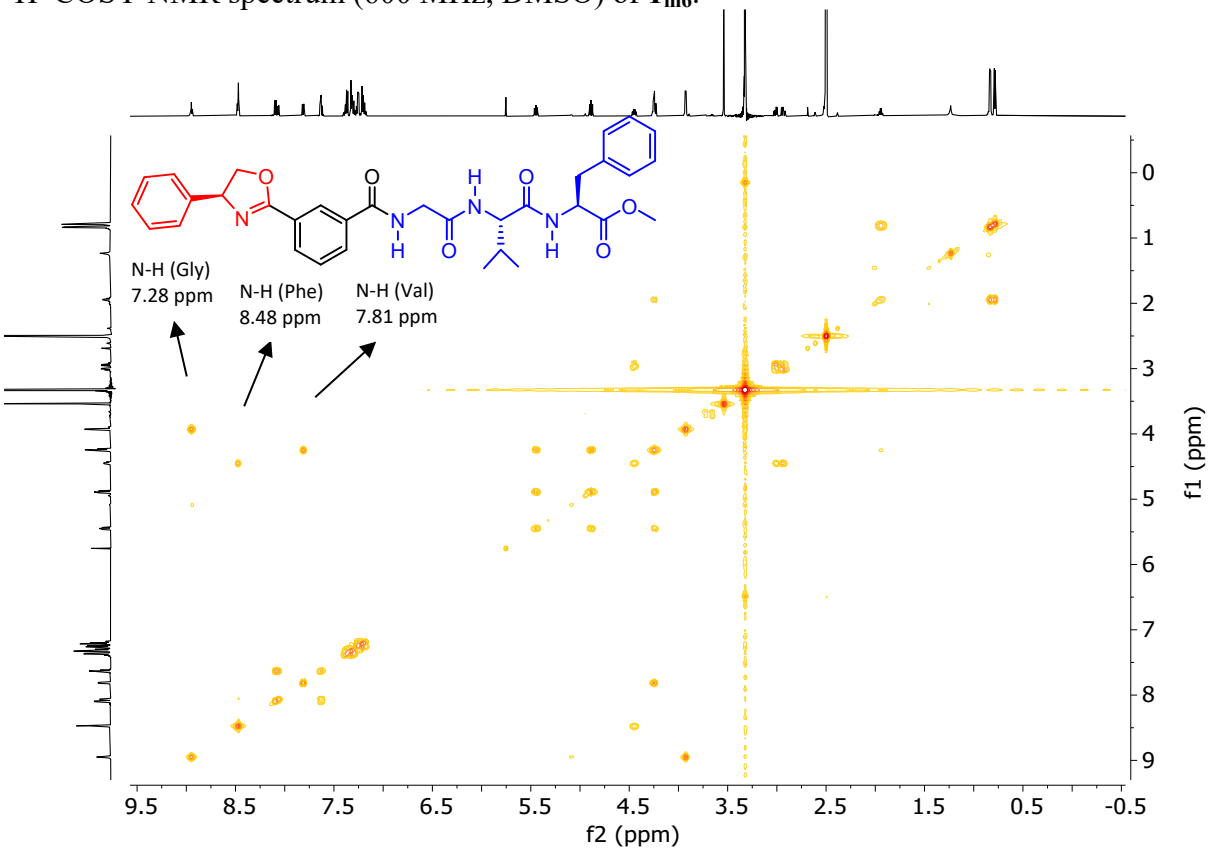

$^1$H COSY NMR spectrum (600 MHz, $CDCl_3$) of $\mathbf{1_{m6}}$.



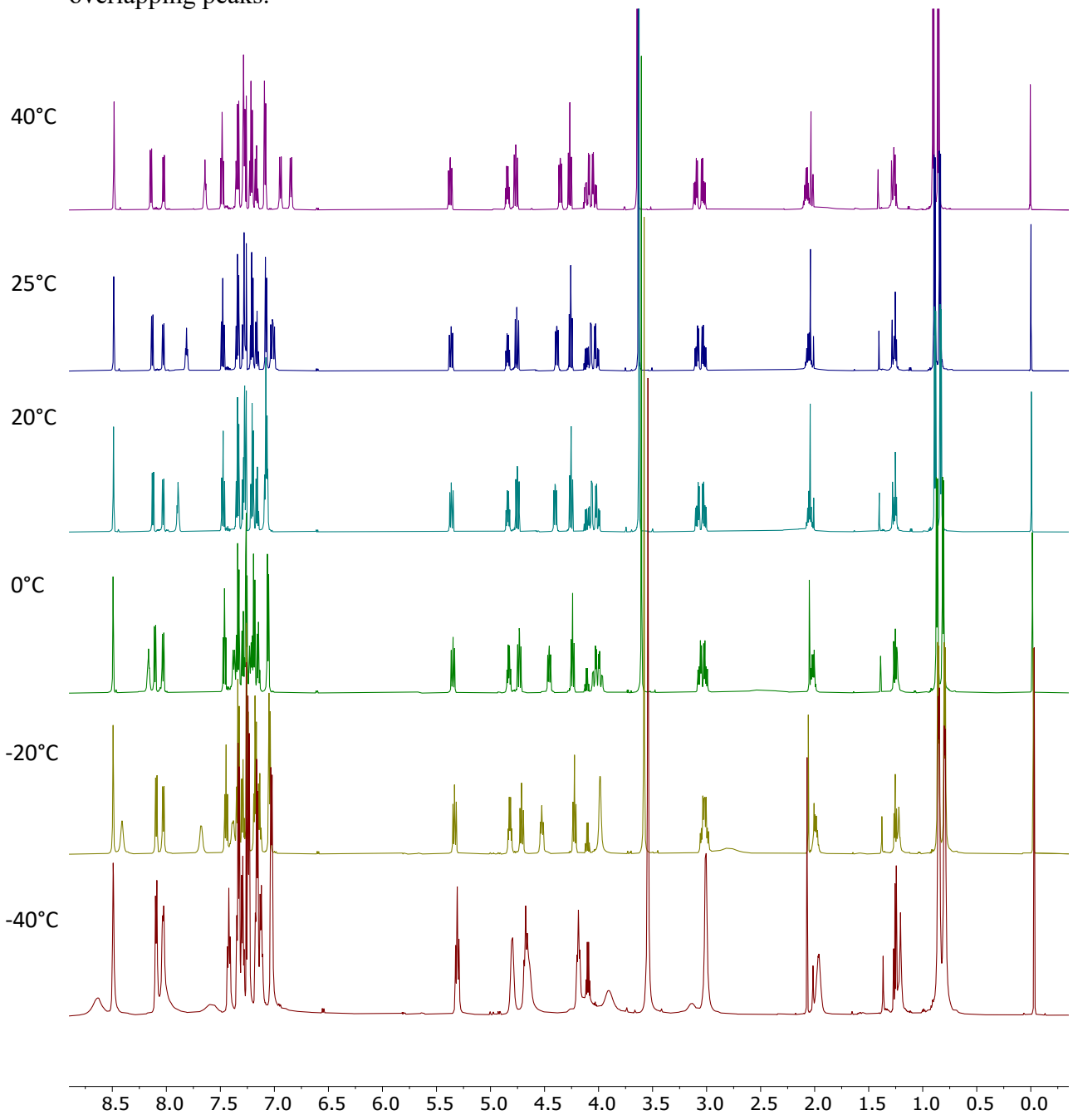
$^{1}$H NMR (600 MHz, DMSO) of $\mathbf{1_{m6}}$, $c$ = 6 mM.



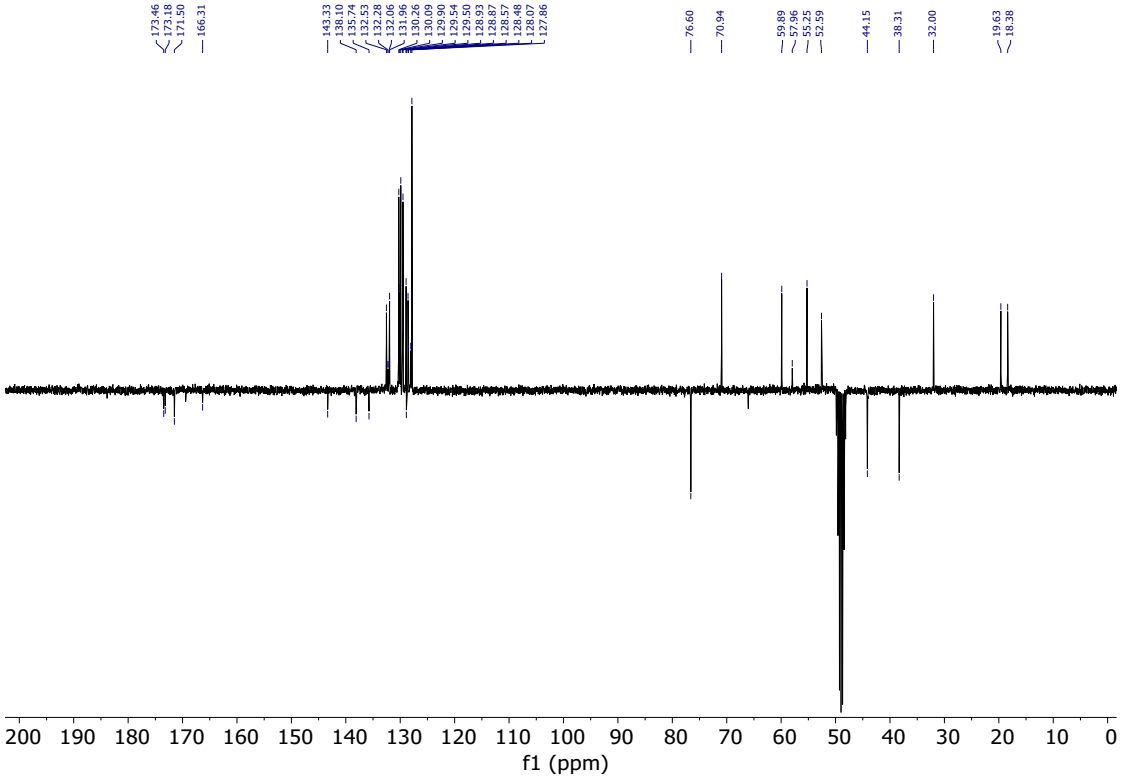

$^{1}$H COSY NMR spectrum (600 MHz, DMSO) of $\mathbf{1_{m6}}$.



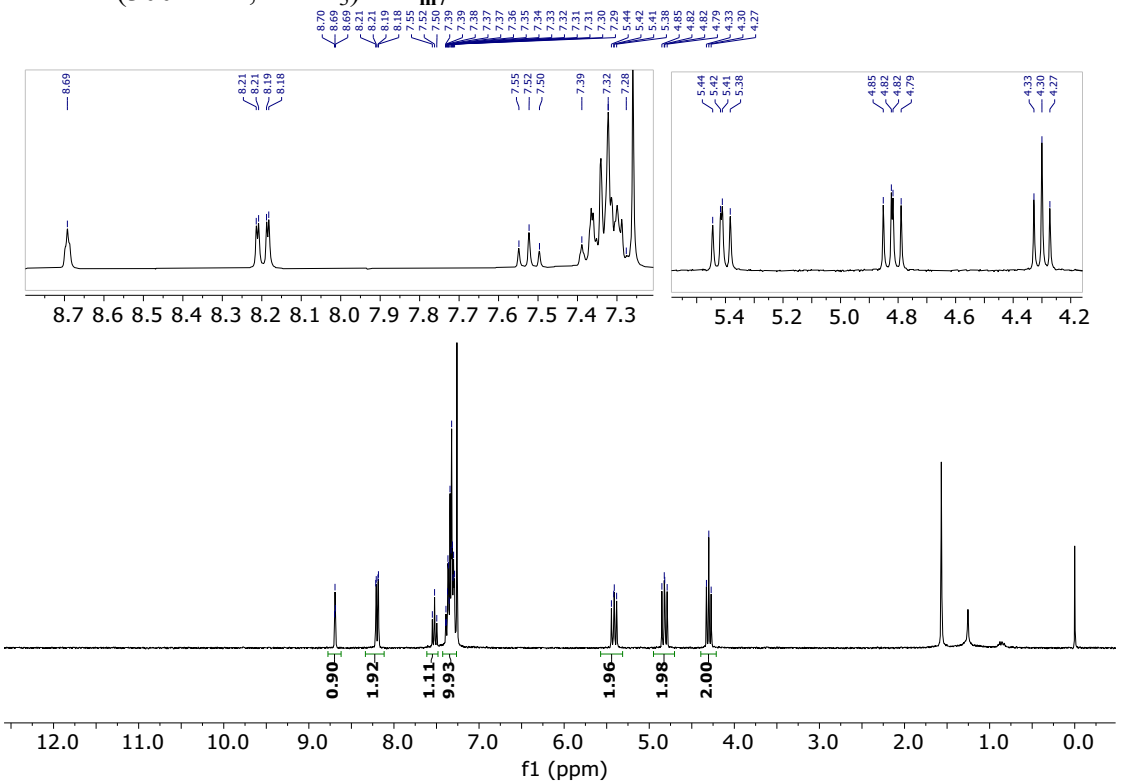
Temperature dependent $^{1}$H NMR spectra of oxazoline $\mathbf{1_{m6}}$, at $c$ = 60 mM. For each temperature a COSY spectrum was recorded as well to determine the chemical shift of overlapping peaks.



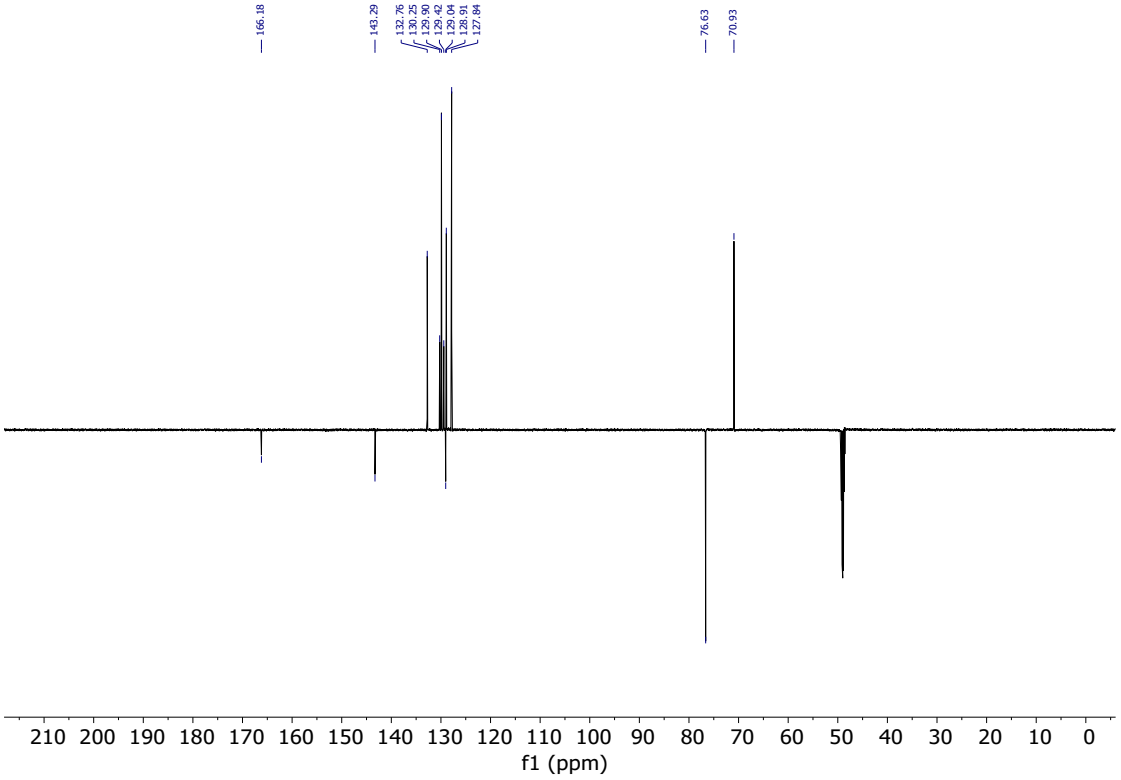
$^{13}$C NMR (75 MHz, $CD_3OD$) of $\mathbf{1_{m6}}$.



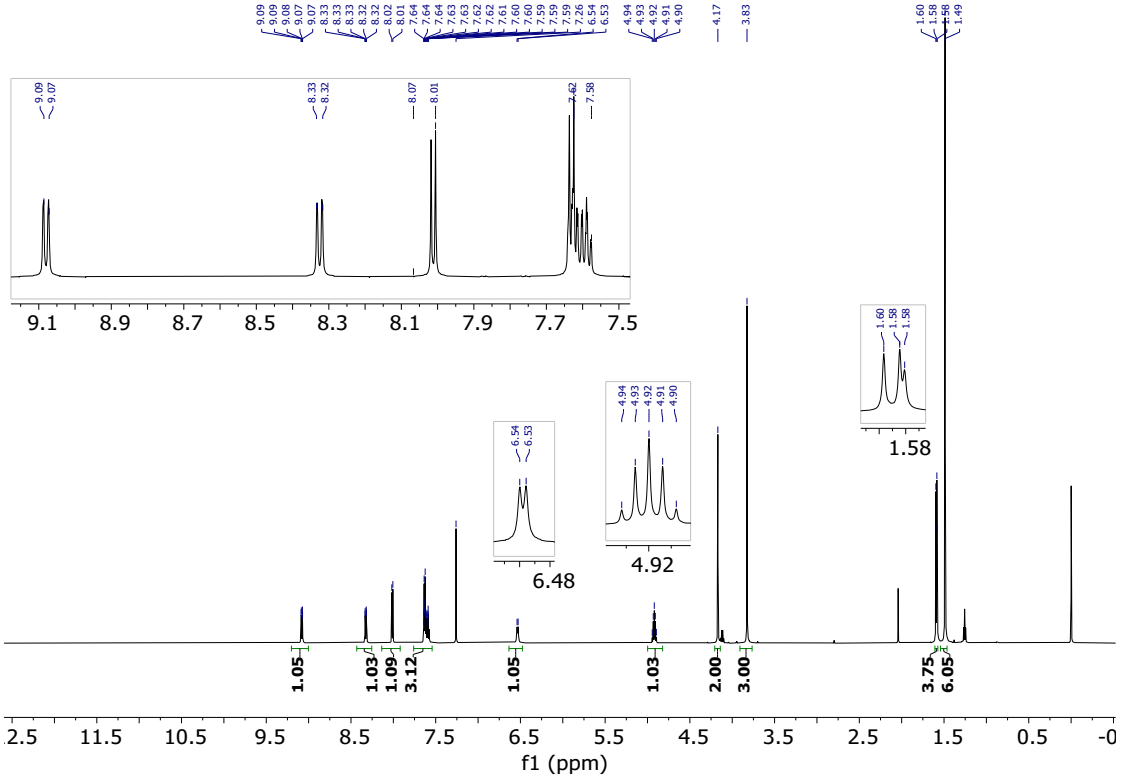
H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{m7}}$.



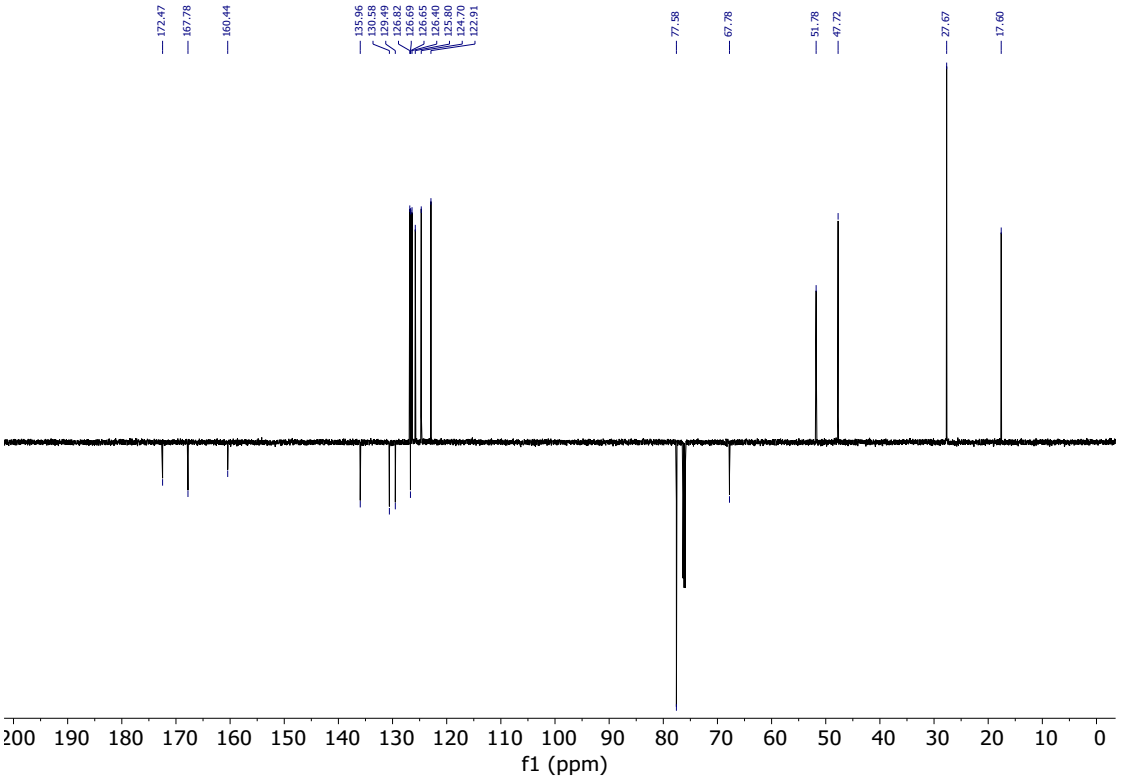

$^{13}C$ NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{m7}}$.



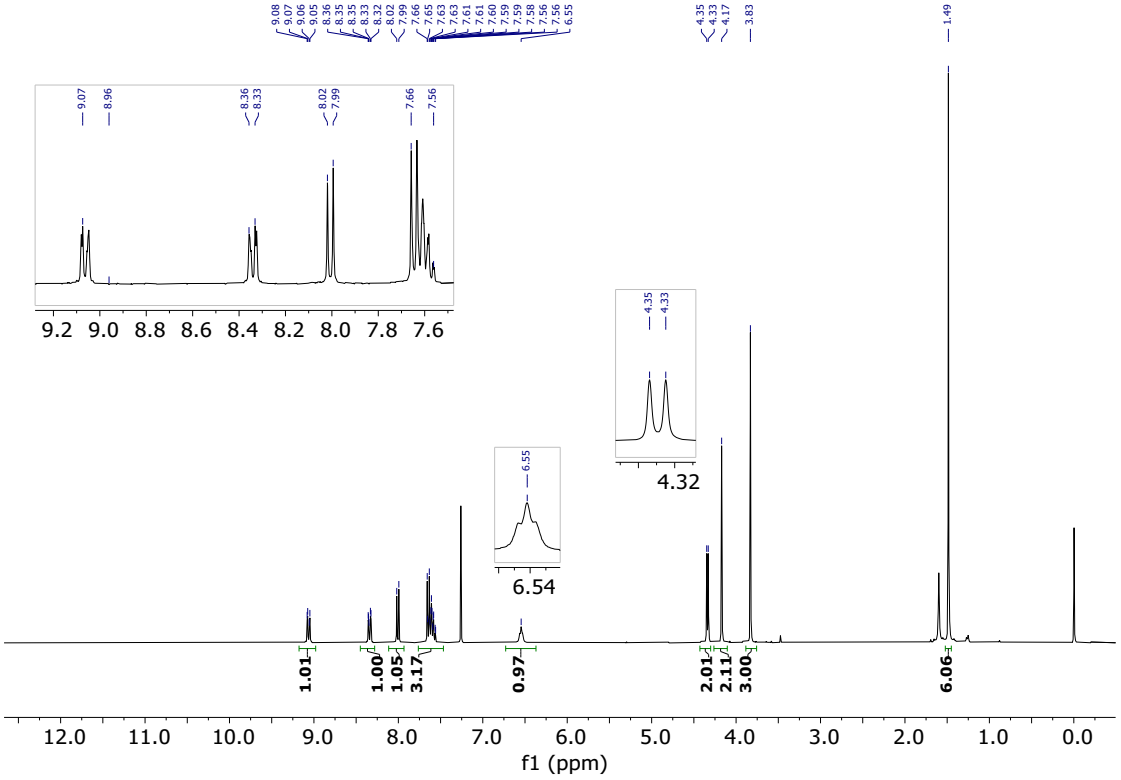
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{n1}}$.



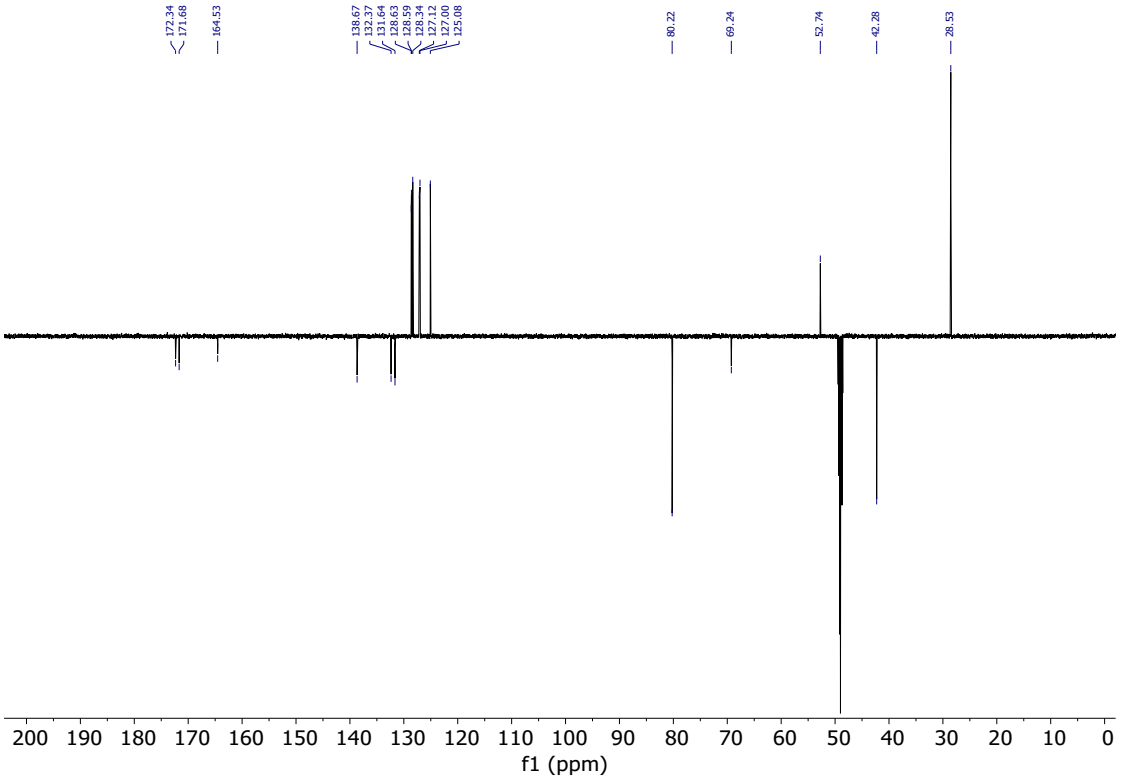
$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{n1}}$.



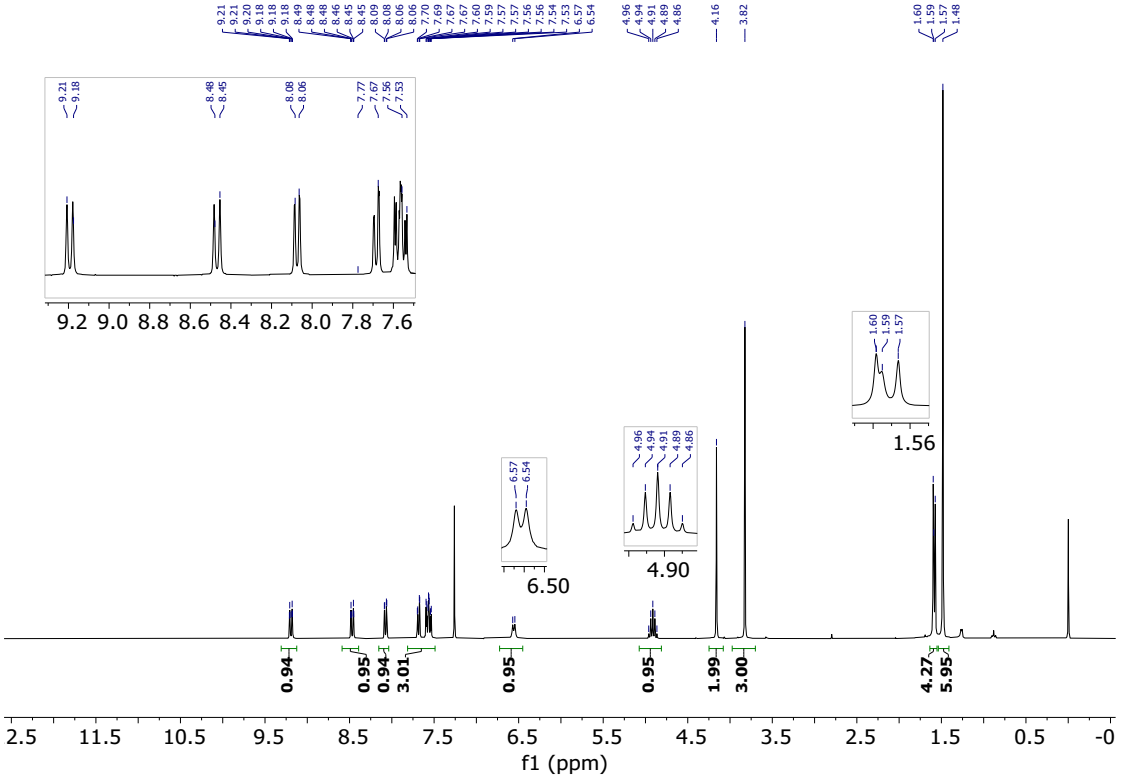
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{n2}}$.



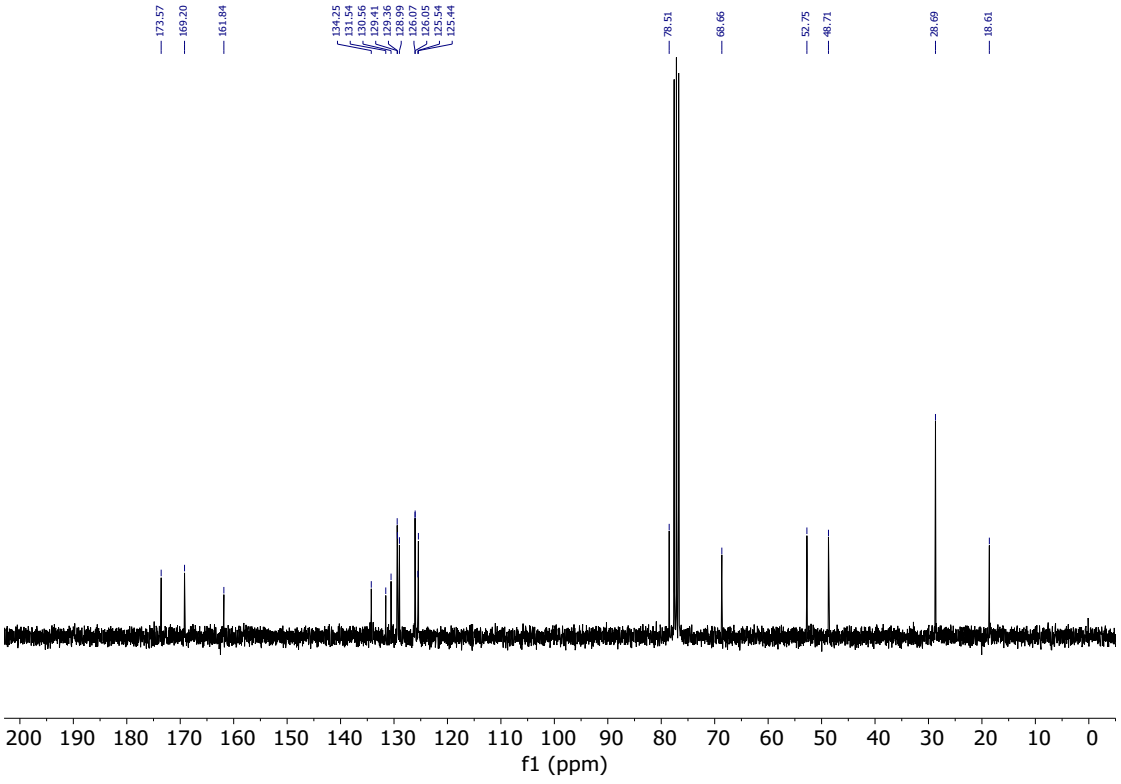

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{n2}}$.



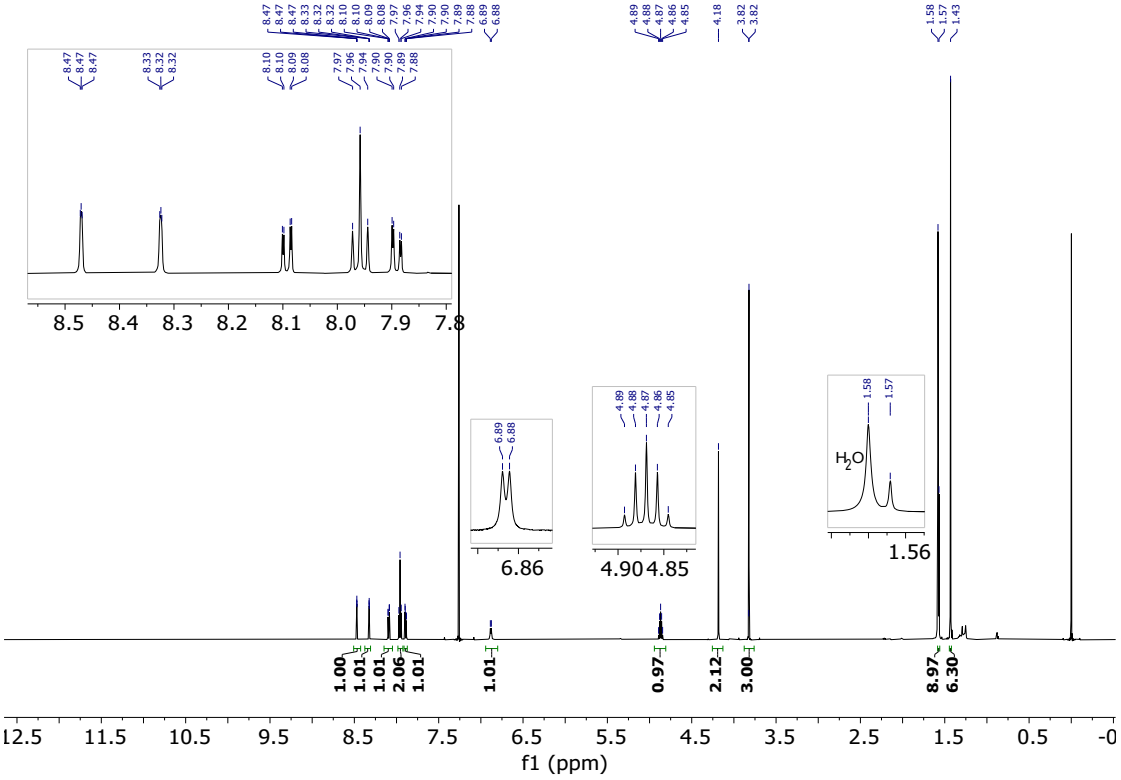
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{n3}}$.



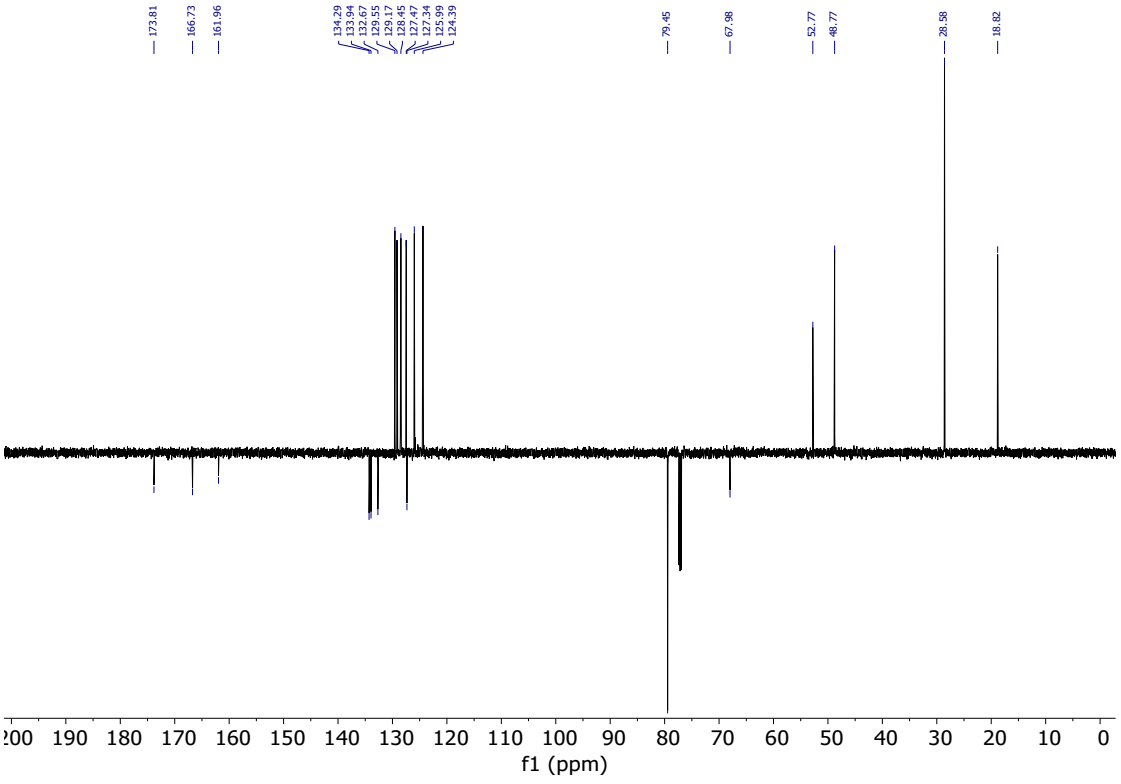

$^{13}$C NMR (75 MHz, $CDCl_3$) of $\mathbf{1_{n3}}$.



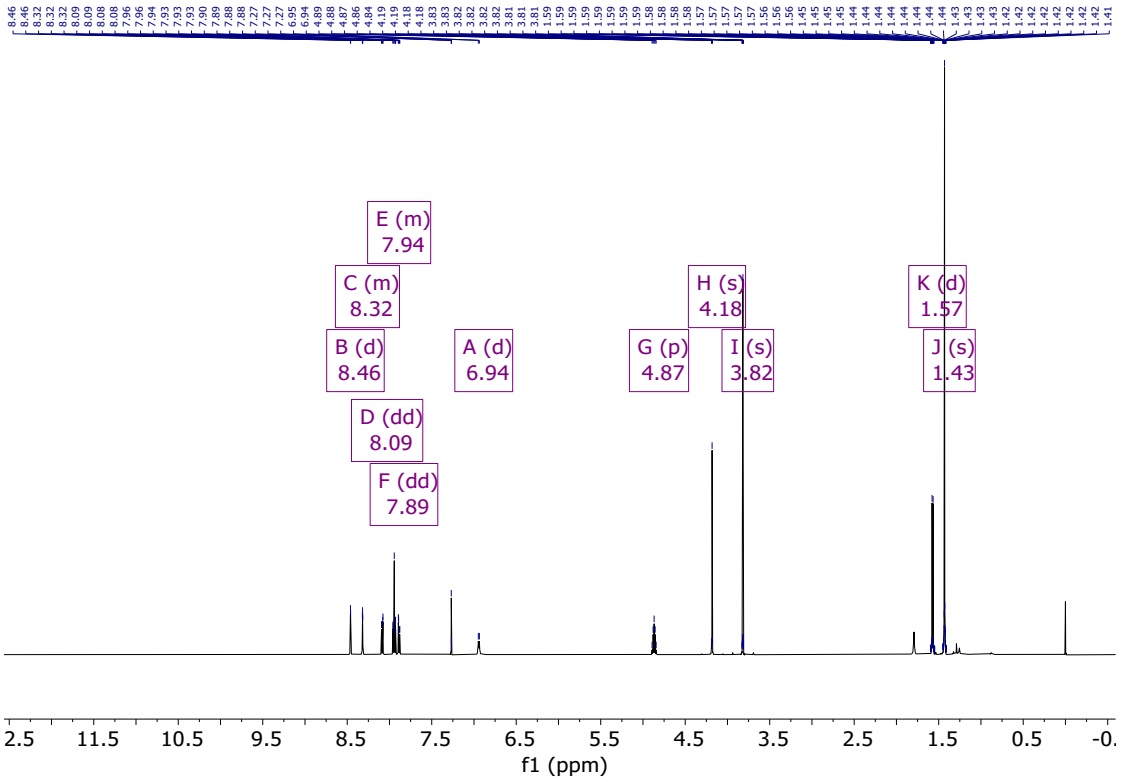
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{n4}}$, $c$ = 6mM.



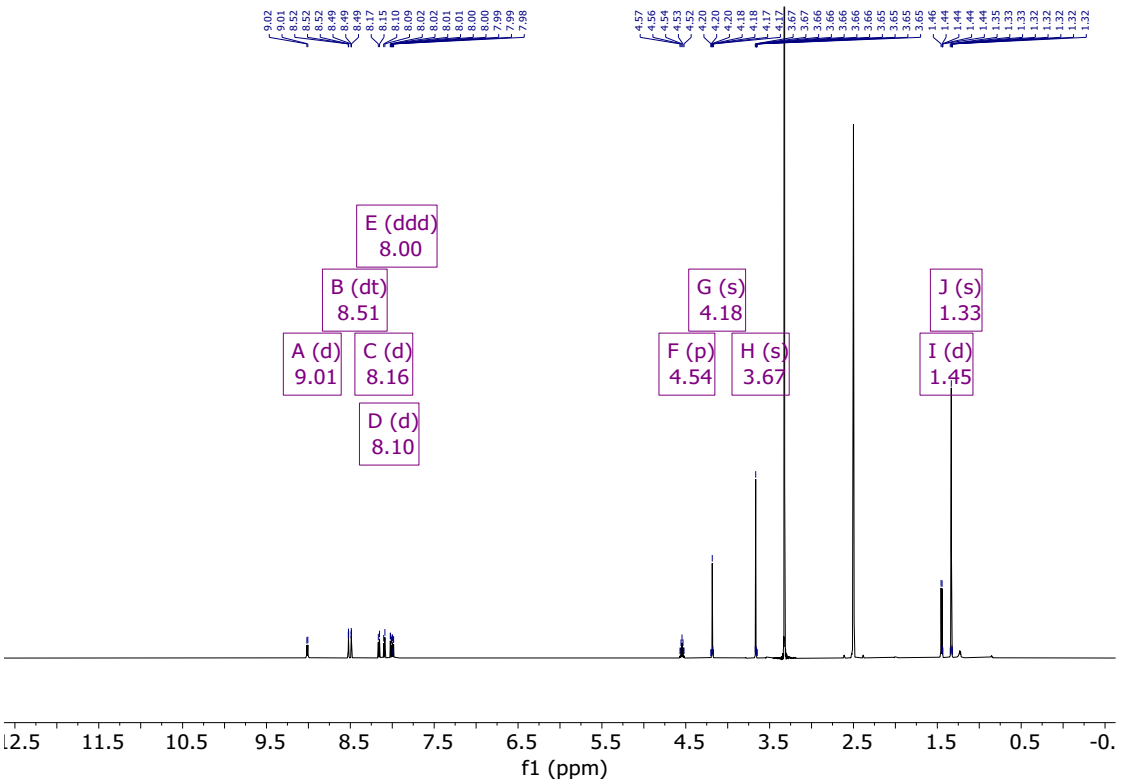

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{n4}}$.



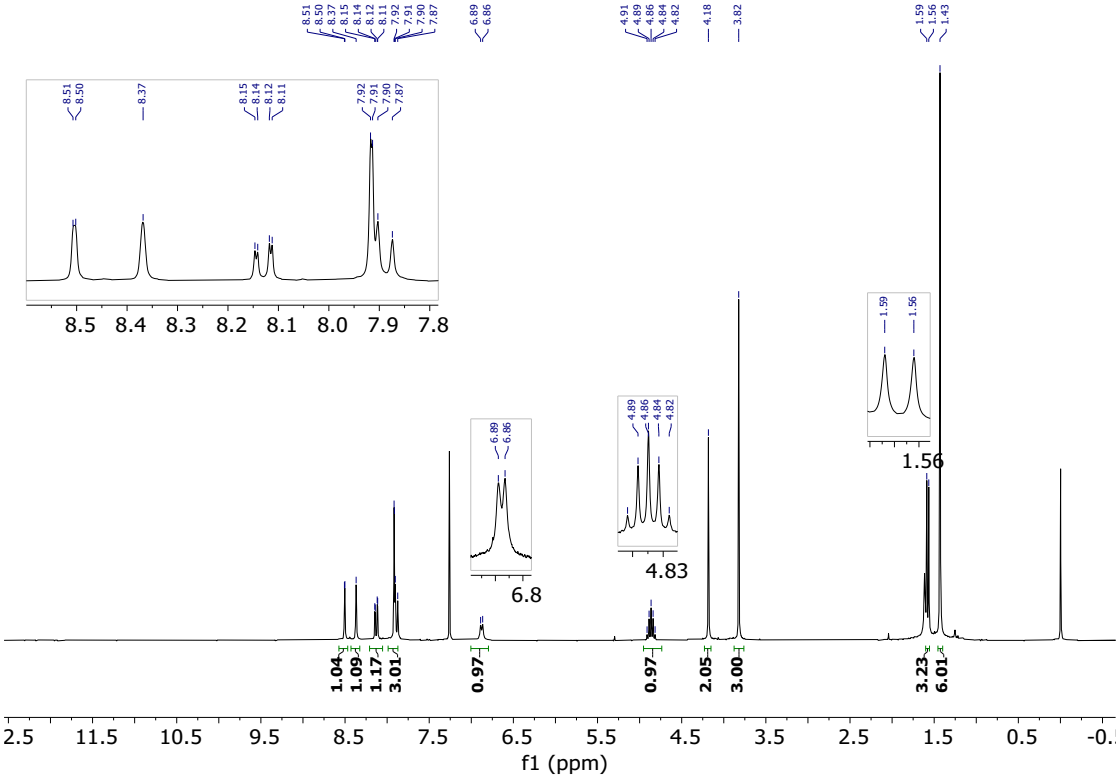
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{n4}}$, $c$ = 60 mM.



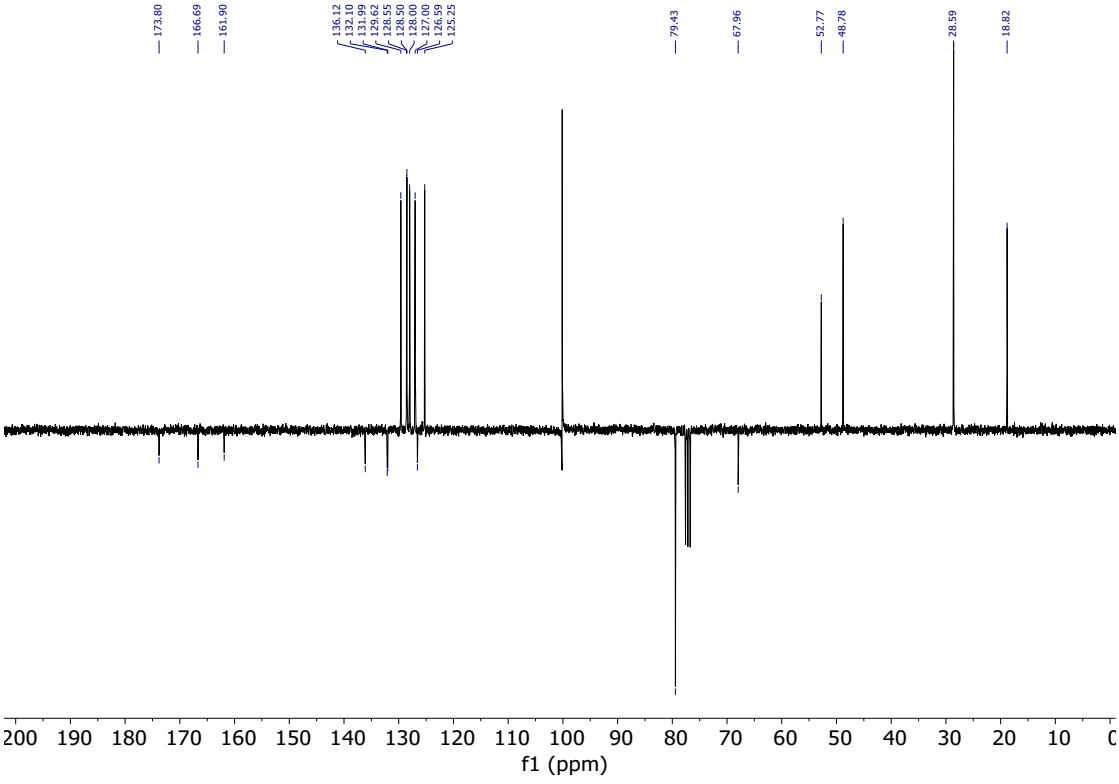

$^1$H NMR (600 MHz, DMSO) of $\mathbf{1_{n4}}$, $c$ = 6 mM.



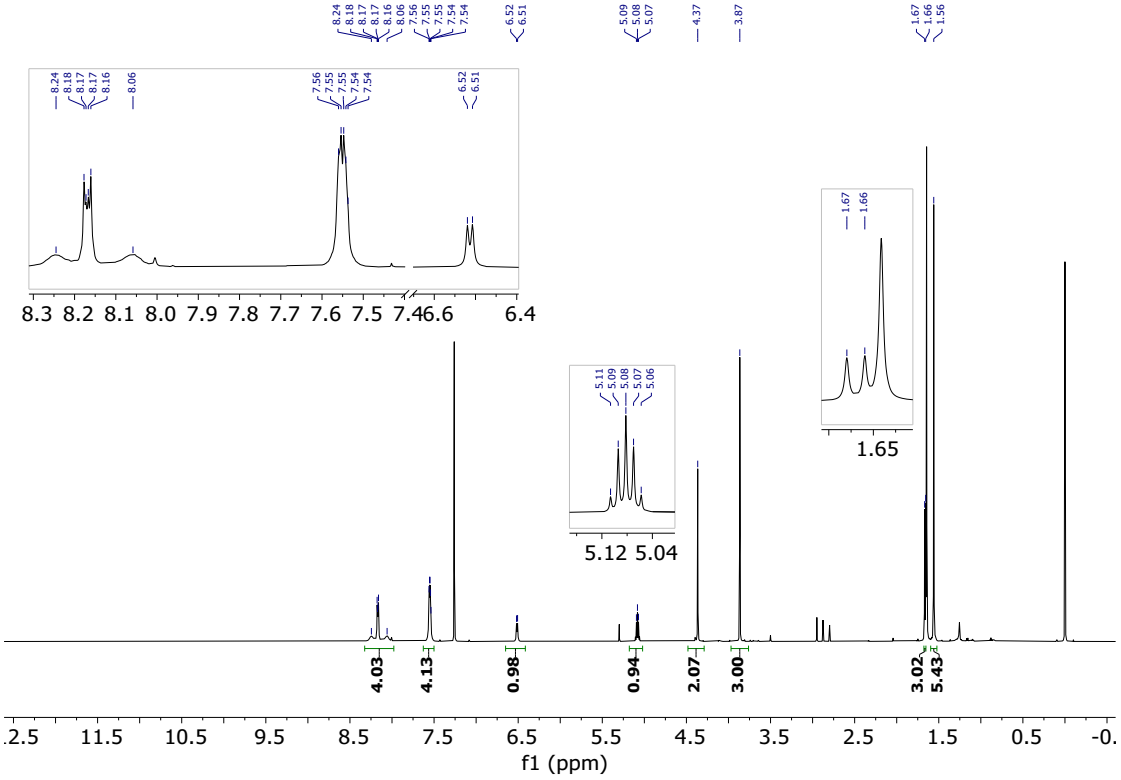
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{1_{n5}}$.



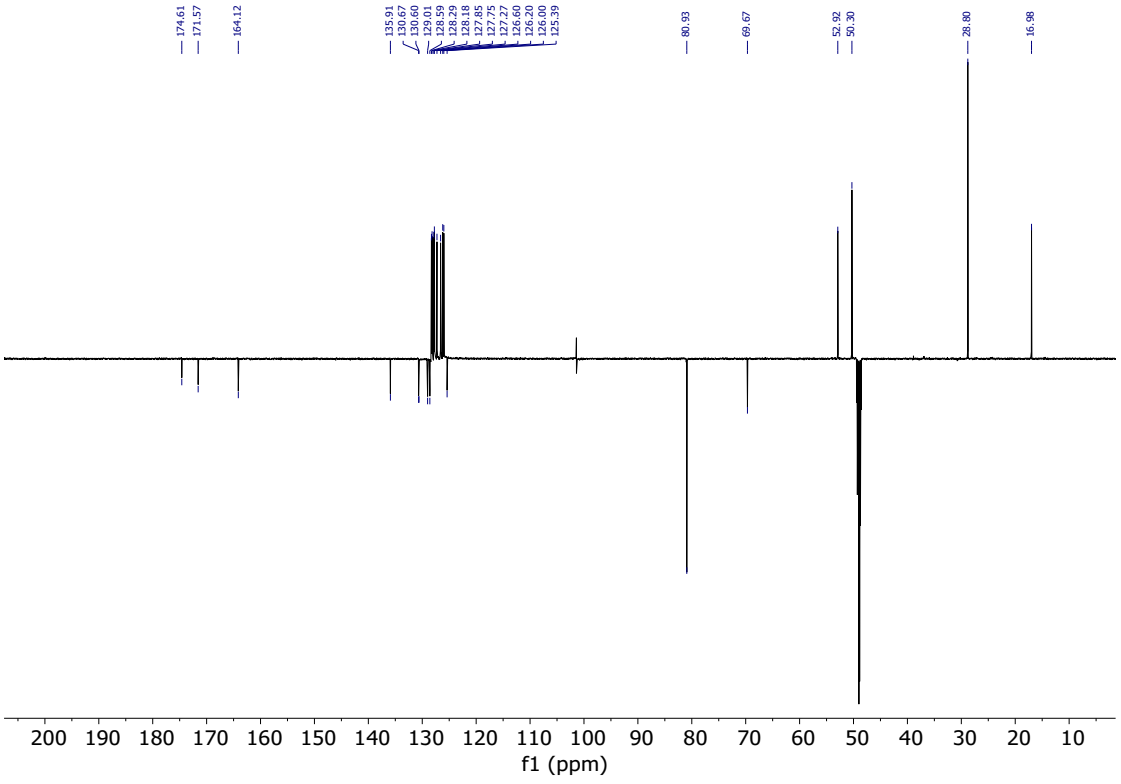

$^{13}$C NMR (75 MHz, $CDCl_3$) of $\mathbf{1_{n5}}$.



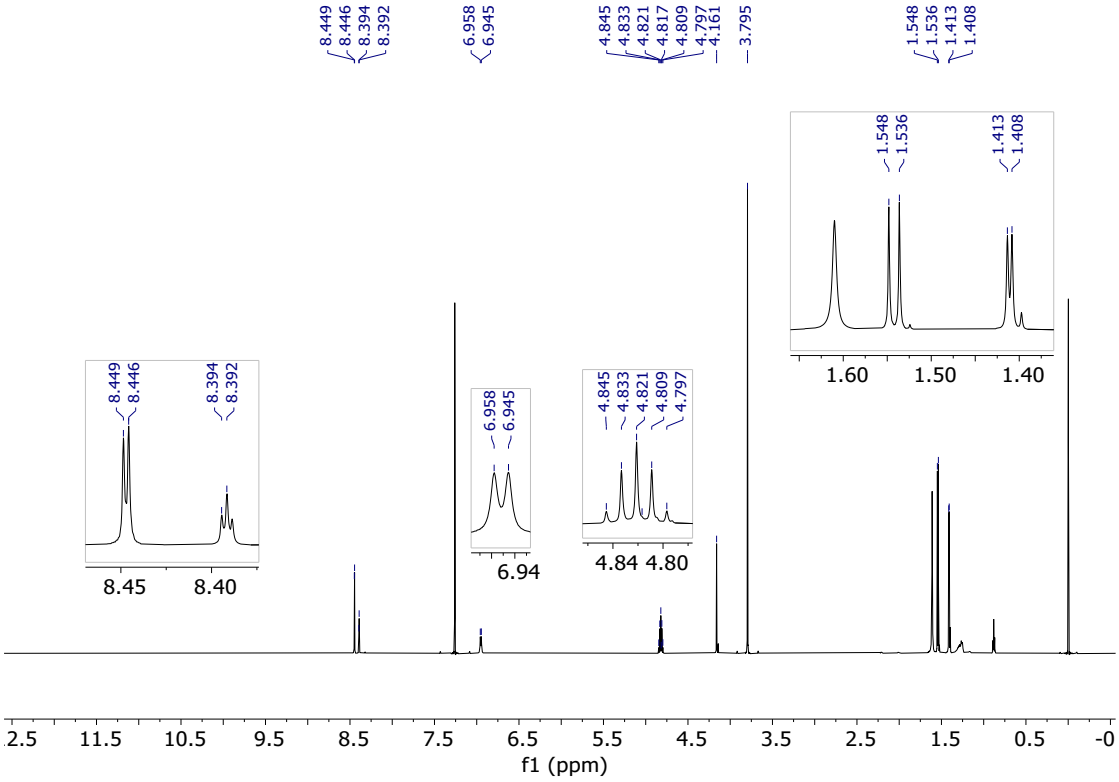
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{a1}}$.



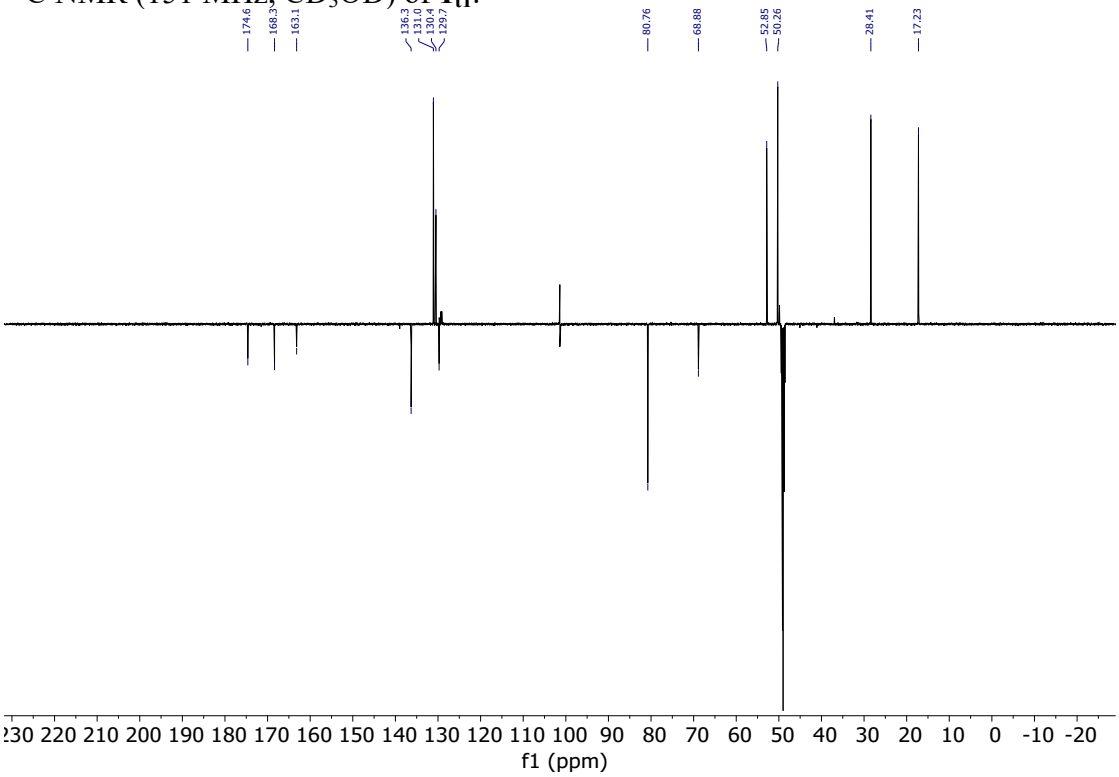

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{1_{a1}}$.



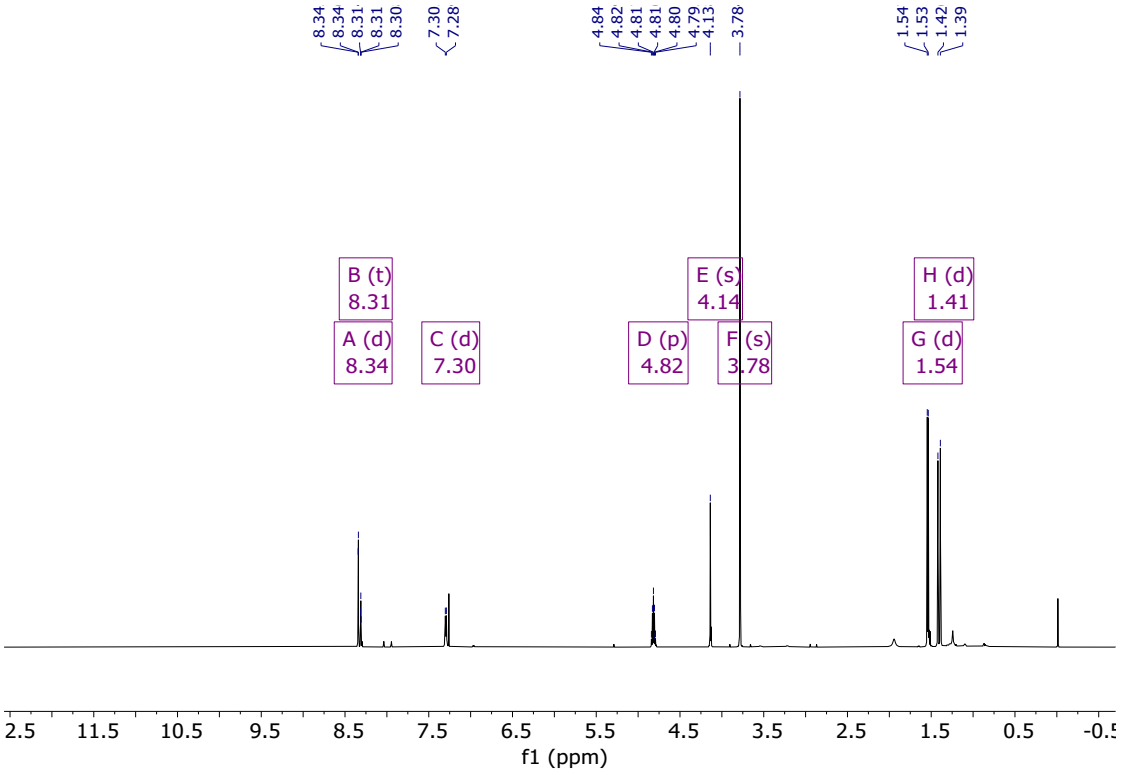
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{t1}}$, $c$ = 6 mM



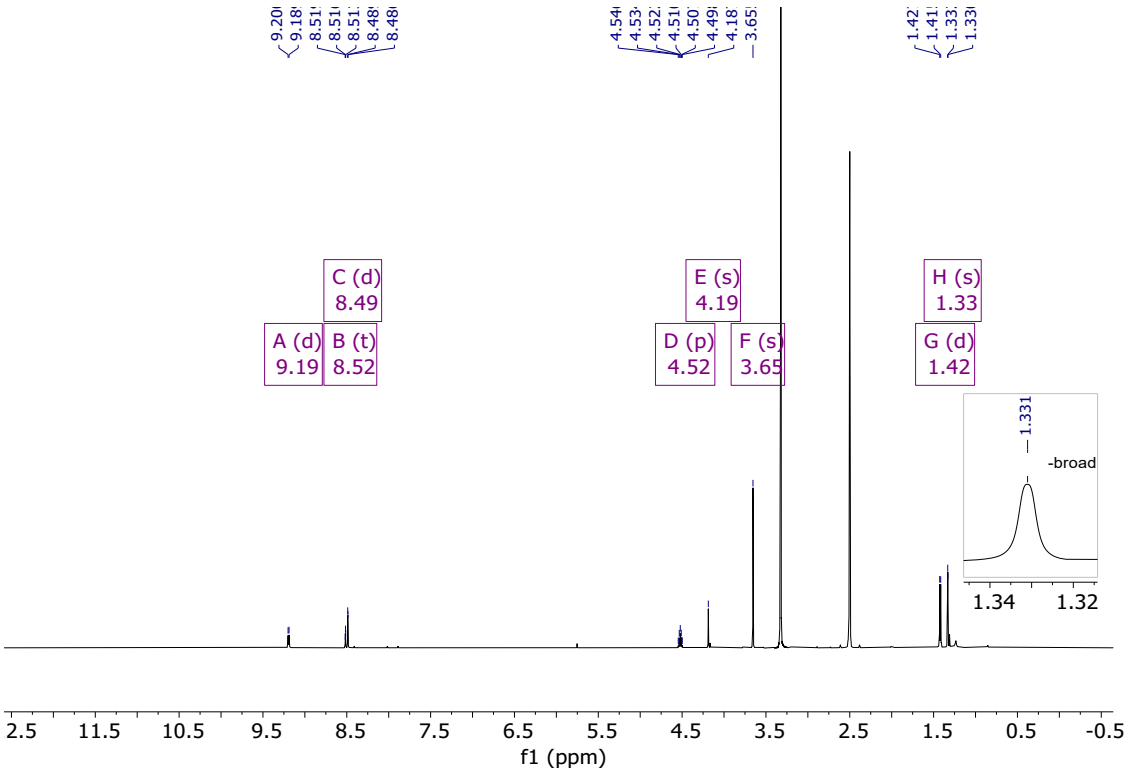

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{t1}}$.



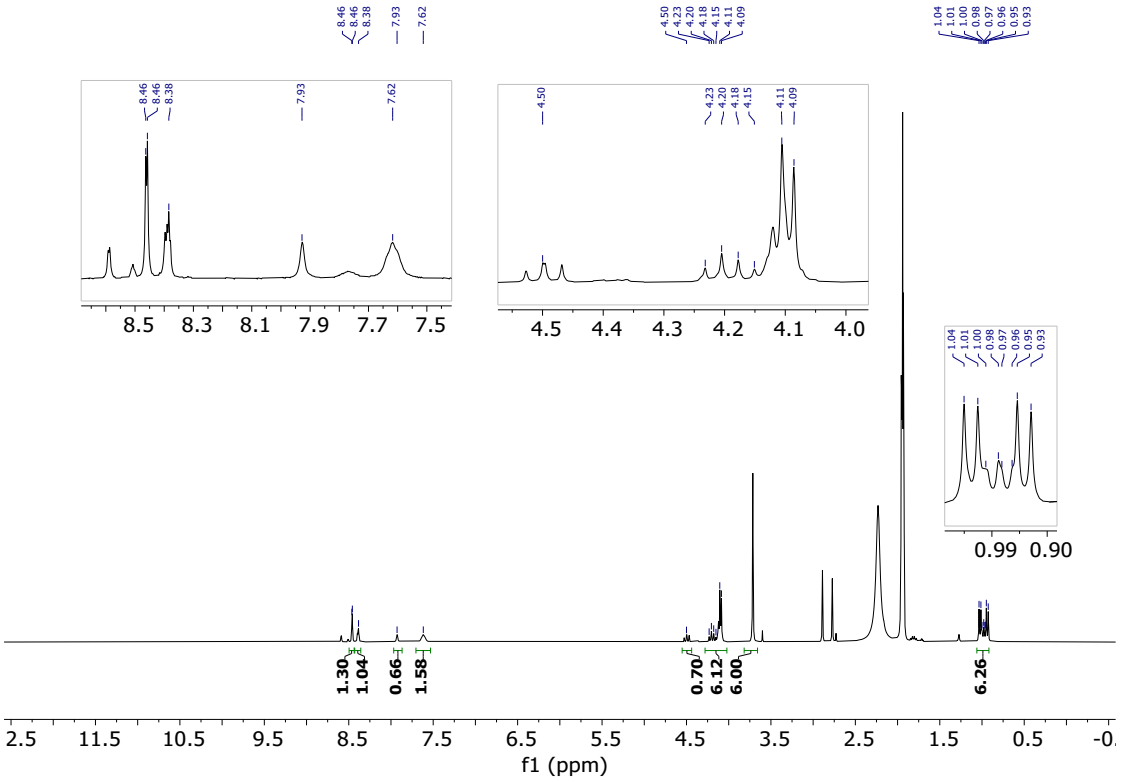
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{t1}}$, $c$ = 60 mM



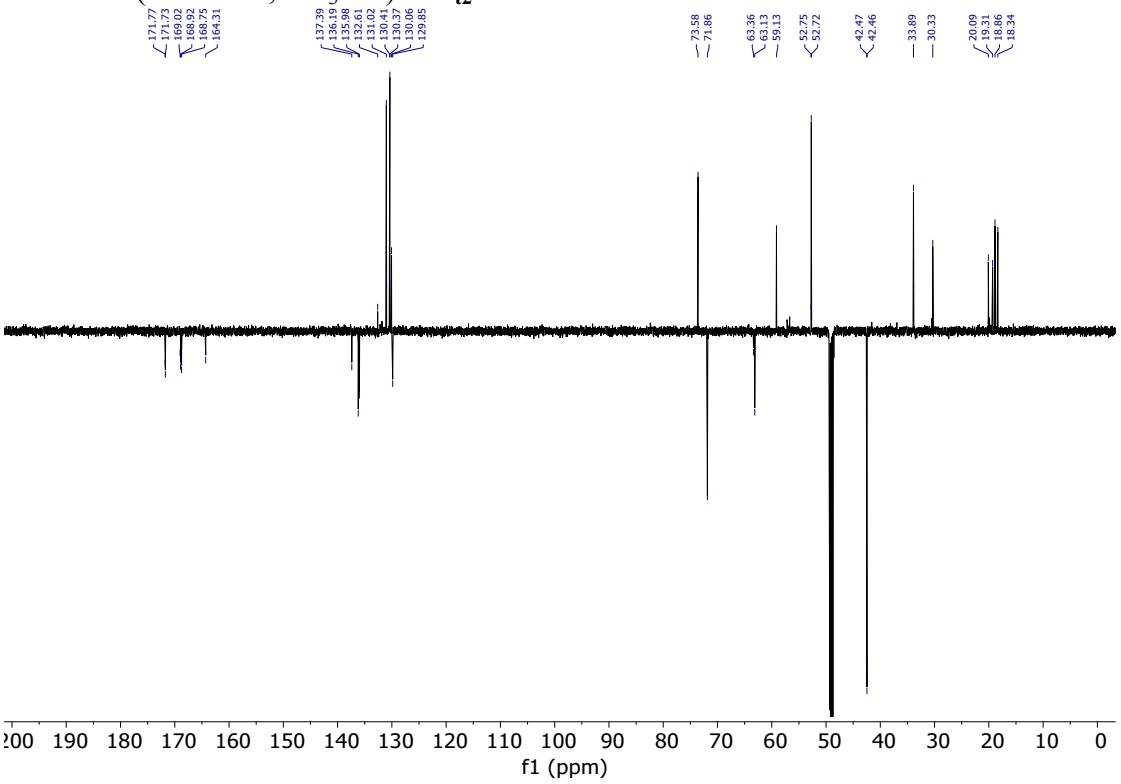

$^{1}$H NMR (600 MHz, DMSO) of $\mathbf{1_{t1}}$, $c$ = 6 mM



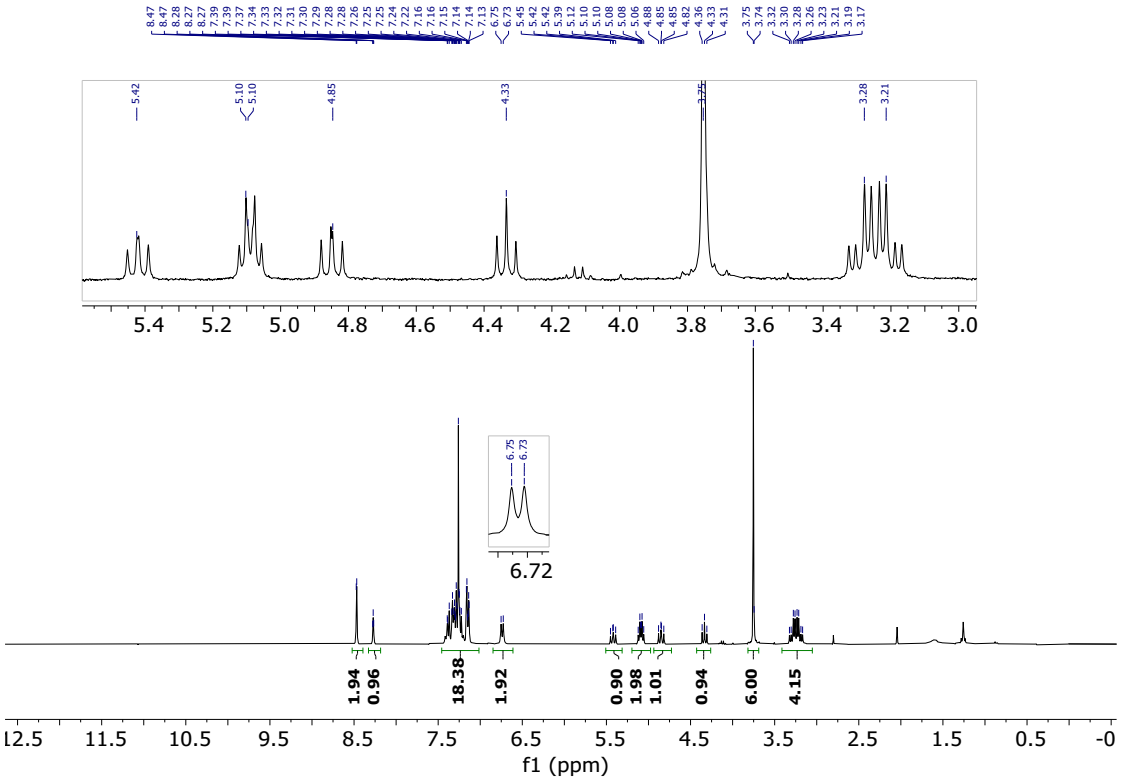
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{1_{t2}}$.



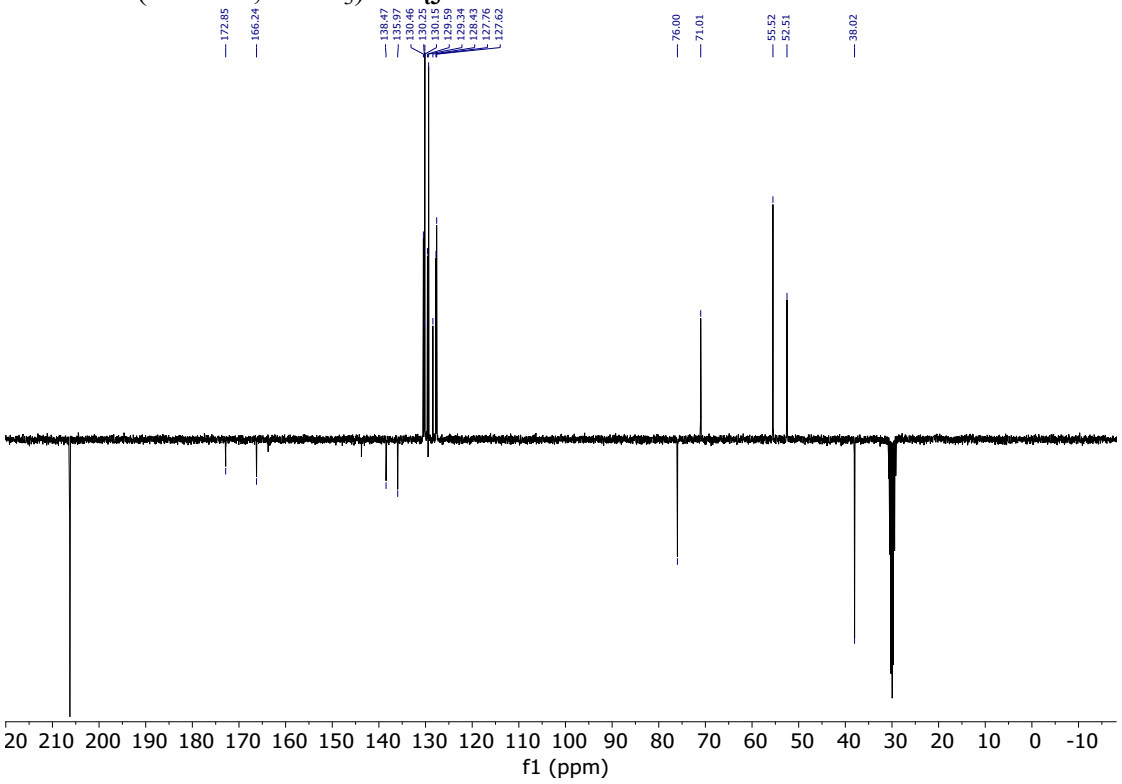

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{t2}}$.



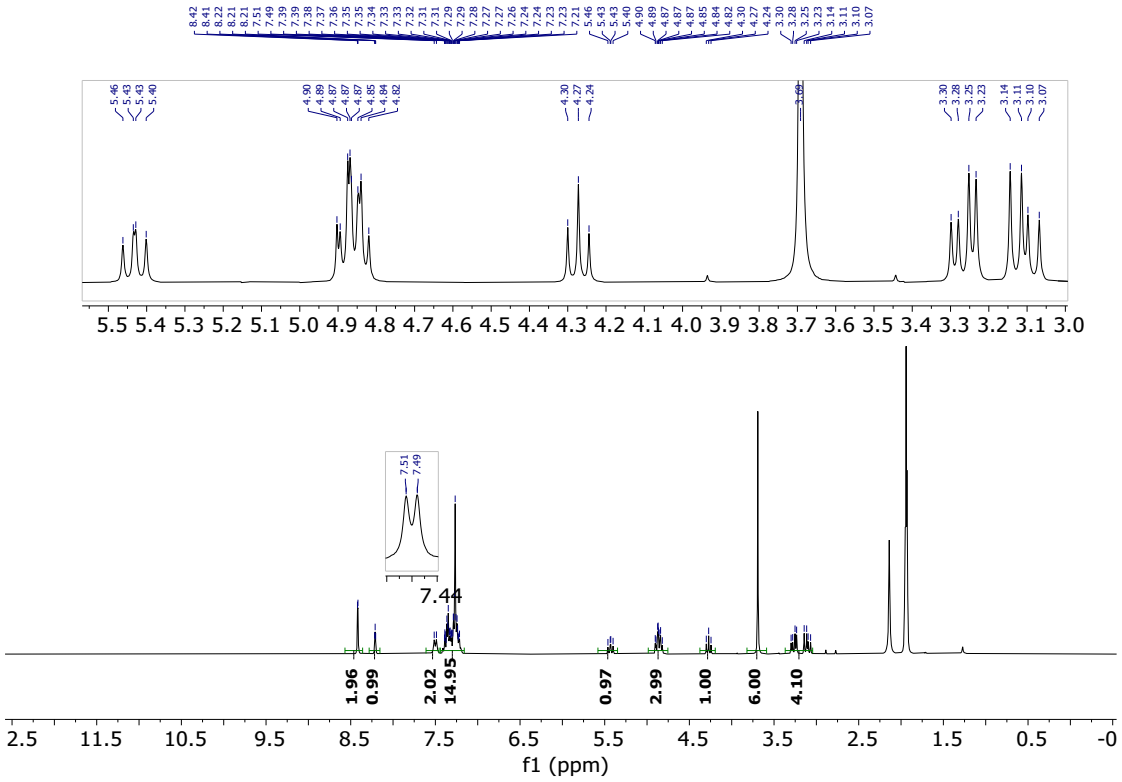
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{1_{t3}}$.



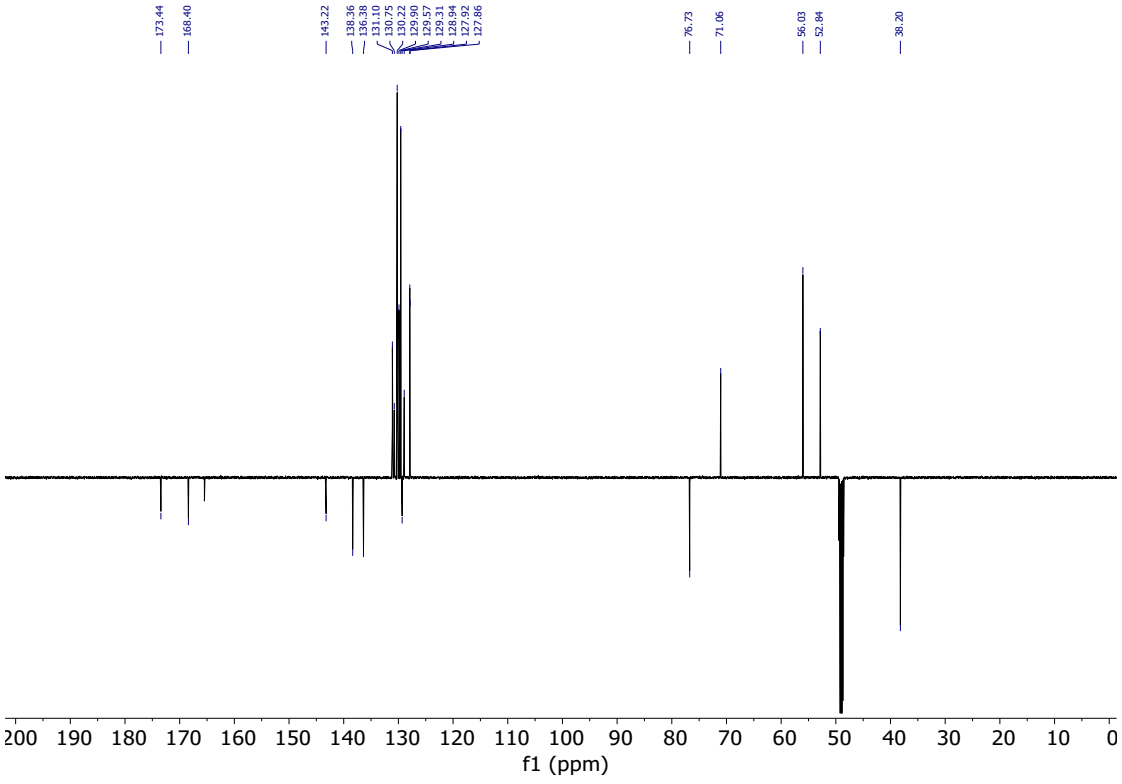

$^{13}$C NMR (75 MHz, $CDCl_3$) of $\mathbf{1_{t3}}$.



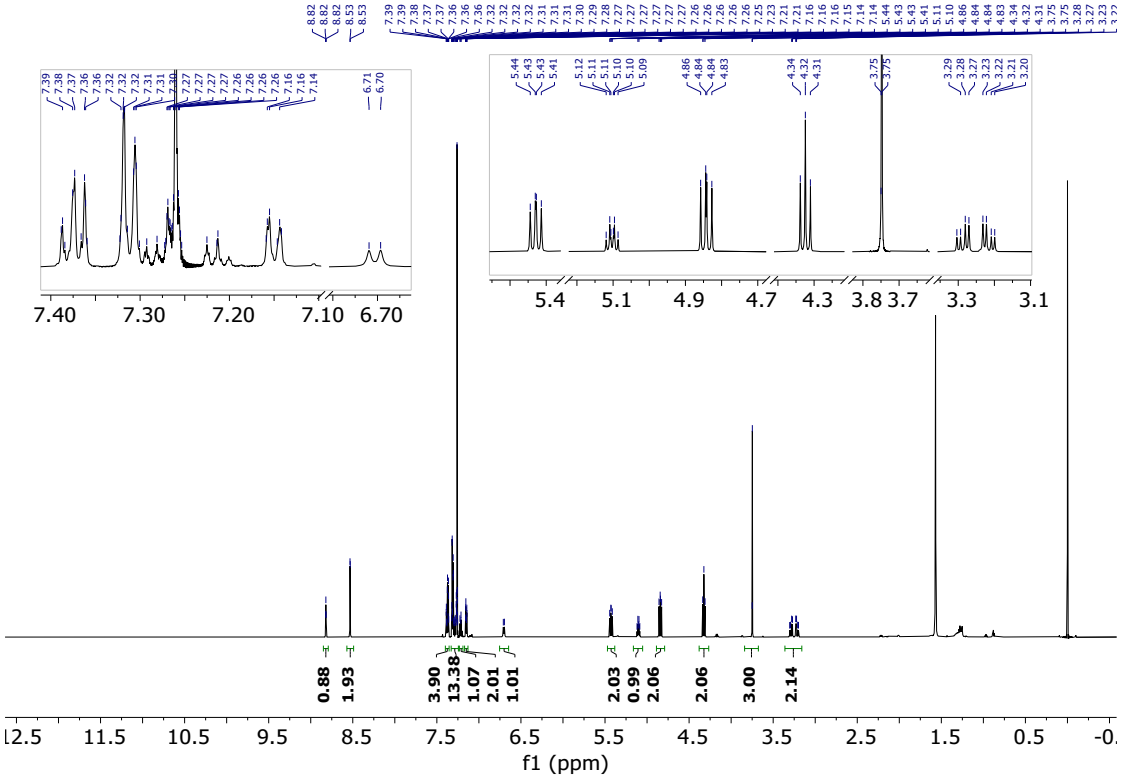
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{1}_{\mathbf{t4}}$.



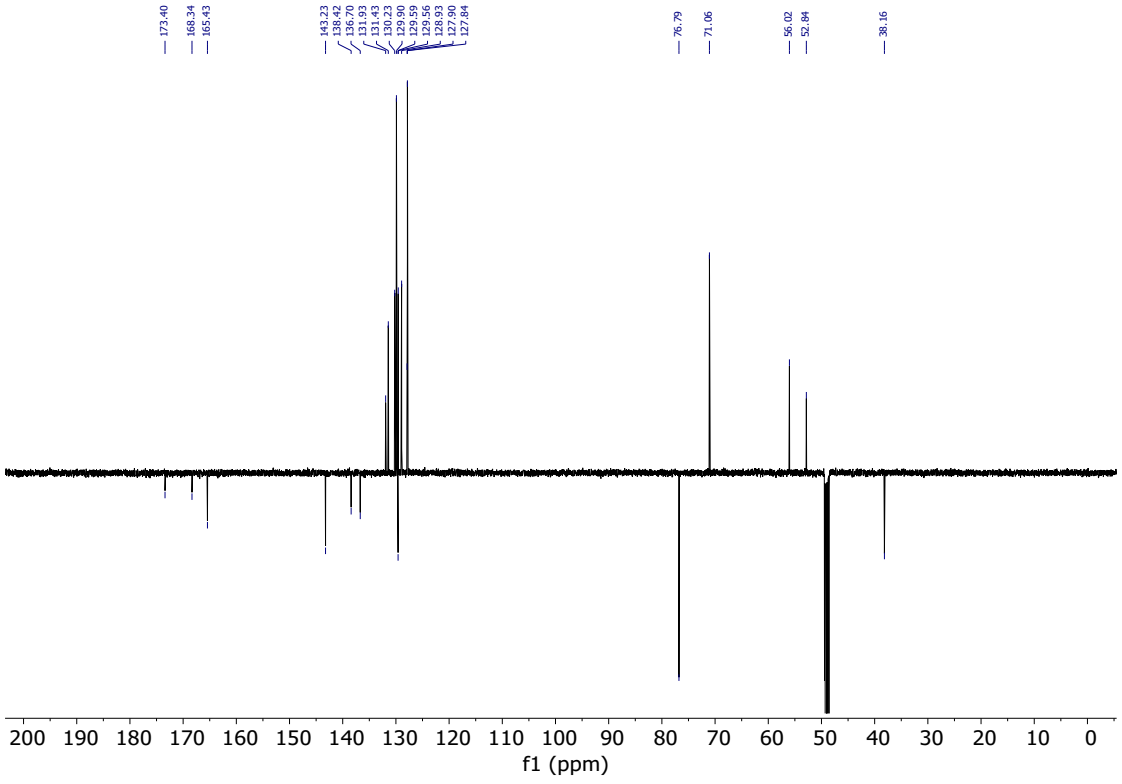

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1}_{\mathbf{t4}}$.



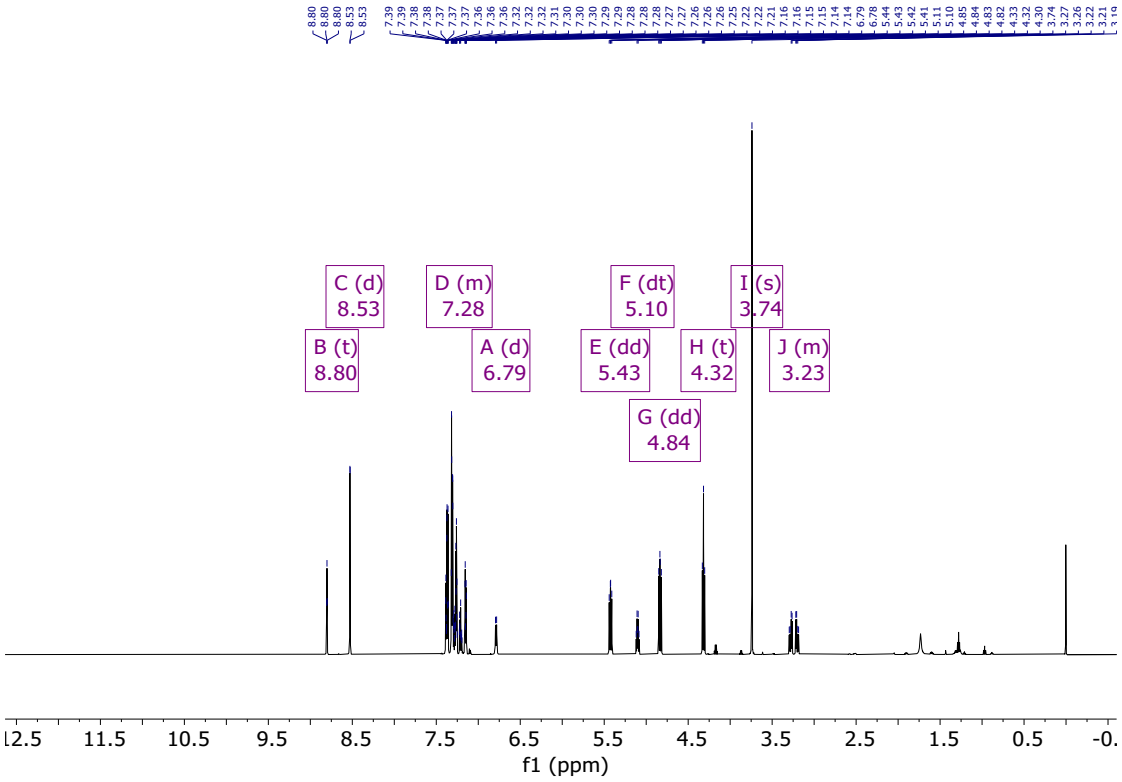
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{t5}}$, $c$ = 6 mM.



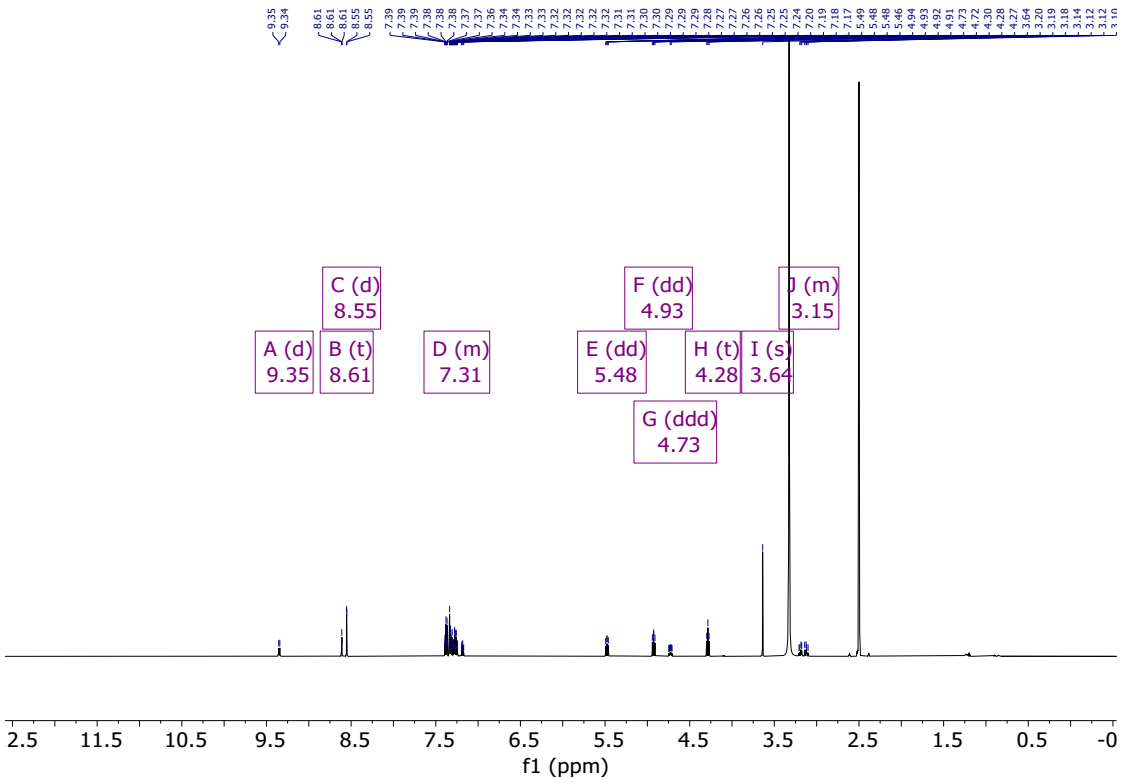

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{t5}}$.



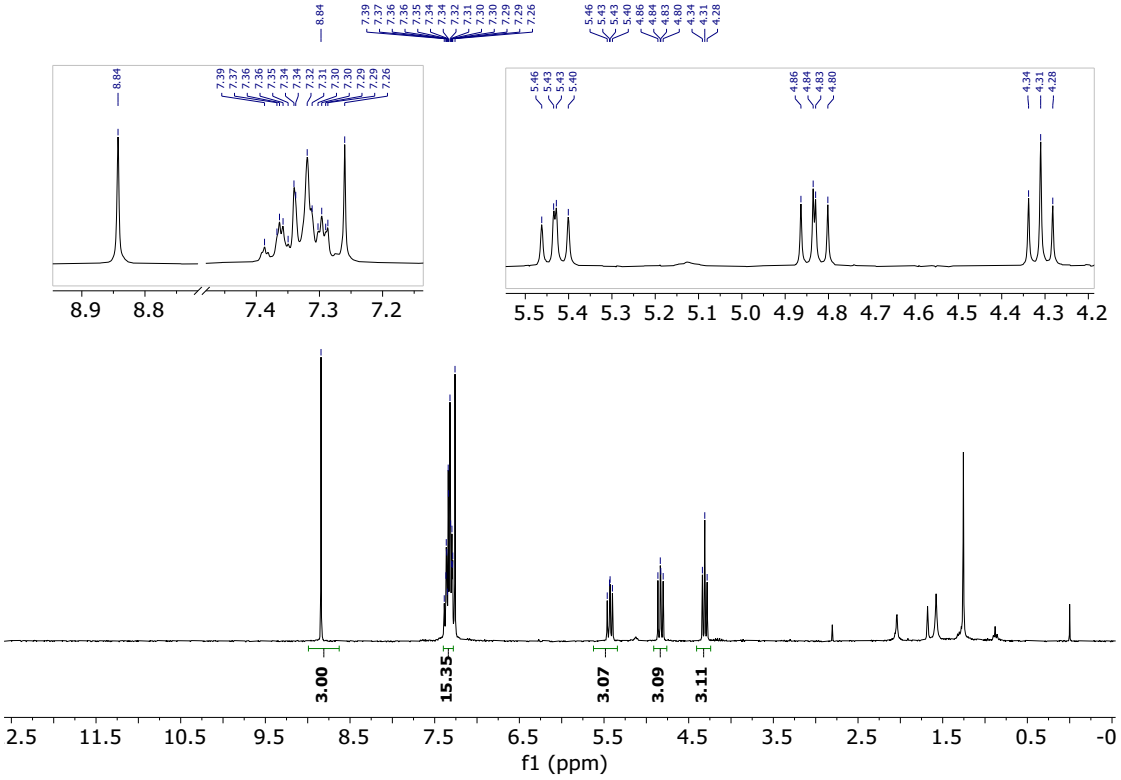
$^1$H NMR (600 MHz, $CDCl_3$) of $\mathbf{1_{t5}}$, $c$ = 60 mM.



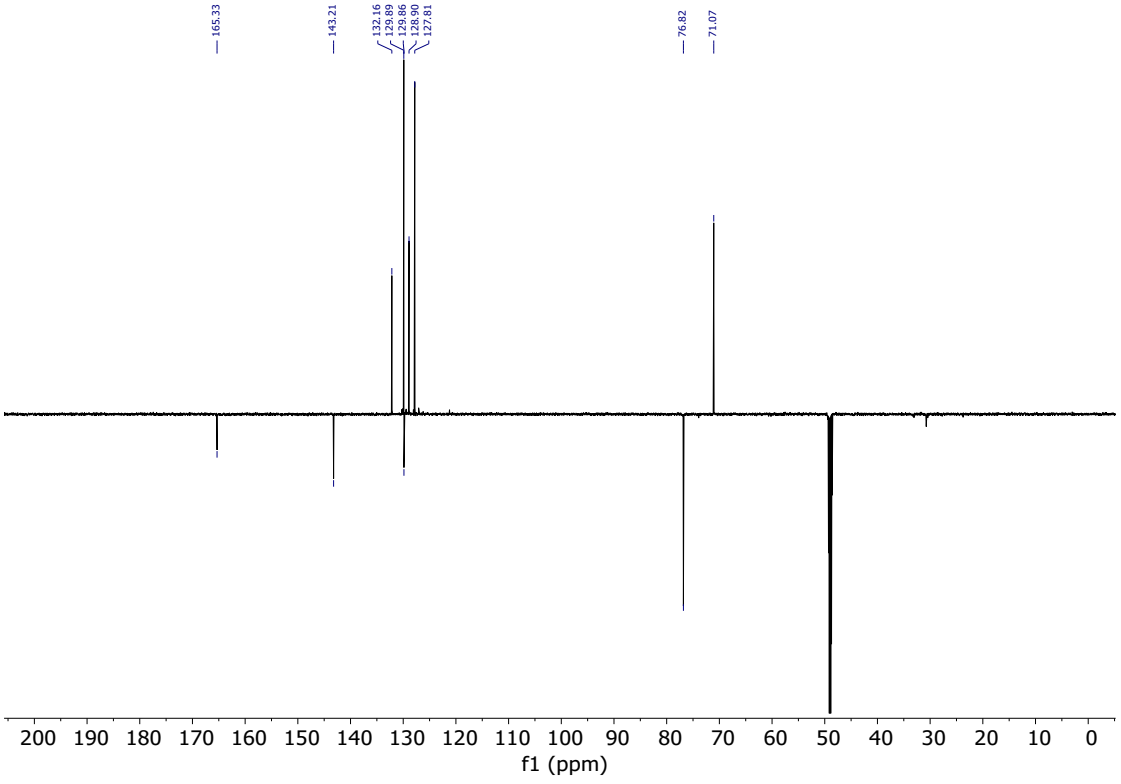

$^1$H NMR (600 MHz, DMSO) of $\mathbf{1_{t5}}$, $c$ = 6 mM.



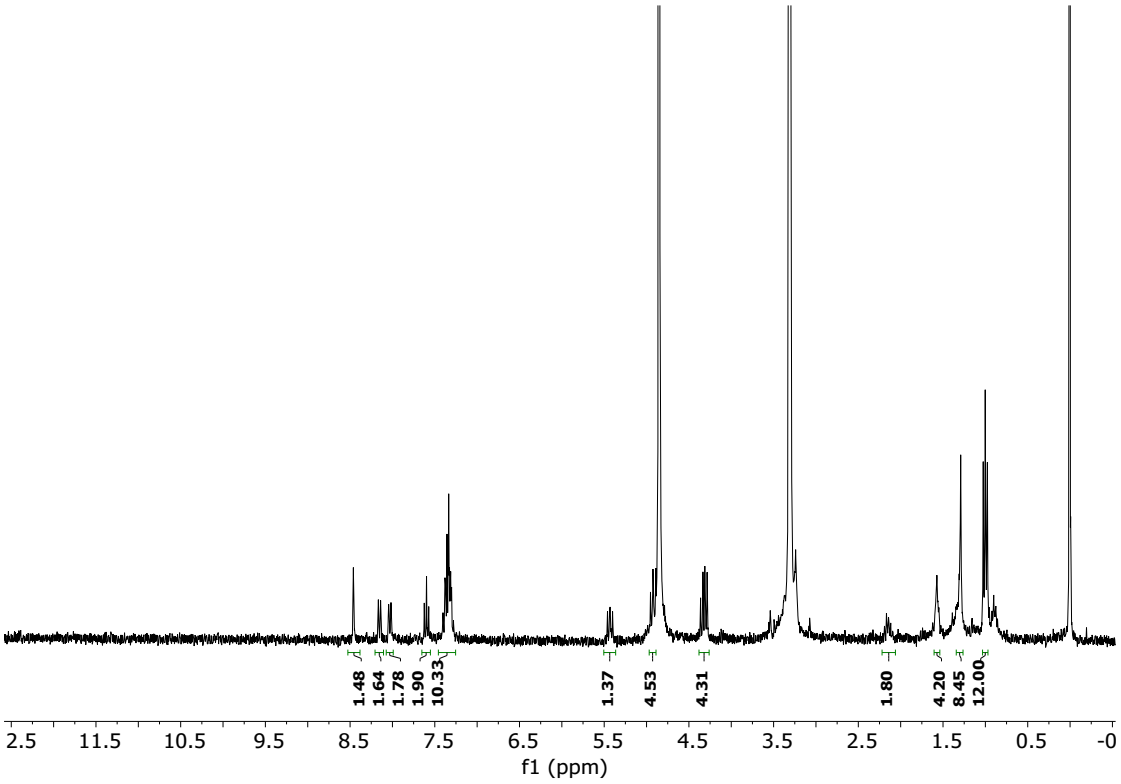
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{1_{t6}}$.



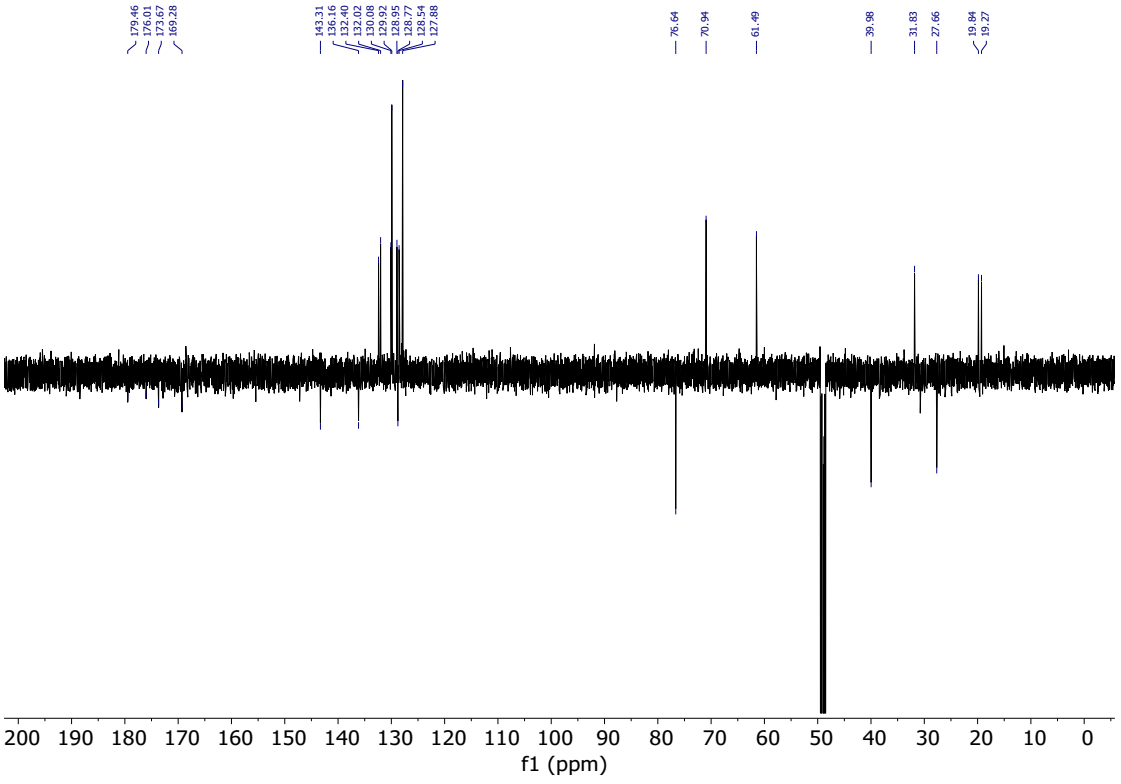

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{1_{t6}}$.



$^{1}$H NMR (300 MHz, $CD_3OD$) of **((Ph-ox)-*m*$C_6H_4$-Val-NH-$CH_2CH_2$)$_2$ ($1_b$).**

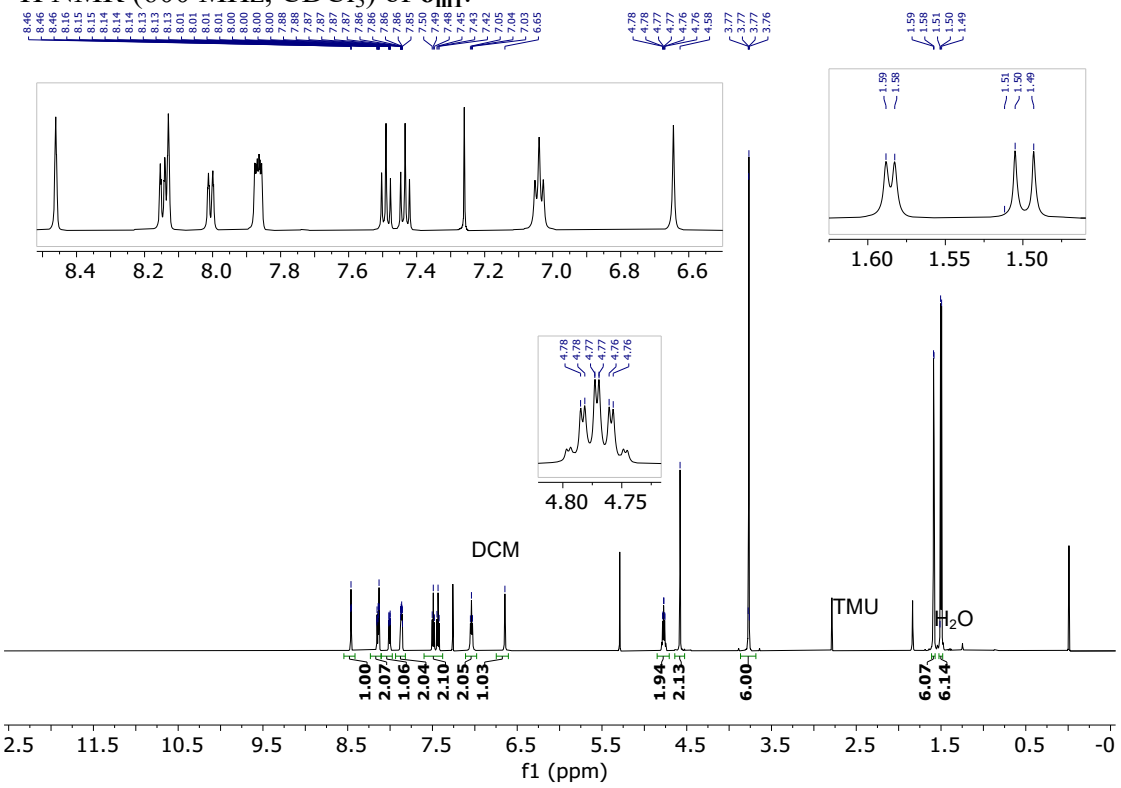



$^{13}$C NMR (151 MHz, $CD_3OD$) of **((Ph-ox)-*m*$C_6H_4$-Val-NH-$CH_2CH_2$)$_2$ ($1_b$).**

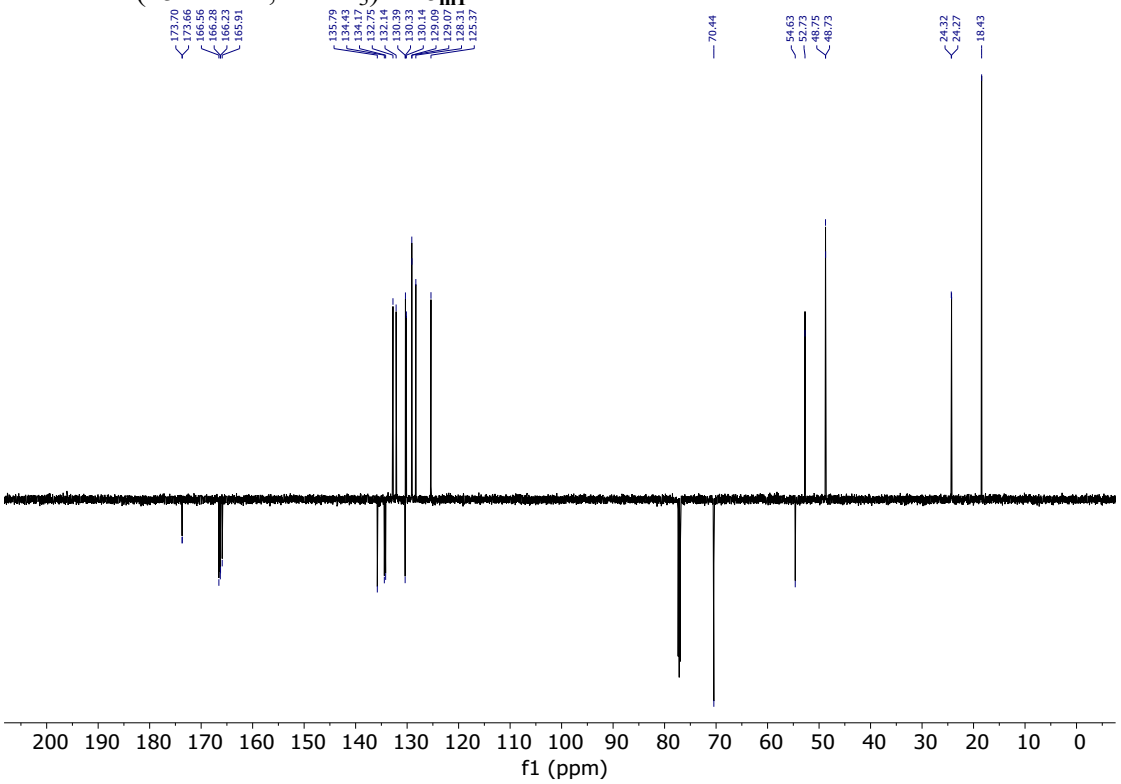


## 2.2. Reaction 1

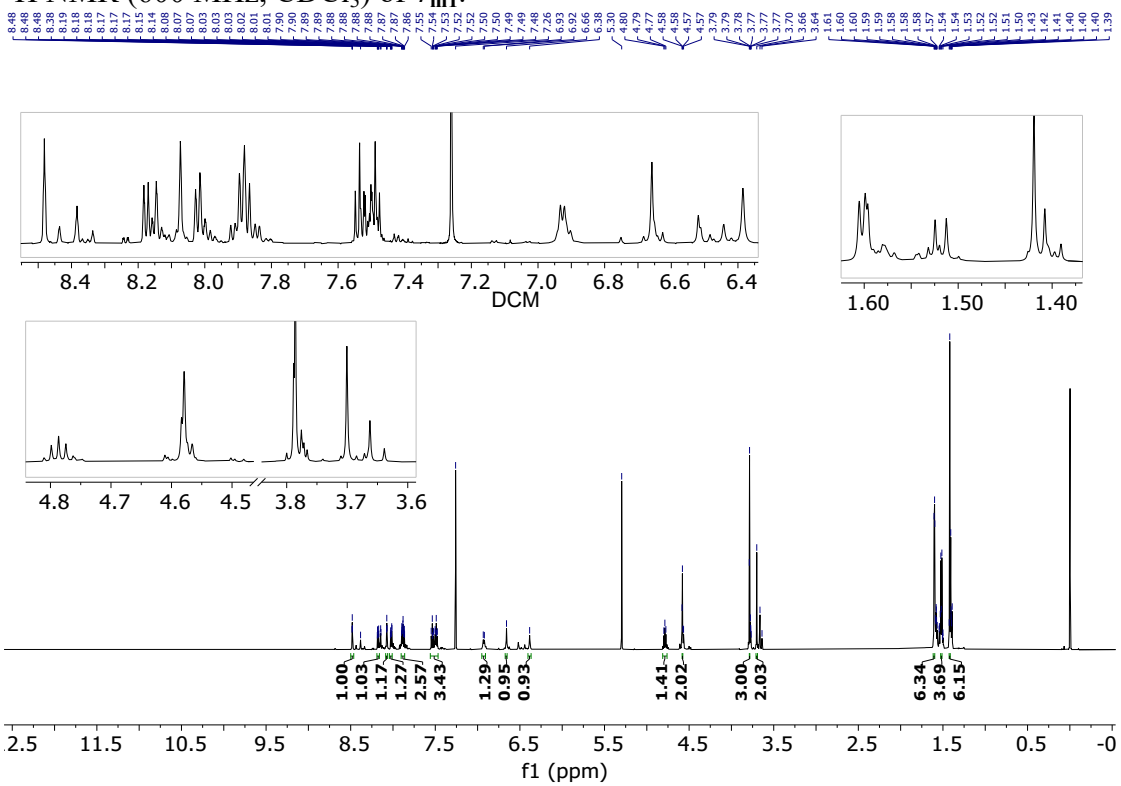
$^{1}$H NMR (600 MHz, $CDCl_3$) of **$6_{m1}$**.



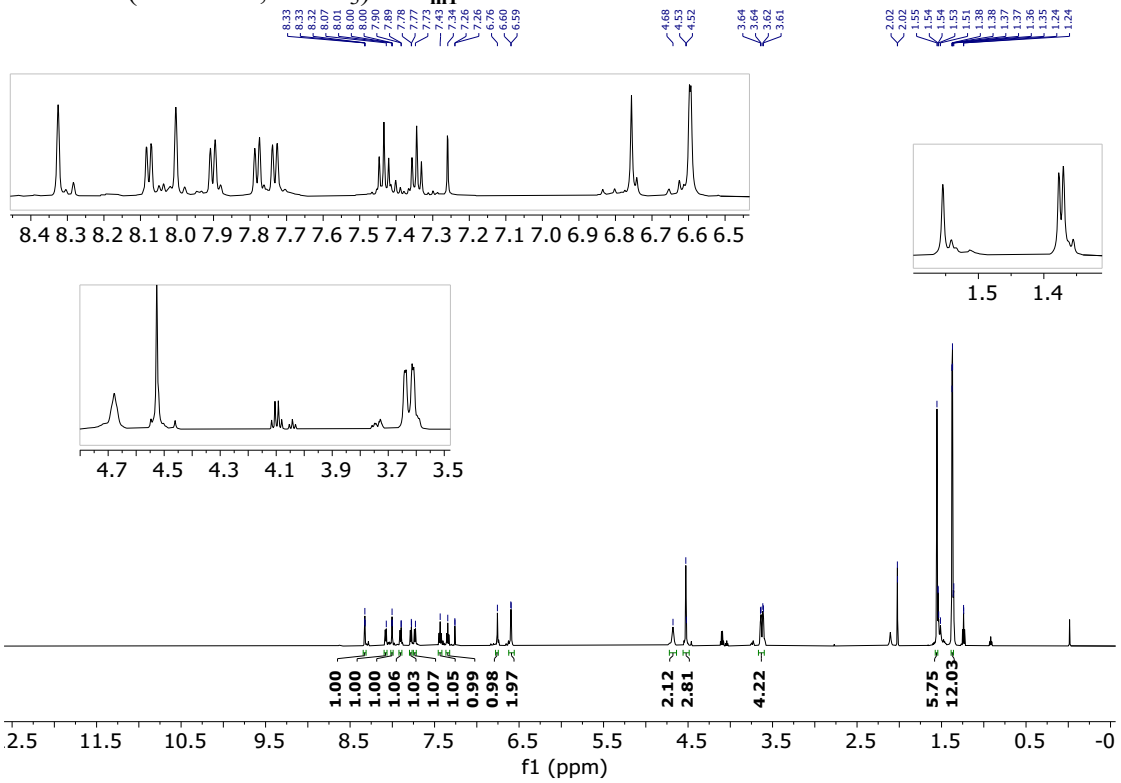

$^{13}$C NMR (151 MHz, $CDCl_3$) of **$6_{m1}$**.



$^1$H NMR (600 MHz, $CDCl_3$) of **$7_{m1}$**.

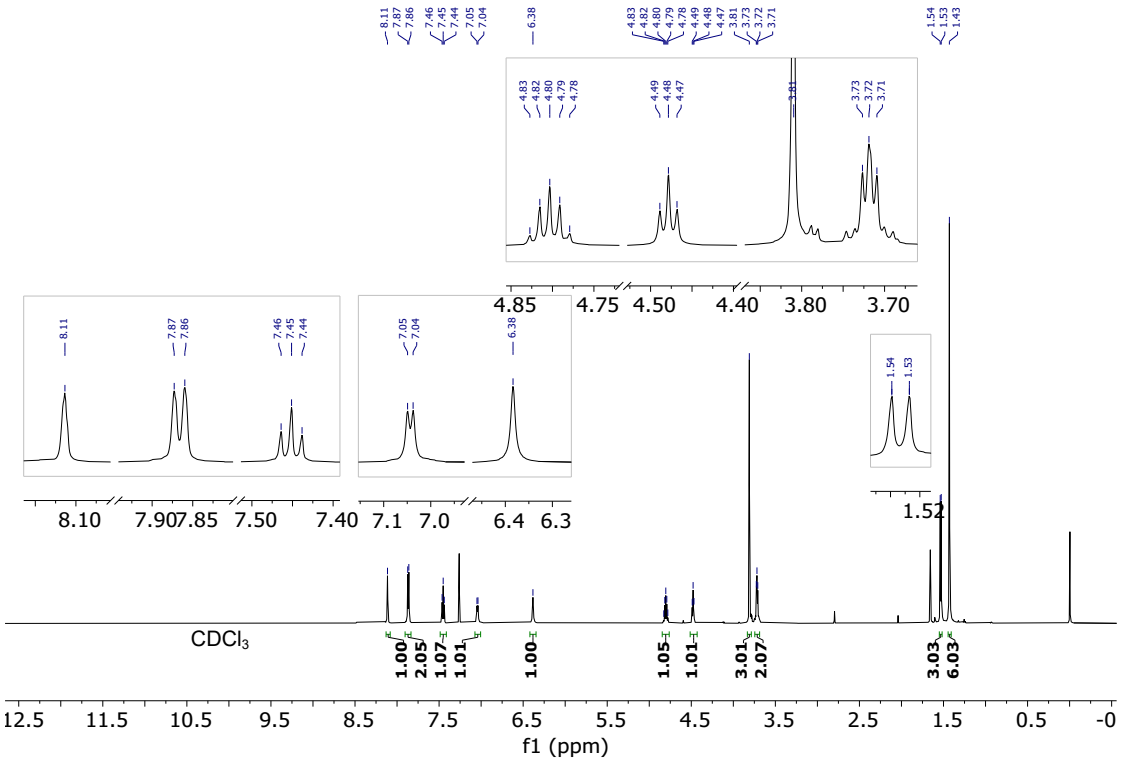



$^1$H NMR (600 MHz, $CDCl_3$) of **$8_{m1}$**.

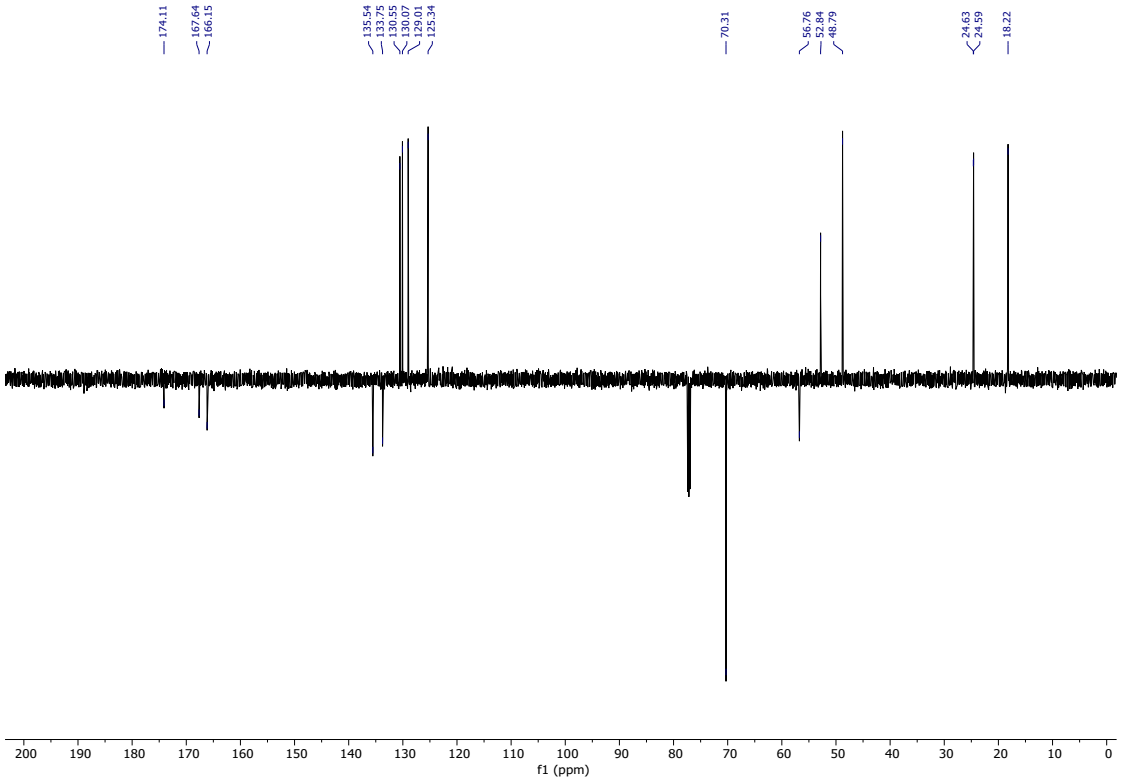


## 2.3. Reaction 5

$^{1}$H NMR (600 MHz, $CDCl_3$) of **$3_{m1}$**.

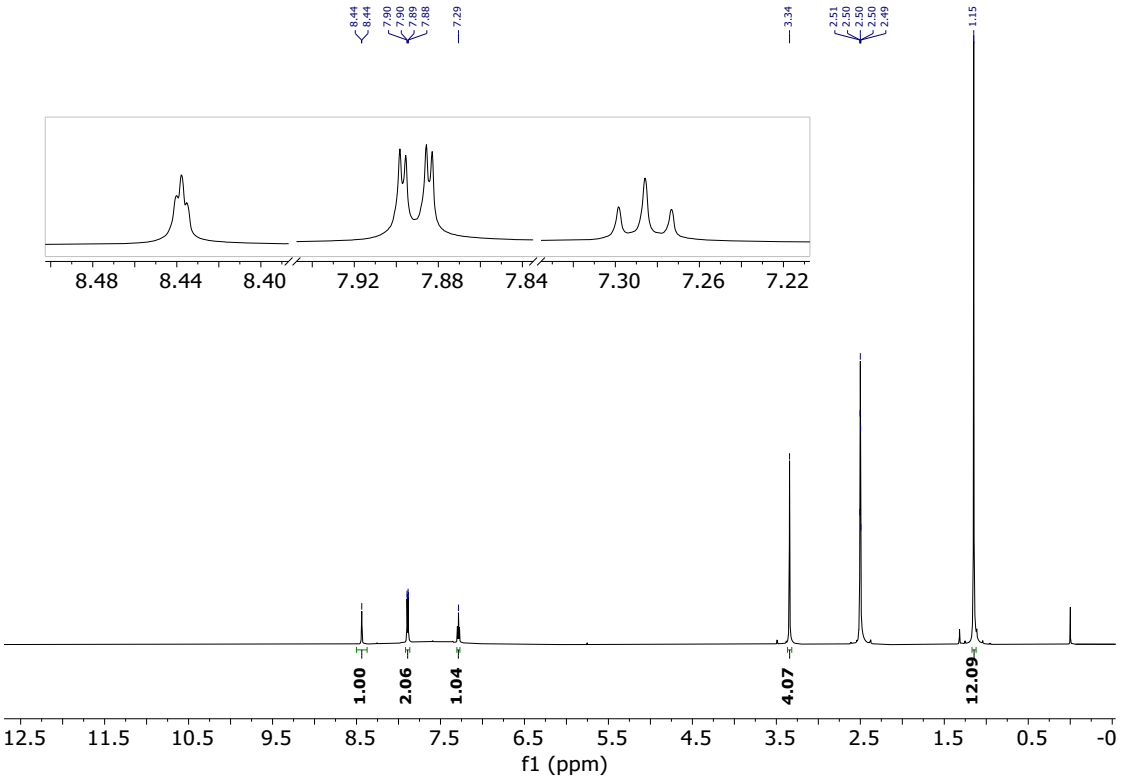



$^{13}$C NMR (151 MHz, $CDCl_3$) of **$3_{m1}$**.

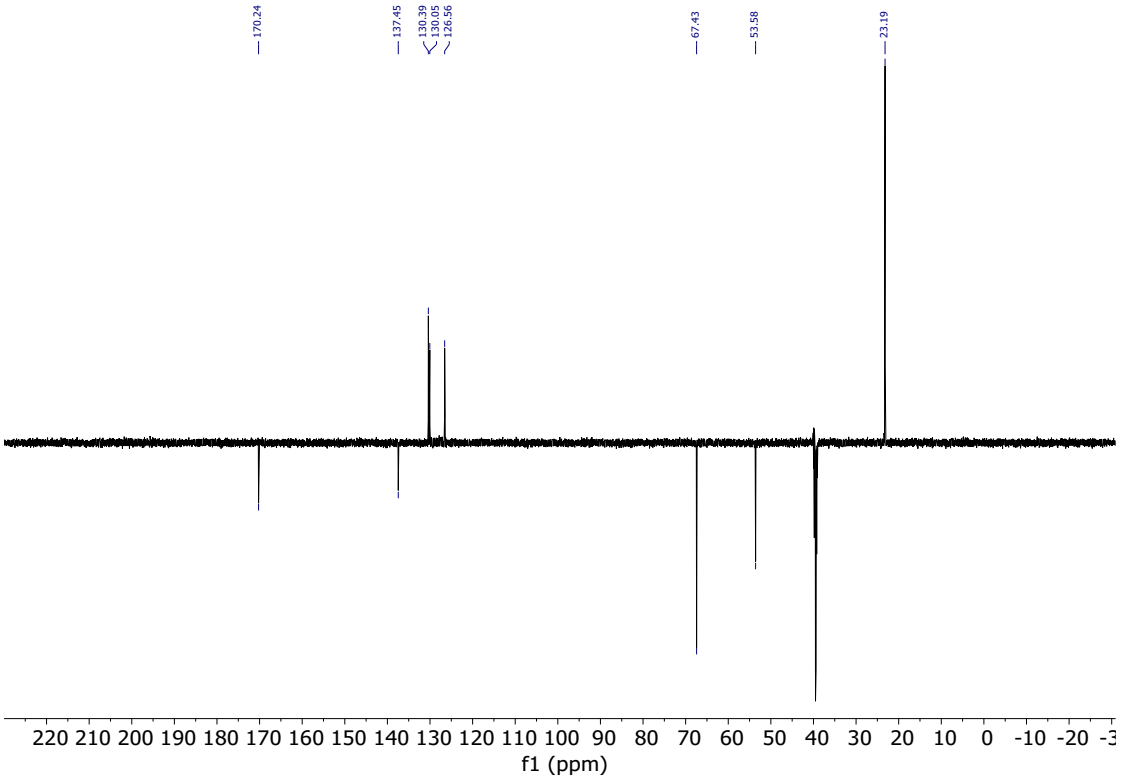


## 2.4. Reaction 6

$^{1}$H NMR (600 MHz, DMSO) of **$4_{m1}$**.

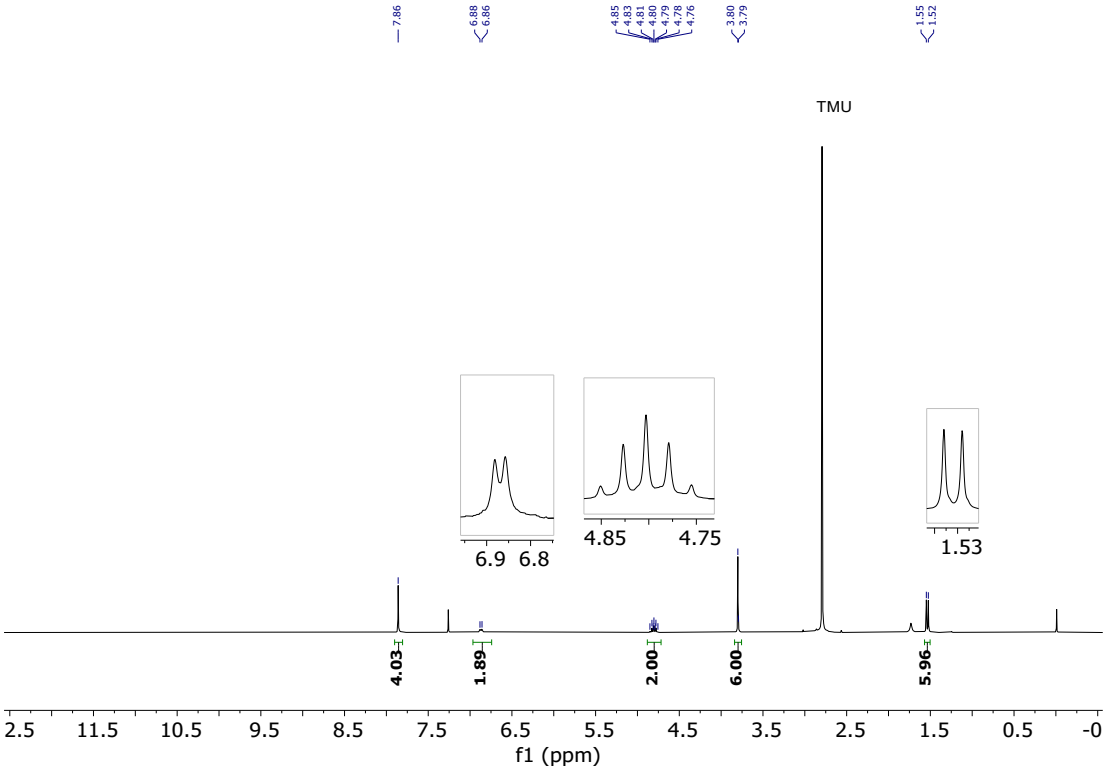



$^{13}$C NMR (151 MHz, DMSO) of **$4_{m1}$**.

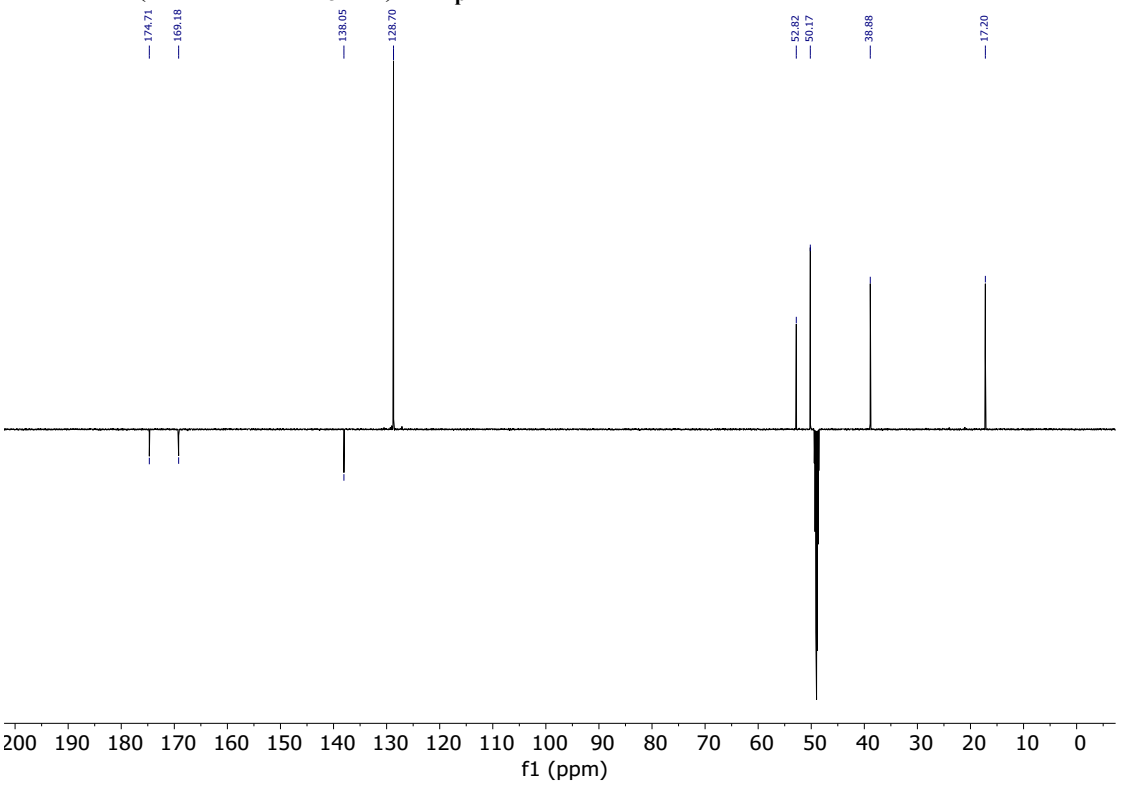


## 2.5. Reaction 7

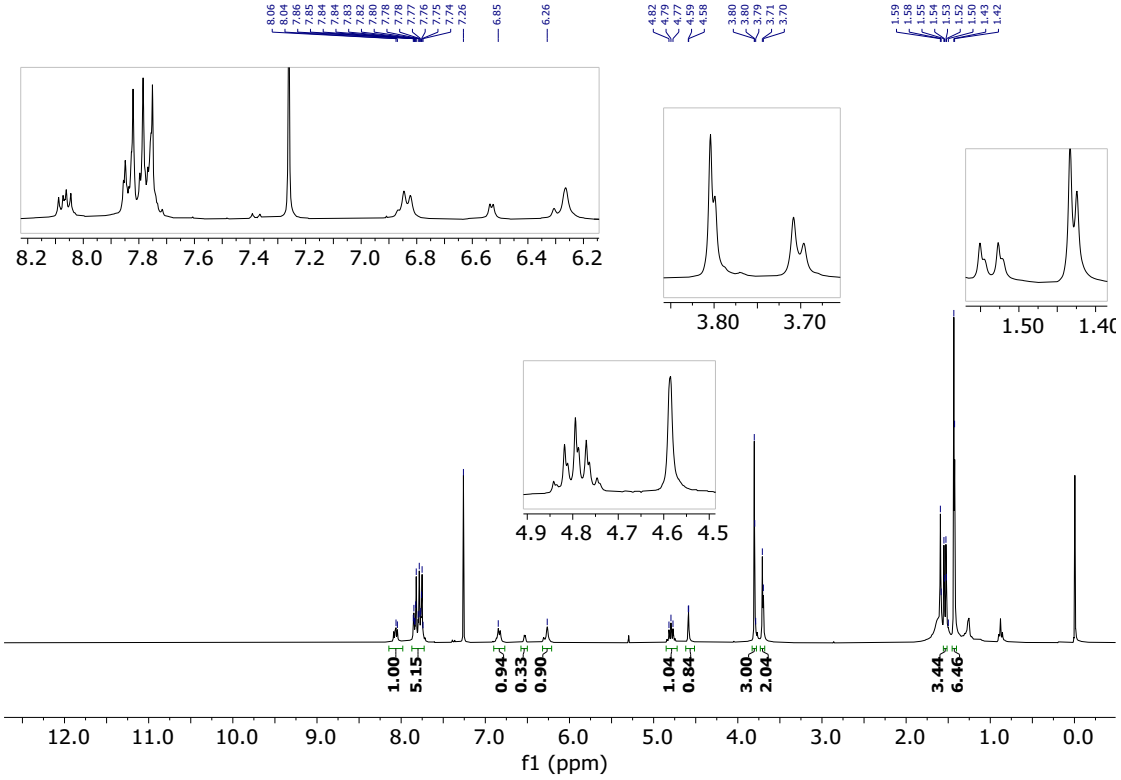
$^{1}$H NMR (300 MHz, $CDCl_3$) of **2**$_p$.



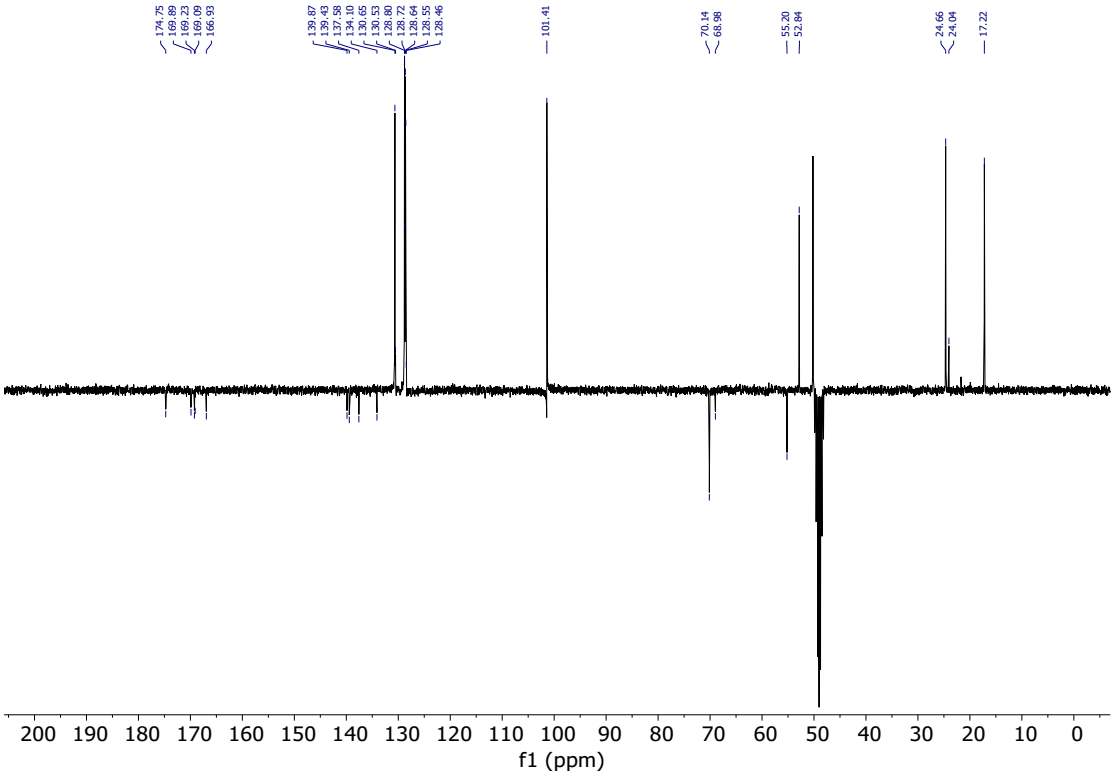

$^{13}$C NMR (151 MHz, $CD_3OD$) of **2**$_p$.



$^{1}$H NMR (300 MHz, $CDCl_3$) of **$3_p$**.

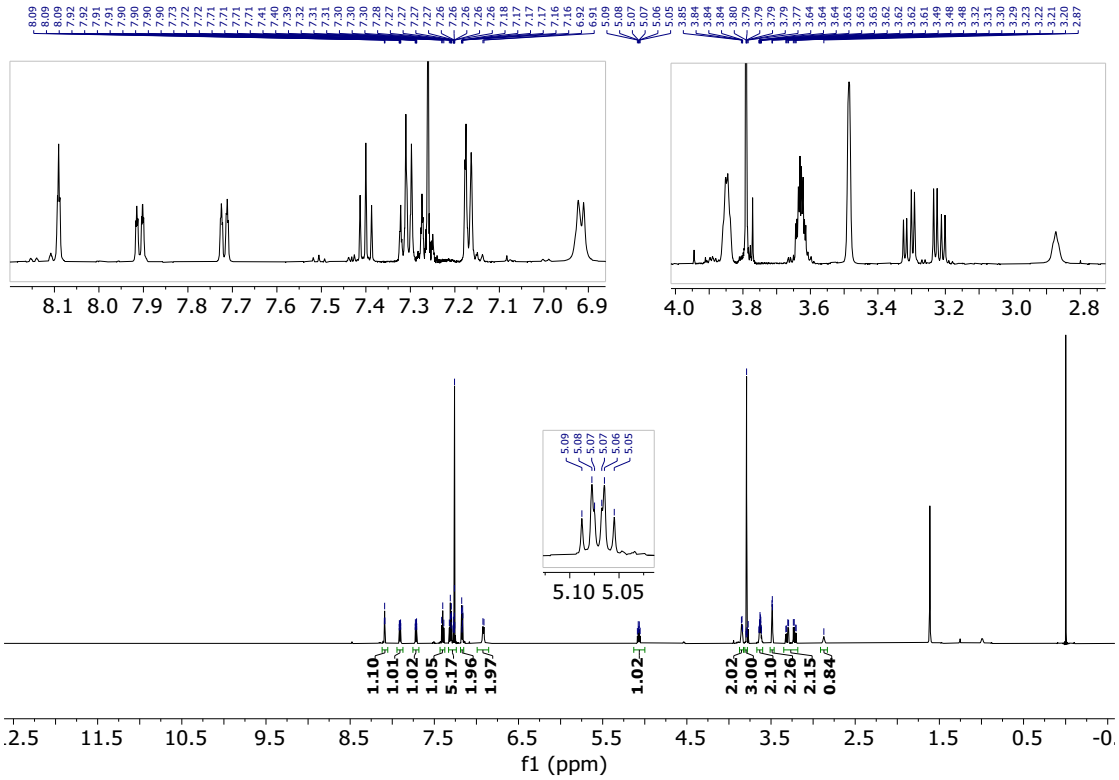



$^{13}$C NMR (75 MHz, $CD_3OD$) of **$3_p$**.

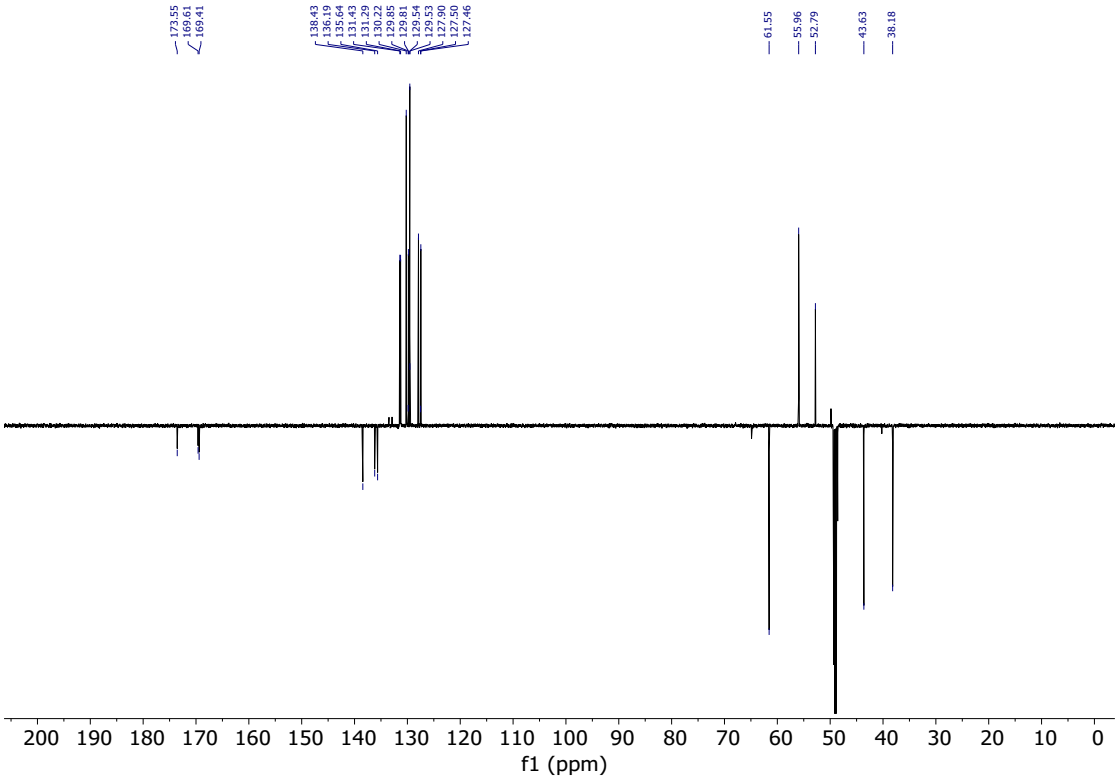


## 2.6. Reaction 8

$^{1}$H NMR (600 MHz, $CDCl_3$) of **$3_{m2}$**.

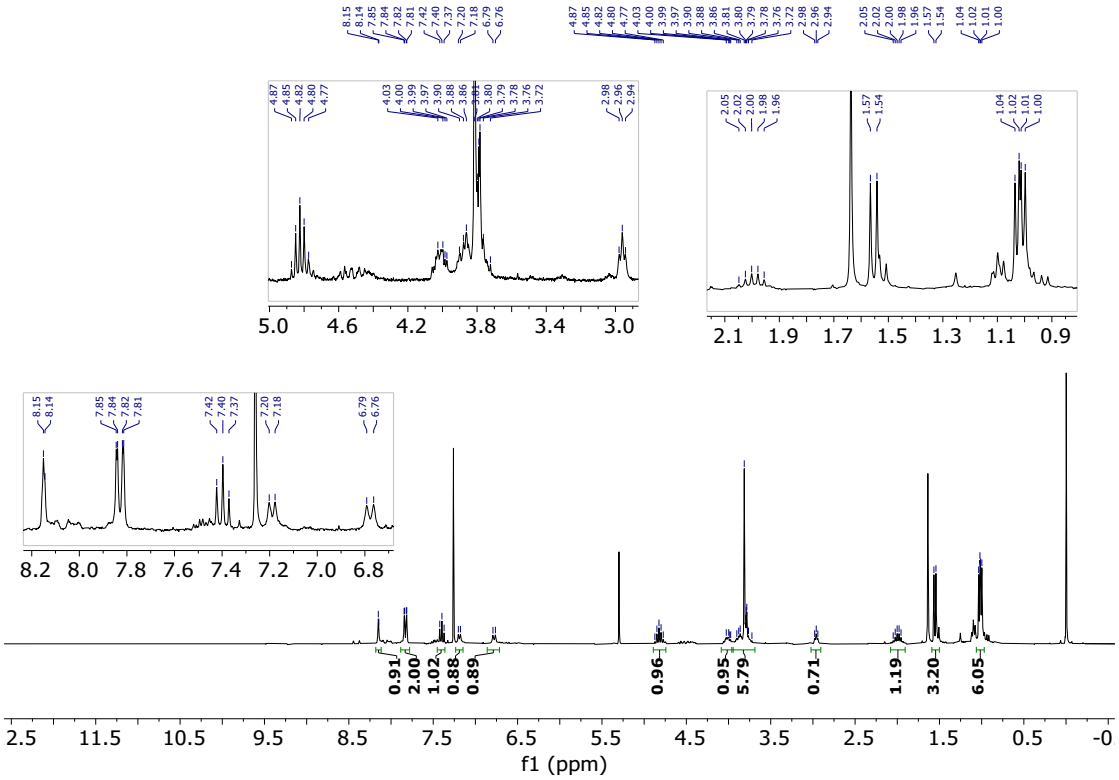



$^{13}$C NMR (151 MHz, $CD_3OD$) of **$3_{m2}$**.



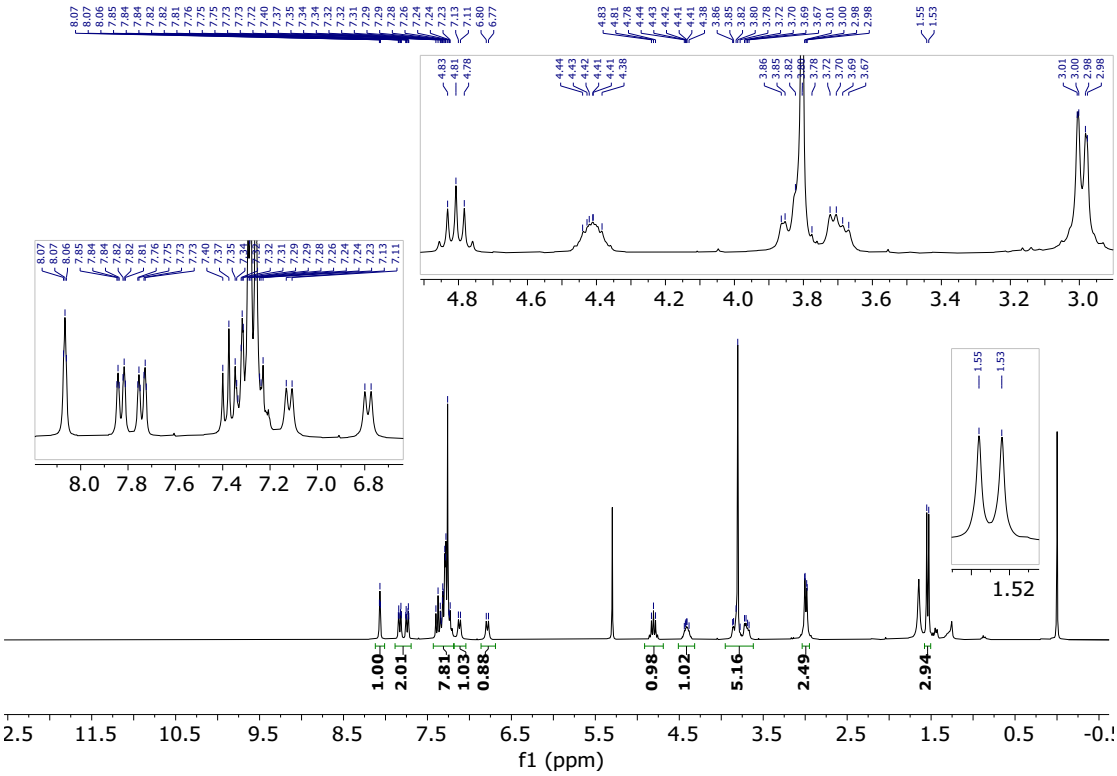
## 2.7. Reaction 9

$^1$H NMR (600 MHz, $CDCl_3$) of **$3_{m3}$**.



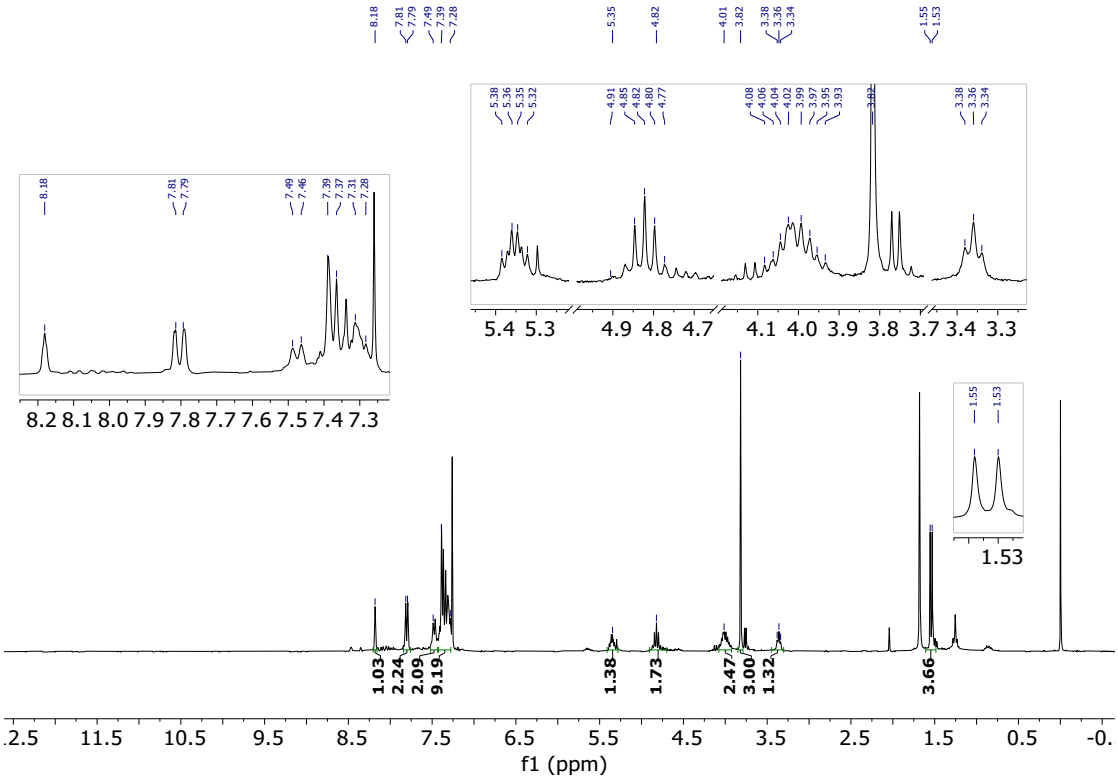
## 2.8. Reaction 10

$^1$H NMR (300 MHz, $CDCl_3$) of **$3_{m4}$**.

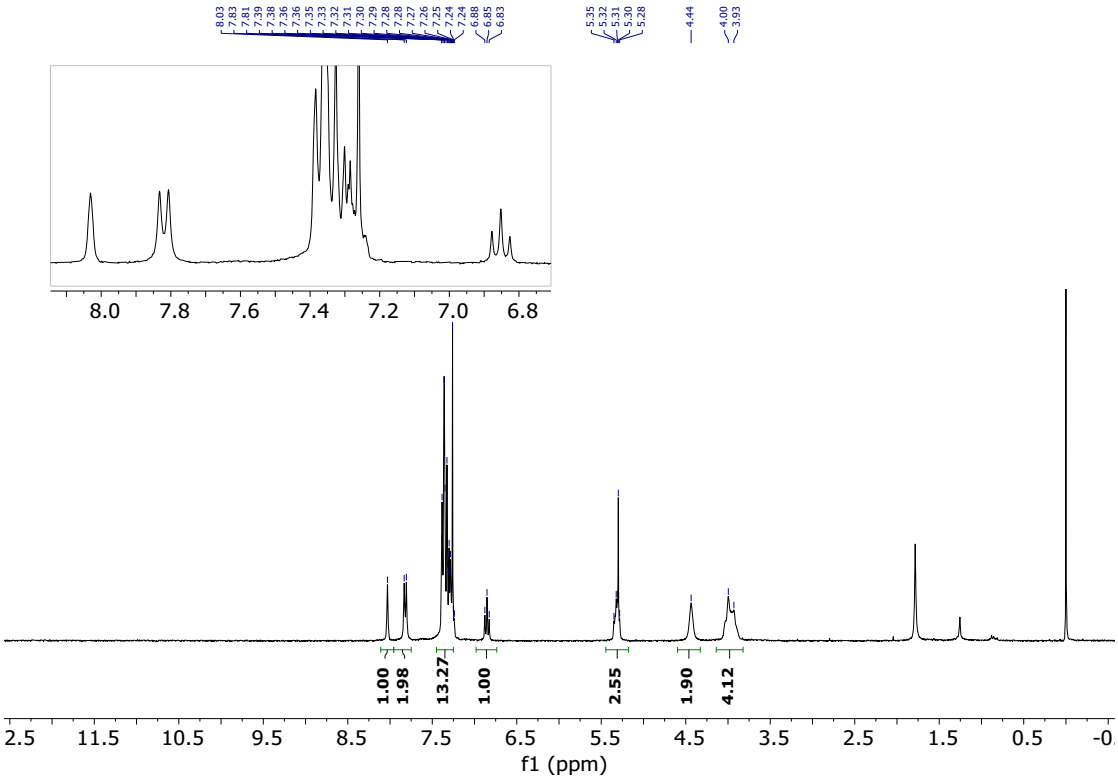


## 2.9. Reaction 11

$^1$H NMR (300 MHz, $CDCl_3$) of **$3_{m5}$**.

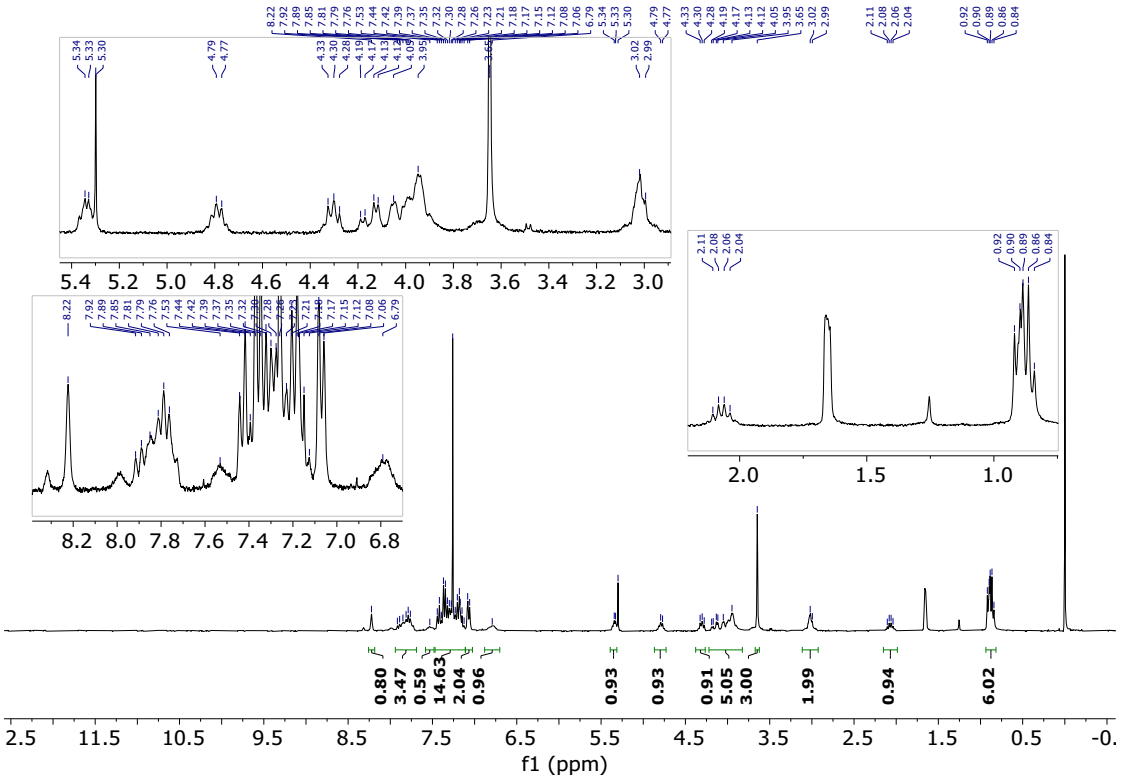



$^1$H NMR (300 MHz, $CDCl_3$) of **$4_{m5}$**.



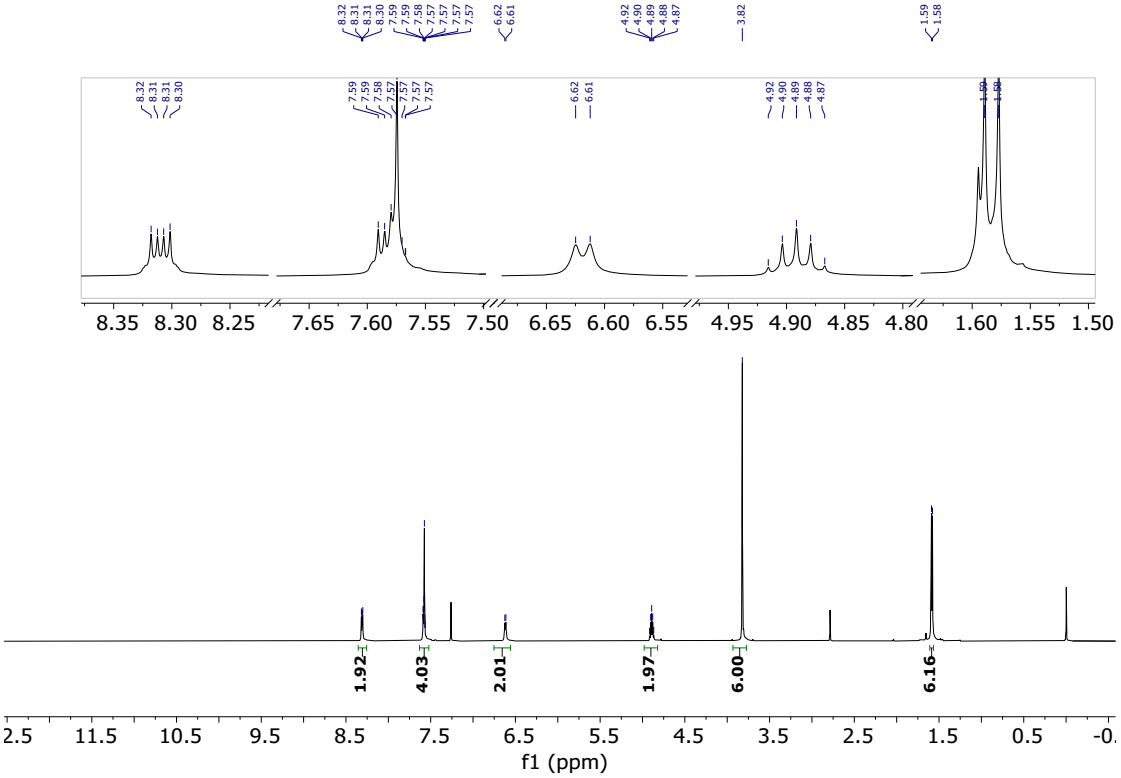
## 2.10. Reaction 12

$^1$H NMR (300 MHz, $CDCl_3$) of **$3_{m6}$**.

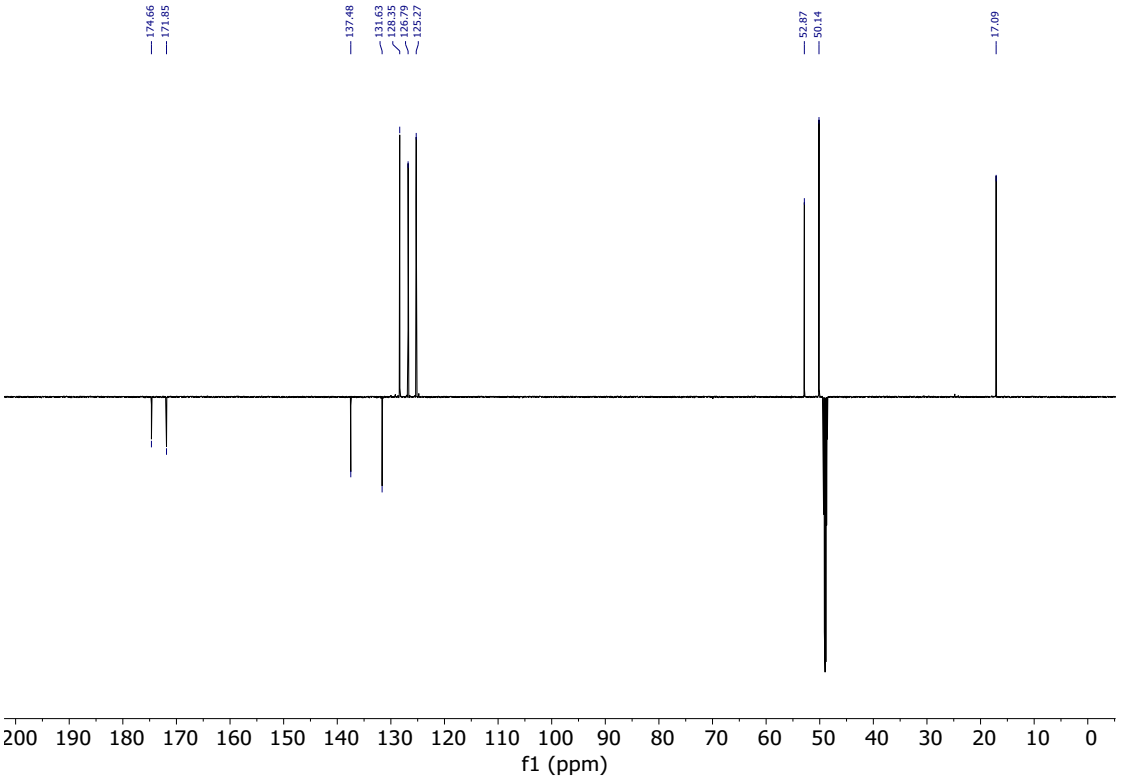


## 2.11. Reaction 13

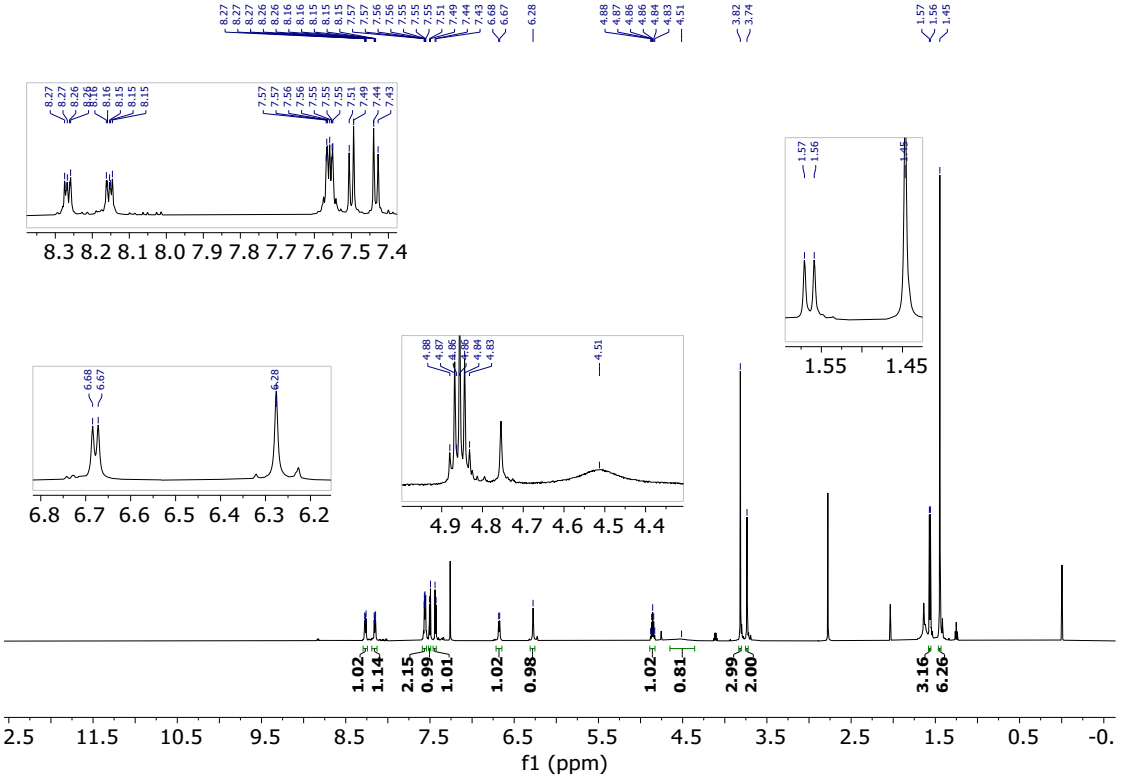
$^{1}$H NMR (600 MHz, $CDCl_3$) of **$2_{n1}$**.



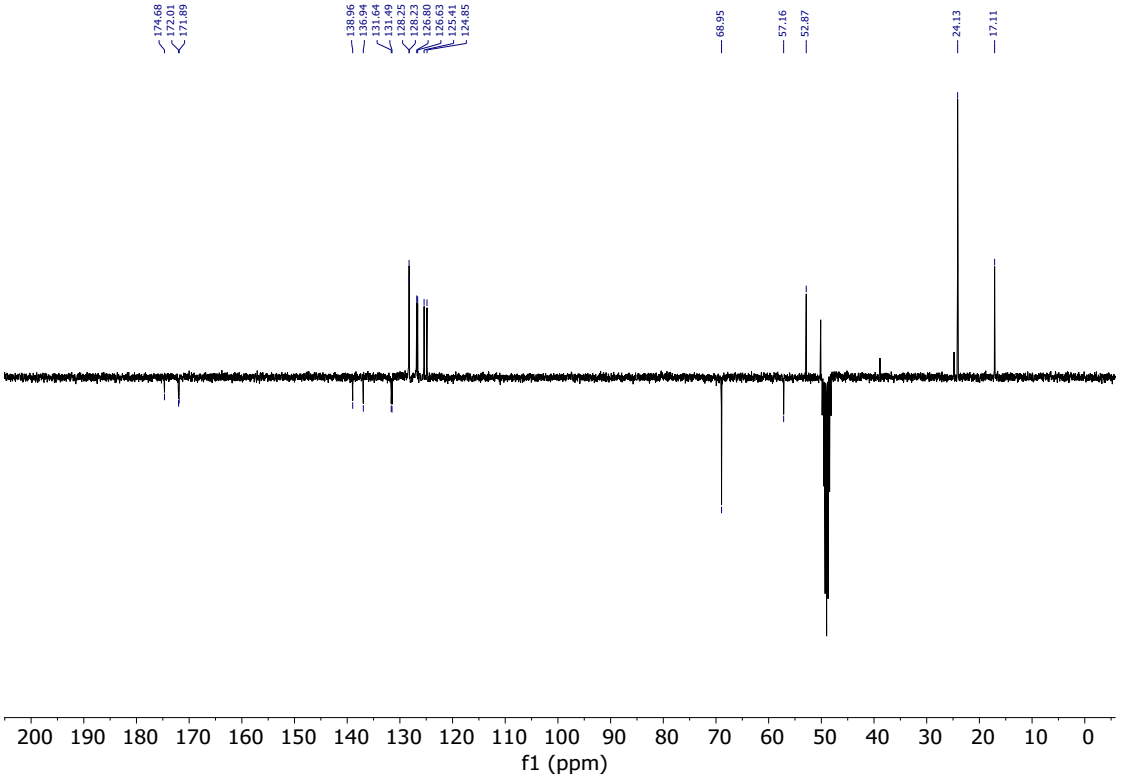

$^{13}$C NMR (151 MHz, $CD_3OD$) of **$2_{n1}$**.



$^{1}$H NMR (600 MHz, $CDCl_3$) of **$3_{n1}$**.

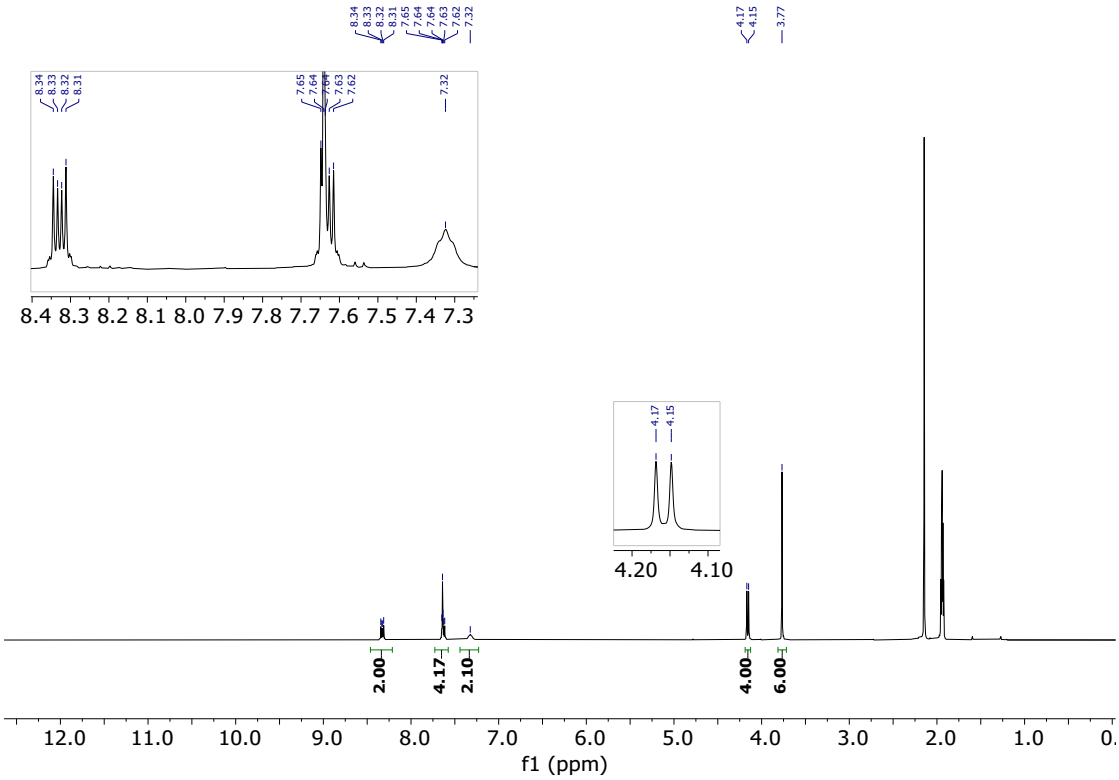



$^{13}$C NMR (75 MHz, $CD_3OD$) of **$3_{n1}$.**

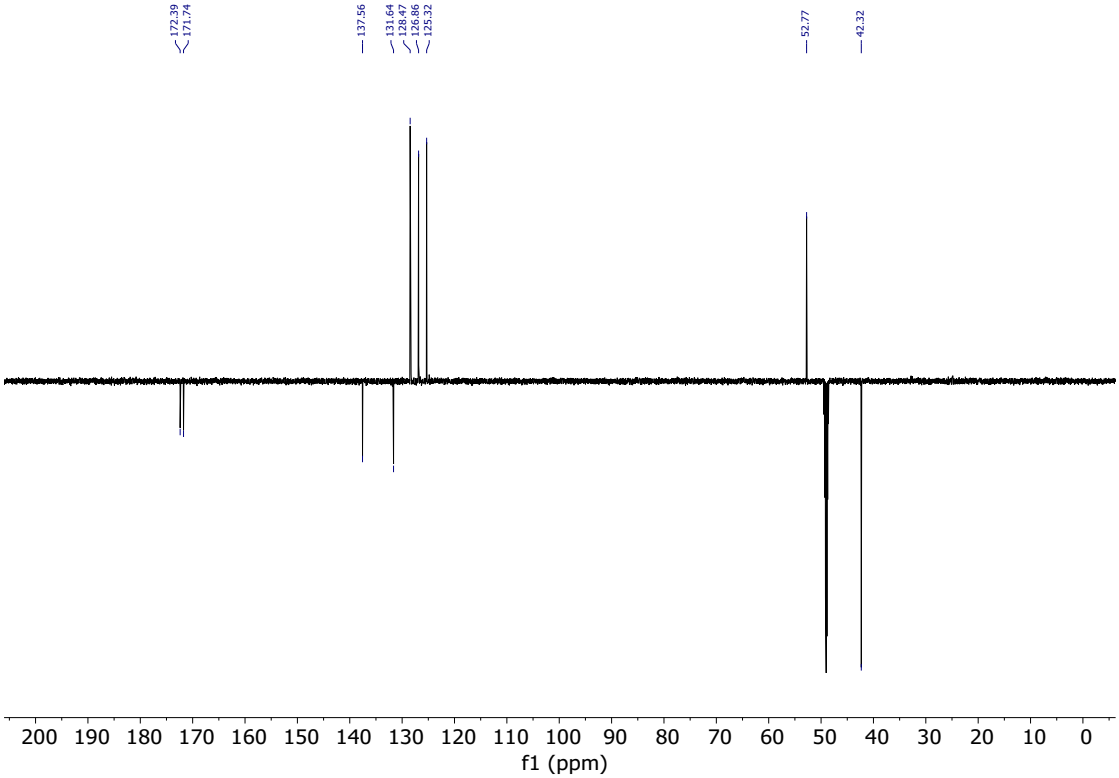


## 2.12. Reaction 14

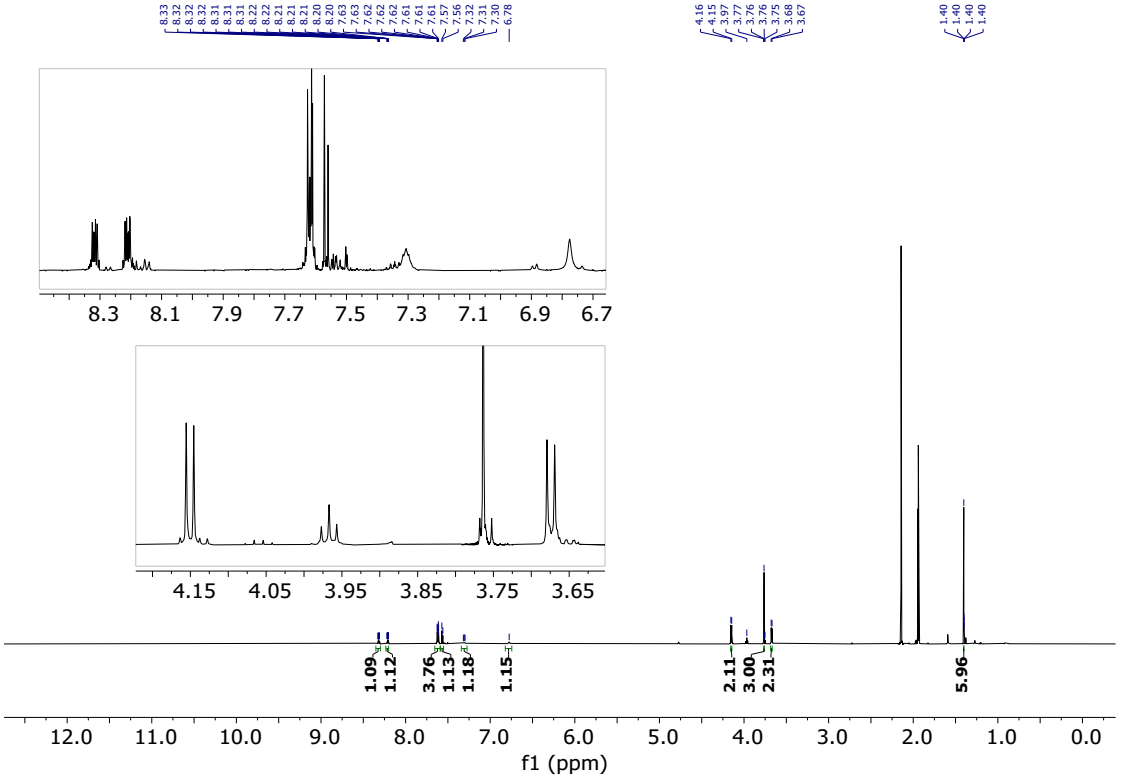
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{2_{n2}}$.



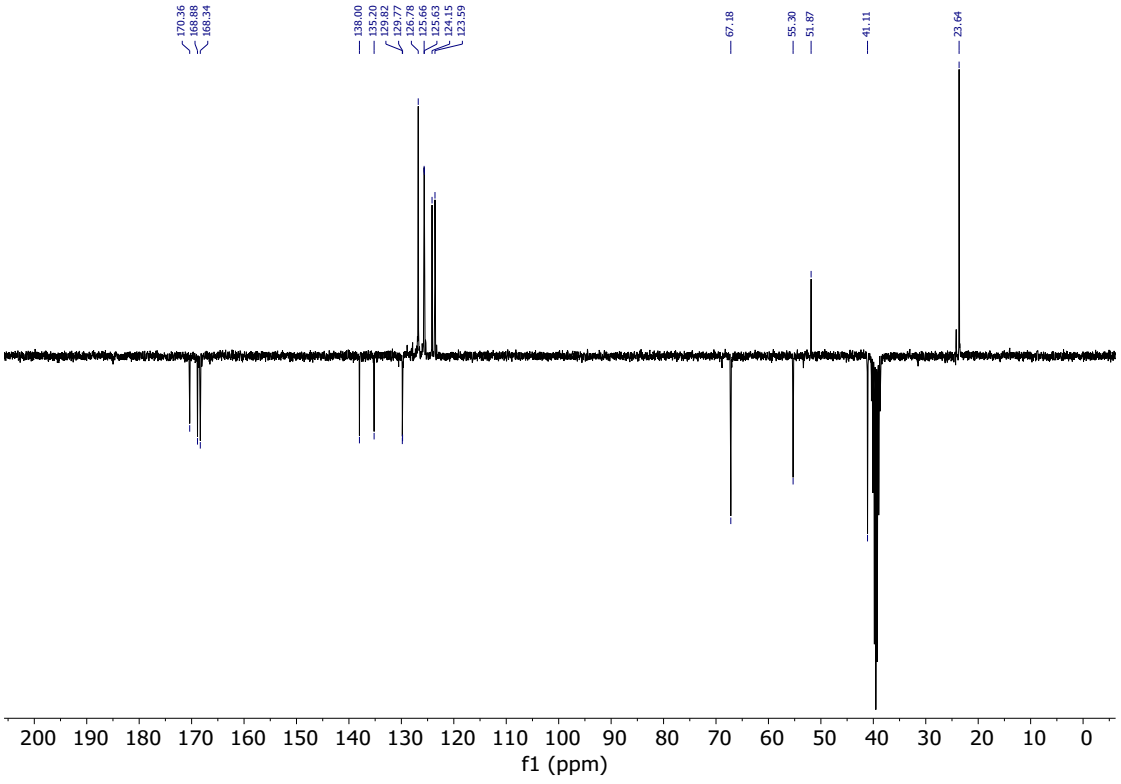

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{2_{n2}}$.



$^{1}$H NMR (600 MHz, $CD_3CN$) of $\mathbf{3_{n2}}$.

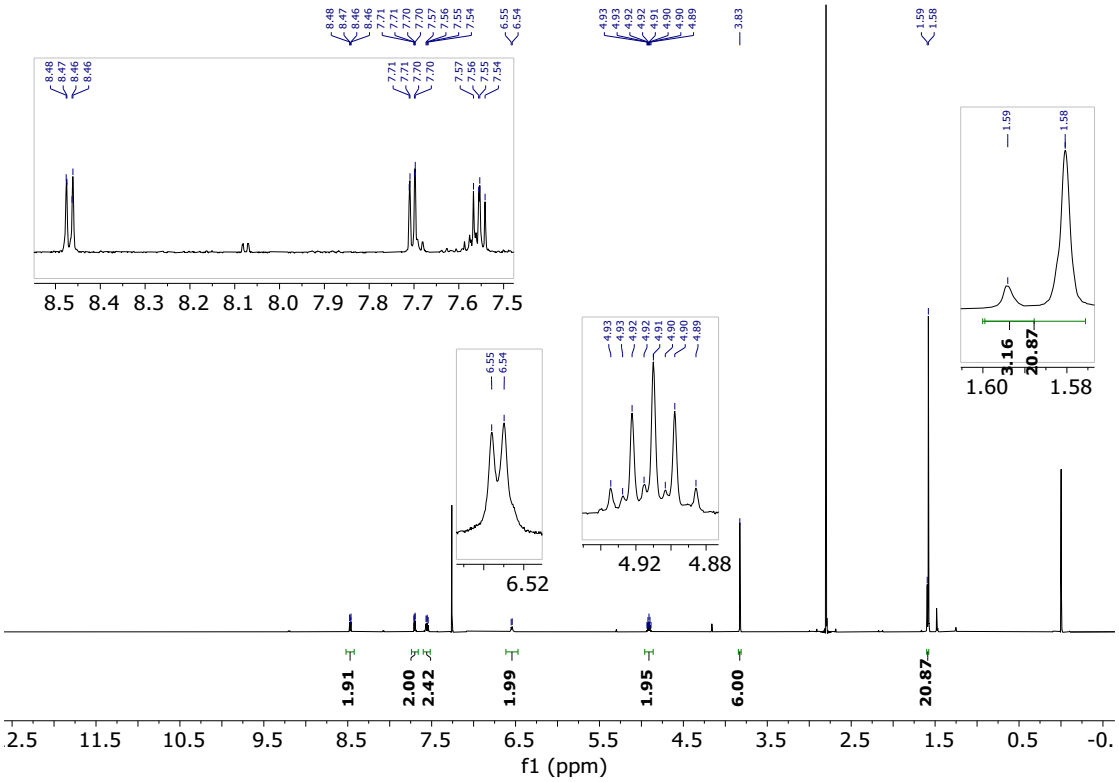



$^{13}$C NMR (75 MHz, DMSO) of $\mathbf{3_{n2}}$.

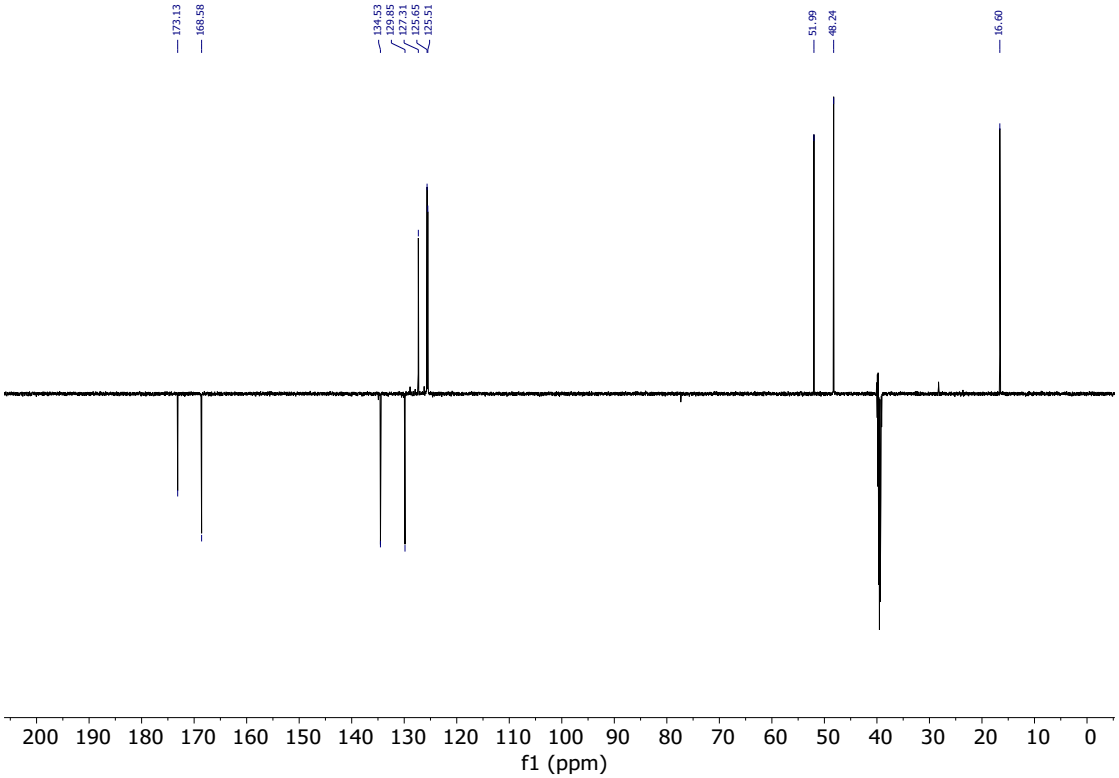


## 2.13. Reaction 15

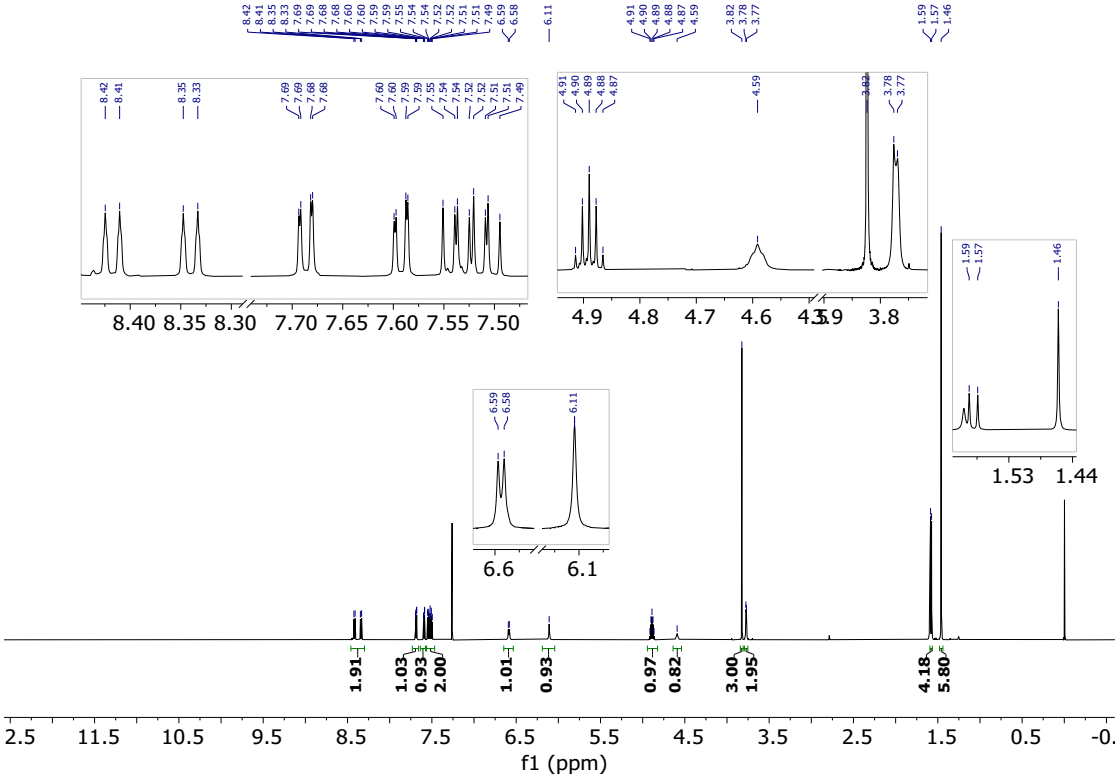
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{2_{n3}}$.



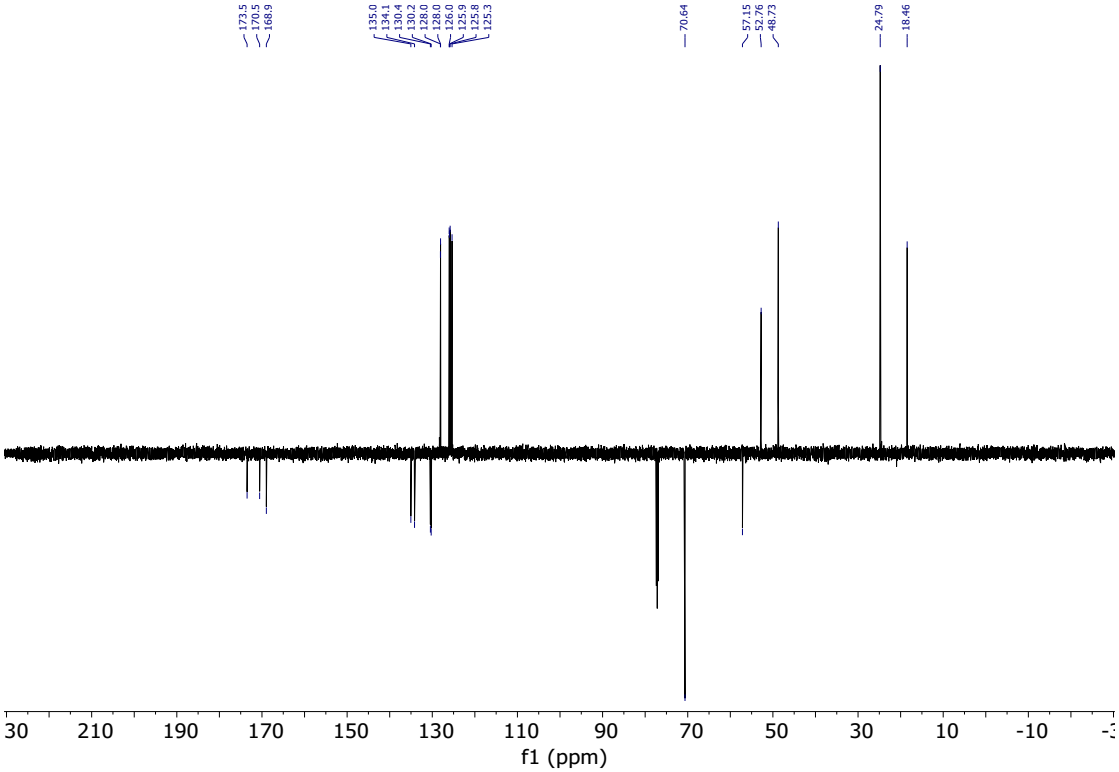

$^{13}$C NMR (151 MHz, DMSO) of $\mathbf{2_{n3}}$.



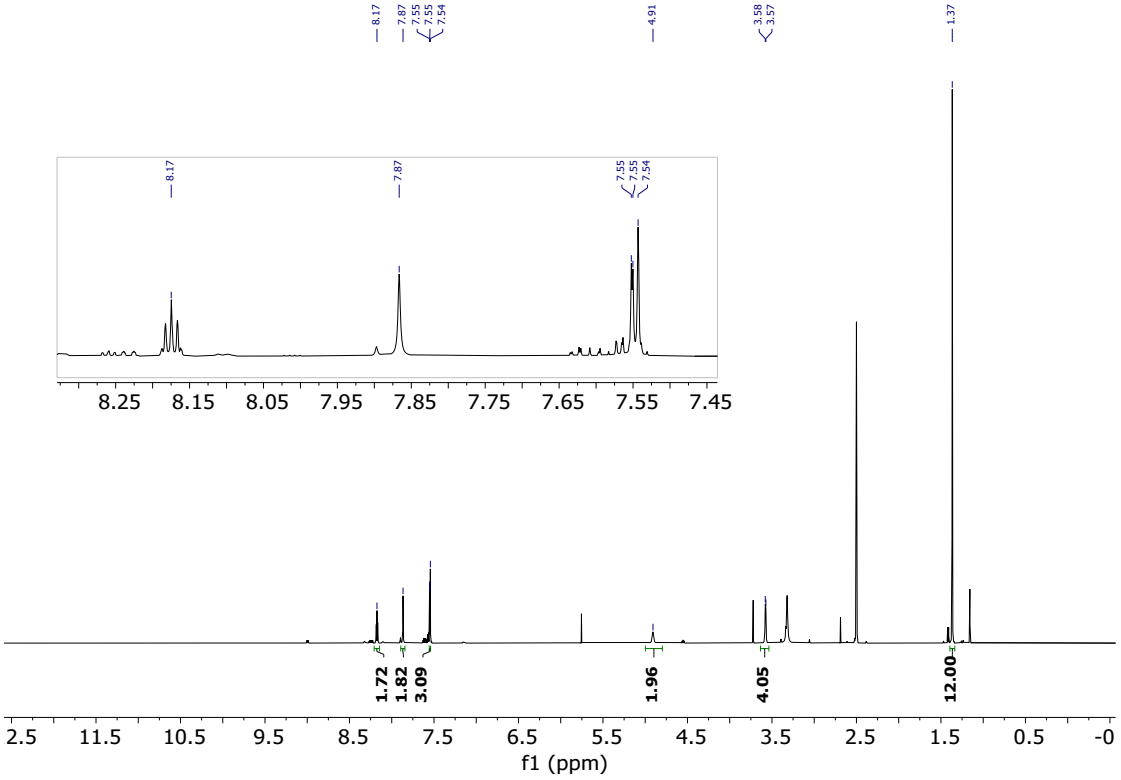
$^{1}$H NMR (600 MHz, $CDCl_3$) of $\mathbf{3_{n3}}$.



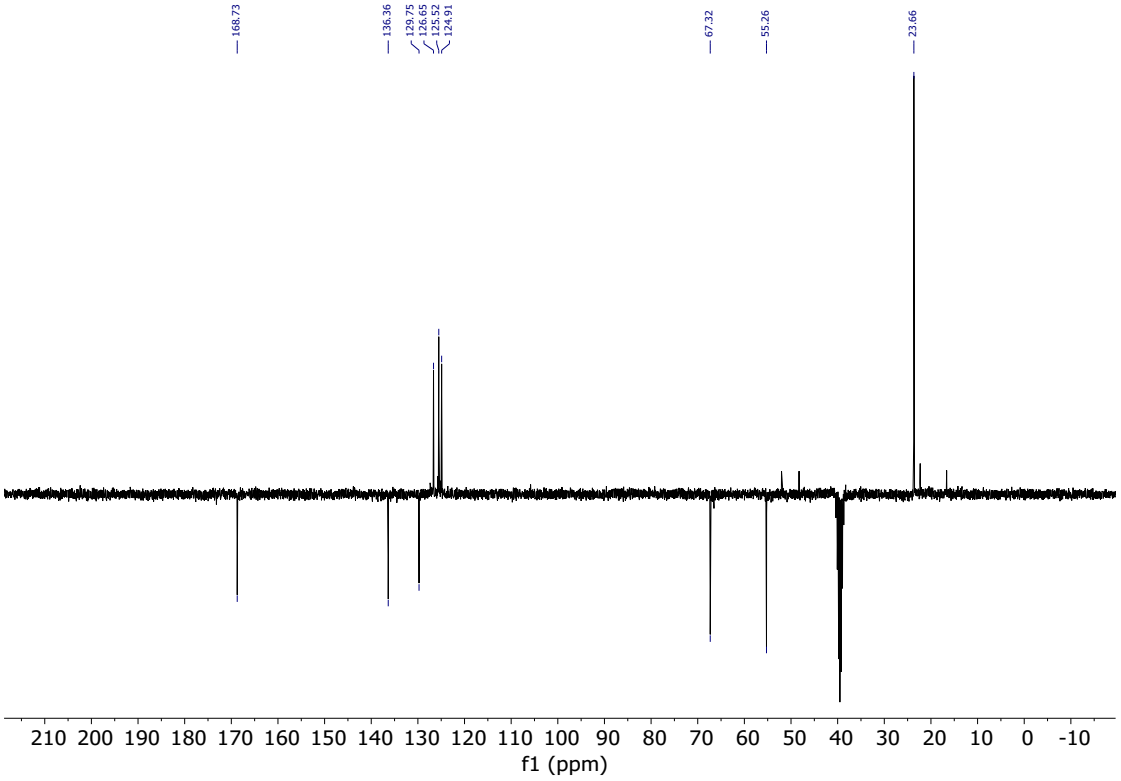

$^{13}$C NMR (151 MHz, $CDCl_3$) of $\mathbf{3_{n3}}$.



$^{1}$H NMR (600 MHz, DMSO) of **$4_{n3}$.**

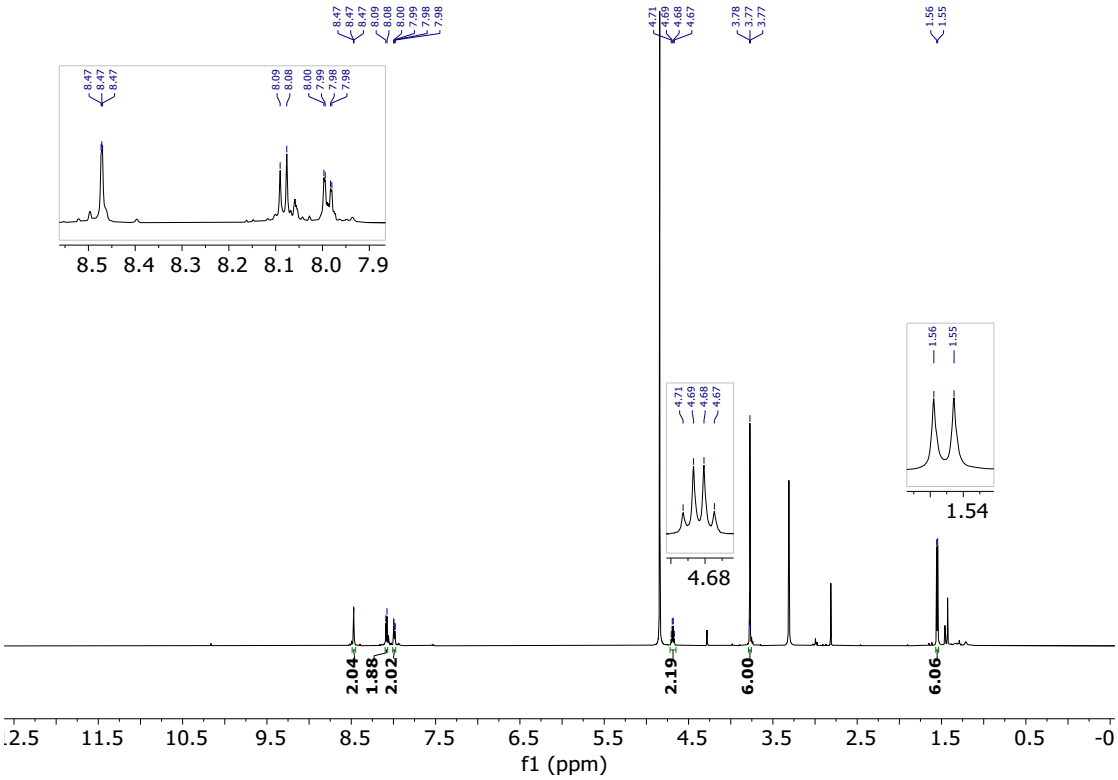



$^{13}$C NMR (75 MHz, DMSO) of **$4_{n3}$**.

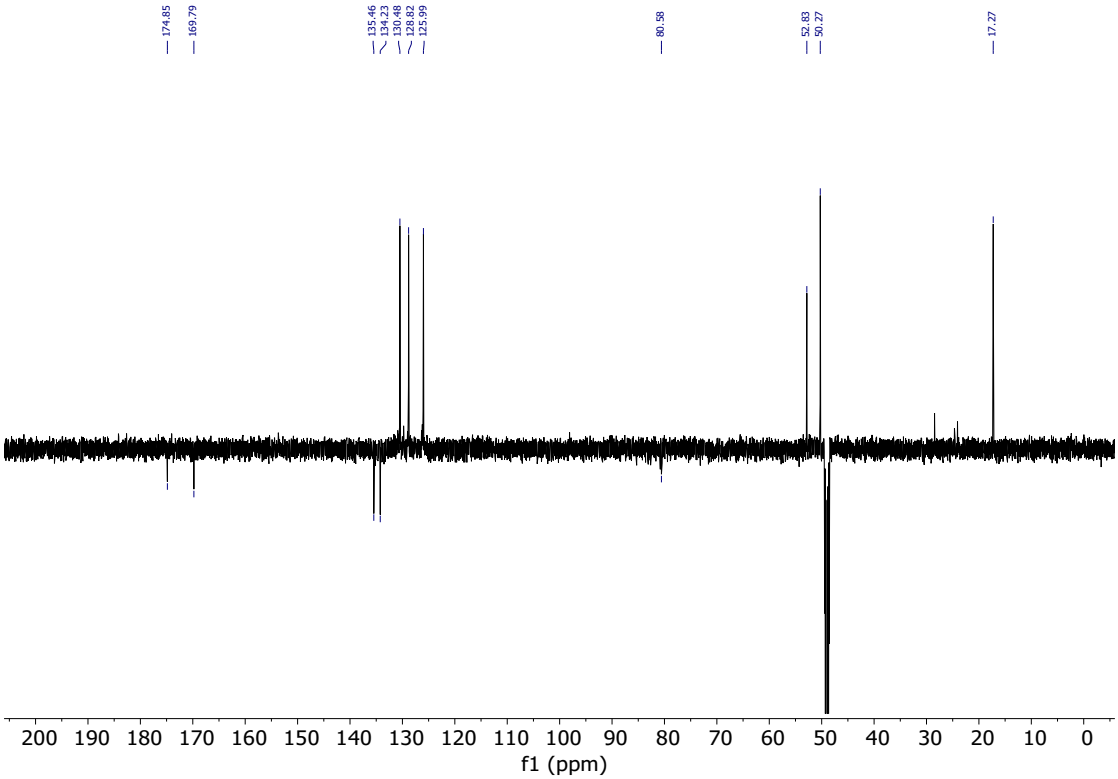


## 2.14. Reaction 16

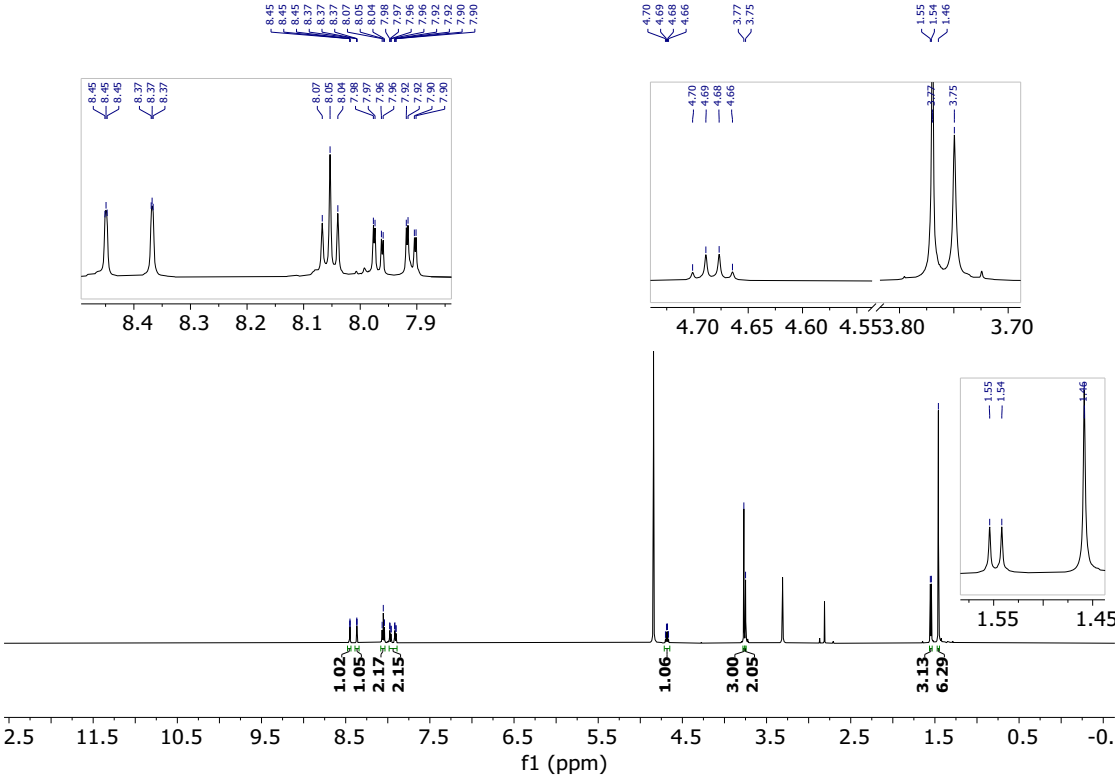
$^{1}$H NMR (600 MHz, $CD_3OD$) of $\mathbf{2_{n4}}$.



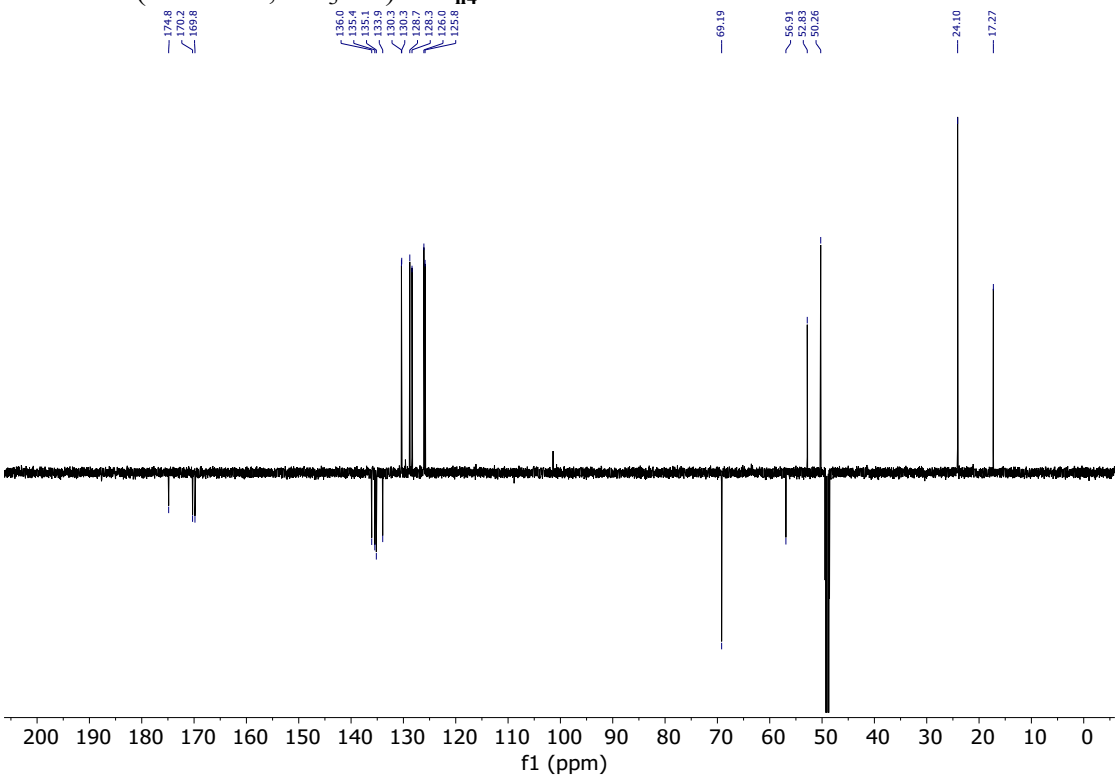

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{2_{n4}}$.



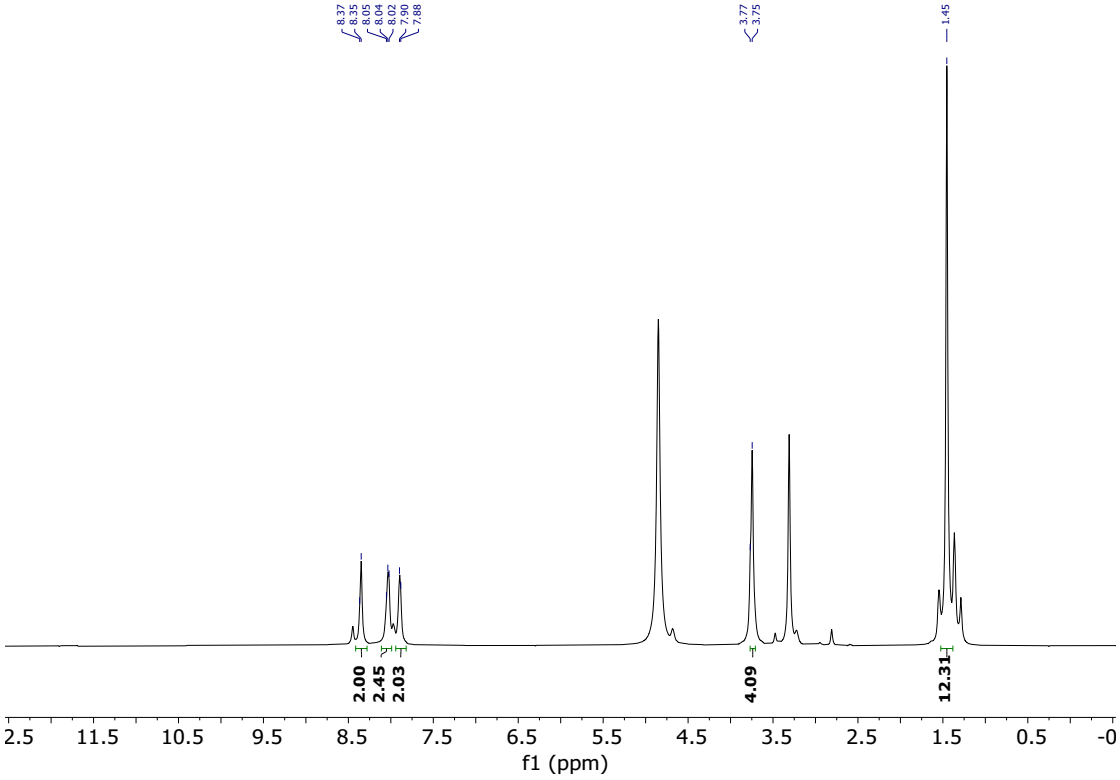
$^{1}$H NMR (600 M Hz, $CD_3OD$) of $\mathbf{3_{n4}}$.



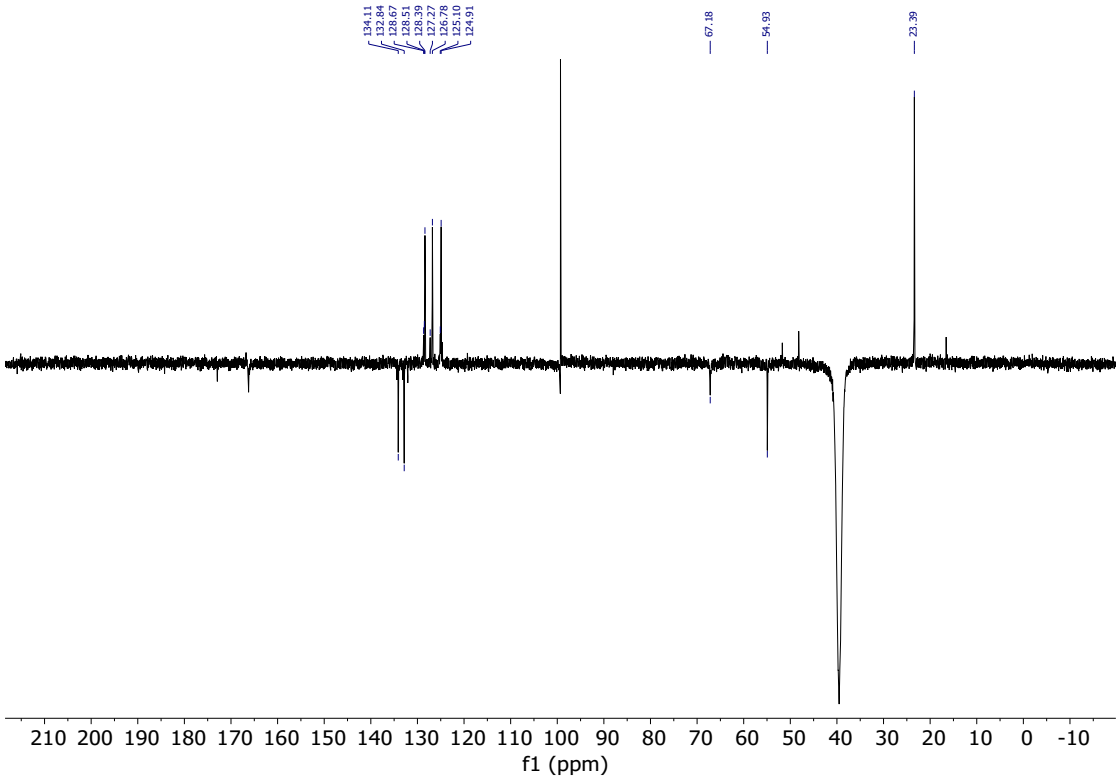

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{3_{n4}}$.



$^{1}$H NMR (600 MHz, $CD_3OD$) of **$4_{n4}$.**

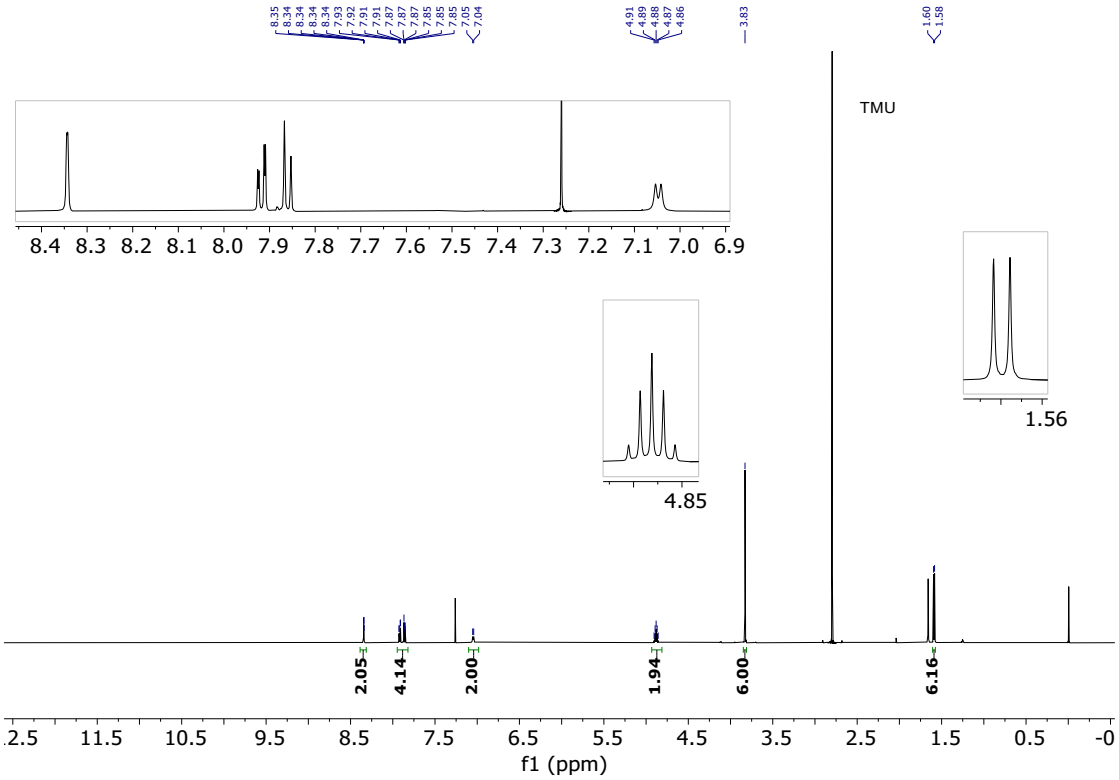



$^{13}$C NMR (75 MHz, DMSO) of **$4_{n4}$**.

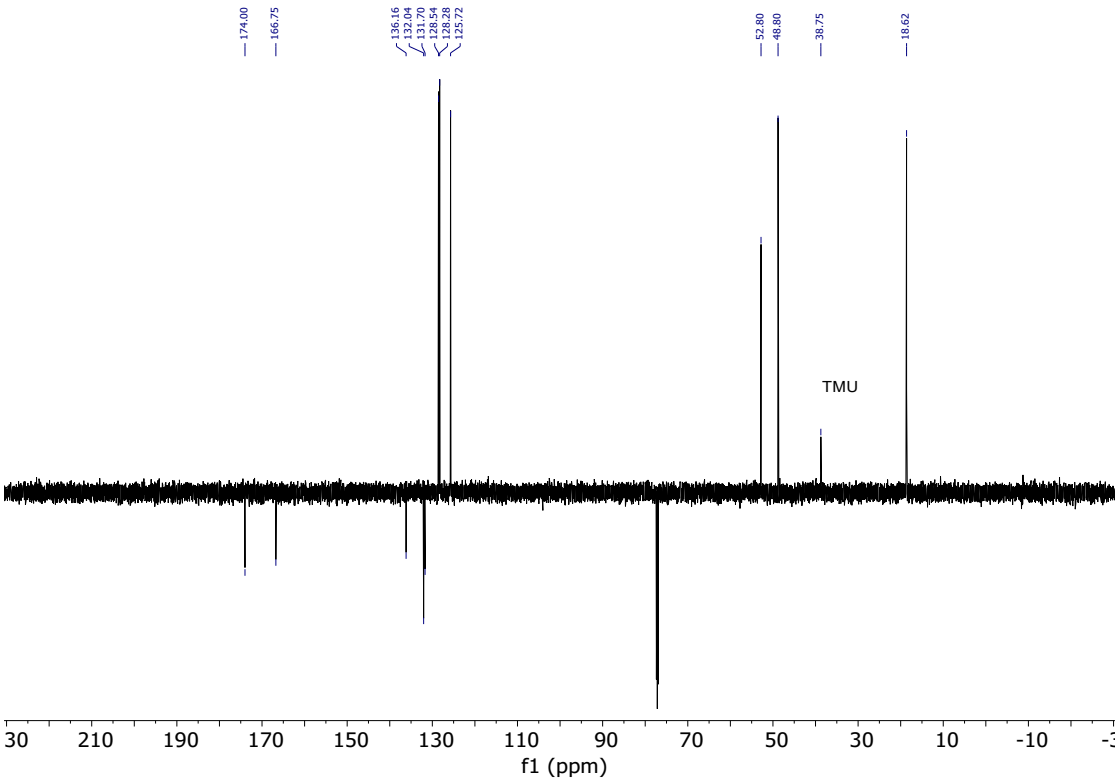


## 2.15. Reaction 17

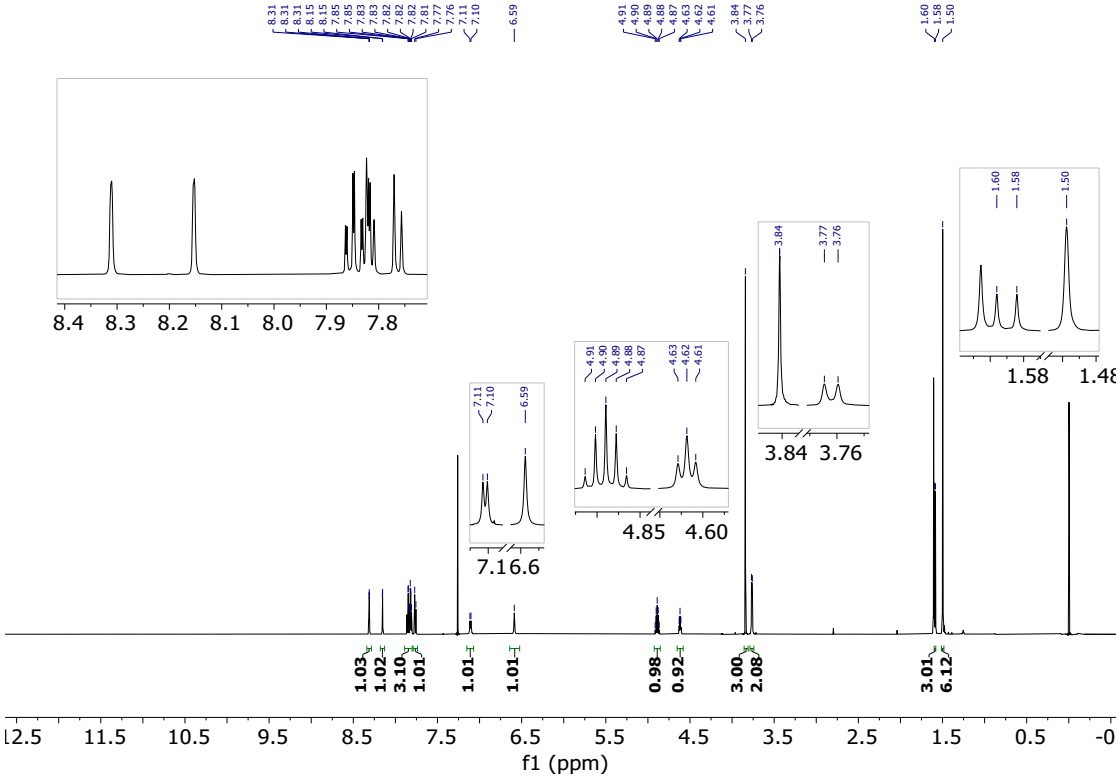
$^{1}$H NMR (600 MHz, $CDCl_3$) of **$2_{n5}$**.



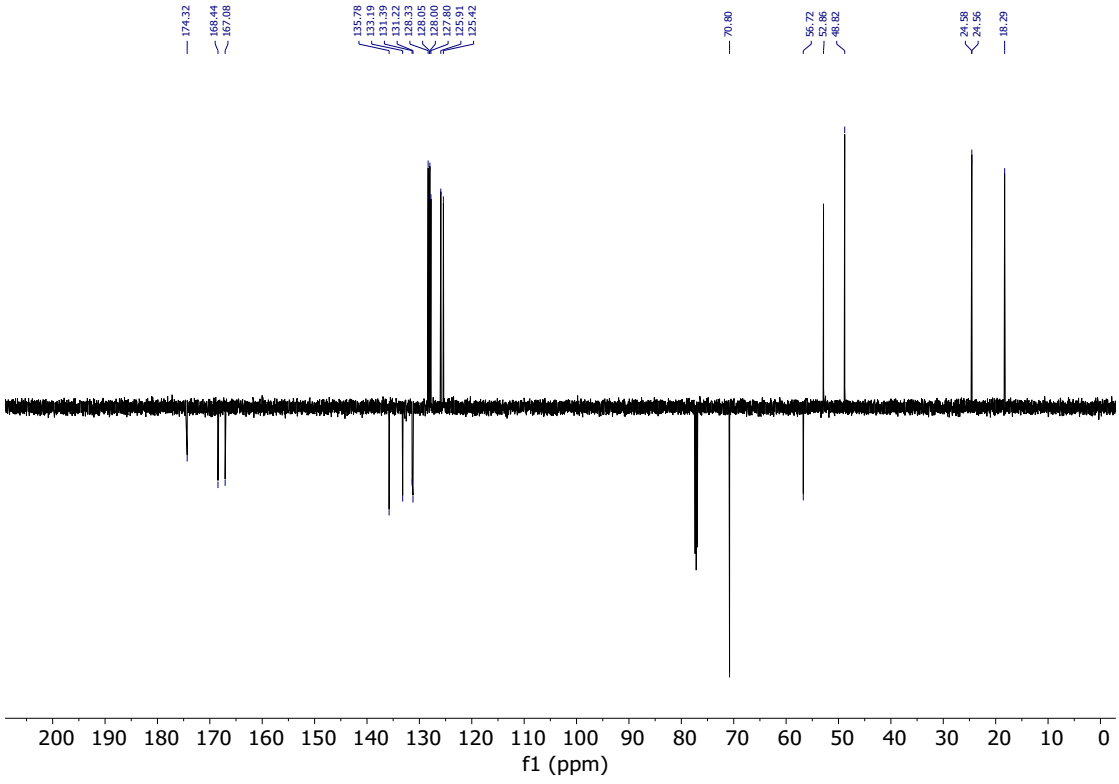

$^{13}$C NMR (151 MHz, $CDCl_3$) of **$2_{n5}$**.



$^{1}$H NMR (600 MHz, $CDCl_3$) of **$3_{n5}$**.

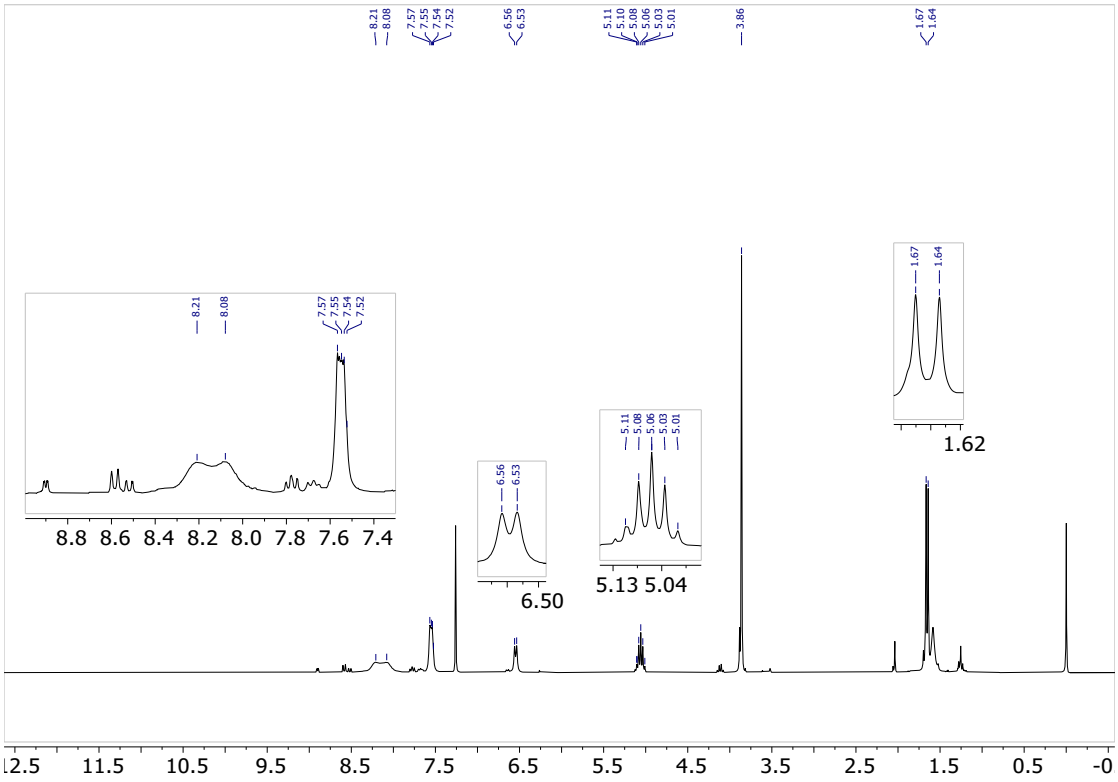



$^{13}$C NMR (151 MHz, $CDCl_3$) of **$3_{n5}$**.

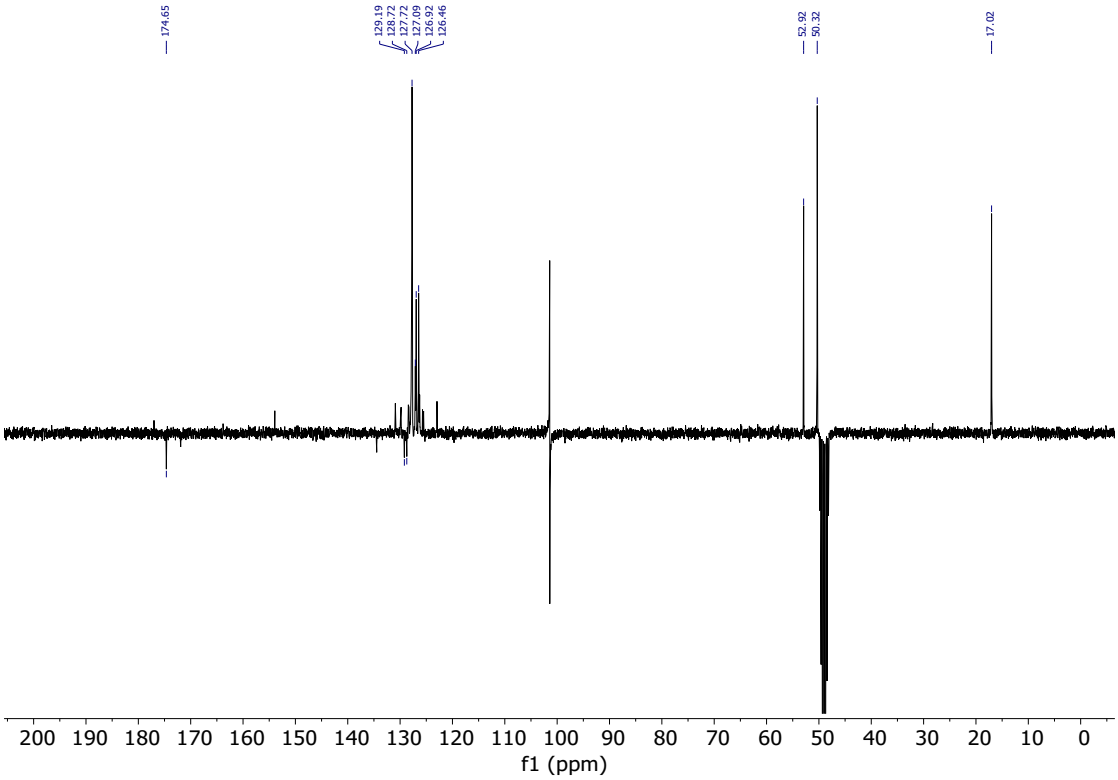


## 2.16. Reaction 18

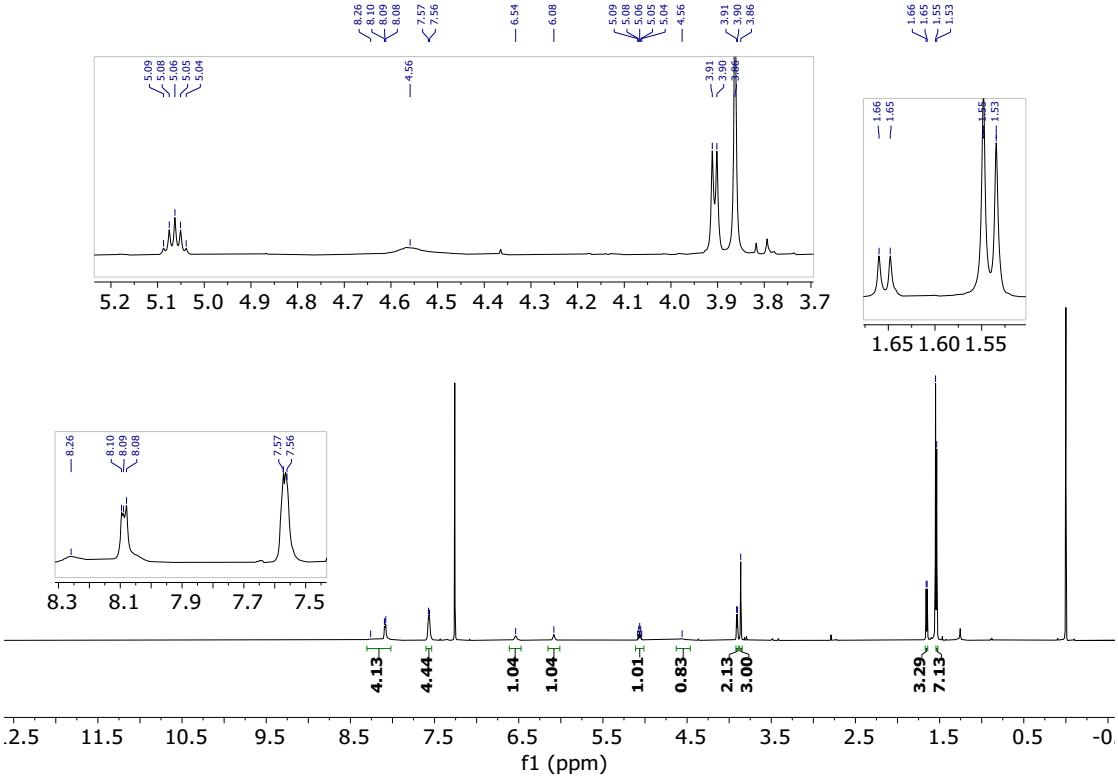
$^{1}$H NMR (300 MHz, $CDCl_3$) of **$2_{a1}$.**



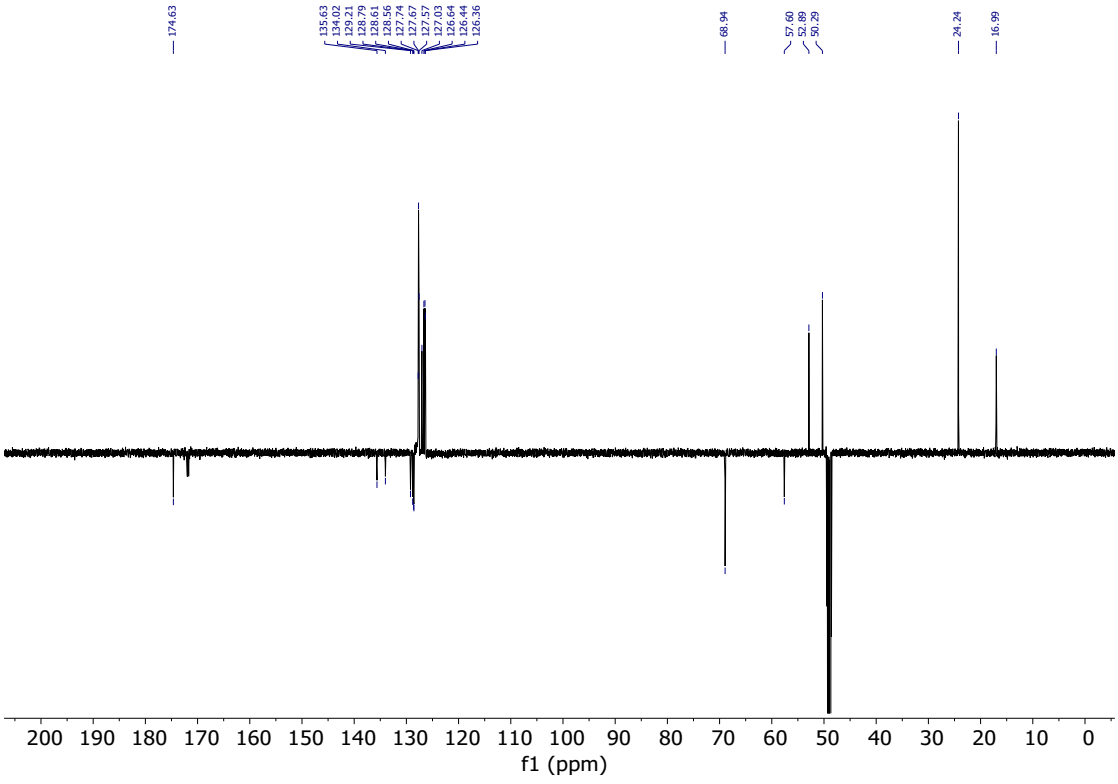

$^{13}$C NMR (75 MHz, $CD_3OD$) of **$2_{a1}$.**



$^{1}$H NMR (300 MHz, $CDCl_3$) of **$3_{a1}$.**

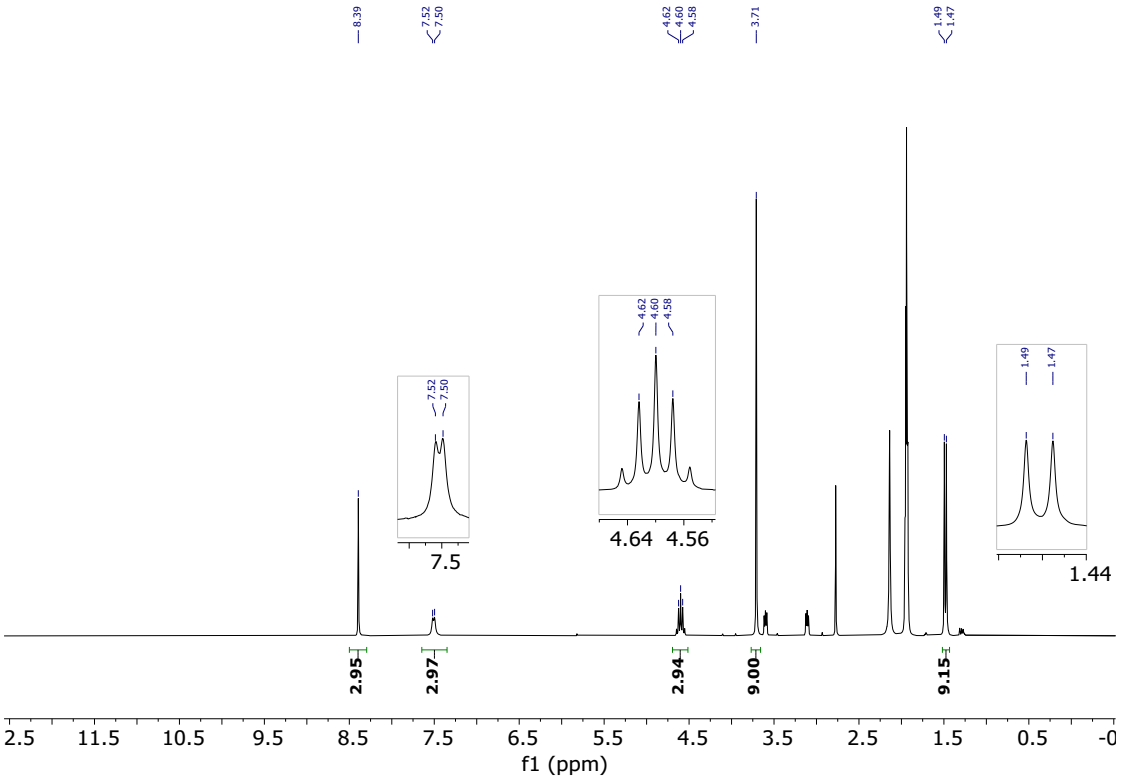



$^{13}$C NMR (151 MHz, $CD_3OD$) of **$3_{a1}$**.

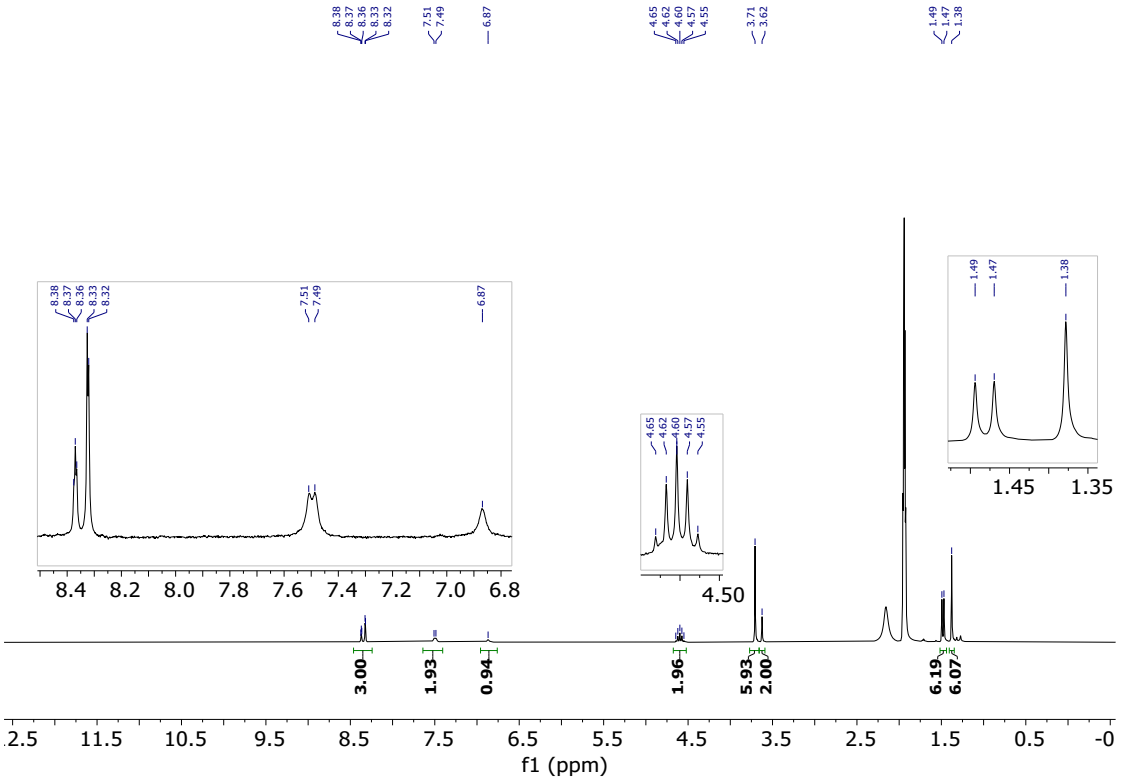


## 2.17. Reaction 19

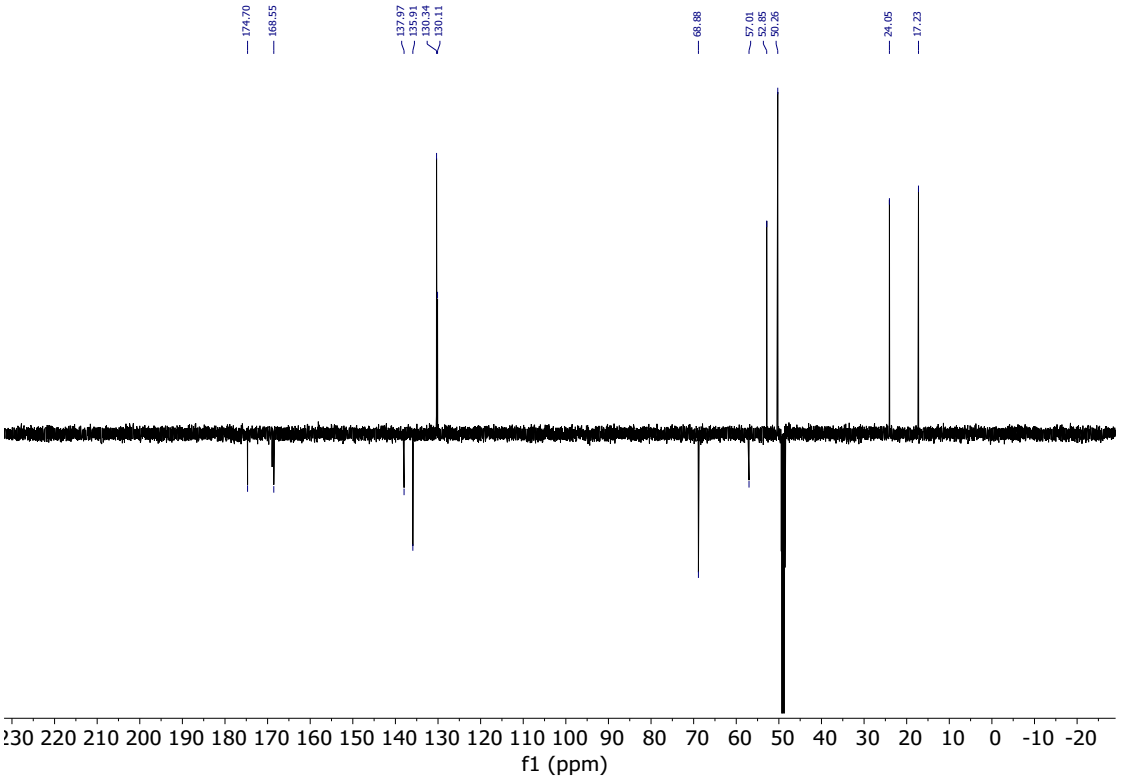
$^1$H NMR (300 MHz, $CD_3CN$) of **$2_{t1}$.**



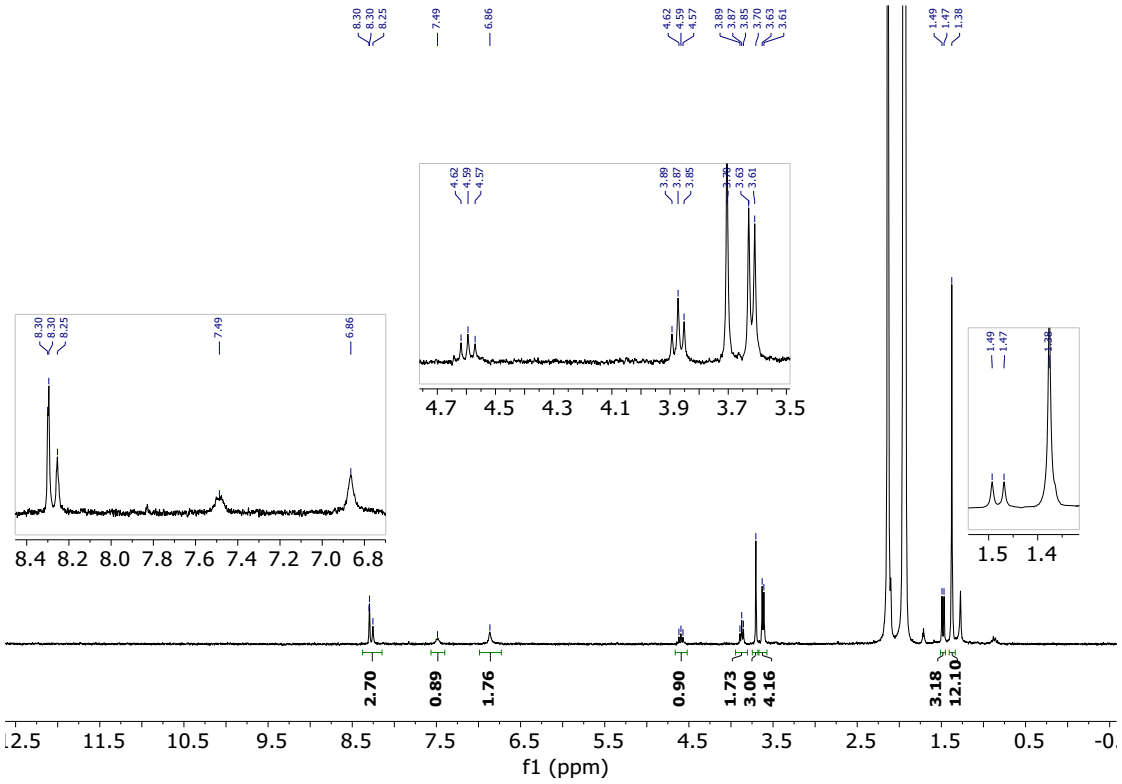
$^{1}$H NMR (300 MHz, $CD_3CN$) of $\mathbf{3_{t1}}$.




$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{3_{t1}}$.

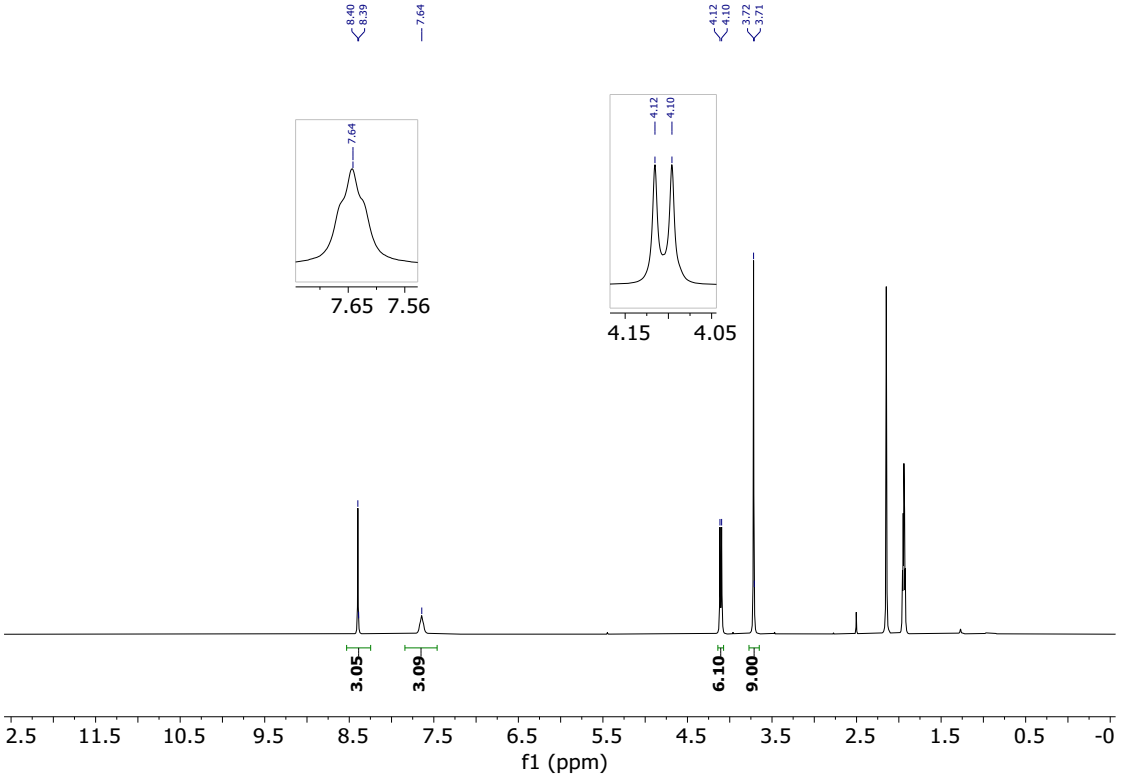


$^{1}$H NMR (300 MHz, $CD_3CN$) of **$4_{t1}$.**

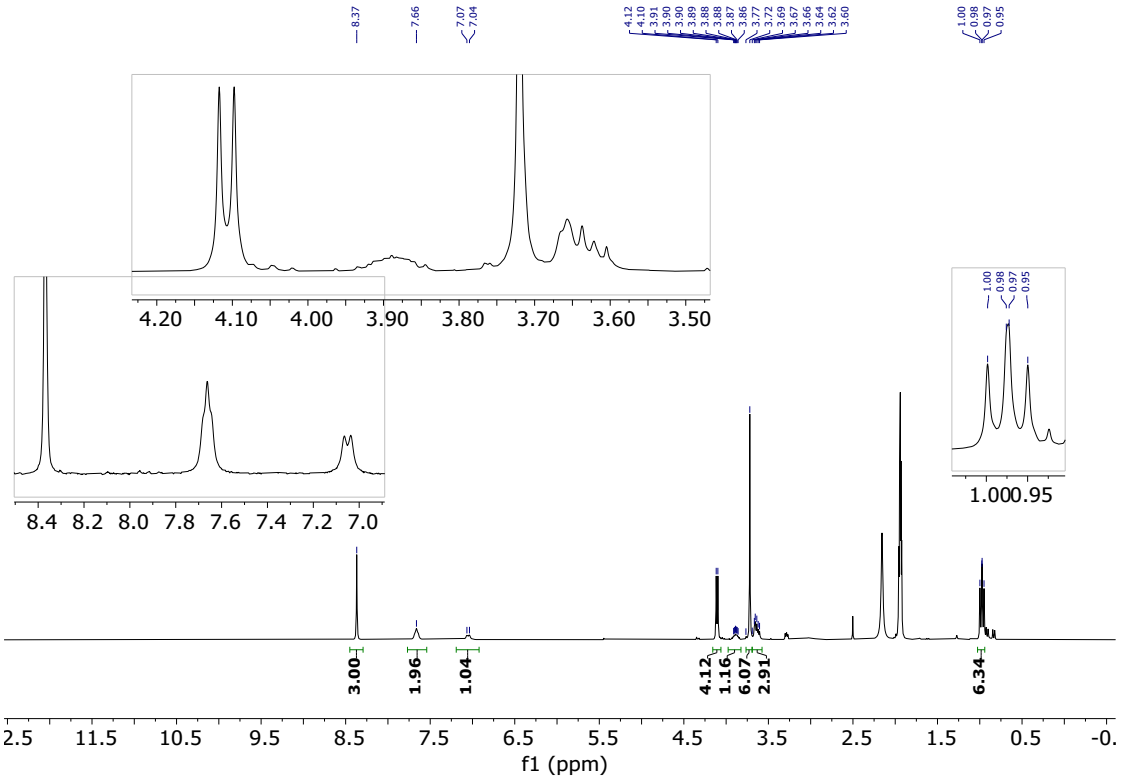


## 2.18. Reaction 20

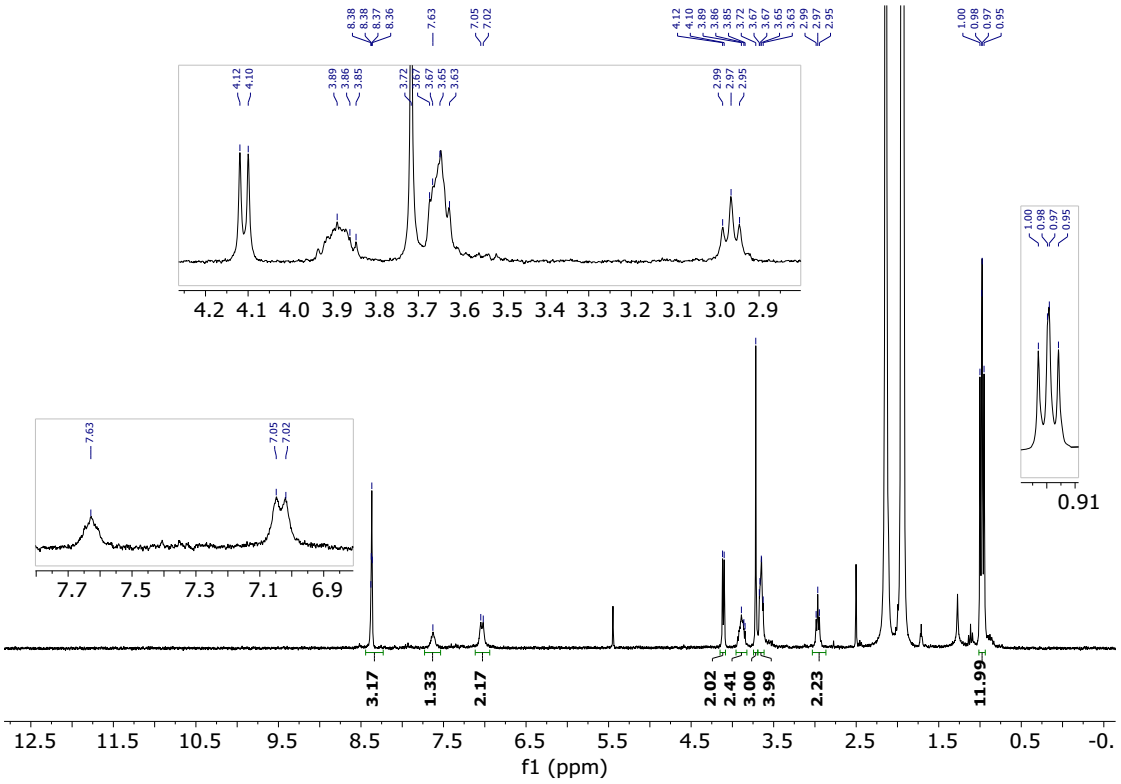
$^1$H NMR (300 MHz, $CD_3CN$) of $\mathbf{2}_{t2}$.




$^1$H NMR (300 MHz, $CD_3CN$) of $\mathbf{3}_{t2}$.

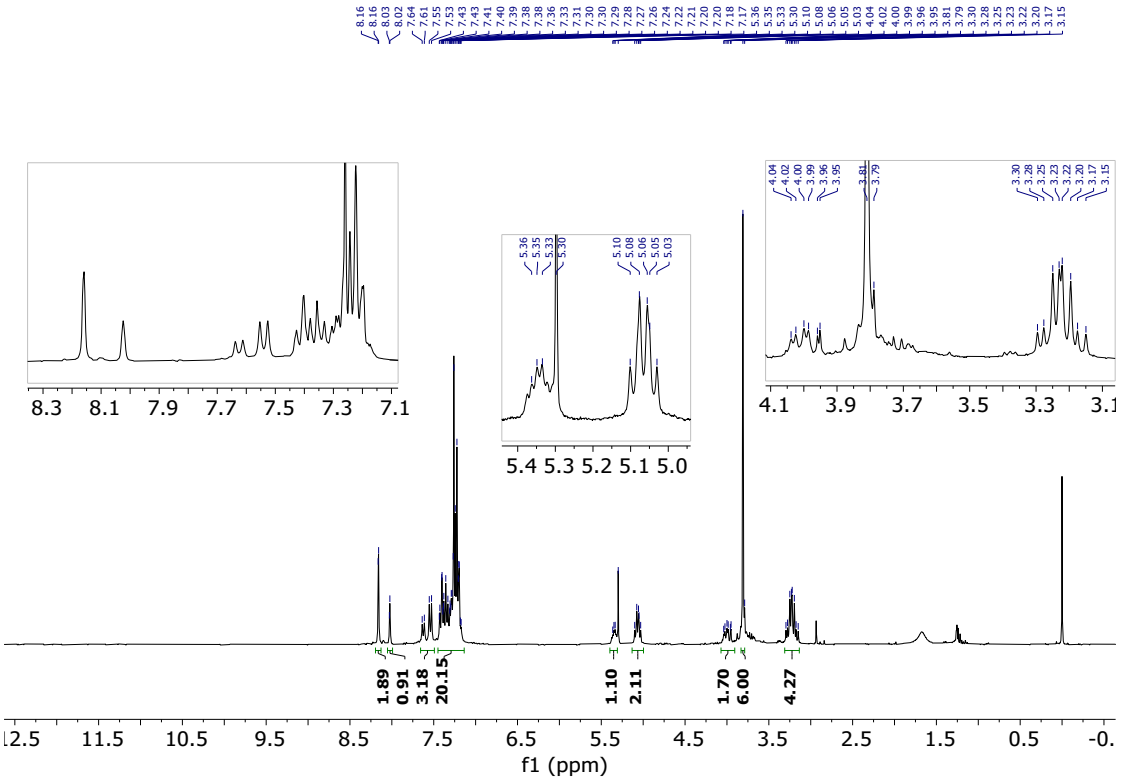


$^{1}$H NMR (300 MHz, $CD_3CN$) of **$4_{t2}$.**

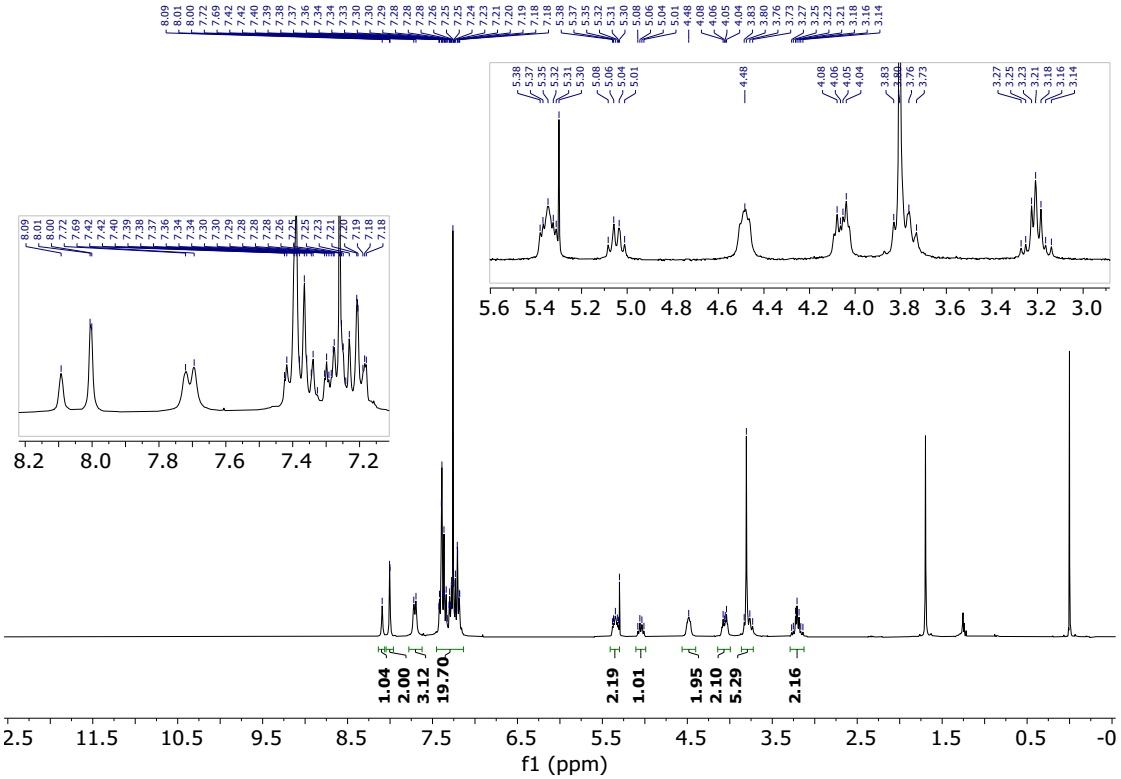


## 2.19. Reaction 21

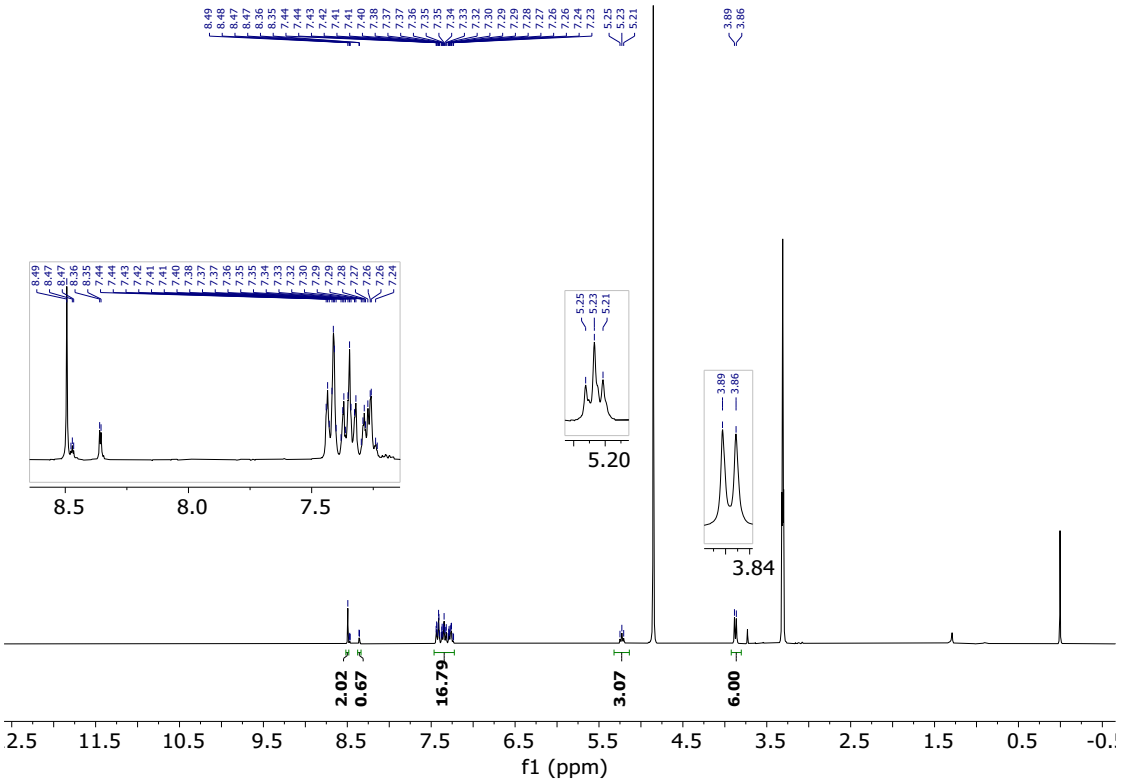
$^1$H NMR (300 MHz, $CDCl_3$) of **$3_{t5}$.**




$^1$H NMR (300 MHz, $CDCl_3$) of **$4_{t5}$.**

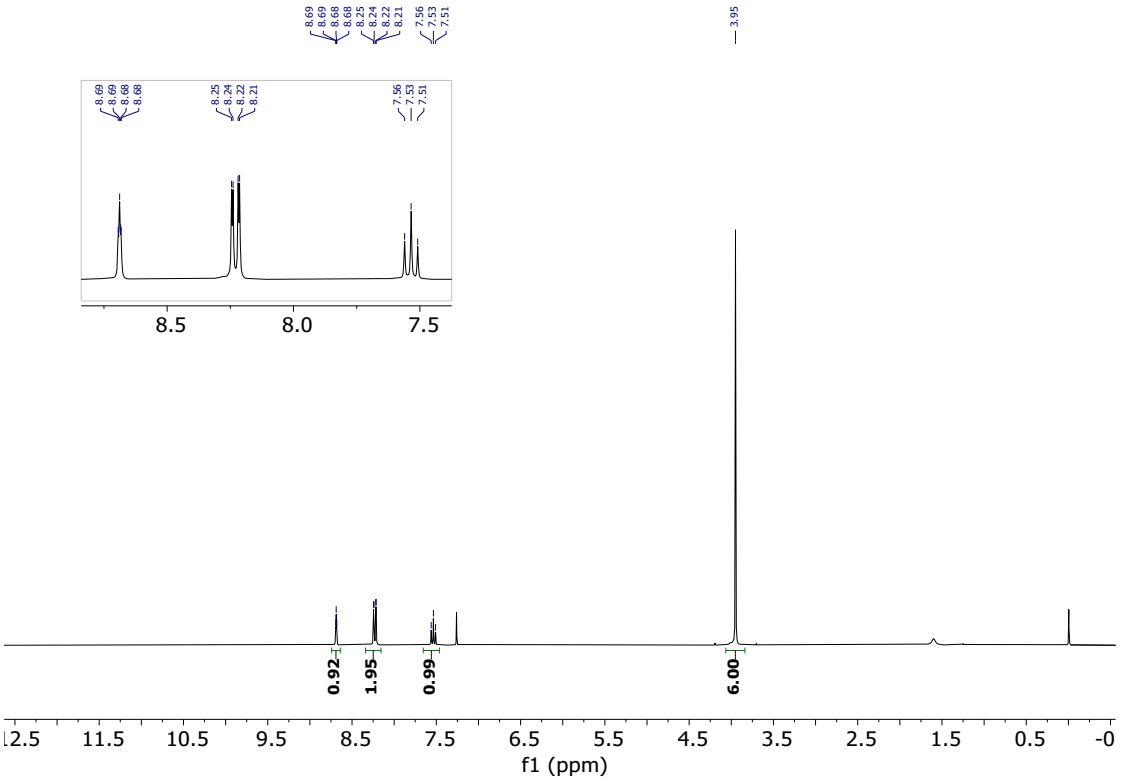


$^{1}$H NMR (300 MHz, $CD_3OD$) of **$5_{t5}$.**

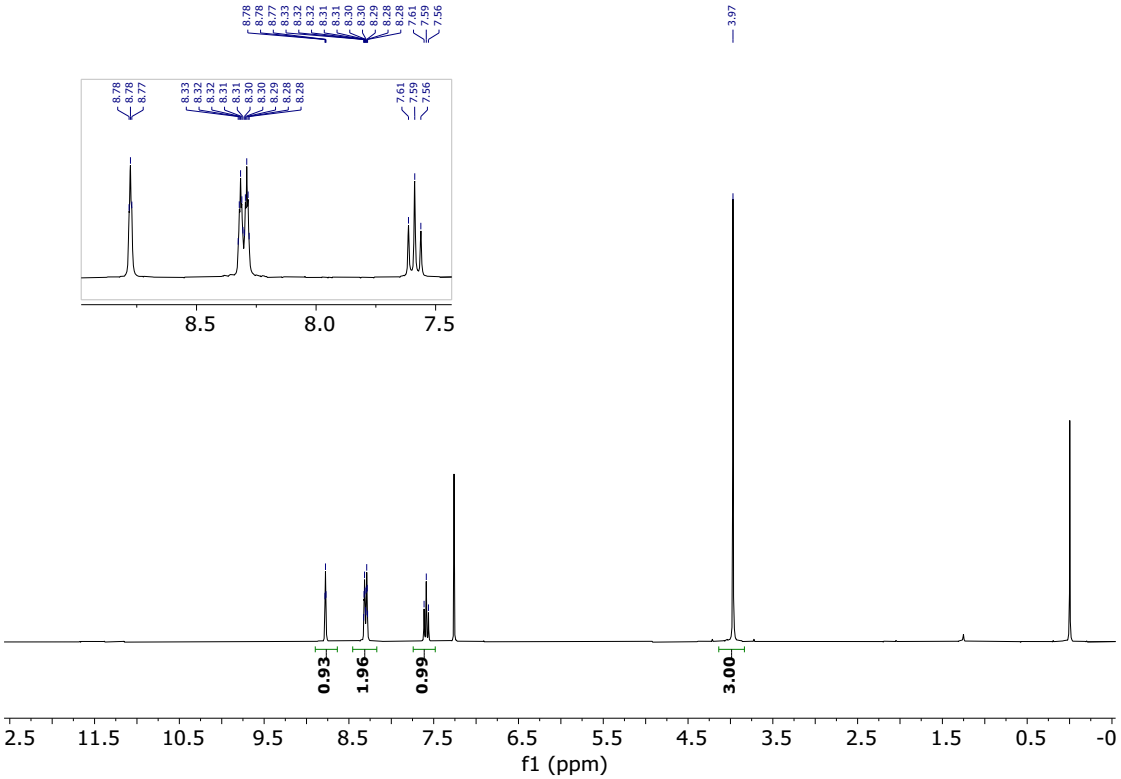


## 2.20. Linear reaction sequence 1

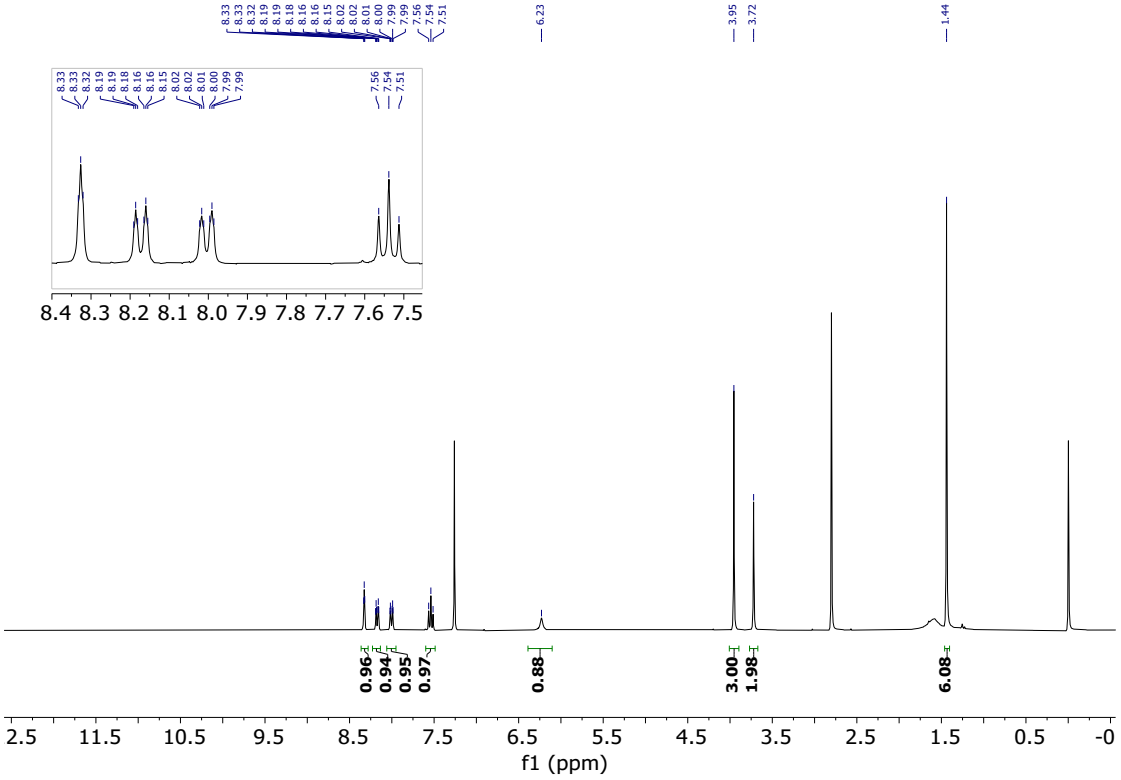
$^1$H NMR (300 MHz, $CDCl_3$) of **$9_{m1}$**.



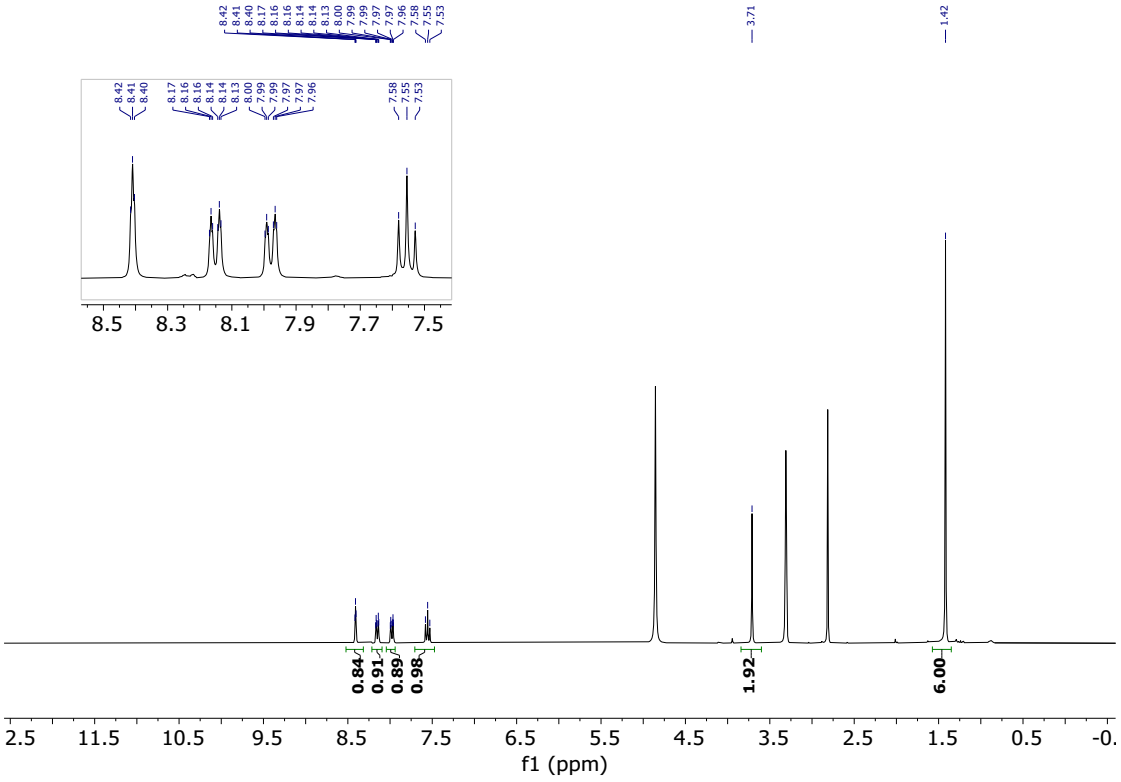

$^1$H NMR (300 MHz, $CDCl_3$) of **$10_{m1}$**.



$^1$H NMR (300 MHz, $CDCl_3$) of **$11_{m1}$**.

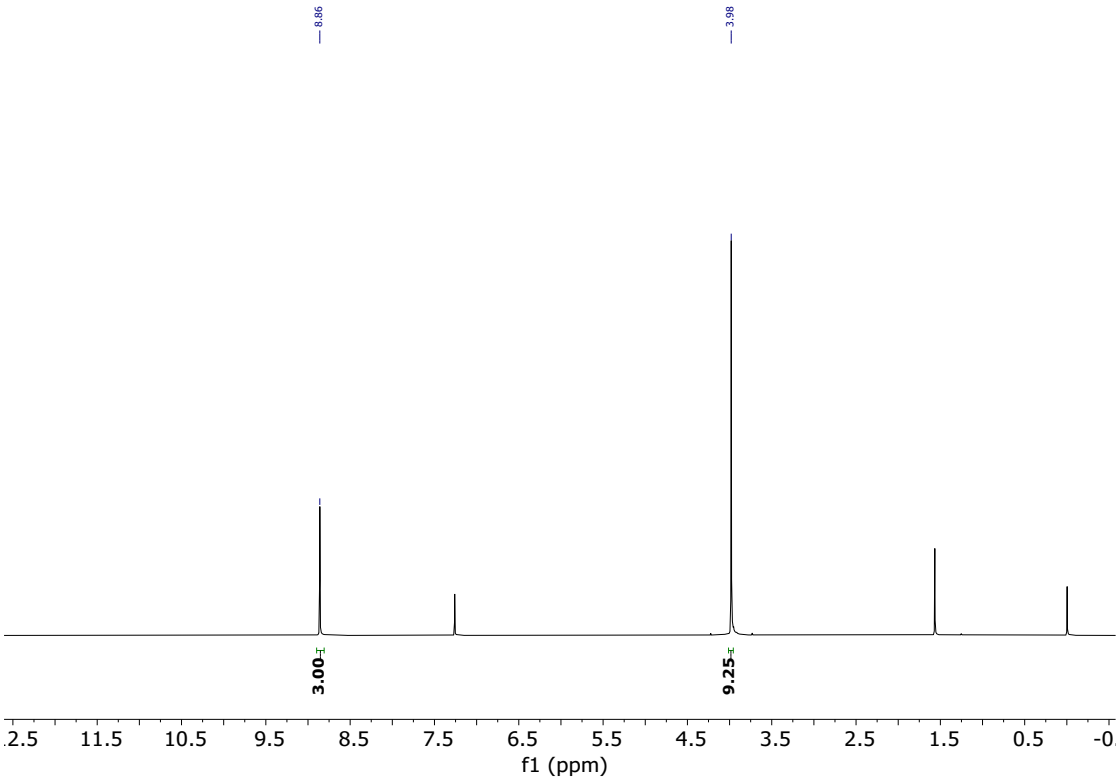



$^1$H NMR (300 MHz, $CD_3OD$) of **$12_{m1}$**.

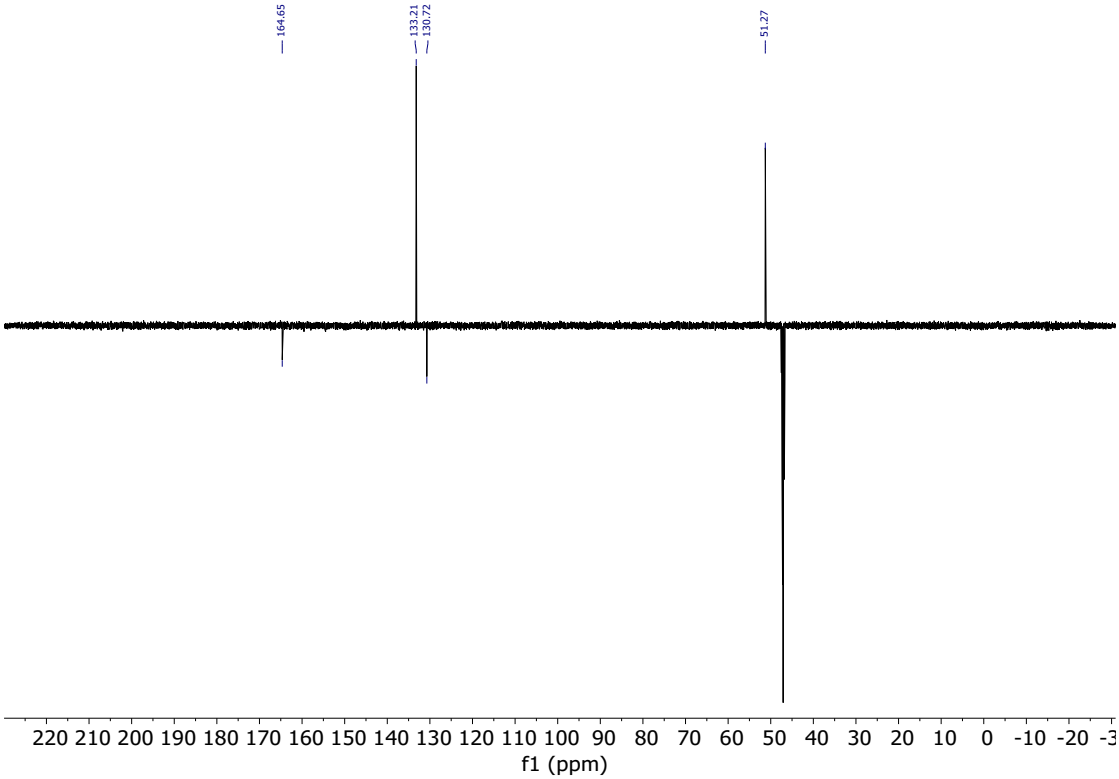


## 2.21. Linear reaction sequence 2

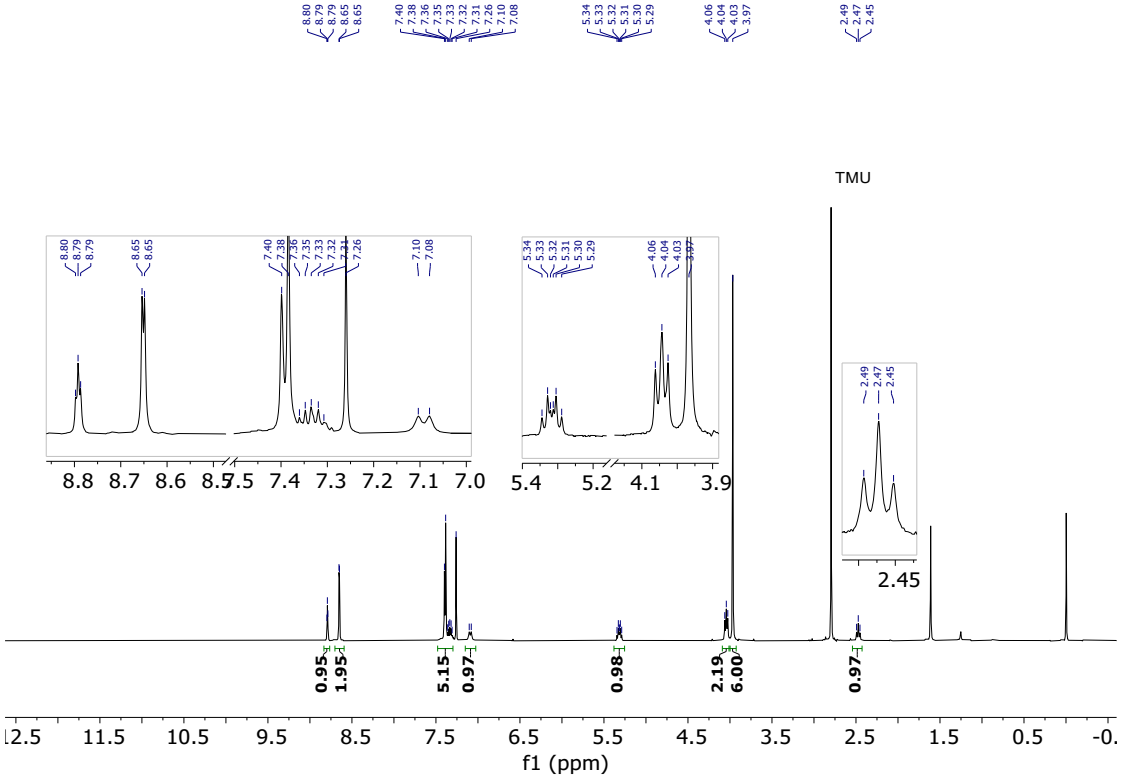
$^{1}$H NMR (300 MHz, $CDCl_3$) of **$13_{t3}$**.



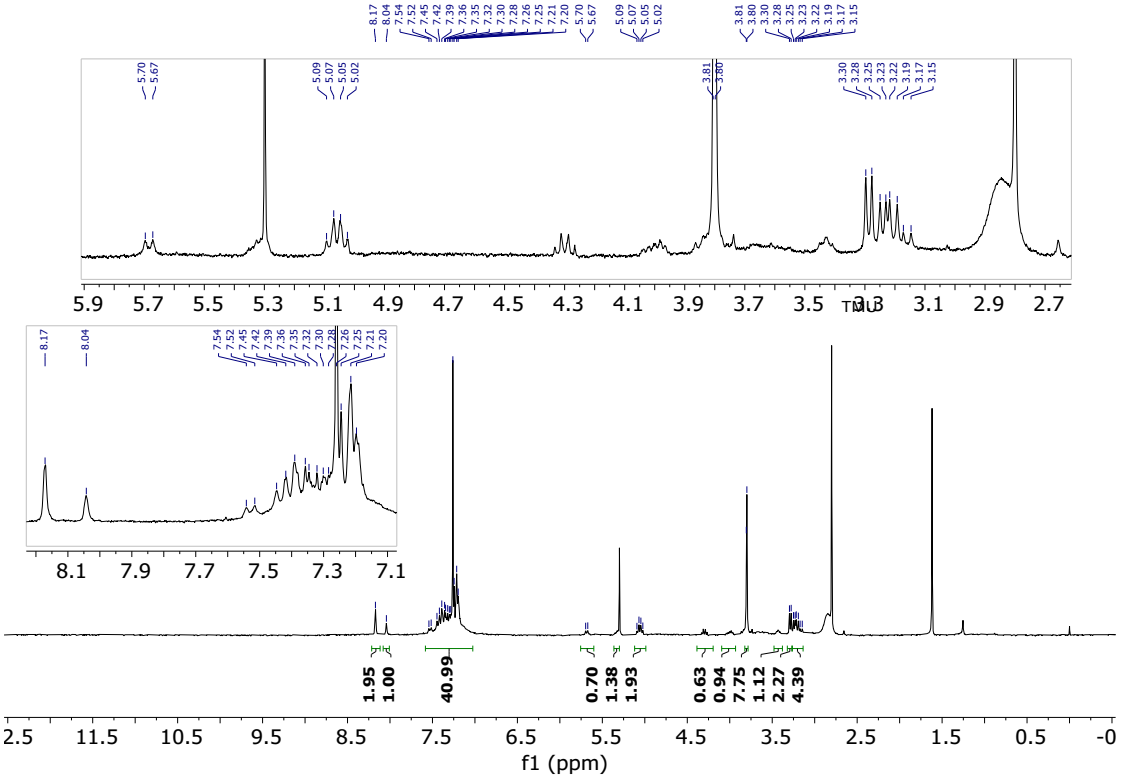

$^{13}$C NMR (151 MHz, $CD_3OD$) of **$13_{t3}$**.



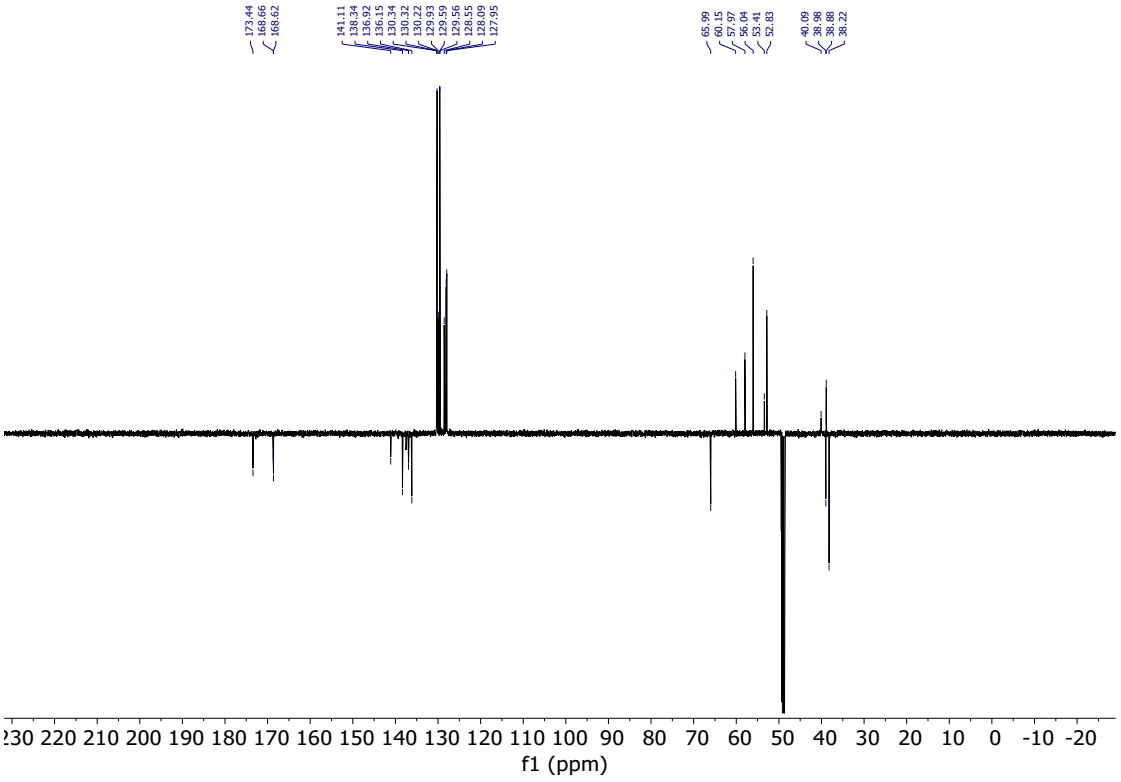
$^{1}$H NMR (300 MHz, $CDCl_3$) of **$15_{t3}$**.



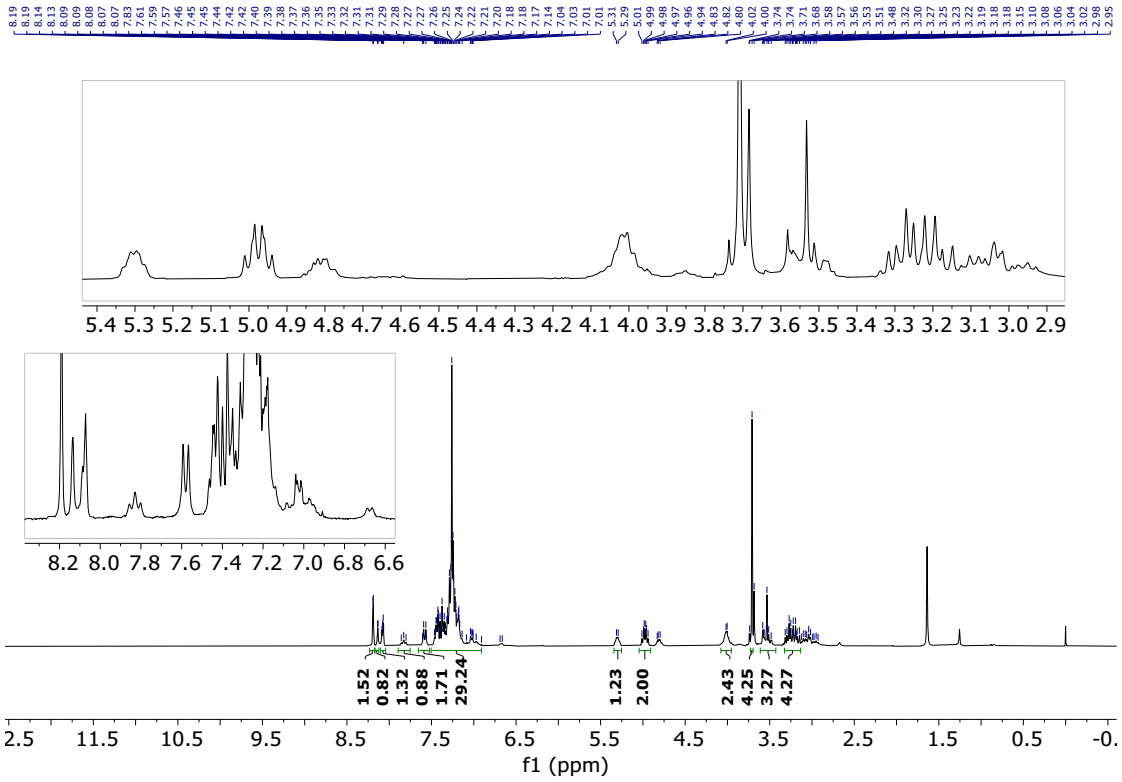
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{3_{t3}}$.



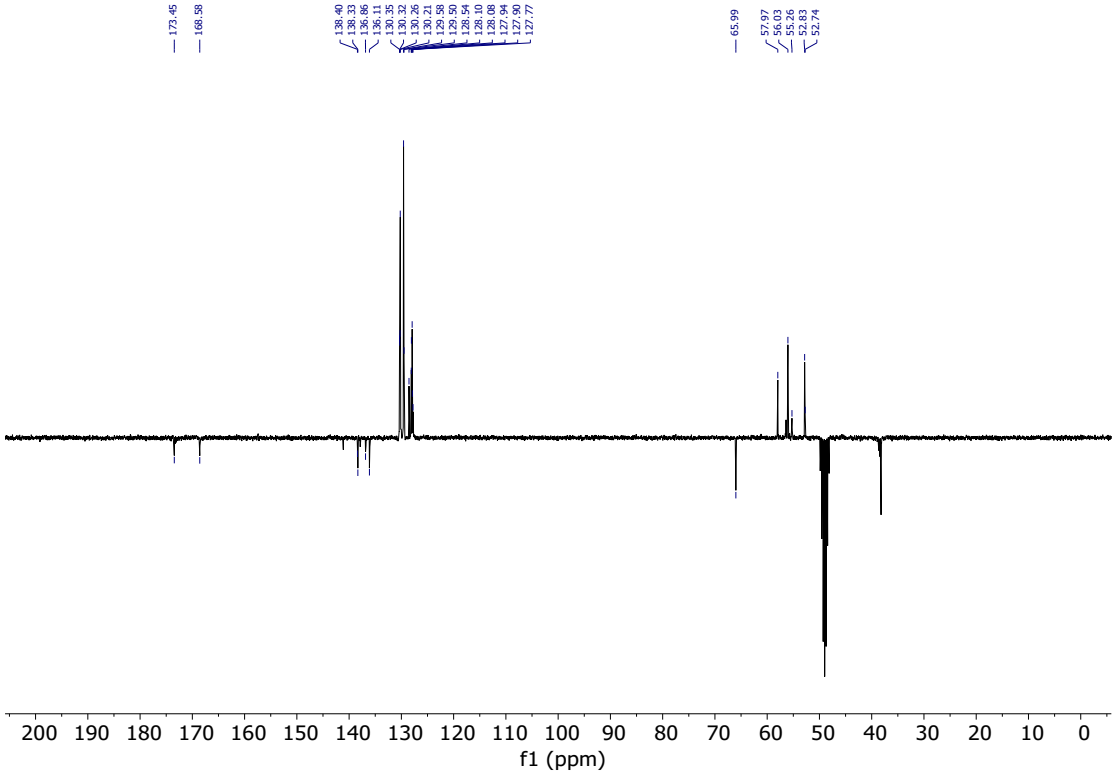

$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{3_{t3}}$.



$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{3_{t4}}$.

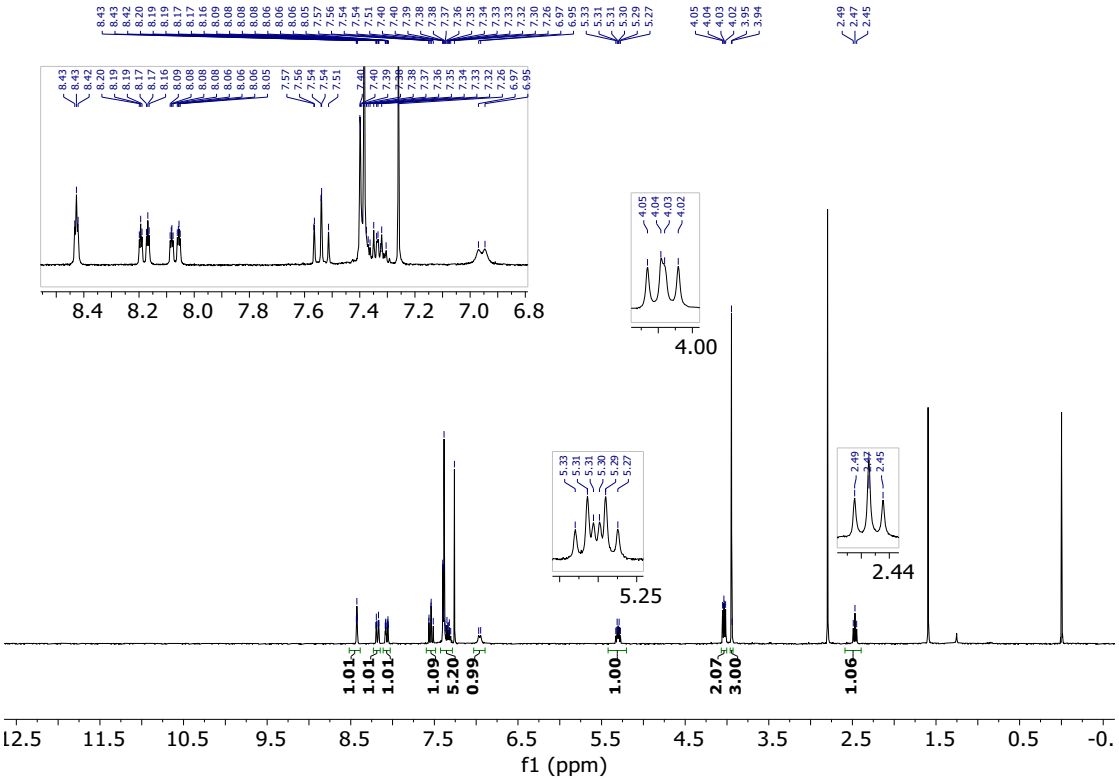



$^{13}$C NMR (151 MHz, $CD_3OD$) of $\mathbf{3_{t4}}$.

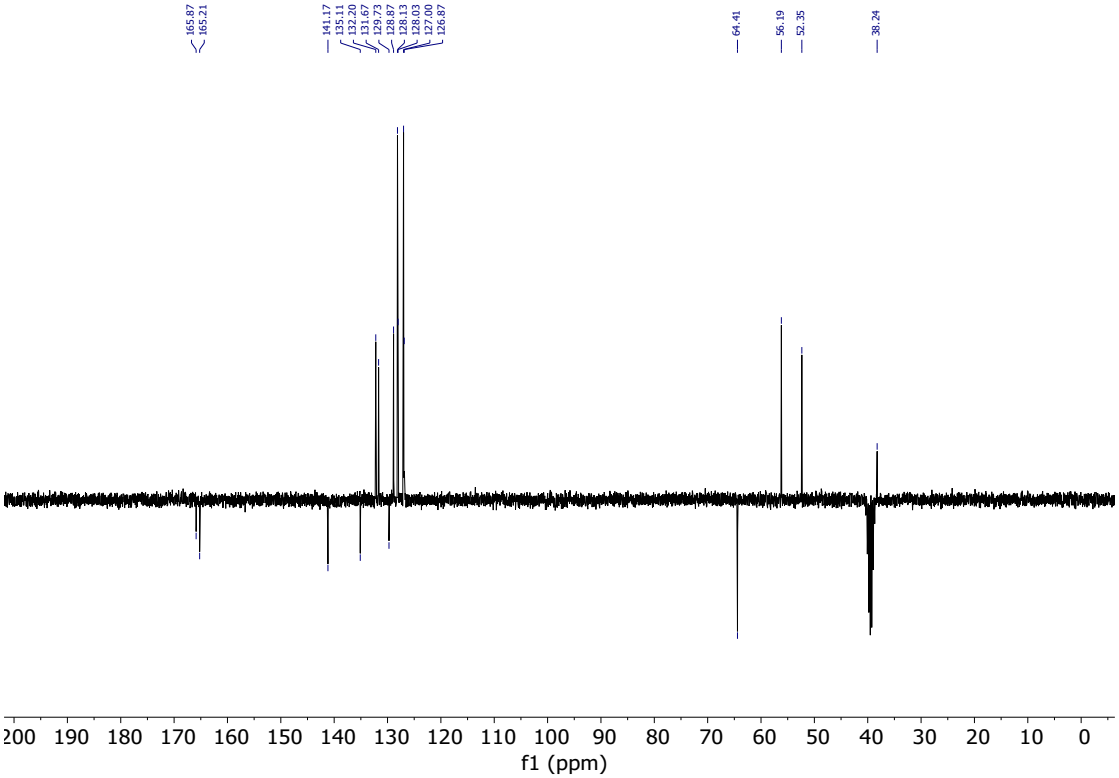


## 2.22. Synthesis of derivative **3b**

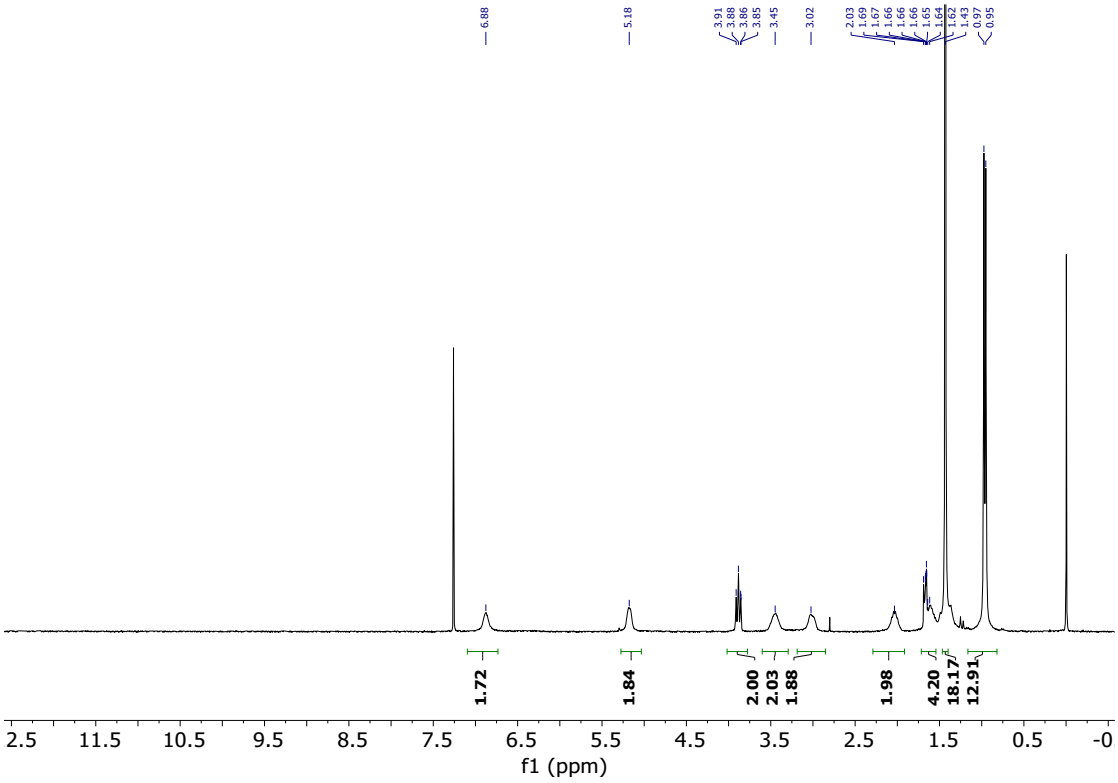
$^{1}$H NMR (300 MHz, $CDCl_3$) of $\mathbf{11_{m5}}$.



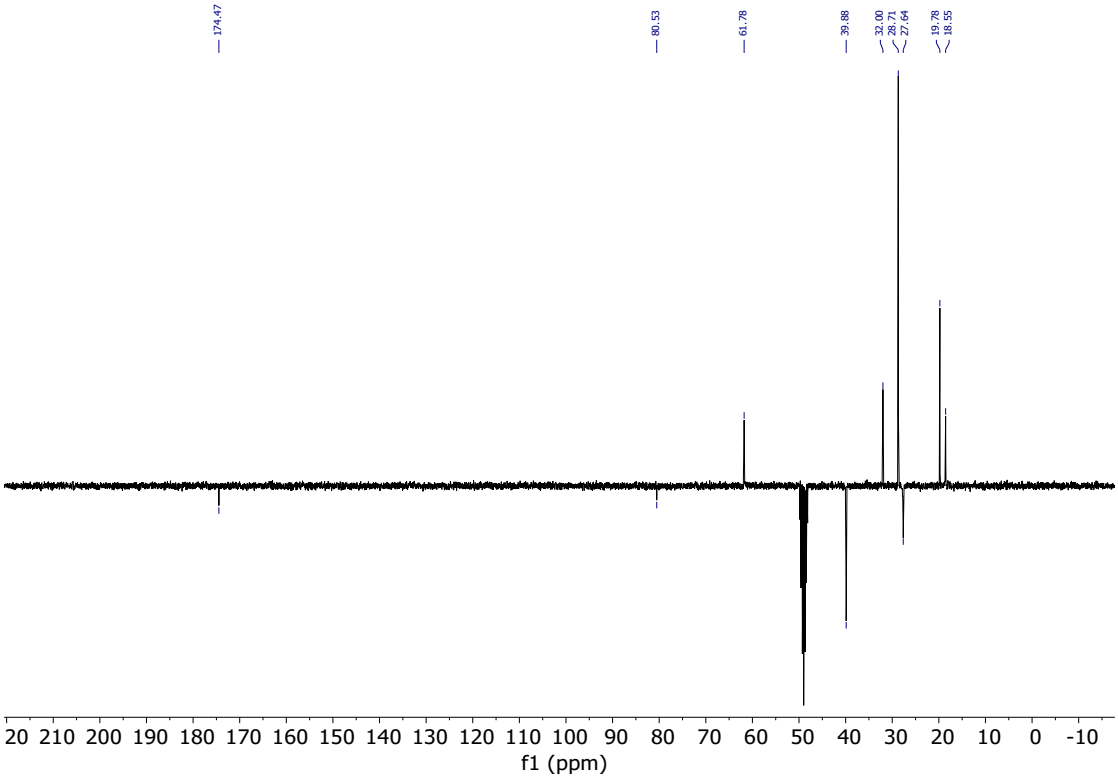

$^{13}$C NMR (75 MHz, DMSO) of $\mathbf{11_{m5}}$.



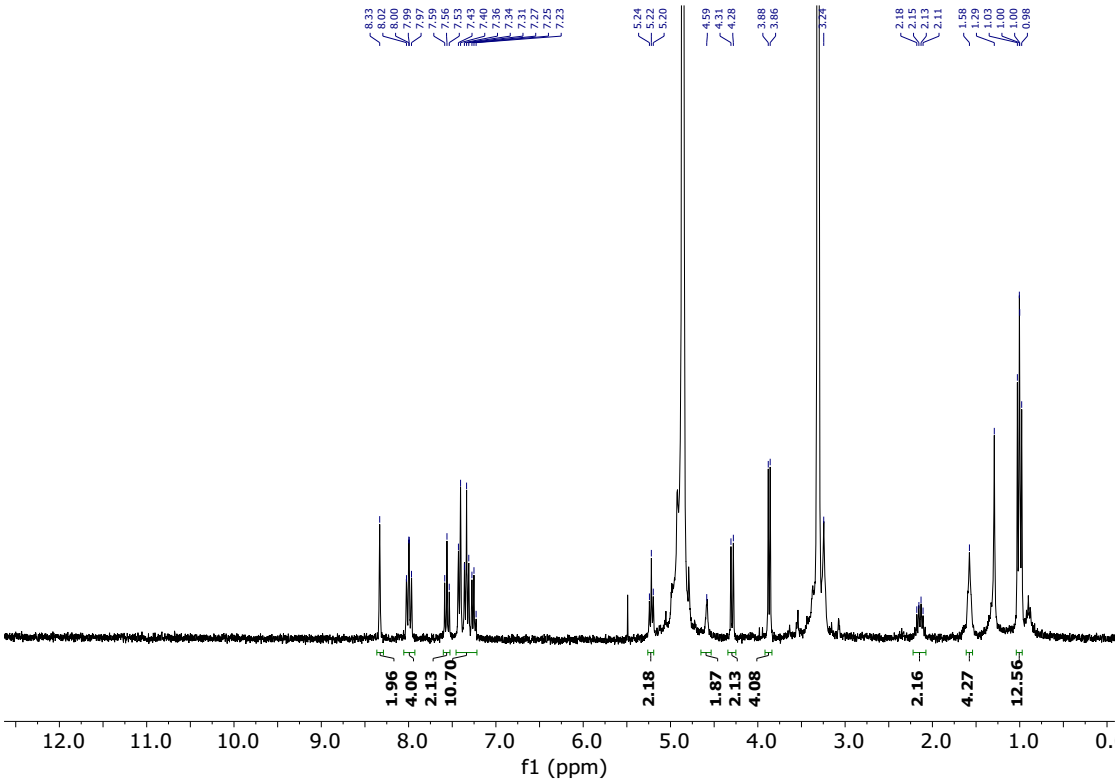
$^{1}$H NMR (300 MHz, $CDCl_3$) of **(Boc-Val-NH-$CH_2CH_2$)$_2$ (17).**




$^{13}$C NMR (75 MHz, $CD_3OD$) of **(Boc-Val-NH-$CH_2CH_2$)$_2$ (17).**



$^{1}$H NMR (300 MHz, $CDCl_3$) of **(Phg$^{\#}$-*m*$C_6H_4$-Val-NH-$CH_2CH_2$)$_2$ ($3_b$).**



## 3. CD spectra.

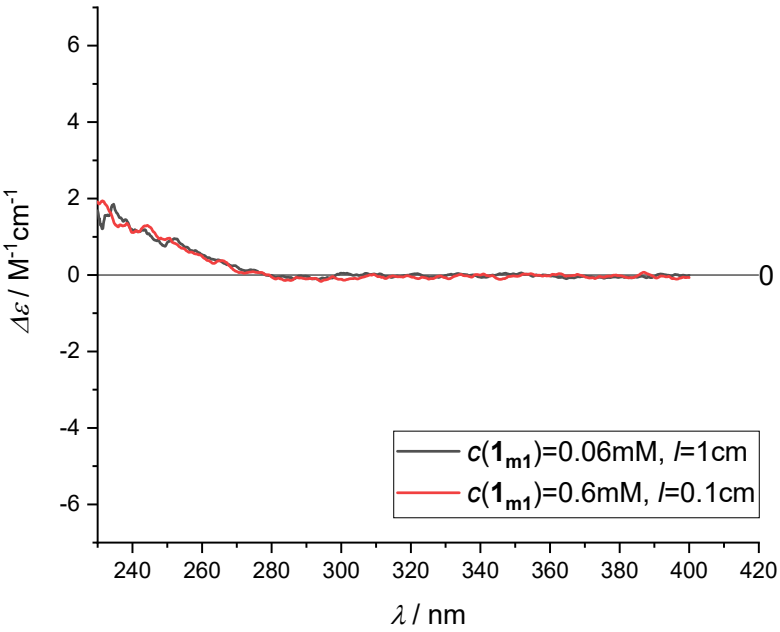



Figure S2. CD spectra (DCM) of $\mathbf{1_{m1}}$ solutions**.**

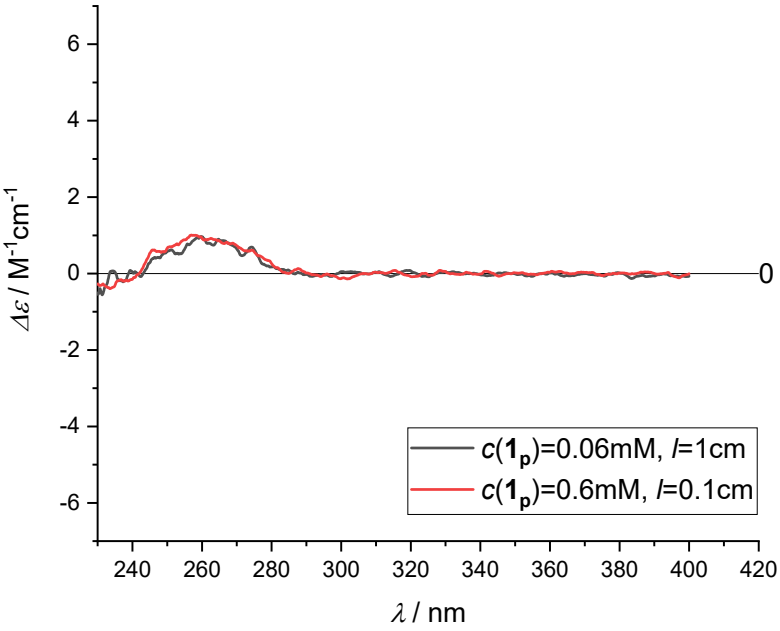



Figure S3. CD spectra (DCM) of $\mathbf{1_p}$ solutions**.**

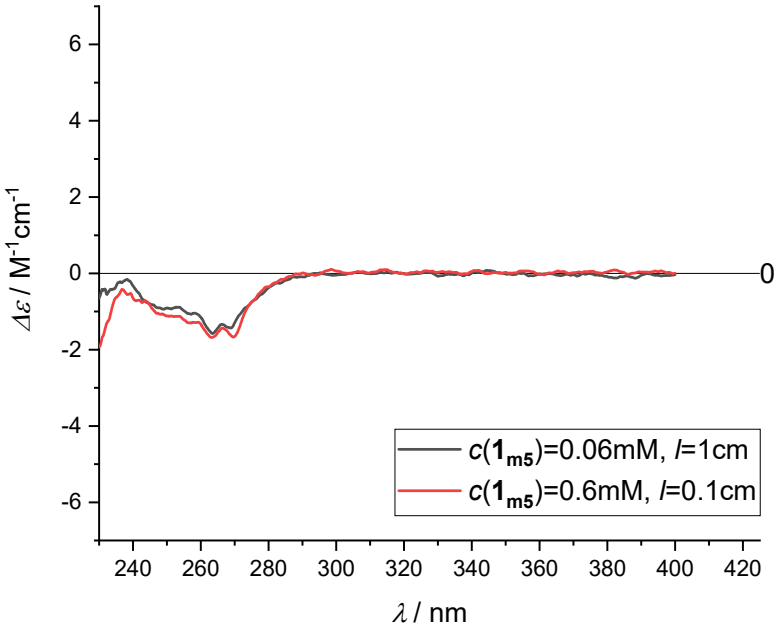



Figure S4.CD spectra (DCM) of $\mathbf{1_{m5}}$ solutions**.**

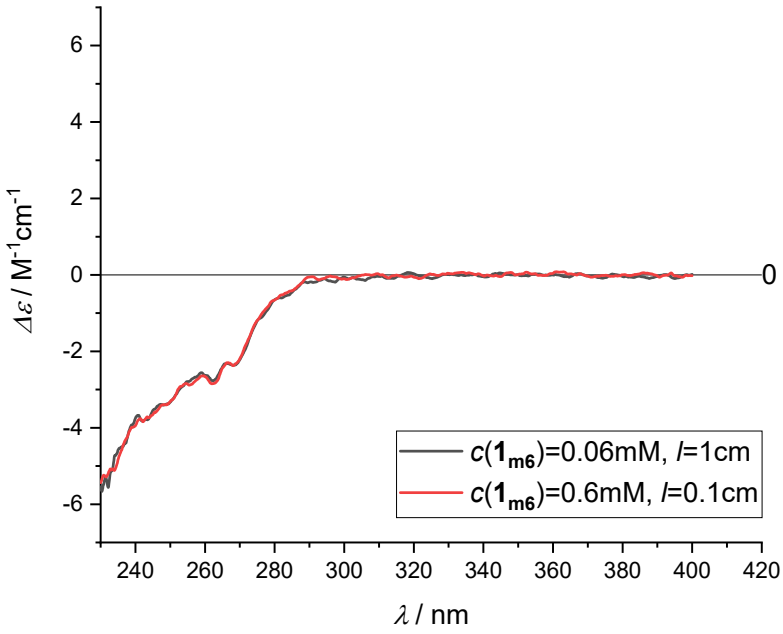



Figure S5. CD spectra (DCM) of $\mathbf{1_{m6}}$ solutions**.**

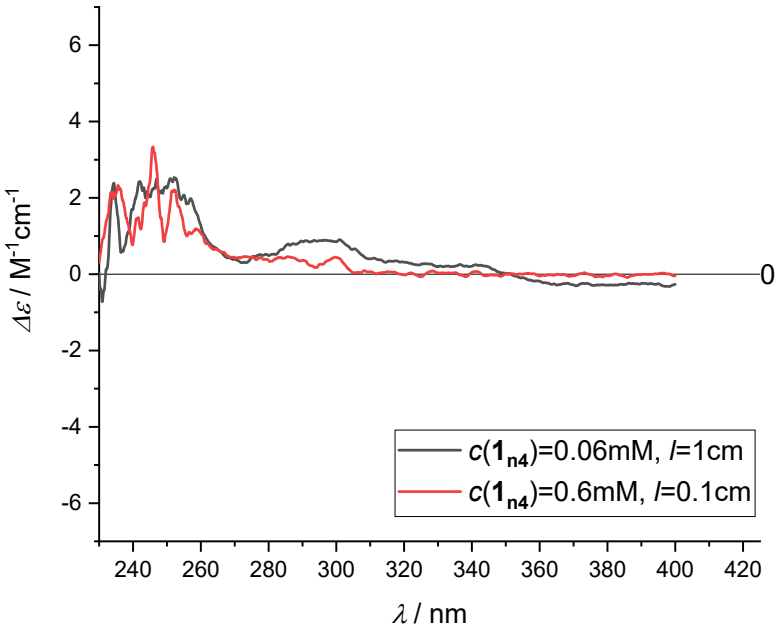



Figure S6. CD spectra (DCM) of $\mathbf{1_{n4}}$ solutions**.**

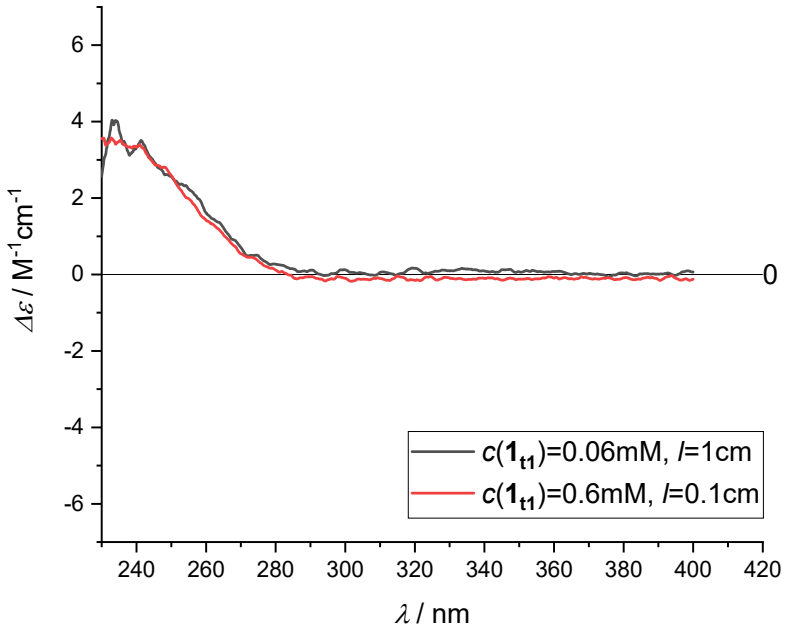



Figure S7. CD spectra (DCM) of $\mathbf{1_{t1}}$ solutions**.**

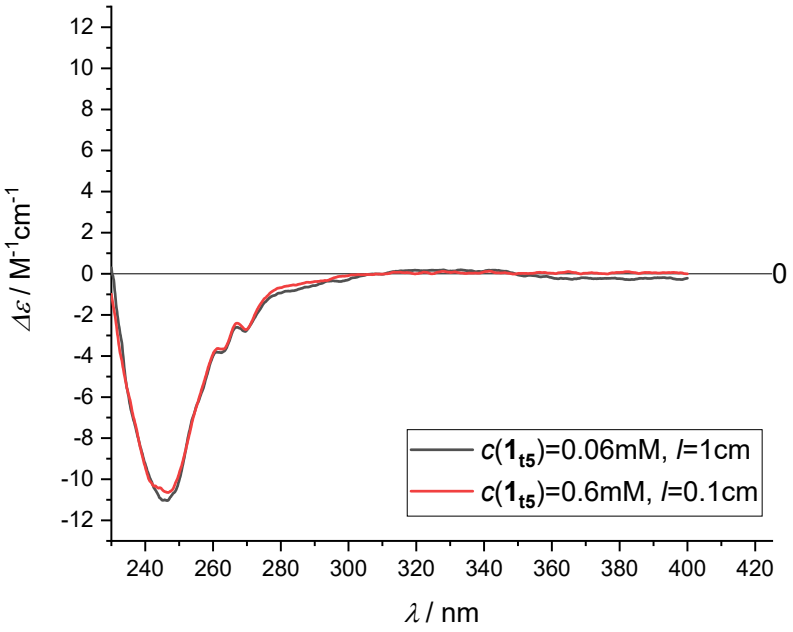
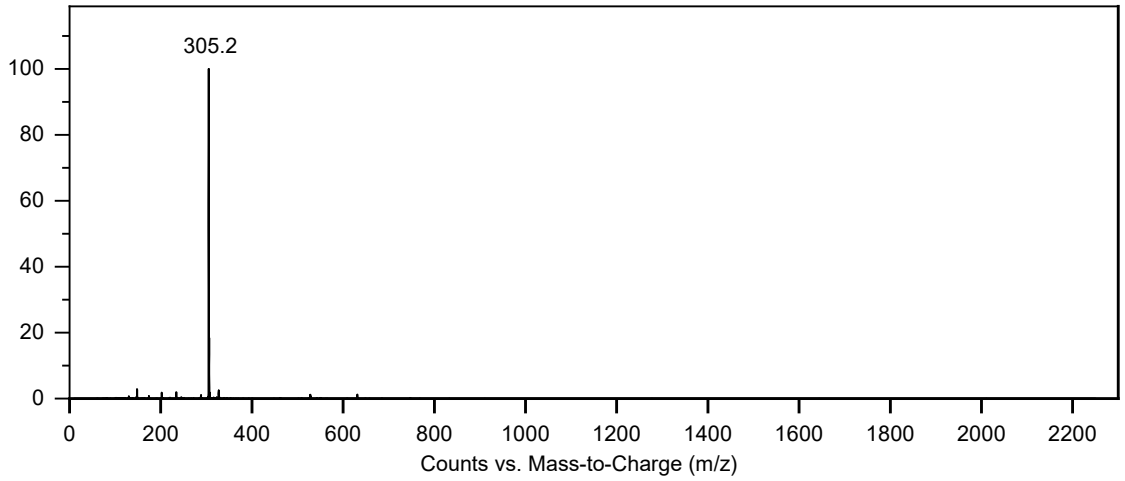



Figure S8. CD spectra (DCM) of $\mathbf{1}_{t5}$ solutions**.**

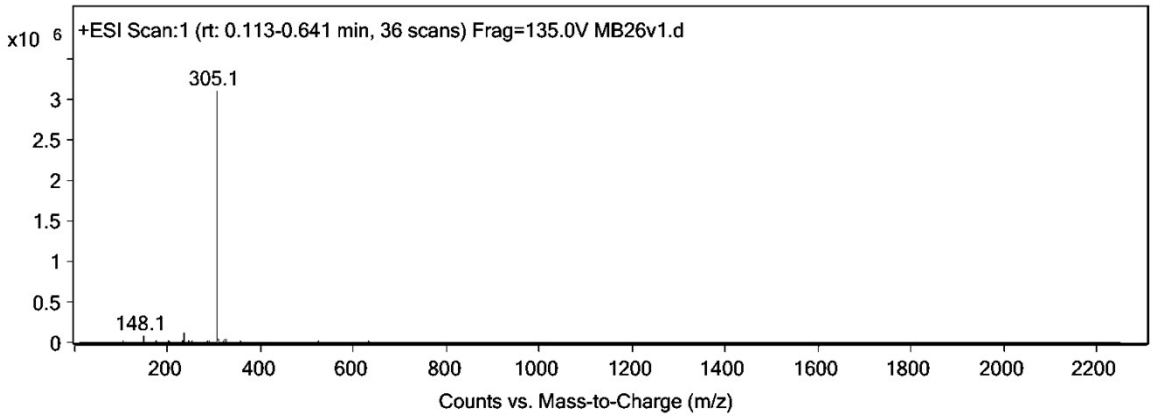
## 4. Mass spectra.

### 4.1. Oxazolines

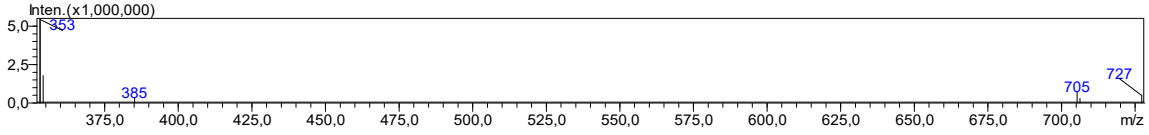
ESI-MS of $\mathbf{1}_{m1}$.



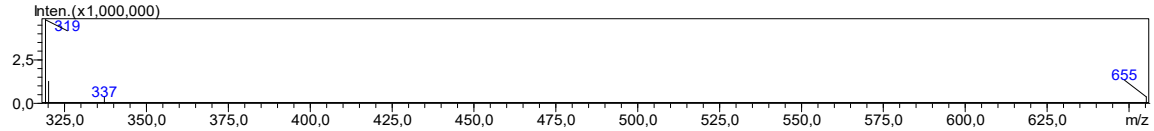

ESI-MS of $\mathbf{1}_{p}$.



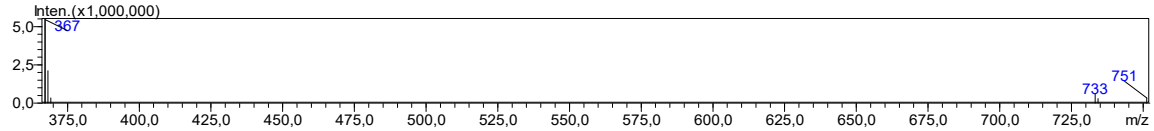

ESI-MS of $\mathbf{1}_{m2}$.



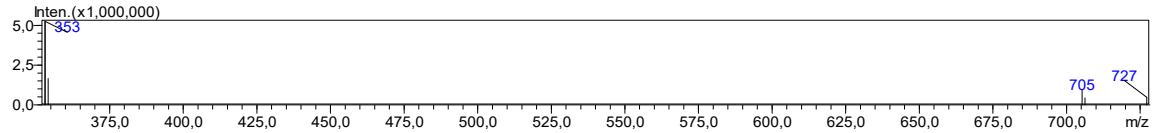
ESI-MS of $\mathbf{1}_{m3}$.



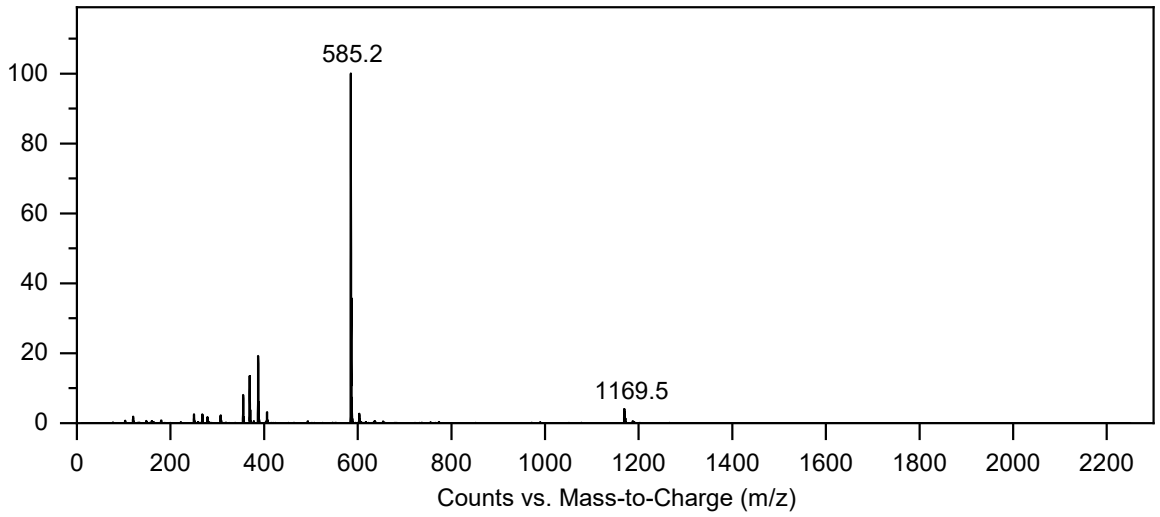

ESI-MS of $\mathbf{1}_{m4}$.



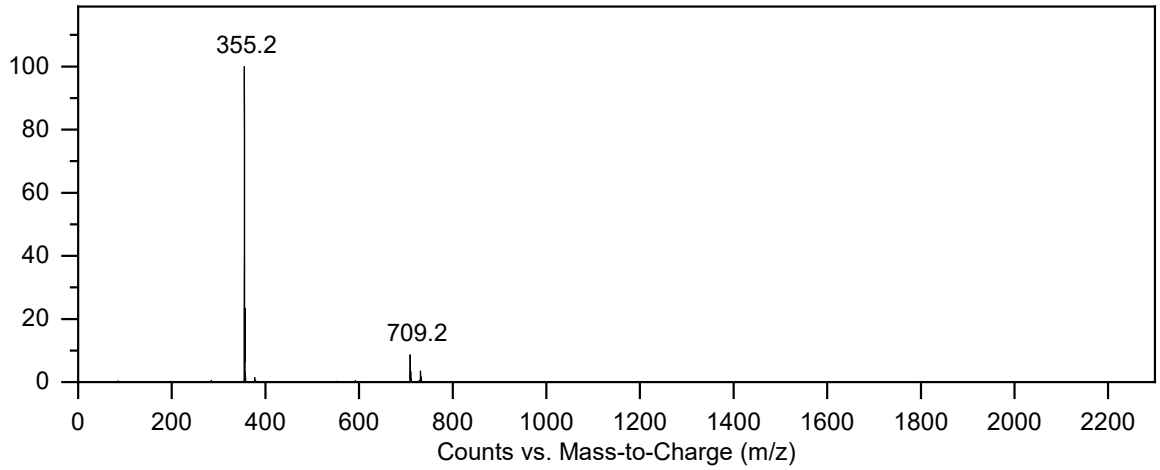

ESI-MS of $\mathbf{1}_{m5}$.



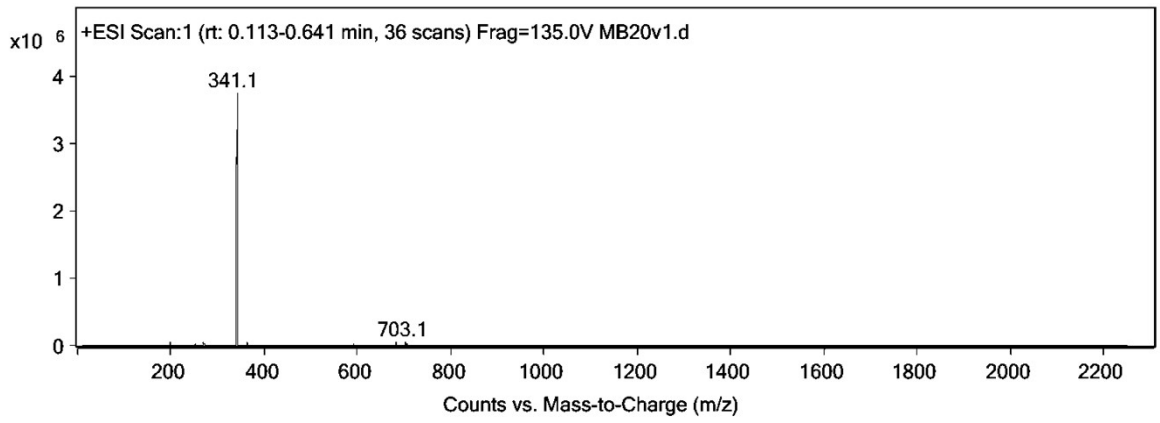

ESI-MS of $\mathbf{1}_{m6}$.



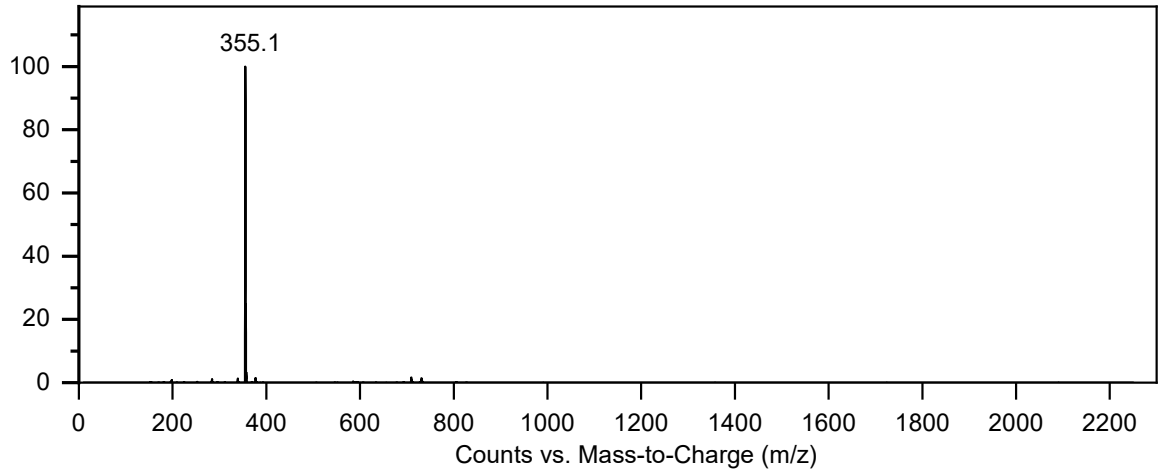
ESI-MS of $\mathbf{1}_{n1}$.



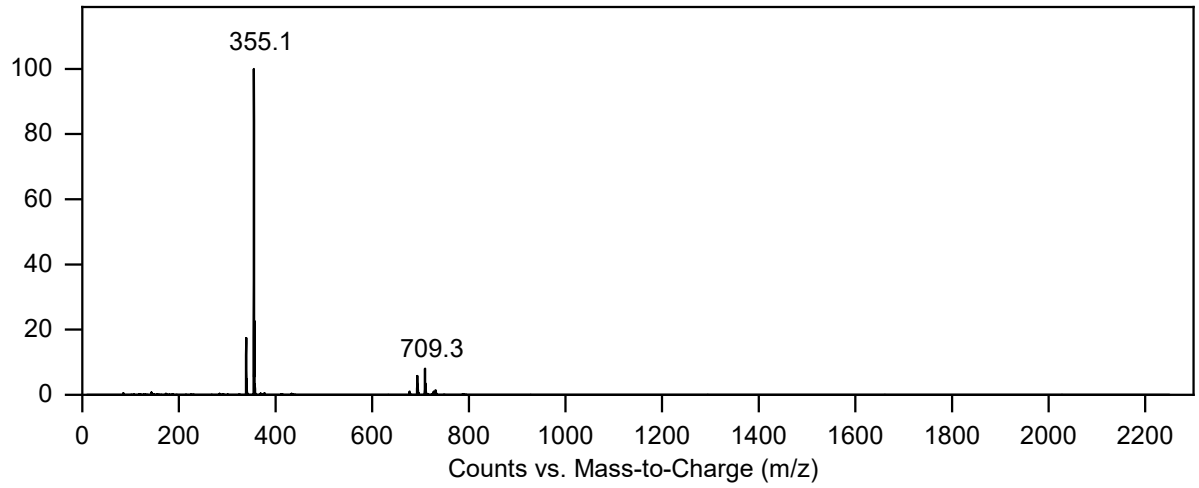

ESI-MS of $\mathbf{1}_{n2}$.



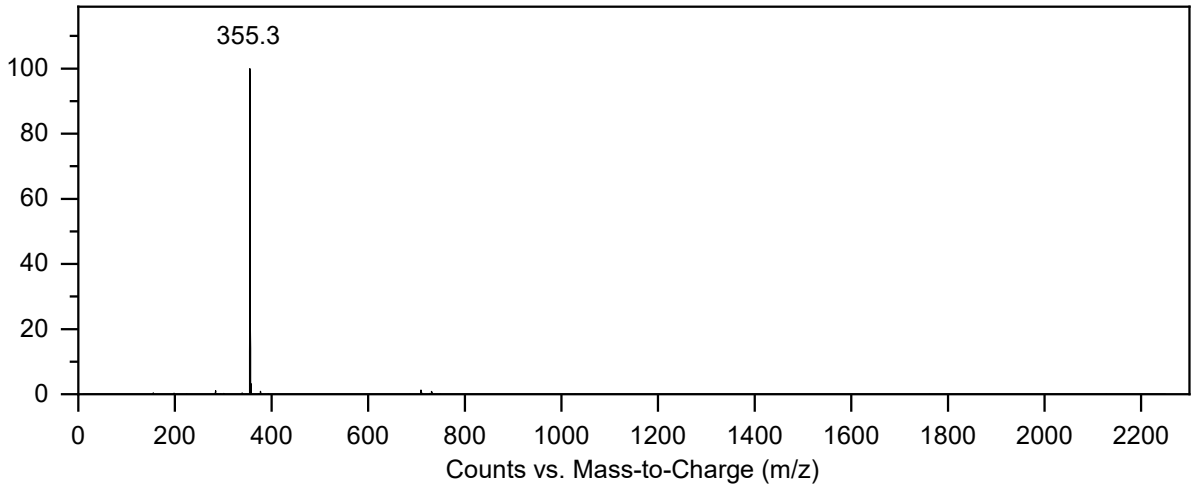

ESI-MS of $\mathbf{1}_{n3}$.



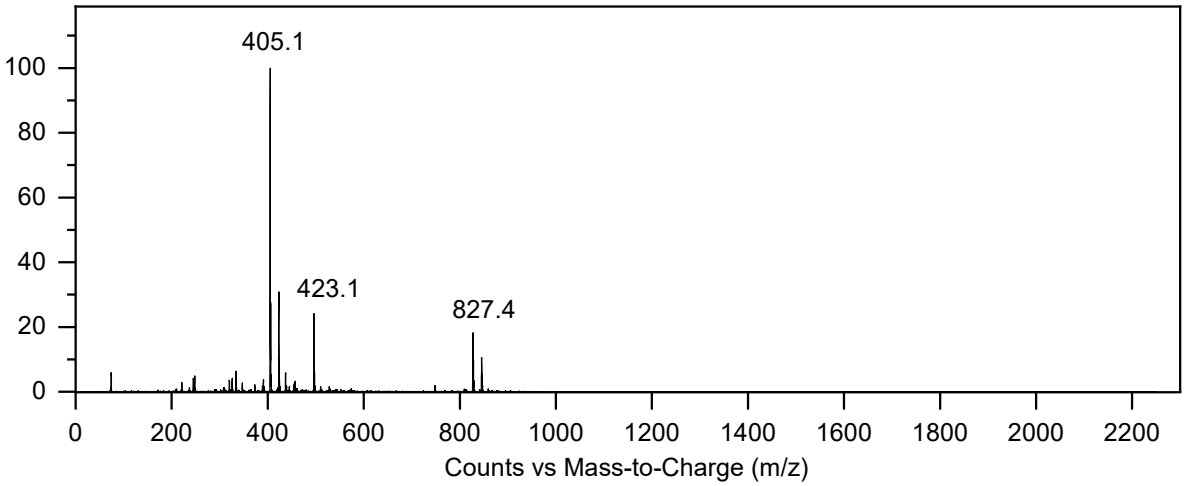
ESI-MS of $\mathbf{1}_{n4}$.



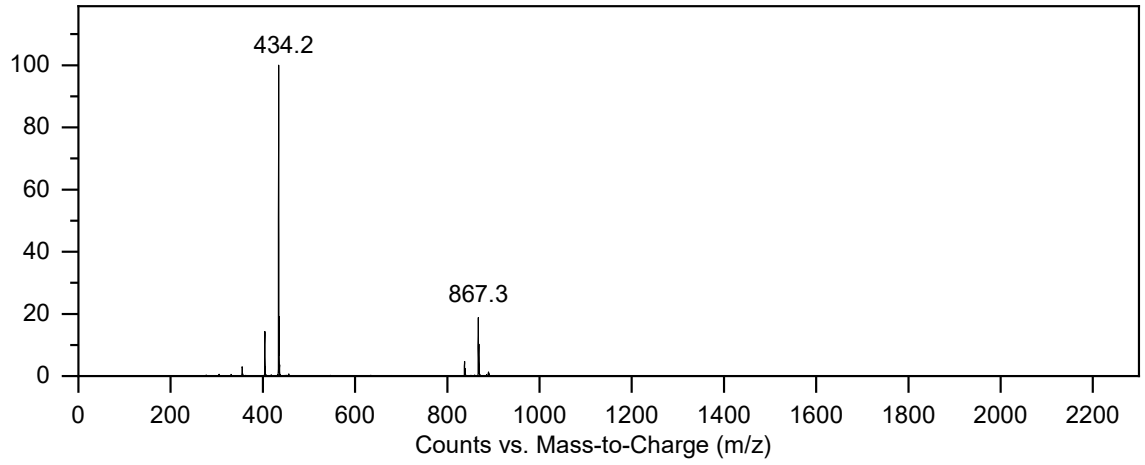

ESI-MS of $\mathbf{1}_{n5}$.



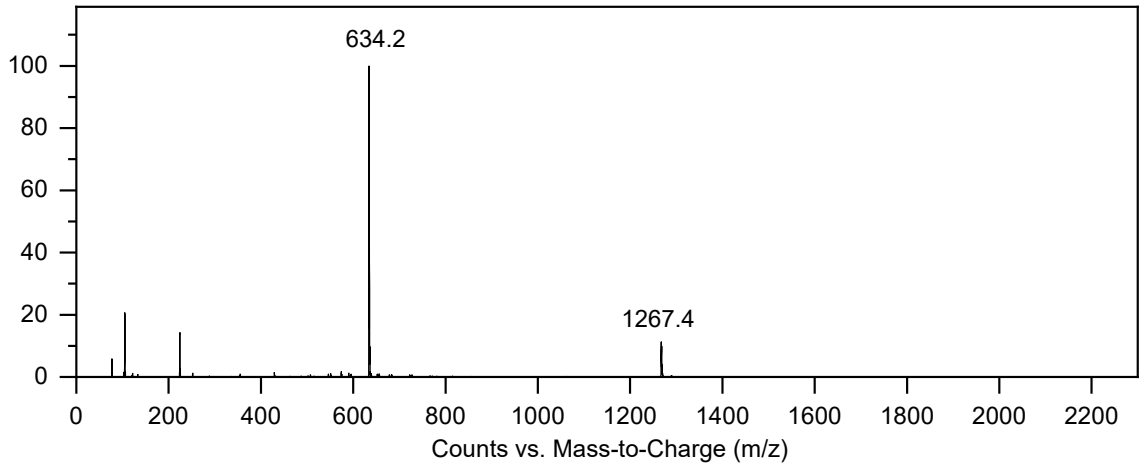

ESI-MS of $\mathbf{1}_{a}$.



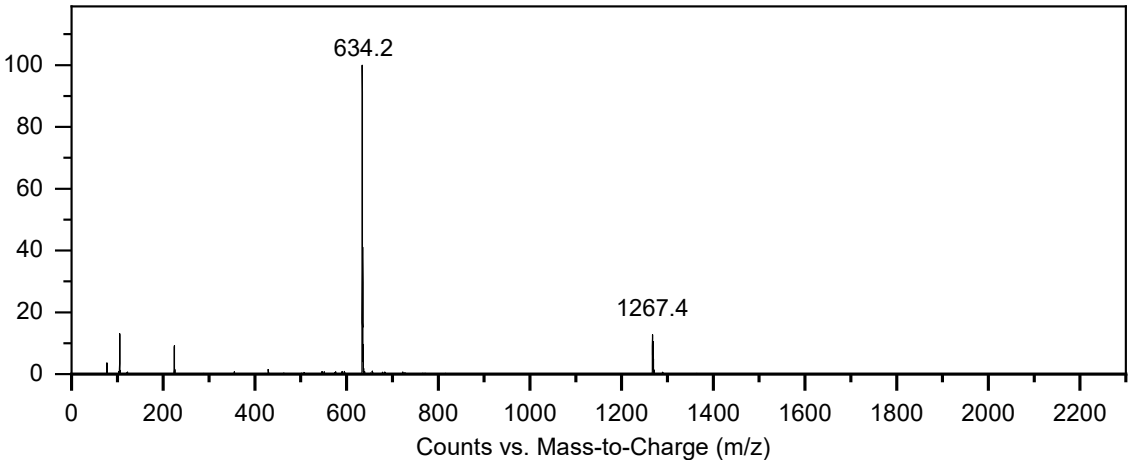
ESI-MS of $\mathbf{1}_{t1}$.



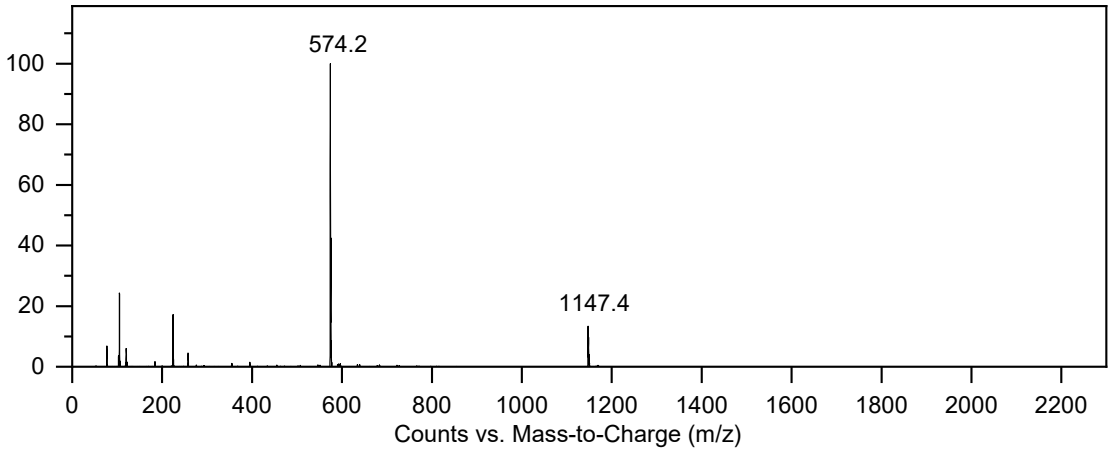

ESI-MS of $\mathbf{1}_{t3}$.



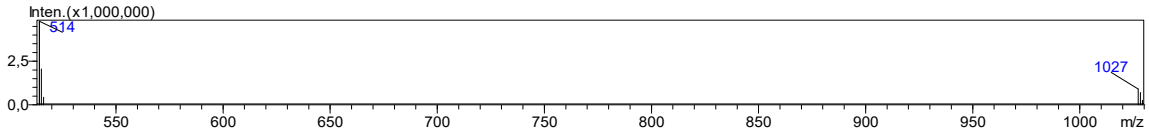

ESI-MS of $\mathbf{1}_{t4}$.



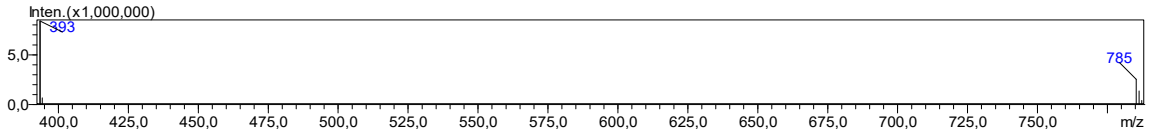
ESI-MS of $\mathbf{1}_{t5}$.




ESI-MS of $\mathbf{1}_{t6}$.

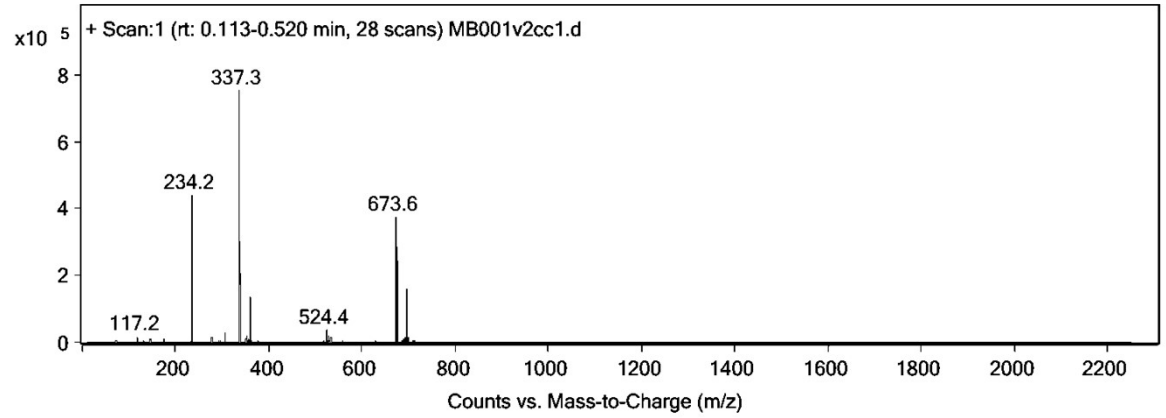



ESI-MS of $\mathbf{1}_{b}$

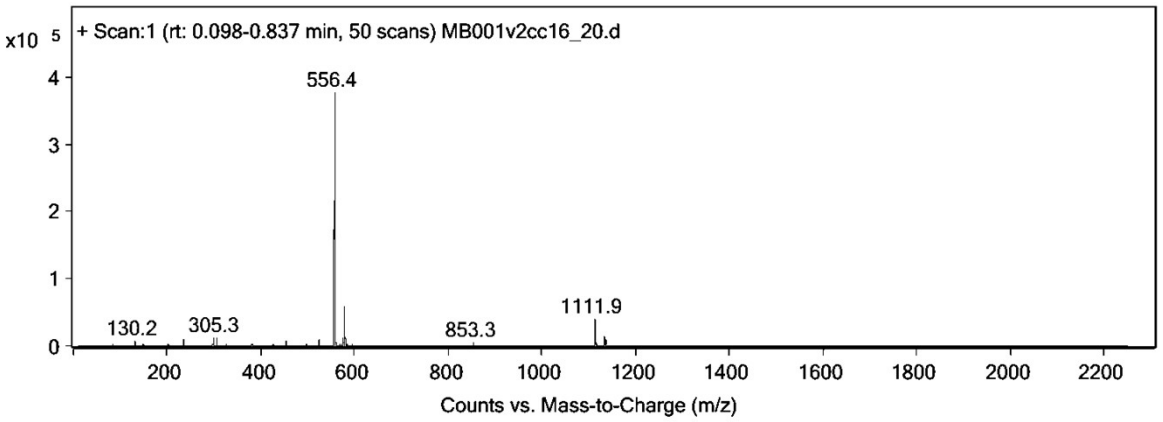


## 4.2. Reaction 1

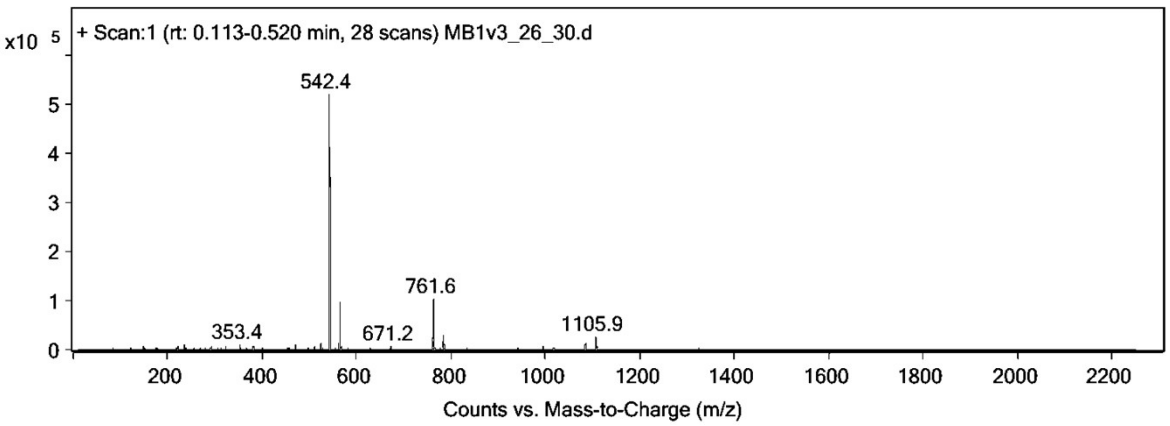
ESI-MS of $\mathbf{2_{m1}}$.



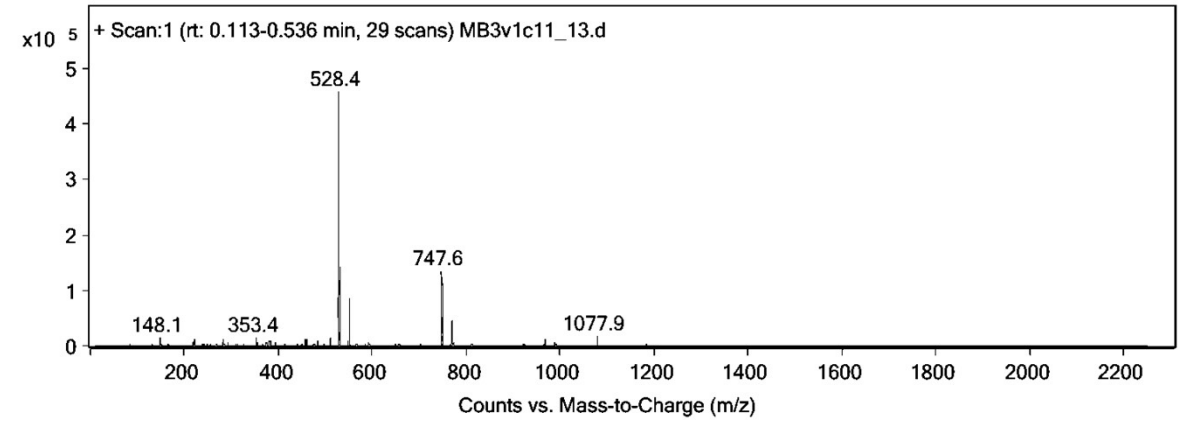

ESI-MS of $\mathbf{6_{m1}}$.




ESI-MS of $\mathbf{7_{m1}}$.

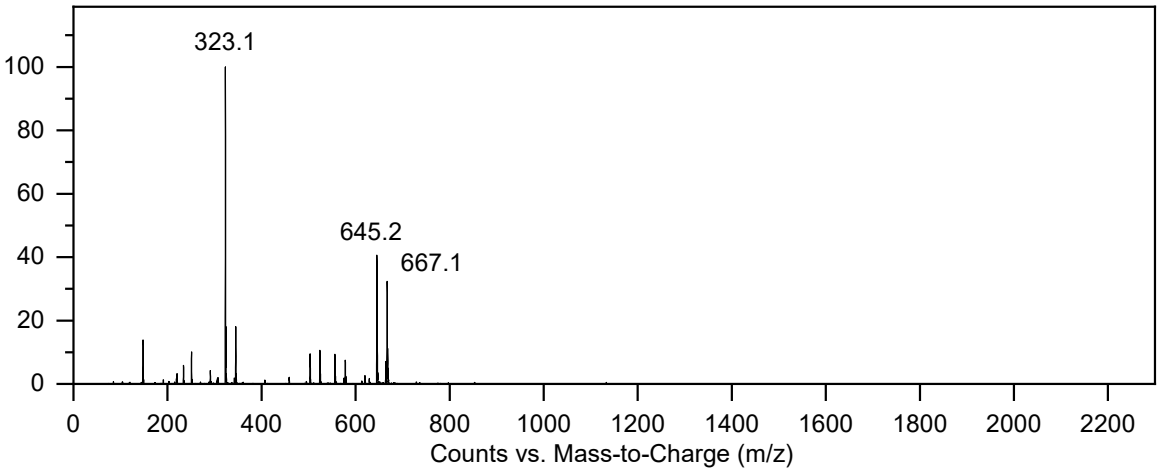


ESI-MS of $\mathbf{8_{m1}}$.



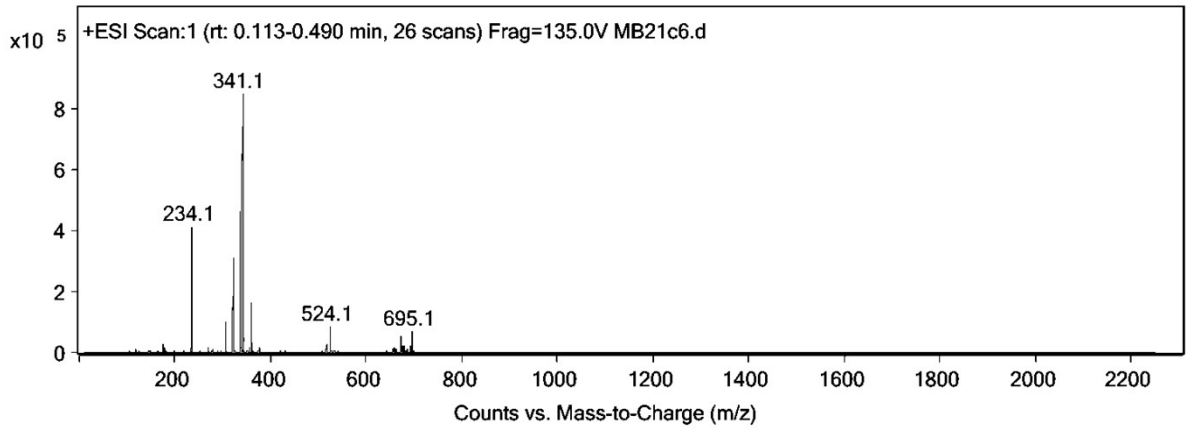

## 4.3. Reaction 5

ESI-MS of $\mathbf{3_{m1}}$.



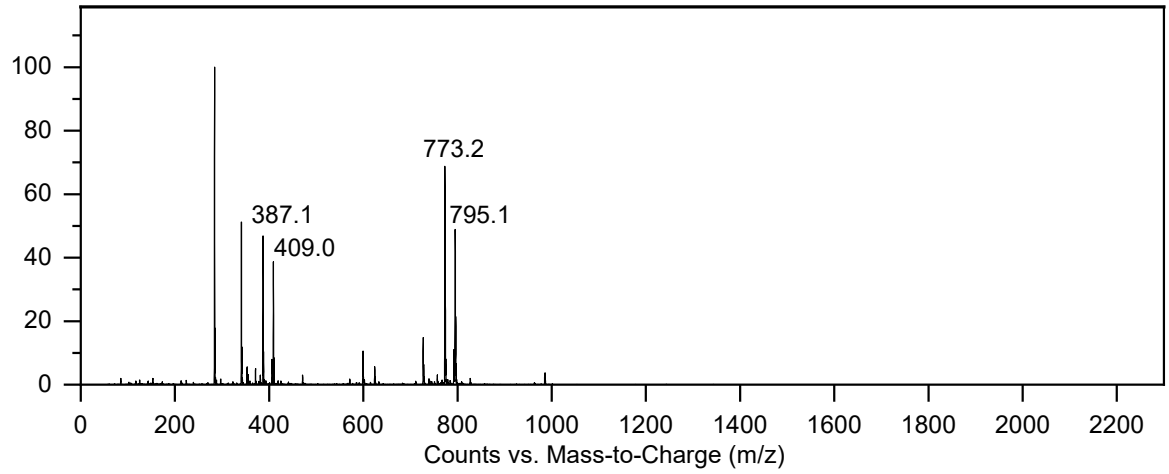

## 4.4. Reaction 7

ESI-MS of $\mathbf{2_p}$.

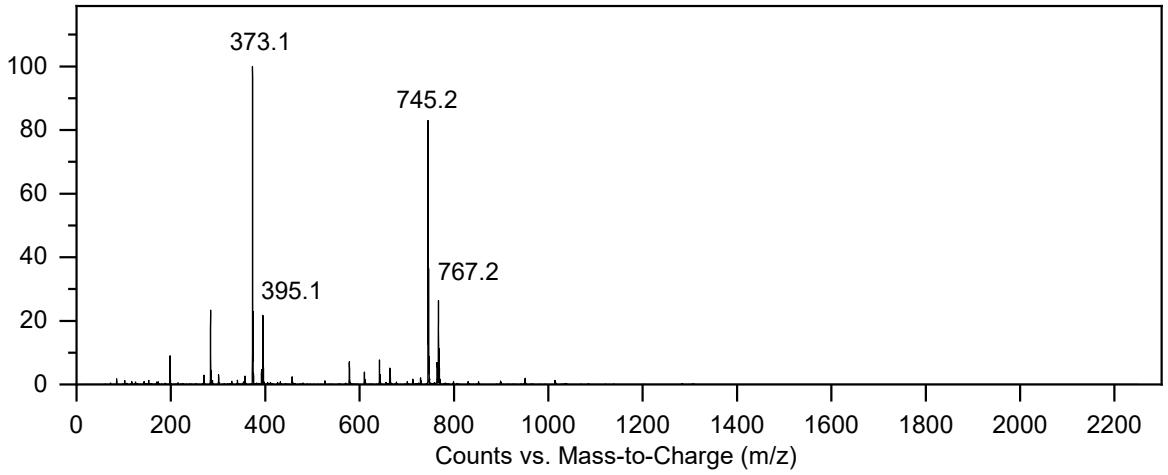


## 4.5. Reaction 13

ESI-MS of **$2_{n1}$**.

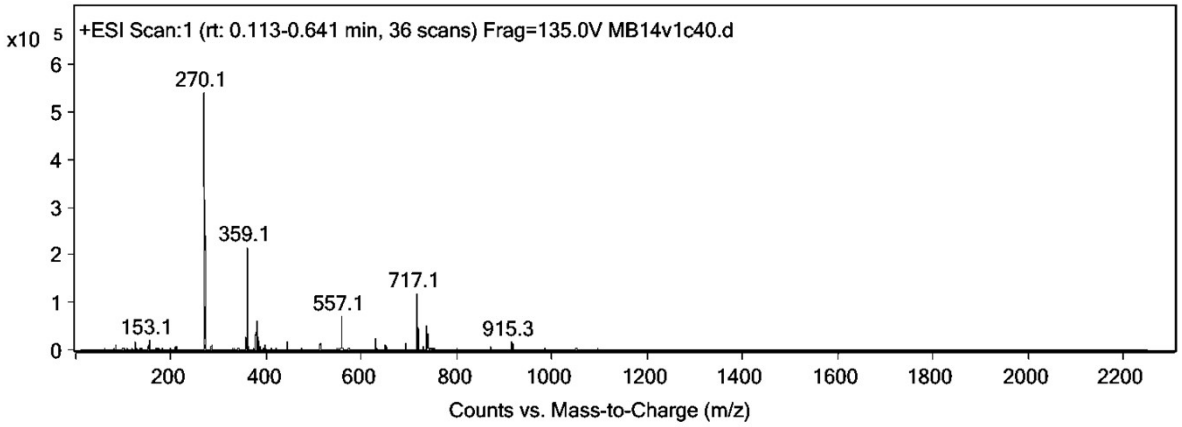



ESI-MS of **$3_{n1}$**.

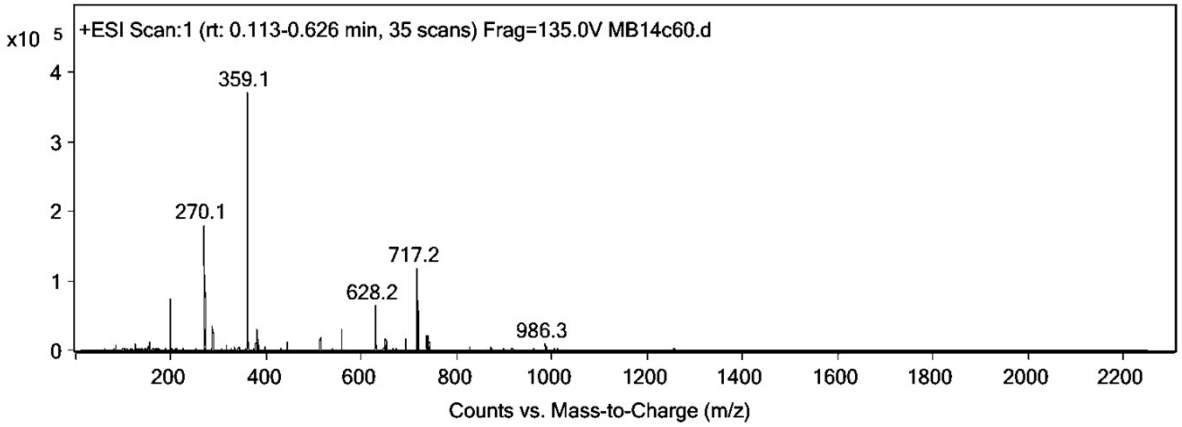


## 4.6. Reaction 14

ESI-MS of $\mathbf{2}_{n2}$.

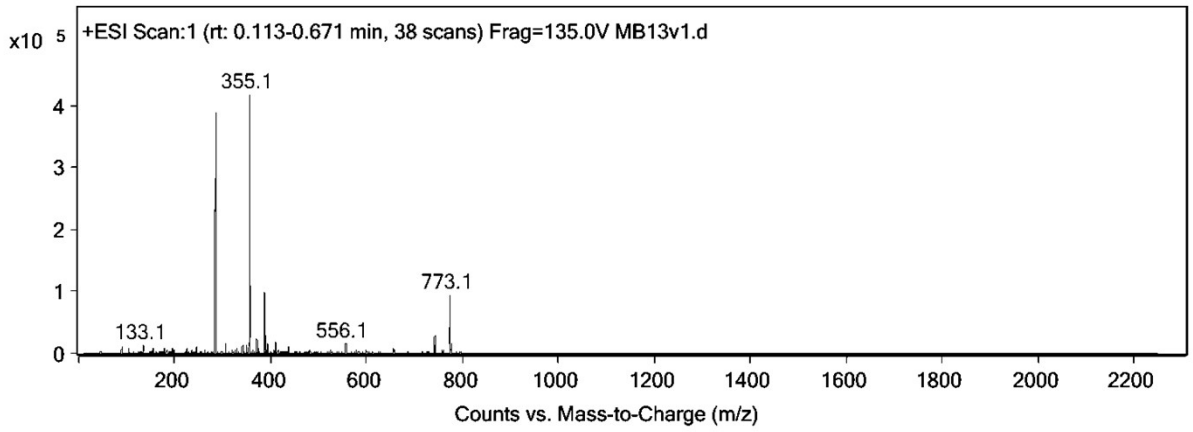



ESI-MS of $\mathbf{3}_{n2}$.

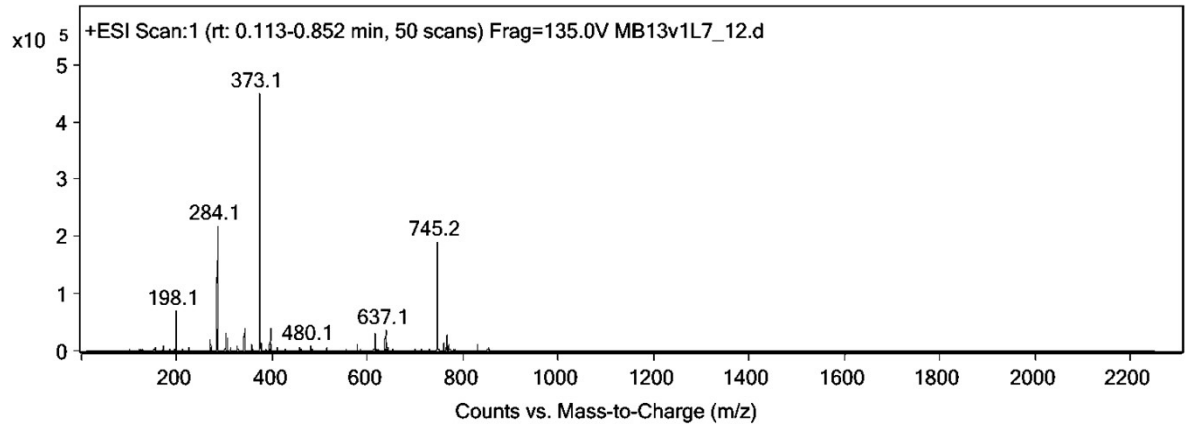


## 4.7. Reaction 15

ESI-MS of $\mathbf{2}_{n3}$.

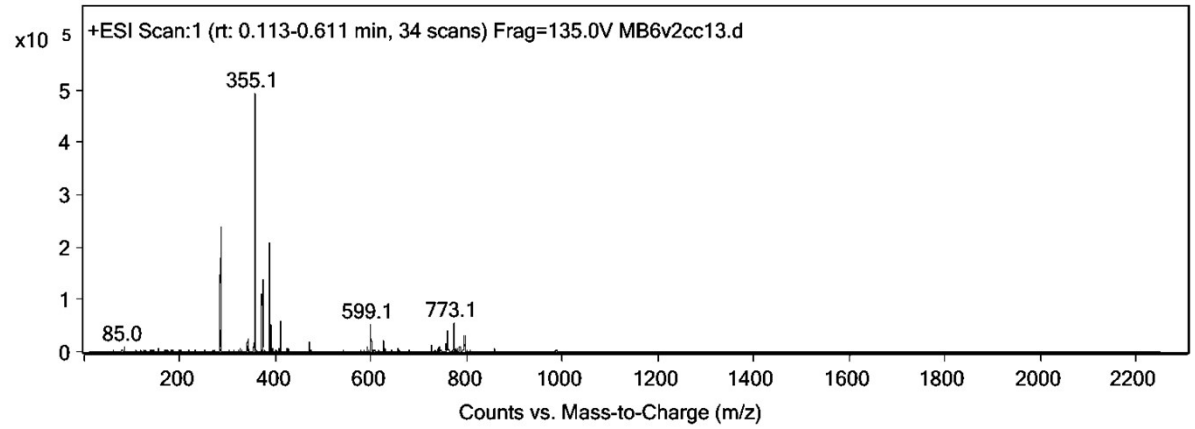



ESI-MS of $\mathbf{3}_{n3}$.

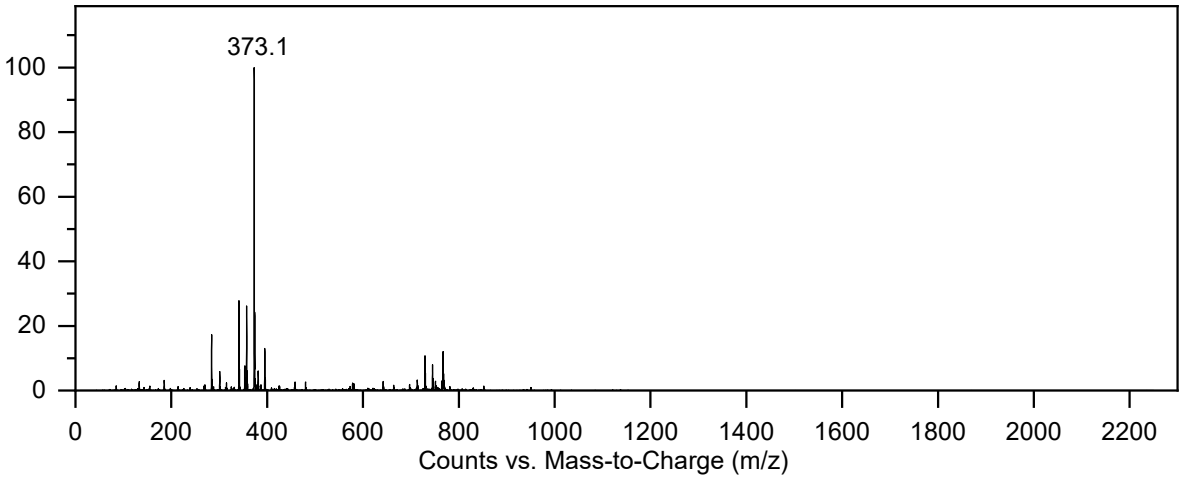


## 4.8. Reaction 16

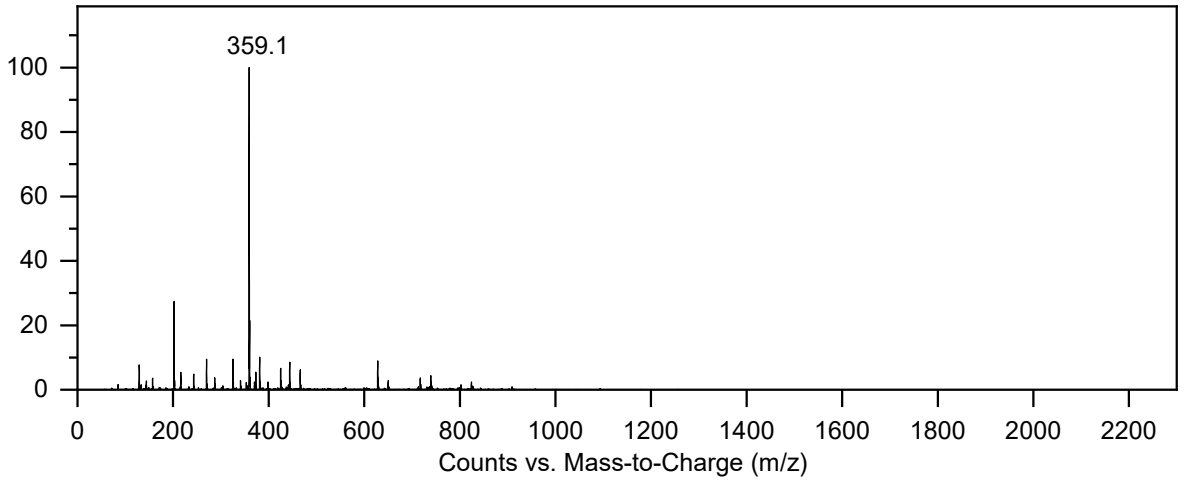
ESI-MS of **2**$_{n4}$.




ESI-MS of **3**$_{n4}$.

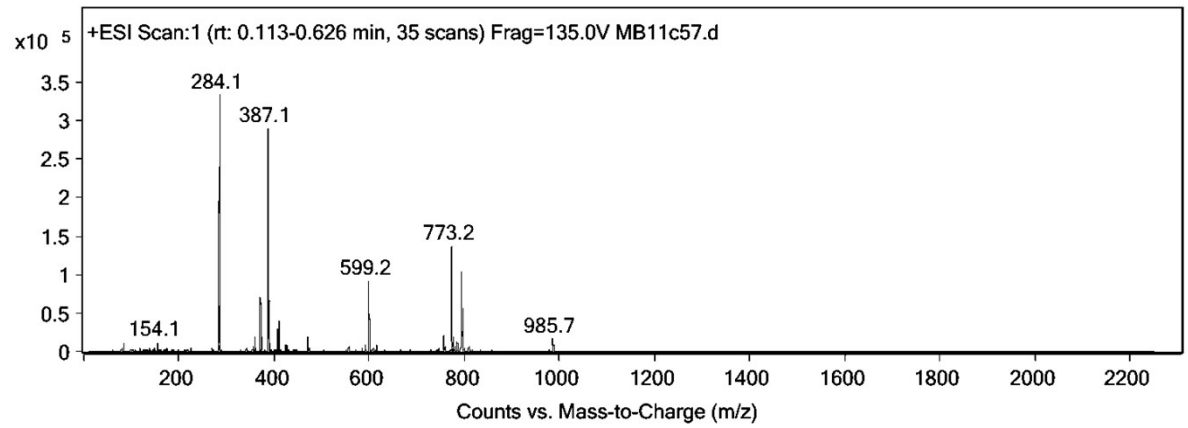



ESI-MS of **4**$_{n4}$.

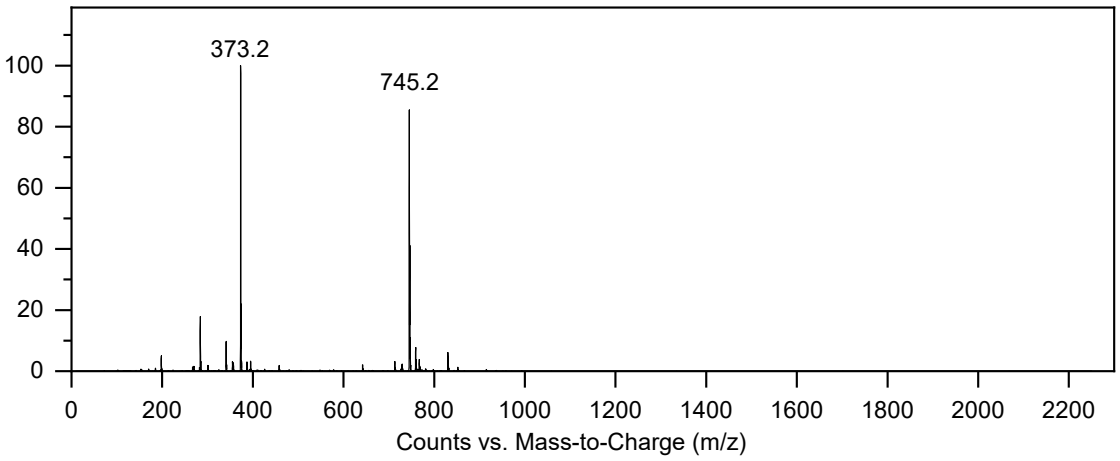


## 4.9. Reaction 17

ESI-MS of $\mathbf{2}_{n5}$.

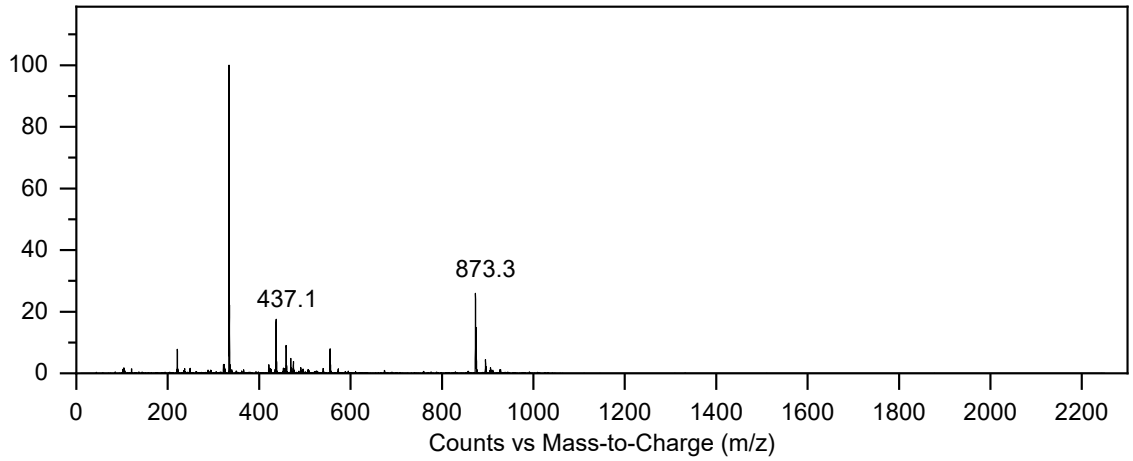



ESI-MS of $\mathbf{3}_{n5}$.

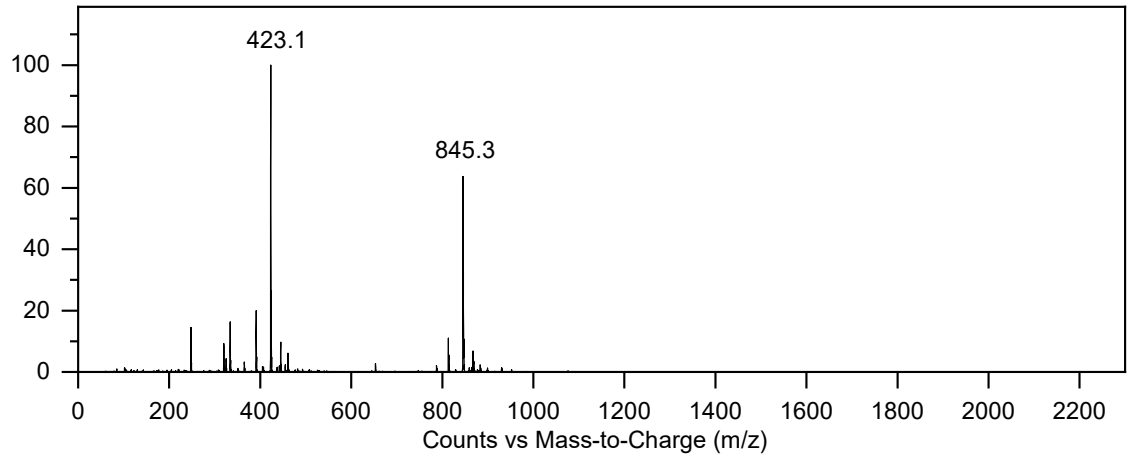


## 4.10. Reaction 18

ESI-MS of $\mathbf{2_{a1}}$.

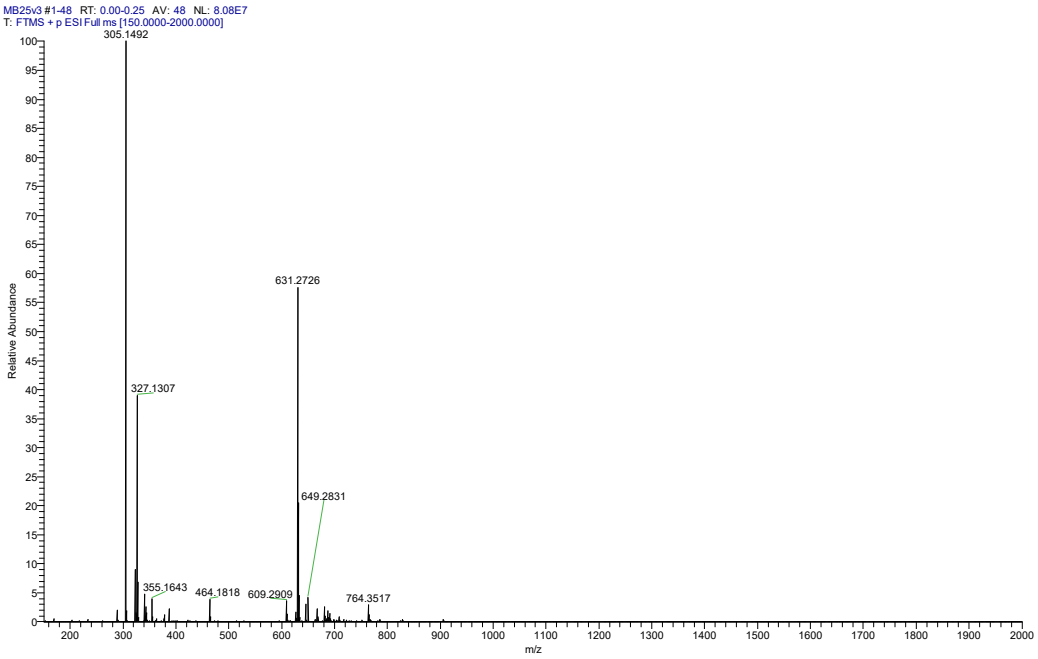



ESI-MS of $\mathbf{3_{a1}}$.

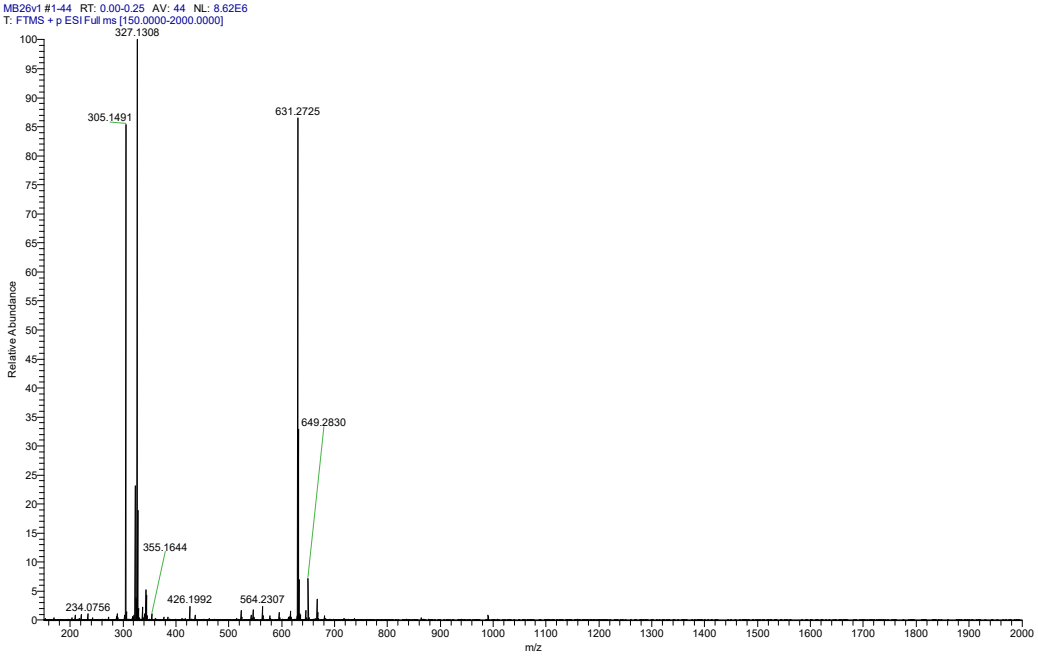


## 5. HRMS

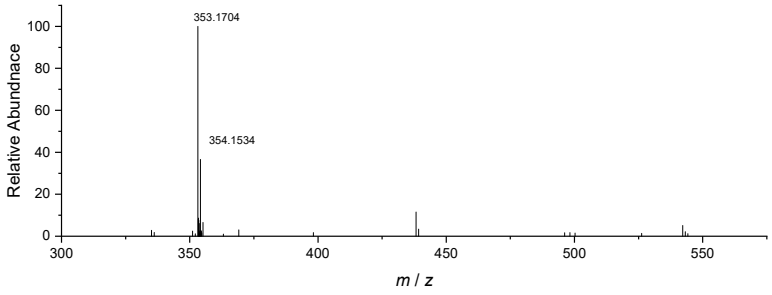
### ESI-HRMS of $\mathbf{1_{m1}}$.



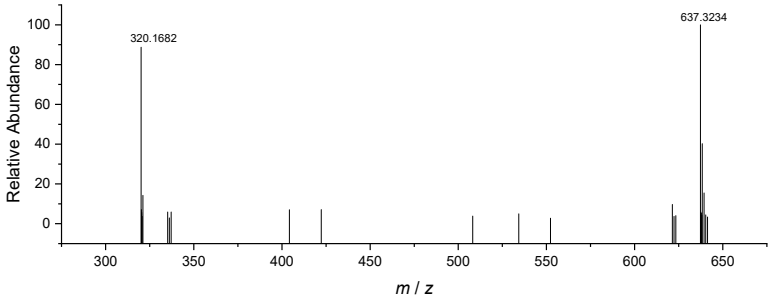

### ESI-HRMS of $\mathbf{1_{p}}$.



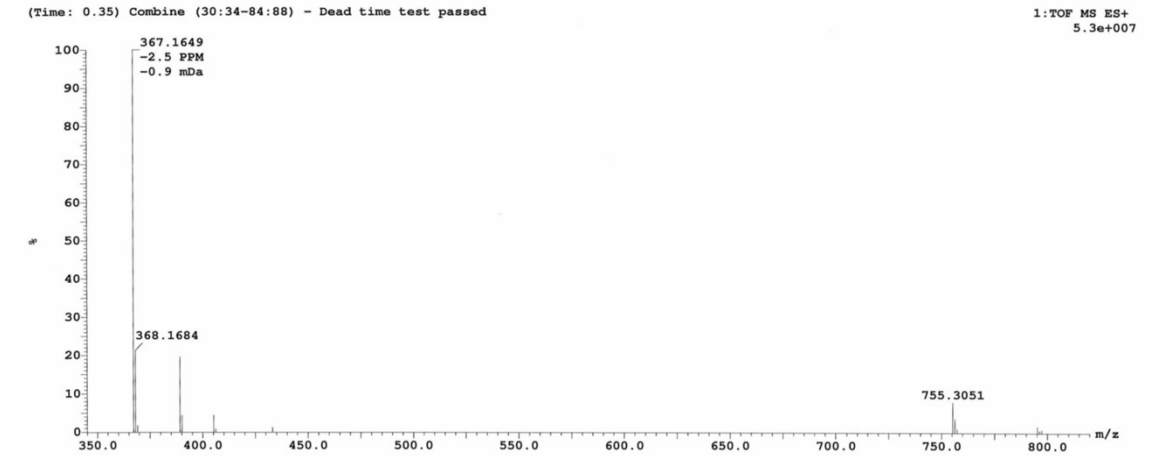
MALDI-HRMS of $\mathbf{1_{m2}}$.



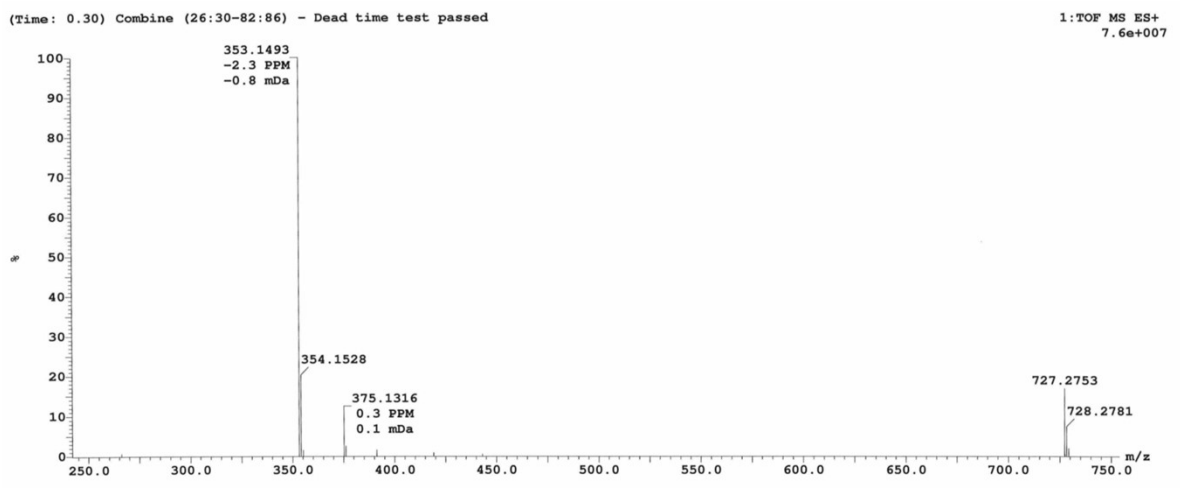

MALDI-HRMS of $\mathbf{1_{m3}}$.



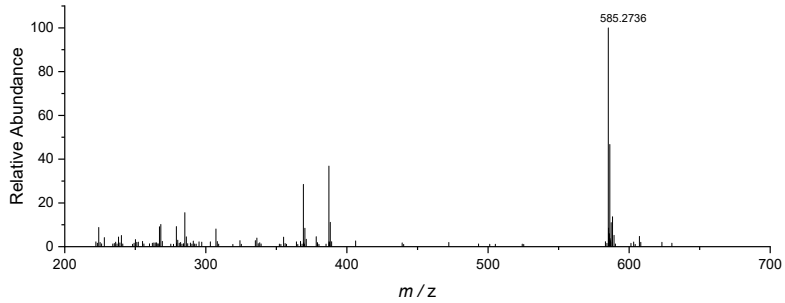

ESI-TOF-HRMS of $\mathbf{1_{m4}}$.



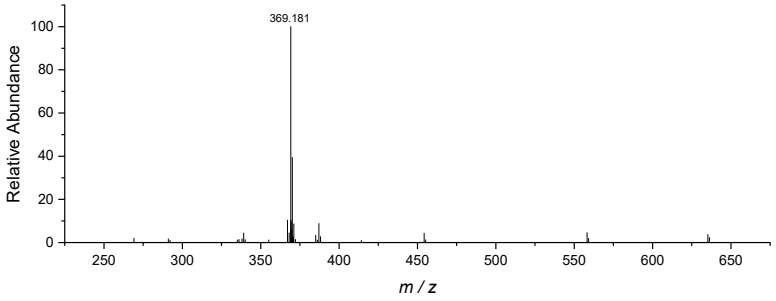
ESI-TOF-HRMS of $\mathbf{1}_{m5}$.



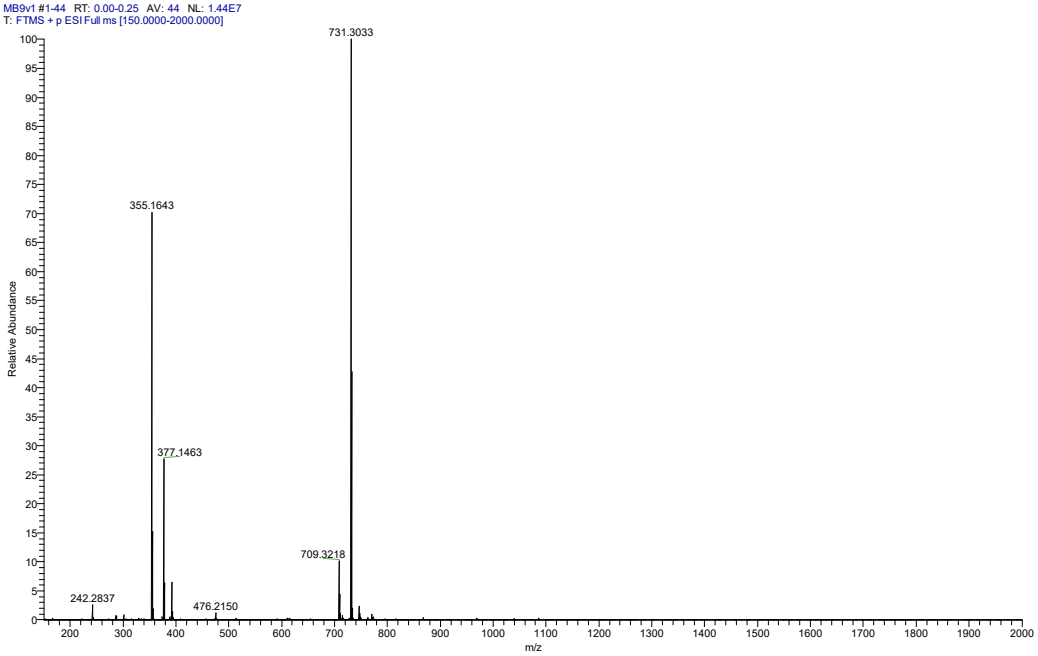

MALDI-HRMS of $\mathbf{1}_{m6}$.



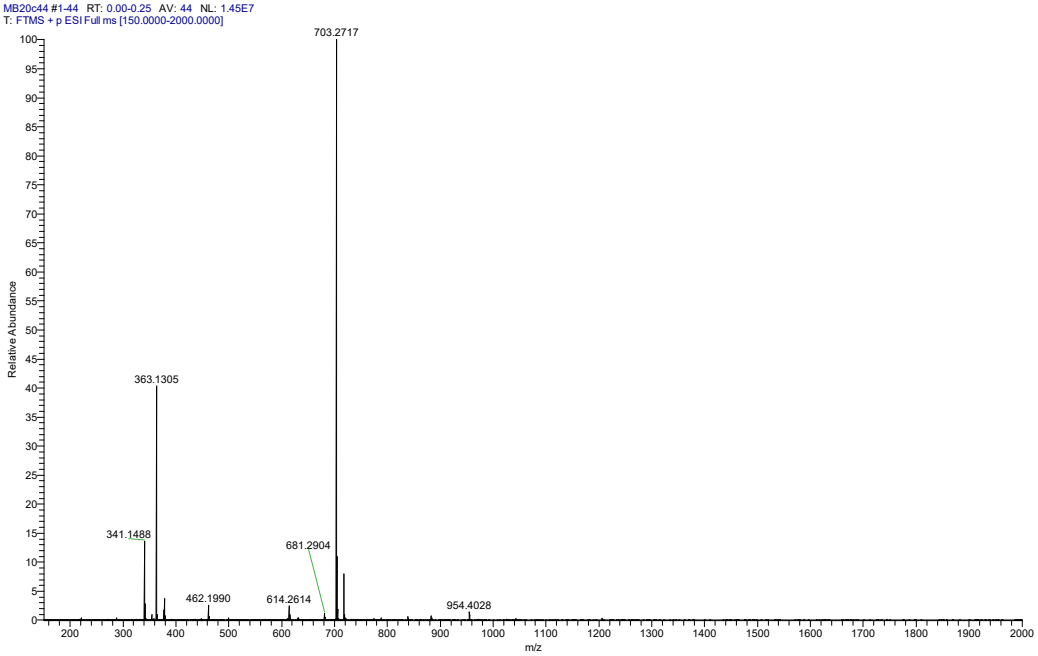

MALDI-HRMS of $\mathbf{1}_{m7}$.



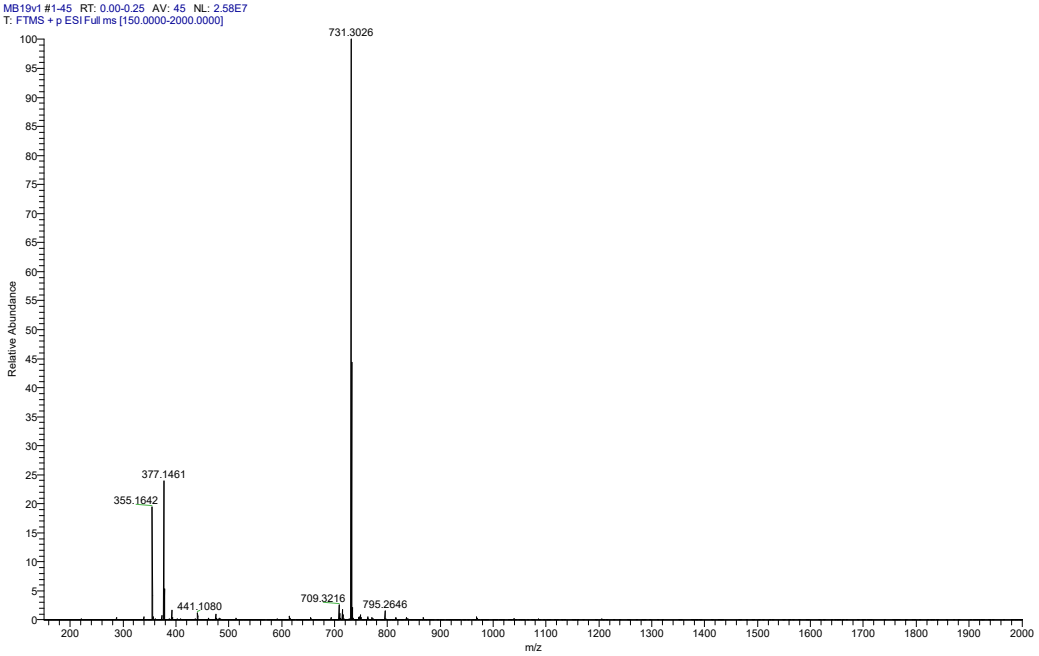
ESI-HRMS of $\mathbf{1_{n1}}$.



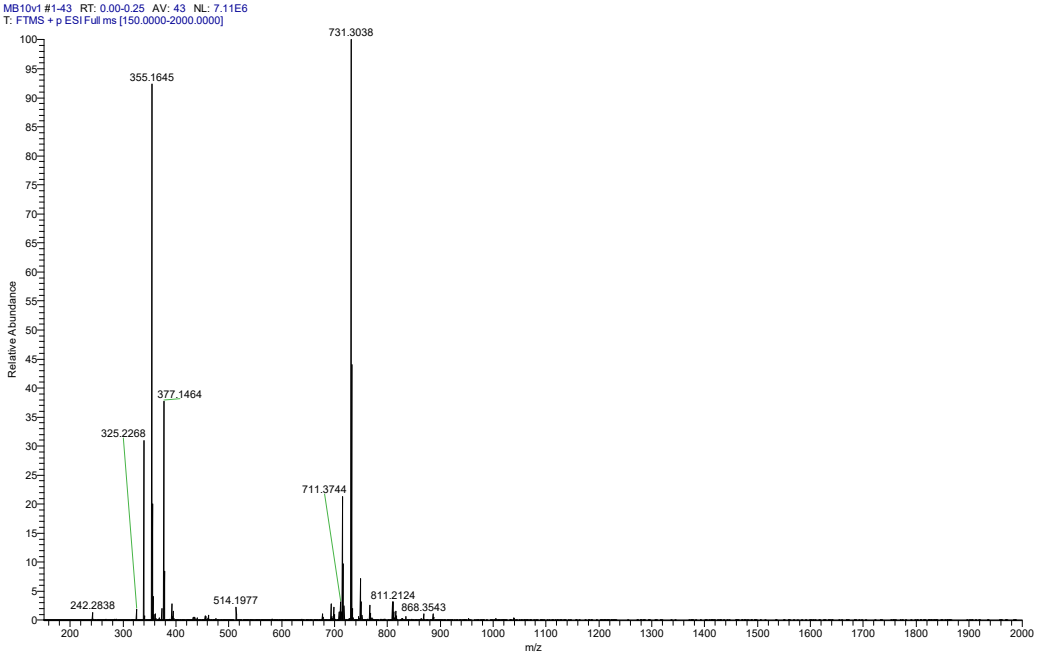

ESI-HRMS of $\mathbf{1_{n2}}$.



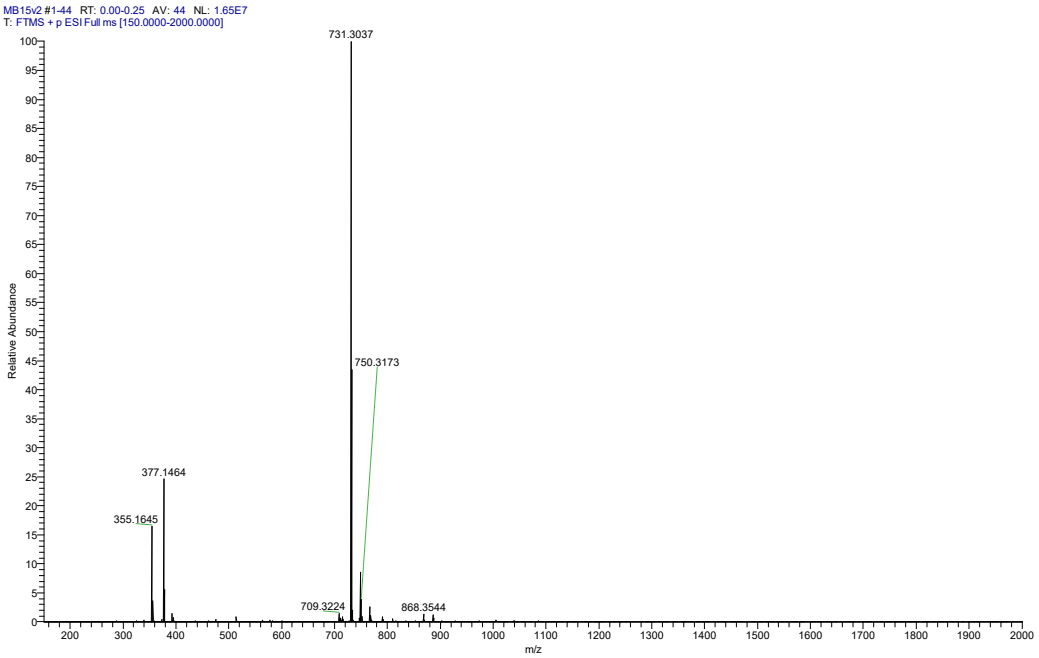
ESI-HRMS of $\mathbf{1}_{n3}$.



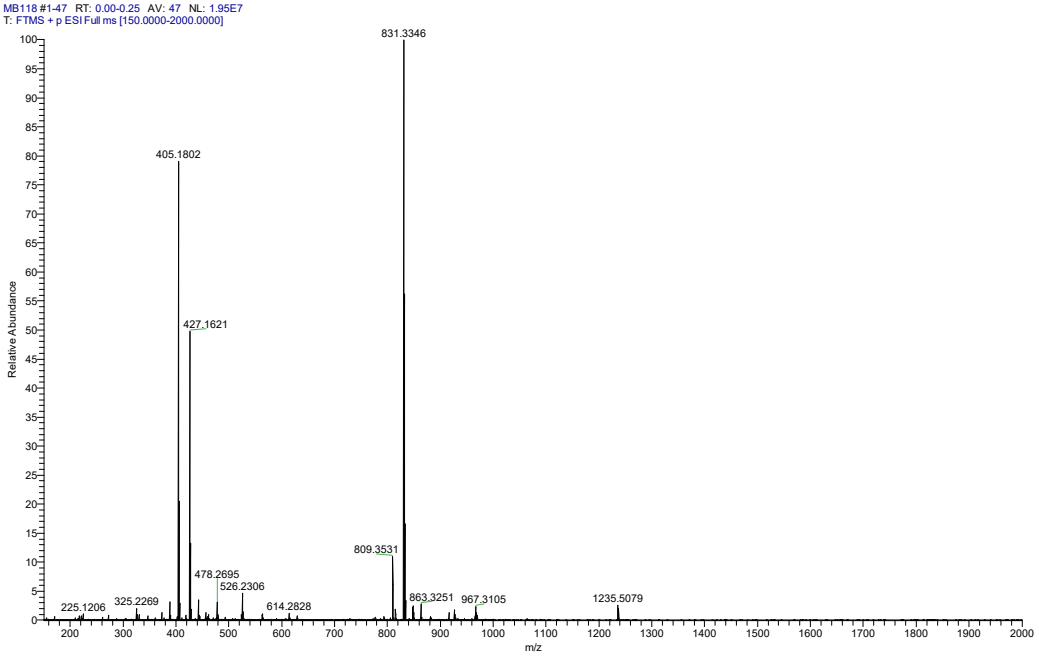

ESI-HRMS of $\mathbf{1}_{n4}$.



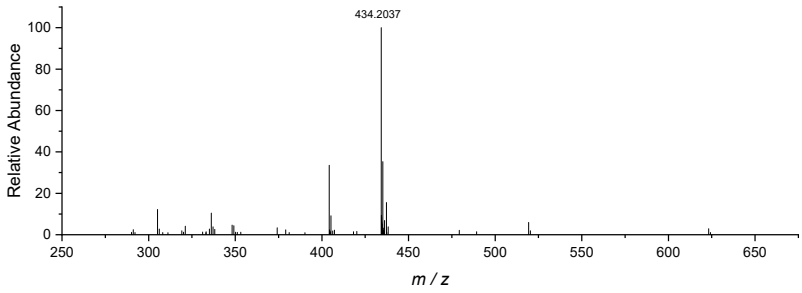
ESI-HRMS of $\mathbf{1}_{\mathbf{n5}}$.



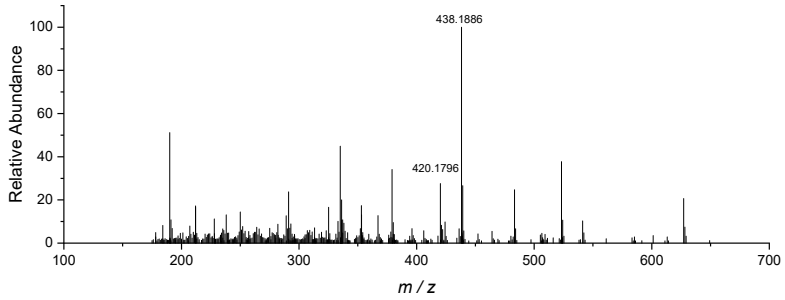

ESI-HRMS of $\mathbf{1}_{\mathbf{a1}}$.



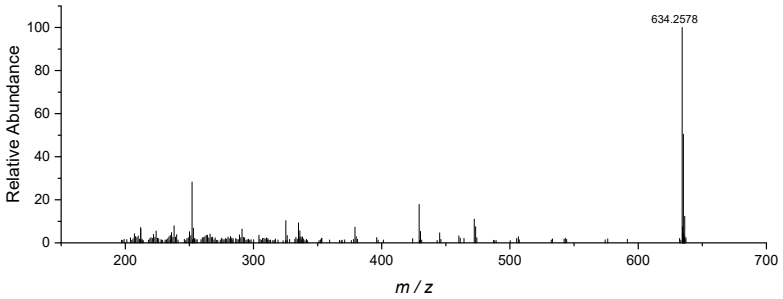
MALDI-HRMS of $\mathbf{1_{t1}}$.



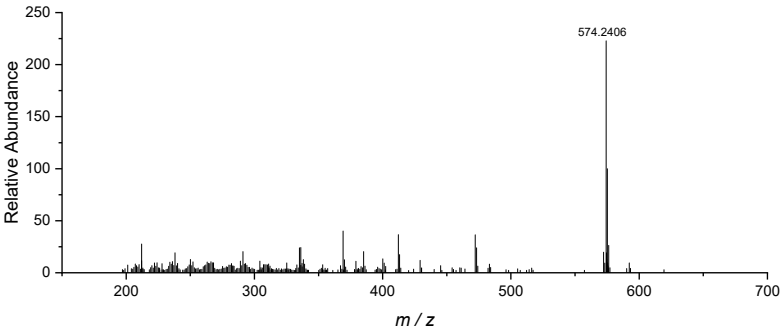

MALDI-HRMS of $\mathbf{1_{t2}}$.



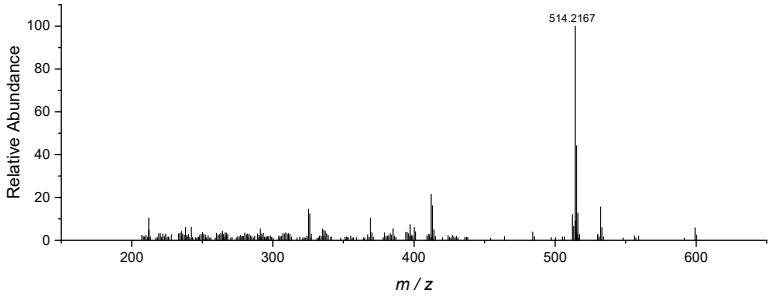

MALDI-HRMS of $\mathbf{1_{t3}}$.



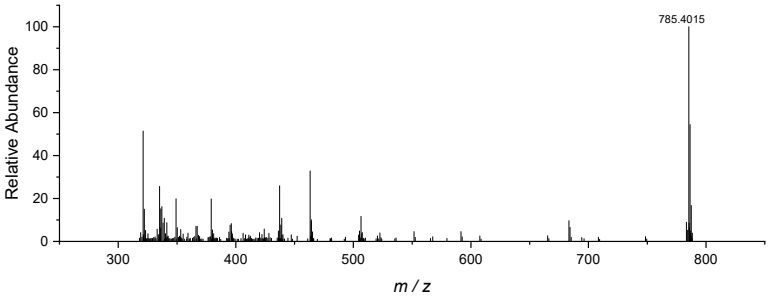

MALDI-HRMS of $\mathbf{1_{t5}}$.



MALDI-HRMS of $\mathbf{1_{t6}}$.

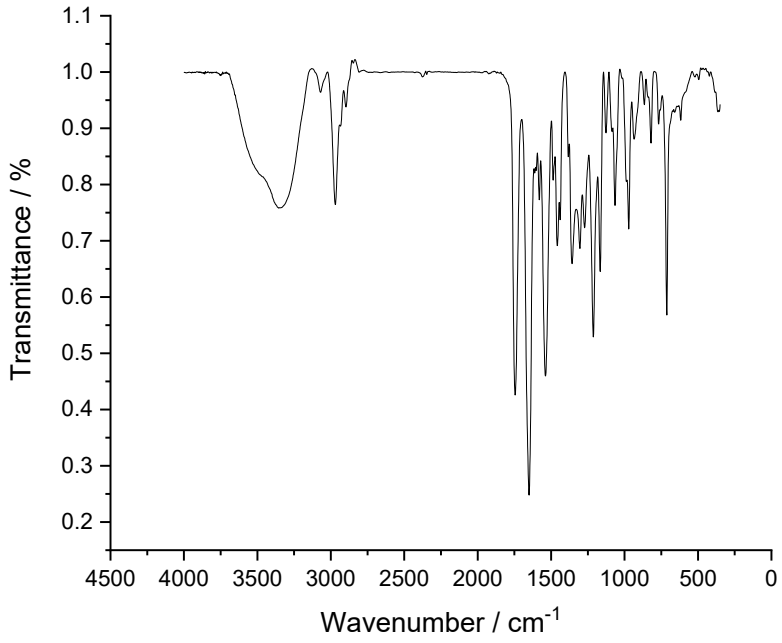



MALDI-HRMS of $\mathbf{1_b}$.

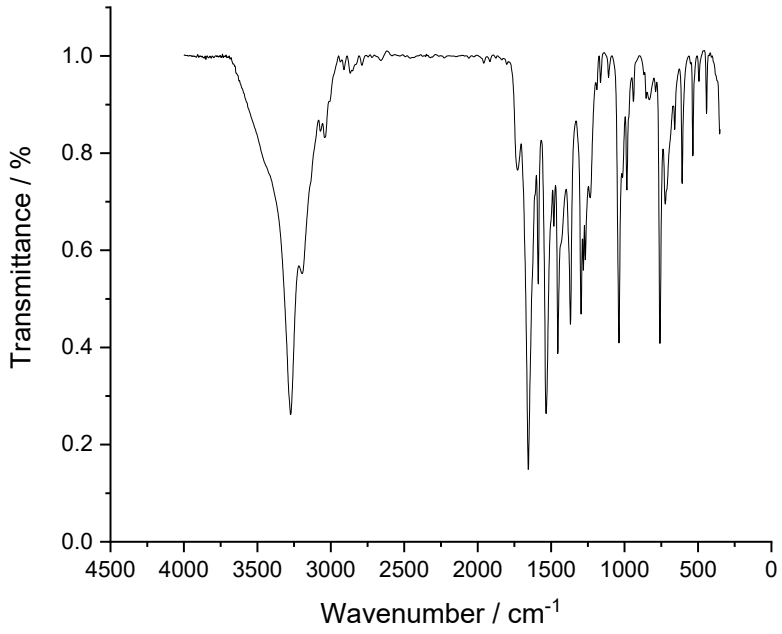


## 6. IR spectra.

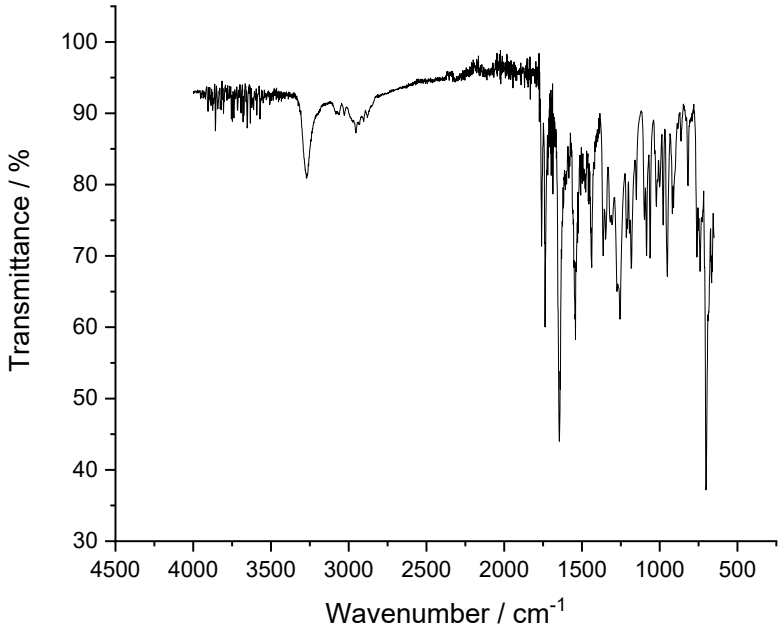
IR (KBr) of $\mathbf{1_{m1}}$.



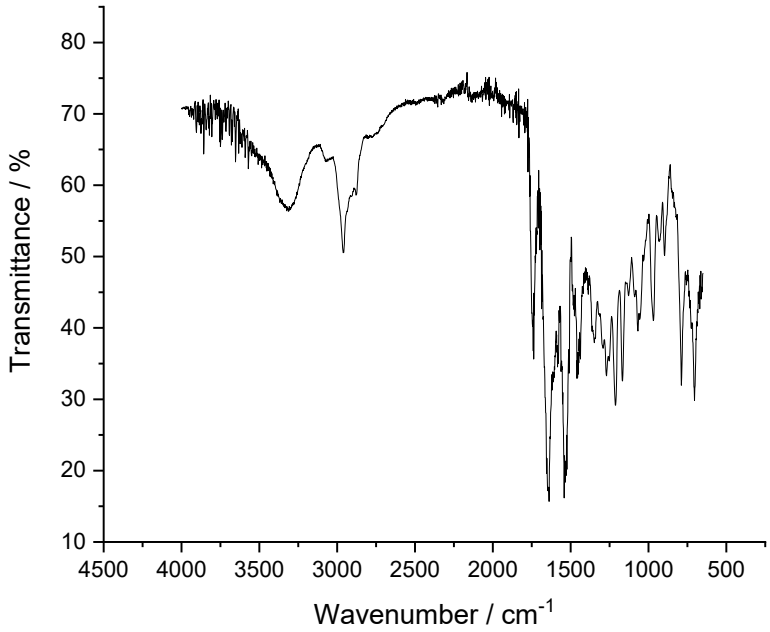

IR (KBr) of $\mathbf{1_{p1}}$.



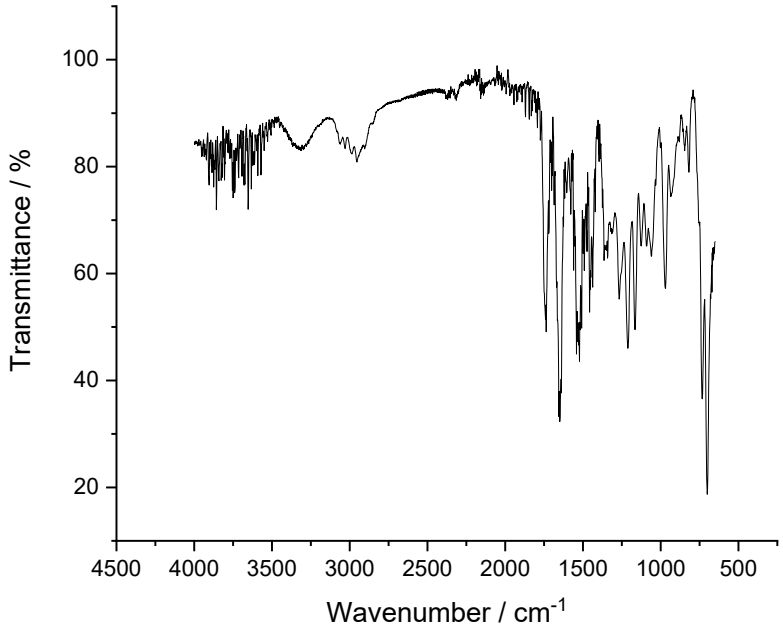
IR (ATR) of $\mathbf{1_{m2}}$.



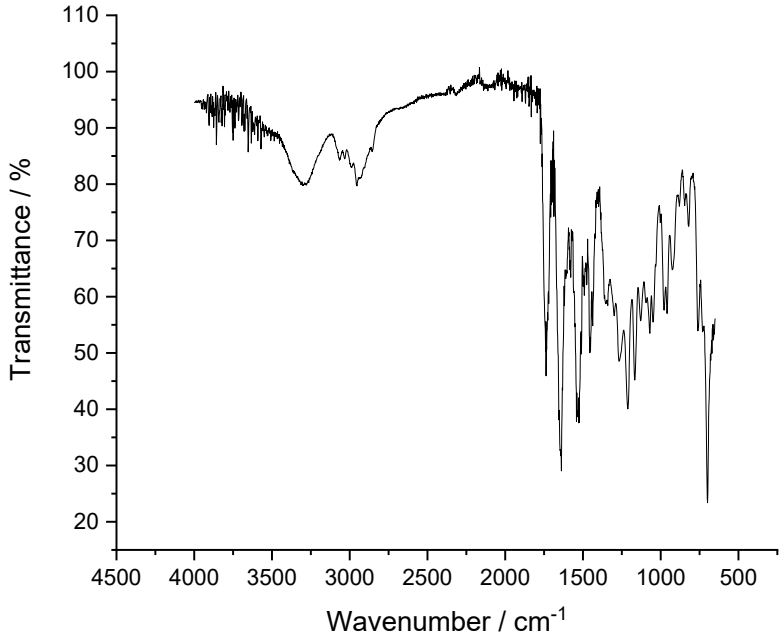

IR (ATR) of $\mathbf{1_{m3}}$.



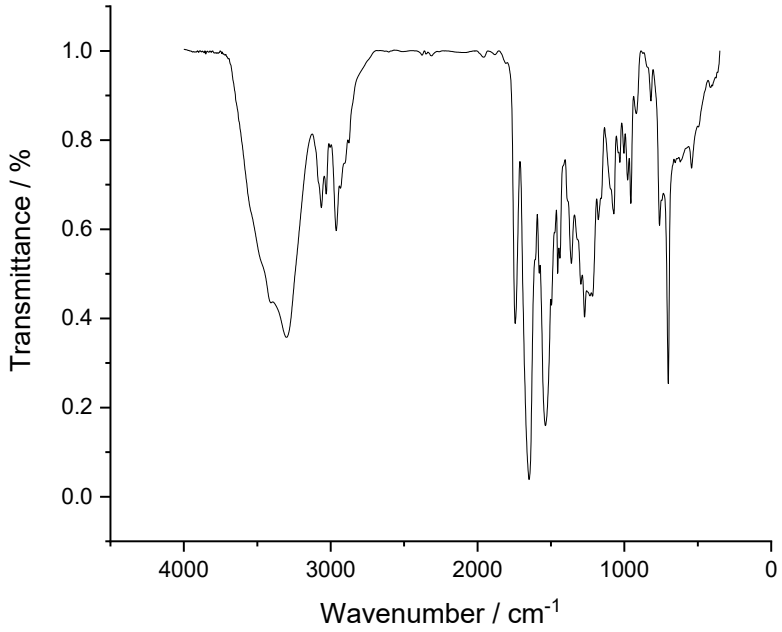
IR (ATR) of $\mathbf{1}_{\mathbf{m4}}$.



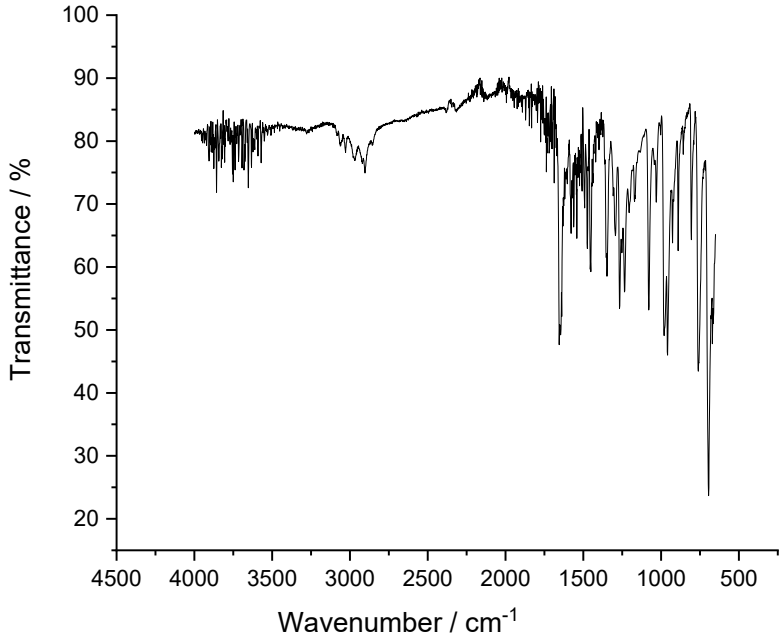

IR (ATR) of $\mathbf{1}_{\mathbf{m5}}$.



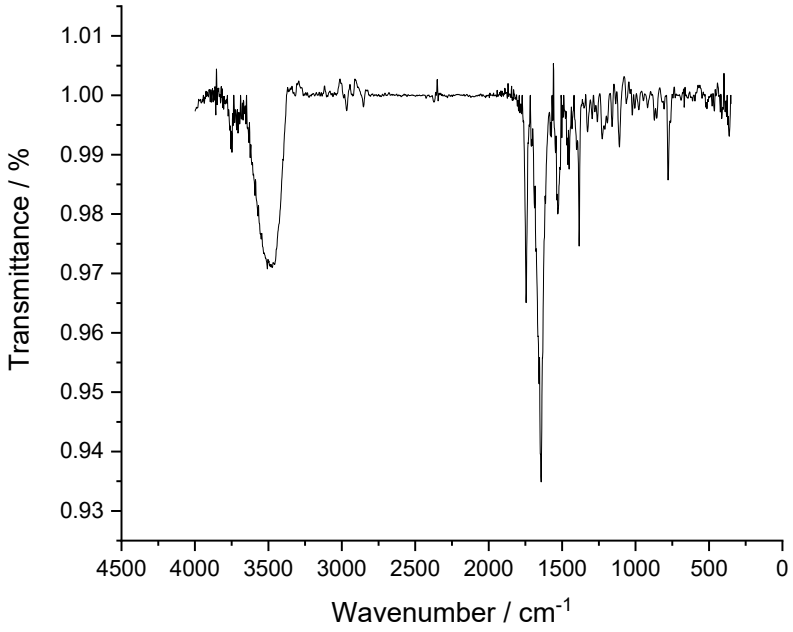
IR (KBr) of $\mathbf{1_{m6}}$.



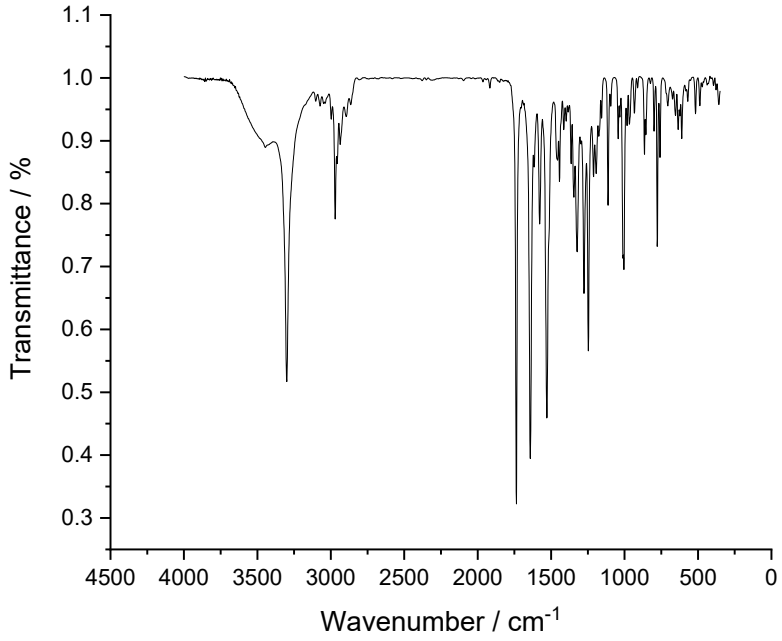

IR (ATR) of $\mathbf{1_{m7}}$.



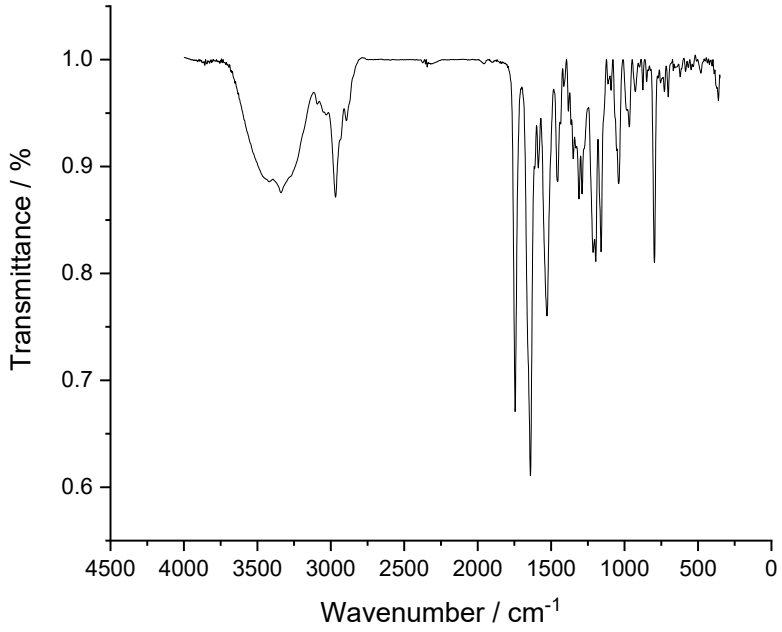
IR (KBr) of $\mathbf{1_{n1}}$.



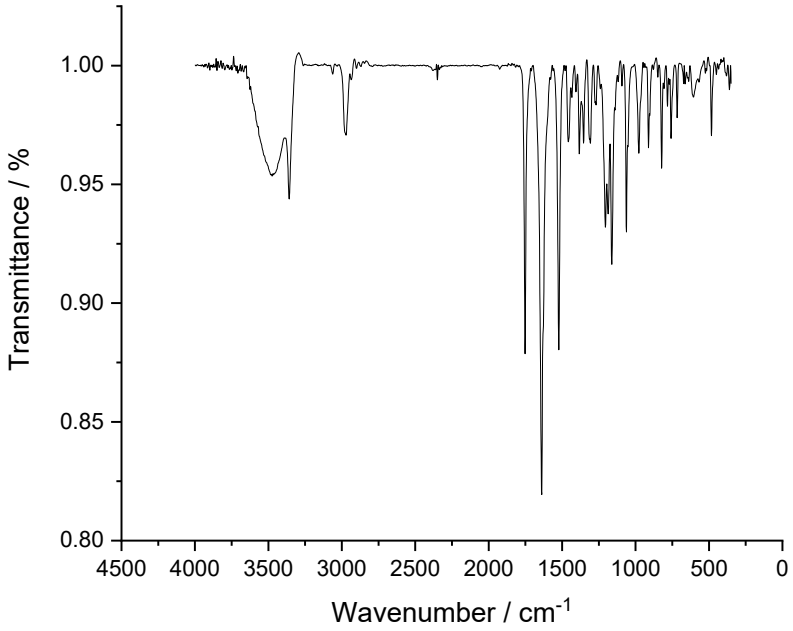

IR (KBr) of $\mathbf{1_{n2}}$.



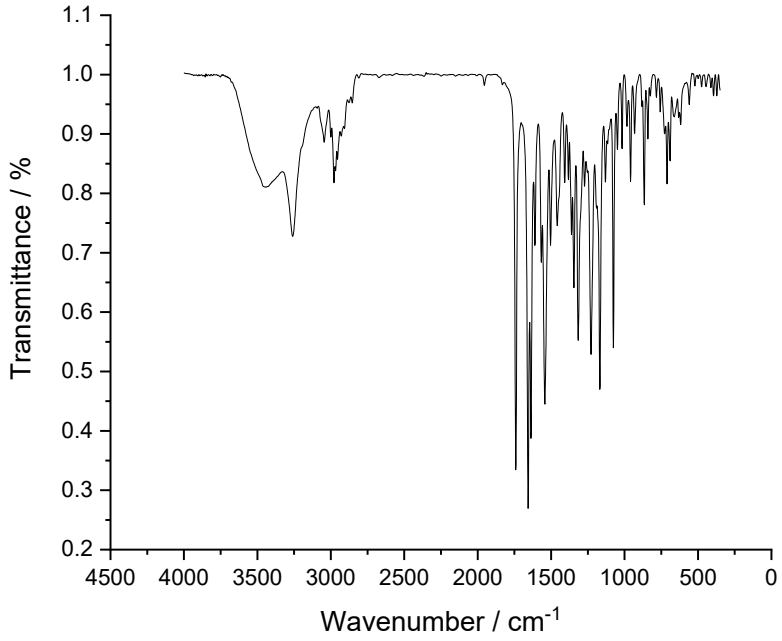
IR (KBr) of $\mathbf{1_{n3}}$.



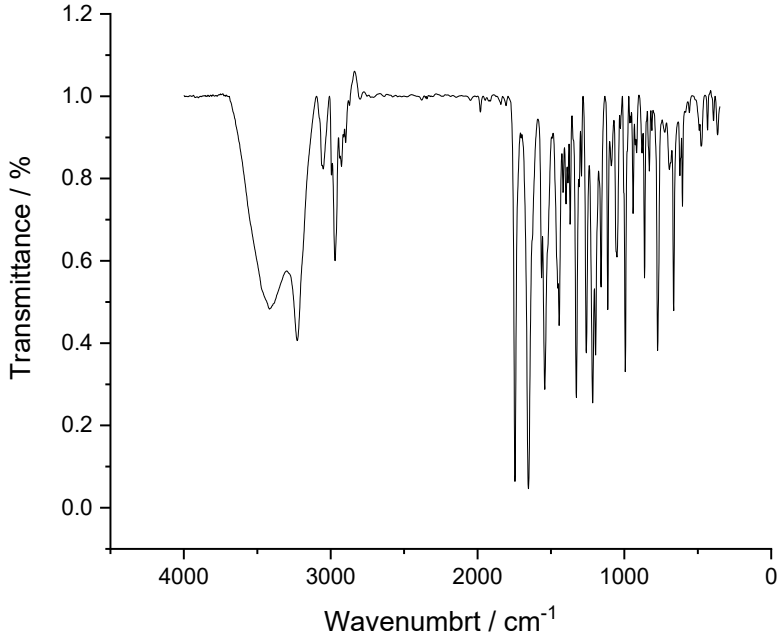

IR (KBr) of $\mathbf{1_{n4}}$.



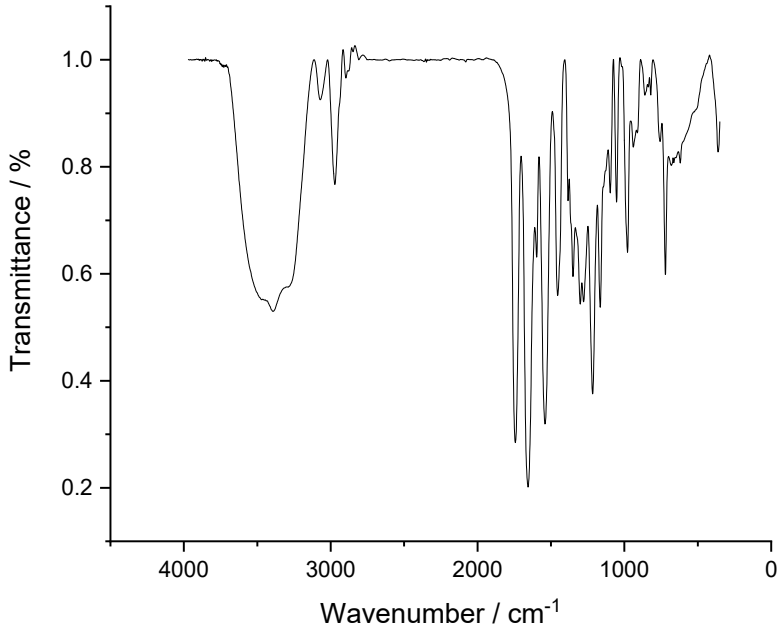
IR (KBr) of $\mathbf{1_{n5}}$.



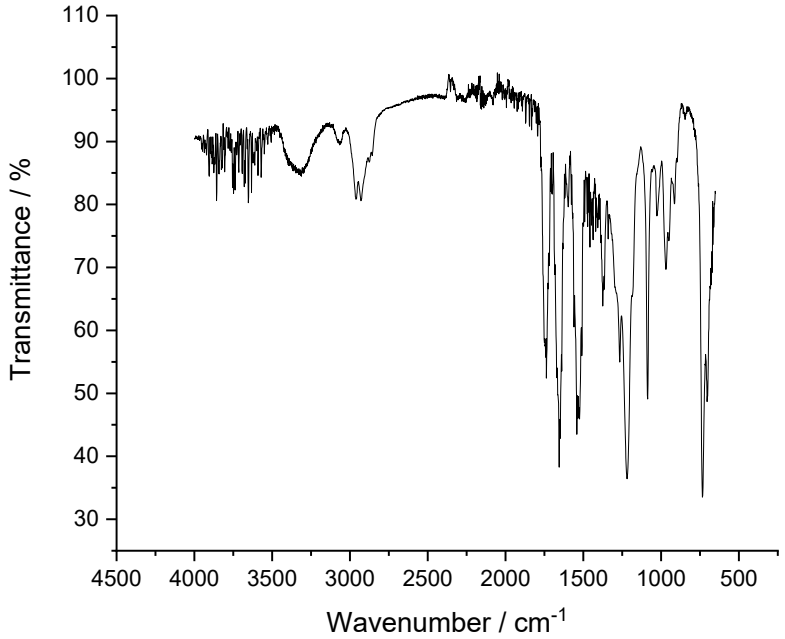

IR (KBr) of $\mathbf{1_{a1}}$.



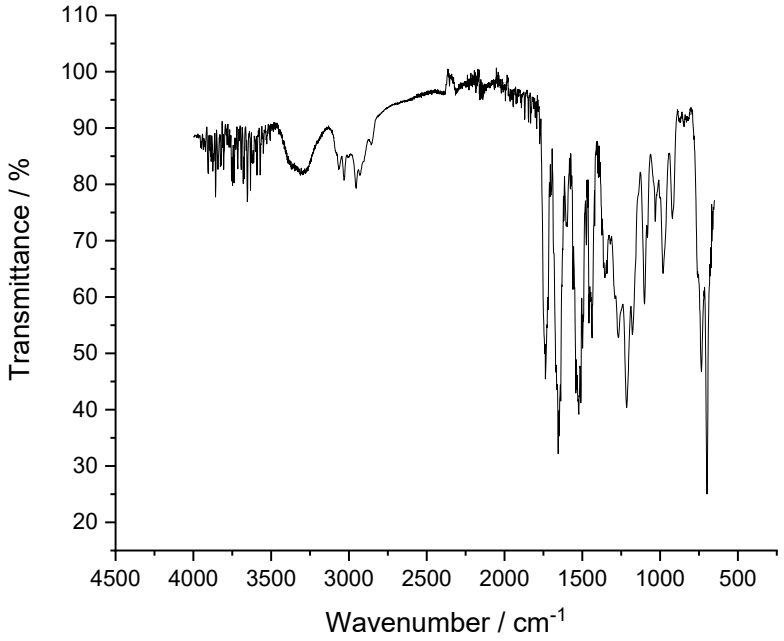
IR (KBr) of $\mathbf{1_{t1}}$.



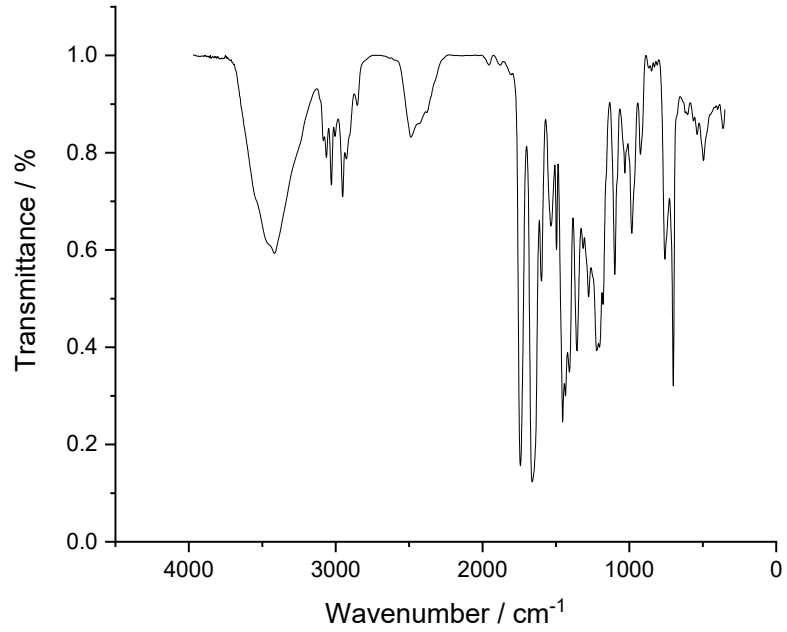

IR (ATR) of $\mathbf{1_{t2}}$.



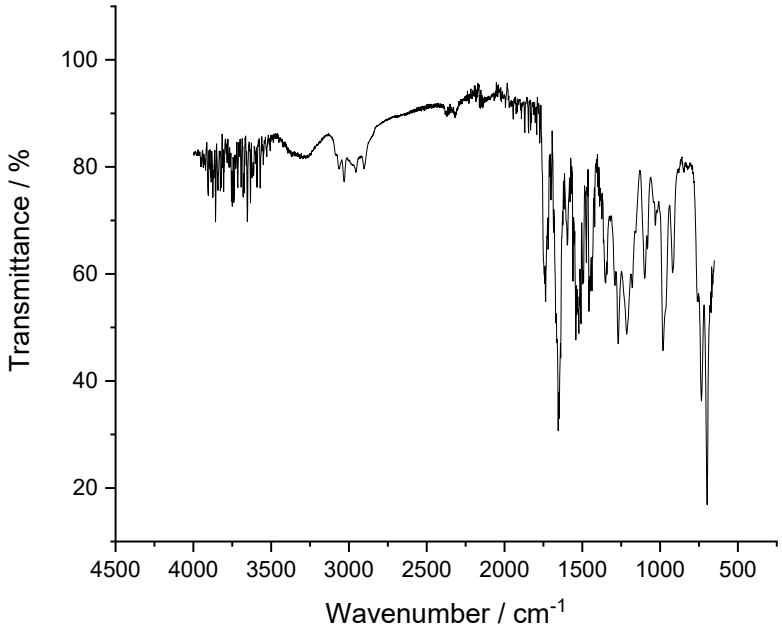
IR (ATR) of $\mathbf{1_{t3}}$.



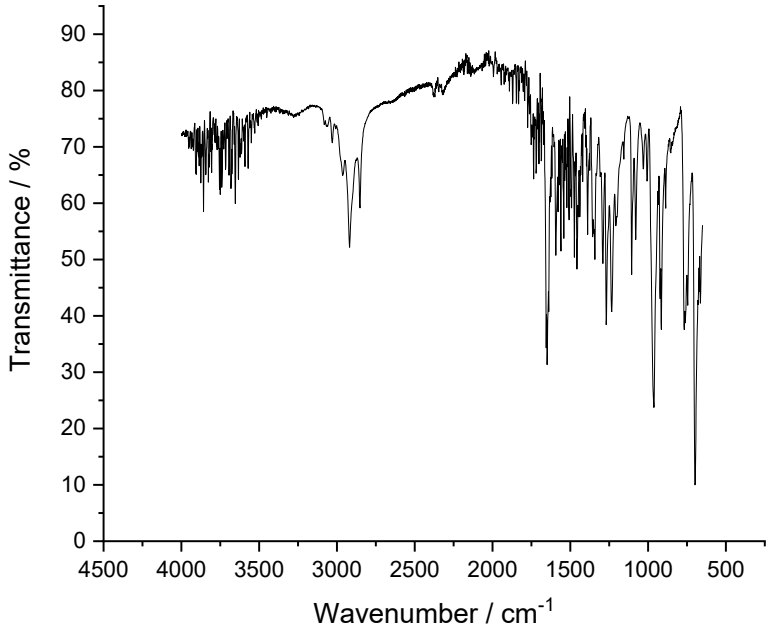

IR (KBr) of $\mathbf{1_{t4}}$.



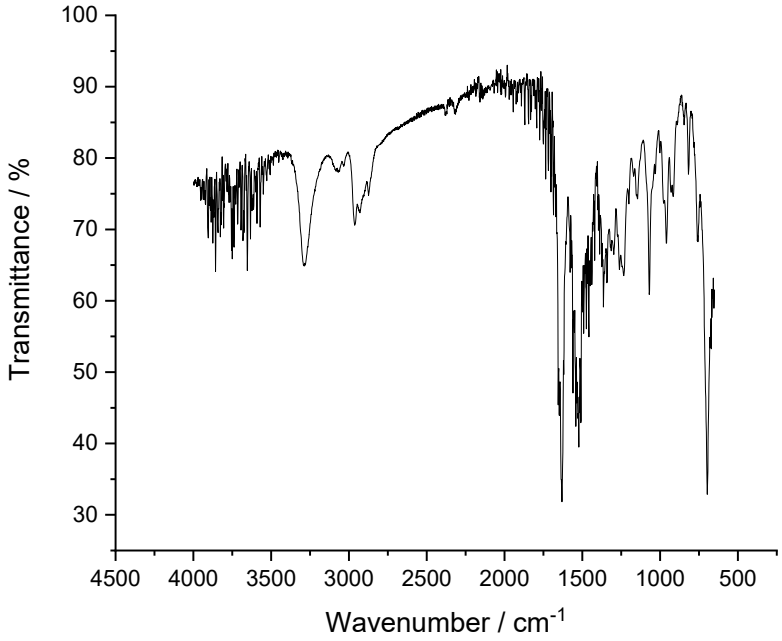
IR (ATR) of $\mathbf{1}_{t5}$.




IR (ATR) of $\mathbf{1}_{t6}$.



IR (ATR) of $\mathbf{1_b}$.



## 7. X-ray single crystal structures.

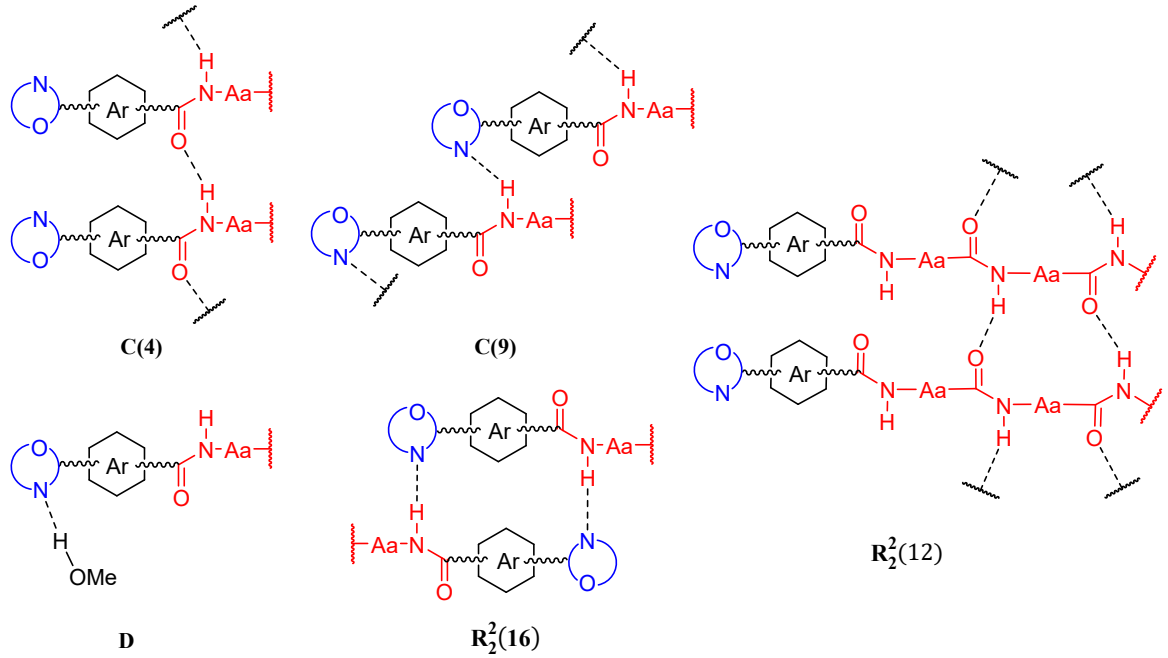



Figure S9. Types of hydrogen bonding interactions that occur in obtained crystal structures. Details are given in Table S5.

Table S5. Types of graph set motifs that appear in each oxazoline compound.

| Oxazoline | Types of hydrogen bonding |
|---|---|
| $\mathbf{1_{p1}}$ | **C(9)** |
| $\mathbf{1_{m6}}^*$ | **C(4)C(4)D**$\mathbf{R_2^2(12)}$* |
| $\mathbf{1_{n2}}$ | **C(4)** |
| $\mathbf{1_{n4}}$ | **C(4)** |
| $\mathbf{1_{n5}}$ | **C(4)** |
| $\mathbf{1_{a1}}$ | **C(9)** |
| $\mathbf{1_{t4}}$ | **C(4)**$\mathbf{R_2^2(16)}$ |

* $\mathbf{R_2^2(12)}$ is a binary graph set motif

Structures of similar oxazoline compounds with motifs disclosed above have been reported previously in literature. These structures can be divided into four categories according to unitary motifs which appear in the structure: oxazoline compounds in which oxazoline rings participate in a) a chain motif[1–8] or b) in a ring motif[9–13] as well as oxazoline compounds in which oxazoline rings do not participate but have c) a chain motif[11,14–20] or d) a ring motif.[12,21] In all of these reported structures, only the oxazoline nitrogen atom acts as a hydrogen bonding acceptor. There are only two reported supramolecular structures (which do not contain a metal atom) in which the oxazoline oxygen atom acts as the hydrogen bonding acceptor.[13,22]

The molecular structure of the oxazoline bioconjugates is dominated by six dihedral angles $\alpha$, $\varphi$, $\theta$, $\phi$, $\psi$, and $\chi$ (Figure S10). Angle $\alpha$ is defined by $N_{ox}=C_{ox}–C_{a1}=O_{a1}$ dihedral angles (Figure S10, a). Values of $\alpha$ give information about relative directionality between the oxazoline and the amide double bond. Angles $\varphi$ and $\theta$, defined by $N_{ox}=C_{ox}–C_{Ar1}=C_{Ar2}$ and $O_{a1}=C_{a1}–C_{A4r}=C_{Ar3}$ atoms, respectively, give insight in coplanarity of the oxazoline and amide C=O double bonds with the central aromatic unit (Figure S10, b and c). Angles $\phi$ and $\psi*$ are the Ramachandran dihedral angles of the amino acid residues, defined by $C_{a1}–N_{a1}–C_{\alpha}–C_{e\,(a2)}$ and $N_{a1}–C_{\alpha}–C_{c\,(a2)}–O_e\,(N_{a2})$ atom (Figure S10, d and e). Angles $\chi$ are defined by angles between two planes of amide and amide, or amide and ester carbonyl bonds (Figure S10, f). If a molecule has more than one $\chi$ value, then the successive values of $\chi$ are reported in order from N-terminus to C-terminus. Angles $\chi$ near 0° indicate a parallel orientation, values of 90° indicate a perpendicular orientation and values near 180° indicate antiparallel orientation. The experimental data of all defined angles for the 7 oxazolines are collected in Table S6. Data from crystal stuctures of similar compounds, amino-acid-aromatic and oxazoline-aromatic conjugates from the crystal base are collected in Table S6 (see below).

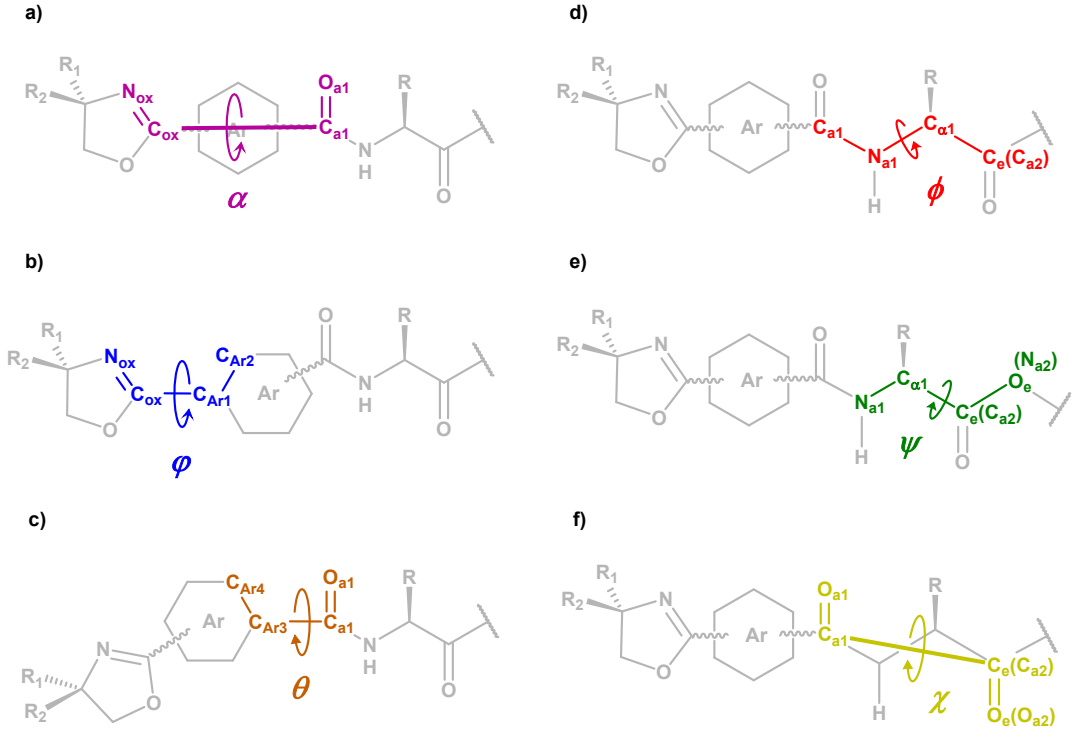



Figure S10. Characteristic dihedral angles: a) $\alpha$, b) $\phi$, c) $\theta$, d) $\varphi$, e) $\psi$ and f) $\chi$ of oxazoline compounds as defined in the text above.

Table S6. Dihedral angles as defined in Figure S10, for reported oxazoline structures and examples of structurally most similar compound from the literature.

| Compound | $\alpha$ /° | $\varphi$ /° | $\theta$ /° | $\phi$ /° | $\psi$ /° | $\chi$ /° |
|---|---|---|---|---|---|---|
| **$1_p$** | -44 | -12 | -31 | -85 | -175 | 86 |
| **$1_{m6}$** | 140 | -5 | -21 | -84 (Gly)<br>-132 (Val)<br>37 (Phe) | 172 (Gly)<br>127 (Val)<br>-179 (Phe) | 87 (Gly-Val)<br>-126 (Val-Phe)<br>-153 (Phe-ester) |
| **$1_{n2}$** | -76 | 22 | -21, -47 | -62 | -31 | 78 |
| **$1_{n4}$** | -50 | -12 | -30 | -73 | 158 | 83 |
| **$1_{n5}$** | 2 | -14 | -16 | -75 | 151 | 89 |
| **$1_a$** | -17 | -93 | 80 | 53 | 42 | 76 |
| **$1_{t4}$*** | -41 ($Phe_1$)<br>136 ($Phe_2$) | -7 | -21 ($Phe_1$)<br>-26 ($Phe_2$) | 95($Phe_1$)<br>61($Phe_2$) | -169 ($Phe_1$)<br>-141 ($Phe_2$) | 80 ($Phe_1$)<br>79 ($Phe_2$) |
| **$2_{m1}$** | -62 | - | -34 | -77 | 156 | -112 |
| **$2_{n5}$** | -61 | - | -34 | -77 | 158 | -111 |
| **$4_{m5}$** | -0.71 | - | -42, 41 | -147, -121 | 56, 50 | - |
| **$3_{t3}$** | -101, -115, 136 | - | 29, 35, 14 | -114(A.al), -75, -115 | 71, 151, -174 | -116, 68 |
| ***p*$C_6H_4$(Gly-OMe)$_2$**[23] | 180 | - | -28, 28 | 65, -65 | -152, 152 | 106, -106 |
| **2-Nph-Phe-OMe**[24] | - | - | 25 | -70 | -37 | 11 |
| **2-Nph-Val-OMe**[24] | - | - | 29 | -72 | 138 | -122 |
| **9,10-Anth(Phe-OMe)**[25] | -178 | - | -67, 66 | 66, -90 | -153, 164 | 106, -115 |
| **9,10-Anth(Val-OMe)$_2$**[25] | 153 | - | -95, 68 | -88, -75 | 141, 137 | -126, -119 |
| **1,3,5-$C_6H_3$-(Phe-OMe)$_3$**[26] | 122,123, 142 | - | 158, -29, 169 | 88, 98, 102 | 21, -32, -45 | -14, -119 -128 |
| **1,3,5-$C_6H_3$-(Gly-OMe)$_3$**[26] | -88,-89, -84 | | | | | |
| **(Phg-ox)*m*$C_6H_4CN$**[27] | -167 | -173 | | | | |
| **(ETA-ox)$_2$*m*$C_6H_4$**[28] | -169 | 178, 19 | | | | |

[#] carbonyl is separated from the aromatic ring by the amide nitrogen.

## 7.1 Oxazolines

Table S7. Experimental data for the X-ray diffraction studies

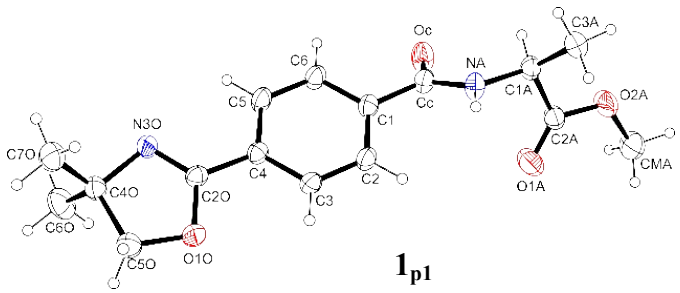
| **Compound** | **$1_{p1}$** | **$1_{m6}$** | **$1_{n2}$** | **$1_{n4}$** |
|---|---|---|---|---|
| Formula | $C_{16}H_{20}N_2O_4$ | $C_{33}H_{36}N_4O_6 \cdot Cl$ O | $C_{19}H_{20}N_2O_4$ | $C_{20}H_{22}N_2O_4$ |
| $F_w$ (g mol$^{-1}$) | 304.34 | 616.70 | 340.37 | 354.39 |
| Crystal system | Tetragonal | Monoclinic | Monoclinic | Monoclinic |
| Space group | $P4_3$ (No. 78) | $P2_1$ (No. 4) | $P2_1/c$ (No. 14) | $C2$ (No. 5) |
| $a$ (Å) | 7.30610(10) | 4.85790(10) | 14.4335(2) | 22.688(4) |
| $b$ (Å) | 7.30610(10) | 21.1948(4) | 13.2892(2) | 5.2784(6) |
| $c$ (Å) | 29.5083(6) | 15.9374(3) | 9.4990(2) | 16.099(2) |
| $\alpha$ (°) | 90 | 90 | 90 | 90 |
| β (°) | 90 | 91.905(2) | 105.099(2) | 105.082(17) |
| $\gamma$ (°) | 90 | 90 | 90 | 90 |
| V (Å$^3$) | 1575.13(5) | 1640.04(6) | 1759.10(5) | 1861.6(5) |
| $Z$ | 4 | 2 | 4 | 4 |
| $D_{calc}$ (g cm$^{-3}$) | 1.283 | 1.249 | 1.285 | 1.264 |
| $F$(000) | 648 | 656 | 720 | 752 |
| Instrument | XtaLAB | Xcalibur | XtaLAB | Xcalibur |
| Radiation (Å) | 1.54184 | 1.54184 | 1.54184 | 1.54184 |
| Temperature ($K$) | 293(2) | 293(2) | 293(2) | 293(2) |
| Reflections collected | 5610 | 8050 | 12736 | 2235 |
| Independent reflections | 2524 | 4801 | 3615 | 1615 |
| $R_{init}$ | 0.0253 | 0.0320 | 0.0349 | 0.0307 |
| Reflections observed | 2375 | 4108 | 3143 | 1209 |
| Parameters | 207 | 423 | 233 | 243 |
| $R_1$ [$I > 2\sigma(I)$][a] | 0.0376 | 0.0504 | 0.0528 | 0.0549 |
| $wR_2$ (all data)[b] | 0.0930 | 0.1596 | 0.1550 | 0.1352 |
| Goof, $S$[c] | 1.105 | 1.169 | 1.063 | 1.030 |
| Maximum/minimum electron density (e Å$^3$) | 0.152/-0.195 | 0.247/-0.228 | 0.306/-0.392 | 0.168/-0.135 |

[a] $R_1 = \Sigma||F_o| - |F_c||/ \Sigma|F_o|$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$. [c] $S = \{\Sigma[w(F_o^2 - F_c^2)^2]/(n - p)\}^{1/2}$ where n is number of reflections and p is the total number of parameters refined

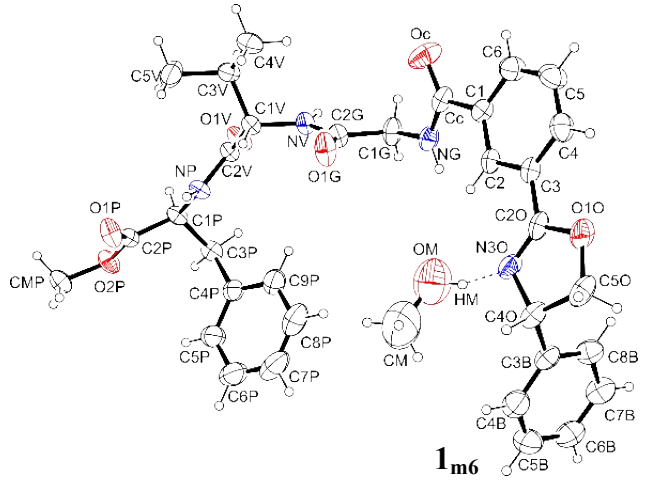
Table S7. Experimental data for the X-ray diffraction studies (continuation)

| **Compound** | **$1_{n5}$** | **$1_{a1}$** | **$1_{t4}$** |
|---|---|---|---|
| Formula | $C_{20}H_{22}N_2O_4$ | $C_{24}H_{24}N_2O_4$ | $C_{37}H_{35}N_3O_7$ |
| $F_w$ (g mol$^{-1}$) | 354.39 | 404.45 | 633.68 |
| Crystal system | Orthorhombic | Orthorhombic | Tetragonal |
| Space group | $P2_12_12_1$ (No. 1 | $P2_12_12$ (No. 18 | $P4_12_12$ (No. 92 |
| *a* (Å) | 5.1830(1) | 13.2430(4) | 18.8070(2) |
| *b* (Å) | 5.5120(1) | 20.7980(6) | 18.8070(2) |
| *c* (Å) | 64.5994(13) | 7.7513(2) | 19.0641(5) |
| $\alpha$ (°) | 90 | 90 | 90 |
| β (°) | 90 | 90 | 90 |
| $\gamma$ (°) | 90 | 90 | 90 |
| V (Å$^3$) | 1845.52(6) | 2134.92(10) | 6743.0(2) |
| *Z* | 4 | 4 | 8 |
| $D_{calc}$ (g cm$^{-3}$) | 1.275 | 1.258 | 1.248 |
| *F*(000) | 752 | 856 | 2672 |
| Instrument | XtaLAB | XtaLAB | Xcalibur |
| Radiation (Å) | 1.54184 | 1.54184 | 1.54184 |
| Temperature (*K*) | 293(2) | 293(2) | 293(2) |
| Reflections collected | 14023 | 8620 | 14949 |
| Independent reflections | 3887 | 4022 | 5899 |
| $R_{init}$ | 0.0353 | 0.0318 | 0.0326 |
| Reflections observed | 3813 | 3596 | 4958 |
| Parameters | 243 | 279 | 434 |
| $R_1$ [$I > 2\sigma(I)$][a] | 0.0867 | 0.0468 | 0.0419 |
| $wR_2$ (all data)[b] | 0.2865 | 0.1288 | 0.1103 |
| Goof, *S*[c] | 1.161 | 1.083 | 1.038 |
| Maximum/minimum electron density (e Å$^3$) | 0.498/-0.350 | 0.218/-0.176 | 0.138/-0.109 |

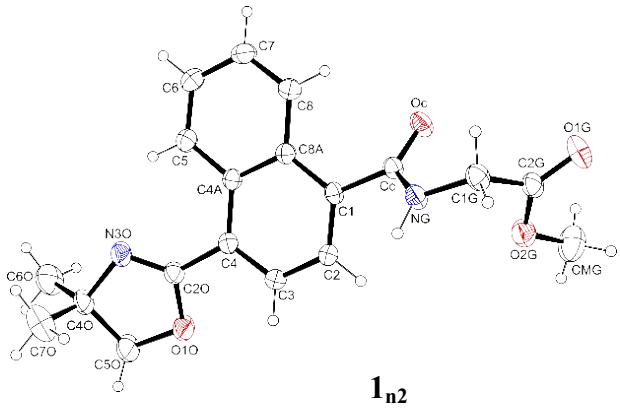
[a] $R_1 = \Sigma||F_o| - |F_c||/ \Sigma|F_o|$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$. [c] $S = \{\Sigma[w(F_o^2 - F_c^2)^2]/(n - p)\}^{1/2}$ where n is number of reflections and p is the total number of parameters refined



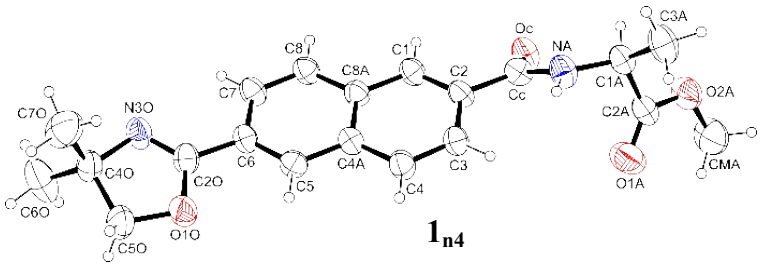

$\mathbf{1_{p1}}$




$\mathbf{1_{m6}}$

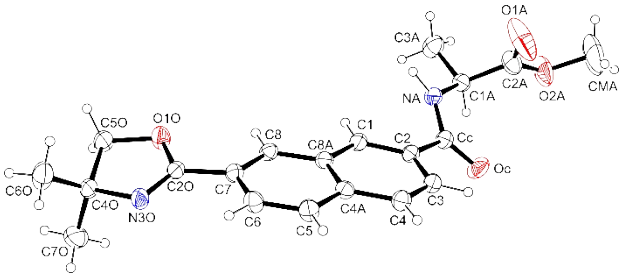



$\mathbf{1_{n2}}$

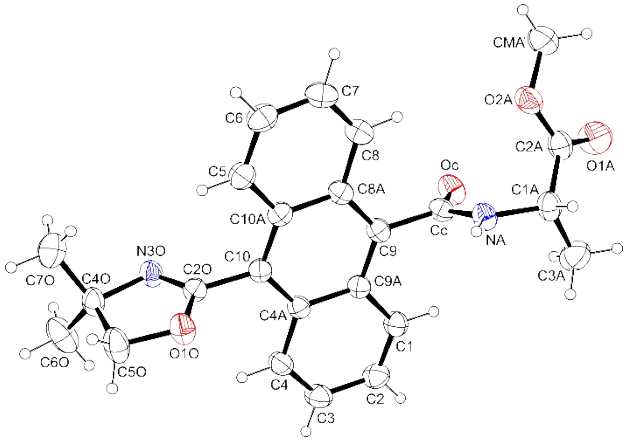



$\mathbf{1_{n4}}$

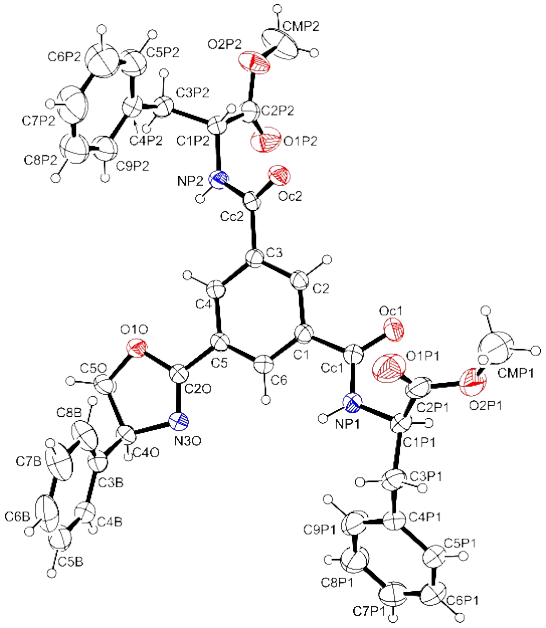
Figure S11. ORTEP-III drawings (Farrugia)[29] for SCXRD determined structures with complete atom numbering schemes and 30 % ellipsoid probability level.




**$1_{n5}$**

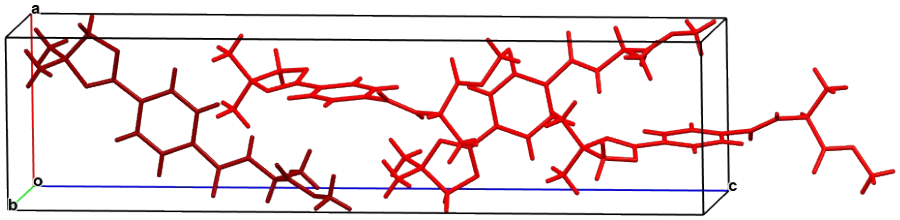



**$1_{a1}$**

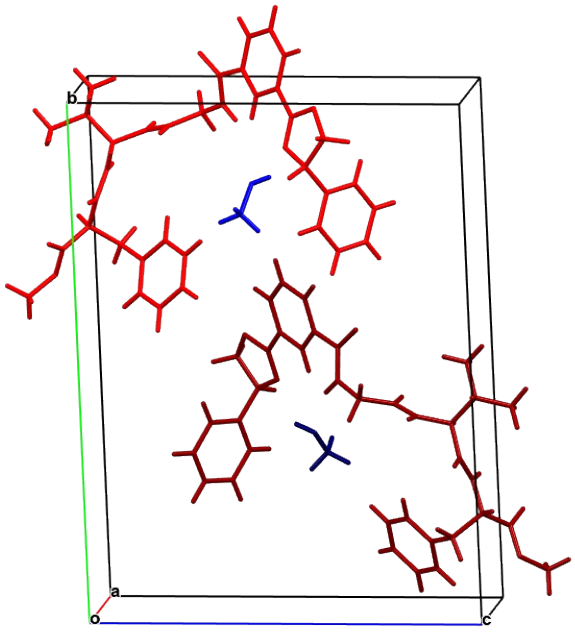



**$1_{t4}$**

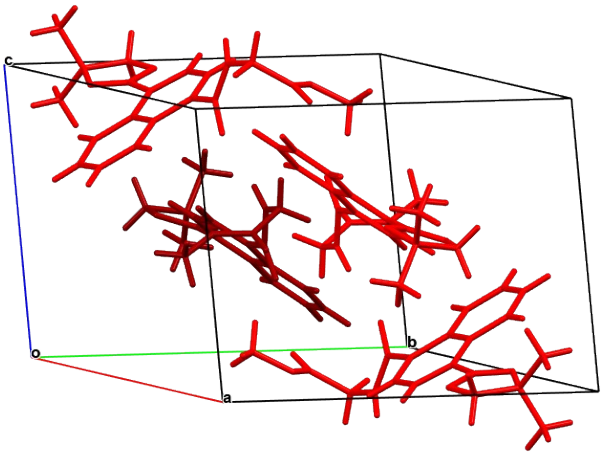
Figure S11. ORTEP-III drawings (Farrugia)[29] for SCXRD determined structures with complete atom numbering schemes and 30 % ellipsoid probability level. (continuation).




**$1_{p1}$**

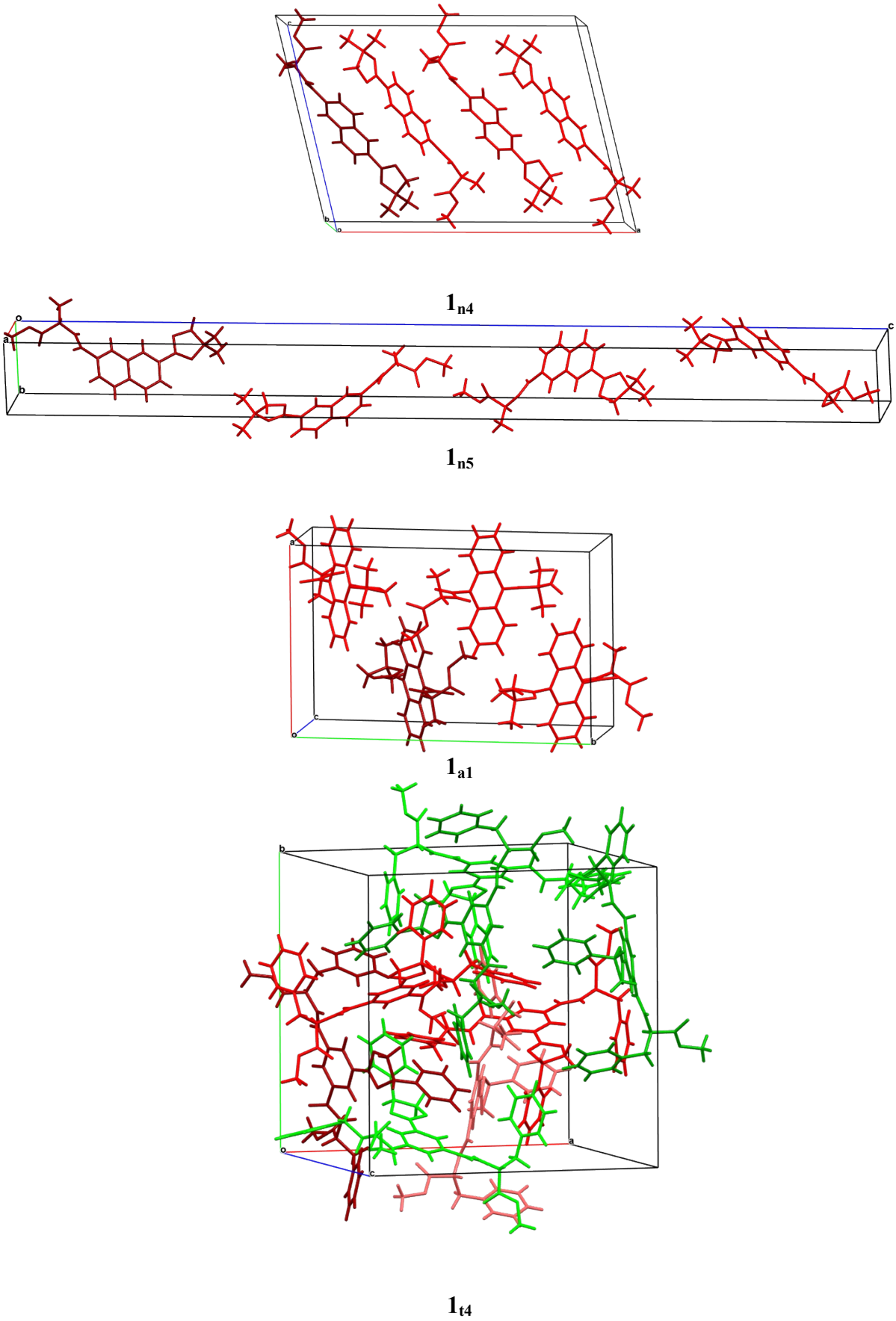



**$1_{m6}$**




**$1_{n2}$**

Figure S12. Crystal packings for SCXRD determined structures. Solvent methanol molecules in **$1_{m6}$** are shown in blue.



$\mathbf{1}_{n4}$

$\mathbf{1}_{n5}$

$\mathbf{1}_{a1}$

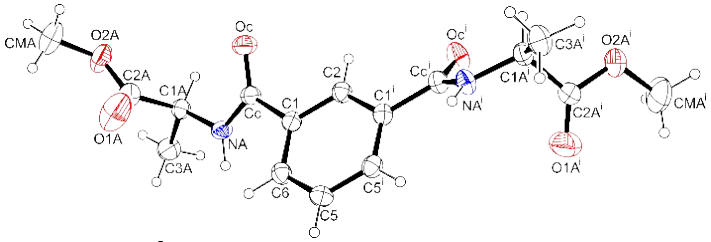
$\mathbf{1}_{t4}$

Figure S12. Crystal packings for SCXRD determined structures. (continuation)

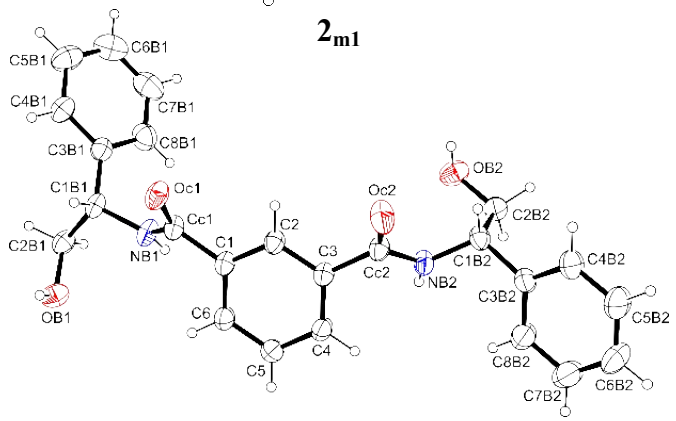
Table S8. Experimental data for the X-ray diffraction studies.

| **Compound** | **$2_{m1}$** | **$4_{m5}$** | **$2_{n5}$** | **$3_{t3}$** |
|---|---|---|---|---|
| Formula | $C_{16}H_{20}N_2O_6$ | $C_{24}H_{24}N_2O_4$ | $C_{20}H_{22}N_2C$ | $C_{37}H_{37}N_3O_8$ |
| $F_w$ (g mol$^{-1}$) | 336.34 | 404.45 | 386.39 | 651.69 |
| Crystal system | Monoclinic | Monoclinic | Monoclini | Tetragonal |
| Space group | *C*2 (No. 5) | *C*2 (No. 5) | *C*2 (No. 5) | $P4_32_12$ (No. 96) |
| *a* (Å) | 6.4358(2) | 20.892(2) | 6.5044(4) | 18.8640(2) |
| *b* (Å) | 8.0804(3) | 4.9926(3) | 8.0195(6) | 18.8640(2) |
| *c* (Å) | 16.4380(6) | 21.517(2) | 18.7137(1 | 19.6976(4) |
| *α* (°) | 90 | 90 | 90 | 90 |
| β (°) | 98.198(3) | 111.246(12) | 95.141(6) | 90 |
| *γ* (°) | 90 | 90 | 90 | 90 |
| V (Å$^3$) | 846.10(5) | 2091.8(4) | 972.22(11 | 7009.4(2) |
| *Z* | 2 | 4 | 2 | 8 |
| $D_{calc}$ (g cm$^{-3}$) | 1.320 | 1.284 | 1.320 | 1.235 |
| *F*(000) | 356 | 856 | 408 | 2755 |
| Instrument | Xcalibur | Xcalibur | Xcalibur | Xcalibur |
| Radiation (Å) | 1.54184 | 1.54184 | 1.54184 | 1.54184 |
| Temperature (*K*) | 293(2) | 293(2) | 293(2) | 293(2) |
| Reflections collected | 1358 | 11420 | 1845 | 22636 |
| Independent reflections | 994 | 3874 | 1343 | 7226 |
| $R_{init}$ | 0.0195 | 0.0849 | 0.0258 | 0.0411 |
| Reflections observed | 980 | 2974 | 1261 | 4601 |
| Parameters | 116 | 281 | 134 | 443 |
| $R_1$ [$I > 2\sigma(I)$][a] | 0.0483 | 0.0671 | 0.0416 | 0.0852 |
| $wR_2$ (all data)[b] | 0.1483 | 0.1950 | 0.1413 | 0.2769 |
| Goof, *S*[c] | 1.165 | 1.060 | 1.179 | 1.048 |
| Maximum/minimum electron density (e Å$^3$) | 0.279/-0.176 | 0.217/-0.222 | 0.292/-0.2( | 0.295/-0.194 |

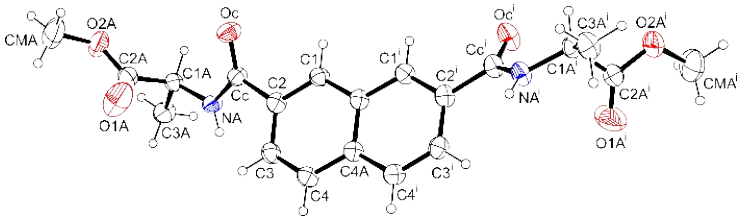
[a] $R_1 = \Sigma||F_o| - |F_c||/ \Sigma|F_o|$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$. [c] $S = \{\Sigma[w(F_o^2 - F_c^2)^2]/(n - p)\}^{1/2}$ where n is number of reflections and p is the total number of parameters refined



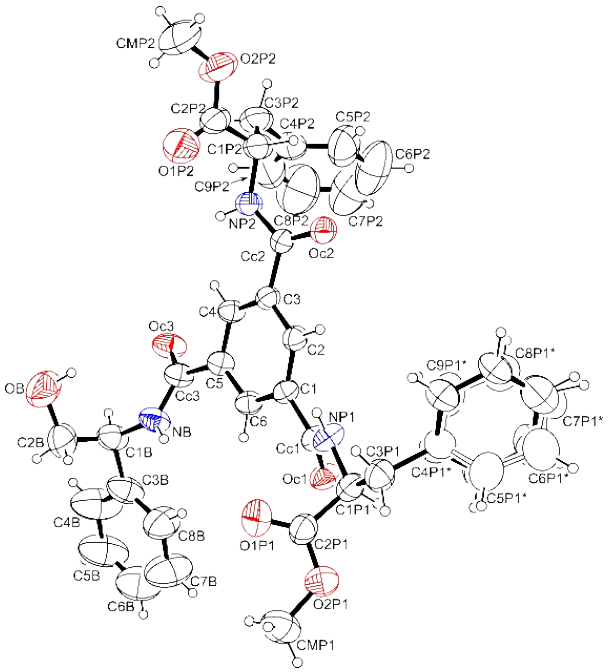

**$2_{m1}$**




**$4_{m5}$**

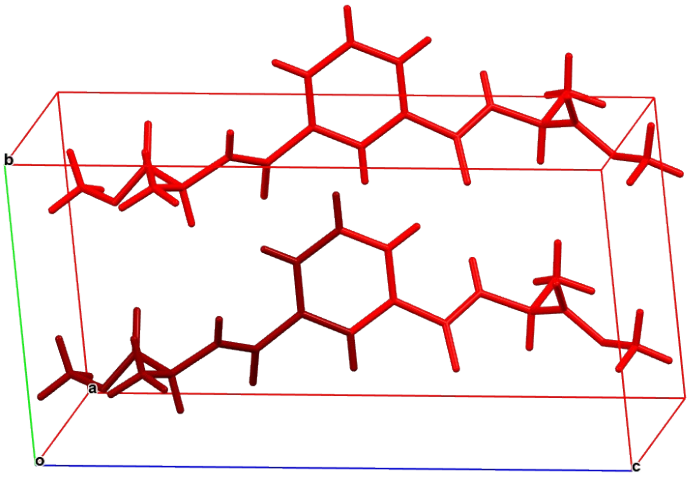



**$2_{n5}$**

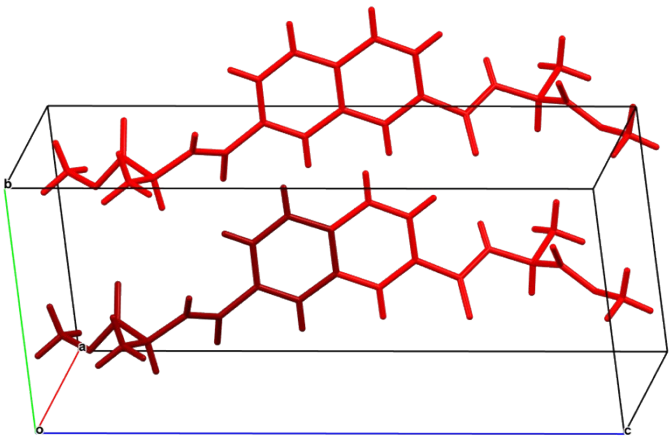



**$3_{t3}$**

Figure S13. ORTEP-III drawings (Farrugia)[29] for SCXRD determined structures with complete atom numbering schemes and 30 % ellipsoid probability level.

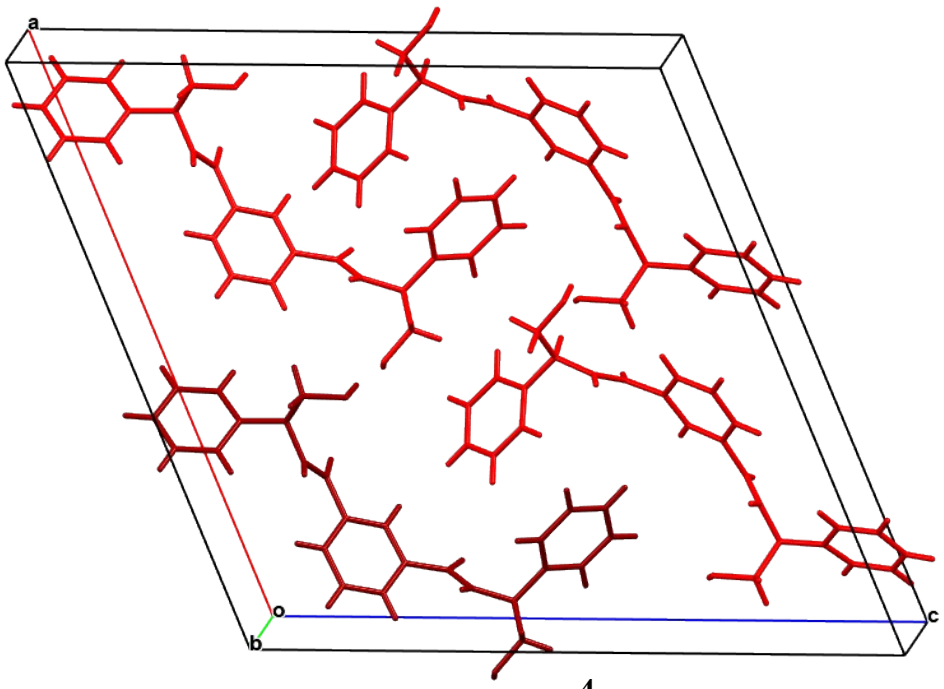



**$2_{m1}$**

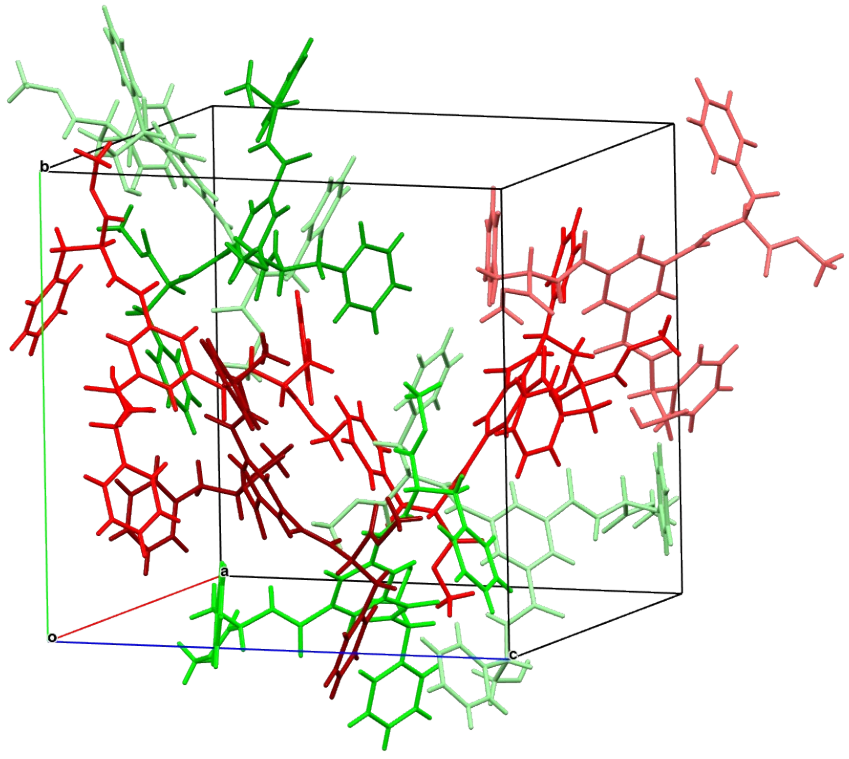



**$2_{n5}$**

Figure S14. Crystal packings for SCXRD determined structures. For reason of clarity, symmetry equivalent molecules are drawn in different shades of red and green.




$\mathbf{4}_{m5}$



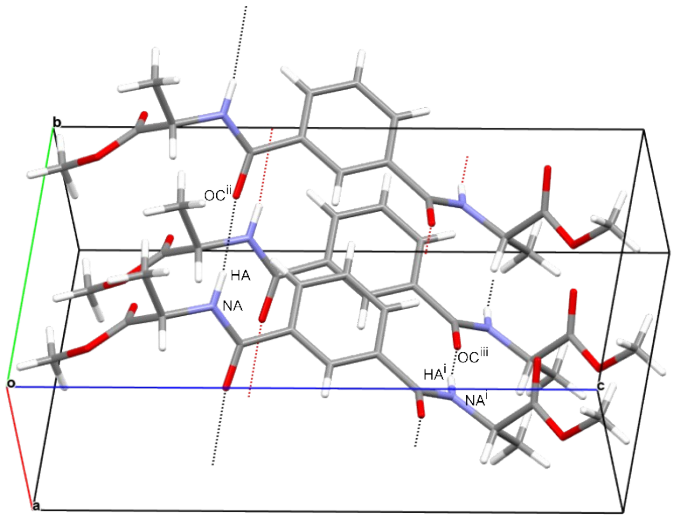

$\mathbf{3}_{t3}$

Figure S15. Crystal packings for SCXRD determined structures. For reason of clarity, symmetry equivalent molecules are drawn in different shades of red and green.

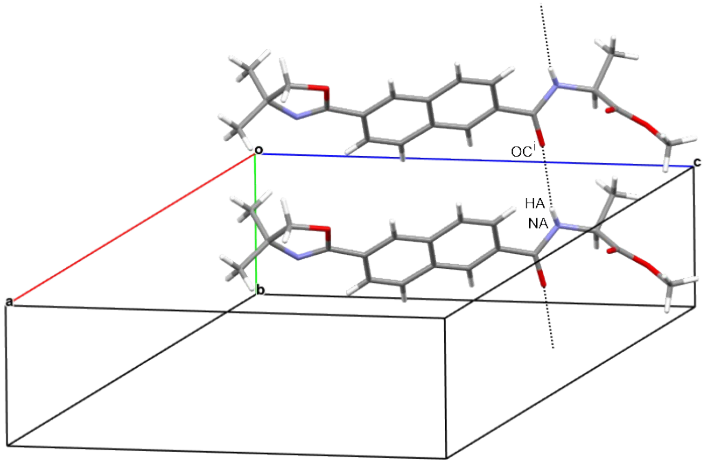
## 7.3. Hydrogen bonds

Table S9. Geometry parameters (Å , °) for hydrogen bonds in SCXRD determined structures.

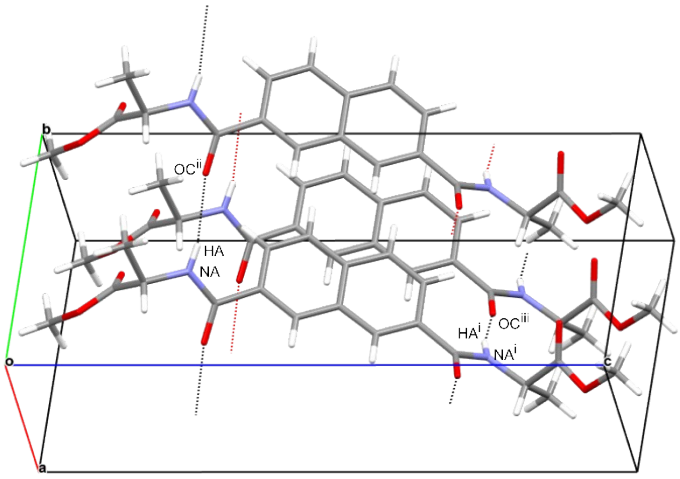
| ***D*-H···*A*, type** | ***D*-H** | **H···*A*** | ***D*···*A*** | ***D*-H···*A*** |
|---|---|---|---|---|
| **$1_{p1}$** | | | | |
| NA-HA···N3O, am···oxz | 0.90(3) | 2.24(3) | 3.119(3) | 166(3) |
| **$1_{m6}$** | | | | |
| NV-HV···O1G, am···am | 0.88(2) | 2.13(2) | 2.988(4) | 167(4) |
| NP-HP···O1V, am···am | 0.86(2) | 2.28(3) | 3.062(4) | 151(4) |
| OM-HM···N3O, dimer with solvent | 0.82 | 2.24 | 2.916(11) | 139.3 |
| **$1_{n2}$** | | | | |
| NG-HG···OC, am···am | 0.89(2) | 2.01(2) | 2.8208(16) | 150.8(16) |
| **$1_{n4}$** | | | | |
| NA-HA···OC, am···am | 0.77(9) | 2.46(9) | 3.158(11) | 152(8) |
| **$1_{n5}$** | | | | |
| NA-HA···OC, am···am | 0.91(6) | 2.14(6) | 3.050(6) | 171(5) |
| **$1_{a1}$** | | | | |
| NA-HA···N3O, am···oxz | 0.97(4) | 2.11(4) | 3.054(3) | 165(3) |
| **$1_{t4}$** | | | | |
| NP2-HP2···OC2, am···am | 0.87(2) | 2.13(3) | 2.956(3) | 159(3) |
| NP1-HP1···N3O, am···oxz | 0.89(2) | 2.29(2) | 3.175(3) | 173(3) |
| **$2_{m1}$** | | | | |
| NA-HA···OC, am···am | 0.87(4) | 2.16(5) | 3.019(4) | 170(3) |
| **$4_{m5}$** | | | | |
| NB1-HB1···OC1, am···am | 0.88(8) | 2.10(8) | 2.974(5) | 179(5) |
| NB2-HB2···OC2, am···am | 0.96(7) | 1.96(7) | 2.911(5) | 173(6) |
| OB1-HOB1···OB2, OH···OH | 0.82 | 1.98 | 2.772(6) | 161.2 |
| OB2-HOB2···OB1, OH···OH | 0.82 | 1.88 | 2.696(6) | 174.2 |
| **$2_{n5}$** | | | | |
| NA-HA···OC, am···am | 0.81(4) | 2.23(4) | 3.020(4) | 166(3) |
| **$3_{t3}$** | | | | |
| NP1-HP1···OC2, am(1)···am(2) | 0.87(3) | 2.01(3) | 2.879(6) | 177(6) |
| NB-HB···OC3, am(3)···am(3) | 0.85(3) | 2.13(3) | 2.967(6) | 168(6) |
| NP2-HP2···OC1, am(2)···am(1) | 0.84(3) | 2.04(4) | 2.813(6) | 153(7) |
| OB-HOB···O1P1, OH···O=C | 0.82 | 2.09 | 2.744(10) | 136.0 |
| OB-HOB···NB, intramolecular | 0.82 | 2.59 | 2.973(10) | 109.7 |




**$2_{m1}$**

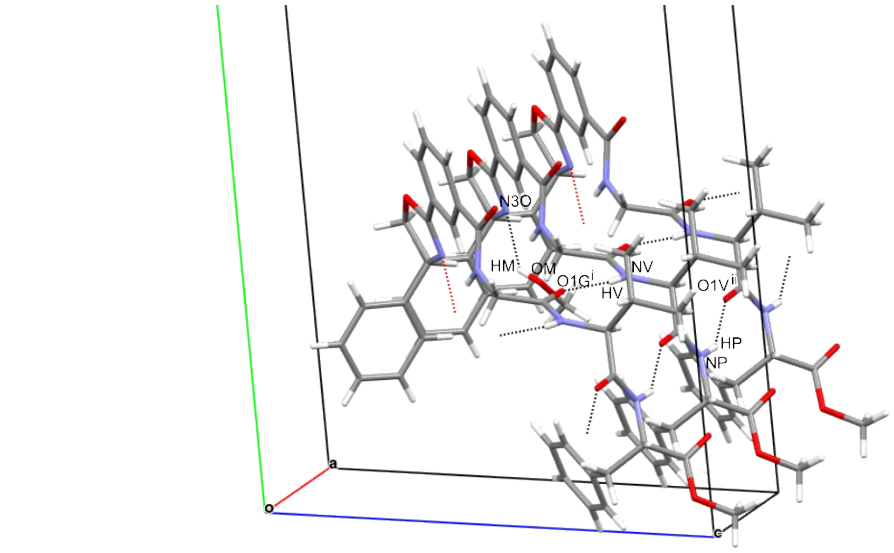



**$1_{n4}$**

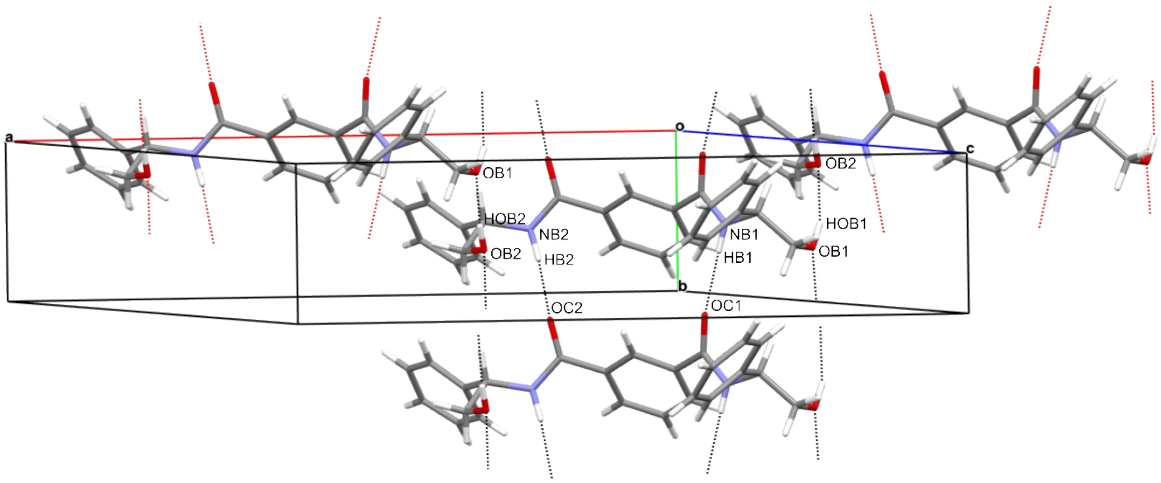



**$2_{n5}$**

Figure S16. Hydrogen bonds (Table S9) for SCXRD determined structures. Symmetry codes: (i) x,y,z, (ii) x,y,z (iii) x,y,z for **$2_{m1}$** and **$2_{n5}$**, (i) x,y,z for **$1_{n4}$**.

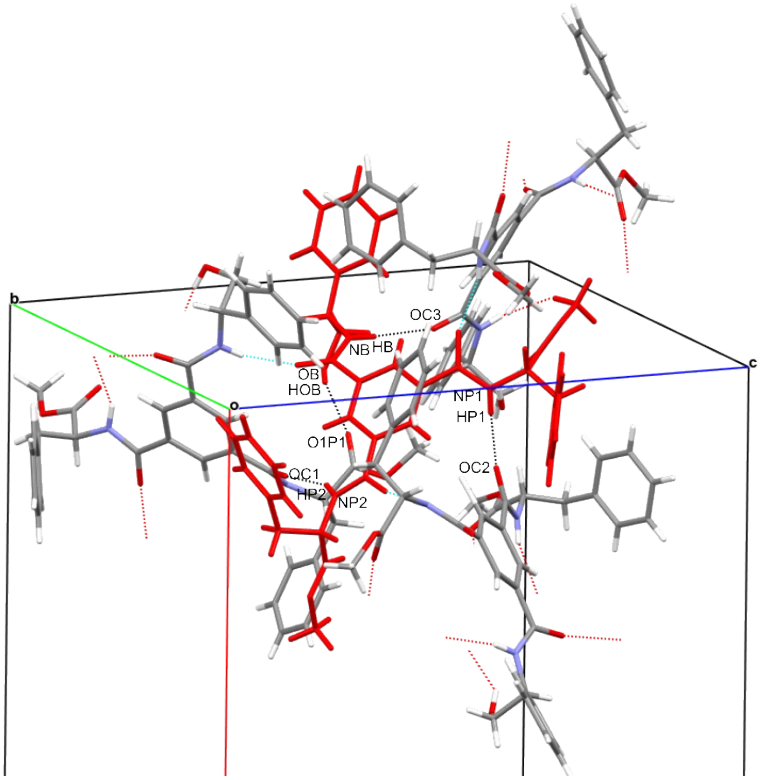



**$1_{m6}$**

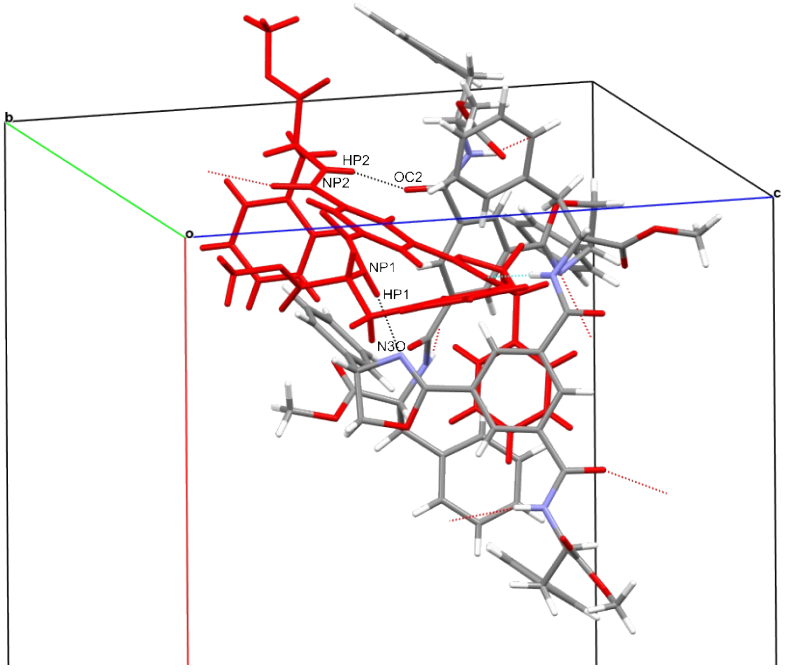



**$4_{m5}$**

Figure S17. Hydrogen bonds (Table S9) for SCXRD determined structures. Symmetry codes: (i) x,y,z, (ii) x,y,z **$1_{m6}$**, (i) x,y,z, (ii) x,y,z and (iii) x,y,z for **$4_{m5}$**.

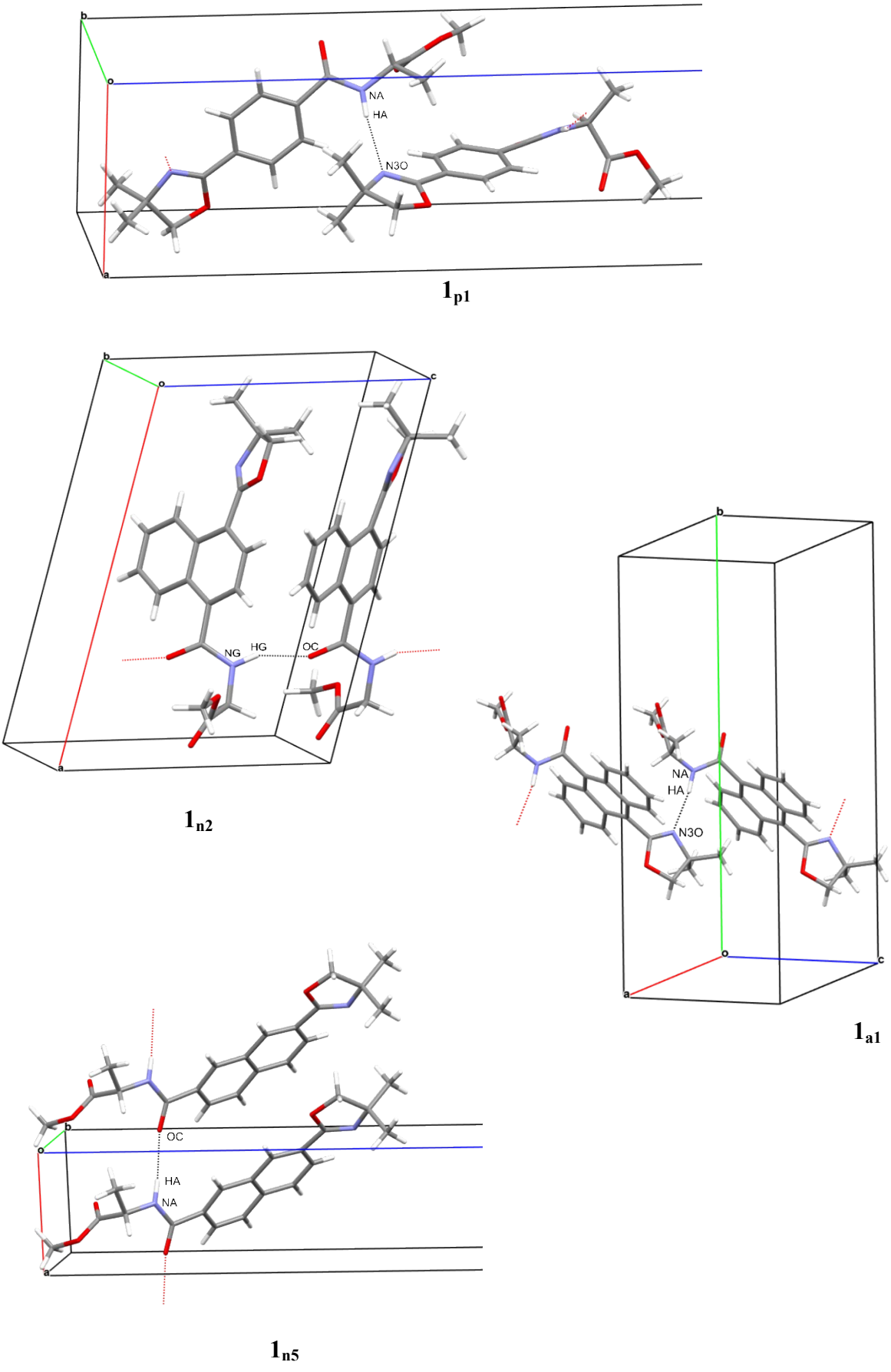



**$3_{t3}$**




**$1_{t4}$**

Figure S18. Hydrogen bonds (Table S9) for SCXRD determined structures. Symmetry codes: (i) x,y,z, (ii) x,y,z and (iii) **$3_{t3}$**; (i) x,y,z and (ii) x,y,z for **$1_{t4}$**. For reason of clarity, origin molecules are drawn in red.



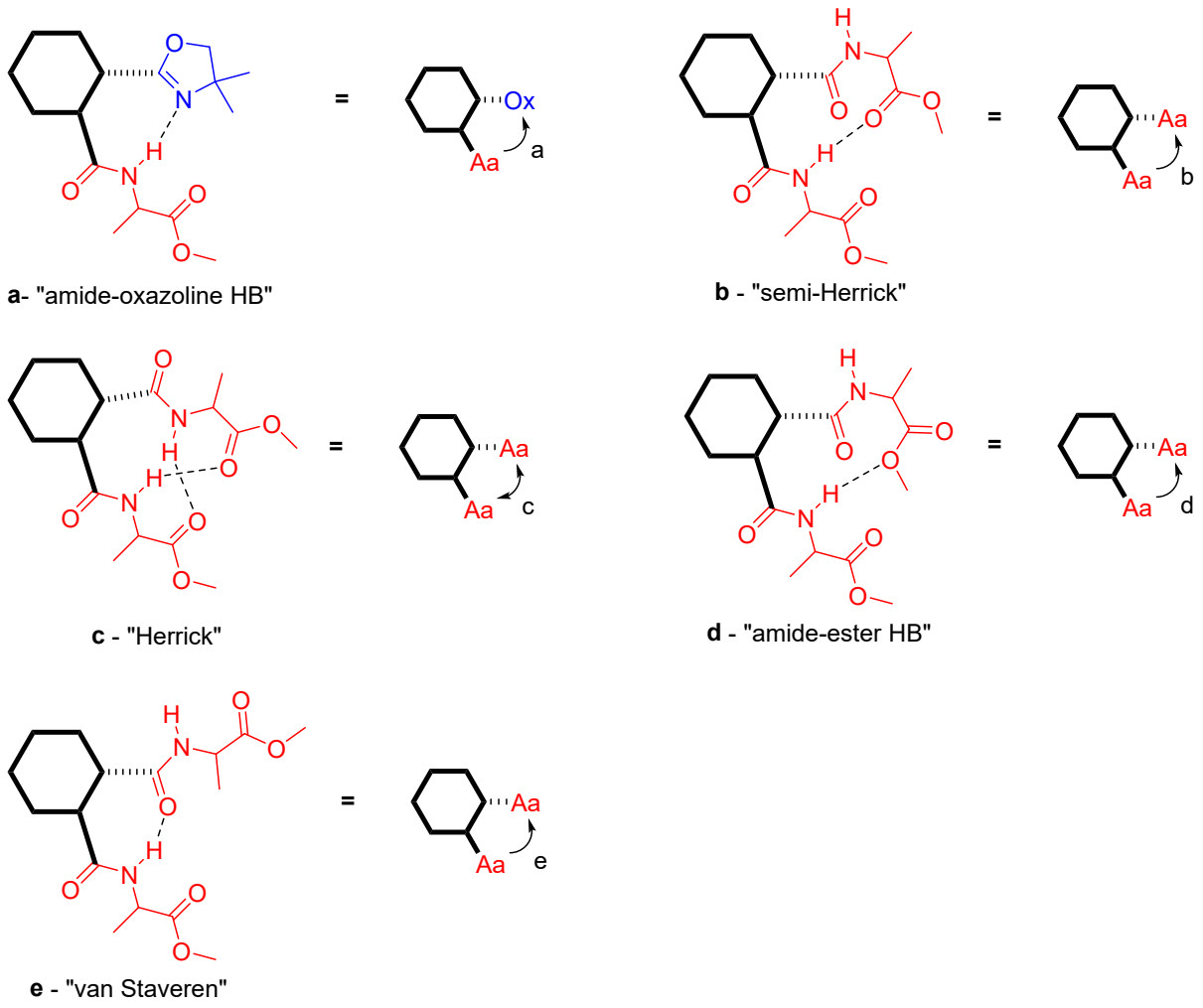

$\mathbf{1}_{p1}$

$\mathbf{1}_{n2}$

$\mathbf{1}_{a1}$

$\mathbf{1}_{n5}$

Figure S19. Hydrogen bonds (Table S9) for SCXRD determined structures. Symmetry codes: (i) x,y,z, for $\mathbf{1}_{p1}$; (i) x,y,z for 1n2; (i) x,y,z for 1a1 and (i) x,y,z for $\mathbf{1}_{n5}$.




**a**- "amide-oxazoline HB"

**b** - "semi-Herrick"

**c** - "Herrick"

**d** - "amide-ester HB"

**e** - "van Staveren"

Figure S20. Types of hydrogen bonding: a-HB with oxazoline, b-semi-Herrick, c-Herrick, d-HB with the methoxy oxygen, e- van Staveren HB. The arrowhead indicates the direction of the amide proton donation (each arrowhead on an arrow represents one amide proton). BW = Boltzmann weight, Ox = oxazoline ring, Aa = amino acid, HBA-hydrogen bond acceptor, HBD-hydrogen bond donor.

'Anti' and 'syn' relative orientations of oxazoline rings in dimers are defined by making a 2D projection of the dimer vertically in relation to the benzene rings (Figure S21, bottom right). Then, the origin of the coordinate system is placed in the center of the benzene rings. We define angles $\alpha_{x1,x2}$ as the angles between two crossed lines of which the first line passes through heteroatom X1 and the origin of the coordinate system, while the second line passes through theteroatom X2 and the origin of the coordinate system. Numbers 1 and 2 in angle indices in Figure S21 are ommitted as it is assumed that one indice denotes a heteroatom from one molecule from the dimer, and the other indice denotes the heteroatom from the other molecule from the dimer.

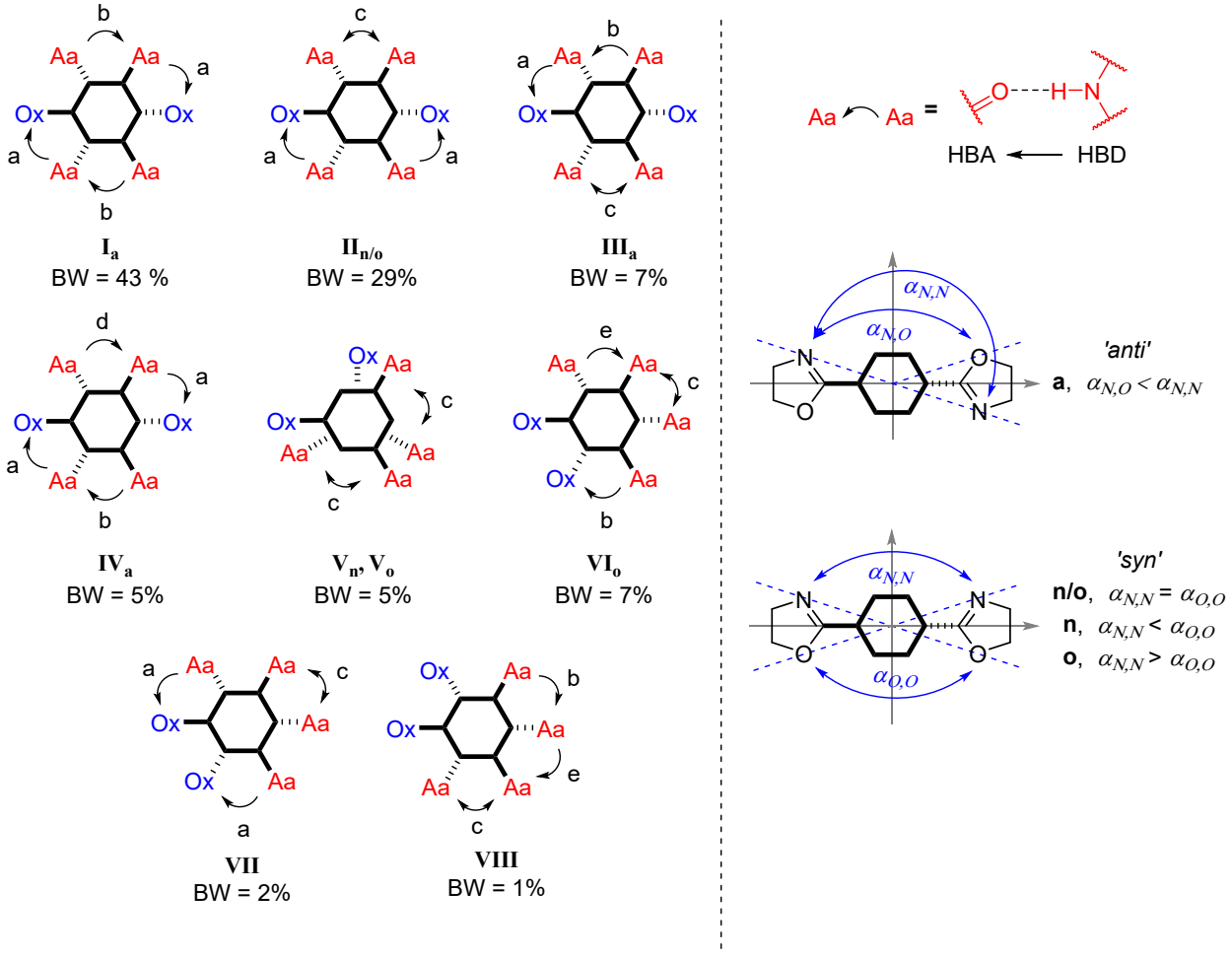



Figure S21. DFT structures of $\mathbf{1_{t1}}$ dimers and corresponding hydrogen bonding with Boltzmann weight values greater than 1%

Table S10. Characteristic parameters of conformers obtained by CREST/CENSO protocol with Boltzmann weight contributions ≥ 1%.

| | | | | Type of hydrogen bonded amide hydrogen atom | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Conf. | Type | Stacked oxazoline relative positions | Oxazoline relative orientation | Herrick | van Staveren | semi-Herrick | oxazoline | $\Delta G_{tot}$ / *kcalmol*$^{-1}$ | Boltzmann weight | BW SUM over type |
| 1 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 0 | 18 | |
| 4 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 0.42 | 9 | |
| 6 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 0.75 | 5 | |
| 7 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 0.95 | 4 | |
| 8 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 0.98 | 3 | 43 |
| 14 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 1.22 | 2 | |
| 18 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 1.59 | 1 | |
| 24 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 1.81 | 1 | |
| 27 | I | 1,4' | *anti* | / | / | ++(3,6') | ++(5,2') | 2.02 | 1 | |
| 2 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 0.27 | 11 | |
| 3 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 0.39 | 9 | |
| 9 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 1.05 | 3 | |
| 11 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 1.08 | 3 | 29 |
| 20 | II | 1,4' | *syn* | ++(5,6'-ester) | / | / | ++(3,2') | 1.63 | 1 | |
| 25 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 1.97 | 1 | |
| 28 | II | 1,4' | *syn* | ++(5,6') | / | / | ++(3,2') | 2.08 | 1 | |
| 5 | III | 1,4' | *anti* | ++(5,6') | / | +(3) | +(2') | 0.59 | 7 | 7 |
| 13 | IV | 1,4' | *anti* | / | / | ++(3-ester,6') | ++(5,2') | 1.18 | 2 | |
| 17 | IV | 1,4' | *anti* | / | / | ++(3-ester,6') | ++(5,2') | 1.45 | 2 | 5 |
| 21 | IV | 1,4' | *anti* | / | / | ++(3-ester,6') | ++(5,2') | 1.67 | 1 | |
| 10 | V | P1,3' | *syn(N away)* | ++/++(3,4'/5,6') | / | / | / | 1.07 | 3 | |
| 19 | V | P1,3' | *syn(N towards each other)* | ++/++(3,4'/5,6') | / | / | / | 1.6 | 1 | 5 |
| 29 | V | P1,3' | *syn(N away)* | ++/++(3,4'/5,6'-ester) | / | / | / | 2.11 | 1 | |
| 12 | VI | P1,6' | *syn(N away)* | ++(3,4') | +(2') | / | +(5) | 1.14 | 3 | |
| 15 | VI | P1,6' | *syn(N away)* | ++(3,4') | +(2') | / | +(5) | 1.23 | 2 | 7 |
| 16 | VI | P1,6' | *syn(N away)* | ++(3,4') | +(2') | / | +(5) | 1.37 | 2 | |
| 22 | VII | P1,6' | *syn(N away)* | ++(3,4') | / | / | ++(5,2') | 1.69 | 1 | 2 |
| 26 | VII | P1,6' | *syn(N away)* | ++(3,4') | / | / | ++(5,2') | 1.99 | 1 | |
| 23 | VIII | P1,6' | *anti* | ++(3,4') | +(5) | | | 1.75 | 1 | 1 |
| | | | | | | | Total BW SUM= | | 97 | |

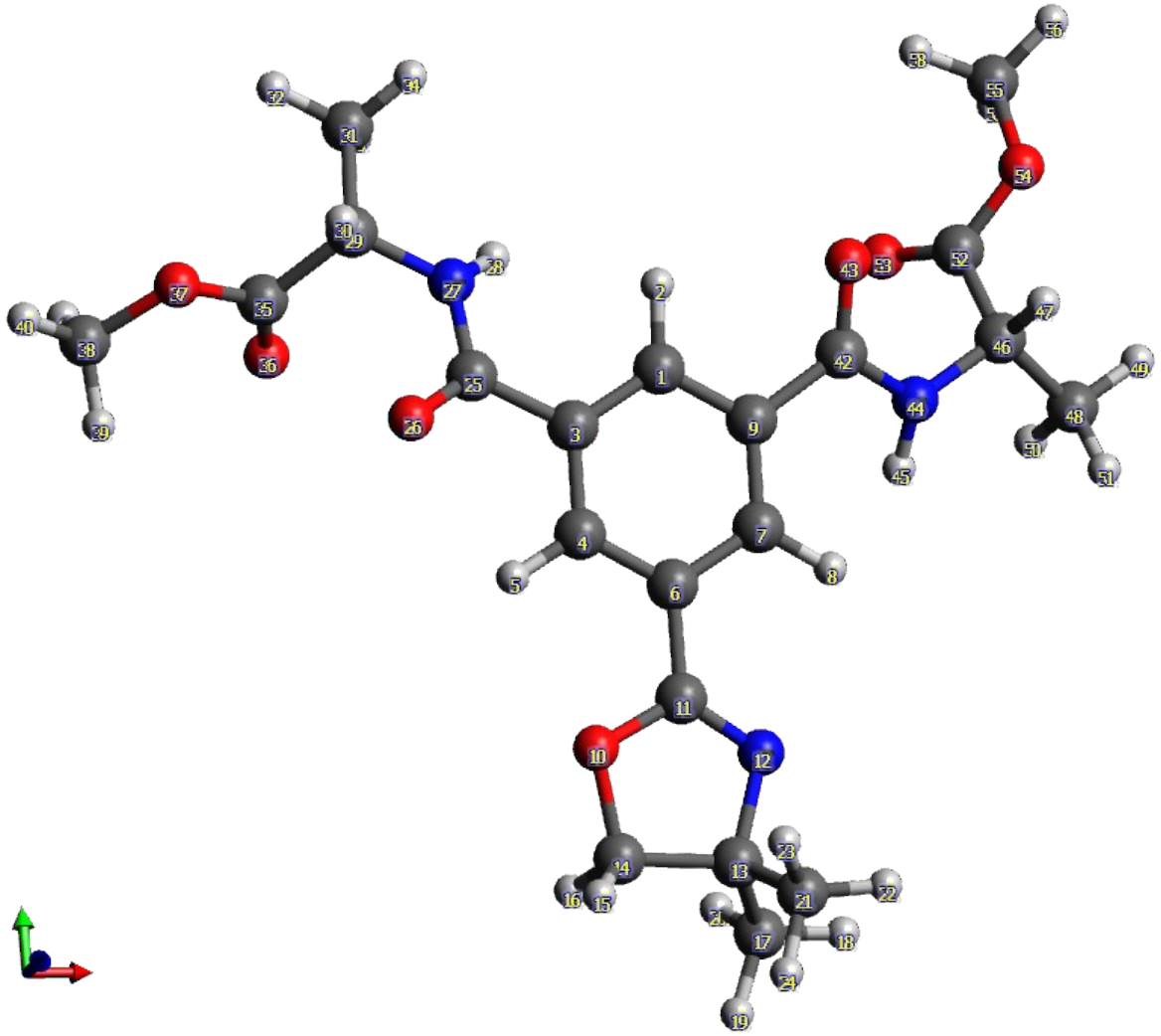


Figure S22. DFT optimized structure of lowest energy conformer of $\mathbf{1}_{t1}$ (CONF1) with atom labels.

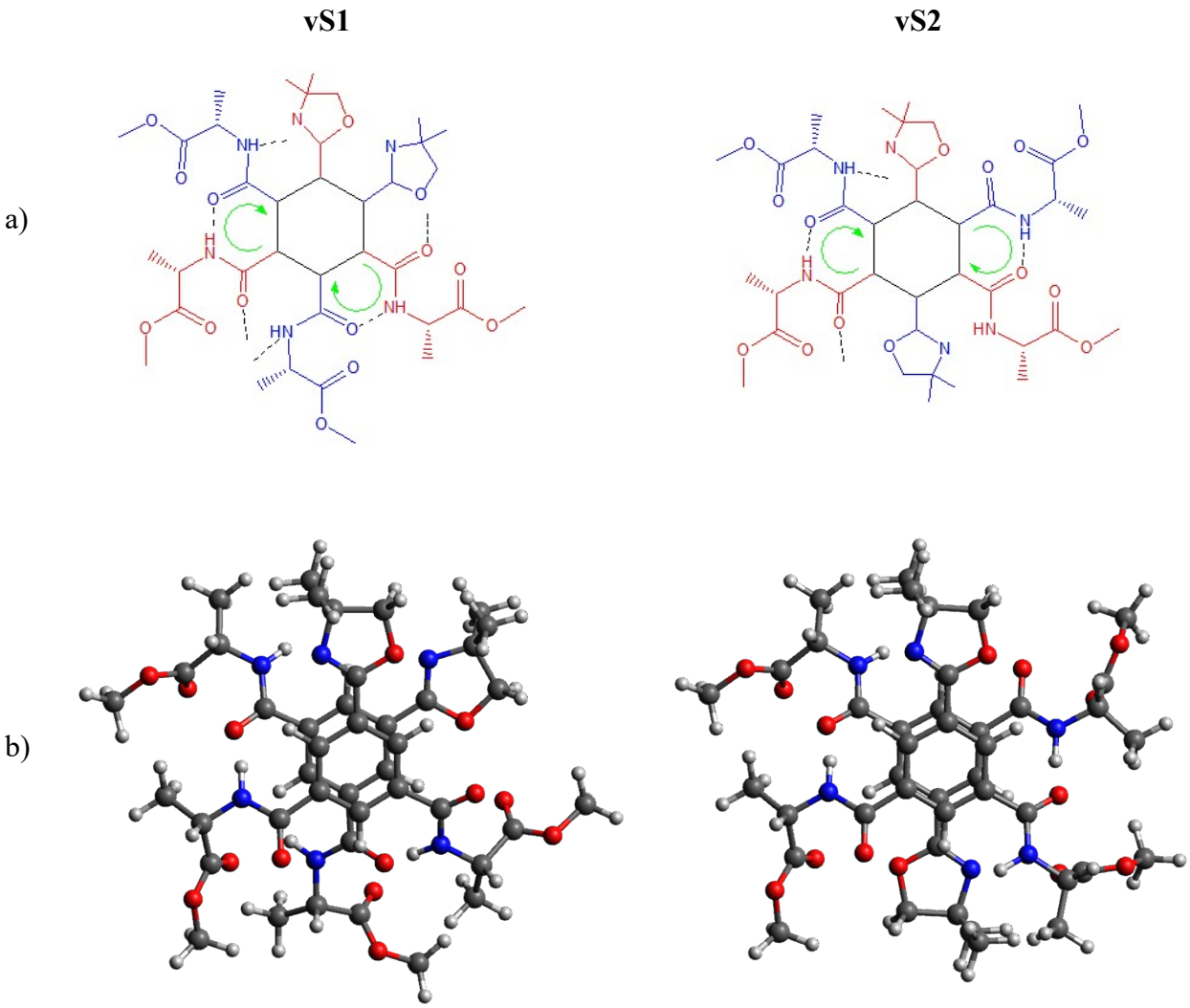



Figure S23. Schematic (a) and 3D “ball and stick” (b) representation of starting dimer models for $\mathbf{1}_{\mathbf{t1}}$ molecules (vS1 and vS2), obtained by the Avogadro software from two copies of the lowest energy conformer of $\mathbf{1}_{\mathbf{t1}}$. Labels of atoms in one part of dimer is identical as in the monomer labelling (Figure S22), labels of the second part of dimer are accordingly increased for 58. (Atom 1 in one part is identical to atom 59 in second part of dimer, atom 2 is identical to atom 60, etc.) In order to mimic the van Staveren hydrogen bonding motifs for vS2 it was necessary to change torsion angles of two amide groups with respect to benzene rings, in particular C(1)-C(3)-C(25)-O(26) and C(65)-C(67)-C(100)-O(101) torsion angles from ≈ -150° in CONF1 to ≈ 150°."

Table S11. Gibbs free energies ($G$) for monomer conformers of $\mathbf{1_{t1}}$ at different temperatures.

| CONF | G [$E_h$] 233 K | ΔG [kcal/mol] 233 K | G [$E_h$] 253 K | ΔG [kcal/mol] 253 K | G [$E_h$] 273 K | ΔG [kcal/mol] 273 K |
|---|---|---|---|---|---|---|
| CONF1 | -1506.7451897 | 0.00 | -1506.7509090 | 0.00 | -1506.7568827 | 0.00 |
| CONF2 | -1506.7447804 | 0.26 | -1506.7505004 | 0.26 | -1506.7564741 | 0.26 |
| CONF3 | -1506.7443329 | 0.54 | -1506.7500520 | 0.54 | -1506.7560282 | 0.54 |
| CONF4 | -1506.7441282 | 0.67 | -1506.7498446 | 0.67 | -1506.7558183 | 0.67 |
| CONF5 | -1506.7440714 | 0.70 | -1506.7497902 | 0.70 | -1506.7557630 | 0.70 |
| CONF6 | -1506.7438705 | 0.83 | -1506.7495897 | 0.83 | -1506.7555655 | 0.83 |
| CONF7 | -1506.7438737 | 0.83 | -1506.7495891 | 0.83 | -1506.7555606 | 0.83 |
| CONF8 | -1506.7438461 | 0.84 | -1506.7495641 | 0.84 | -1506.7555391 | 0.84 |
| CONF9 | -1506.7438008 | 0.87 | -1506.7495135 | 0.88 | -1506.7554789 | 0.88 |
| CONF10 | -1506.7436885 | 0.94 | -1506.7494037 | 0.94 | -1506.7553739 | 0.95 |
| CONF11 | -1506.7435880 | 1.01 | -1506.7493114 | 1.00 | -1506.7552884 | 1.00 |
| CONF12 | -1506.7434740 | 1.08 | -1506.7491924 | 1.08 | -1506.7551650 | 1.08 |
| CONF13 | -1506.7433286 | 1.17 | -1506.7490587 | 1.16 | -1506.7550463 | 1.15 |
| CONF14 | -1506.7433336 | 1.16 | -1506.7490488 | 1.17 | -1506.7550212 | 1.17 |
| CONF15 | -1506.7433183 | 1.17 | -1506.7490368 | 1.17 | -1506.7550122 | 1.17 |
| CONF16 | -1506.7432941 | 1.19 | -1506.7490112 | 1.19 | -1506.7549852 | 1.19 |
| CONF17 | -1506.7431828 | 1.26 | -1506.7489051 | 1.26 | -1506.7548807 | 1.26 |
| CONF18 | -1506.7429376 | 1.41 | -1506.7486535 | 1.42 | -1506.7546249 | 1.42 |
| CONF19 | -1506.7429500 | 1.41 | -1506.7486599 | 1.41 | -1506.7546248 | 1.42 |
| CONF20 | -1506.7428644 | 1.46 | -1506.7485814 | 1.46 | -1506.7545544 | 1.46 |
| CONF21 | -1506.7427883 | 1.51 | -1506.7485189 | 1.50 | -1506.7545056 | 1.49 |
| CONF22 | -1506.7424890 | 1.69 | -1506.7482067 | 1.70 | -1506.7541817 | 1.69 |
| CONF23 | -1506.7424365 | 1.73 | -1506.7481663 | 1.72 | -1506.7541534 | 1.71 |
| CONF24 | -1506.7424369 | 1.73 | -1506.7481575 | 1.73 | -1506.7541388 | 1.72 |
| CONF25 | -1506.7423019 | 1.81 | -1506.7480287 | 1.81 | -1506.7540121 | 1.80 |
| CONF26 | -1506.7422470 | 1.85 | -1506.7479516 | 1.86 | -1506.7539147 | 1.86 |
| CONF27 | -1506.7420906 | 1.94 | -1506.7478268 | 1.93 | -1506.7538185 | 1.92 |
| CONF28 | -1506.7421297 | 1.92 | -1506.7478474 | 1.92 | -1506.7538219 | 1.92 |
| CONF29 | -1506.7420525 | 1.97 | -1506.7477827 | 1.96 | -1506.7537689 | 1.95 |
| CONF30 | -1506.7418123 | 2.12 | -1506.7475292 | 2.12 | -1506.7535057 | 2.12 |
| CONF31 | -1506.7417322 | 2.17 | -1506.7474637 | 2.16 | -1506.7534522 | 2.15 |
| CONF32 | -1506.7416213 | 2.24 | -1506.7473470 | 2.24 | -1506.7533335 | 2.23 |
| CONF33 | -1506.7415279 | 2.30 | -1506.7472467 | 2.30 | -1506.7532217 | 2.30 |
| CONF34 | -1506.7415045 | 2.31 | -1506.7472216 | 2.31 | -1506.7531994 | 2.31 |
| CONF35 | -1506.7412985 | 2.44 | -1506.7470144 | 2.44 | -1506.7529888 | 2.44 |
| CONF36 | -1506.7409763 | 2.64 | -1506.7466693 | 2.66 | -1506.7526216 | 2.67 |
| CONF37 | -1506.7405839 | 2.89 | -1506.7462834 | 2.90 | -1506.7522415 | 2.91 |
| CONF38 | -1506.7404543 | 2.97 | -1506.7461561 | 2.98 | -1506.7521174 | 2.99 |
| CONF39 | -1506.7403628 | 3.03 | -1506.7460853 | 3.03 | -1506.7520681 | 3.02 |
| CONF40 | -1506.7403688 | 3.03 | -1506.7460783 | 3.03 | -1506.7520478 | 3.03 |
| CONF41 | -1506.7402343 | 3.11 | -1506.7459260 | 3.13 | -1506.7518759 | 3.14 |
| CONF42 | -1506.7400646 | 3.22 | -1506.7457682 | 3.23 | -1506.7517318 | 3.23 |
| CONF43 | -1506.7400251 | 3.24 | -1506.7457362 | 3.25 | -1506.7517070 | 3.25 |
| CONF44 | -1506.7399567 | 3.28 | -1506.7456541 | 3.30 | -1506.7516092 | 3.31 |
| CONF45 | -1506.7398280 | 3.36 | -1506.7455551 | 3.36 | -1506.7515418 | 3.35 |
| CONF46 | -1506.7399157 | 3.31 | -1506.7456008 | 3.33 | -1506.7515436 | 3.35 |
| CONF47 | -1506.7397351 | 3.42 | -1506.7454458 | 3.43 | -1506.7514167 | 3.43 |

Table S11(continuation). Gibbs free energies ($G$) for monomer conformers of $\mathbf{1_{t1}}$ at different temperatures.

| CONF | G [$E_h$] 293 K | ΔG [kcal/mol] 293 K | G [$E_h$] 298 K | ΔG [kcal/mol] 298 K | G [$E_h$] 313 K | ΔG [kcal/mol] 313 K |
|---|---|---|---|---|---|---|
| CONF1 | -1506.7631071 | 0.00 | -1506.7647019 | 0.00 | -1506.7695789 | 0.00 |
| CONF2 | -1506.7626979 | 0.26 | -1506.7642926 | 0.26 | -1506.7691686 | 0.26 |
| CONF3 | -1506.7622573 | 0.53 | -1506.7638537 | 0.53 | -1506.7687361 | 0.53 |
| CONF4 | -1506.7620453 | 0.67 | -1506.7636413 | 0.67 | -1506.7685222 | 0.66 |
| CONF5 | -1506.7619860 | 0.70 | -1506.7635804 | 0.70 | -1506.7684560 | 0.70 |
| CONF6 | -1506.7617941 | 0.82 | -1506.7633904 | 0.82 | -1506.7682722 | 0.82 |
| CONF7 | -1506.7617842 | 0.83 | -1506.7633792 | 0.83 | -1506.7682568 | 0.83 |
| CONF8 | -1506.7617671 | 0.84 | -1506.7633633 | 0.84 | -1506.7682448 | 0.84 |
| CONF9 | -1506.7616932 | 0.89 | -1506.7632853 | 0.89 | -1506.7681535 | 0.89 |
| CONF10 | -1506.7615954 | 0.95 | -1506.7631896 | 0.95 | -1506.7680648 | 0.95 |
| CONF11 | -1506.7615154 | 1.00 | -1506.7631108 | 1.00 | -1506.7679892 | 1.00 |
| CONF12 | -1506.7613881 | 1.08 | -1506.7629827 | 1.08 | -1506.7678585 | 1.08 |
| CONF13 | -1506.7612875 | 1.14 | -1506.7628870 | 1.14 | -1506.7677788 | 1.13 |
| CONF14 | -1506.7612468 | 1.17 | -1506.7628424 | 1.17 | -1506.7677223 | 1.17 |
| CONF15 | -1506.7612408 | 1.17 | -1506.7628370 | 1.17 | -1506.7677190 | 1.17 |
| CONF16 | -1506.7612121 | 1.19 | -1506.7628079 | 1.19 | -1506.7676886 | 1.19 |
| CONF17 | -1506.7611058 | 1.26 | -1506.7627007 | 1.26 | -1506.7675773 | 1.26 |
| CONF18 | -1506.7608479 | 1.42 | -1506.7624426 | 1.42 | -1506.7673195 | 1.42 |
| CONF19 | -1506.7608408 | 1.42 | -1506.7624337 | 1.42 | -1506.7673047 | 1.43 |
| CONF20 | -1506.7607796 | 1.46 | -1506.7623749 | 1.46 | -1506.7672537 | 1.46 |
| CONF21 | -1506.7607446 | 1.48 | -1506.7623434 | 1.48 | -1506.7672326 | 1.47 |
| CONF22 | -1506.7604101 | 1.69 | -1506.7620064 | 1.69 | -1506.7668884 | 1.69 |
| CONF23 | -1506.7603938 | 1.70 | -1506.7619930 | 1.70 | -1506.7668840 | 1.69 |
| CONF24 | -1506.7603767 | 1.71 | -1506.7619759 | 1.71 | -1506.7668677 | 1.70 |
| CONF25 | -1506.7602482 | 1.79 | -1506.7618463 | 1.79 | -1506.7667336 | 1.79 |
| CONF26 | -1506.7601324 | 1.87 | -1506.7617261 | 1.87 | -1506.7666012 | 1.87 |
| CONF27 | -1506.7600618 | 1.91 | -1506.7616616 | 1.91 | -1506.7665537 | 1.90 |
| CONF28 | -1506.7600495 | 1.92 | -1506.7616456 | 1.92 | -1506.7665268 | 1.92 |
| CONF29 | -1506.7600073 | 1.95 | -1506.7616059 | 1.94 | -1506.7664945 | 1.94 |
| CONF30 | -1506.7597377 | 2.11 | -1506.7613352 | 2.11 | -1506.7662218 | 2.11 |
| CONF31 | -1506.7596938 | 2.14 | -1506.7612933 | 2.14 | -1506.7661851 | 2.13 |
| CONF32 | -1506.7595766 | 2.22 | -1506.7611770 | 2.21 | -1506.7660727 | 2.20 |
| CONF33 | -1506.7594492 | 2.30 | -1506.7610451 | 2.29 | -1506.7659257 | 2.29 |
| CONF34 | -1506.7594338 | 2.31 | -1506.7610320 | 2.30 | -1506.7659211 | 2.30 |
| CONF35 | -1506.7592177 | 2.44 | -1506.7608143 | 2.44 | -1506.7656977 | 2.44 |
| CONF36 | -1506.7588291 | 2.68 | -1506.7604204 | 2.69 | -1506.7652883 | 2.69 |
| CONF37 | -1506.7584543 | 2.92 | -1506.7600468 | 2.92 | -1506.7649182 | 2.92 |
| CONF38 | -1506.7583341 | 3.00 | -1506.7599277 | 3.00 | -1506.7648027 | 3.00 |
| CONF39 | -1506.7583069 | 3.01 | -1506.7599061 | 3.01 | -1506.7647982 | 3.00 |
| CONF40 | -1506.7582731 | 3.03 | -1506.7598690 | 3.03 | -1506.7647508 | 3.03 |
| CONF41 | -1506.7580800 | 3.15 | -1506.7596703 | 3.16 | -1506.7645350 | 3.17 |
| CONF42 | -1506.7579514 | 3.24 | -1506.7595459 | 3.24 | -1506.7644234 | 3.24 |
| CONF43 | -1506.7579335 | 3.25 | -1506.7595296 | 3.25 | -1506.7644122 | 3.24 |
| CONF44 | -1506.7578180 | 3.32 | -1506.7594095 | 3.32 | -1506.7642773 | 3.33 |
| CONF45 | -1506.7577841 | 3.34 | -1506.7593842 | 3.34 | -1506.7642785 | 3.33 |
| CONF46 | -1506.7577402 | 3.37 | -1506.7593286 | 3.37 | -1506.7641872 | 3.38 |
| CONF47 | -1506.7576436 | 3.43 | -1506.7592399 | 3.43 | -1506.7641230 | 3.42 |

Table S12. Gibbs free energies ($G$) for dimer conformers of $\mathbf{1_{t1}}$ at different temperatures.

| CONF (dimer) | G [$E_h$] 233 K | ΔG [kcal/mol] 233 K | G [$E_h$] 253 K | ΔG [kcal/mol] 253 K | G [$E_h$] 273 K | ΔG [kcal/mol] 273 K |
|---|---|---|---|---|---|---|
| CONF1 | -1506.7451897 | 0.00 | -1506.7509090 | 0.00 | -1506.7568827 | 0.00 |
| CONF2 | -1506.7447804 | 0.28 | -1506.7505004 | 0.28 | -1506.7564741 | 0.28 |
| CONF3 | -1506.7443329 | 0.29 | -1506.7500520 | 0.32 | -1506.7560282 | 0.35 |
| CONF4 | -1506.7441282 | 0.42 | -1506.7498446 | 0.42 | -1506.7558183 | 0.42 |
| CONF5 | -1506.7440714 | 0.59 | -1506.7497902 | 0.58 | -1506.7557630 | 0.58 |
| CONF6 | -1506.7438705 | 0.77 | -1506.7495897 | 0.77 | -1506.7555655 | 0.76 |
| CONF7 | -1506.7438737 | 0.88 | -1506.7495891 | 0.90 | -1506.7555606 | 0.92 |
| CONF8 | -1506.7438461 | 0.92 | -1506.7495641 | 0.94 | -1506.7555391 | 0.96 |
| CONF9 | -1506.7438008 | 1.02 | -1506.7495135 | 1.03 | -1506.7554789 | 1.04 |
| CONF10 | -1506.7436885 | 0.99 | -1506.7494037 | 1.01 | -1506.7553739 | 1.04 |
| CONF11 | -1506.7435880 | 1.12 | -1506.7493114 | 1.11 | -1506.7552884 | 1.10 |
| CONF12 | -1506.7434740 | 1.16 | -1506.7491924 | 1.15 | -1506.7551650 | 1.15 |
| CONF13 | -1506.7433286 | 1.14 | -1506.7490587 | 1.15 | -1506.7550463 | 1.17 |
| CONF14 | -1506.7433336 | 1.21 | -1506.7490488 | 1.21 | -1506.7550212 | 1.21 |
| CONF15 | -1506.7433183 | 1.18 | -1506.7490368 | 1.19 | -1506.7550122 | 1.21 |
| CONF16 | -1506.7432941 | 1.31 | -1506.7490112 | 1.32 | -1506.7549852 | 1.34 |
| CONF17 | -1506.7431828 | 1.41 | -1506.7489051 | 1.42 | -1506.7548807 | 1.43 |
| CONF18 | -1506.7429376 | 1.50 | -1506.7486535 | 1.53 | -1506.7546249 | 1.55 |
| CONF19 | -1506.7429500 | 1.42 | -1506.7486599 | 1.47 | -1506.7546248 | 1.53 |
| CONF20 | -1506.7428644 | 1.69 | -1506.7485814 | 1.67 | -1506.7545544 | 1.66 |
| CONF21 | -1506.7427883 | 1.61 | -1506.7485189 | 1.62 | -1506.7545056 | 1.64 |
| CONF22 | -1506.7424890 | 1.66 | -1506.7482067 | 1.66 | -1506.7541817 | 1.67 |
| CONF23 | -1506.7424365 | 1.74 | -1506.7481663 | 1.74 | -1506.7541534 | 1.74 |
| CONF24 | -1506.7424369 | 1.74 | -1506.7481575 | 1.76 | -1506.7541388 | 1.78 |
| CONF25 | -1506.7423019 | 1.89 | -1506.7480287 | 1.91 | -1506.7540121 | 1.94 |
| CONF26 | -1506.7422470 | 1.98 | -1506.7479516 | 1.98 | -1506.7539147 | 1.98 |
| CONF27 | -1506.7420906 | 1.97 | -1506.7478268 | 1.98 | -1506.7538185 | 1.99 |
| CONF28 | -1506.7421297 | 2.06 | -1506.7478474 | 2.06 | -1506.7538219 | 2.07 |
| CONF29 | -1506.7420525 | 2.09 | -1506.7477827 | 2.09 | -1506.7537689 | 2.10 |
| CONF30 | -1506.7418123 | 2.05 | -1506.7475292 | 2.08 | -1506.7535057 | 2.11 |
| CONF31 | -1506.7417322 | 2.18 | -1506.7474637 | 2.20 | -1506.7534522 | 2.22 |
| CONF32 | -1506.7416213 | 2.25 | -1506.7473470 | 2.25 | -1506.7533335 | 2.25 |
| CONF33 | -1506.7415279 | 2.31 | -1506.7472467 | 2.36 | -1506.7532217 | 2.40 |
| CONF34 | -1506.7415045 | 2.34 | -1506.7472216 | 2.37 | -1506.7531994 | 2.41 |
| CONF35 | -1506.7412985 | 2.43 | -1506.7470144 | 2.44 | -1506.7529888 | 2.45 |
| CONF36 | -1506.7409763 | 2.44 | -1506.7466693 | 2.46 | -1506.7526216 | 2.48 |
| CONF37 | -1506.7405839 | 2.62 | -1506.7462834 | 2.64 | -1506.7522415 | 2.65 |
| CONF38 | -1506.7404543 | 2.82 | -1506.7461561 | 2.86 | -1506.7521174 | 2.89 |
| CONF39 | -1506.7403628 | 2.86 | -1506.7460853 | 2.89 | -1506.7520681 | 2.93 |
| CONF40 | -1506.7403688 | 3.11 | -1506.7460783 | 3.17 | -1506.7520478 | 3.23 |
| CONF41 | -1506.7402343 | 3.24 | -1506.7459260 | 3.31 | -1506.7518759 | 3.37 |

Table S12. Gibbs free energies ($G$) for dimer conformers of $\mathbf{1_{t1}}$ at different temperatures. (continuation)

| CONF | G [$E_h$] 293 K | ΔG [kcal/mol] 293 K | G [$E_h$] 298 K | ΔG [kcal/mol] 298 K | G [$E_h$] 313 K | ΔG [kcal/mol] 313 K |
|---|---|---|---|---|---|---|
| CONF1 | -1506.7631071 | 0.00 | -1506.7647019 | 0.00 | -1506.7695789 | 0.00 |
| CONF2 | -1506.7626979 | 0.27 | -1506.7642926 | 0.27 | -1506.7691686 | 0.27 |
| CONF3 | -1506.7622573 | 0.39 | -1506.7638537 | 0.39 | -1506.7687361 | 0.42 |
| CONF4 | -1506.7620453 | 0.42 | -1506.7636413 | 0.42 | -1506.7685222 | 0.42 |
| CONF5 | -1506.7619860 | 0.59 | -1506.7635804 | 0.59 | -1506.7684560 | 0.59 |
| CONF6 | -1506.7617941 | 0.75 | -1506.7633904 | 0.75 | -1506.7682722 | 0.74 |
| CONF7 | -1506.7617842 | 0.95 | -1506.7633792 | 0.95 | -1506.7682568 | 0.98 |
| CONF8 | -1506.7617671 | 0.98 | -1506.7633633 | 0.98 | -1506.7682448 | 0.99 |
| CONF9 | -1506.7616932 | 1.05 | -1506.7632853 | 1.05 | -1506.7681535 | 1.06 |
| CONF10 | -1506.7615954 | 1.06 | -1506.7631896 | 1.07 | -1506.7680648 | 1.09 |
| CONF11 | -1506.7615154 | 1.09 | -1506.7631108 | 1.08 | -1506.7679892 | 1.08 |
| CONF12 | -1506.7613881 | 1.14 | -1506.7629827 | 1.14 | -1506.7678585 | 1.15 |
| CONF13 | -1506.7612875 | 1.18 | -1506.7628870 | 1.18 | -1506.7677788 | 1.20 |
| CONF14 | -1506.7612468 | 1.22 | -1506.7628424 | 1.22 | -1506.7677223 | 1.22 |
| CONF15 | -1506.7612408 | 1.22 | -1506.7628370 | 1.23 | -1506.7677190 | 1.24 |
| CONF16 | -1506.7612121 | 1.36 | -1506.7628079 | 1.37 | -1506.7676886 | 1.38 |
| CONF17 | -1506.7611058 | 1.44 | -1506.7627007 | 1.45 | -1506.7675773 | 1.45 |
| CONF18 | -1506.7608479 | 1.58 | -1506.7624426 | 1.59 | -1506.7673195 | 1.61 |
| CONF19 | -1506.7608408 | 1.59 | -1506.7624337 | 1.60 | -1506.7673047 | 1.65 |
| CONF20 | -1506.7607796 | 1.64 | -1506.7623749 | 1.63 | -1506.7672537 | 1.62 |
| CONF21 | -1506.7607446 | 1.66 | -1506.7623434 | 1.67 | -1506.7672326 | 1.68 |
| CONF22 | -1506.7604101 | 1.69 | -1506.7620064 | 1.69 | -1506.7668884 | 1.70 |
| CONF23 | -1506.7603938 | 1.75 | -1506.7619930 | 1.75 | -1506.7668840 | 1.75 |
| CONF24 | -1506.7603767 | 1.80 | -1506.7619759 | 1.81 | -1506.7668677 | 1.83 |
| CONF25 | -1506.7602482 | 1.96 | -1506.7618463 | 1.97 | -1506.7667336 | 1.99 |
| CONF26 | -1506.7601324 | 1.99 | -1506.7617261 | 1.99 | -1506.7666012 | 2.00 |
| CONF27 | -1506.7600618 | 2.01 | -1506.7616616 | 2.02 | -1506.7665537 | 2.03 |
| CONF28 | -1506.7600495 | 2.07 | -1506.7616456 | 2.08 | -1506.7665268 | 2.09 |
| CONF29 | -1506.7600073 | 2.11 | -1506.7616059 | 2.11 | -1506.7664945 | 2.12 |
| CONF30 | -1506.7597377 | 2.14 | -1506.7613352 | 2.15 | -1506.7662218 | 2.17 |
| CONF31 | -1506.7596938 | 2.24 | -1506.7612933 | 2.25 | -1506.7661851 | 2.26 |
| CONF32 | -1506.7595766 | 2.25 | -1506.7611770 | 2.25 | -1506.7660727 | 2.25 |
| CONF33 | -1506.7594492 | 2.44 | -1506.7610451 | 2.45 | -1506.7659257 | 2.48 |
| CONF34 | -1506.7594338 | 2.45 | -1506.7610320 | 2.46 | -1506.7659211 | 2.49 |
| CONF35 | -1506.7592177 | 2.47 | -1506.7608143 | 2.47 | -1506.7656977 | 2.48 |
| CONF36 | -1506.7588291 | 2.51 | -1506.7604204 | 2.52 | -1506.7652883 | 2.54 |
| CONF37 | -1506.7584543 | 2.67 | -1506.7600468 | 2.68 | -1506.7649182 | 2.70 |
| CONF38 | -1506.7583341 | 2.93 | -1506.7599277 | 2.94 | -1506.7648027 | 2.97 |
| CONF39 | -1506.7583069 | 2.97 | -1506.7599061 | 2.98 | -1506.7647982 | 3.01 |
| CONF40 | -1506.7582731 | 3.29 | -1506.7598690 | 3.30 | -1506.7647508 | 3.35 |
| CONF41 | -1506.7580800 | 3.45 | -1506.7596703 | 3.46 | -1506.7645350 | 3.52 |

Table S13. Boltzmann averaged free energy $G$ of ensemble of 47 monomers of $\mathbf{1_{t1}}$ ($E_h$):

| $T$ / K | $\langle E_{gas} \rangle$ | $\langle G_{mRRHO} \rangle$ | $\langle G_{solv} \rangle$ | $\langle G \rangle$ |
|---|---|---|---|---|
| 233 | -1507.1118680 | 0.4091322 | -0.0414216 | -1506.7441574 |
| 253 | -1507.1117665 | 0.4034176 | -0.0414428 | -1506.7497917 |
| 273 | -1507.1116754 | 0.3974478 | -0.0414598 | -1506.7556874 |
| 293 | -1507.1115927 | 0.3912264 | -0.0414738 | -1506.7618401 |
| 298 | -1507.1115732 | 0.3896321 | -0.0414769 | -1506.7634180 |
| 313 | -1507.1115171 | 0.3847563 | -0.0414854 | -1506.7682461 |

Table S14. Boltzmann averaged free energy $G$ of ensemble of 41 dimer structures of $\mathbf{1_{t1}}$ ($E_h$):

| $T$ / K | $\langle E_{gas} \rangle$ | $\langle G_{mRRHO} \rangle$ | $\langle G_{solv} \rangle$ | $\langle G \rangle$ |
|---|---|---|---|---|
| 233 | -3014.2977470 | 0.8458926 | -0.0506042 | -3013.5024586 |
| 253 | -3014.2975688 | 0.8363840 | -0.0506951 | -3013.5118799 |
| 273 | -3014.2974074 | 0.8263455 | -0.0507776 | -3013.5218394 |
| 293 | -3014.2972638 | 0.8157857 | -0.0508500 | -3013.5323280 |
| 298 | -3014.2972306 | 0.8130652 | -0.0508666 | -3013.5350319 |
| 313 | -3014.2971361 | 0.8047120 | -0.0509137 | -3013.5433377 |

Table S15. Gibbs free energy of formation as calculated from equation $\Delta G = G(\text{dimer}) - 2xG(\text{monomer})$.

| $T$ / K | $\Delta G/[E_h]$ | $\Delta G$/kcal mol$^{-1}$ |
|---|---|---|
| 233 | 0.014144 | 8.88 |
| 253 | 0.012297 | 7.72 |
| 273 | 0.010465 | 6.57 |
| 293 | 0.008648 | 5.43 |
| 298 | 0.008196 | 5.14 |
| 313 | 0.006846 | 4.30 |

Table S16. Experimental and calculated NMR parameters for monomer ensemble of $\mathbf{1_{t1}}$ at different temperatures.

Part 1: $^1$H NMR experimental shifts and calculated shieldings and shifts*

| Lab. ($^1$H) | shift exp. (233 K) | shield. averaged (233 K) | shift calc. (233 K) | shift exp. (253 K) | shield. averaged (253 K) | shift calc. (253 K) | shift exp. (273 K) | shield. averaged (273 K) | shift calc. (273 K) |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 8.220 | 22.483 | 8.195 | 8.260 | 22.493 | 8.229 | 8.290 | 22.492 | 8.264 |
| 5 | 8.190 | 22.252 | 8.397 | 8.240 | 22.254 | 8.442 | 8.290 | 22.254 | 8.478 |
| 15 | 4.180 | 26.892 | 4.314 | 4.170 | 26.892 | 4.316 | 4.161 | 26.894 | 4.315 |
| 16 | 4.160 | 27.080 | 4.149 | 4.160 | 27.082 | 4.147 | 4.159 | 27.080 | 4.149 |
| 18 | 1.420 | 29.970 | 1.606 | 1.410 | 29.971 | 1.577 | 1.410 | 29.972 | 1.554 |
| 22 | 1.530 | 30.049 | 1.537 | 1.490 | 30.049 | 1.508 | 1.460 | 30.048 | 1.486 |
| 28 | 8.120 | 24.388 | 6.518 | 7.870 | 24.385 | 6.546 | 7.610 | 24.382 | 6.569 |
| 30 | 4.860 | 26.851 | 4.351 | 4.850 | 26.854 | 4.349 | 4.840 | 26.855 | 4.350 |
| 32 | 1.610 | 29.856 | 1.706 | 1.590 | 29.855 | 1.680 | 1.570 | 29.855 | 1.659 |
| 39 | 3.820 | 27.537 | 3.747 | 3.810 | 27.542 | 3.737 | 3.810 | 27.544 | 3.732 |
| | | | | | | | | | |
| | | MAE(C-H): | 0.13881 | | | 0.13778 | | | 0.13402 |
| | | AE(N-H): | 1.60189 | | | 1.32362 | | | 1.04140 |

| Lab. ($^1$H) | shift exp. (293 K) | shield. averaged (293 K) | shift calc. (293 K) | shift exp. (298 K) | shield. averaged (298 K) | shift calc. (298 K) | shift exp. (313 K) | shield. averaged (313 K) | shift calc. (313 K) |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 8.310 | 22.492 | 8.299 | 8.320 | 22.492 | 8.308 | 8.330 | 22.491 | 8.325 |
| 5 | 8.330 | 22.254 | 8.513 | 8.340 | 22.254 | 8.523 | 8.370 | 22.255 | 8.540 |
| 15 | 4.150 | 26.987 | 4.240 | 4.150 | 26.987 | 4.239 | 4.140 | 26.987 | 4.241 |
| | | | | | | | | | |
| 18 | 1.404 | 29.975 | 1.542 | 1.403 | 29.975 | 1.535 | 1.420 | 29.976 | 1.525 |
| 22 | 1.440 | 30.044 | 1.479 | 1.434 | 30.044 | 1.472 | 1.399 | 30.043 | 1.464 |
| 28 | 7.380 | 24.370 | 6.603 | 7.330 | 24.369 | 6.608 | 7.170 | 24.368 | 6.620 |
| 30 | 4.830 | 26.849 | 4.364 | 4.830 | 26.849 | 4.364 | 4.820 | 26.849 | 4.366 |
| 32 | 1.560 | 29.854 | 1.651 | 1.550 | 29.854 | 1.644 | 1.550 | 29.854 | 1.636 |
| 39 | 3.800 | 27.544 | 3.737 | 3.800 | 27.544 | 3.735 | 3.790 | 27.545 | 3.734 |
| | | | | | | | | | |
| | | MAE(C-H): | 0.13506 | | | 0.13488 | | | 0.13024 |
| | | AE(N-H): | 0.77710 | | | 0.72172 | | | 0.54950 |

* Shift calc. is obtained by using linear regression equation between shield. averaged (x) and shift exp (y), see Figure S22-S27. Linear regression equation is calculated for all $^1$H nuclei bonded to carbon atoms, independently for each *T*. MAE(C-H) is the mean absolute error for $^1$H nuclei with respect to the calculated linear regression equation. AE(N-H) is absolute error for $^1$H amide nuclei with respect to the calculated linear regression equation.

Part 2: Experimental and calculated $^{1}$H-$^{1}$H *J* couplings**

| | 2-bond | | | 3-bond | | | | | 4-bond | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *T* (K) | *J*(15-16) | exp. | | *J*(28-30) | exp. | *J*(15-16) | exp. | | *J*(2-5) | exp. | *J*(5-8) | exp. | *J*(15-18) | *J*(16-18) | *J*(18-22) | *J*(28-32) |
| 233 | -9.00 | 7.9 | | 5.94 | 7.9 | 7.04 | 7.4 | | 0.90 | | 0.75 | | 0.13 | -0.10 | 0.24 | -0.29 |
| 253 | -9.00 | 7.8 | | 5.84 | 7.6 | 7.13 | 7.4 | | 0.89 | 1.7 | 0.75 | 1.7 | 0.13 | -0.10 | 0.24 | -0.29 |
| 273 | -9.00 | | | 5.81 | 7.6 | 7.13 | 7.3 | | 0.89 | | 0.75 | | 0.13 | -0.10 | 0.24 | -0.29 |
| 293 | -9.00 | | | 5.76 | 7.5 | 7.13 | 7.3 | | 0.89 | 1.7 | 0.75 | 1.7 | 0.13 | -0.10 | 0.24 | -0.28 |
| 298 | -9.00 | | | 5.76 | 7.5 | 7.13 | 7.3 | | 0.89 | 1.7 | 0.75 | 1.7 | 0.13 | -0.10 | 0.24 | -0.28 |
| 313 | -9.00 | | | 5.74 | 7.5 | 7.13 | 7.2 | | 0.89 | 1.7 | 0.75 | 1.7 | 0.13 | -0.10 | 0.24 | -0.28 |

** Experimentally observed *J* couplings and their corresponding calculated values (left from exp. values) are shaded grey.

Part 3: $^{13}$C NMR experimental shifts and calculated shieldings and shifts for T = 298 K***

| Lab. ($^{13}$C) | shield. averaged (293 K) | shift exp. (293 K) | shift calc. (293 K) |
|---|---|---|---|
| 1 | 44.735 | 129.679 | 129.213 |
| 3 | 39.860 | 134.903 | 133.767 |
| 4 | 43.546 | 129.083 | 130.324 |
| 6 | 46.157 | 128.334 | 127.884 |
| 11 | 10.697 | 161.781 | 161.008 |
| 13 | 110.184 | 67.472 | 68.077 |
| 14 | 98.519 | 79.352 | 78.973 |
| 17 | 154.933 | 27.002 | 26.277 |
| 25 | 6.169 | 166.965 | 165.238 |
| 29 | 128.827 | 48.850 | 50.663 |
| 31 | 167.004 | 15.823 | 15.001 |
| 35 | -4.962 | 173.230 | 175.635 |
| 38 | 127.566 | 51.445 | 51.840 |
| | | | |
| | | MAE: | 0.99512 |

*** Shift calc. is obtained by using linear regression equation between shield. averaged (x) and shift exp (y), see Figure S25. Linear regression equation is calculated for all $^{13}$C nuclei. MAE is the mean absolute error for $^{13}$C nuclei with respect to the calculated linear regression equation.

Table S17. Experimental and calculated NMR parameters for dimer ensemble of $\mathbf{1_{t1}}$ at different temperatures.

Part 1: $^1$H NMR experimental shifts and calculated shieldings and shifts*

| Lab. ($^1$H) | shift exp. (233 K) | shield. averaged (233 K) | shift calc. (233 K) | shift exp. (253 K) | shield. averaged (253 K) | shift calc. (253 K) | shift exp. (273 K) | shield. averaged (273 K) | shift calc. (273 K) |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 8.220 | 22.535 | 8.416 | 8.260 | 22.549 | 8.447 | 8.290 | 22.563 | 8.473 |
| 5 | 8.190 | 22.961 | 8.011 | 8.240 | 22.957 | 8.055 | 8.290 | 22.953 | 8.095 |
| 15 | 4.180 | 26.917 | 4.256 | 4.170 | 26.917 | 4.256 | 4.161 | 26.917 | 4.260 |
| 16 | 4.160 | 26.990 | 4.187 | 4.160 | 26.994 | 4.183 | 4.159 | 26.993 | 4.187 |
| 18 | 1.420 | 29.916 | 1.409 | 1.410 | 29.918 | 1.378 | 1.410 | 29.917 | 1.357 |
| 22 | 1.530 | 29.714 | 1.602 | 1.490 | 29.714 | 1.574 | 1.460 | 29.720 | 1.548 |
| 28 | 8.120 | 22.276 | 8.662 | 7.870 | 22.280 | 8.705 | 7.610 | 22.282 | 8.745 |
| 30 | 4.860 | 26.407 | 4.741 | 4.850 | 26.406 | 4.747 | 4.840 | 26.409 | 4.752 |
| 32 | 1.610 | 29.728 | 1.588 | 1.590 | 29.731 | 1.557 | 1.570 | 29.732 | 1.536 |
| 39 | 3.820 | 27.415 | 3.784 | 3.810 | 27.415 | 3.779 | 3.810 | 27.415 | 3.778 |
| | | | | | | | | | |
| | | MAE(C-H): | 0.08180 | | | 0.08488 | | | 0.08862 |
| | | AE(N-H): | 0.54169 | | | 0.83490 | | | 1.13510 |

| Lab. ($^1$H) | shift exp. (293 K) | shield. averaged (293 K) | shift calc. (293 K) | shift exp. (298 K) | shield. averaged (298 K) | shift calc. (298 K) | shift exp. (313 K) | shield. averaged (313 K) | shift calc. (313 K) |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 8.310 | 22.567 | 8.503 | 8.320 | 22.568 | 8.513 | 8.330 | 22.569 | 8.525 |
| 5 | 8.330 | 22.951 | 8.129 | 8.340 | 22.951 | 8.138 | 8.370 | 22.950 | 8.152 |
| 15 | 4.150 | 26.955 | 4.231 | 4.150 | 26.955 | 4.232 | 4.140 | 26.955 | 4.231 |
| | | | | | | | | | |
| 18 | 1.404 | 29.917 | 1.348 | 1.403 | 29.917 | 1.342 | 1.420 | 29.917 | 1.330 |
| 22 | 1.440 | 29.722 | 1.537 | 1.434 | 29.723 | 1.532 | 1.399 | 29.724 | 1.519 |
| 28 | 7.380 | 22.283 | 8.779 | 7.330 | 22.283 | 8.790 | 7.170 | 22.284 | 8.804 |
| 30 | 4.830 | 26.409 | 4.763 | 4.830 | 26.409 | 4.765 | 4.820 | 26.408 | 4.766 |
| 32 | 1.560 | 29.733 | 1.527 | 1.550 | 29.733 | 1.522 | 1.550 | 29.733 | 1.510 |
| 39 | 3.800 | 27.415 | 3.784 | 3.800 | 27.415 | 3.783 | 3.790 | 27.415 | 3.780 |
| | | | | | | | | | |
| | | MAE(C-H): | 0.09311 | | | 0.09320 | | | 0.10213 |
| | | AE(N-H): | 1.39946 | | | 1.46029 | | | 1.63419 |

* Shift calc. is obtained by using linear regression equation between shield. averaged (x) and shift exp (y), see Figure S22-Figure S27. Linear regression equation is calculated for all $^1$H nuclei bonded to carbon atoms, independently for each *T*. MAE(C-H) is the mean absolute error for $^1$H nuclei with respect to the calculated linear regression equation. AE(N-H) is absolute error for $^1$H amide nuclei with respect to the calculated linear regression equation.

Part 2: Experimental and calculated $^{1}$H-$^{1}$H *J* couplings**

| | 2-bond | | | 3-bond | | | | | 4-bond | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *T* (K) | *J*(15-16) | exp. | | *J*(28-30) | exp. | *J*(15-16) | exp. | | *J*(2-5) | exp. | *J*(5-8) | exp. | *J*(15-18) | *J*(16-18) | *J*(18-22) | *J*(28-32) |
| 233 | -8.49 | 7.9 | | 7.62 | 7,9 | 6.82 | 7,4 | | 0,87 | | 0.64 | | 0.12 | -0.08 | 0.23 | -0.21 |
| 253 | -8.88 | 7.8 | | 7.89 | 7,6 | 7.12 | 7,4 | | 0,90 | 1.7 | 0.67 | 1.7 | 0.12 | -0.09 | 0.24 | -0.21 |
| 273 | -8.90 | | | 7.85 | 7,6 | 7.12 | 7,3 | | 0,90 | | 0.68 | | 0.12 | -0.09 | 0.24 | -0.22 |
| 293 | -8.90 | | | 7.85 | 7,5 | 7.12 | 7,3 | | 0,90 | 1.7 | 0.68 | 1.7 | 0.12 | -0.09 | 0.24 | -0.22 |
| 298 | -8.90 | | | 7.85 | 7,5 | 7.12 | 7,3 | | 0,90 | 1.7 | 0.68 | 1.7 | 0.12 | -0.09 | 0.24 | -0.22 |
| 313 | -8.90 | | | 7.85 | 7,5 | 7.12 | 7,2 | | 0,90 | 1.7 | 0.68 | 1.7 | 0.13 | -0.09 | 0.24 | -0.22 |

** Experimentally observed *J* couplings and their corresponding calculated values (left from exp. values) are shaded grey.

Part 3: $^{13}$C NMR experimental shifts and calculated shieldings and shifts for T = 298 K***

| Lab. ($^{13}$C) | shield. averaged (293 K) | shift exp. (293 K) | shift calc. (293 K) |
|---|---|---|---|
| 1 | 43.181 | 129.679 | 130.235 |
| 3 | 40.622 | 134.903 | 132.612 |
| 4 | 43.442 | 129.083 | 129.993 |
| 6 | 46.960 | 128.334 | 126.724 |
| 11 | 8.045 | 161.781 | 162.876 |
| 13 | 110.004 | 67.472 | 68.156 |
| 14 | 98.491 | 79.352 | 78.852 |
| 17 | 155.372 | 27.002 | 26.010 |
| 25 | 6.772 | 166.965 | 164.059 |
| 29 | 129.526 | 48.850 | 50.020 |
| 31 | 166.668 | 15.823 | 15.515 |
| 35 | -6.212 | 173.230 | 176.121 |
| 38 | 126.685 | 51.445 | 52.660 |
| | | | |
| | | MAE: | 1.31755 |

*** Shift calc. is obtained by using linear regression equation between shield. averaged (x) and shift exp (y), see Figure S27. Linear regression equation is calculated for all $^{13}$C nuclei. MAE is the mean absolute error for $^{13}$C nuclei with respect to the calculated linear regression equation.

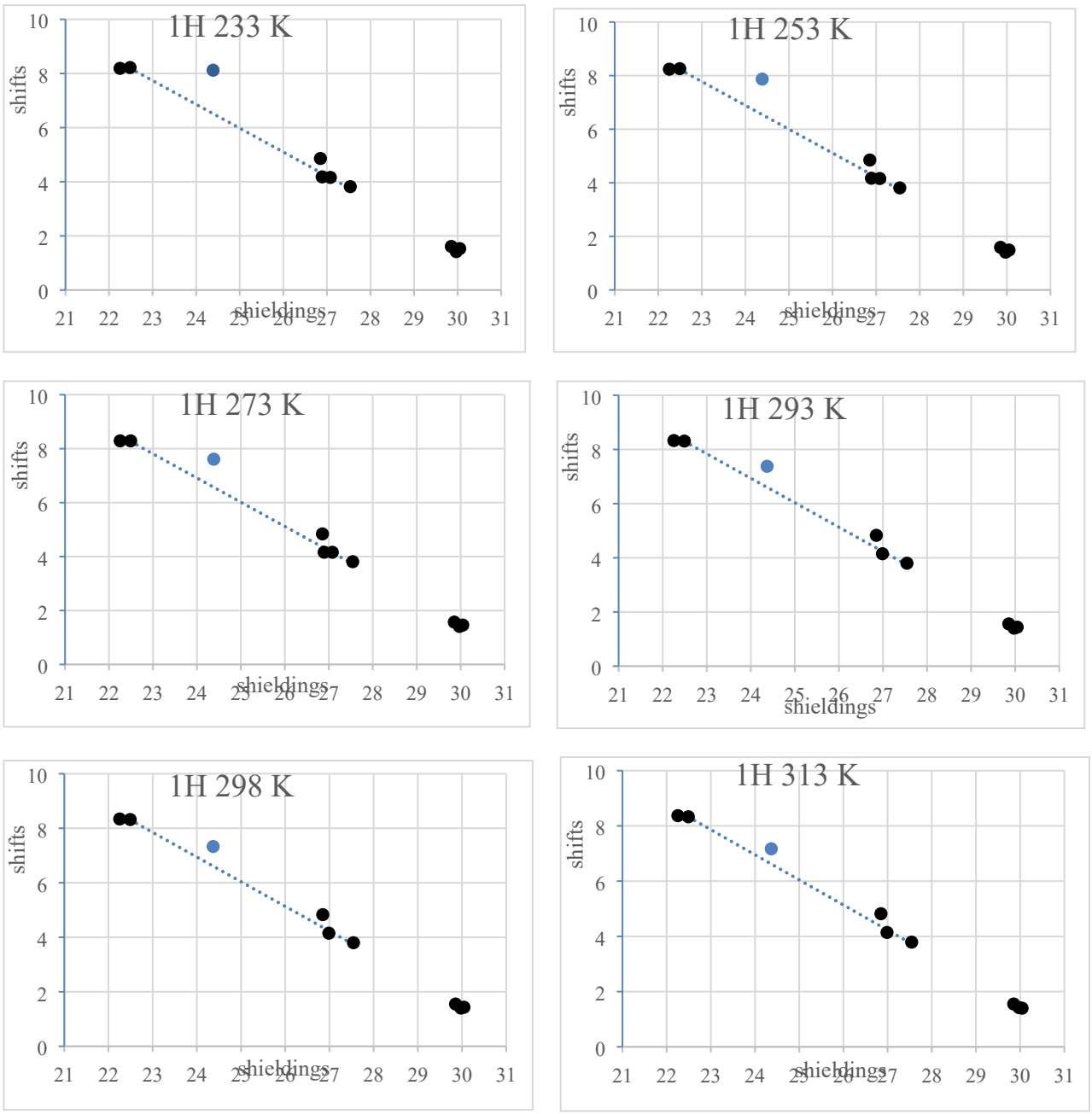



Figure S24. Linear regressions at different temperatures between $^{1}$H calculated shieldings and $^{1}$H experimental shifts for monomer ensemble of $\mathbf{1}_{\mathbf{tt}}$.

* $^{1}$H nuclei bonded to carbon atoms are black, $^{1}$H amide nucleus is blue.

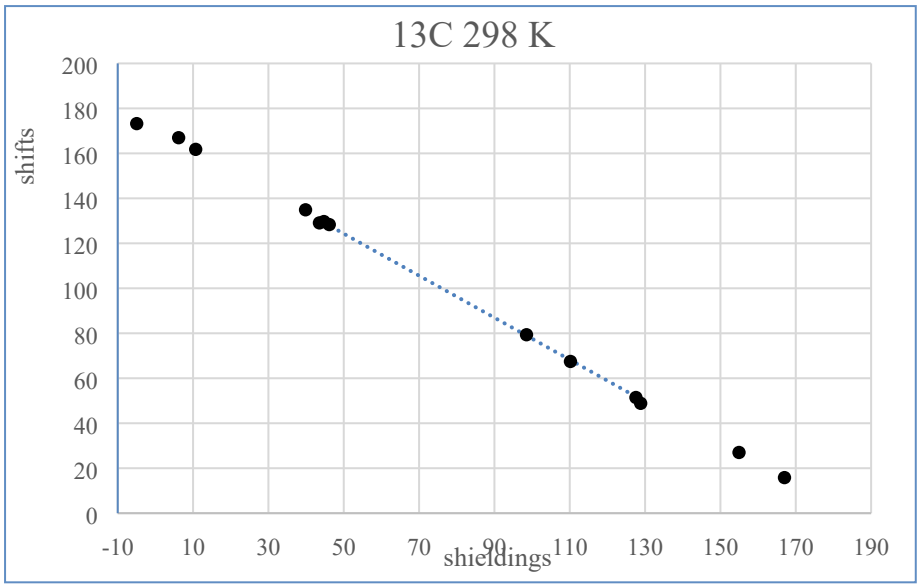



Figure S25. Linear regression at 298 K between $^{13}C$ calculated shieldings and $^{13}C$ experimental shifts for monomer ensemble of $\mathbf{1_{t1}}$.

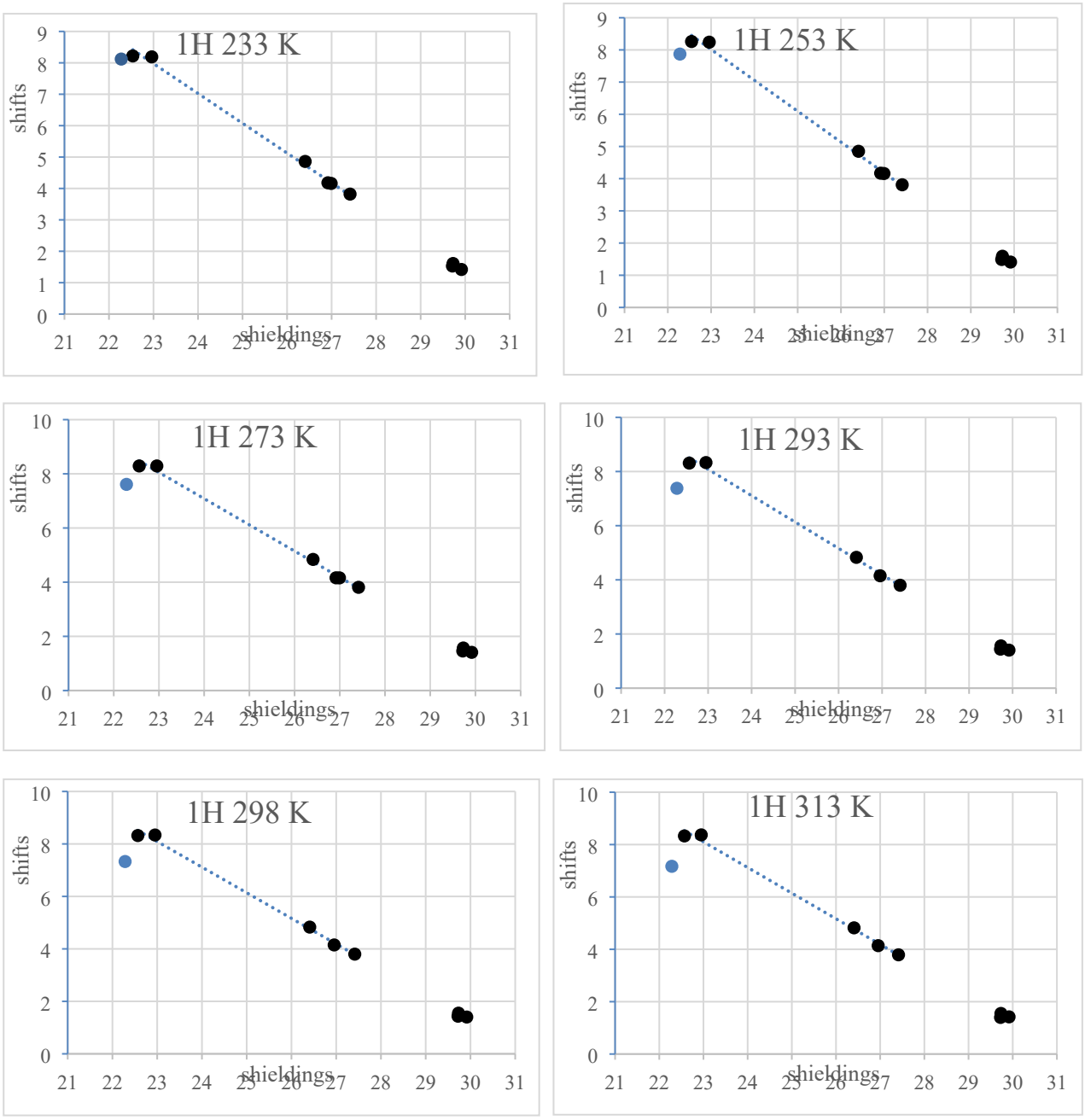



Figure S26. Linear regressions at different temperatures between $^{1}$H calculated shieldings and $^{1}$H experimental shifts for dimer ensemble of $\mathbf{1}_{\mathbf{t1}}$.

* $^{1}$H nuclei bonded to carbon atoms are black, $^{1}$H amide nucleus is blue.

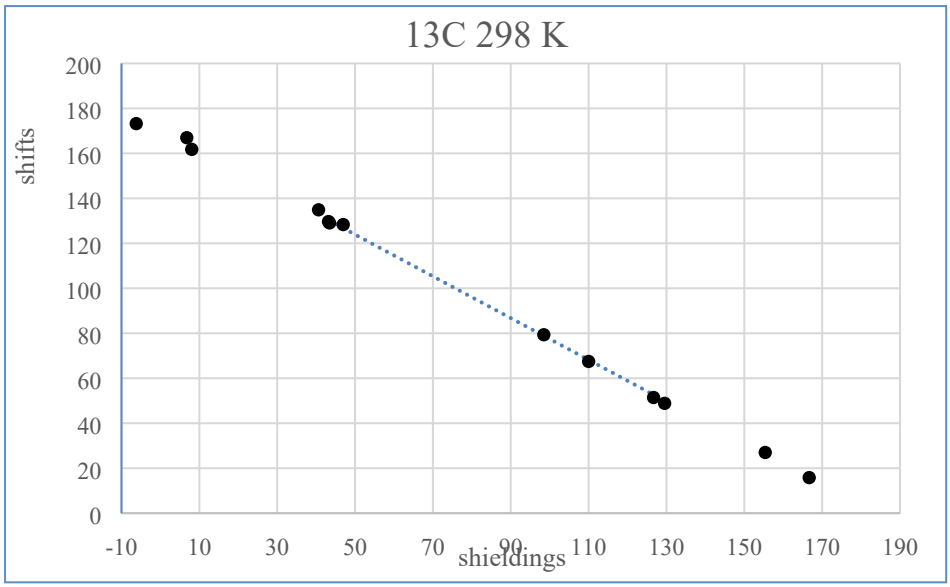



Figure S27. Linear regression at 298 K between $^{13}C$ calculated shieldings and $^{13}C$ experimental shifts for dimer ensemble of **1t1**.

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