Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Visible light-driven Metal-free Synthesis of Highly Substituted Pyrroles through C–H Functionalisation

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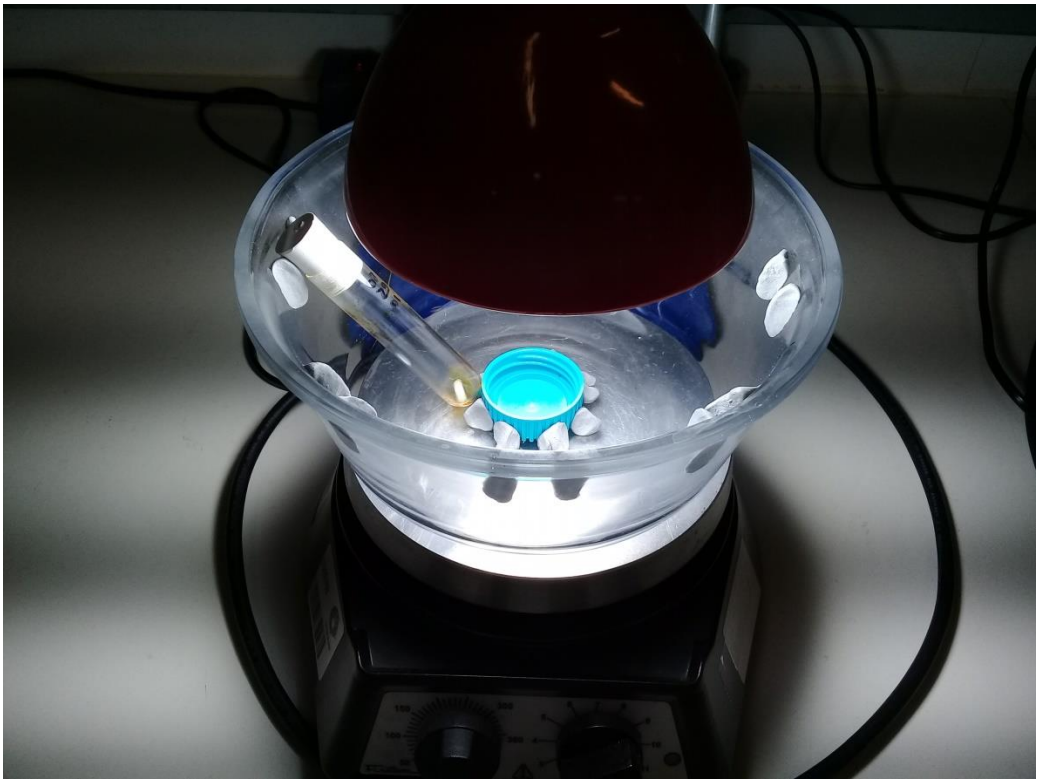
1. General Information

All reagents were purchased from commercial suppliers (Sigma-Aldrich, Oakwood and Combi-Blocks) and used without further purification, all solvents were analytical grade. Thin layer chromatography (TLC) was performed using silica gel GF254, 0.25 mm thickness, visualization was accomplished with short wave UV light or $KMnO_4$ staining solution followed by heating. Hydrogen nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 500 MHz in $CDCl_3$ solutions, at ambient temperature. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 125 MHz in $CDCl_3$ solutions, at ambient temperature. Chemicals shifts (δ) are given in ppm and the residual solvent signals were used as references for ^{1}H and ^{13}C NMR spectra ($CDCl_3$: δH = 7.27 ppm, δC = 77.00 ppm). High resolution mass spectra were recorded on Thermo Scientific LTQ FT Ultra and Q Exactive Orbitrap spectrometers working with an electronspray ionization (ESI). The Gas Chromatography coupled to Mass Spectrometry (CG-MS) analyses were performed using a Network GC system 6890N (Agilent Technologies Inc., Palo Alto, CA, USA), equipped with a HP-5MS 5% Phenyl Methyl Silox (25.0 m × 250 µm × 0.25 µ nominal) capillary column. The GC analyses were carried out in split mode (ratio 150:1) using helium as carrier gas at a flow rate of 504 mL/min (7.65 psi). The injection port temperature was 250 °C; the oven was maintained at an initial temperature of 50 °C for 3 minutes, then programmed at 40 °C/min to a temperature of 280 °C, where it was held, post-run, for 2 minutes. The MS detector was at 250 °C, using H_2 flow at 40.00 mL/min, air at 400 mL/min and He makeup flow at 45.0 mL/min.

2. General Procedure

Benzophenone (0.5 mmol, 50 mol%), amines (1.0 mmol), methyl acetoacetate (2.0 mmol) and acid (1.0 mmol) were added to a test tube and capped with a rubber septum. The reaction mixture was stirred and irradiated using a compact fluorescent lamp (CFL, 50 W) at room temperature (kept at around 35 °C using a fan) for 72 h. After completion of the reaction (followed by TLC), the whole mixture was added to the top of a silica column and eluted using ethyl acetate/n-hexane (20:80) to afford the targeted product. For reactions employing levulinic acid the eluent was changed to ethyl acetate/n-hexane (30:70).

A description of the apparatus for the photoreaction is shown in Figure S1.



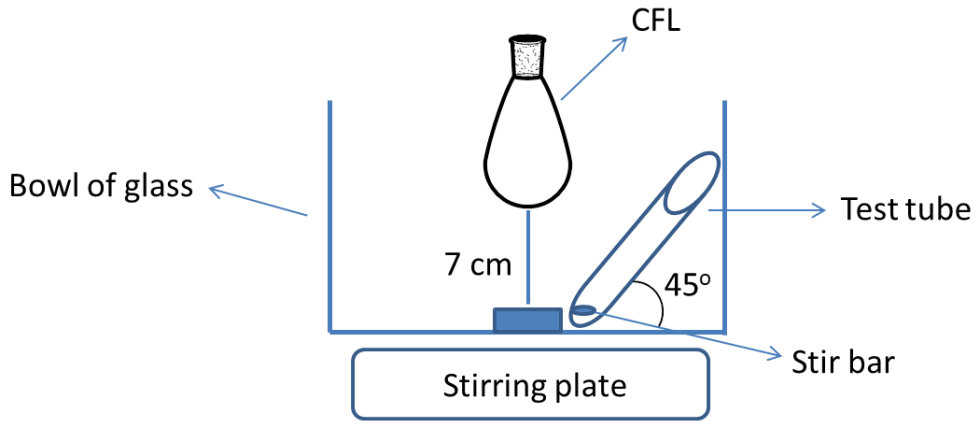


Figure S1. Homemade apparatus for the photochemical reaction.

Figure S2 presents the emission profile of the CFL lamp employed in this method. The overlap between benzophenone absorption band (< 380 nm)[1] and CFL emission bands can be considered small. Under such conditions, access to the triplet state of benzophenone may be impaired and longer reaction times can be observed (e.g. 72 h reaction time). Alternatively, the triplet state of benzophenone might decay with different lifetimes depending on the solvent and media.[2] Under the neat condition described in our method, benzophenone triplet state lifetime may be reduced in such a way that productive quenching processes would be more difficult, thus having an effect

[1] https://webbook.nist.gov/cgi/cbook.cgi?ID=C119619&Mask=400. Accessed on July, 2021.
[2] G. Dormán, H. Nakamura, A. Pulsipher and G. D. Prestwich, *Chem. Rev.*, 2016, **116**, 15284–15398.

on the reaction time. For a brief discussion about even longer reaction times observed in our study, see item 6 of this Supporting Information.

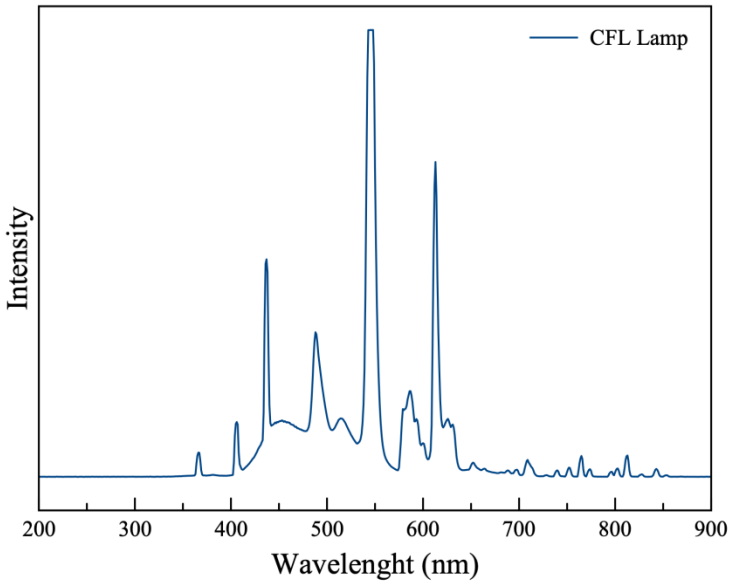
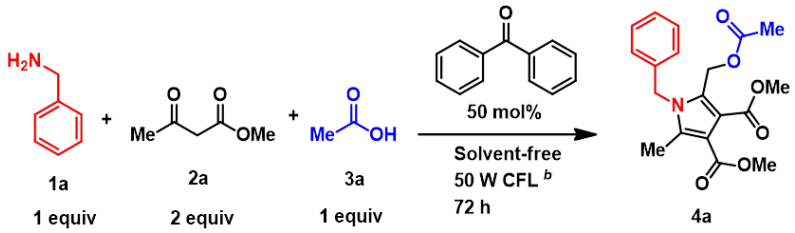
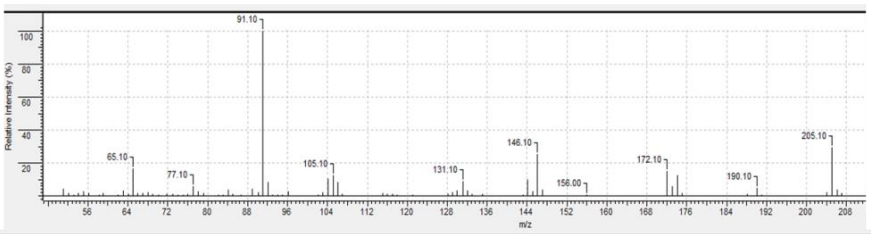


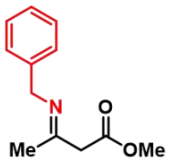
Figure S2. Emission profile for CFL lamp.

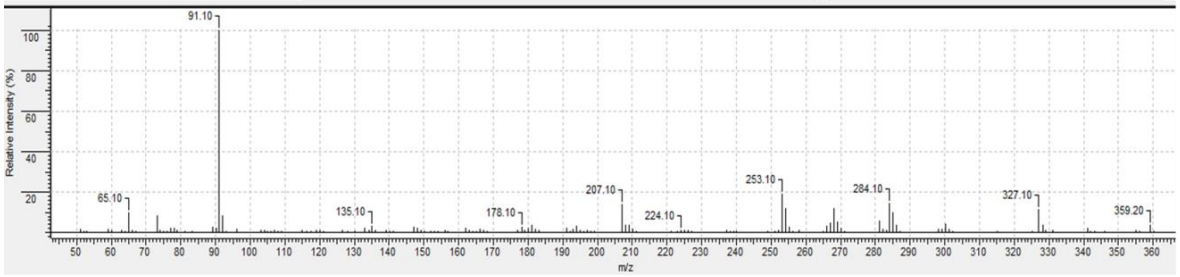
3. Kinetic profile



Benzophenone (0.5 mmol, 50 mol%), benzylamine (1.0 mmol), methyl acetoacetate (2.0 mmol) and acetic acid (1.0 mmol) were employed following the **General Procedure**. Aliquots of the reaction mixture were taken (10 min, 24 h, 48 h, 72 h and 96 h), diluted with ethyl acetate and analyzed by GC-MS (Figure S3). The experiment was done in triplicate.


91.10
65.10
77.10
105.10
131.10
146.10
156.00
172.10
190.10
205.10
Relative Intensity (%)
m/z


N
O
Me
OMe


91.10
65.10
135.10
178.10
207.10
224.10
253.10
284.10
327.10
359.20
Relative Intensity (%)
m/z


O
Me
O
OMe
N
Me
O
OMe
O

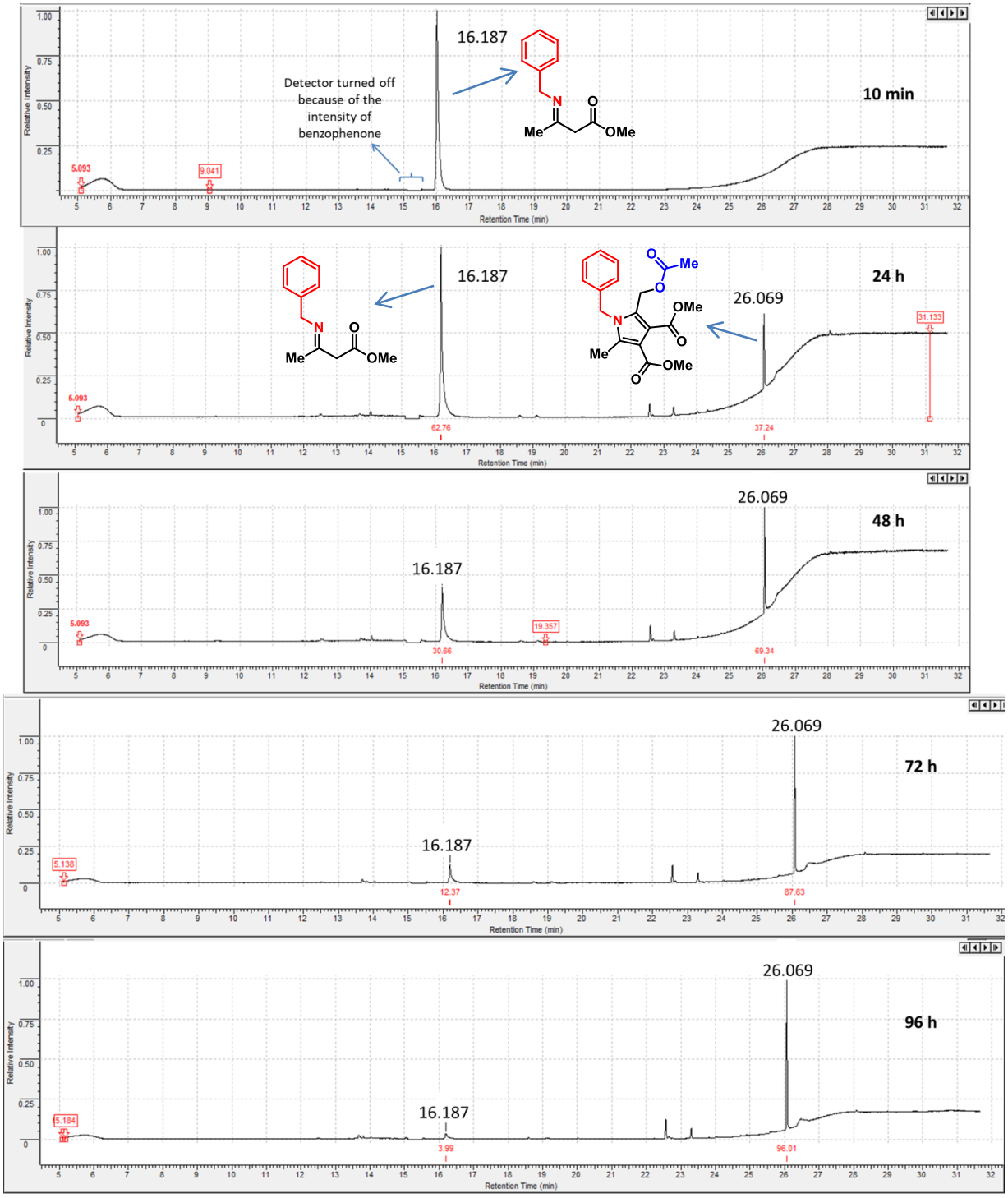


Figure S3. Kinetic profile.

4. Intermediate pyrroles

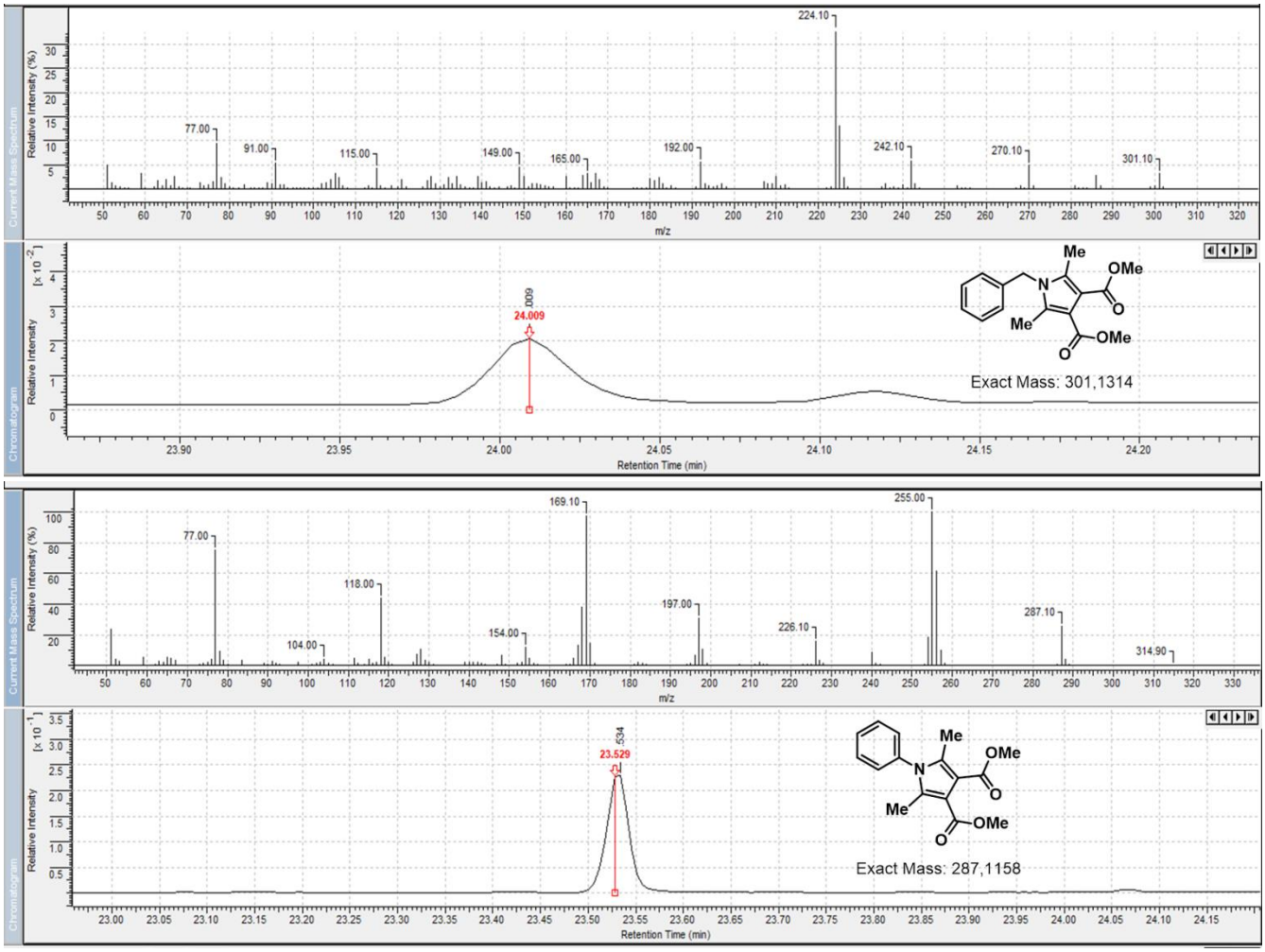
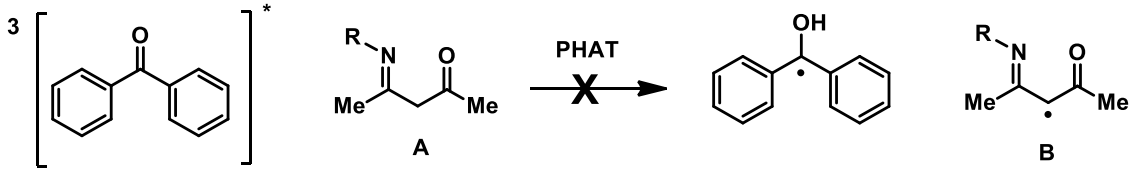


Figure S4. Intermediate pyrroles observed when employing benzylamine or aniline in the reaction.

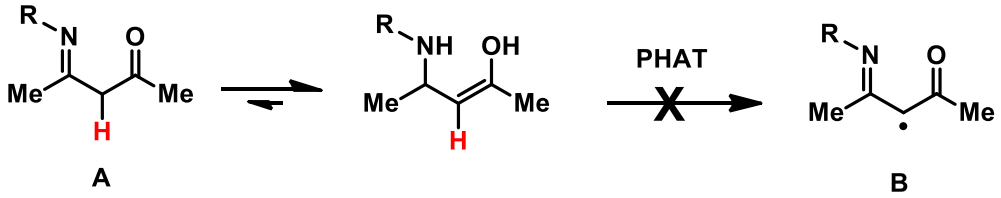
5. Possible reason for reaction failure when using either acetylacetone or dimethyl malonate.

Following the **General Procedure** with acetylacetone, benzylamine and acetic acid, we could observe by GC-MS the formation of the corresponding imine **A** in accordance to the mechanistic studies described in the manuscript. However, no product was obtained after 72 h irradiation and the imine remained unreacted.

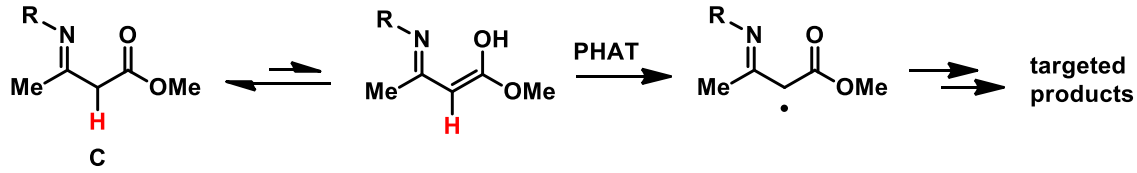
It suggests that photoinduced HAT transfer from imine **A** to the triplet state of benzophenone to furnish radical **B** is strongly unfavourable:



We hypothesize that, under our conditions, the enol form of imine **A** is highly favoured and considering that HAT parallels bond dissociation energies[3], hydrogen transfer from sp^2 carbon becomes more difficult compared to the same transfer from sp^3 carbons:



On the other hand, the keto form of imine **C**, coming from methyl acetoacetate, might be favoured due to higher pK_a of α-hydrogens next to an ester group. In this scenario, imine **C** undergoes HAT more easily (from sp^3 carbon) allowing the transformation reach completion:



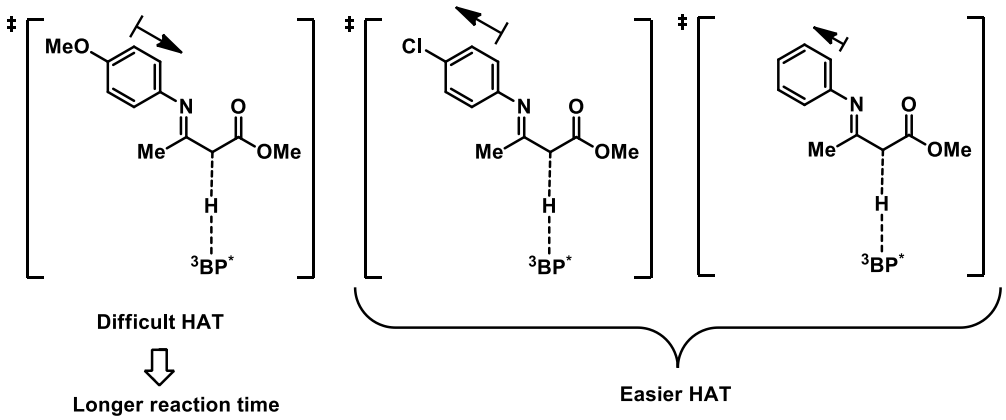
When employing dimethyl malonate, it is recovered unreacted and the process is shut down. This result emphasizes the necessity of imine formation to carry the transformation on.

6. Possible reason for longer reaction time when employing 4-methoxyaniline.

As reported in the manuscript, electron-rich 4-methoxyaniline has taken 6 days to reach 75% yield of the targeted product whereas other anilines have taken 72 h to furnish products in even higher yields. This outcome suggests an influence of electronic nature of anilines in the transformation. Here, we hypothesize that HAT step is the determining step in the reaction and possibly the electronic nature of anilines determines how fast the hydrogen transfer may occurs. The conjugation of the imines coming from anilines extends from the C–H bond susceptible to HAT towards the ring; hence, the influence of the electronics of the ring might be more substantial in this scenario.

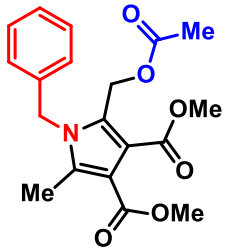
[3] J. M. Mayer, *Acc. Chem. Res.*, 2011, **44**, 36–46.

Lanzalunga and collaborators[4] reported polar effects in hydrogen atom transfer reactions from activated phenols and we believe we have the same kind of effect in the reaction employing 4-methoxyaniline. The polarization of the hydrogen atom transfer transition state because of the partial charge transfer may determine stabilization or destabilization of the transition state:



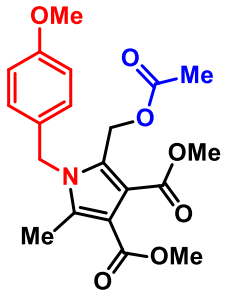
[4] M. Bietti, E. Cucinotta, G. A. Dilabio, O. Lanzalunga, A. Lapi, M. Mazzonna, E. Romero-Montalvo and M. Salamone, *J. Org. Chem.*, 2019, **84**, 1778–1786.

7. Characterization of the products



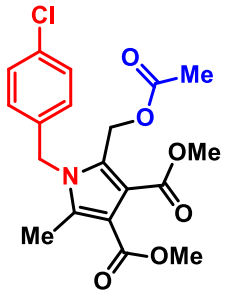
4a

Prepared from benzylamine, methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (82% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.32–7.26 (m, 3H), 6.88 (d, 2H, J = 7.55 Hz), 5.22 (s, 2H), 5.15 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.34 (s, 3H), 1.77 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.35, 165.32, 165.24, 136.10, 135.85, 129.44, 128.93, 127.68, 125.43, 116.93, 112.88, 55.12, 51.86, 51.47, 47.40, 20.41, 10.92.
HRMS m/z (ESI): calcd. for $C_{19}H_{22}NO_6$ $[M+H]^+$ 360.1447, found 360.1444.



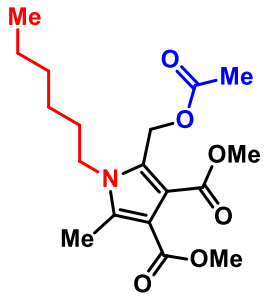
4b

Prepared from 4-methoxybenzylamine, methyl acetoacetate and acetic acid following the general procedure to give the product as pale orange oil (80% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.83 (m, 4H), 5.21 (s, 2H), 5.08 (s, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 2.34 (s, 3H), 1.83 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.60, 165.57, 165.49, 159.34, 136.29, 129.62, 128.00, 126.98, 117.11, 114.54, 113.05, 55.53, 55.40, 52.08, 51.70, 47.19, 20.76, 11.19.
HRMS m/z (ESI): calcd. for $C_{20}H_{27}NO_7$ $[M+H]^+$ 390.1553, found 390.1552.



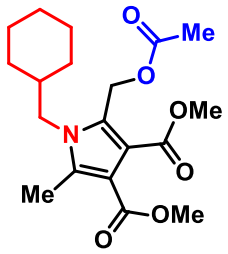
4c

Prepared from 4-chlorobenzylamine, methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (85% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.28 (d, 2H, J = 8.17 Hz), 6.81 (d, 2H, J = 8.17 Hz), 5.20 (s, 2H), 5.11 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.32 (s, 3H), 1.80 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.27, 165.17, 165.11, 135.85, 134.42, 133.64, 129.30, 129.09, 126.85, 117.11, 113.08, 55.02, 51.89, 51.51, 46.83, 20.44, 10.89.
HRMS m/z (ESI): calcd. for $C_{19}H_{21}ClNO_6$ $[M+H]^+$ 394.1057, found 394.1055.



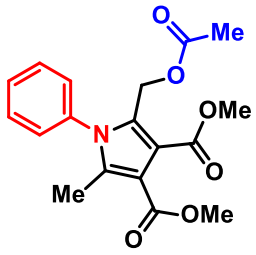
4d

Prepared from hexylamine, methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (94% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.23 (s, 2H), 3.84–3.79 (m+s+s, 8H), 2.42 (s, 3H), 2.05 (s, 3H), 1.66–1.60 (m, 2H), 1.38–1.27 (m, 6H), 0.89 (t, 3H, J = 6.92 Hz)
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.40, 165.36, 165.33, 135.32, 128.42, 116.65, 112.46, 55.31, 51.76, 51.36, 44.37, 31.32, 30.80, 26.43, 22.42, 20.81, 13.89, 10.92.
HRMS m/z (ESI): calcd. for $C_{18}H_{28}NO_6$ $[M+H]^+$ 354.1917, found 354,1915.



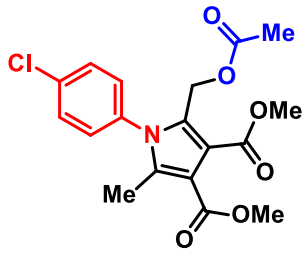
4e

Prepared from cyclohexanemethylamine, methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (95% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.23 (s, 2H), 3.83 (s, 3H), 3.79 (s, 3H), 3.69 (d, 2H, J = 6.92 Hz), 2.41 (s, 3H), 2.05 (s, 3H), 1.75–1.59 (m, 6H), 1.16 (m, 3H), 0.98 (m, 2H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.51, 165.43, 165.36, 135.80, 128.98, 116.76, 112.51, 55.48, 51.75, 51.36, 50.28, 39.35, 30.74, 26.04, 25.79, 20.82, 11.49.
HRMS m/z (ESI): calcd. for $C_{19}H_{28}NO_6$ $[M+H]^+$ 366.1917, found 366.1914.



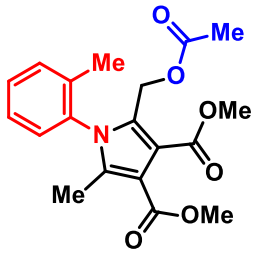
4f

Prepared from aniline, methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (81% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.50–7.54 (m, 3H), 7.20–7.24 (m, 2H), 4.96 (s, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.19 (s, 3H), 1.91 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.03, 165.32, 165.21, 136.79, 135.81, 129.97, 129.62, 129.57, 128.16, 116.85, 112.65, 55.64, 51.94, 51.55, 20.61, 11.86.
HRMS m/z (ESI): calcd. for $C_{18}H_{20}NO_6$ $[M+H]^+$ 346.1291, found 346.1293.



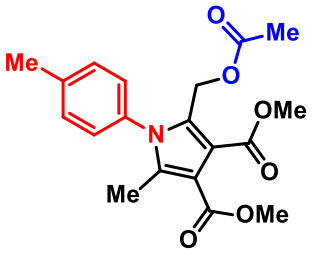
4g

Prepared from 4-chloro aniline, methyl acetoacetate and acetic acid following the general procedure to give the product as pale orange oil (84% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.48 (d, 2H, J = 8.80 Hz), 7.16 (d, 2H, J = 8.80 Hz), 4.95 (s, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.19 (s, 3H), 1.93 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 169.97, 165.13, 165.04, 136.64, 135.84, 134.30, 129.88, 129.51, 117.21, 112.96, 55.54, 51.99, 51.61, 20.63, 11.85.
HRMS m/z (ESI): calcd. for $C_{18}H_{19}ClNO_6$ $[M+H]^+$ 380.0901, found 380.0903.



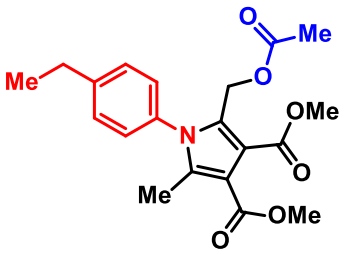
4h

Prepared from *o*-toluidine (2-methyl aniline), methyl acetoacetate and acetic acid following the general procedure to give the product as pale yellow oil (83% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.41 (dd, 1H, *J* = 6.92, 7.55 Hz), 7.36 (d, 1H, *J* = 6.92 Hz), 7.32 (ap t, 1H, *J* = 7.55 Hz), 7.12 (d, 1H, *J* = 7.55 Hz), 4.93 (d, 2H, *J* = 13.20 Hz), 4.85 (d, 2H, *J* = 13.20 Hz), 3.87 (s, 3H), 3.85 (s, 3H), 2.11 (s, 3H), 1.98 (s, 3H), 1.87 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 169.93, 165.29, 165.17, 136.58, 134.82, 131.13, 129.98, 129.39, 128.50, 127.08, 116.84, 112.60, 55.60, 51.87, 51.49, 20.49, 17.10, 11.41.
HSQC, HMBC, COSY, DEPT135, NOESY: See Spectral Data Section.
HRMS m/z (ESI): calcd. for $C_{19}H_{22}NO_6$ $[M+H]^+$ 360.1447, found 360.1445.



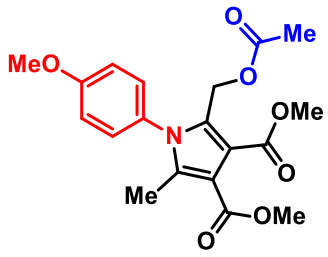
4i

Prepared from 4-methyl aniline, methyl acetoacetate and acetic acid following the general procedure to give the product as pale brown oil (82% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.28 (d, 2H, *J* = 8.17 Hz), 7.08 (d, 2H, *J* = 8.17 Hz), 4.94 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 2.43 (s, 3H), 2.18 (s, 3H), 1.92 (s, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.09, 165.33, 165.22, 139.73, 136.90, 133.10, 130.13, 130.03, 127.84, 116.69, 112.51, 55.72, 51.87, 51.49, 21.19, 20.65, 11.84.
HRMS m/z (ESI): calcd. for $C_{19}H_{22}NO_6$ $[M+H]^+$ 360.1447, found 360.1446.



4j

Prepared from 4-ethyl aniline, methyl acetoacetate and acetic acid following the general procedure to give the product as pale orange oil (89% yield).
^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.31 (d, 2H, *J* = 8.17 Hz), 7.11 (d, 2H, *J* = 8.17 Hz), 4.94 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 2.73 (q, 2H, *J* = 7.80 Hz), 2.19 (s, 3H), 1.92 (s, 3H), 1.30 (t, 3H, *J* = 7.55 Hz).
^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.08, 165.35, 165.22, 145.88, 136.92, 133.24, 130.05, 128.90, 127.91, 116.66, 112.49, 55.76, 51.87, 51.51, 28.49, 20.63, 15.20, 11.88.
HRMS m/z (ESI): calcd. for $C_{20}H_{24}NO_6$ $[M+H]^+$ 374.1604, found 374.1607.



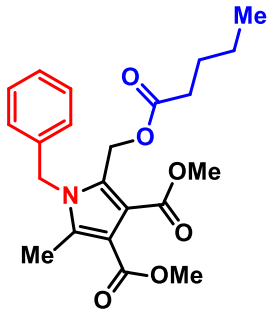
4k

Prepared from 4-methoxy aniline, methyl acetoacetate and acetic acid following the general procedure to give the product as pale brown oil (71% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.12 (d, 2H, J = 8.80 Hz), 6.98 (d, 2H, J = 8.80 Hz), 4.95 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 2.18 (s, 3H), 1.94 (s, 3H).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 170.09, 165.33, 165.24, 160.16, 137.14, 130.21, 129.22, 128.24, 116.61, 114.62, 112.41, 55.72, 55.53, 51.89, 51.51, 20.66, 11.83.

HRMS m/z (ESI): calcd. for $C_{19}H_{22}NO_7$ $[M+H]^+$ 376.1396, found 376.1397.



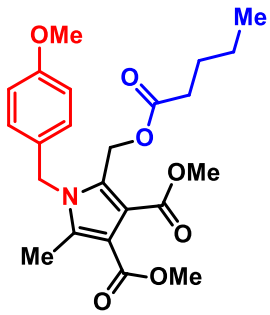
4l

Prepared from benzylamine, methyl acetoacetate and valeric acid following the general procedure to give the product as pale yellow oil (82% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.30–7.26 (m, 3H), 6.88 (d, 2H, J = 6.95 Hz), 5.22 (s, 2H), 5.16 (s, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 2.35 (s, 3H), 2.02 (t, 2H, J = 7.55 Hz), 1.43 (quint, 2H, J = 7.55 Hz), 1.24 (sext, 2H, J = 7.55 Hz), 0.85 (t, 3H, J = 7.55 Hz).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 173.18, 165.33, 165.22, 136.04, 135.89, 129.60, 128.91, 127.68, 125.43, 116.82, 112.89, 55.00, 51.84, 51.47, 47.39, 33.50, 26.65, 22.10, 13.59, 10.93.

HRMS m/z (ESI): calcd. for $C_{22}H_{28}NO_6$ $[M+H]^+$ 402.1917, found 402.1915.



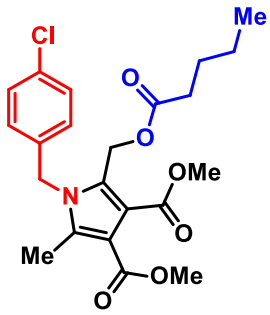
4m

Prepared from 4-methoxybenzylamine, methyl acetoacetate and valeric acid following the general procedure to give the product as pale yellow oil (87% yield)

^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.83 (m, 4H), 5.21 (s, 2H), 5.08 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 2.33 (s, 3H), 2.07 (t, 2H, J = 7.55 Hz), 1.44 (quint, 2H, J = 7.55 Hz), 1.22 (sext, 2H, J = 7.55 Hz), 0.85 (t, 3H, J = 7.55 Hz).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 173.17, 165.35, 165.23, 159.10, 136.00, 129.54, 127.80, 126.73, 116.77, 114.28, 112.84, 55.26, 55.04, 51.82, 51.45, 46.93, 33.59, 26.70, 22.12, 13.59, 10.96.

HRMS m/z (ESI): calcd. for $C_{23}H_{30}NO_7$ $[M+H]^+$ 432.2022, found 432.2019.



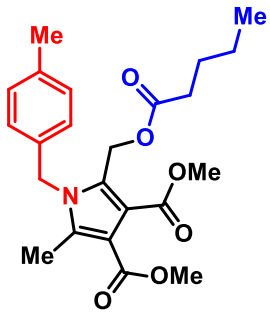
4n

Prepared from 4-chlorobenzylamine, methyl acetoacetate and valeric acid following the general procedure to give the product as pale yellow oil (88% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.28 (d, 2H, J = 8.17 Hz), 6.82 (d, 2H, J = 8.17 Hz), 5.20 (s, 2H), 5.11 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.32 (s, 3H), 2.02 (t, 2H, J = 7.65 Hz), 1.41 (quint, 2H, J = 7.55 Hz), 1.21 (sext, 2H, J = 7.55 Hz), 0.85 (t, 3H, J = 7.55 Hz).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 173.14, 165.24, 165.12, 135.81, 134.48, 133.67, 129.50, 129.11, 126.87, 117.05, 113.14, 54.90, 51.90, 51.53, 46.83, 33.55, 26.68, 22.12, 13.59, 10.92.

HRMS m/z (ESI): calcd. for $C_{22}H_{27}ClNO_6$ $[M+H]^+$ 436.1527, found 436.1524.



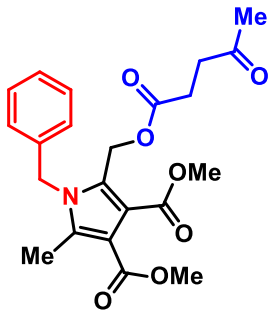
4o

Prepared from 4-methylbenzylamine, methyl acetoacetate and valeric acid following the general procedure to give the product as pale yellow oil (80% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.10 (d, 2H, J = 7.55 Hz), 6.77 (d, 2H, J = 7.55 Hz), 5.20 (s, 2H), 5.10 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.04 (t, 2H, J = 7.55 Hz), 1.43 (quint, 2H, J = 7.55 Hz), 1.22 (sext, 2H, J = 7.55 Hz), 0.84 (t, 3H, J = 7.55 Hz).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 173.18, 165.38, 165.25, 137.43, 136.07, 132.84, 129.56, 125.41, 116.77, 112.81, 55.04, 51.83, 51.46, 47.23, 33.57, 26.68, 22.14, 20.97, 13.59, 10.96.

HRMS m/z (ESI): calcd. for $C_{23}H_{30}NO_6$ $[M+H]^+$ 416.2073, found 416.2076.



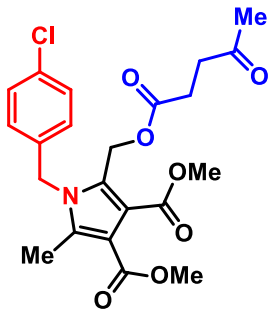
4p

Prepared from benzylamine, methyl acetoacetate and levulinic acid following the general procedure to give the product as pale yellow oil (81% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.32–7.24 (m, 3H), 6.88 (d, 2H, J = 6.92 Hz), 5.20 (s, 2H), 5.16 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 2.58 (t, 2H, J = 6.92 Hz), 2.34 (s, 3H), 2.29 (t, 2H, J = 6.92 Hz), 2.12 (s, 3H).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 206.37, 172.09, 165.30, 165.17, 136.13, 135.93, 129.28, 128.91, 127.67, 125.46, 116.92, 112.84, 55.42, 51.84, 51.46, 47.35, 37.72, 29.72, 27.56, 10.93.

HRMS m/z (ESI): calcd. for $C_{22}H_{26}NO_7$ $[M+H]^+$ 416.1709, found 416.1710.



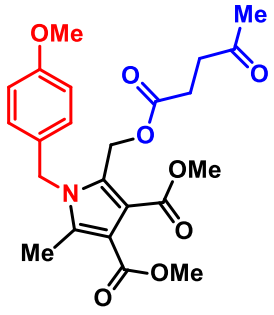
4q

Prepared from 4-chlorobenzylamine, methyl acetoacetate and levulinic acid following the general procedure to give the product as pale yellow oil (79% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.26 (d, 2H, J = 8.17 Hz), 6.82 (d, 2H, J = 8.80 Hz), 5.17 (s, 2H), 5.12 (s, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 2.60 (t, 2H, J = 6.92 Hz), 2.31–2.29 (s+m, 5H), 2.12 (s, 3H).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 206.40, 172.06, 165.17, 165.05, 135.91, 134.50, 133.55, 129.11, 129.04, 126.92, 117.03, 113.00, 55.34, 51.84, 51.47, 46.75, 37.66, 29.65, 27.53, 10.87.

HRMS m/z (ESI): calcd. for $C_{22}H_{25}ClNO_7$ $[M+H]^+$ 450.1320, found 450.1317.



4r

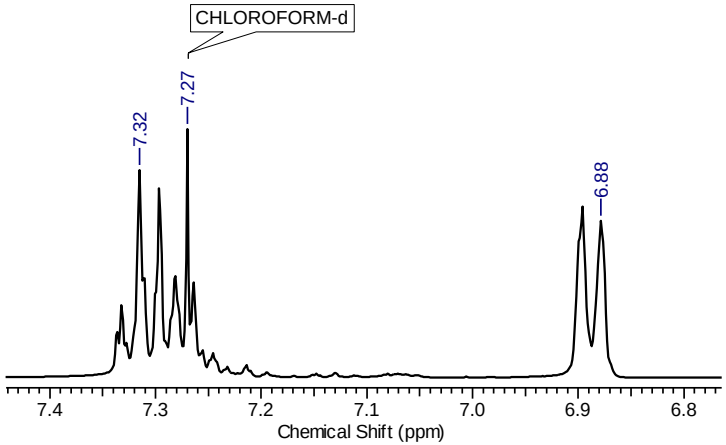
Prepared from 4-methoxybenzylamine, methyl acetoacetate and levulinic acid following the general procedure to give the product as pale yellow oil (78% yield).

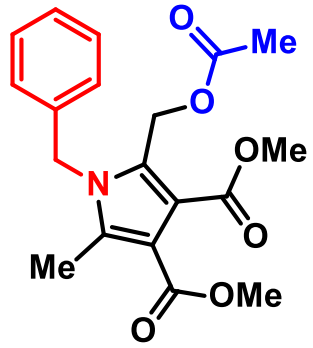
^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.83 (s, 4H), 5.20 (s, 2H), 5.09 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 3.77 (s, 3H), 2.61 (t, 2H, J = 6.29 Hz), 2.36–2.33 (s+m, 5H), 2.13 (s, 3H).

^{13}C NMR (125 MHz, Chloroform-*d*): δ 206.42, 172.12, 165.35, 165.22, 159.09, 136.12, 129.23, 127.84, 126.79, 116.87, 114.30, 112.80, 55.48, 55.28, 51.86, 51.46, 46.91, 37.77, 29.72, 27.64, 10.98.

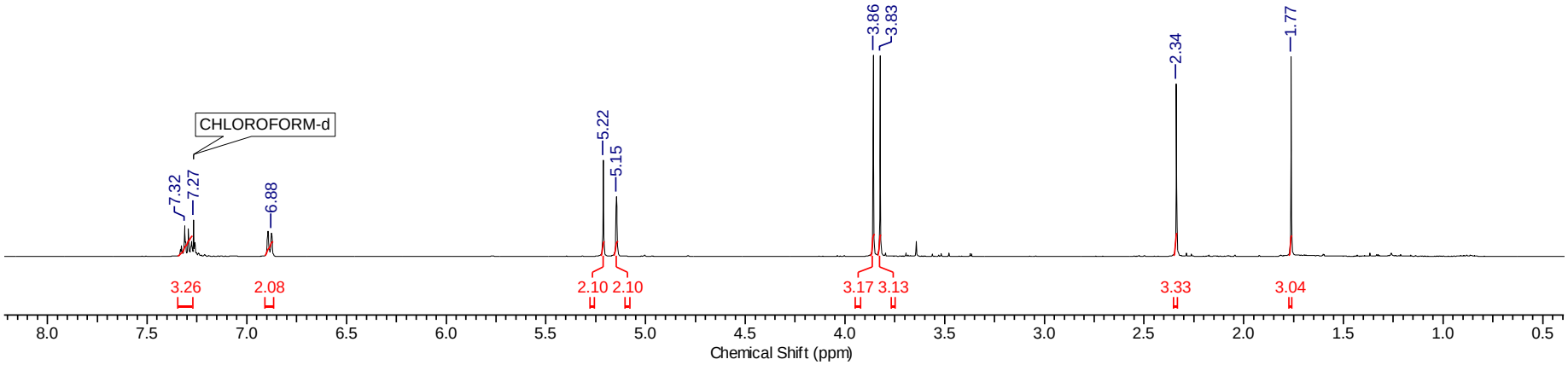
HRMS m/z (ESI): calcd. for $C_{23}H_{28}NO_8$ $[M+H]^+$ 446.1815, found 446.1817.

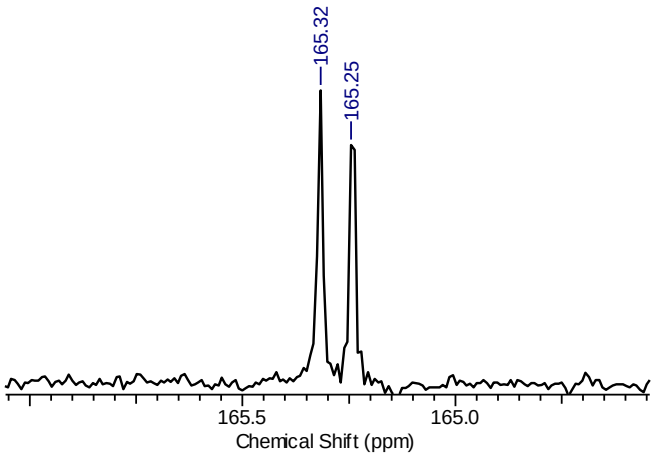
8. Spectral Data

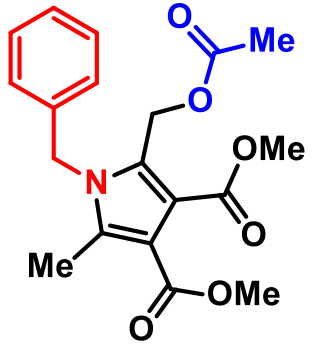




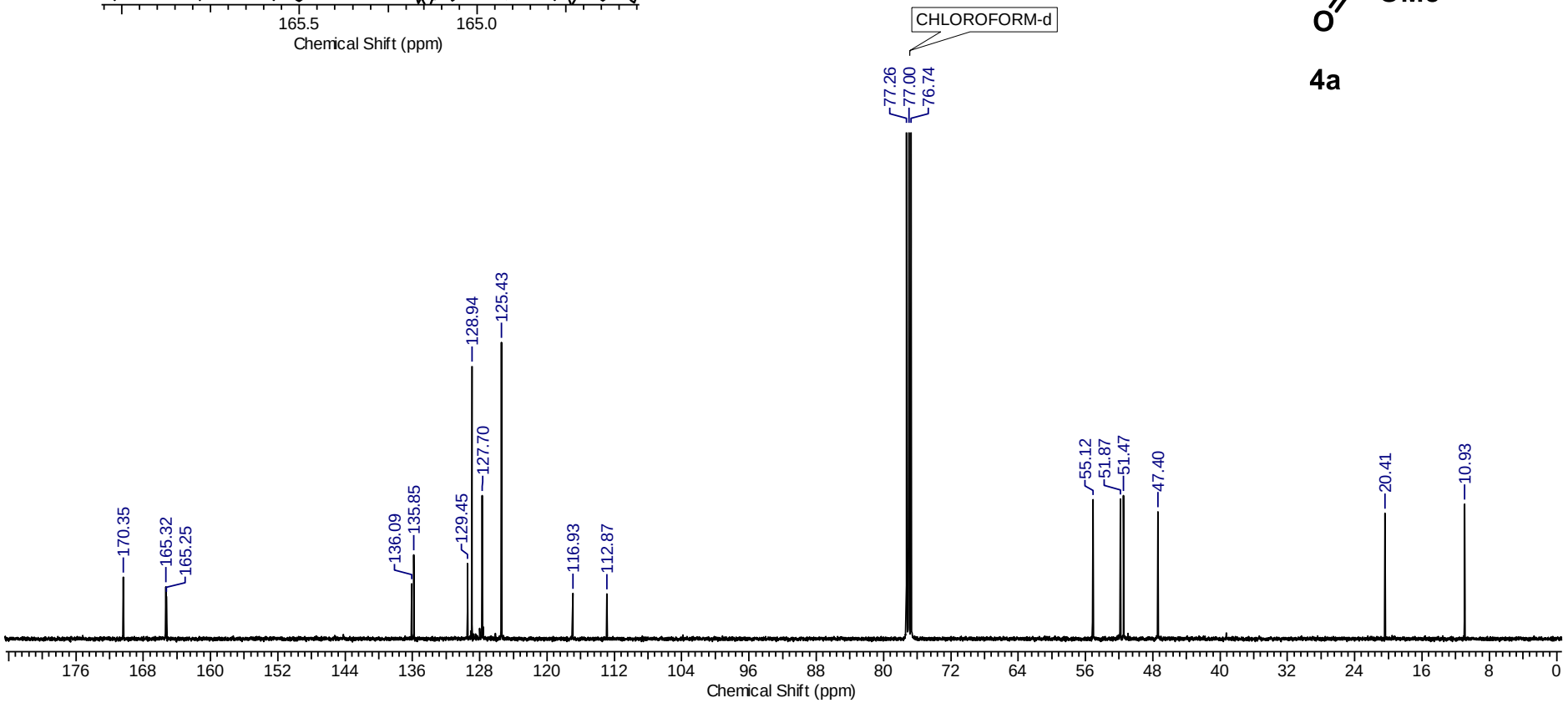
4a

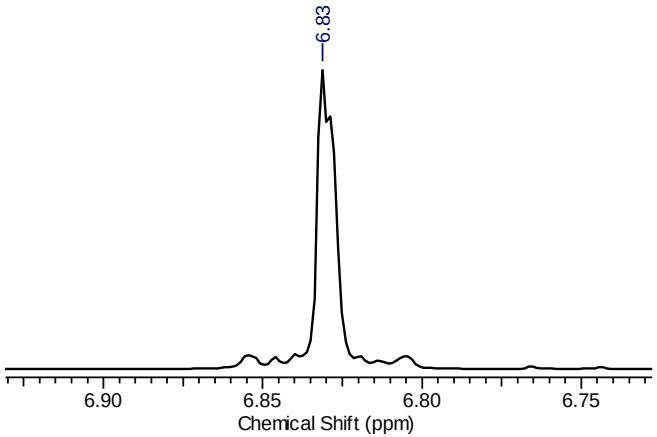


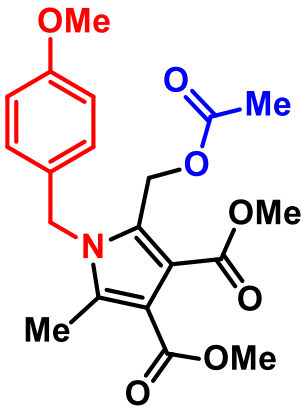

165.32
165.25
165.5
165.0
Chemical Shift (ppm)


O
Me
O
OMe
N
O
Me
OMe
O

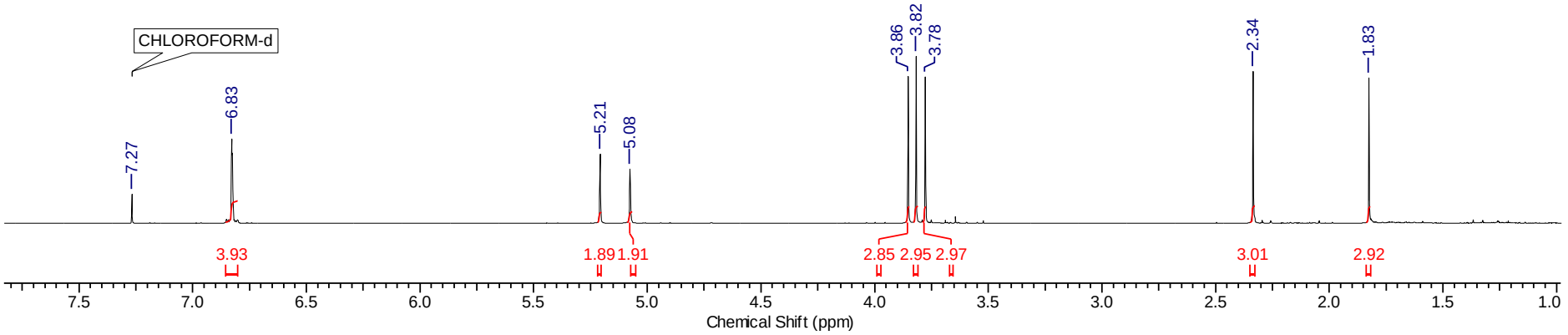
4a


CHLOROFORM-d
77.26
77.00
76.74
170.35
165.32
165.25
136.09
135.85
129.45
128.94
127.70
125.43
116.93
112.87
55.12
51.87
51.47
47.40
20.41
10.93
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


6.83
6.90
6.85
6.80
6.75
Chemical Shift (ppm)


OMe
O
Me
O
OMe
N
O
Me
OMe
O

4b


CHLOROFORM-d
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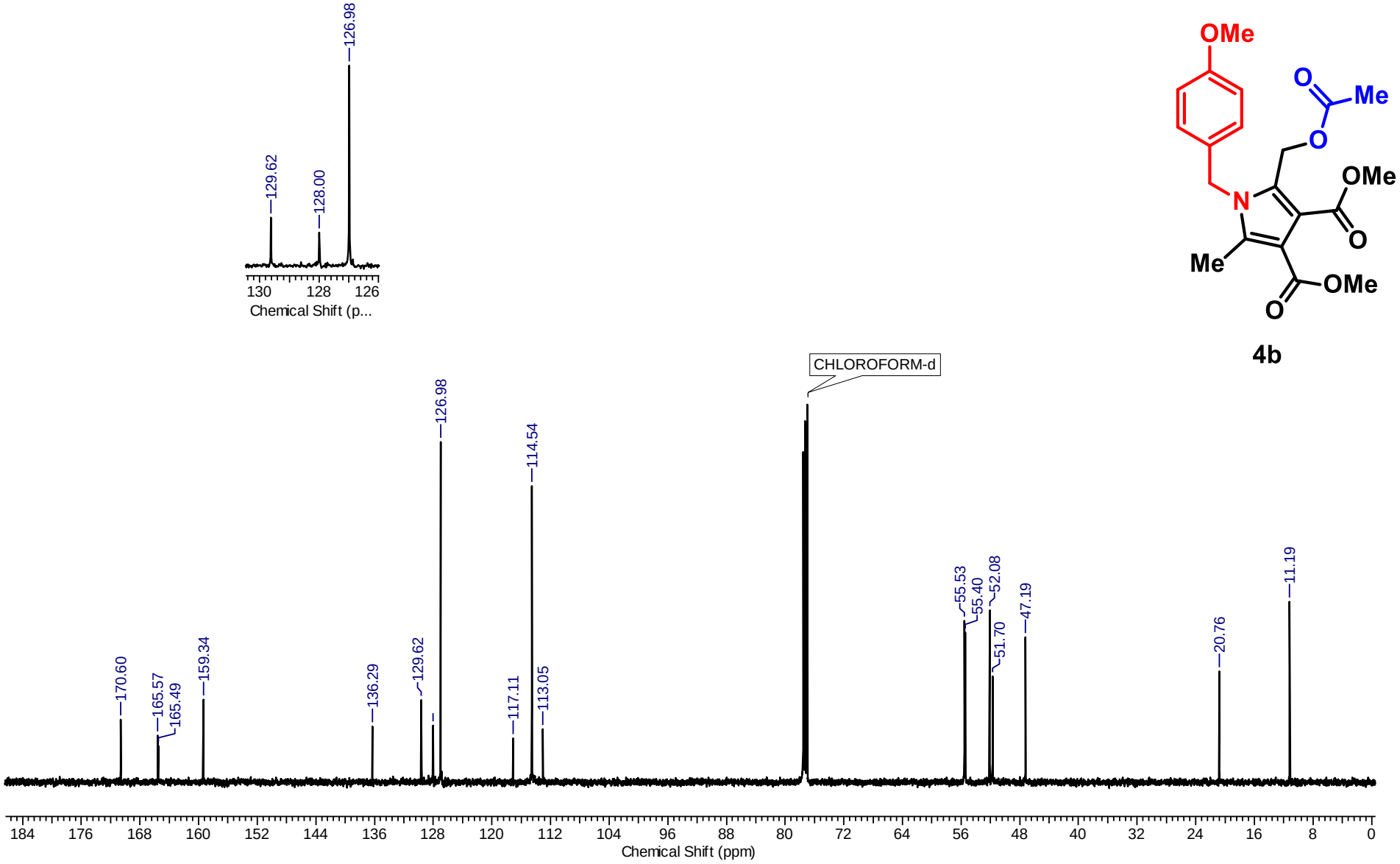
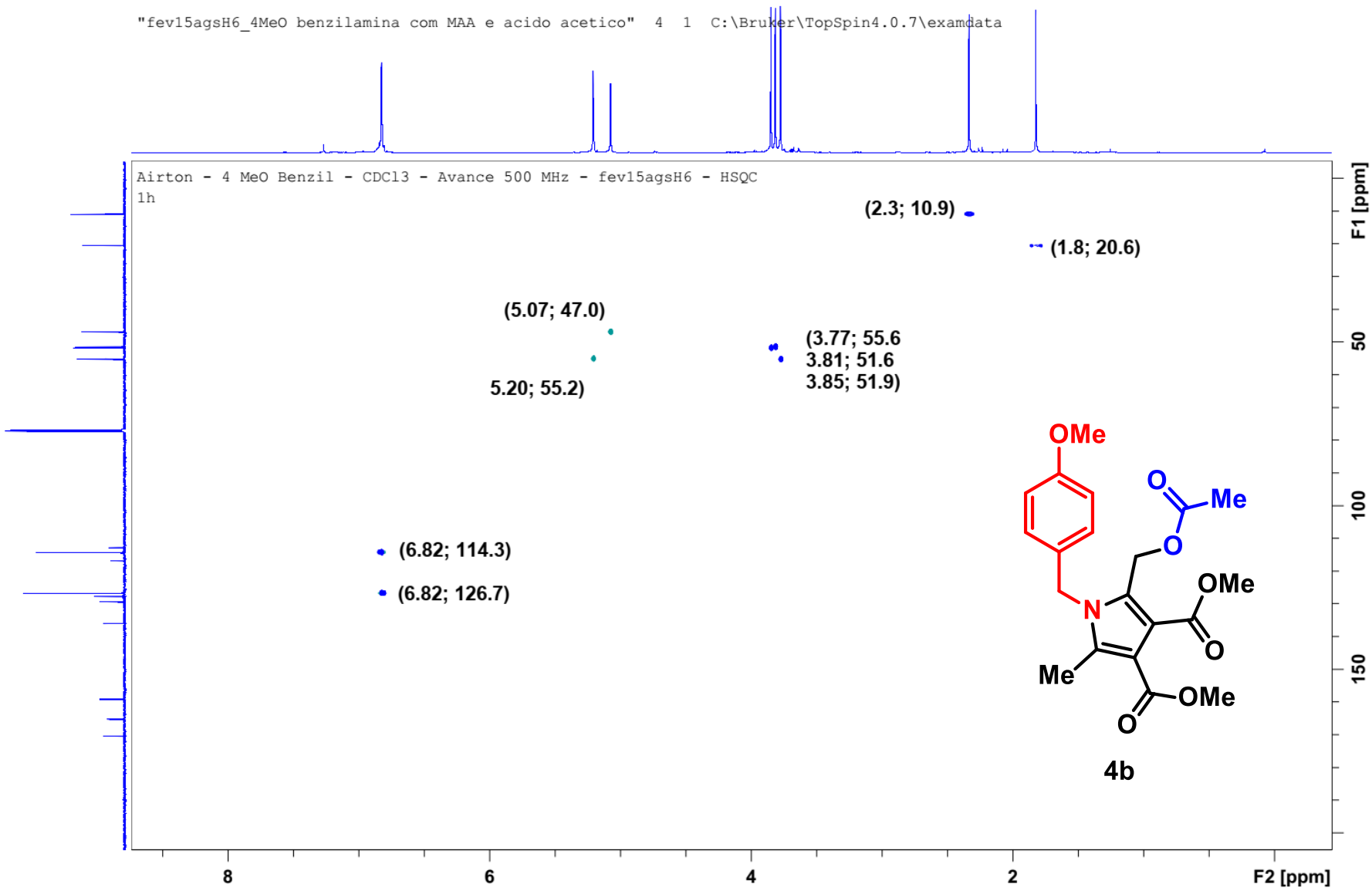
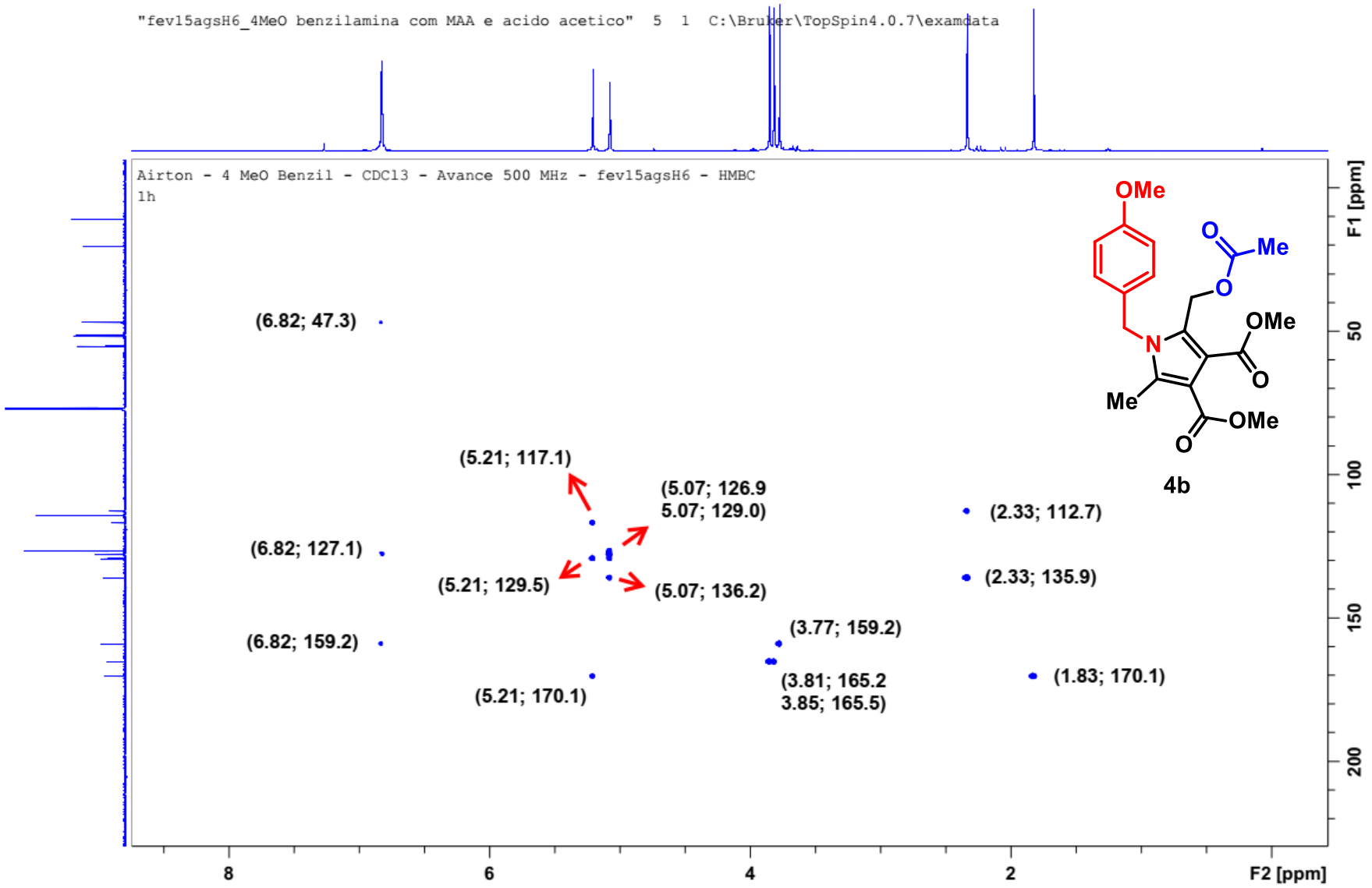
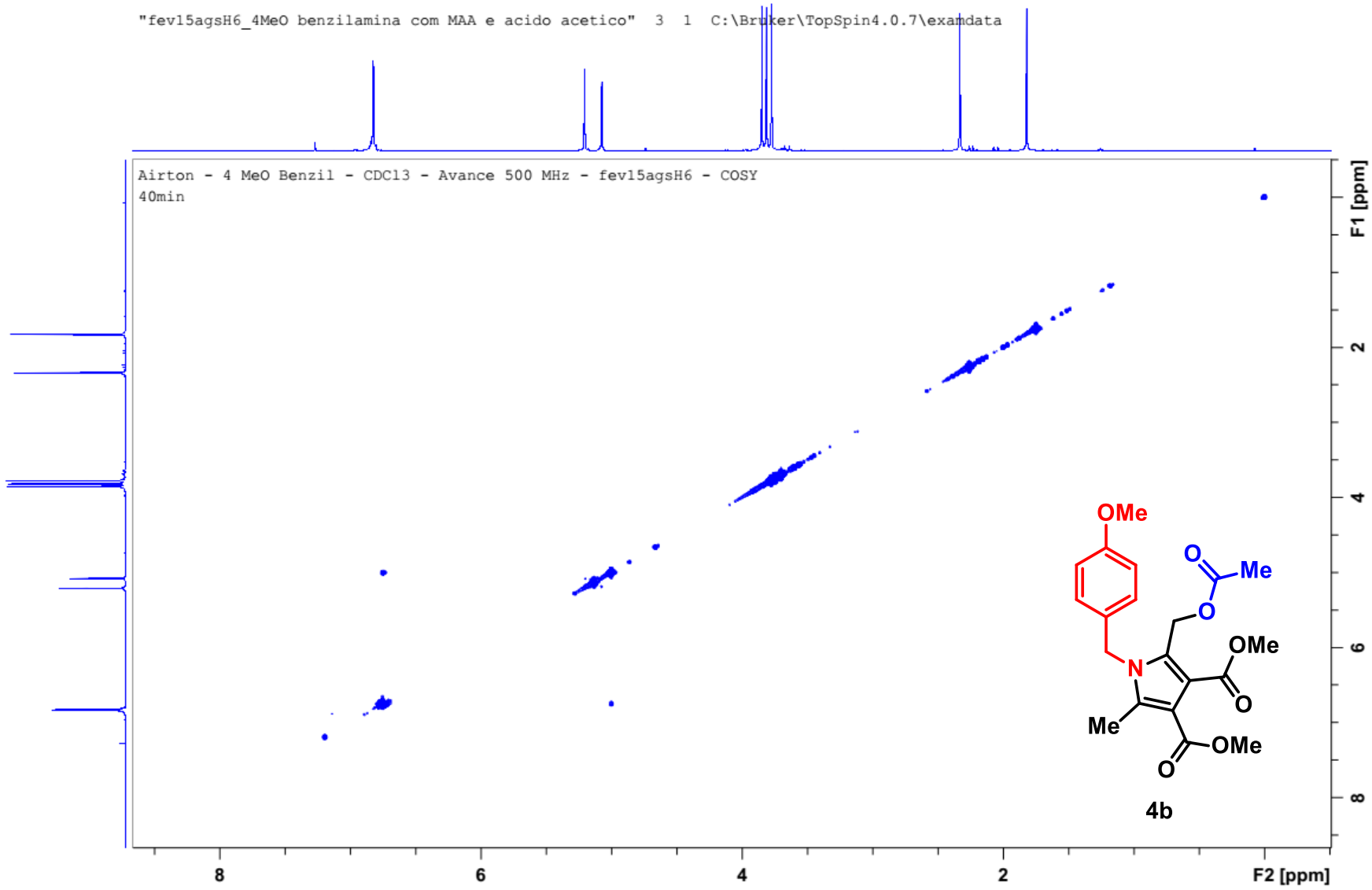
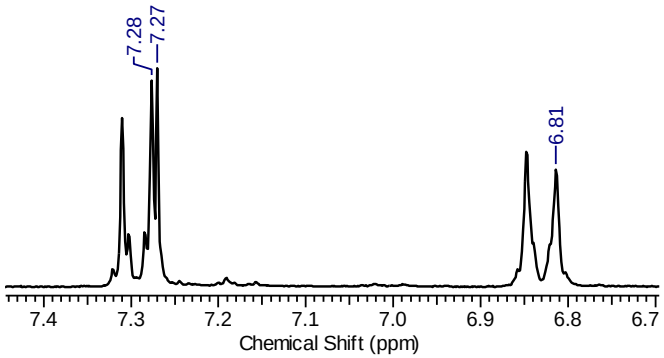
6.83
5.21
5.08
3.86
3.82
3.78
2.34
1.83
3.93
1.89
1.91
2.85
2.95
2.97
3.01
2.92
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

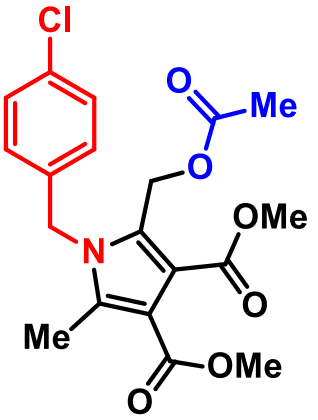

126.98
129.62
128.00
130
128
126
Chemical Shift (p...
OMe
O
Me
O
OMe
N
O
Me
OMe
O
4b
CHLOROFORM-d
126.98
114.54
170.60
165.57
165.49
159.34
136.29
129.62
117.11
113.05
55.53
55.40
52.08
51.70
47.19
20.76
11.19
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


"fev15agsH6_4MeO benzilamina com MAA e acido acetico" 4 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 4 MeO Benzil - CDCl3 - Avance 500 MHz - fev15agsH6 - HSQC
1h
(2.3; 10.9)
(1.8; 20.6)
(5.07; 47.0)
5.20; 55.2)
(3.77; 55.6
3.81; 51.6
3.85; 51.9)
(6.82; 114.3)
(6.82; 126.7)
OMe
O
Me
O
OMe
N
Me
O
OMe
O
4b
F1 [ppm]
50
100
150
8
6
4
2
F2 [ppm]

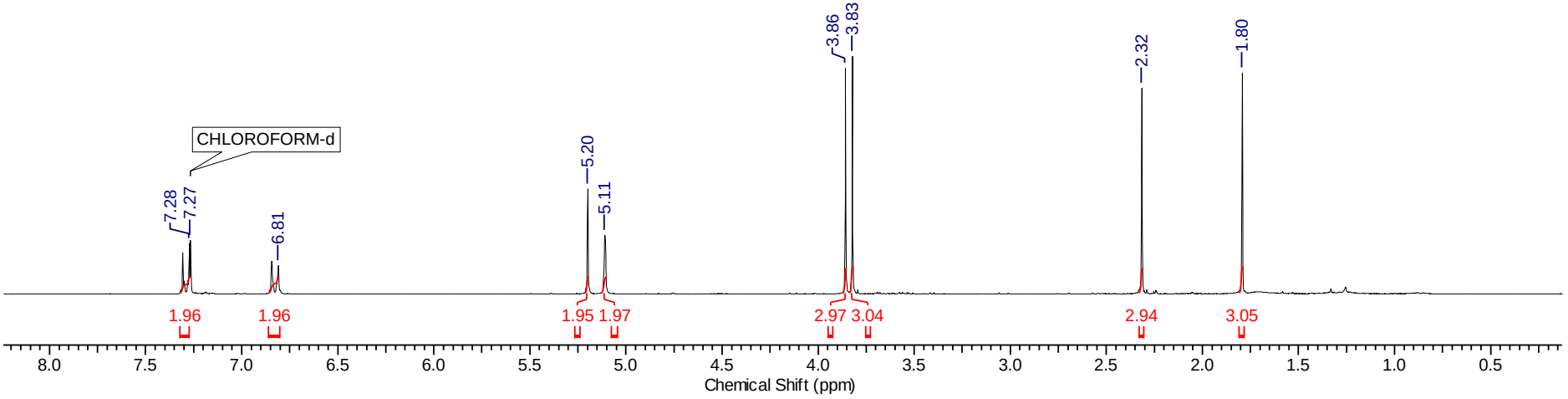

"fev15agsH6_4MeO benzilamina com MAA e acido acetico" 5 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 4 MeO Benzil - CDCl3 - Avance 500 MHz - fev15agsH6 - HMBC
1h
(6.82; 47.3)
(5.21; 117.1)
(5.07; 126.9
5.07; 129.0)
(6.82; 127.1)
(5.21; 129.5)
(5.07; 136.2)
(6.82; 159.2)
(3.77; 159.2)
(5.21; 170.1)
(3.81; 165.2
3.85; 165.5)
(2.33; 112.7)
(2.33; 135.9)
(1.83; 170.1)
OMe
O
Me
O
OMe
N
Me
O
OMe
4b
F1 [ppm]
50
100
150
200
8
6
4
2
F2 [ppm]

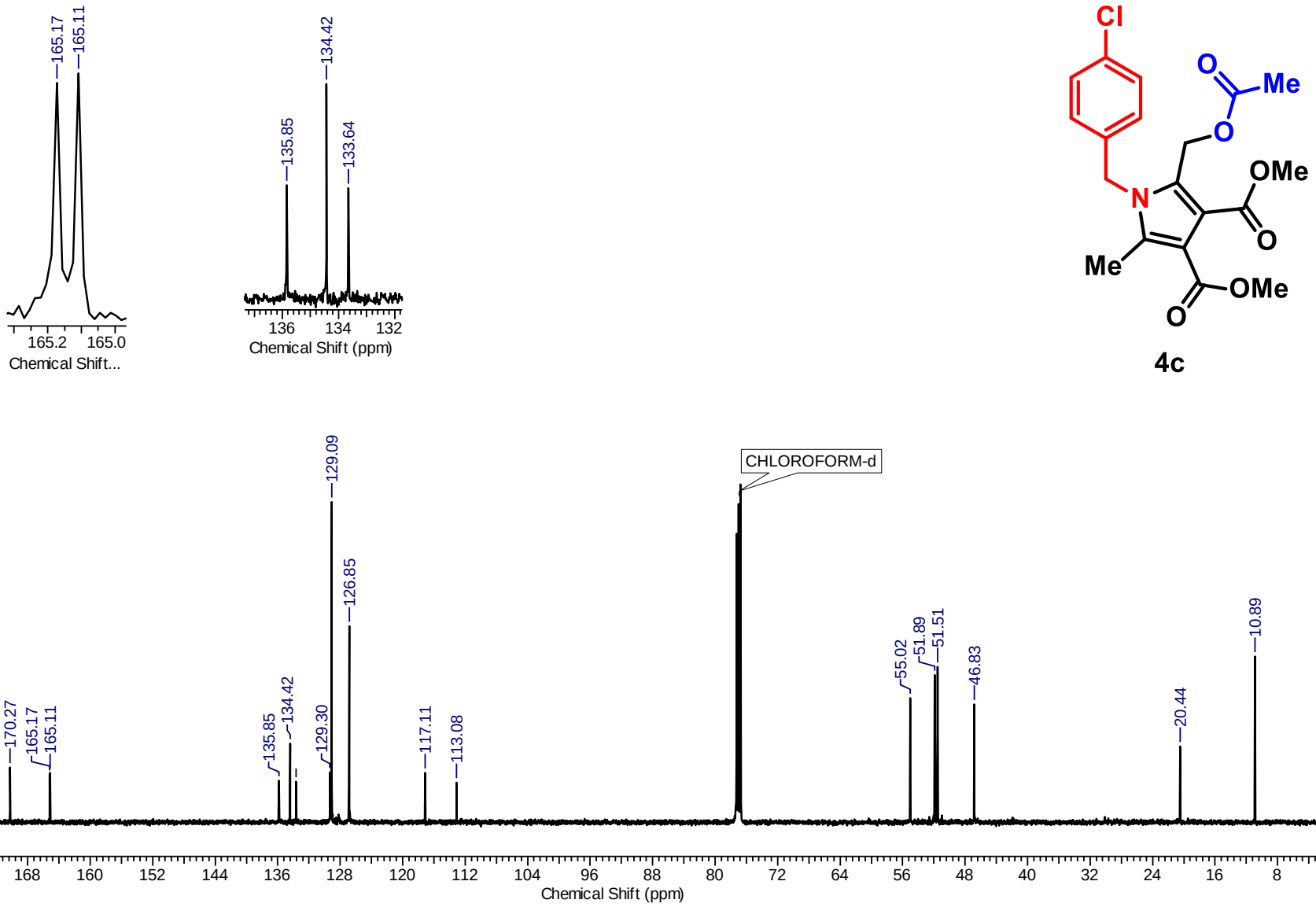

"fev15agsH6_4MeO benzilamina com MAA e acido acetico" 3 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 4 MeO Benzil - CDCl3 - Avance 500 MHz - fev15agsH6 - COSY
40min
F1 [ppm]
F2 [ppm]
8
6
4
2
OMe
O
Me
O
N
OMe
Me
O
OMe
O
4b


7.28
7.27
6.81
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
Chemical Shift (ppm)


Cl
O
Me
O
OMe
N
O
Me
OMe
O

4c


CHLOROFORM-d
7.28
7.27
6.81
5.20
5.11
3.86
3.83
2.32
1.80
1.96
1.96
1.95
1.97
2.97
3.04
2.94
3.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


165.17
165.11
165.2
165.0
Chemical Shift...
134.42
135.85
133.64
136
134
132
Chemical Shift (ppm)
Cl
O
Me
O
OMe
N
O
Me
OMe
O
4c
CHLOROFORM-d
129.09
126.85
170.27
165.17
165.11
135.85
134.42
129.30
117.11
113.08
55.02
51.89
51.51
46.83
20.44
10.89
184
176
168
160
152
144
136
128
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96
88
80
72
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56
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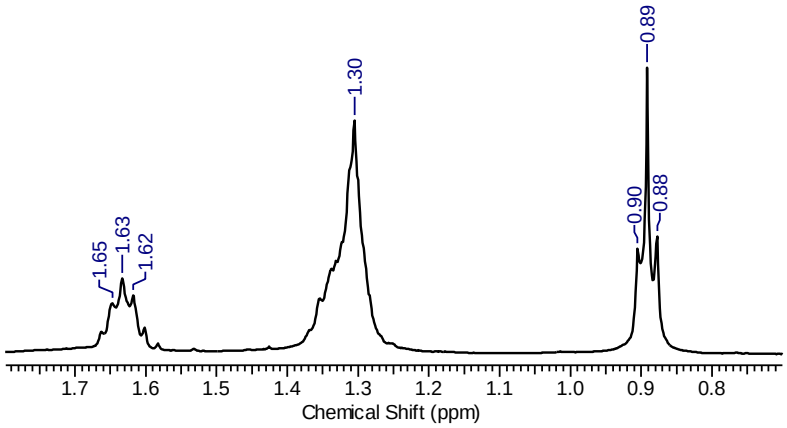
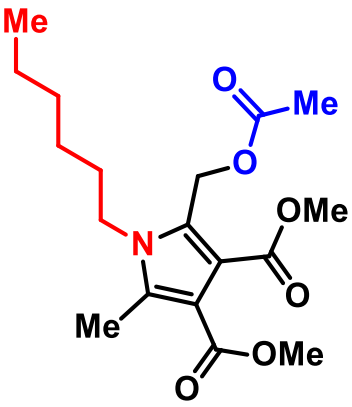
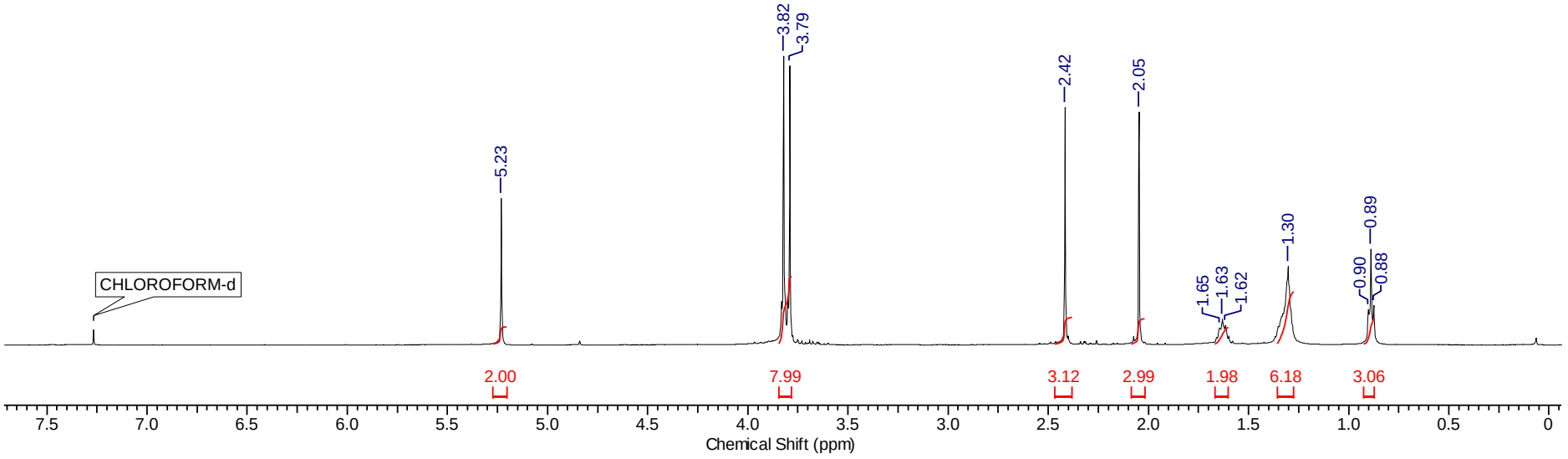
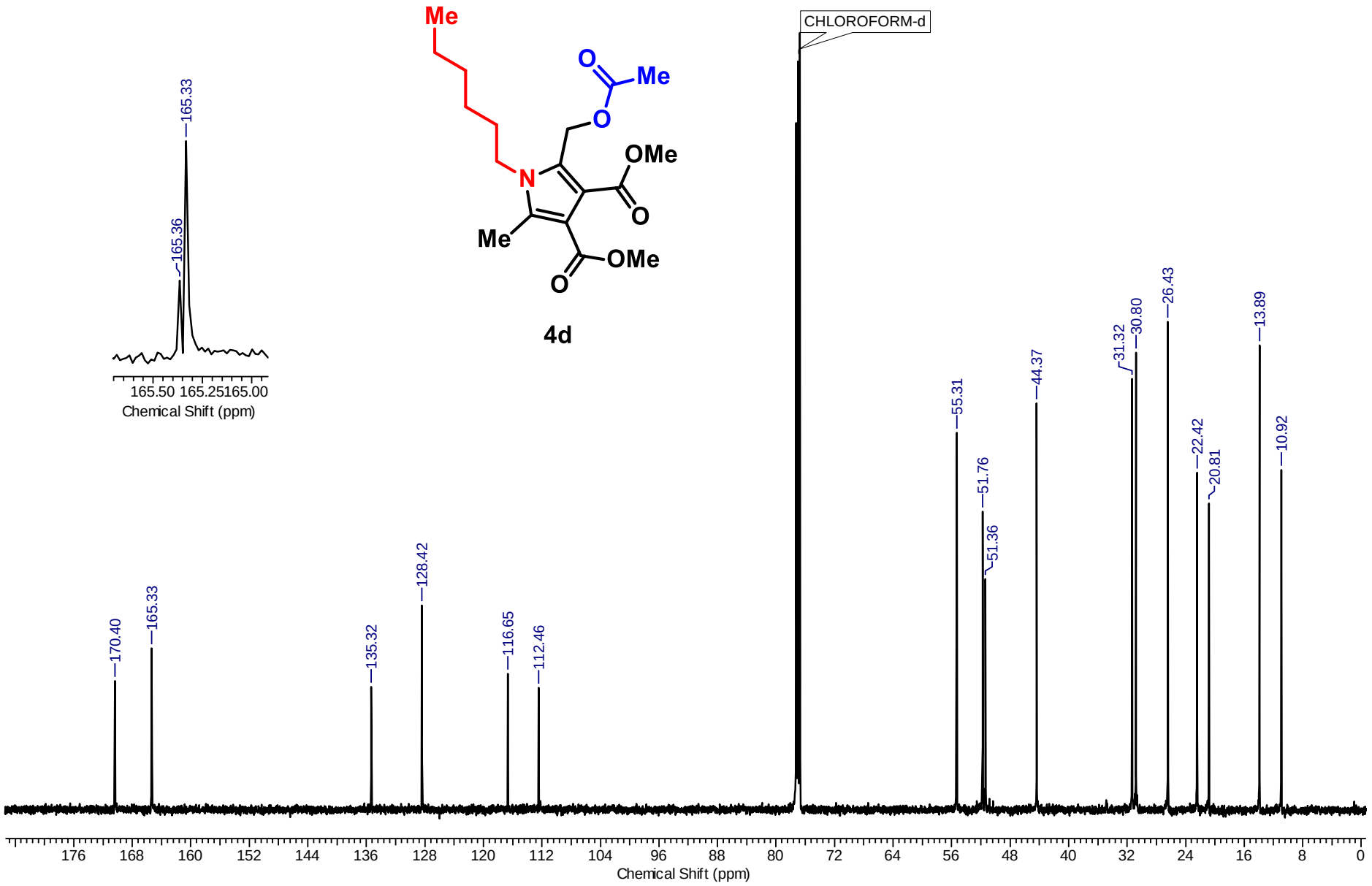
40
32
24
16
8
0
Chemical Shift (ppm)

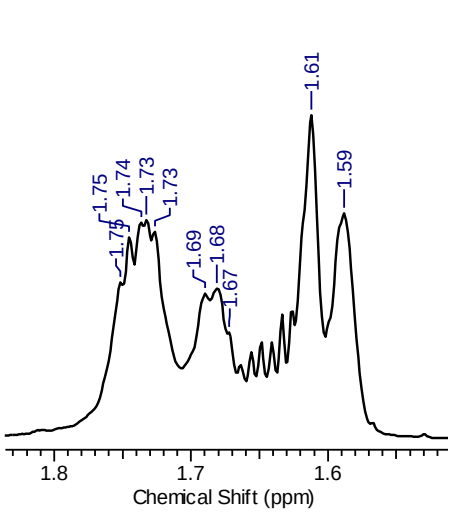

1.65
1.63
1.62
1.30
0.90
0.89
0.88
1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
Chemical Shift (ppm)

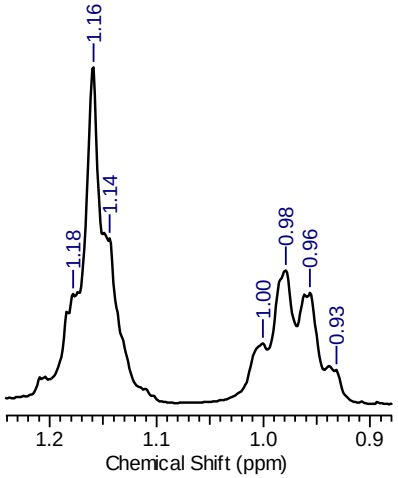

Me
O
Me
O
OMe
N
O
Me
OMe
O

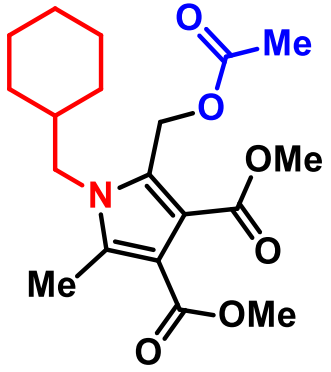
4d


CHLOROFORM-d
5.23
3.82
3.79
2.42
2.05
1.65
1.63
1.62
1.30
0.90
0.89
0.88
2.00
7.99
3.12
2.99
1.98
6.18
3.06
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

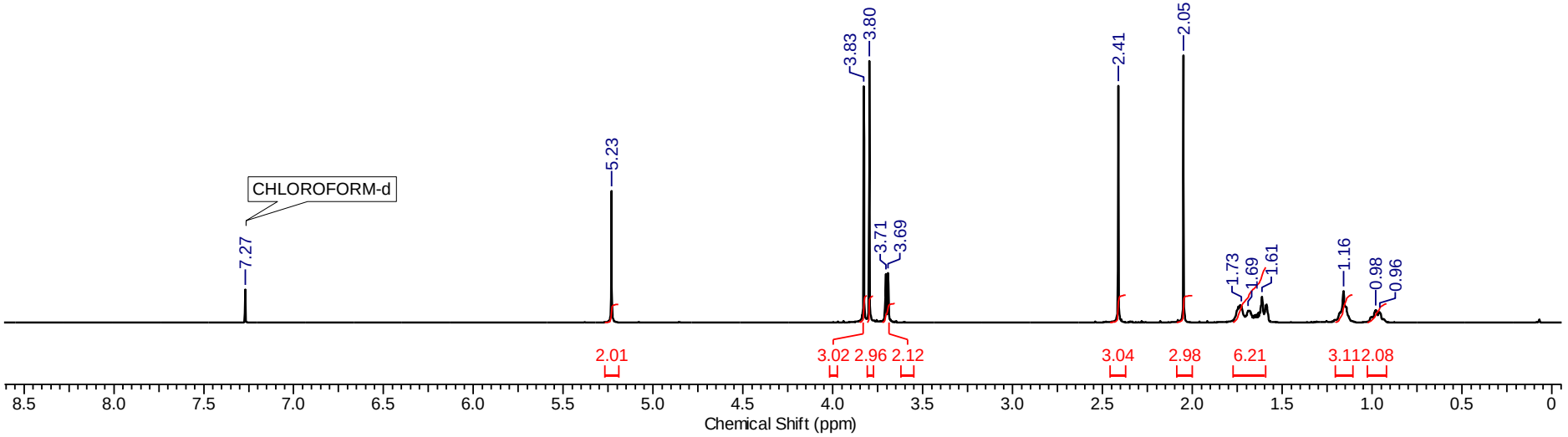

Me
O
Me
O
OMe
N
O
Me
OMe
O
4d
CHLOROFORM-d
165.33
165.36
165.50 165.25165.00
Chemical Shift (ppm)
170.40
165.33
135.32
128.42
116.65
112.46
55.31
51.76
51.36
44.37
31.32
30.80
26.43
22.42
20.81
13.89
10.92
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

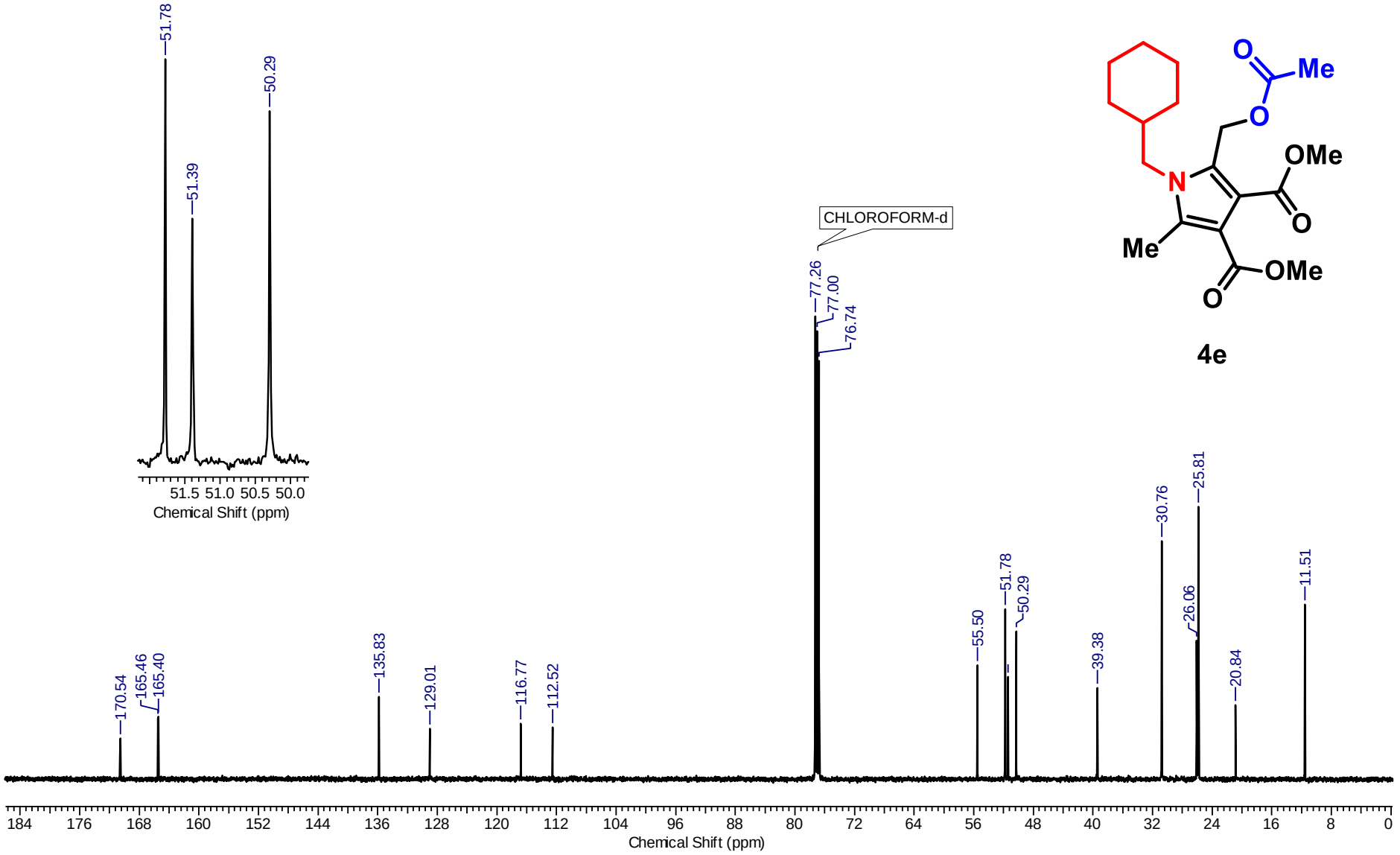

1.75
1.74
1.73
1.73
1.69
1.68
1.67
1.61
1.59
1.8
1.7
1.6
Chemical Shift (ppm)

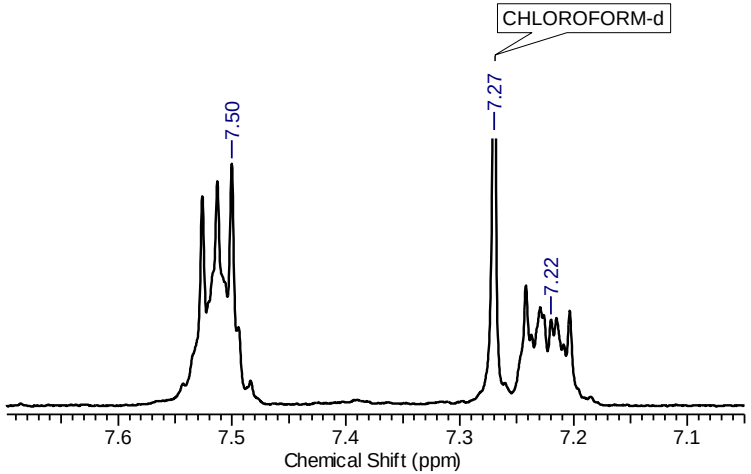

1.16
1.18
1.14
0.98
0.96
1.00
0.93
1.2
1.1
1.0
0.9
Chemical Shift (ppm)

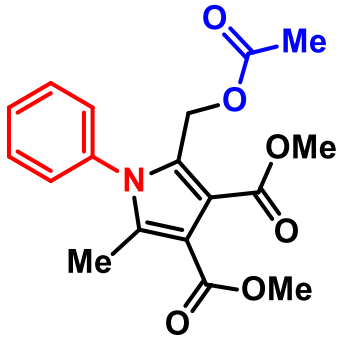

O
Me
O
OMe
N
O
Me
OMe
O

4e

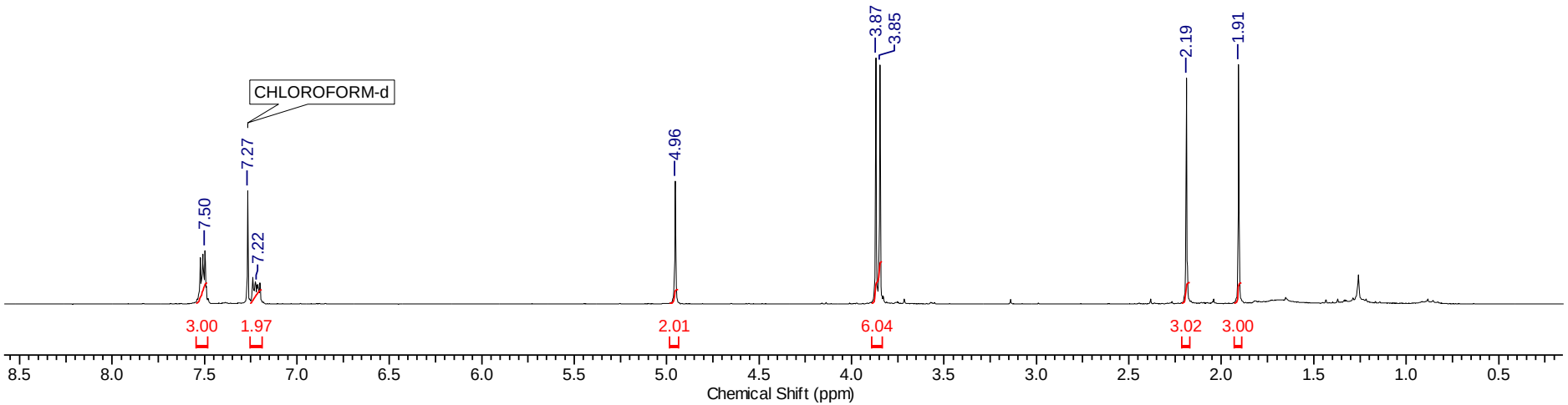

CHLOROFORM-d
7.27
5.23
3.83
3.80
3.71
3.69
2.41
2.05
1.73
1.69
1.61
1.16
0.98
0.96
2.01
3.02
2.96
2.12
3.04
2.98
6.21
3.11
2.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

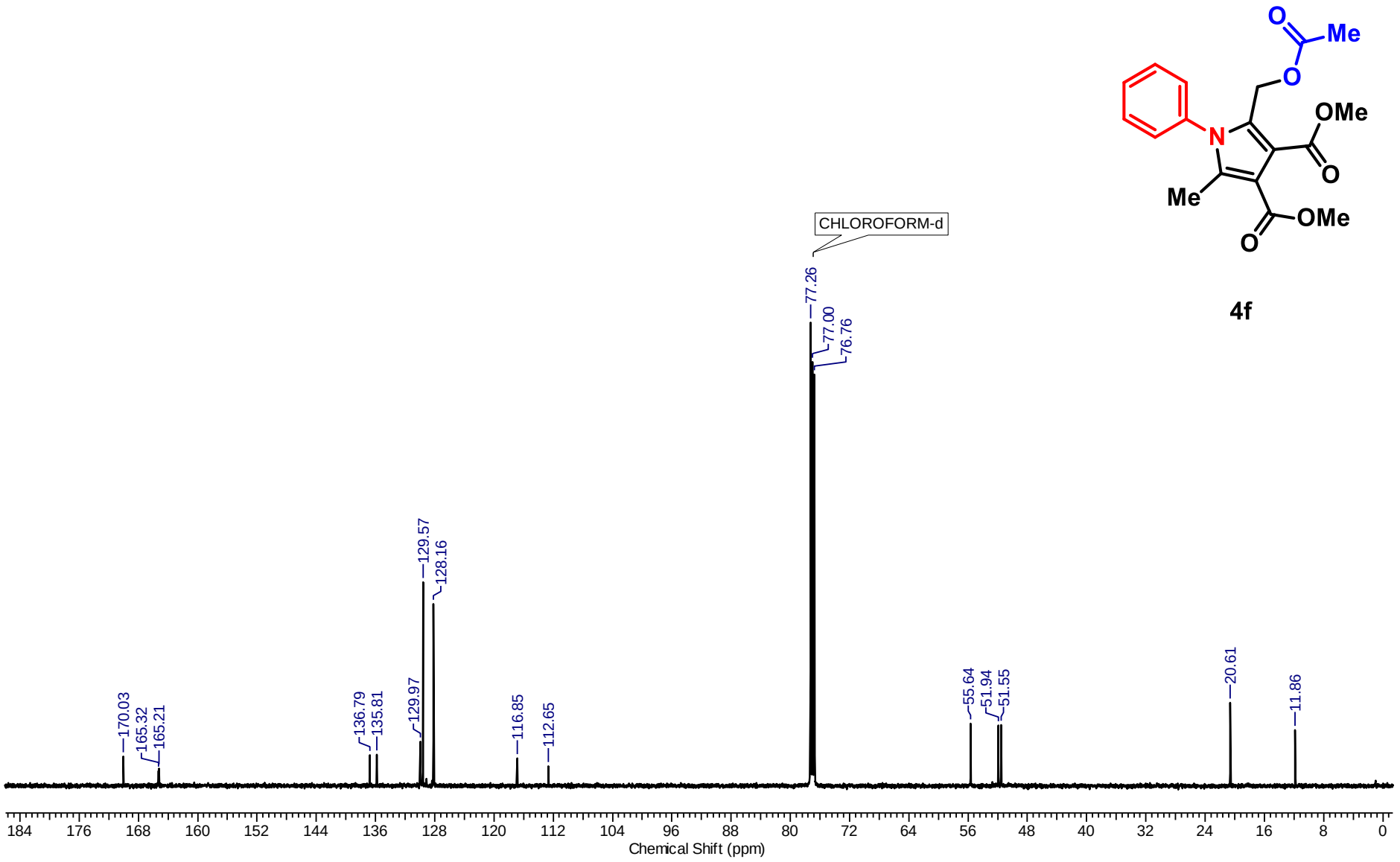

51.78
51.39
50.29
51.5 51.0 50.5 50.0
Chemical Shift (ppm)
CHLOROFORM-d
77.26
77.00
76.74
O
Me
O
OMe
N
Me
O
OMe
4e
170.54
165.46
165.40
135.83
129.01
116.77
112.52
55.50
51.78
50.29
39.38
30.76
26.06
25.81
20.84
11.51
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


CHLOROFORM-d
7.50
7.27
7.22
7.6
7.5
7.4
7.3
7.2
7.1
Chemical Shift (ppm)

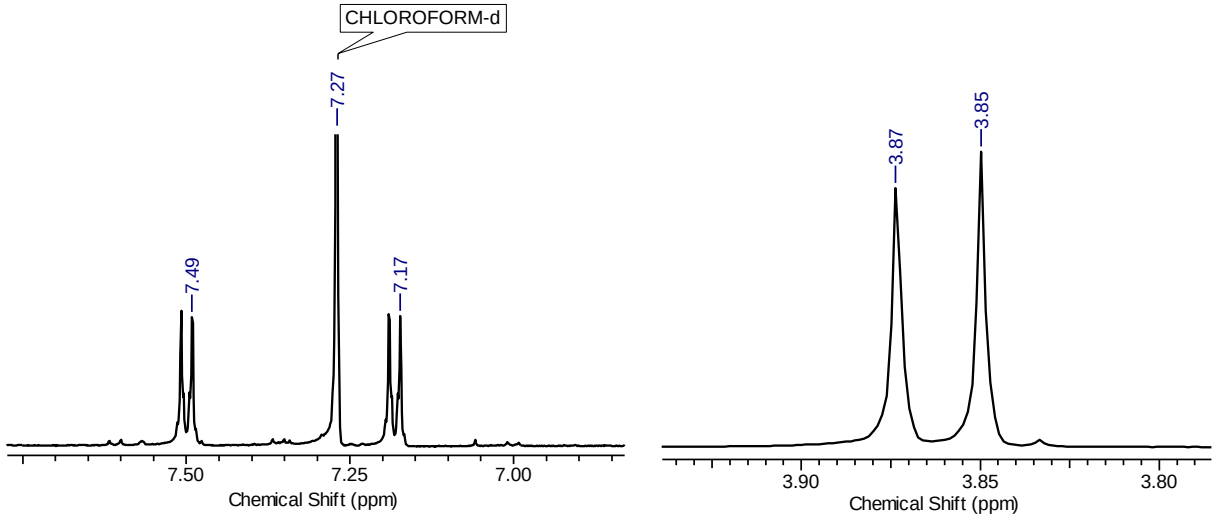

O
Me
O
OMe
N
O
Me
OMe
O

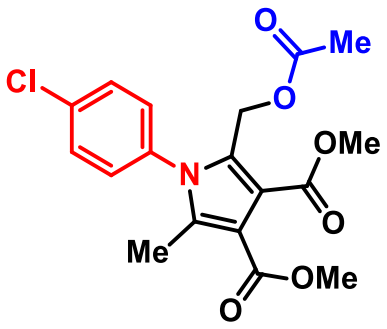
4f


CHLOROFORM-d
7.50
7.27
7.22
4.96
3.87
3.85
2.19
1.91
3.00
1.97
2.01
6.04
3.02
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

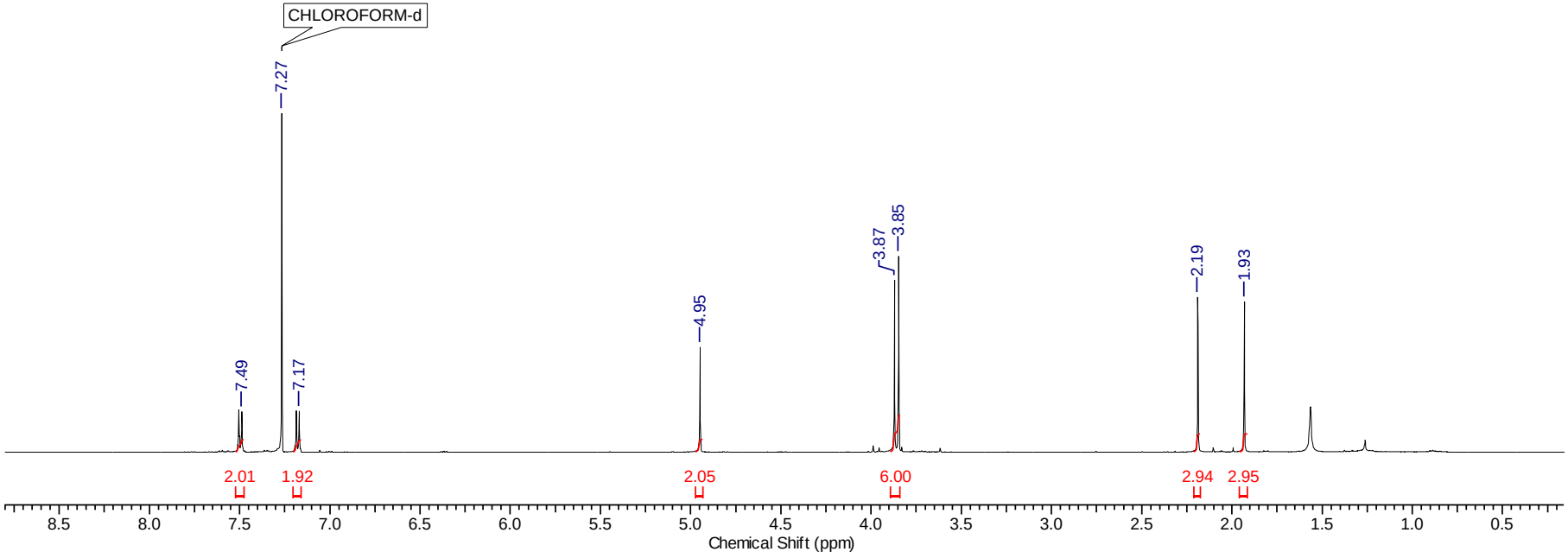

CHLOROFORM-d
77.26
77.00
76.76
170.03
165.32
165.21
136.79
135.81
129.97
129.57
128.16
116.85
112.65
55.64
51.94
51.55
20.61
11.86
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

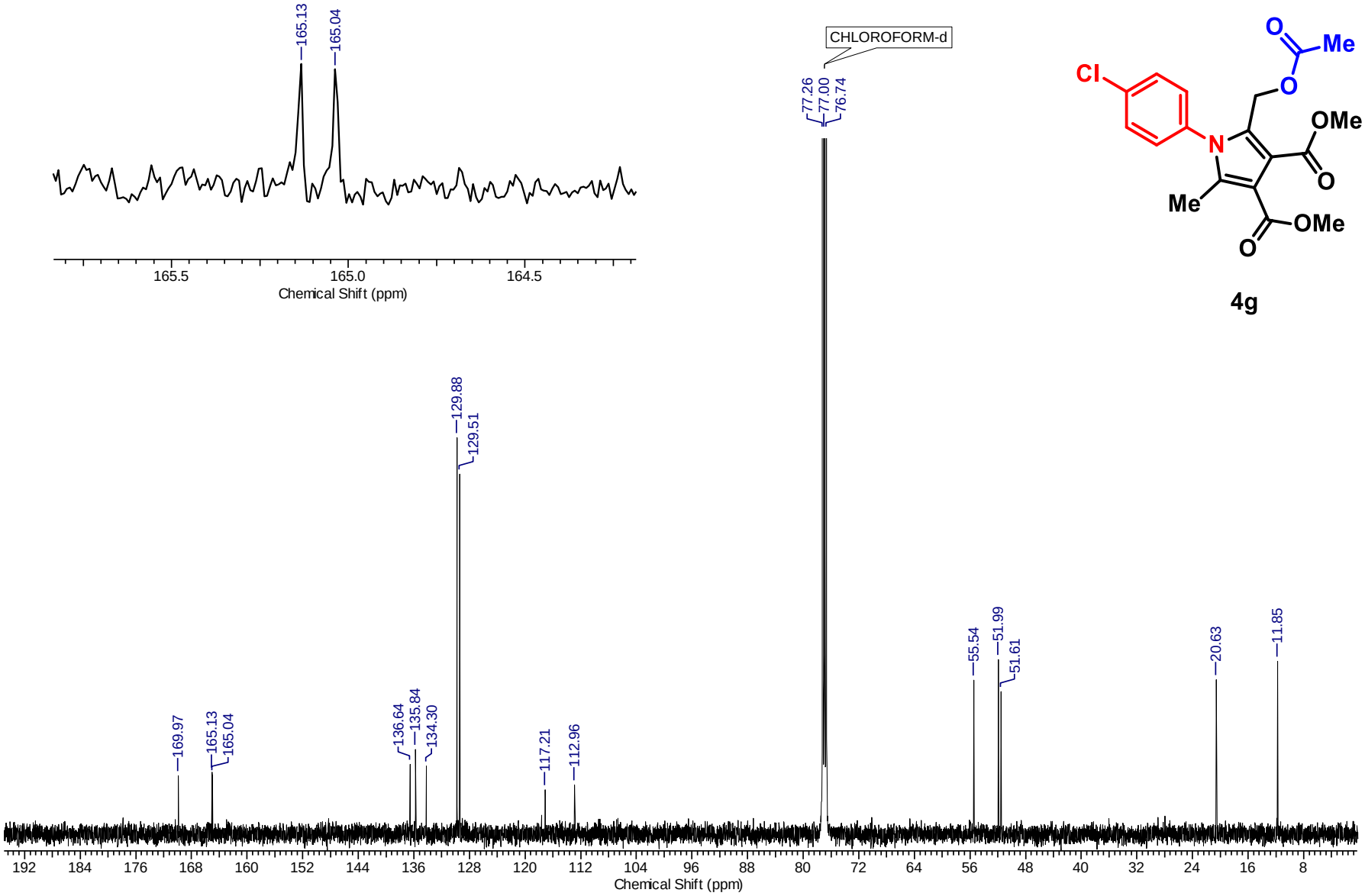
4f

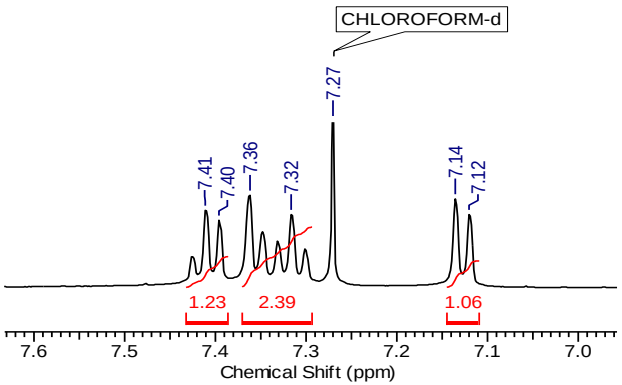

CHLOROFORM-d
7.27
7.49
7.17
7.50
7.25
7.00
Chemical Shift (ppm)
3.87
3.85
3.90
3.85
3.80
Chemical Shift (ppm)

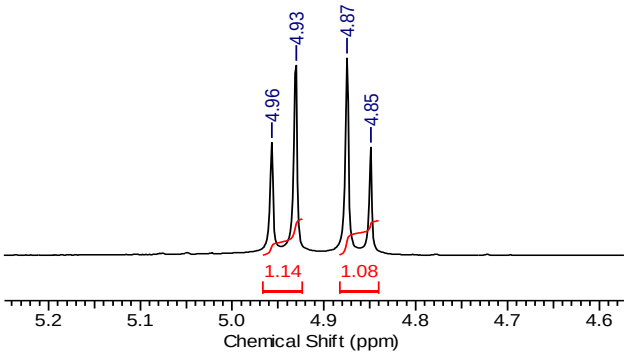

O
Me
Cl
O
OMe
N
O
Me
OMe
O

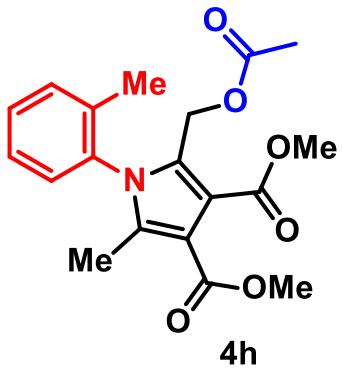
4g


CHLOROFORM-d
7.27
7.49
7.17
4.95
3.87
3.85
2.19
1.93
2.01
1.92
2.05
6.00
2.94
2.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


165.13
165.04
165.5
165.0
164.5
Chemical Shift (ppm)
CHLOROFORM-d
77.26
77.00
76.74
Cl
N
O
Me
OMe
O
Me
OMe
O
4g
129.88
129.51
169.97
165.13
165.04
136.64
135.84
134.30
117.21
112.96
55.54
51.99
51.61
20.63
11.85
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

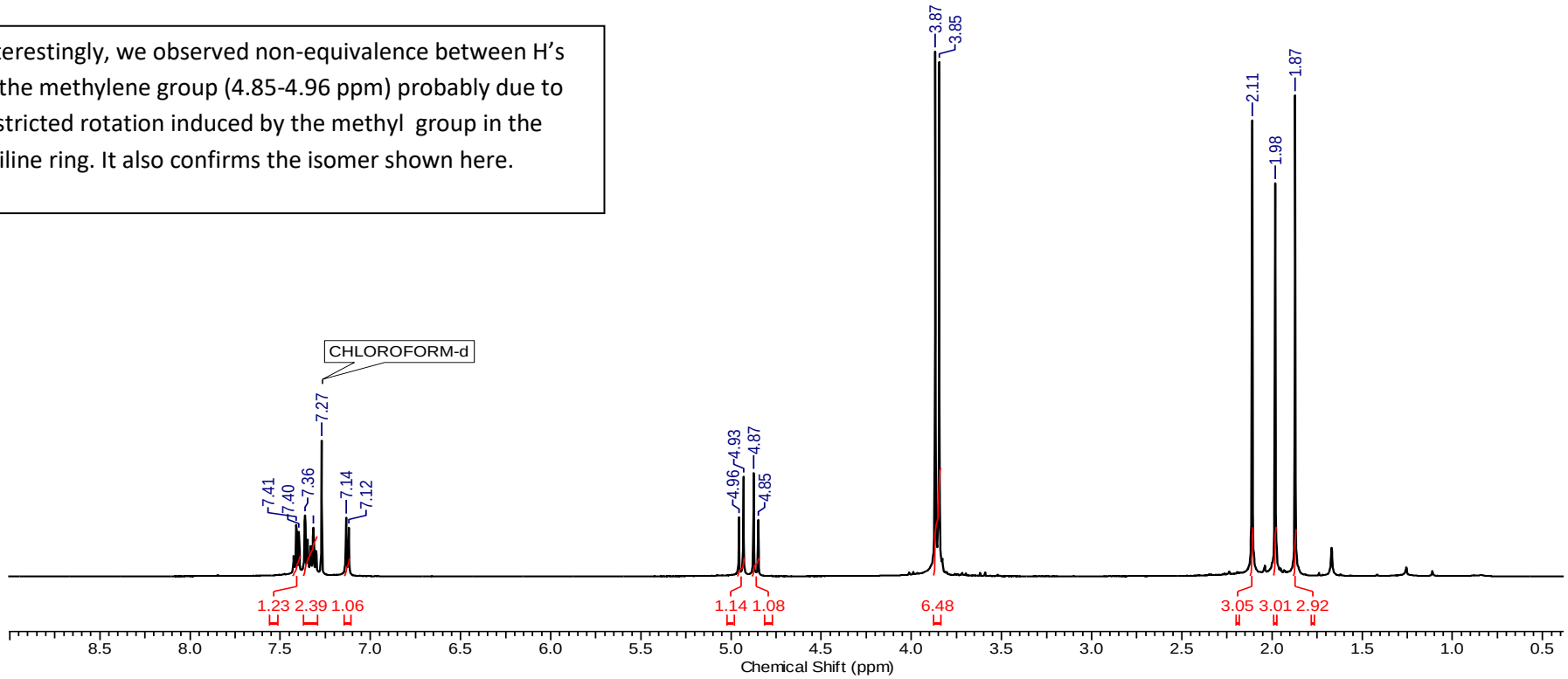


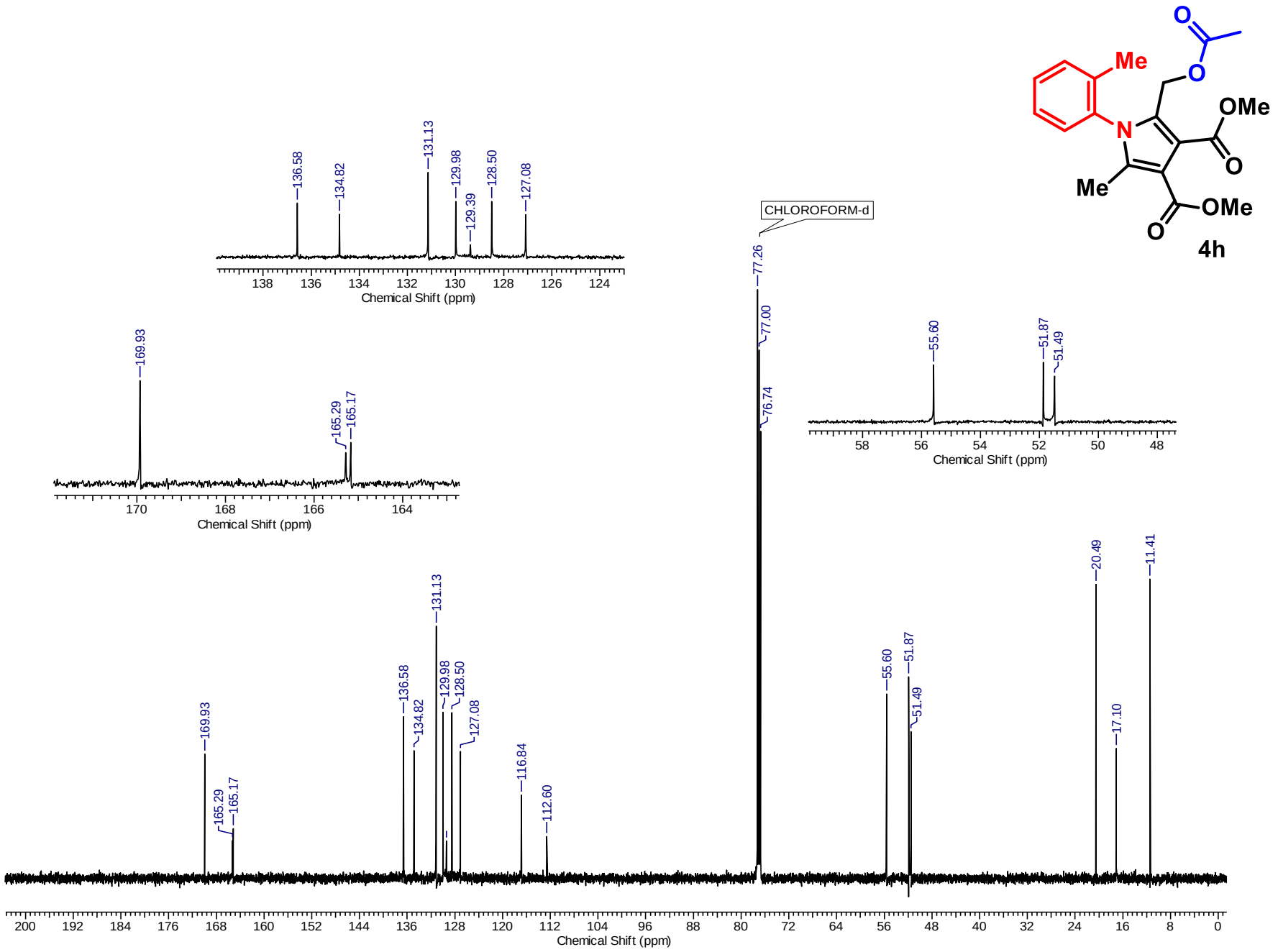


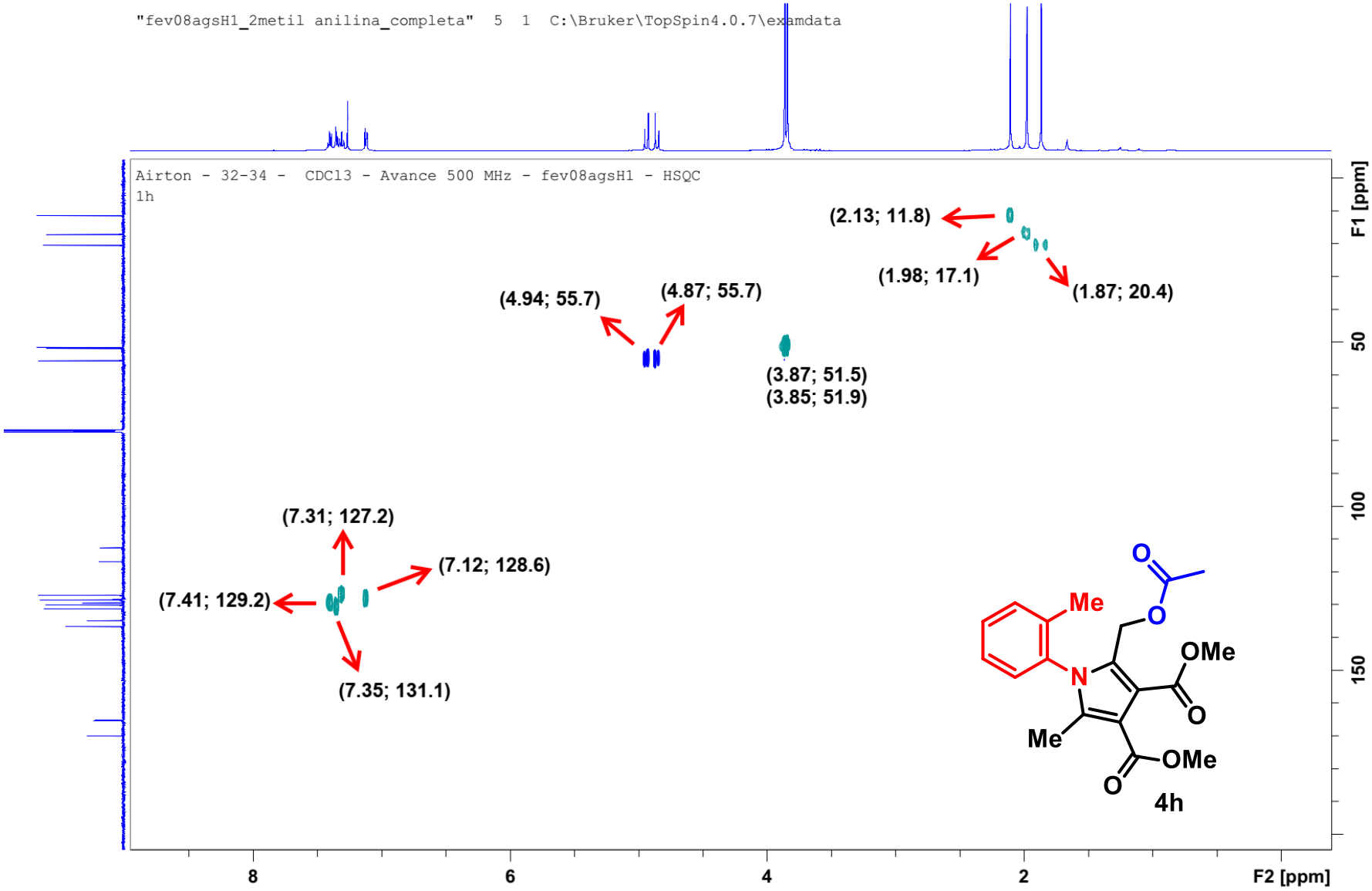


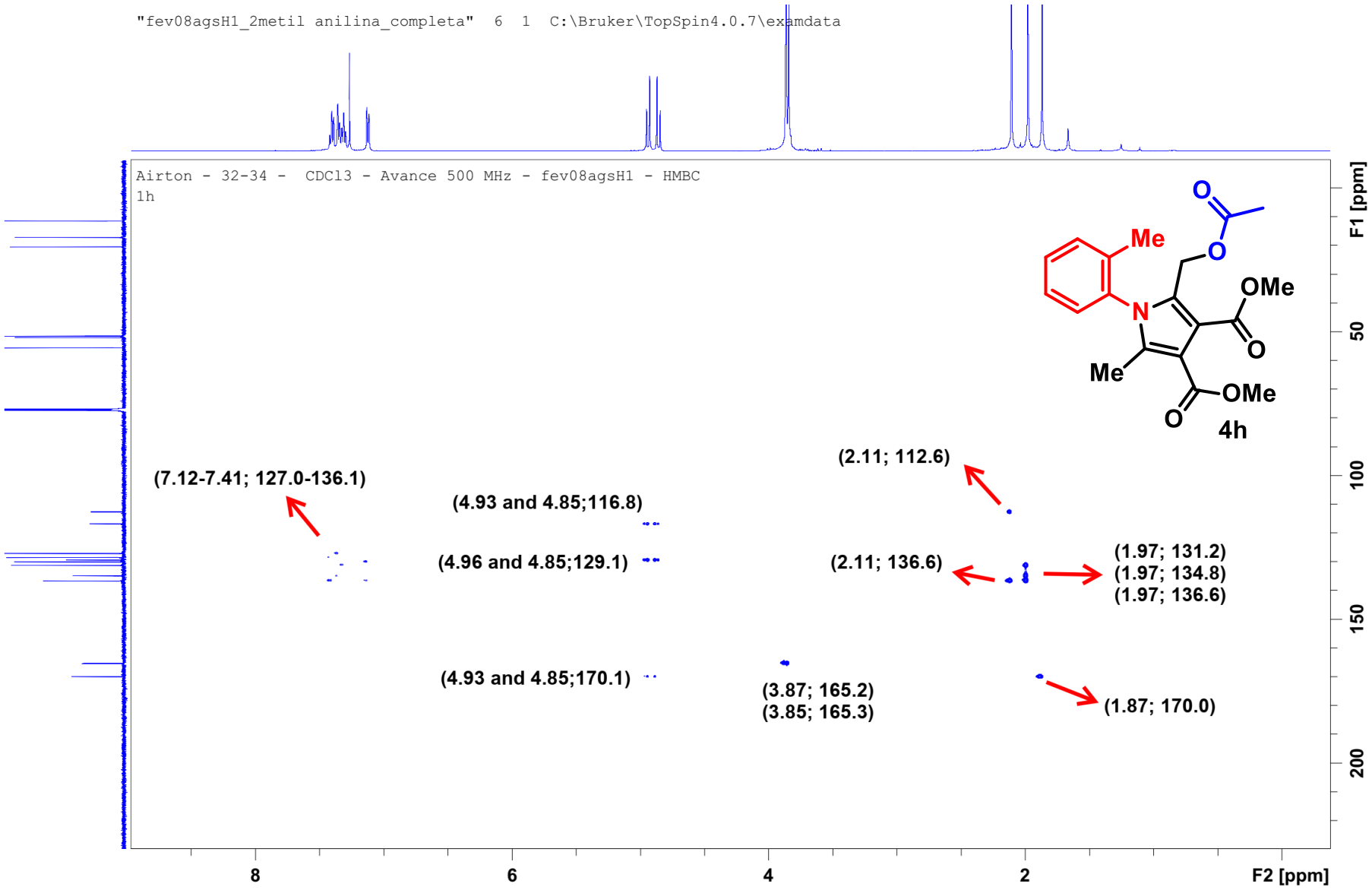
4h

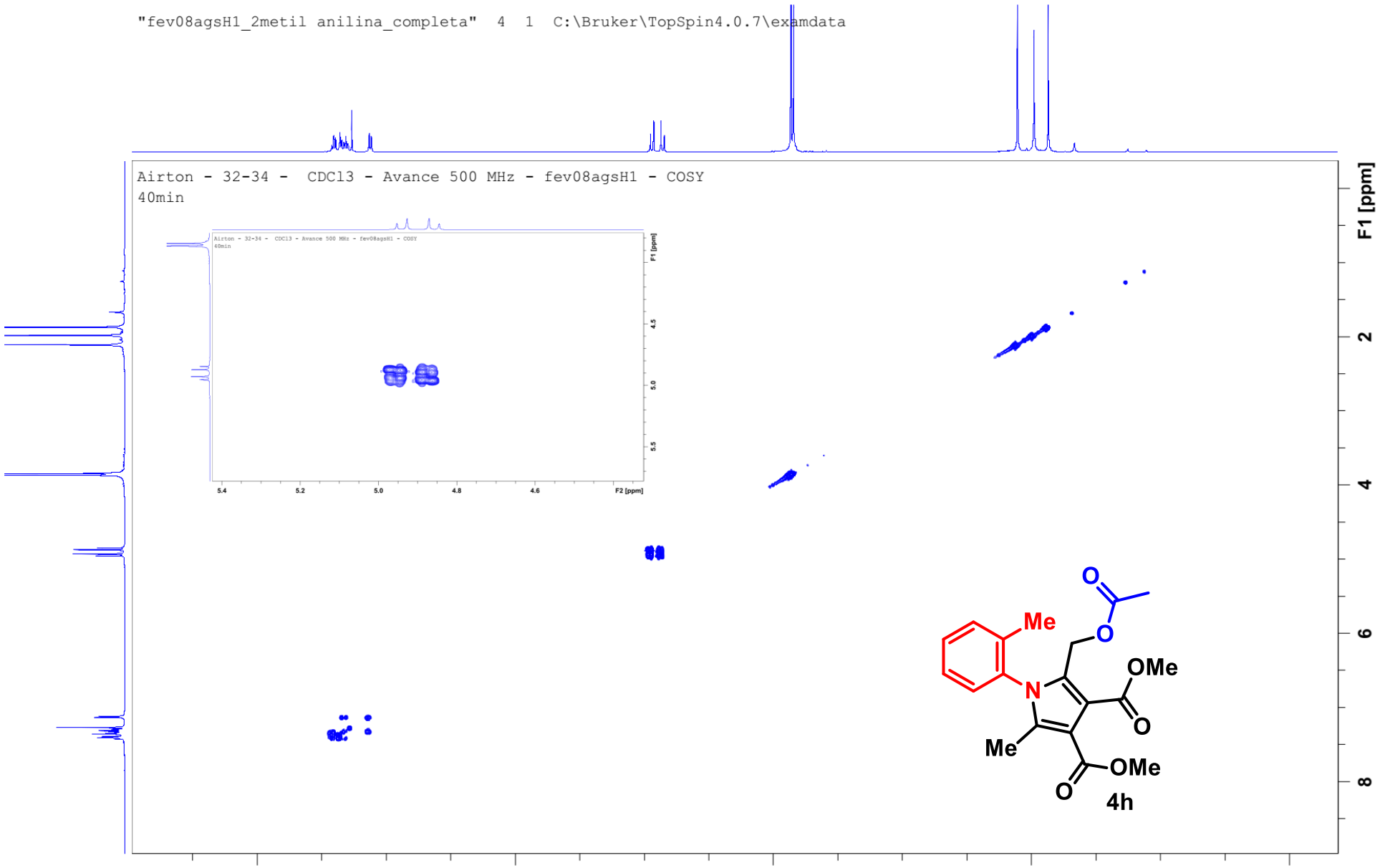
Interestingly, we observed non-equivalence between H's in the methylene group (4.85-4.96 ppm) probably due to restricted rotation induced by the methyl group in the aniline ring. It also confirms the isomer shown here.

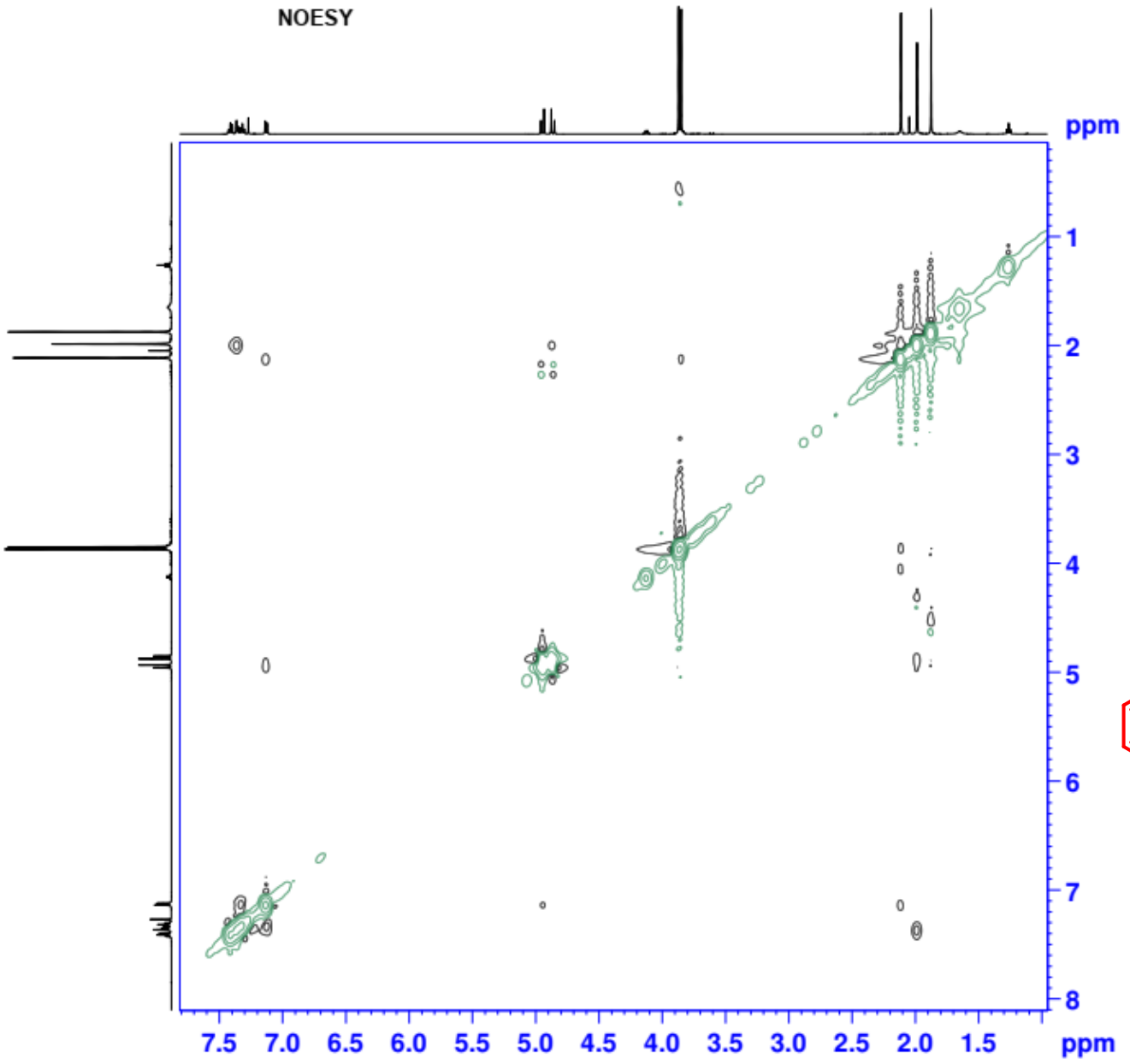


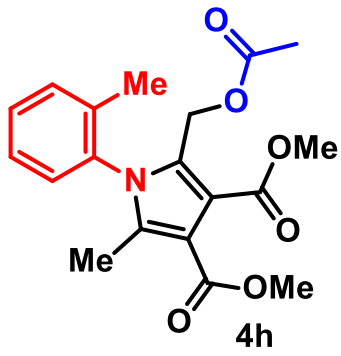

Me
O
O
OMe
N
O
Me
OMe
O
4h
CHLOROFORM-d
136.58
134.82
131.13
129.98
129.39
128.50
127.08
Chemical Shift (ppm)
169.93
165.29
165.17
Chemical Shift (ppm)
77.26
77.00
76.74
55.60
51.87
51.49
Chemical Shift (ppm)
169.93
165.29
165.17
136.58
134.82
131.13
129.98
128.50
127.08
116.84
112.60
55.60
51.87
51.49
20.49
17.10
11.41
Chemical Shift (ppm)


"fev08agsH1_2metil anilina_completa" 5 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 32-34 - CDCl3 - Avance 500 MHz - fev08agsH1 - HSQC
1h
(2.13; 11.8)
(1.98; 17.1)
(1.87; 20.4)
(4.94; 55.7)
(4.87; 55.7)
(3.87; 51.5)
(3.85; 51.9)
(7.31; 127.2)
(7.12; 128.6)
(7.41; 129.2)
(7.35; 131.1)
Me
N
OMe
Me
OMe
4h
F1 [ppm]
F2 [ppm]
8
6
4
2
50
100
150

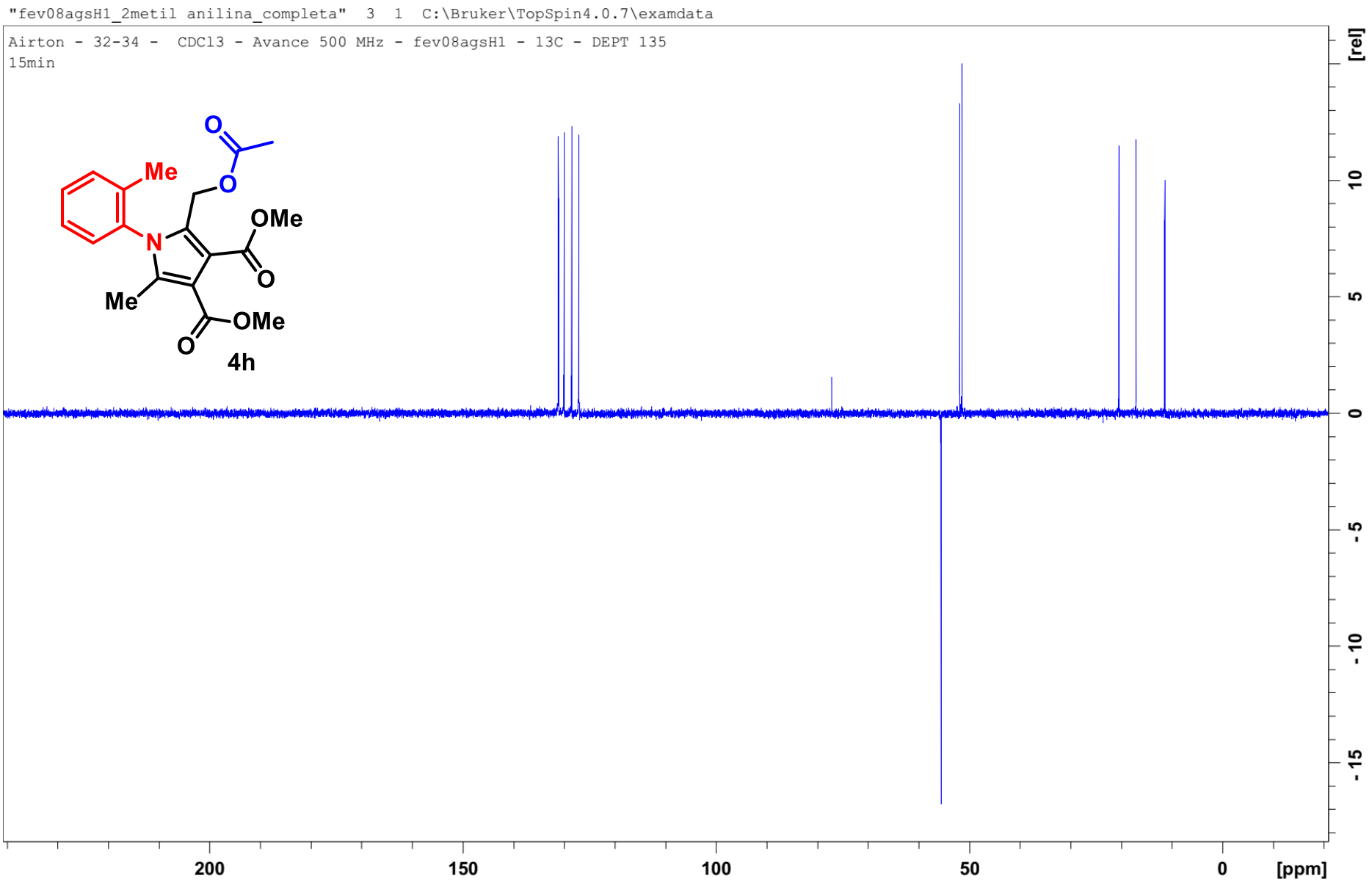

"fev08agsH1_2metil anilina_completa" 6 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 32-34 - CDCl3 - Avance 500 MHz - fev08agsH1 - HMBC
1h
Me
O
O
OMe
N
O
Me
OMe
O
4h
(7.12-7.41; 127.0-136.1)
(4.93 and 4.85;116.8)
(4.96 and 4.85;129.1)
(4.93 and 4.85;170.1)
(2.11; 112.6)
(2.11; 136.6)
(1.97; 131.2)
(1.97; 134.8)
(1.97; 136.6)
(3.87; 165.2)
(3.85; 165.3)
(1.87; 170.0)
F1 [ppm]
50
100
150
200
8
6
4
2
F2 [ppm]

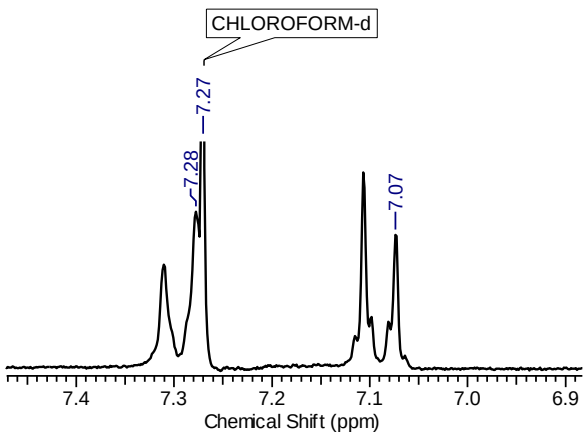

"fev08agsH1_2metil anilina_completa" 4 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 32-34 - CDCl3 - Avance 500 MHz - fev08agsH1 - COSY
40min
F1 [ppm]
F2 [ppm]
Me
N
Me
O
O
OMe
O
OMe
O
4h

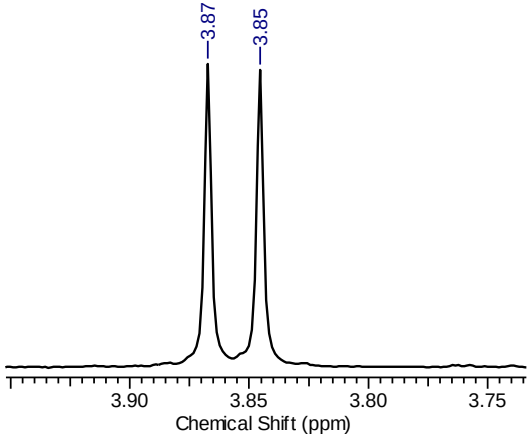

NOESY
ppm
1
2
3
4
5
6
7
8
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

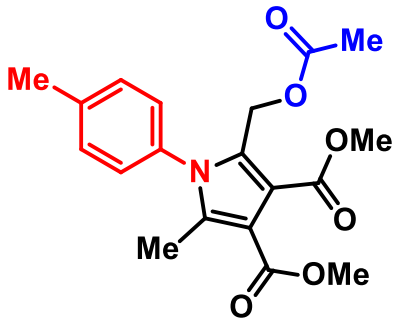

Me
N
O
O
OMe
O
Me
OMe
O

4h

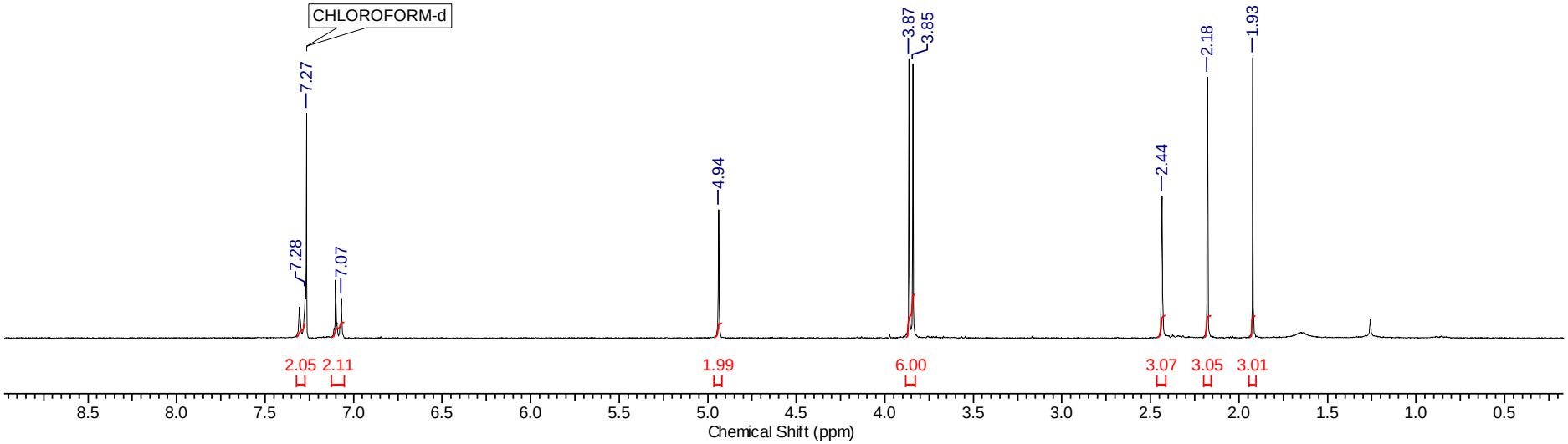

"fev08agsH1_2metil anilina_completa" 3 1 C:\Bruker\TopSpin4.0.7\examdata
Airton - 32-34 - CDCl3 - Avance 500 MHz - fev08agsH1 - 13C - DEPT 135
15min
Me
N
Me
O
O
OMe
O
OMe
O
4h
[rel]
10
5
0
-5
-10
-15
200
150
100
50
0
[ppm]

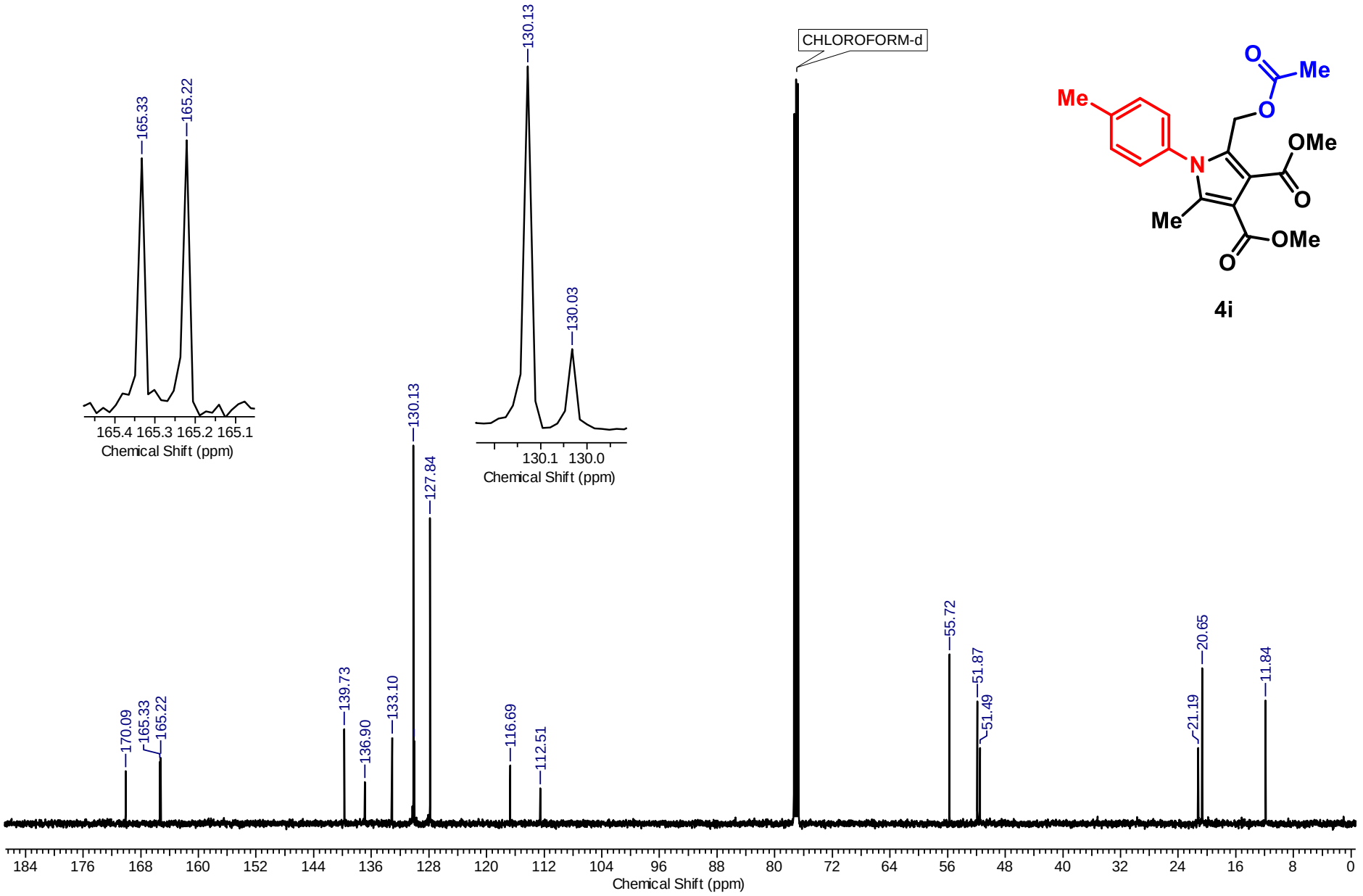

CHLOROFORM-d
7.27
7.28
7.07
7.4
7.3
7.2
7.1
7.0
6.9
Chemical Shift (ppm)

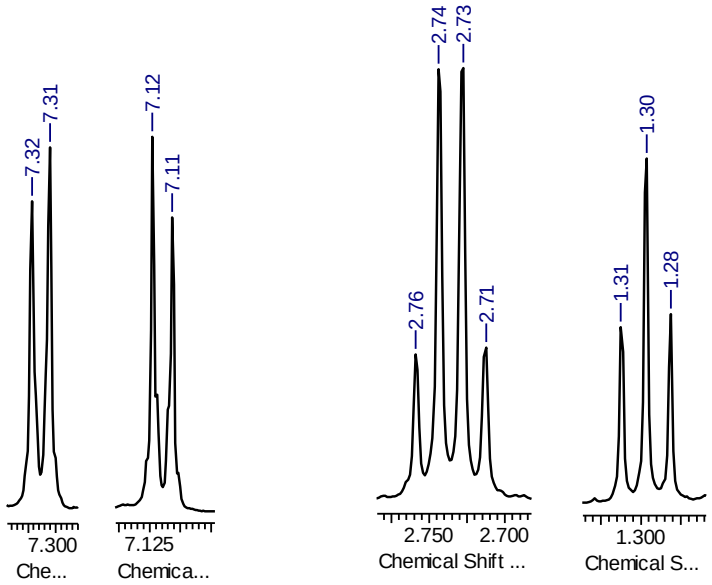

3.87
3.85
3.90
3.85
3.80
3.75
Chemical Shift (ppm)

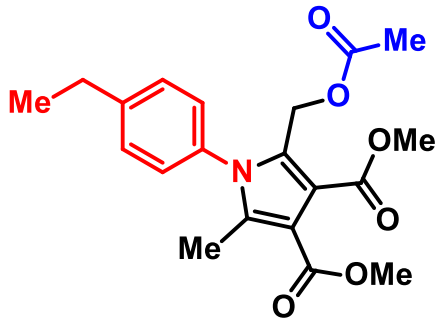

Me
O
Me
O
N
OMe
O
Me
OMe
O

4i

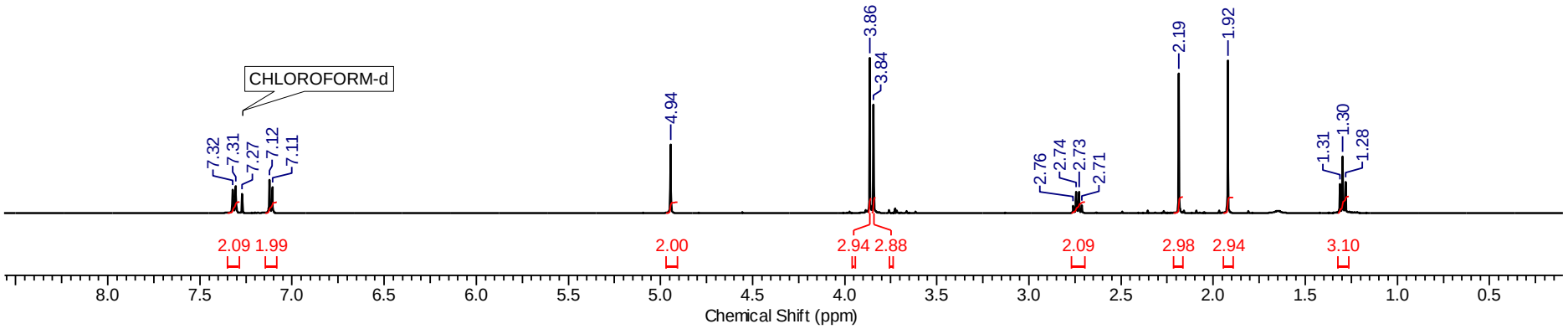

CHLOROFORM-d
7.27
7.28
7.07
4.94
3.87
3.85
2.44
2.18
1.93
2.05
2.11
1.99
6.00
3.07
3.05
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

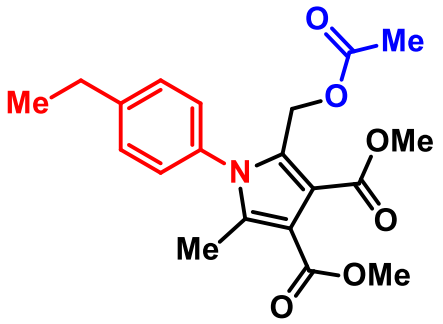

165.33
165.22
165.4 165.3 165.2 165.1
Chemical Shift (ppm)
130.13
130.03
130.1 130.0
Chemical Shift (ppm)
CHLOROFORM-d
Me
O
Me
O
OMe
N
Me
O
OMe
O
4i
170.09
165.33
165.22
139.73
136.90
133.10
130.13
127.84
116.69
112.51
55.72
51.87
51.49
21.19
20.65
11.84
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


7.32
7.31
7.12
7.11
2.74
2.73
2.76
2.71
1.30
1.31
1.28
7.300
7.125
2.750
2.700
1.300
Che...
Chemica...
Chemical Shift ...
Chemical S...

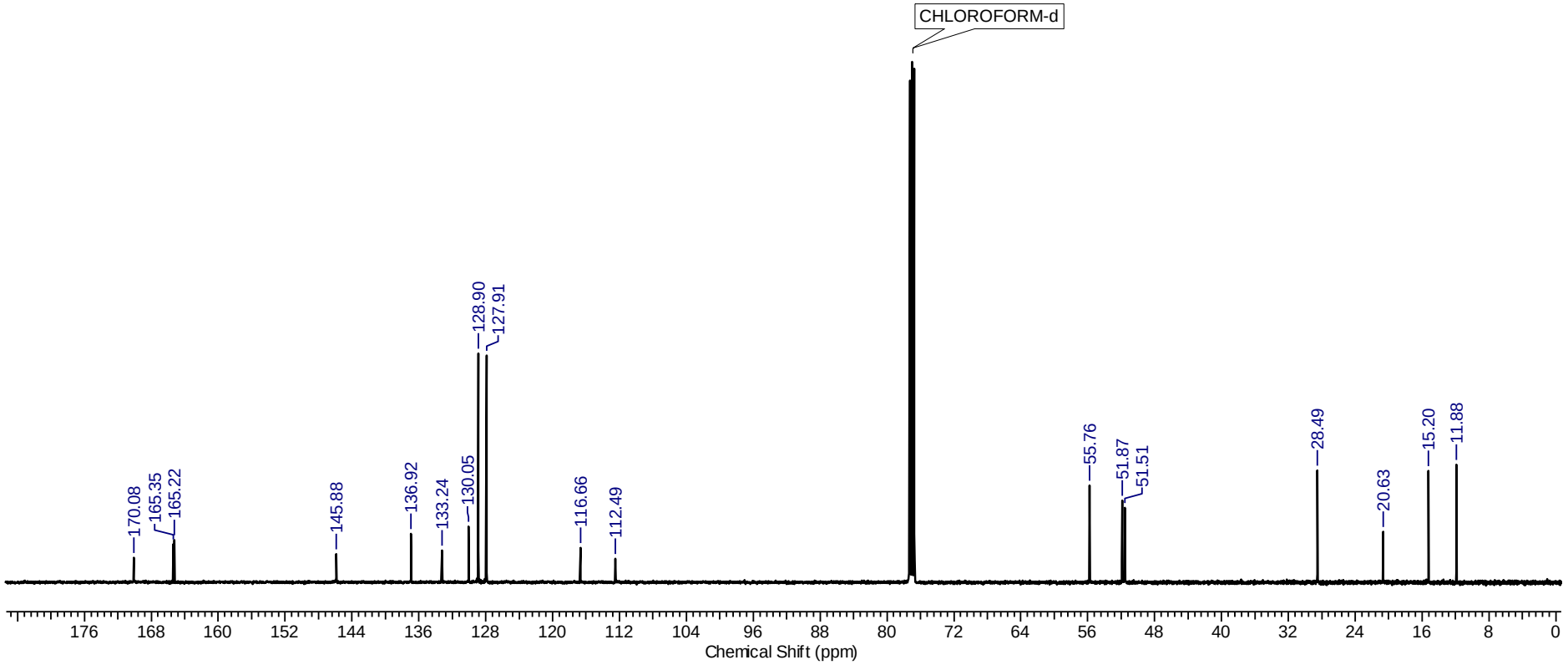

O
Me
O
OMe
N
Me
O
OMe
O

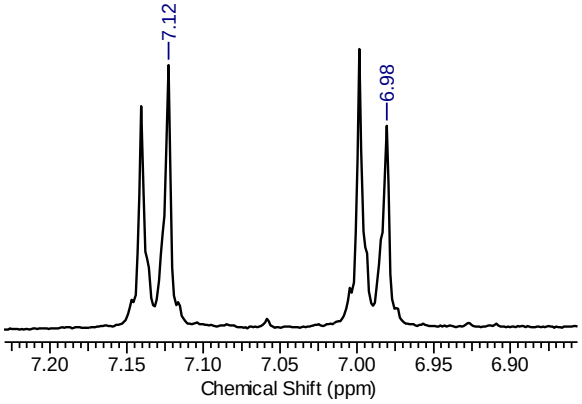
4j

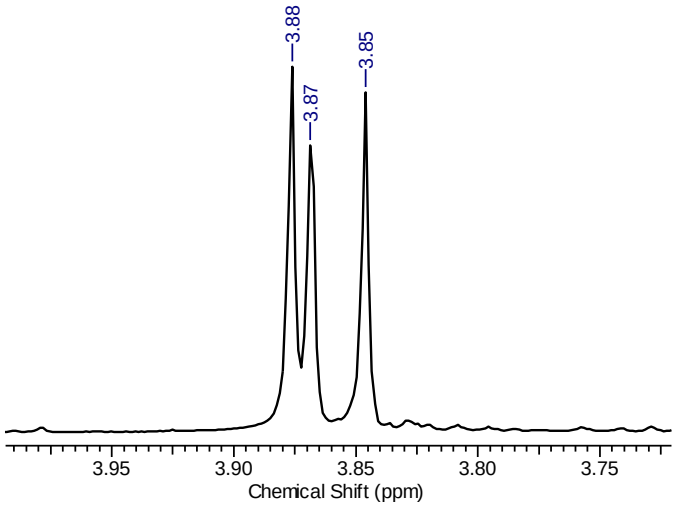

CHLOROFORM-d
7.32
7.31
7.27
7.12
7.11
4.94
3.86
3.84
2.76
2.74
2.73
2.71
2.19
1.92
1.31
1.30
1.28
2.09
1.99
2.00
2.94
2.88
2.09
2.98
2.94
3.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

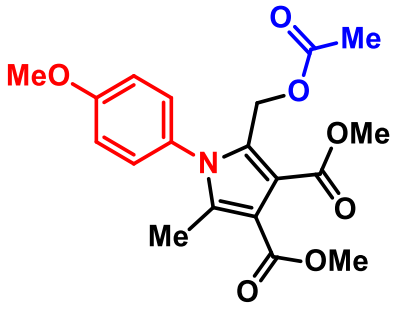

O
Me
O
Me
OMe
N
O
Me
OMe
O

4j

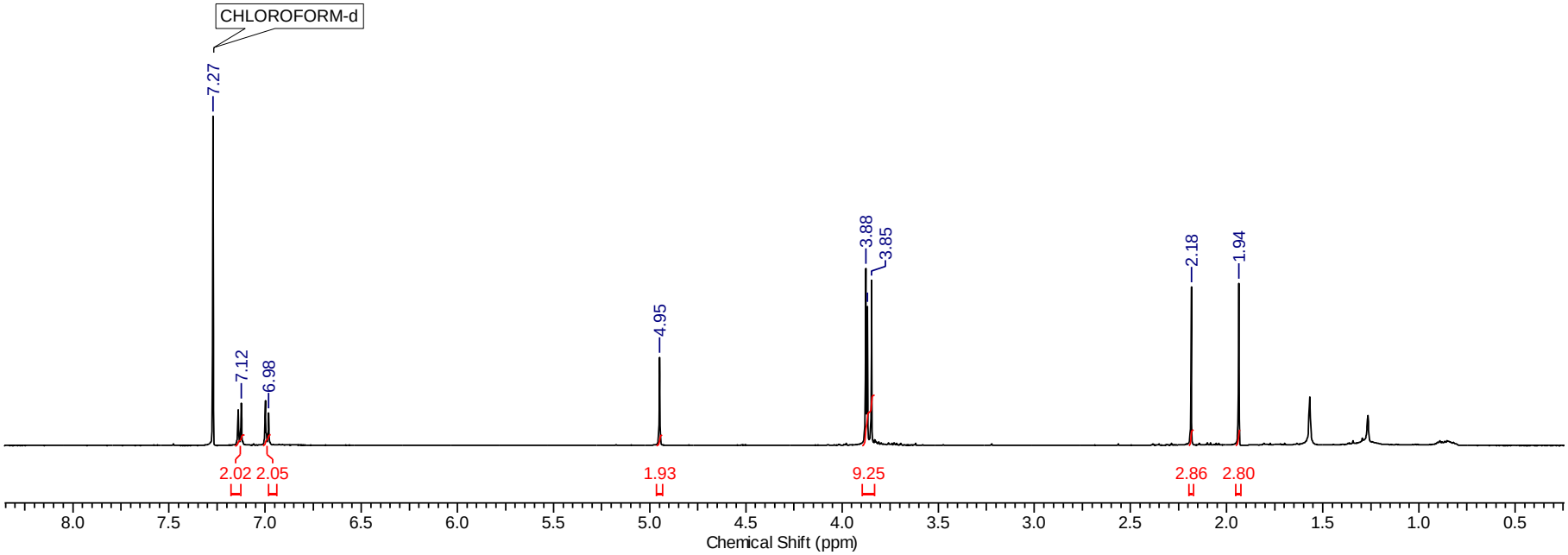

CHLOROFORM-d
170.08
165.35
165.22
145.88
136.92
133.24
130.05
128.90
127.91
116.66
112.49
55.76
51.87
51.51
28.49
20.63
15.20
11.88
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

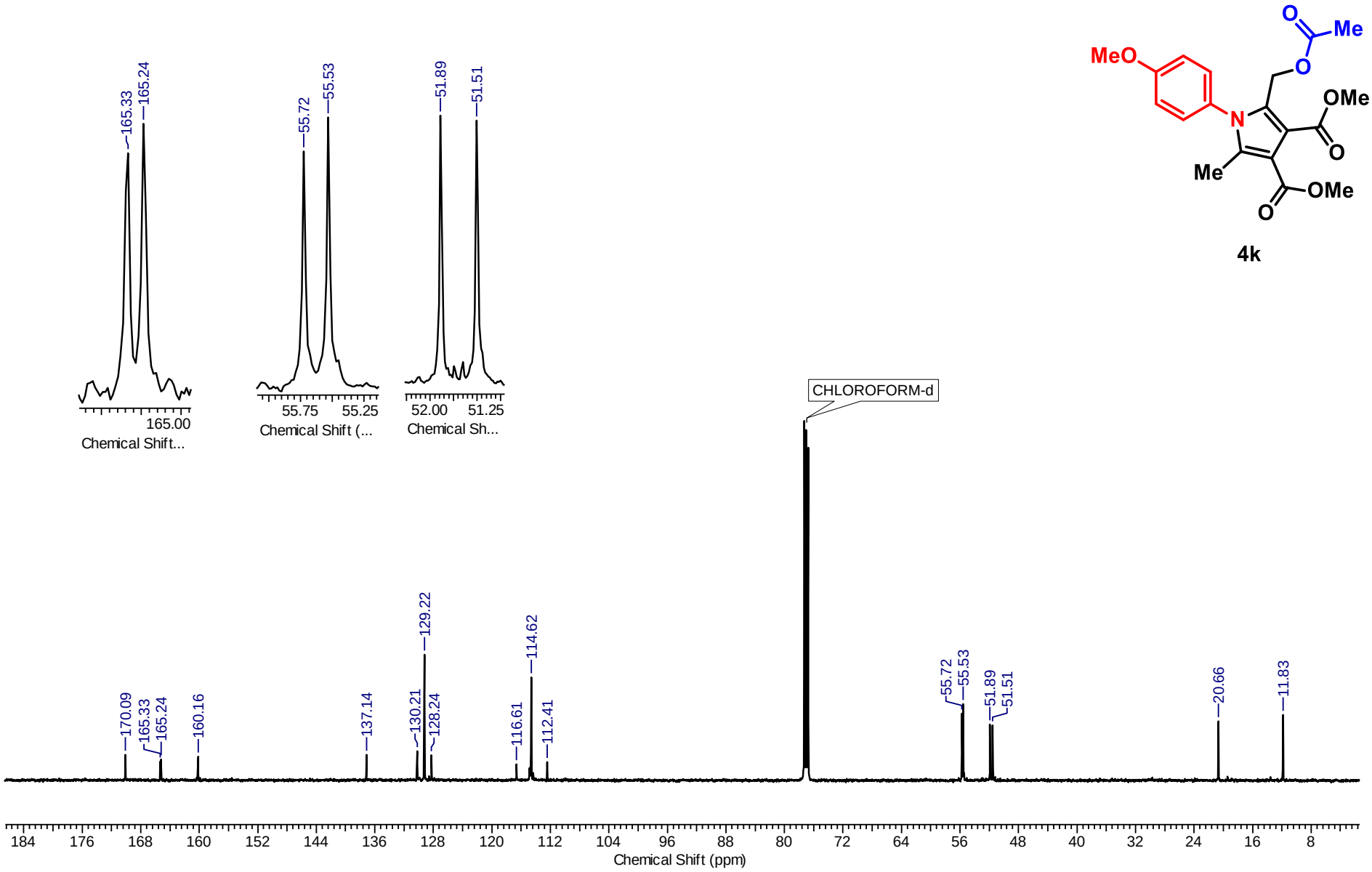

7.12
6.98
7.20
7.15
7.10
7.05
7.00
6.95
6.90
Chemical Shift (ppm)

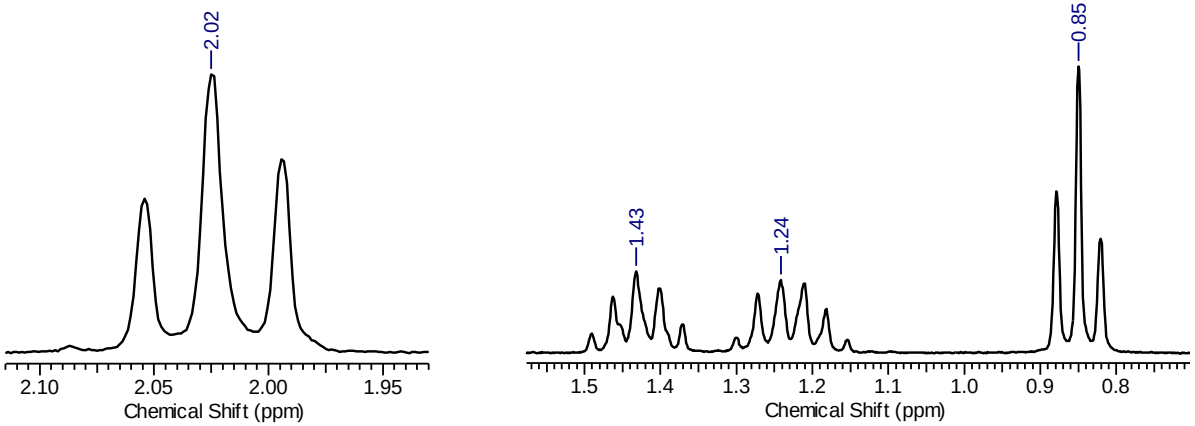

3.88
3.87
3.85
3.95
3.90
3.85
3.80
3.75
Chemical Shift (ppm)

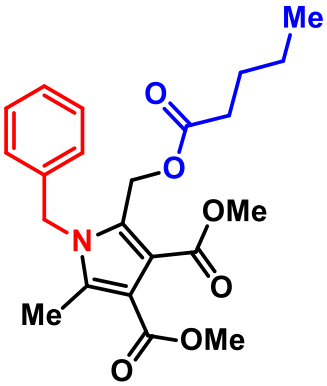

MeO
O
Me
O
N
OMe
O
Me
OMe
O

4k

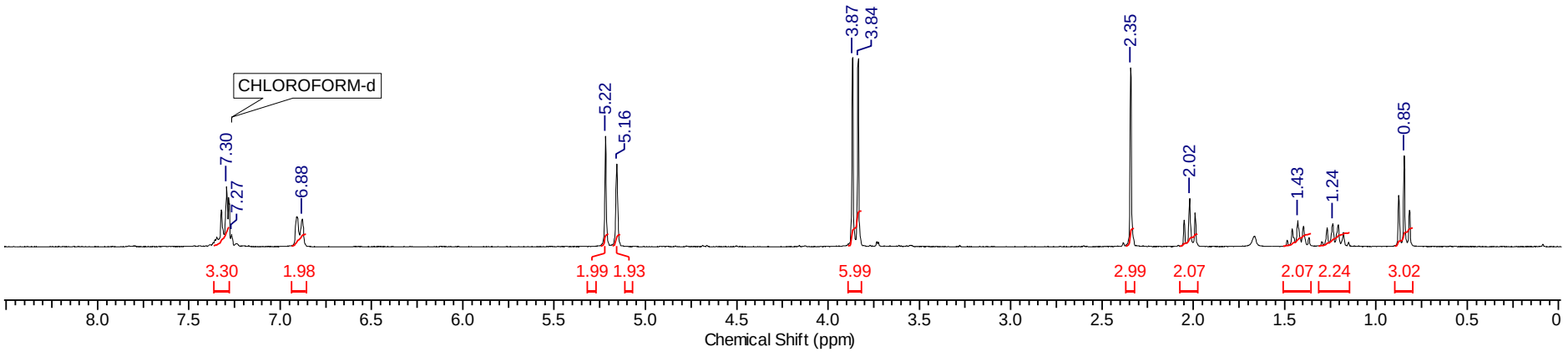

CHLOROFORM-d
7.27
7.12
6.98
4.95
3.88
3.85
2.18
1.94
2.02
2.05
1.93
9.25
2.86
2.80
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

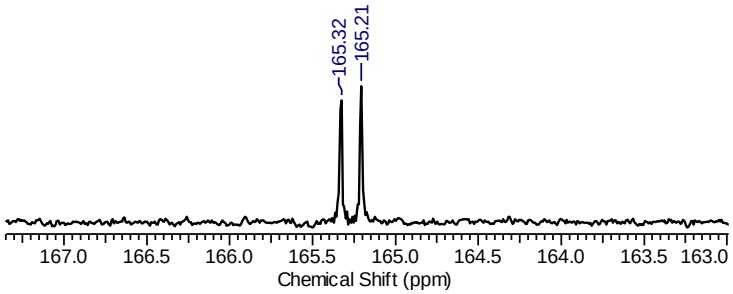

MeO
O
Me
O
OMe
N
Me
O
OMe
O
4k
165.33
165.24
55.72
55.53
51.89
51.51
165.00
Chemical Shift...
55.75
55.25
Chemical Shift (...
52.00
51.25
Chemical Sh...
CHLOROFORM-d
170.09
165.33
165.24
160.16
137.14
130.21
129.22
128.24
116.61
114.62
112.41
55.72
55.53
51.89
51.51
20.66
11.83
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

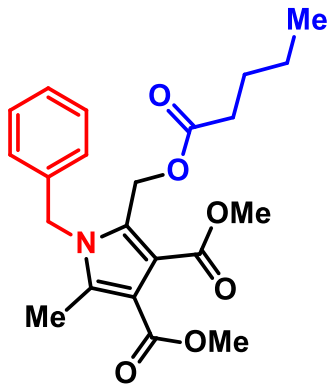

2.02
1.43
1.24
0.85
2.10
2.05
2.00
1.95
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
Chemical Shift (ppm)
Chemical Shift (ppm)


Me
O
O
OMe
N
O
Me
OMe
O

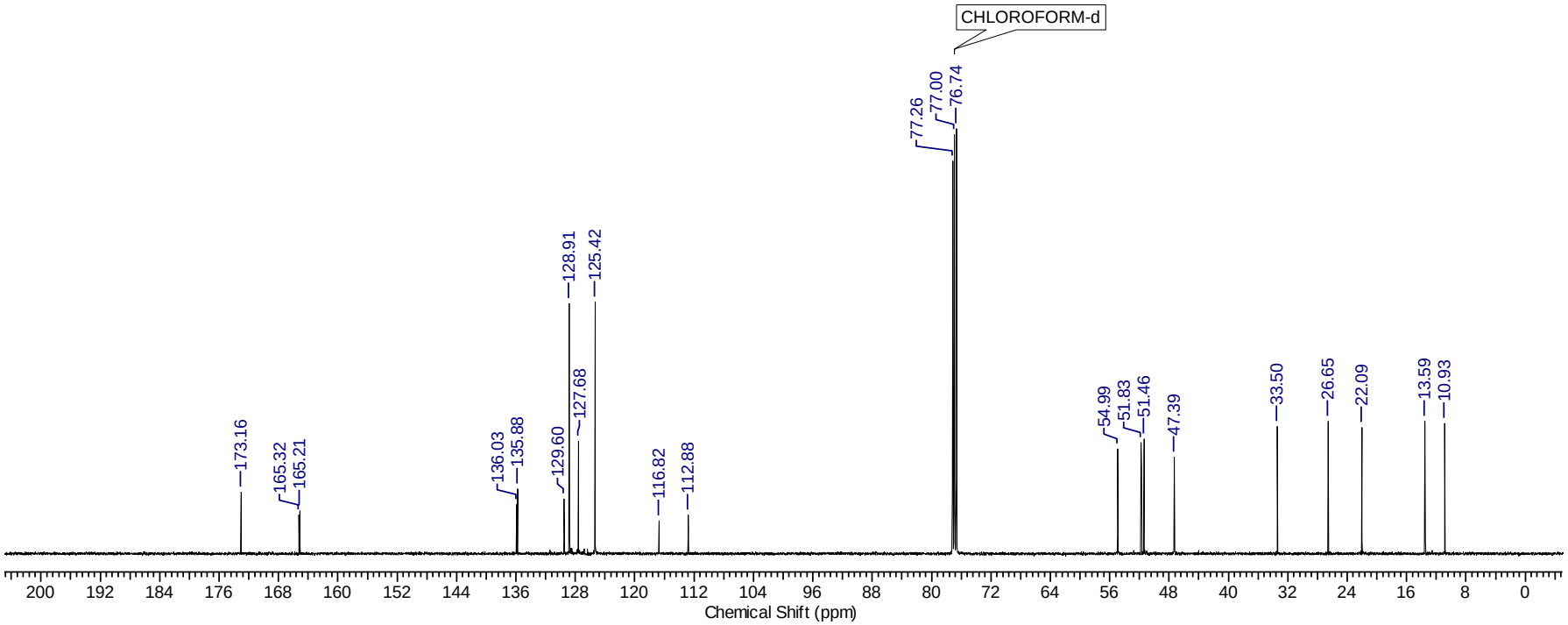
4l

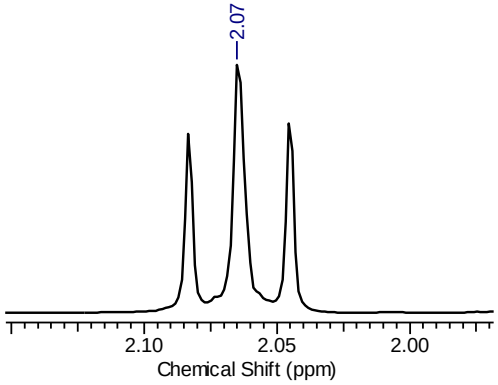

CHLOROFORM-d
7.30
7.27
6.88
5.22
5.16
3.87
3.84
2.35
2.02
1.43
1.24
0.85
3.30
1.98
1.99
1.93
5.99
2.99
2.07
2.07
2.24
3.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

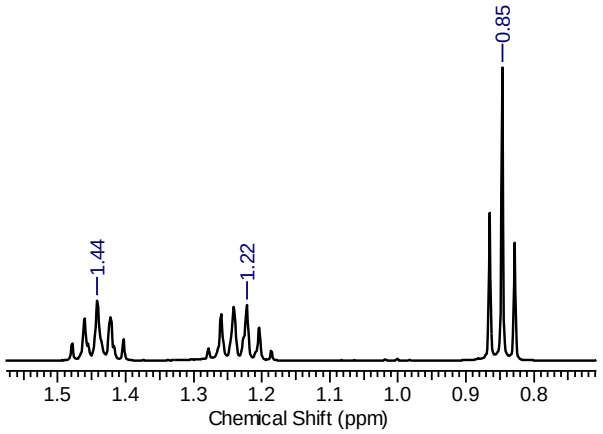

165.32
165.21
167.0
166.5
166.0
165.5
165.0
164.5
164.0
163.5
163.0
Chemical Shift (ppm)

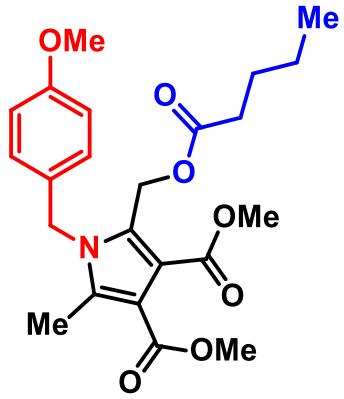

Me
O
O
OMe
N
O
Me
OMe
O

4l

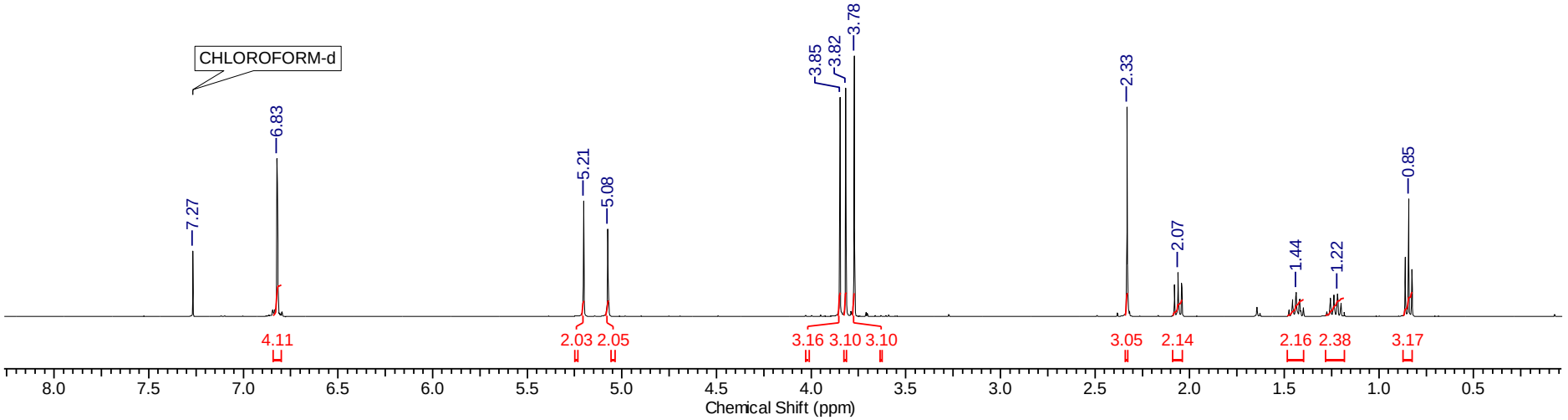

CHLOROFORM-d
77.26
77.00
76.74
173.16
165.32
165.21
136.03
135.88
129.60
128.91
127.68
125.42
116.82
112.88
54.99
51.83
51.46
47.39
33.50
26.65
22.09
13.59
10.93
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

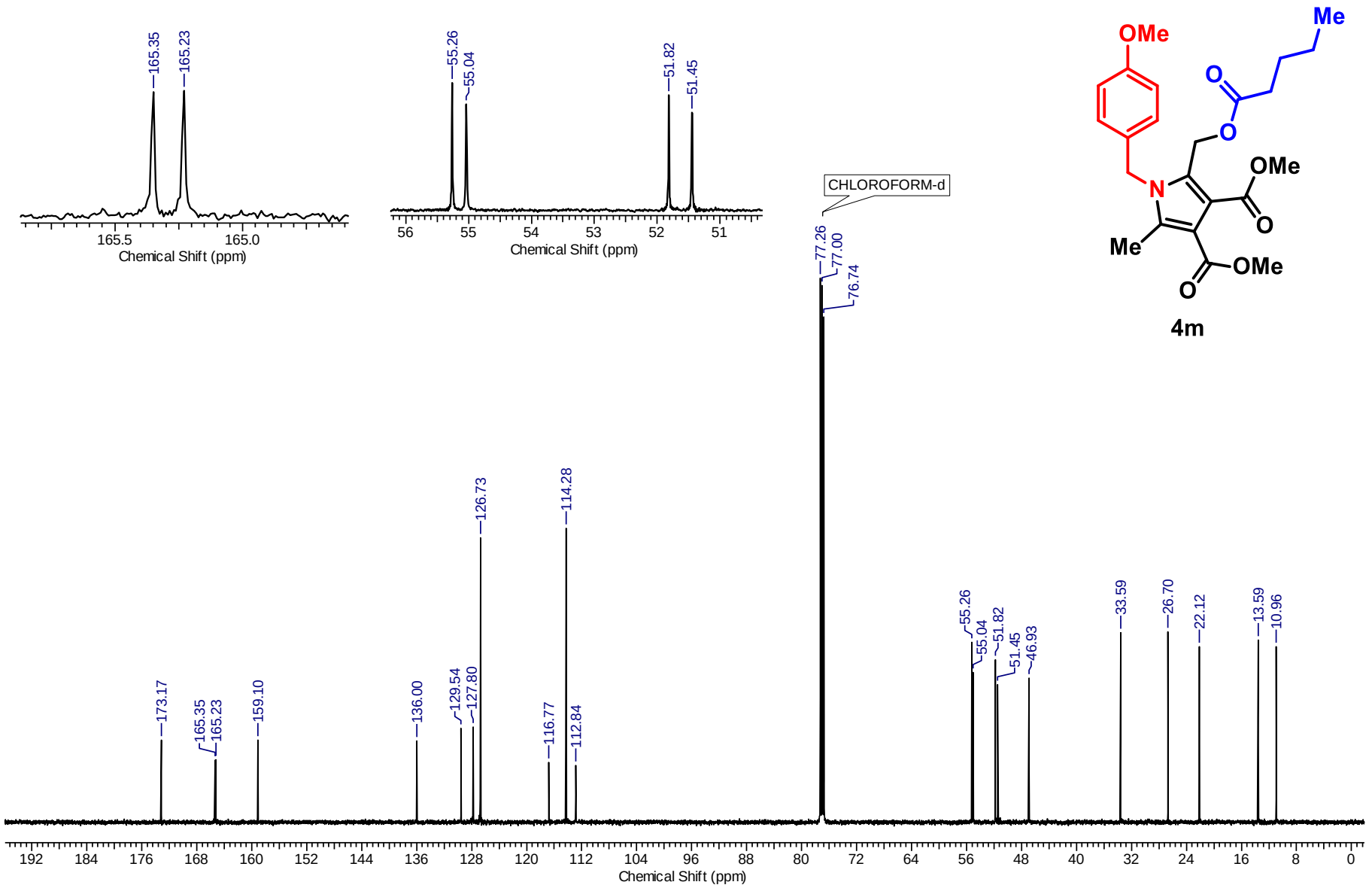

2.07
2.10
2.05
2.00
Chemical Shift (ppm)

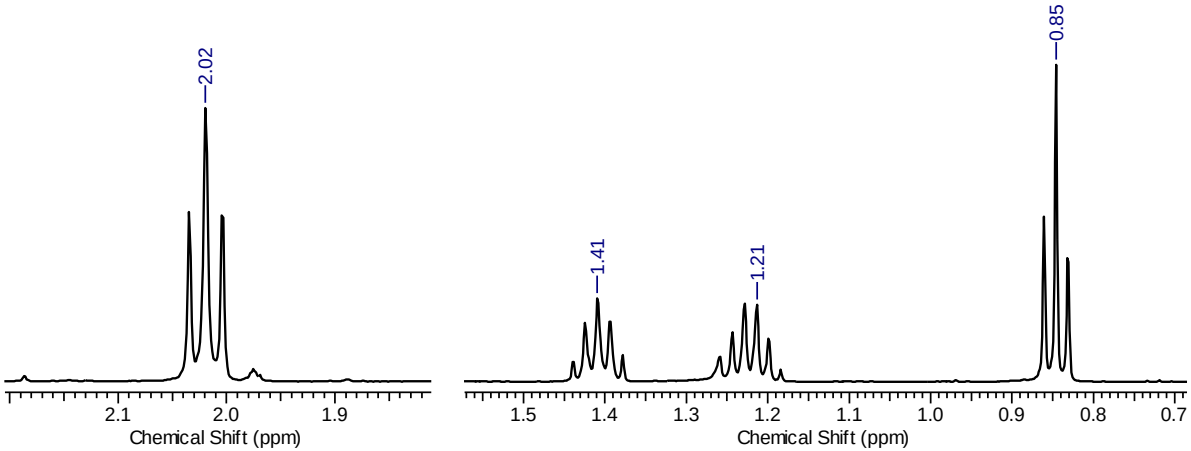

0.85
1.44
1.22
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
Chemical Shift (ppm)

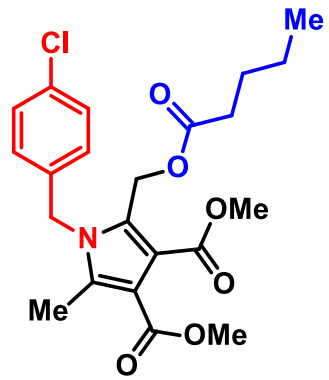

OMe
Me
O
O
OMe
N
O
Me
OMe
O

4m

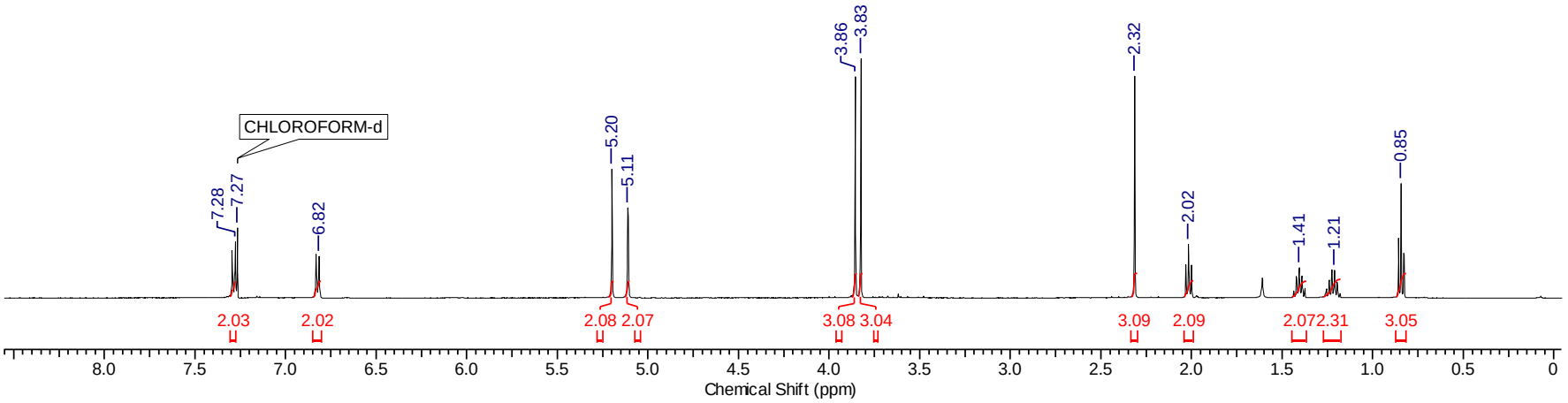

CHLOROFORM-d
7.27
6.83
5.21
5.08
3.85
3.82
3.78
2.33
2.07
1.44
1.22
0.85
4.11
2.03
2.05
3.16
3.10
3.10
3.05
2.14
2.16
2.38
3.17
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

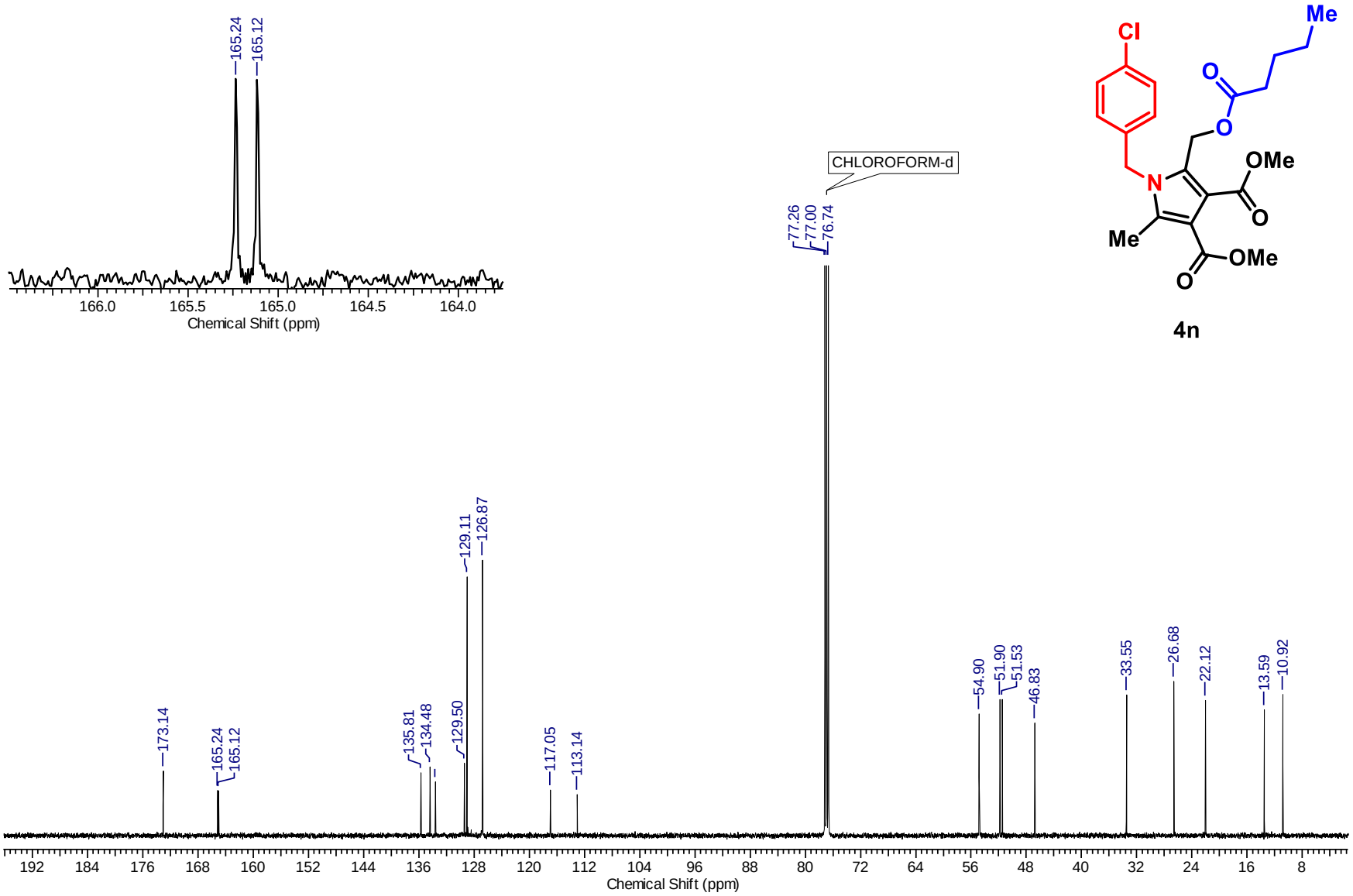

165.35
165.23
165.5
165.0
Chemical Shift (ppm)
55.26
55.04
51.82
51.45
56
55
54
53
52
51
Chemical Shift (ppm)
CHLOROFORM-d
77.26
77.00
76.74
OMe
Me
O
O
OMe
N
Me
O
OMe
O
4m
173.17
165.35
165.23
159.10
136.00
129.54
127.80
126.73
116.77
114.28
112.84
55.26
55.04
51.82
51.45
46.93
33.59
26.70
22.12
13.59
10.96
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

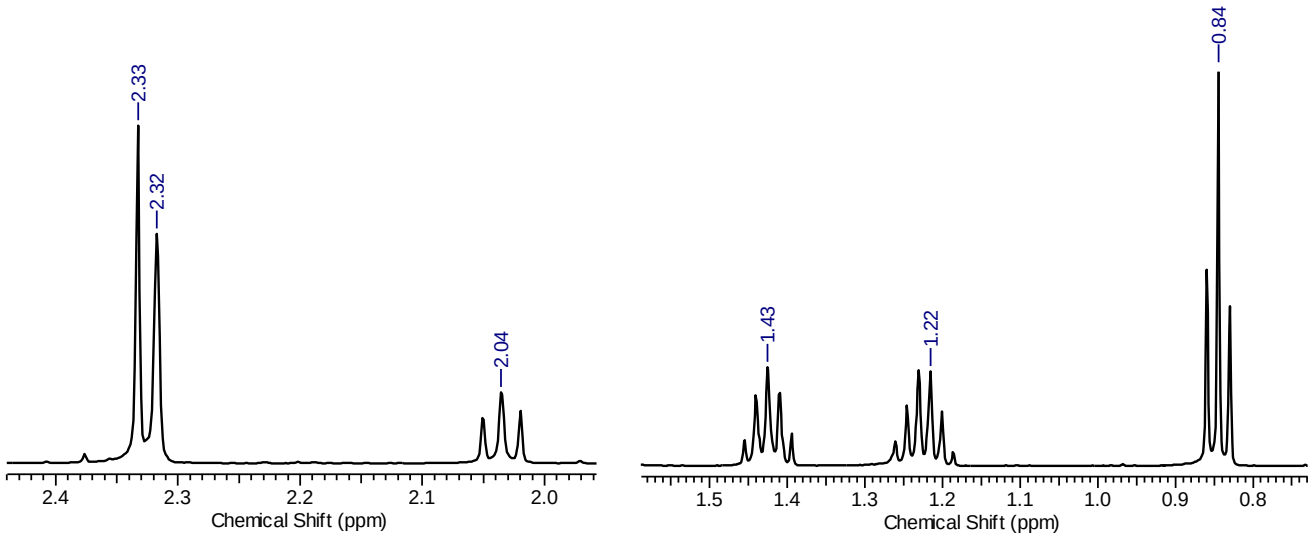

2.02
1.41
1.21
0.85
Chemical Shift (ppm)
Chemical Shift (ppm)

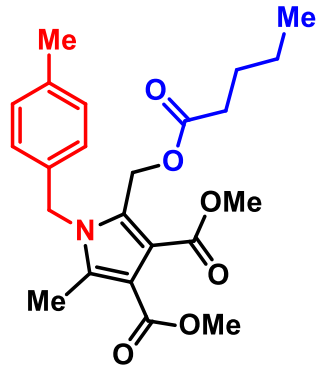

Cl
Me
O
O
N
OMe
O
Me
OMe
O

4n

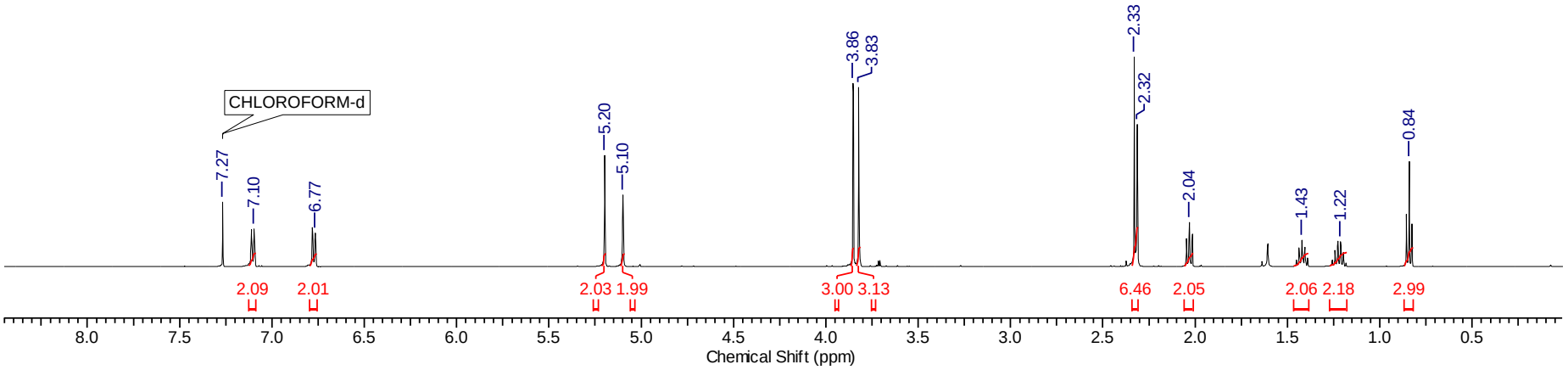

CHLOROFORM-d
7.28
7.27
6.82
5.20
5.11
3.86
3.83
2.32
2.02
1.41
1.21
0.85
2.03
2.02
2.08
2.07
3.08
3.04
3.09
2.09
2.07
2.31
3.05
Chemical Shift (ppm)

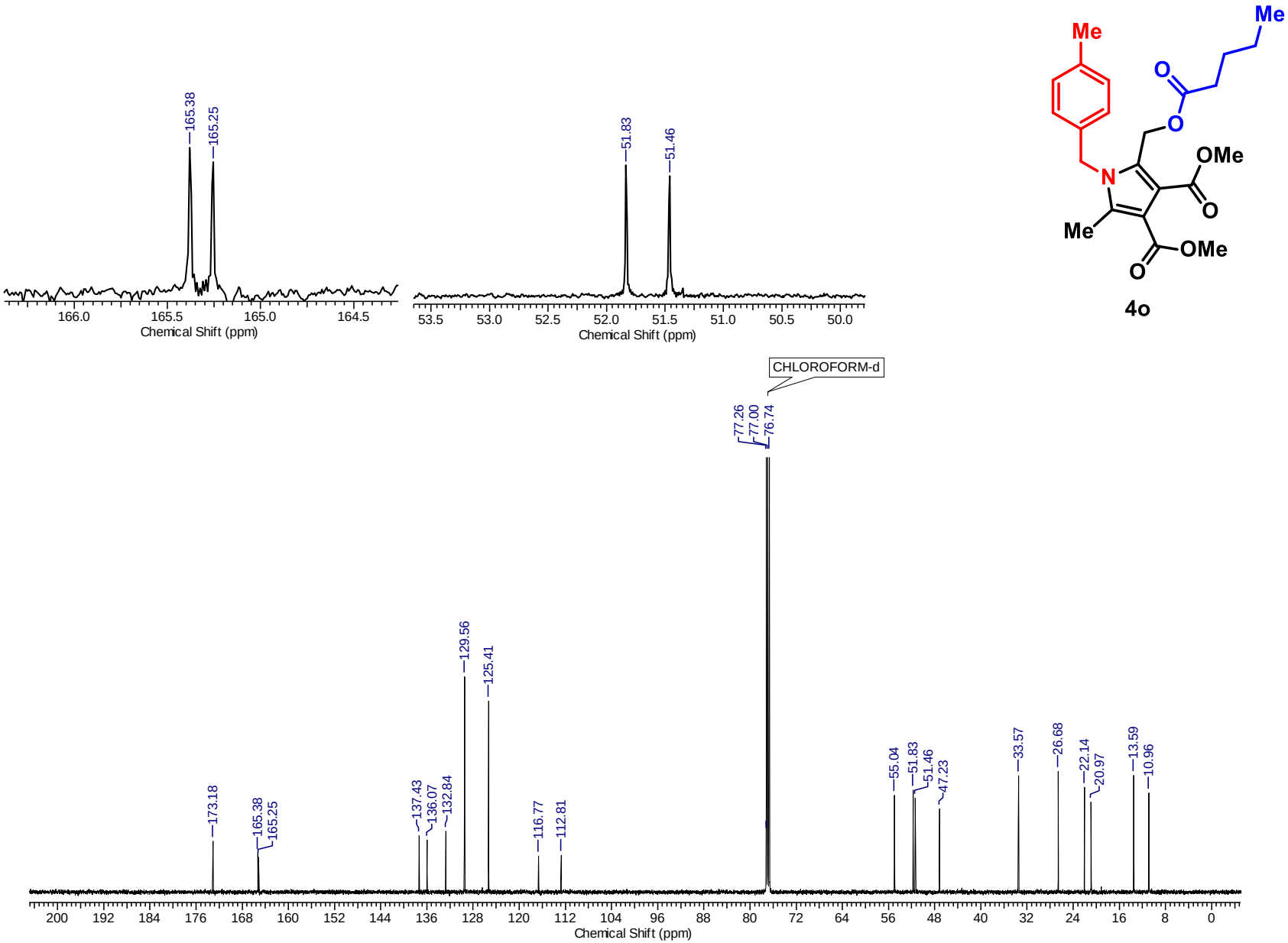

165.24
165.12
166.0
165.5
165.0
164.5
164.0
Chemical Shift (ppm)
CHLOROFORM-d
77.26
77.00
76.74
Cl
Me
O
O
N
OMe
O
Me
OMe
O
4n
173.14
165.24
165.12
135.81
134.48
129.50
129.11
126.87
117.05
113.14
54.90
51.90
51.53
46.83
33.55
26.68
22.12
13.59
10.92
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

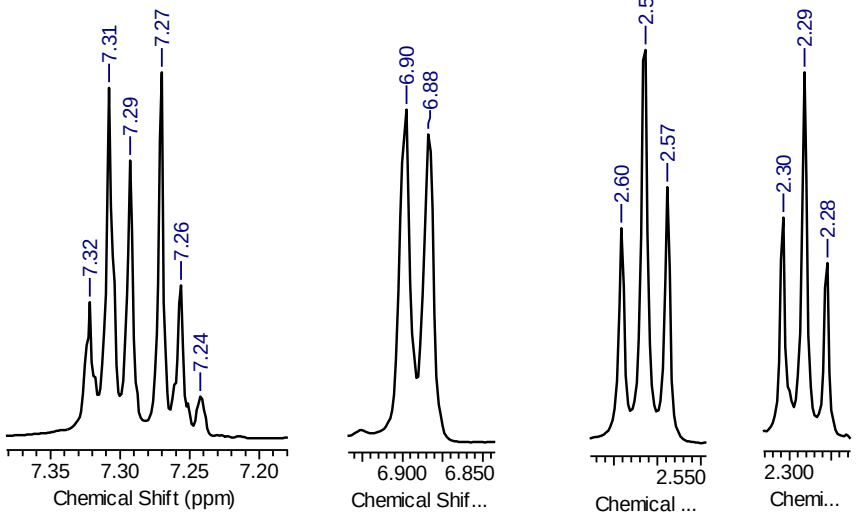

2.33
2.32
2.04
0.84
1.43
1.22
Chemical Shift (ppm)
Chemical Shift (ppm)

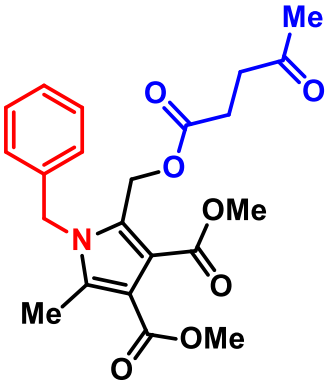

Me
Me
O
O
N
OMe
O
Me
OMe
O

4o

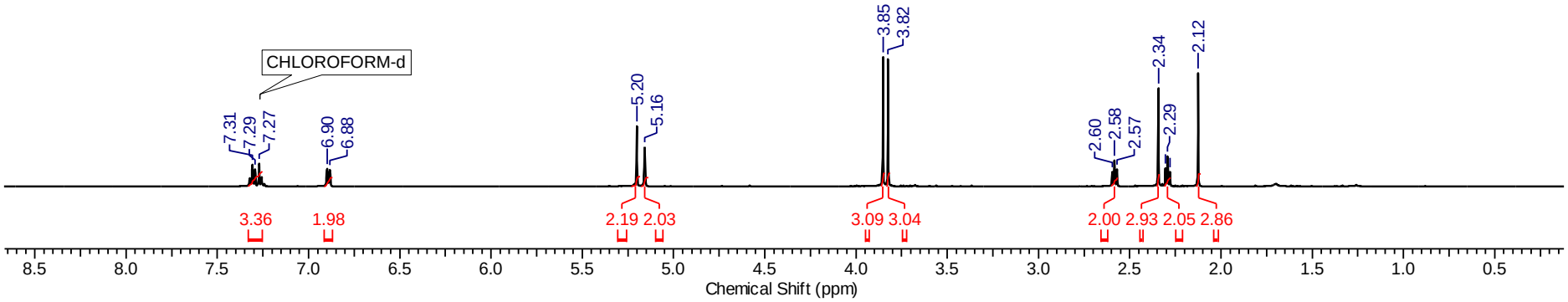

CHLOROFORM-d
7.27
7.10
6.77
5.20
5.10
3.86
3.83
2.33
2.32
2.04
1.43
1.22
0.84
2.09
2.01
2.03
1.99
3.00
3.13
6.46
2.05
2.06
2.18
2.99
Chemical Shift (ppm)

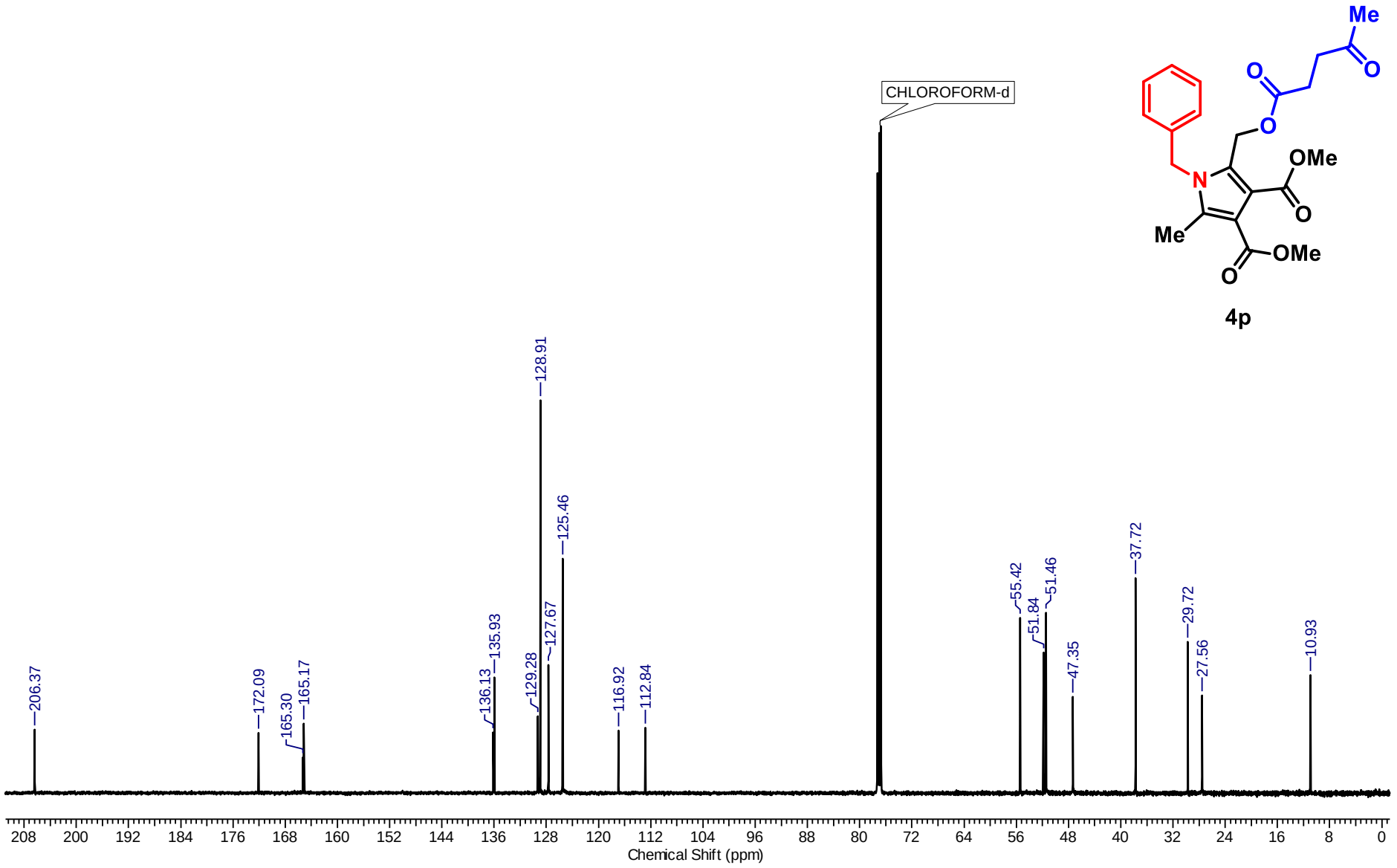

Me
Me
O
O
OMe
O
N
Me
OMe
O
4o
165.38
165.25
51.83
51.46
166.0
165.5
165.0
164.5
53.5
53.0
52.5
52.0
51.5
51.0
50.5
50.0
Chemical Shift (ppm)
CHLOROFORM-d
77.26
77.00
76.74
173.18
165.38
165.25
137.43
136.07
132.84
129.56
125.41
116.77
112.81
55.04
51.83
51.46
47.23
33.57
26.68
22.14
20.97
13.59
10.96
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


7.32
7.31
7.29
7.27
7.26
7.24
7.35 7.30 7.25 7.20
Chemical Shift (ppm)
6.90
6.88
6.900 6.850
Chemical Shif...
2.60
2.58
2.57
2.550
Chemical ...
2.30
2.29
2.28
2.300
Chemi...

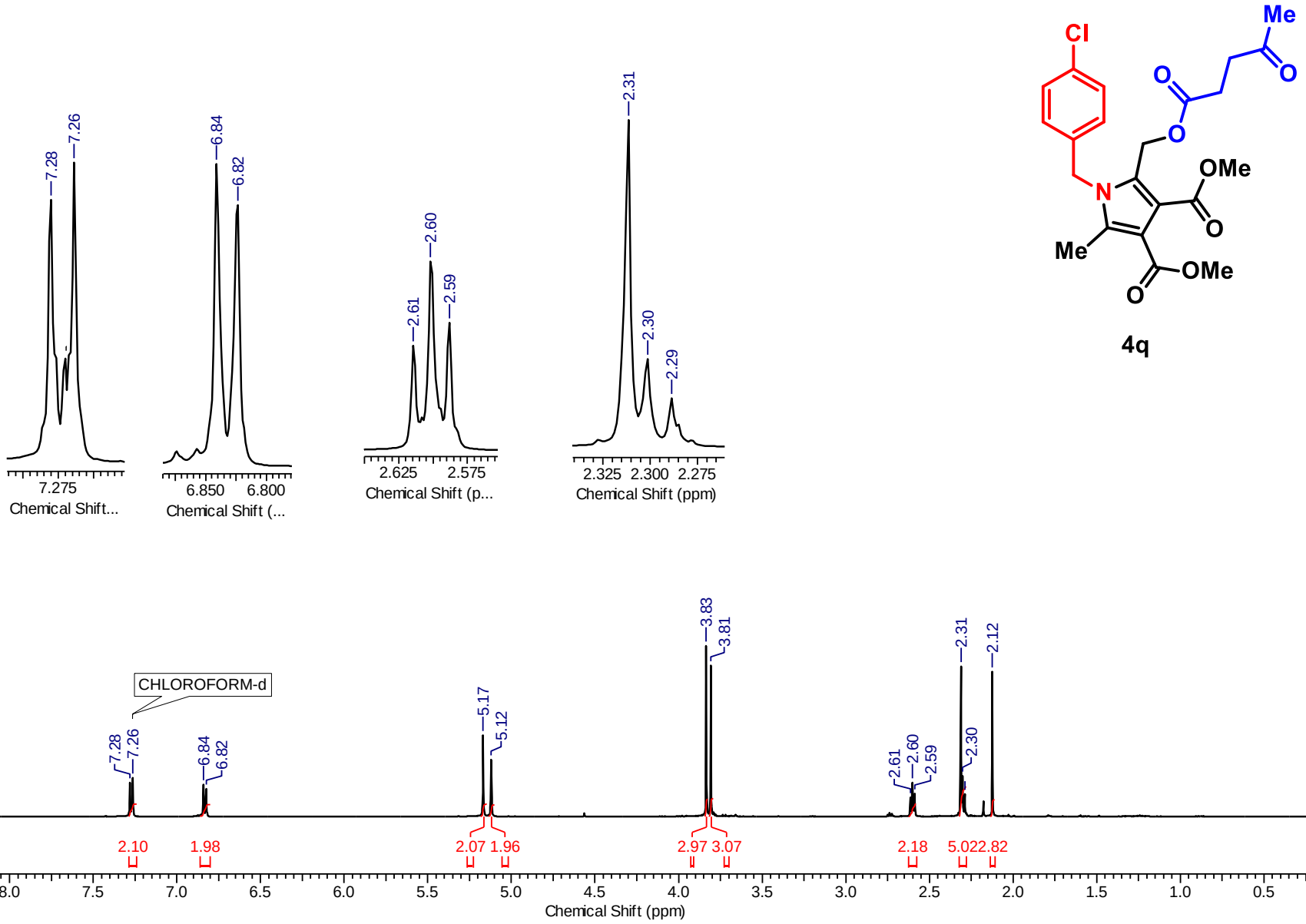

Me
O
O
O
OMe
N
O
Me
OMe
O

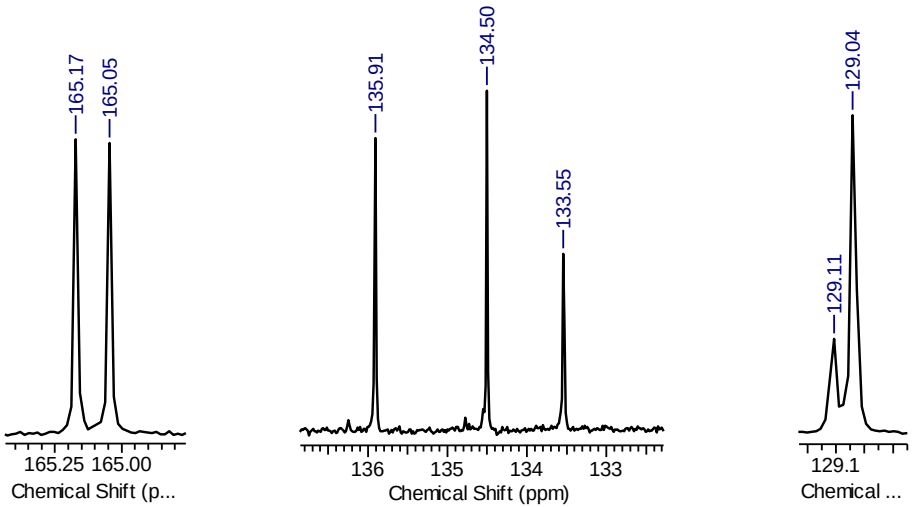
4p

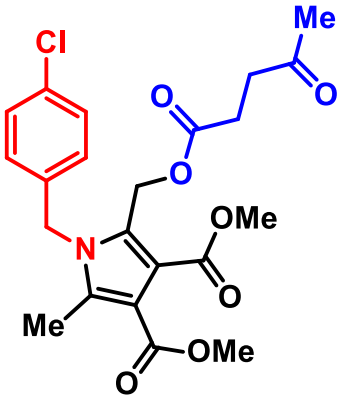

CHLOROFORM-d
7.31
7.29
7.27
6.90
6.88
5.20
5.16
3.85
3.82
2.60
2.58
2.57
2.34
2.29
2.12
3.36
1.98
2.19 2.03
3.09 3.04
2.00 2.93 2.05 2.86
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)


CHLOROFORM-d
206.37
172.09
165.30
165.17
136.13
135.93
129.28
128.91
127.67
125.46
116.92
112.84
55.42
51.84
51.46
47.35
37.72
29.72
27.56
10.93
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)
Me
O
O
O
N
OMe
O
Me
O
OMe

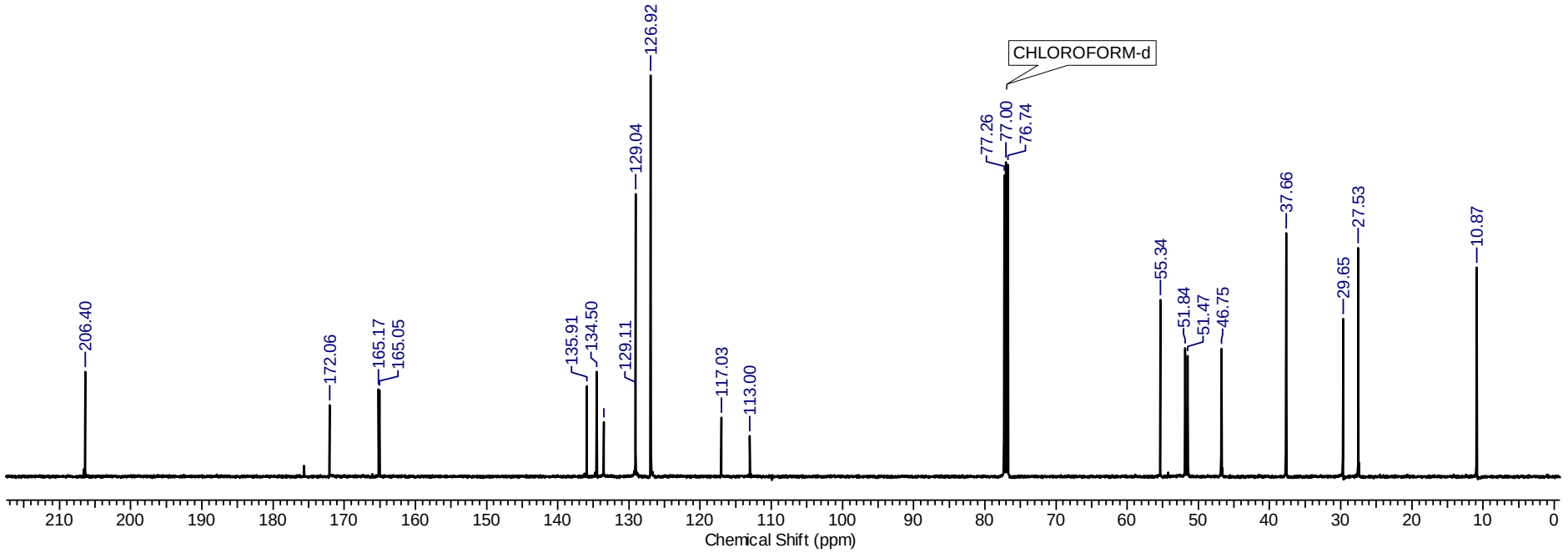
4p

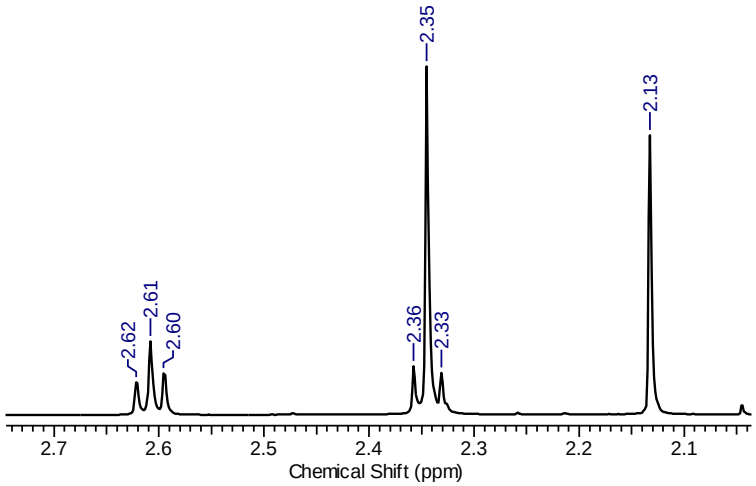

7.28
7.26
6.84
6.82
2.61
2.60
2.59
2.31
2.30
2.29
Chemical Shift...
Chemical Shift (...
Chemical Shift (p...
Chemical Shift (ppm)
Cl
Me
O
O
O
OMe
N
Me
O
OMe
O
4q
CHLOROFORM-d
5.17
5.12
3.83
3.81
2.12
2.10
1.98
2.07
1.96
2.97
3.07
2.18
5.02
2.82
Chemical Shift (ppm)

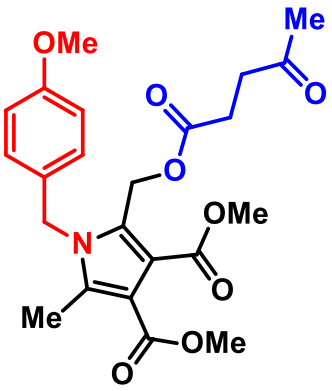

165.17
165.05
165.25 165.00
Chemical Shift (p...
135.91
134.50
133.55
136 135 134 133
Chemical Shift (ppm)
129.04
129.11
129.1
Chemical ...


Cl
Me
O
O
O
OMe
N
O
Me
O
OMe

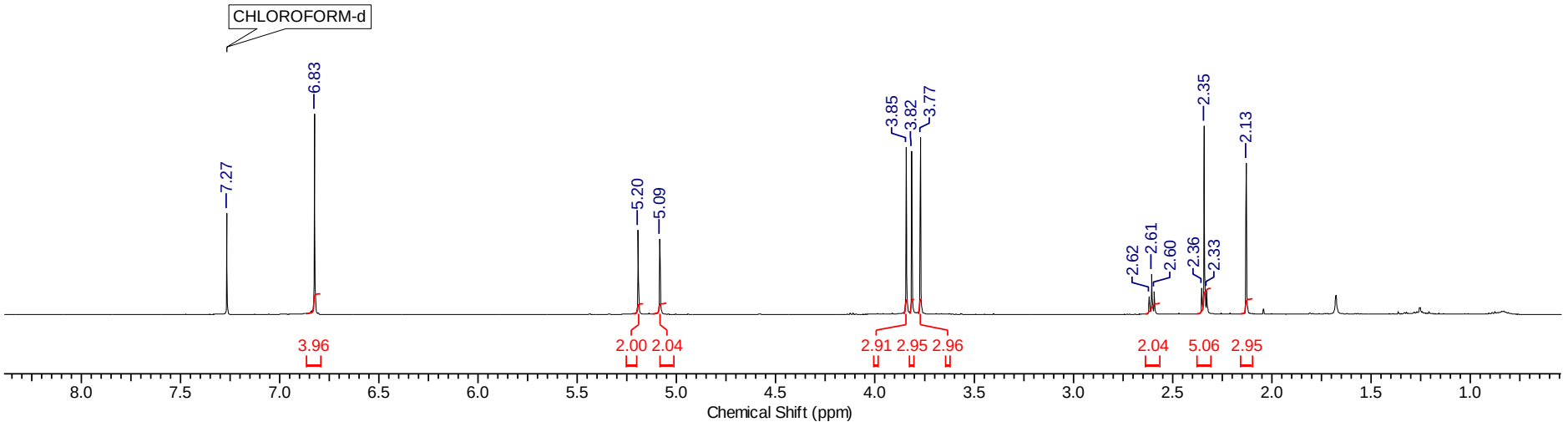
4q

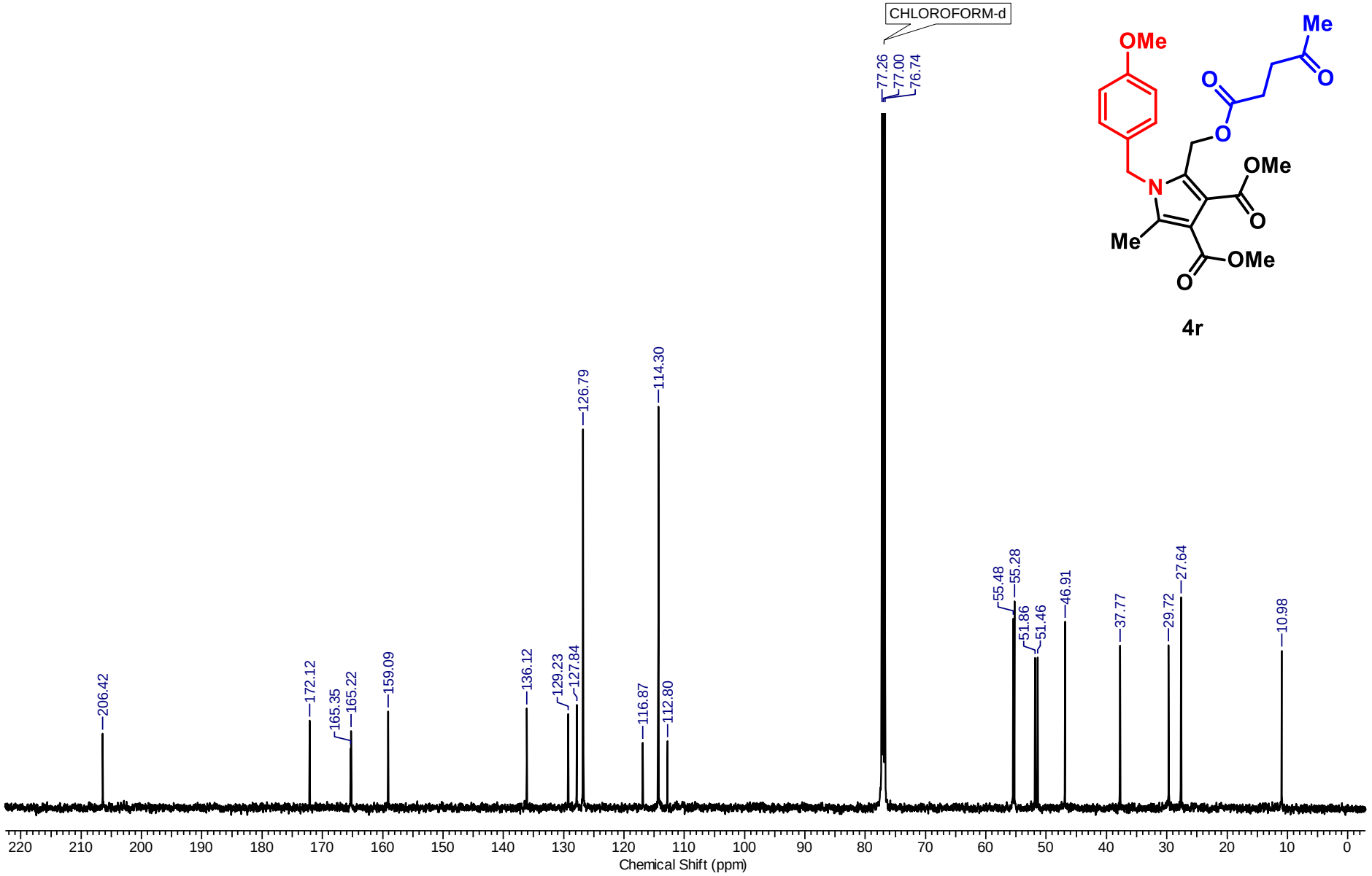

206.40
172.06
165.17
165.05
135.91
134.50
129.11
129.04
126.92
117.03
113.00
CHLOROFORM-d
77.26
77.00
76.74
55.34
51.84
51.47
46.75
37.66
29.65
27.53
10.87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


2.62
2.61
2.60
2.36
2.33
2.35
2.13
2.7
2.6
2.5
2.4
2.3
2.2
2.1
Chemical Shift (ppm)


OMe
Me
O
O
O
N
OMe
O
Me
OMe
O

4r


CHLOROFORM-d
7.27
6.83
5.20
5.09
3.85
3.82
3.77
2.62
2.61
2.60
2.36
2.33
2.35
2.13
3.96
2.00
2.04
2.91
2.95
2.96
2.04
5.06
2.95
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


CHLOROFORM-d
77.26
77.00
76.74
206.42
172.12
165.35
165.22
159.09
136.12
129.23
127.84
126.79
116.87
114.30
112.80
55.48
55.28
51.86
51.46
46.91
37.77
29.72
27.64
10.98
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)
OMe
Me
O
O
O
N
OMe
O
Me
OMe
O

4r