Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Antimicrobial Peptide-Inspired NH125 Analogues: Bacterial and Fungal Biofilm-Eradicating Agents and Rapid Killers of MRSA Persisters

Akash Basak,[a] Yasmeen Abouelhassan,[b] Ran Zuo,[b] Hussain Yousaf,[b] Yousong Ding,[b] Robert W. Huigens III[a,b*]

[a]*Department of Chemistry, University of Florida, Gainesville, Florida 32610;* [b]*Department of Medicinal Chemistry, College of Pharmacy, University of Florida, Gainesville, Florida 32610.*

*Corresponding Author: rhuigens@cop.ufl.edu

Supporting Information

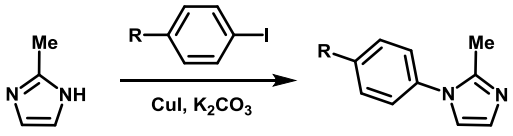
1.) General Information:

All reactions were carried out under an atmosphere of argon using anhydrous solvents unless otherwise specified. All chemical reagents for synthesis were used without further purification. Analytical thin layer chromatography (TLC) was performed using 250 μm Silica Gel 60 F254 pre-coated plates (EMD Chemicals Inc.). Flash column chromatography was performed using 230-400 Mesh 60Å Silica Gel from Sorbent Technologies.

NMR experiments were recorded using broadband probes on a Varian Mercury-Plus-400 spectrometer via VNMR-J software (400 MHz for ^{1}H and 100 MHz for ^{13}C). All spectra are presented using MestReNova (Mnova) software and ^{1}H NMR are displayed without the use of the signal suppression function. Spectra were obtained in the following solvents (reference peaks also included for ^{1}H and ^{13}C NMRs): $CDCl_3$ (^{1}H NMR: 7.26 ppm; ^{13}C NMR: 77.23 ppm) and d_6-DMSO (^{1}H NMR: 2.50 ppm; ^{13}C NMR: 39.52 ppm). All NMR experiments were performed at room temperature. Chemical shift values (δ) are reported in parts per million (ppm) for all ^{1}H NMR and ^{13}C NMR spectra. ^{1}H NMR multiplicities are reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. High-resolution mass spectra were obtained for all new compounds from the Chemistry Department at the University of Florida.

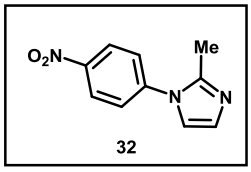
Bacterial strains used during these investigations included: methicillin-sensitive *Staphylococcus aureus* ATCC 29213, methicillin-resistant *Staphylococcus aureus* ATCC MRSA BAA-44 and MRSA BAA-1707, Clinical Isolates of *S. aureus*, including MRSA strains, from Shands Hospital, Gainesville, FL: MRSA-1, MRSA-2, SA-129, SA-138, SA-147, SA-156, methicillin-resistant *Staphylococcus epidermidis* (MRSE, ATCC 35984), vancomycin-resistant *Enterococcus faecium* (VRE, ATCC 700221), *Pseudomonas aeruginosa* (PAO1), multi-drug resistant *Acinetobacter baumannii* (ATCC 1794), *Klebsiella pneumoniae* (ATCC 13883) and *Escherichia coli* (UAEC-1; clinical isolate, University of Arkansas for Medical Sciences). DMSO stocks of compounds tested were stored at room temperature in the absence of light for several months at a time without observing a loss in biological activity. To ensure compound integrity of our DMSO stock solutions, we did not subject DMSO stocks to freeze-thaw cycles.

2.) Synthetic Procedures and Characterization Data:



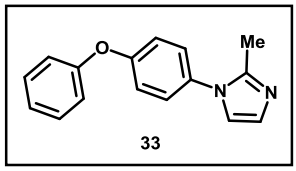
32-36

General Procedure for the *N*-arylation of 2-Methyl-1H-imidazole (Synthesis of 32-36): 1-Chloro-4-iodobenzene (726 mg, 3.04 mmol), copper(I) iodide (58 mg, 0.30 mmol) and anhydrous potassium carbonate (630 mg, 4.57 mmol) were sequentially added to a stirring solution of 2-methyl-1H-imidazole (250 mg, 3.04 mmol) in 5 mL anhydrous dimethyl sulfoxide in a glass tube under argon. The reaction tube was then sealed and stirred at 130 °C for 48 hours until the reaction was completed. The reaction mixture was then cooled to room temperature and transferred to a separatory funnel containing ethyl acetate (100 mL). The organic layer was then washed using water (3 x 30 mL) then brine (2 x 30 mL) before the organic layer was collected, dried with anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was then purified via flash column chromatography using hexanes:ethyl acetate (2:1 to 1:2) to elute pure **35** as a clear oil.



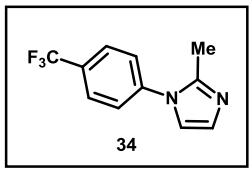
32

Yield: 45% yield; 285 mg of **32** was isolated as yellow solid.
Note: 32 is a known compound. Our NMR spectra and melting point matched those previously reported for this compound.[1]
MP: 142-143 °C, lit. 140-141 °C.[1]



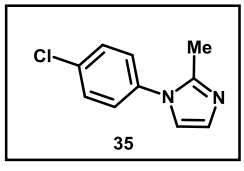
33

Yield: 40% yield; 240 mg of **33** was isolated as a clear oil.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 - 7.36 (m, 2H), 7.24 (m, 1H), 7.22 (m, 1H), 7.18 (m, 1H), 7.09 - 7.05 (m, 4H), 7.02 (d, *J* = 1.4 Hz, 1H), 6.98 (d, *J* = 1.4 Hz, 1H), 2.35 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 156.5, 145.1, 133.0, 130.2, 127.9, 127.2, 124.3, 121.0, 119.7, 119.1, 13.9.
HRMS (ESI): calc. for $C_{16}H_{15}N_2O$ **$[M+H]^+$**: 251.1179, found: 251.1168.



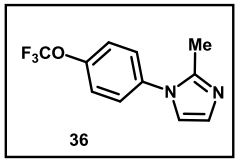
34

Yield: 38% yield; 210 mg of **34** was isolated as a clear oil.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.15 - 6.88 (m, 2H), 2.36 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 141.1, 130.4 (q, *J* = 33.0 Hz), 128.4, 126.9 (q, *J* = 3.7 Hz), 125.8, 123.7 (q, *J* = 272.3 Hz), 120.6, 14.0.
HRMS (ESI) m/z: calc. for $C_{11}H_{10}F_3N_2$ **$[M+H^+]$**: 227.0791, found: 227.0784.
Note: 34 is a known compound[2]; however, we could not locate NMR data following a literature search.



35

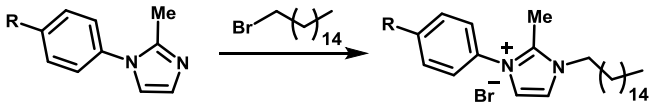
Yield: 45% yield; 260 mg of **35** was isolated.
Note: 35 is a known compound (CAS No. 132026-81-4). Our NMR spectra match those previously reported for this compound.[3]



36

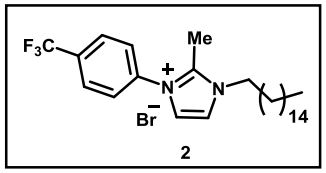
Yield: 36% yield; 160 mg of **36** was isolated as a clear oil.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 - 7.28 (m, 4H), 7.00 (d, *J* = 1.3 Hz, 1H), 6.96 (dd, *J* = 1.4, 0.5 Hz, 1H), 2.33 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7 (q, *J* = 1.8 Hz), 144.8, 136.6, 128.2, 127.1, 122.1 (d, *J* = 1.2 Hz), 120.7, 120.5 (q, *J* = 258.1 Hz), 13.9.

HRMS (ESI) m/z: calc. for $C_{11}H_{10}F_3N_2O$ **[M+H$^+$]**: 243.0740, found: 243.0737.



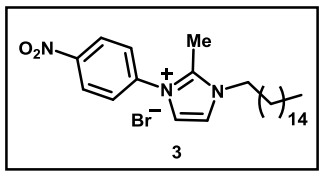
1-7

General Procedure for Alkylation Reactions to Generate Analogues 1-7: 1-Bromohexadecane (0.29 mL, 0.93 mmol) was added to a stirring solution of 1-(4-chlorophenyl)-2-methyl-1H-imidazole **35** (120 mg, 0.62 mmol) in 5 mL anhydrous acetonitrile in a glass tube at room temperature. The reaction mixture was then sealed and heated to 110 °C and allowed to stir for 24 hours. After this time, the reaction mixture was allowed to cool to room temperature before acetonitrile was evaporated *in vacuo*. The resulting crude product was then stirred in anhydrous ether under argon for 5 hours and resulting white precipitate, which was filtered under an argon environment. The resulting precipitate was washed with cold anhydrous ether and dried under vacuum to obtain **6** as a white solid (170 mg, 53%).



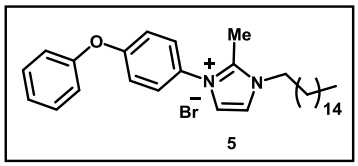
2

Yield: 51% yield; 180 mg of **2** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 2.1 Hz, 1H), 7.47 (d, *J* = 2.1 Hz, 1H), 4.29 (t, *J* = 7.7 Hz, 2H), 2.77 (s, 3H), 1.98 - 1.88 (m, 2H), 1.41 - 1.12 (m, 26H), 0.86 (t, *J* = 6.8 Hz, 3H).
13C NMR (100 MHz, CDCl3): δ 144.6, 137.4 (d, *J* = 1.8 Hz), 132.9 (q, *J* = 33.3 Hz), 127.5 (q, *J* = 3.7 Hz), 127.3, 123.2 (q, *J* = 272.9 Hz), 122.5, 122.3, 49.6, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.4, 29.1, 26.6, 22.7, 14.1, 12.2. **Note**: 23 of the 25 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{27}H_{42}F_3N_2$ **[M$^+$]**: 451.3295, found: 451.3303.
MP: 78-79 °C.



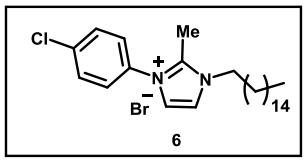
3

Yield: 88% yield; 330 mg of **3** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 8.39 (m, 2H), 8.10 (m, 2H), 7.73 (d, *J* = 2.2 Hz, 1H), 7.65 (d, *J* = 2.2 Hz, 1H), 4.25 (t, *J* = 7.8 Hz, 2H), 2.78 (s, 3H), 1.92 (p, *J* = 7.7 Hz, 2H), 1.49 - 1.14 (m, 26H), 0.84 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 148.9, 145.0, 139.4, 128.3, 125.7, 122.6, 122.4, 49.7, 32.0, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.2, 26.7, 22.8, 14.3, 12.5. **Note**: 21 of the 24 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{26}H_{42}N_3O_2$ **[M$^+$]**: 428.3272, found: 428.3256.
MP: 87-88 °C.



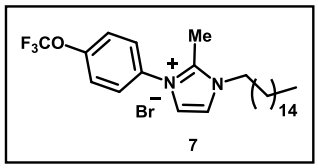
5

Yield: 60% yield; 220 mg of **5** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.70 (d, *J* = 2.1 Hz, 1H), 7.60 (m, 2H), 7.39 (m, 2H), 7.34 (d, *J* = 2.1 Hz, 1H), 7.19 (tt, *J* = 7.5 Hz, 1.1 Hz, 1H), 7.12 - 7.02 (m, 4H), 4.32 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H), 1.98 - 1.85 (m, 2H), 1.41 - 1.12 (m, 26H), 0.85 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 160.0, 155.5, 144.9, 130.4, 128.9, 128.1, 125.0, 122.6, 122.1, 120.2, 119.1, 49.7, 32.1, 29.9, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.5, 29.3, 26.7, 22.9, 14.3, 12.2. **Note**: 26 of the 28 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{32}H_{47}N_2O$ **[M$^+$]**: 475.3683, found: 475.3686.
MP: 66-67 °C.



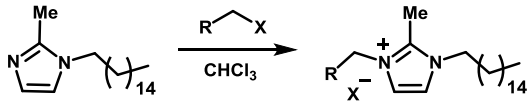
6

Yield: 53% yield; 170 mg of **6** was isolated as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.6, Hz, 2H), 7.64 (m, 1H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.39 (m, 1H), 4.28 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H), 1.92 (p, *J* = 7.8 Hz, 2H), 1.45 - 1.18 (m, 26 H), 0.86 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 137.4, 133.2, 130.7, 128.1, 122.4, 122.1, 49.8, 32.1, 29.9, 29.9, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.3, 26.8, 22.9, 14.3, 12.4. **Note**: 23 of the 24 ^{13}C NMR signals could be found, likely due to signal overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{26}H_{42}ClN_2$ **[M^+]**: 417.3031, found: 417.3037.
MP: 65-66 °C.



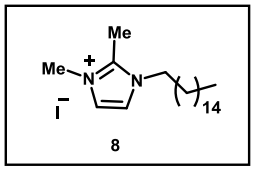
7

Yield: 60% yield; 220 mg of **7** was isolated as a pale white solid.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 2.1 Hz, 1H), 7.42 (d, *J* = 2.1 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 4.26 (t, *J* = 7.7 Hz, 2H), 2.73 (s, 3H), 1.97 - 1.86 (m, 2H), 1.41 - 1.12 (m, 26 H), 0.85 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7 (q, *J* = 1.9 Hz), 145.1, 132.9, 128.6, 122.5 (d, *J* = 0.8 Hz), 122.5, 122.3, 120.4 (q, *J* = 259.3 Hz), 49.7, 32.1, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.3, 26.7, 22.8, 14.3, 12.3. **Note**: 22 of the 25 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{27}H_{42}F_3N_2O$ **[M^+]**: 467.3244, found: 467.3240.
MP: 42-43 °C.



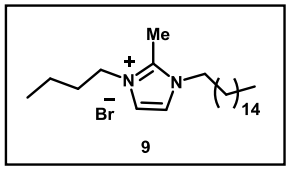
23 8-21

General Procedure for Alkylation of 23 to Generate Analogues 8-21: 3-Bromoprop-1-ene (42 µL, 0.49 mmol) was added to a stirring solution of **23** (100 mg, 0.33 mmol) in 5 mL anhydrous chloroform in a glass tube at room temperature. The reaction tube was then sealed and heated at 90 °C for 24 hours while the reaction occurred. Upon completion of the reaction, the solution was allowed to cool to room temperature and chloroform was then evaporated *in vacuo*. The crude product was then stirred in anhydrous ether under argon for 3 hours and the resulting white precipitate was filtered in an argon environment. The resulting precipitate was then washed with anhydrous ether and dried under vacuum to obtain pure **10** as a white solid (112 mg, 80%).



8

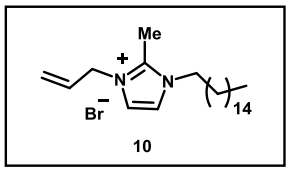
Yield: 82% yield; 120 mg of **8** was isolated as a white solid.
^{1}H NMR (400 MHz, *d_6*-DMSO): δ 7.65 (d, *J* = 2.1 Hz, 1H), 7.61 (d, *J* = 2.1 Hz, 1H), 4.09 (dt, *J* = 7.3, 2.5 Hz, 2H), 3.74 (s, 3H), 2.57 (s, 3H), 1.69 (p, *J* = 7.1 Hz, 2H), 1.32 - 1.15 (m, 26H), 0.85 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (100 MHz, *d_6*-DMSO): δ 144.2, 122.3, 120.9, 47.5, 34.8, 31.3, 29.2, 29.1, 29.0, 29.0, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.3. **Note**: 17 of the 21 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{21}H_{41}N_2$ **[M^+]**: 321.3264, found: 321.3258.
MP: 72-73 °C.



9

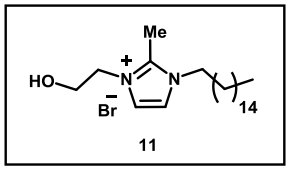
Yield: 32% yield; 46 mg of **9** was isolated as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 2.1 Hz, 1H), 7.54 (d, *J* = 2.1 Hz, 1H), 4.25 (t, *J* = 7.4 Hz, 2H), 4.22 (t, *J* = 7.5 Hz, 2H), 2.77 (s, 3H), 1.92 - 1.68 (m, 4H), 1.42 - 1.08 (m, 28H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.83 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 121.9, 121.7, 49.2, 49.0, 32.0, 31.9, 30.0, 29.8,

29.8, 29.7, 29.6, 29.5, 29.5, 29.2, 26.5, 22.8, 19.7, 14.2, 13.7, 11.1. **Note**: 21 of the 24 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{24}H_{47}N_2$ **[M$^+$]**: 363.3734, found: 363.3745.
MP: 68-69 °C.



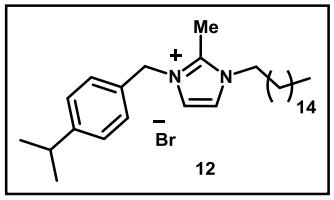
10

Yield: 80% yield; 112 mg of **10** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.74 (d, *J* = 2.1 Hz, 1H), 7.66 (d, *J* = 2.1 Hz, 1H), 6.03 (m, 1H), 5.30 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.11 (dd, *J* = 17.2, 1.4 Hz, 1H), 4.82 (dt, *J* = 5.5, 1.7 Hz, 2H), 4.11 (t, *J* = 7.4 Hz, 2H), 2.58 (s, 3H), 1.71 (p, *J* = 8.0 Hz, 2H), 1.32 - 1.16 (m, 26H), 0.85 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 144.0, 131.6, 121.5, 121.4, 118.8, 49.6, 47.6, 31.3, 29.1, 29.0, 29.0, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.2. **Note**: 18 of the 23 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{23}H_{43}N_2$ **[M$^+$]**: 347.3421, found: 347.3423.
MP: 82-83 °C.



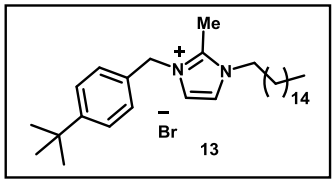
11

Yield: 69% yield; 195 mg of **11** was isolated as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 2.1 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 4.89 (t, *J* = 6.8 Hz, 1H), 4.37 (t, *J* = 4.8 Hz, 2H), 4.08 (t, *J* = 7.6 Hz, 2H), 3.91 (q, *J* = 5.4 Hz, 2H), 2.77 (s, 3H), 1.81 (p, *J* = 7.2 Hz, 2H), 1.43 - 1.13 (m, 26H), 0.85 (t, *J* = 6.6 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 122.6, 121.0, 60.4, 51.8, 49.1, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.2, 26.6, 22.8, 14.3, 11.4. **Note**: 18 of the 22 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{22}H_{43}N_2O$ **[M$^+$]**: 351.3370, found: 351.3380.
MP: 58-59 °C.



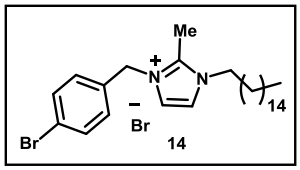
12

Yield: 71% yield; 180 mg of **12** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.81 - 7.72 (m, 2H), 7.31 - 7.21 (m, 4H), 5.37 (m, 2H), 4.11 (t, *J* = 7.5 Hz, 2H), 2.88 (septet, *J* = 7.0 Hz, 1H), 2.63 (s, 3H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.31 - 1.12 (m, 26H), 1.18 (d, *J* = 6.9 Hz, 6H), 0.85 (t, *J* = 6.6 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 148.7, 143.9, 132.0, 127.8, 126.8, 121.6, 121.5, 50.4, 47.6, 33.1, 31.3, 29.0, 29.0, 28.9, 28.9, 28.8, 28.7, 28.4, 25.6, 23.7, 22.1, 13.9, 9.5. **Note**: 23 of the 27 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{30}H_{51}N_2$ **[M$^+$]**: 439.4047, found: 439.4051.
MP: 72-73 °C.



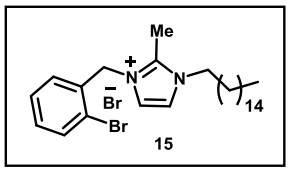
13

Yield: 69% yield; 195 mg of **13** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.77 (d, *J* = 2.1 Hz, 1H), 7.75 (d, *J* = 2.1 Hz, 1H), 7.42 (dt, *J* = 8.4, 2.5, 2H), 7.25 (dt, *J* = 8.3, 2.0 Hz, 2H), 5.38 (s, 2H), 4.10 (t, *J* = 7.4 Hz, 2H), 2.63 (s, 3H), 1.76 - 1.66 (m, 2H), 1.26 (s, 9H), 1.26 - 1.18 (m, 26H), 0.85 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 151.0, 144.0, 131.7, 127.5, 125.7, 121.7, 121.6, 50.3, 47.6, 34.3, 31.3, 31.0, 29.1, 29.0, 29.0, 28.9, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.5. **Note**: 23 of the 27 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{31}H_{53}N_2$ **[M$^+$]**: 453.4203, found: 453.4188.
MP: 89-90 °C.



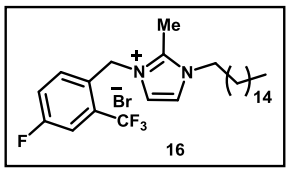
14

Yield: 51% yield; 92 mg of **14** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.73 (m, 2H), 7.62 (m, 2H), 7.29 (m, 2H), 5.39 (s, 2H), 4.09 (t, *J* = 7.4 Hz, 2H), 2.61 (s, 3H), 1.71 (p, *J* = 7.2 Hz, 2H), 1.33 - 1.16 (m, 26H), 0.85 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 144.2, 134.0, 131.9, 130.1, 121.8, 121.7, 121.6, 49.9, 47.7, 31.3, 29.1, 29.0, 28.9, 28.9, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.5. **Note**: 21 of the 25 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{27}H_{44}BrN_2$ **[M$^+$]**: 475.2682, found: 475.2690.
MP: 66-67 °C.



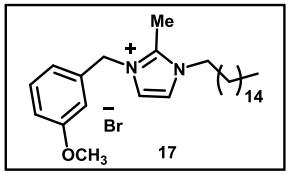
15

Yield: 31% yield; 55 mg of **15** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.78 (d, *J* = 2.2 Hz, 1H), 7.74 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.56 (d, *J* = 2.1 Hz, 1H), 7.44 (m, 1H), 7.36 (td, *J* = 7.7, 1.7 Hz, 1H), 7.08 (dd, *J* = 7.6, 1.7 Hz, 1H), 5.46 (s, 2H), 4.15 (t, *J* = 7.3 Hz, 2H), 2.63 (s, 3H), 1.74 (p, *J* = 7.4Hz, 2H), 1.44 - 1.14 (m, 26H), 0.85 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 144.7, 133.3, 133.2, 130.7, 129.5, 128.5, 122.5, 121.8, 121.6, 51.0, 47.7, 31.3, 29.0, 29.0, 28.9, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.6. **Note**: 22 of the 27 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{27}H_{44}BrN_2$ **[M$^+$]**: 475.2682, found: 475.2705.
MP: 64-65 °C.



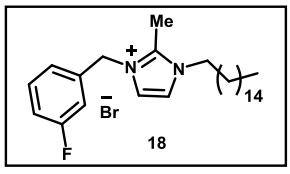
16

Yield: 76% yield; 210 mg of **16** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.82 (dd, *J* = 4.2, 2.7 Hz, 1H), 7.79 (d, *J* = 2.1 Hz, 1H), 7.61 (td, *J* = 8.5, 2.8 Hz, 1H), 7.54 (d, *J* = 2.1 Hz, 1H), 7.22 (dd, *J* = 8.8, 5.3 Hz, 1H), 5.56 (s, 2H), 4.15 (t, *J* = 7.3 Hz, 2H), 2.57 (s, 3H), 1.74 (p, *J* = 7.3 Hz, 2H), 1.36 - 1.15 (m, 26H), 0.85 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 161.5 (d, *J* = 248.1 Hz), 144.8, 132.3 (d, *J* = 8.5 Hz), 128.8 (td, *J* = 31.7, 7.9 Hz), 128.3, 124.5 (d, *J* = 2.5 Hz), 121.8 (d, *J* = 16.0 Hz), 120.3 (d, *J* = 21.0 Hz), 120.2 (q, *J* = 236.8 Hz), 114.6 (dq, *J* = 25.7, 5.8 Hz), 47.8, 47.3, 31.3, 29.1, 29.1, 29.0, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.6. **Note**: 23 of the 28 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{28}H_{43}F_4N_2$ **[M$^+$]**: 483.3357, found: 483.3355.
MP: 49-50 °C.



17

Yield: 36% yield; 60 mg of **17** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.79 - 7.73 (m, 2H), 7.33 (t, *J* = 7.9 Hz, 1H), 6.94 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.90 (m, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 5.37 (s, 2H), 4.10 (t, *J* = 7.4 Hz, 2H), 3.75 (s, 3H), 2.62 (s, 3H), 1.72 (p, *J* = 7.4 Hz, 2H), 1.34 - 1.14 (m, 26H), 0.85 (t, *J* = 6.6 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 159.6, 144.0, 135.9, 130.1, 121.7, 121.5, 119.6, 113.6, 113.6, 55.1, 50.5, 47.6, 31.2, 29.0, 28.9, 28.9, 28.8, 28.8, 28.6, 28.4, 25.6, 22.0, 13.9, 9.5. **Note:** 24 of the 28 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{28}H_{47}N_2O$ **[M$^+$]**: 427.3683, found: 427.3683.
MP: 61-62 °C.



18

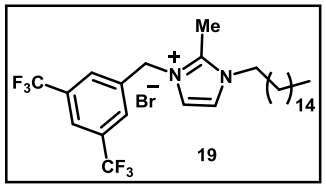
Yield: 59% yield; 190 mg of **18** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.78 (d, *J* = 2.1 Hz, 1H), 7.77 (d, *J* = 2.1 Hz, 1H), 7.50 - 7.11 (m, 4H), 5.44 (s, 2H), 4.10 (t, *J* = 7.4 Hz, 2H), 2.63 (s, 3H), 1.72 (p, *J* = 7.5 Hz, 2H), 1.32 - 1.17 (m, 26H), 0.83 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 162.3 (d, *J* = 244.5 Hz), 144.3, 137.3 (d, *J* = 7.6 Hz), 131.0 (d, *J* = 8.3 Hz), 123.9 (d, *J* = 2.9 Hz), 121.7, 115.4 (d, *J* = 20.8 Hz), 114.8 (d, *J* = 22.3 Hz), 49.9,

47.7, 31.3, 29.1, 29.0, 29.0, 28.9, 28.7, 28.5, 25.7, 22.1, 14.0, 9.6. **Note**: 21 of the 27 ^{13}C NMR signals could be found, one aromatic signal missing and multiple signals overlap at 29 ppm. All ^{13}C NMR signals were found in $CDCl_3$, which is reported below.

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1 (d, *J* = 248.5 Hz), 144.1, 135.7 (d, *J* = 7.4 Hz), 131.3 (d, *J* = 8.3 Hz), 124.3 (d, *J* = 3.1 Hz), 122.7, 121.4, 116.3 (d, *J* = 20.9 Hz), 115.4 (d, *J* = 22.3 Hz), 52.0 (d, *J* = 1.9 Hz), 49.2, 32.1, 30.0, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.2, 26.6, 22.9, 14.3, 11.6.

HRMS (ESI) m/z: calc. for $C_{27}H_{44}FN_2$ **[M$^+$]**: 415.3483, found: 415.3492.

MP: 64-65 °C.



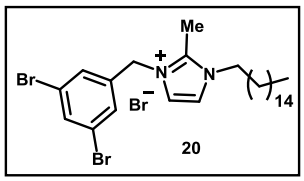
Yield: 37% yield; 75 mg of **19** was isolated as a white solid.

^{1}H NMR (400 MHz, *d*$_6$-DMSO): δ 8.17 (s, 1H), 8.10 (s, 2H), 7.81 (d, *J* = 2.1 Hz, 1H), 7.76 (d, *J* = 2.1 Hz, 1H), 5.58 (s, 2H), 4.10 (t, *J* = 7.4 Hz, 2H), 2.65 (s, 3H), 1.72 (p, *J* = 7.3 Hz, 2H), 1.32 - 1.18 (m, 26H), 0.85 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, *d*$_6$-DMSO): δ 144.8, 137.8, 130.7 (q, *J* = 33.1 Hz), 129.2 (br m), 123.1 (q, *J* = 272.9 Hz), 122.5 (septet, *J* = 3.7 Hz), 121.9, 121.5, 49.4, 47.7, 31.3, 29.0, 29.0, 28.9, 28.9, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.7. **Note**: 22 of the 26 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.

HRMS (ESI) m/z: calc. for $C_{29}H_{43}F_6N_2$ **[M$^+$]**: 533.3324, found: 533.3307.

MP: 54-55 °C.



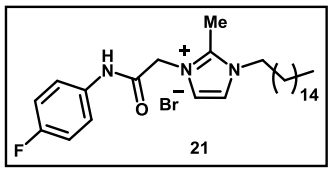
Yield: 42% yield; 130 mg of **20** was isolated as a white solid.

^{1}H NMR (400 MHz, *d*$_6$-DMSO): δ 7.86 (m, 1H), 7.80 (m, 1H), 7.77 (m, 1H), 7.63 (m, 2H), 5.43 (s, 2H), 4.10 (t, *J* = 7.4 Hz, 2H), 2.64 (s, 3H), 1.72 (p, *J* = 7.3 Hz, 2H), 1.47 - 1.09 (m, 26H), 0.85 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, *d*$_6$-DMSO): δ 144.6, 139.0, 133.5, 130.0, 122.9, 121.8, 121.5, 49.1, 47.7, 31.3, 29.1, 29.0, 29.0, 28.9, 28.9, 28.9, 28.7, 28.5, 25.6, 22.1, 14.0, 9.6. **Note**: 22 of the 25 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.

HRMS (ESI) m/z: calc. for $C_{27}H_{43}Br_2N_2$ **[M$^+$]**: 553.1788, found: 553.1796.

MP: 73-74 °C.



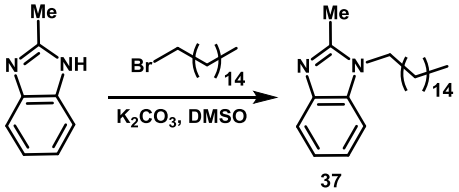
Yield: 69% yield; 195 mg of **21** was isolated as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.77 - 7.70 (m, 2H), 7.20 (d, *J* = 2.1 Hz, 1H), 6.97 - 6.87 (m, 2H), 5.57 (s, 2H), 4.05 (t, *J* = 7.5 Hz, 2H), 2.77 (s, 3H), 1.80 (p, *J* = 7.3 Hz, 2H), 1.40 - 1.17 (m, 26H), 0.86 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 159.6 (d, *J* = 243.5 Hz), 145.1, 134.2 (d, *J* = 2.9 Hz), 123.5, 121.9 (d, *J* = 7.8 Hz), 120.5, 115.5 (d, *J* = 22.4 Hz), 51.8, 49.2, 32.1, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.1, 26.5, 22.8, 14.3, 11.2. **Note:** 25 of the 26 ^{13}C NMR signals could be found, likely due to signal overlap at 29 ppm.

HRMS (ESI) m/z: calc. for $C_{28}H_{45}FN_3O$ **[M$^+$]**: 458.3541, found: 458.3562.

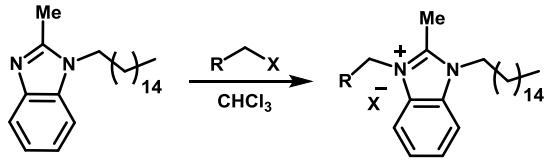
MP: 69-70 °C.



37

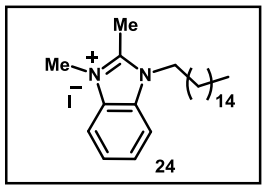
Synthesis of 37: 1-Bromohexadecane (0.50 mL, 1.65 mmol) was added via syringe to a stirring solution of 2-methyl-1H-benzimidazole (1.08 g, 8.20 mmol) and potassium carbonate (230 mg, 1.65 mmol) in 10 mL anhydrous dimethyl sulfoxide (DMSO). The resulting reaction mixture was heated to 110 °C and allowed to

stir for sixteen hours. After this time, the reaction mixture was transferred to a separatory funnel containing ethyl acetate (100 mL). The crude product was washed using water (3 x 30 mL), then brine (2 x 30 mL) before the organic layer was collected and dried with anhydrous sodium sulfate. The dried organic layer was then filtered and concentrated *in vacuo* to give crude product, which was purified via flash column chromatography using 1:1 hexanes:ethyl acetate to elute pure **37** as a clear oil which turned white semisolid upon standing (330 mg, 57%). **Note: 37** is a known compound (CAS No. 405152-04-7). ^{1}H NMR spectra match those previously reported.[4] We found the melting point for **37** to be 44-45 °C.

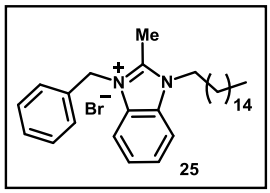


24-27

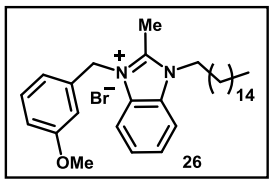
General Procedure for Alkylation of 1-Hexadecyl-2-methyl-1H-benzimidazole to Afford 24-27: Benzyl bromide (42 µL, 0.35 mmol) was added to a stirring solution of 1-hexadecyl-2-methyl-1H-benzimidazole (105 mg, 0.46 mmol) in 5 mL anhydrous chloroform in a glass tube at room temperature. The tube was then sealed and the reaction was heated to 90 °C and allowed to stir for 24 hours. After this time, the reaction mixture was allowed to cool to room temperature and chloroform was evaporated *in vacuo*. The crude product was then stirred in anhydrous ether under argon for 5 hours and resulting white precipitate was filtered in an argon environment. The resulting precipitate was washed with anhydrous ether and dried under vacuum to obtain pure **25** as a white solid (82 mg, 56%).



Yield: 64% yield; 121 mg of **24** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.75 (m, 1H), 7.67 - 7.55 (m, 3H), 4.45 (t, *J* = 7.6 Hz, 2H), 4.17 (s, 3H), 3.21 (s, 3H), 1.91 (p, *J* = 7.5 Hz, 2H), 1.48 - 1.15 (m, 26H), 0.87 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 151.0, 132.0, 131.2, 127.0, 126.9, 113.0, 112.5, 46.9, 33.9, 32.1, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.3, 27.0, 22.9, 14.3, 14.1.
HRMS (ESI) m/z: calc. for $C_{25}H_{43}N_2$ **[M$^+$]**: 371.3421, found: 371.3437.
MP: 67-68 °C.

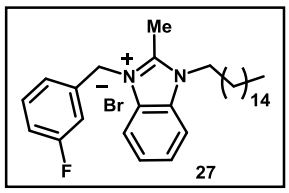


Yield: 56% yield; 82 mg of **25** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.70 (t, *J* = 2.2 Hz, 1H), 7.68 (t, *J* = 2.1 Hz, 1H), 7.63 - 7.53 (m, 2H), 7.40 - 7.31 (m, 3H), 7.30 - 7.24 (m, 2H), 5.95 (s, 2H), 4.54 (t, *J* = 7.6 Hz, 2H), 3.23 (s, 3H), 1.92 (p, *J* = 7.9 Hz, 2H), 1.47 - 1.18 (m, 26H), 0.88 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 151.5, 133.2, 131.7, 131.2, 129.5, 128.9, 127.2, 127.1, 126.9, 113.2, 112.8, 50.0, 46.8, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 29.2, 26.9, 22.8, 14.2, 13.3.
HRMS (ESI) m/z: calc. for $C_{31}H_{47}N_2$ **[M$^+$]**: 447.3734, found: 447.3747.
MP: 72-73 °C.

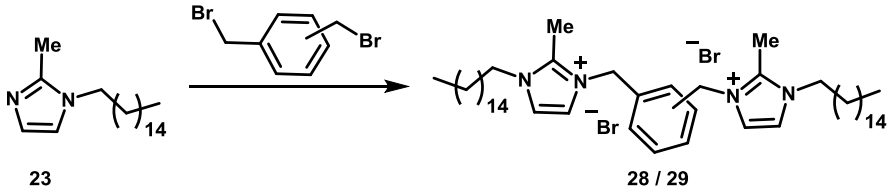


Yield: 31% yield; 48 mg of **26** was isolated as a white solid.
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.71 - 7.62 (m, 2H), 7.60 - 7.49 (m, 2H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 7.3 Hz, 1H), 6.80 (s, 1H), 6.74 (d, *J* = 7.7 Hz, 1H), 5.88 (s, 2H), 4.51 (t, *J* = 7.5 Hz, 2H), 3.75 (s, 3H), 3.18 (s, 3H), 1.88 (p, *J* = 7.8 Hz, 2H), 1.45 - 1.10 (m, 26H), 0.84 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 160.4, 151.6, 134.7, 131.8, 131.2, 130.7, 127.1, 126.9, 119.0, 114.1, 113.2, 113.1, 112.7, 55.7, 49.8, 46.8, 32.0, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 29.3, 26.9, 22.8, 14.3, 13.2. **Note**: 31 of the 32 ^{13}C NMR signals could be found, likely due to signal overlap at 29 ppm.

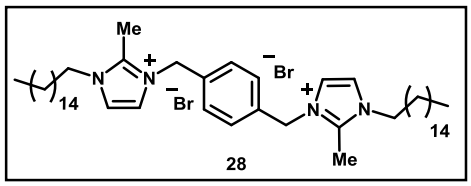
HRMS (ESI) m/z: calc. for $C_{32}H_{49}N_2O$ **[M$^+$]**: 477.3839, found: 477.3841.
MP: 66-67 °C.



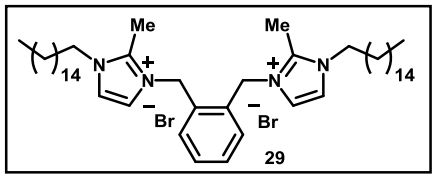
Yield: 33% yield; 51 mg of **27** was isolated as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 - 7.64 (m, 2H), 7.63 - 7.52 (m, 2H), 7.32 (m, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.00 (td, *J* = 8.4, 2.3 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 6.01 (s, 2H), 4.51 (t, *J* = 6.8 Hz, 2H), 3.22 (s, 3H), 1.91 (p, *J* = 6.8 Hz, 2H), 1.48 - 1.13 (m, 26H), 0.86 (t, *J* = 6.6 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2 (d, *J* = 248.6 Hz), 151.8 , 135.8, 135.7, 131.5 (d, *J* = 50.1 Hz), 131.4 (d, *J* = 8.5 Hz), 127.3, 127.1, 123.2 (d, *J* = 2.8 Hz), 116.1 (d, *J* = 21.0 Hz), 114.3, 114.1, 113.0 (d, *J* = 44.2 Hz), 49.6, 47.0, 32.1, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.3, 27.0, 22.9, 14.3, 13.6.
HRMS (ESI) m/z: calc. for $C_{31}H_{46}FN_2$ **[M$^+$]**: 465.3640, found: 465.3639.
MP: 64-65 °C.



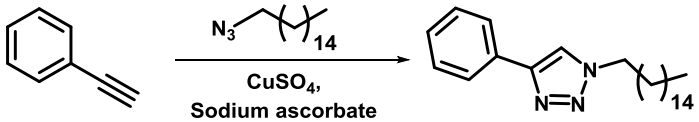
General Bis-benzylation Procedure for the Synthesis of Dimeric Analogues 28 and 29: 1,4-Bis(bromomethyl)benzene (51 mg, 0.195 mmol) was added to a stirring solution of **23** (120 mg, 0.39 mmol) in 50 mL anhydrous chloroform in a reaction tube at room temperature. The reaction tube was then sealed and heated at 120 °C for 24 hours. After that time, the reaction mixture was allowed to cool to room temperature before chloroform was evaporated *in vacuo*. The crude product was stirred in anhydrous ether under argon for 5 hours and resulting white precipitate was filtered in an argon environment. The white precipitate was washed with anhydrous ether and dried under vacuum to obtain compound pure **28** as a white solid (76 mg, 44%).



Yield: 44% yield; 76 mg of **28** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.75 (d, *J* = 2.2 Hz, 2H), 7.74 (d, *J* = 2.1 Hz, 2H), 7.35 (s, 4H), 5.42 (s, 4H), 4.09 (t, *J* = 7.5 Hz, 4H), 2.61 (s, 6H), 1.71 (p, *J* = 7.2 Hz, 4H), 1.33 - 1.16 (m, 52H), 0.85 (t, *J* = 6.6 Hz, 6H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 143.9, 134.5, 128.1, 121.4, 121.4, 78.9, 50.1, 47.6, 30.9, 28.7, 28.6, 28.6, 28.5, 28.3, 28.1, 25.4, 21.7, 13.5, 9.3. **Note**: 19 of the 24 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{48}H_{84}N_4$ **[M^{2+}]**: 358.3343, found: 358.3334.
MP: 81-82 °C.

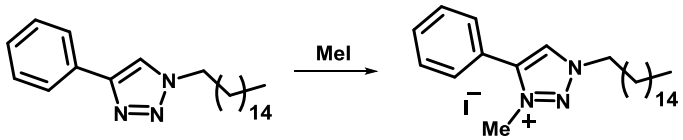


Yield: 72% yield; 123 mg of **29** was isolated as a white solid.
^{1}H NMR (400 MHz, d_6-DMSO): δ 7.82 (d, *J* = 2.1 Hz, 2H), 7.60 (d, *J* = 1.8 Hz, 2H), 7.39 (m, 2H), 6.85 (m, 2H), 5.63 (s, 4H), 4.17 (t, *J* = 7.4 Hz, 4H), 2.63 (s, 6H), 1.78 (p, *J* = 7.2 Hz, 4H), 1.32 - 1.15 (m, 52H), 0.85 (t, *J* = 6.6 Hz, 6H).
^{13}C NMR (100 MHz, d_6-DMSO): δ 144.7, 132.2, 128.9, 127.0, 121.9, 121.7, 48.1, 47.8, 31.3, 29.1, 29.0, 29.0, 28.9, 28.7, 28.5, 25.7, 22.1, 14.0, 9.6. **Note**: 19 of the 24 ^{13}C NMR signals could be found, multiple signals overlap at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{48}H_{84}N_4$ **[M^{2+}]**: 358.3343, found: 358.3355.
MP: 87-88 °C.



38

Click Reaction to Synthesize 38: Phenyl acetylene (20 mg, 0.19 mmol) and 1-hexadecylazide (50 mg, 0.19 mmol) were sequentially added to a 9:1 mixture (10 mL) of *tert*-butanol and water containing copper sulfate (6 mg, 0.04 mmol) and sodium ascorbate (15 mg, 0.08 mmol). The solution was allowed to stir for 30 minutes before the reaction mixture was concentrated *in vacuo*. The crude reaction contents was transferred to a separatory funnel in ethyl acetate (100 mL), which was washed with water (3 x 30 mL), then brine (2 x 30 mL) before the organic layer was collected and dried with anhydrous sodium sulfate. The organic layer was then filtered, and concentrated *in vacuo* before being purified via flash column chromatography using hexanes:ethyl acetate (4:1 to 3:1) as an eluent to afford pure triazole **38** as a white solid (36 mg, 52%). **Note: 38** is a known compound (CAS No. 1009089-53-5). Our NMR data matched those previously reported for this compound.[5]



38 **30**

Methylation to Synthesize Agent 30: Iodomethane (0.18 mL, 0.12 mmol) was added to a stirring solution of **38** (30 mg, 0.81 mmol) in 5 mL anhydrous acetonitrile in a 10 mL glass tube at room temperature. The resulting mixture was sealed and heated at 110 °C and allowed to stir for 24 hours. After this time, the reaction mixture was allowed to cool to room temperature and acetonitrile was evaporated *in vacuo*. The crude product was stirred in anhydrous ether under argon for 5 hours and the resulting white precipitate was filtered under an argon environment. The filtered product was then washed with cold anhydrous ether and dried under vacuum to obtain pure **30** as a white solid (25 mg, 61%). **Note:** Due to a missing aromatic signal in the ^{13}C NMR spectra in $CDCl_3$, NMR spectra were obtained in d_6-DMSO with corresponding tabulated data below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.44 (s, 1H), 7.78 - 7.71 (m, 2H), 7.64 - 7.54 (m, 3H), 4.80 (t, *J* = 7.5 Hz, 2H), 4.31 (s, 3H), 2.10 (p, *J* = 7.6 Hz, 2H), 1.47 - 1.17 (s, 26H), 0.87 (t, *J* = 6.7 Hz, 3H).
^{1}H NMR (400 MHz, d_6-DMSO): δ 9.19 (s, 1H), 7.78 - 7.73 (m, 2H), 7.70 - 7.65 (m, 3H), 4.64 (t, *J* = 7.2 Hz, 2H), 4.29 (s, 3H), 1.96 (p, *J* = 7.0 Hz, 2H), 1.44 - 1.17 (m, 26H), 0.85 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2, 132.3, 130.0, 129.8, 121.9, 55.0, 39.2, 32.1, 29.9, 29.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.1, 26.5, 22.9, 14.3. **Note:** Missing one ^{13}C signal from aromatic region, which was found in d_6-DMSO. 19 of the 22 ^{13}C NMR signals could be found, several signals buried at 29 ppm.
^{13}C NMR (100 MHz, d_6-DMSO): δ 142.3, 131.5, 129.4, 129.3, 128.7, 122.7, 53.2, 31.3, 29.1, 29.0, 29.0, 29.0, 28.8, 28.7, 28.6, 28.3, 25.4, 22.1, 14.0. **Note**: 19 of the 22 ^{13}C NMR signals could be found, several signals buried at 29 ppm.
HRMS (ESI) m/z: calc. for $C_{25}H_{42}N_3$ **[M^+]**: 384.3373, found: 384.3382.
MP: 64-65 °C.

3.) Biological Methods:

A.) Bacterial Minimum Inhibitory Concentration (MIC) Susceptibility Assay (in 96-well plate):

The minimum inhibitory concentration (MIC) for each compound was determined by the broth microdilution method as recommended by the Clinical and Laboratory Standards Institute (CLSI).[6] In a 96-well plate, eleven two-fold serial dilutions of each compound were made in a final volume of 100 μL Luria Broth. Each well was inoculated with ~10^5 bacterial cells at the initial time of incubation, prepared from a fresh log phase culture (OD_{600} of 0.5 to 1.0 depending on bacterial strain). The MIC was defined as the lowest concentration of test compound that prevented bacterial growth after incubating 16 to 18 hours at 37 °C. The concentration range tested for each compound during this study was 0.10 to 100 μM. DMSO served as our vehicle and negative control in each microdilution MIC assay. DMSO was serially diluted with a top concentration of 1% v/v. All MIC values were obtained from a minimum of three independent experiments.

Supporting Table 1. Summary of antibacterial (MIC) assay for select compounds against a panel of *S. aureus* strains, including several clinical/MRSA isolates. All concentrations are reported as micromolar (μM).

Compound	*S. aureus* 29213	MRSA-2	MRSA-1	SA-129	SA-147	SA-138	SA-156	MRSA BAA-44	MRSA BAA-1707
NH125	4.69[a]	3.13	6.25	4.69[a]	4.69[a]	6.25	6.25	4.69[a]	2.35[a]
1	2.35[a]	3.13	2.35[a]	1.56	1.17[a]	1.56	2.35[a]	2.35	1.56
2	3.13	3.13	--	--	--	--	--	--	4.69[a]
4	2.35[a]	4.69[a]	3.13	1.56	1.56	1.56	2.35[a]	3.13	3.13
5	4.69[a]	4.69[a]	--	--	--	--	--	--	4.69[a]
6	3.13	3.13	--	--	--	--	--	--	3.13
7	2.35[a]	3.13	--	--	--	--	--	--	4.69[a]
8	1.56	1.17[a]	1.56	1.56	1.17[a]	2.35[a]	1.56	1.56	0.39
9	2.35[a]	2.35[a]	1.56	1.56	1.17[a]	1.17[a]	2.35[a]	2.35[a]	2.35[a]
11	1.17[a]	1.17[a]	1.17[a]	1.56	1.17[a]	1.56	1.56	1.56	0.39
17	3.13	2.35[a]	4.69[a]	3.13	2.35[a]	3.13	2.35[a]	2.35[a]	1.56
18	4.69[a]	2.35[a]	3.13	3.13	2.35[a]	3.13	3.13	2.35[a]	1.56
25	12.5	3.13	12.5	3.13	6.25	6.25	12.5	12.5	12.5
30	3.13	6.25	4.69[a]	1.56	1.56	2.35[a]	2.35[a]	4.69[a]	3.13
QAC-10	4.69[a]	3.13	4.69[a]	2.35[a]	3.13	2.35[a]	2.35[a]	2.35[a]	1.56

Note: [a] Represents midpoint of a two-fold range in MIC assays. All MICs were obtained from a minimum of three independent experiments.

B.) Fungal Minimum Inhibitory Concentration (MIC) Susceptibility Assay (in 96-well plate):

Fungal minimum inhibition concentrations (MICs) were determined using standard microdilution methods according to the Clinical and Laboratory Standards Institute document M27-A3. The test compound concentration ranged from 0.01 to 100 μM. Amphotericin B (AmB) and itraconazole (ITC) (Fisher Scientific) were included as positive controls. DMSO, the vehicle control, was used at ≤ 1% v/v for these experiments. The fungal M27-A3 standard MIC assay protocol requires the following inoculum preparation protocol: The organisms were cultured onto PDA medium at 35 ºC. The inoculum is prepared by picking five colonies from 24-hour old culture of Candida spp. or 48-hour old culture of *C. neoformans*. The inoculum was suspended in 5 ml of sterile water, the resulting suspension was vortexed for 15 seconds and the cell density adjusted (by adding more sterile water) to an OD_{530} = 0.30, which yields a suspension of 1×10^6 to 5×10^6 cells per mL. The suspension was diluted 50 times and then 20 times using RPMI 1640 medium to obtain the two times test inoculum (1×10^3 to 5×10^3 cells per mL). The following steps are the same with the standard bacterial MIC protocol using 96-well plates. NOTE: RPMI 1640 medium was used in the fungal MIC assay (for both cell inoculum and compound dilution).

Supporting Table 2. Complete summary of antibacterial (MIC), antifungal (MIC) and haemolysis (HC_{50}) studies with NH125, analogues and other membrane-active antimicrobials and controls. All MIC and HC_{50} values are recorded in micromolar (μM) concentrations.

Agent	MRSA-2	MRSA 1707	MRSE 35984	VRE 700221	*A. bau.* 1794	PAO1	UAEC-1	*K. pneu.* 13883	*C. albicans* SC5314	*C. neof.* 66031	RBC HC_{50}
NH125	4.69[a]	2.35[a]	4.69[a]	3.13	37.5[a]	>100	18.8[a]	18.8[a]	3.13	3.13	12.3
1	3.13	1.56	1.17[a]	3.13	12.5	>100	6.25	6.25	3.13	6.25	7.8
2	3.13	4.69[a]	1.56	1.56	18.8[a]	>100	12.5	12.5	--	--	--
3	6.25	3.13	3.13	2.35[a]	25	>100	12.5	50	3.13	6.25	14.2
4	4.69[a]	3.13	2.35[a]	1.56	18.8[a]	>100	6.25	6.25	3.13	3.13	13.4
5	4.69[a]	4.69[a]	--	--	37.5[a]	>100	--	--	--	--	--
6	3.13	3.13	1.17[a]	1.56	12.5	>100	6.25	6.25	--	--	--
7	3.13	4.69[a]	--	--	18.8[a]	>100	--	--	--	--	--
8	1.17[a]	0.39	1.17[a]	2.35[a]	12.5	>100	12.5	12.5	3.13	6.25	13.0
9	2.35[a]	2.35[a]	1.17[a]	1.17[a]	12.5	>100	--	--	--	--	--
10	2.35[a]	--	0.78	2.35[a]	9.38[a]	>100	--	--	--	--	--
11	1.17[a]	0.39	0.59[a]	1.56	6.25	>100	12.5	18.8[a]	3.13	6.25	6.8
12	6.25	--	2.35[a]	3.13	>100	>100	--	--	--	--	--
13	12.5	--	9.38[a]	4.69[a]	>100	>100	--	--	--	--	--
14	6.25	--	6.25	4.69[a]	>100	>100	--	--	--	--	--
15	3.13	--	3.13	2.35[a]	>100	>100	--	--	--	--	--
16	3.13	4.69[a]	3.13	1.56	>100	>100	--	--	--	--	10.7
17	2.35[a]	1.56	2.35[a]	1.56	>100	>100	--	--	--	--	--
18	2.35[a]	1.56	1.17[a]	1.56	25	>100	--	--	--	--	16.7
19	12.5	--	12.5	9.38[a]	>100	>100	--	--	--	--	--
20	37.5	--	12.5	6.25	>100	>100	--	--	--	--	--
21	25	25	>100	6.25	>100	>100	--	--	--	--	46.3
22	>100	--	>100	>100	>100	>100	--	--	--	--	--
23	6.25	--	3.13	2.35[a]	>100	>100	--	--	--	--	--
24	3.13	--	4.69[a]	2.35[a]	37.5[a]	>100	--	--	--	--	--
25	3.13	9.38[a]	3.13	1.56	>100	>100	--	--	--	--	10.4
26	3.13	--	6.25	1.56	>100	>100	--	--	--	--	--
27	6.25	--	9.38[a]	3.13	>100	>100	--	--	--	--	--
28	>100	>100	>100	>100	>100	>100	>100	>100	50	25	--
29	>100	>100	>100	>100	>100	>100	>100	>100	--	--	34.5
30	3.13	3.13	1.56	3.13	12.5	>100	--	--	--	--	12.6
31	25	12.5	9.38[a]	50	>100	>100	25	100	--	--	>100
BAC-12	6.25	6.25	3.13	25	75[a]	>100	50	75[a]	--	--	>100
BAC-16	1.56	1.56	1.56	3.13	6.25	>100	6.25	9.38[a]	3.13	6.25	21.8
QAC-10	3.13	4.69[a]	2.35[a]	2.35[a]	6.25	9.38[a]	12.5	25	--	--	7.9
Dapto.	4.69[a]	3.13	3.13	125	>100	>100	>100	>100	--	--	>100
Amp. B	--	--	--	--	--	--	--	--	0.78	0.1	--

Note: [a] corresponds to a midpoint of a 2-fold range in values. Dapto. = Daptomycin. Amp. B = Amphotericin B. *A. bau.* = *A. baumannii*; *K. pneu.* = *K. pneumoniae*; *C. neof.* = *C. neoformans;* UAEC-1 = *E. coli* (clinical isolate). RBC = red blood cells. MIC = minimum inhibitory concentration (antibacterial activity). HC_{50} = concentration required to lyse 50% of red blood cells (haemolysis assays). All values are the result of a minimum of three independent experiments.

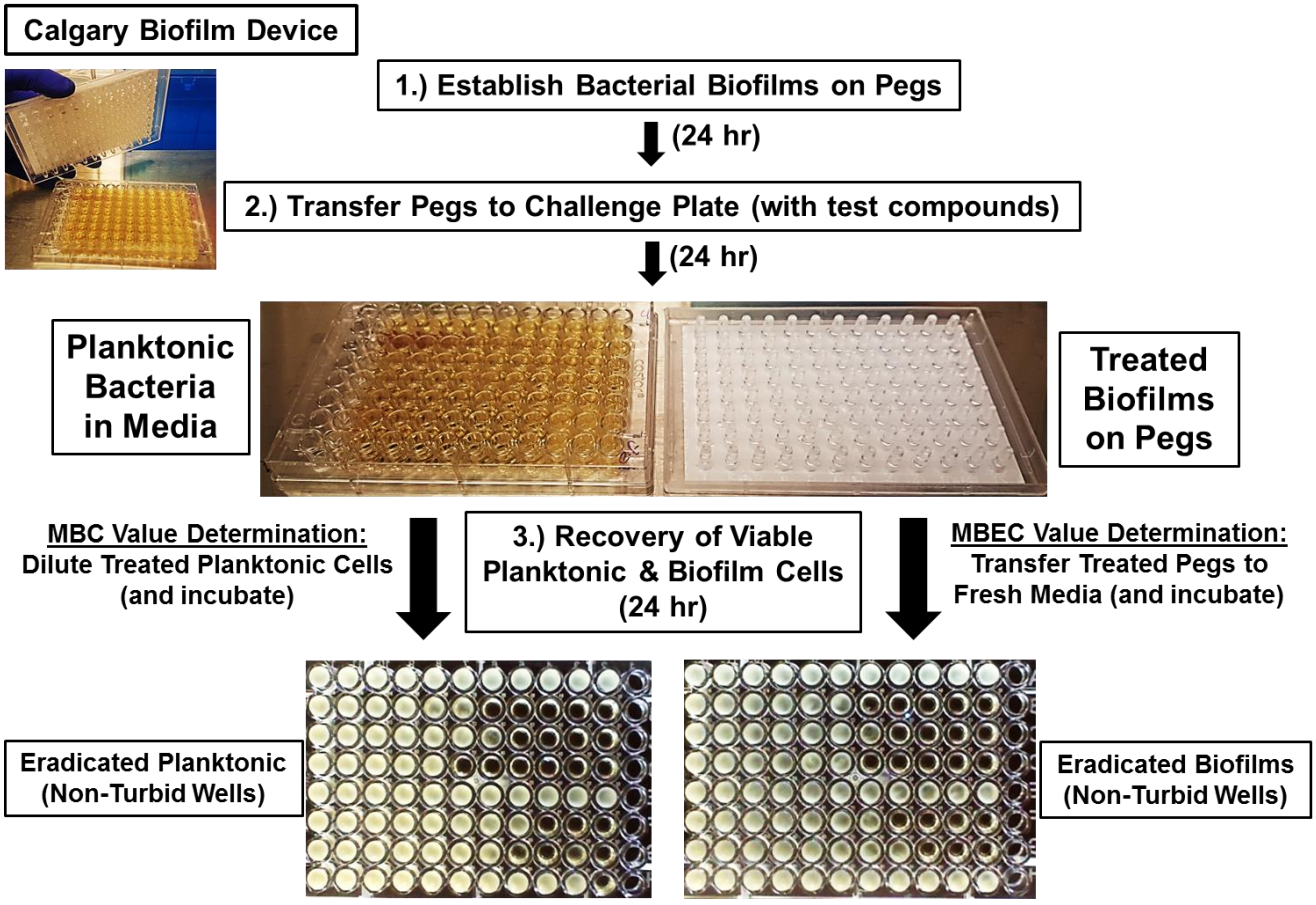
C.) Calgary Biofilm Device Experiments to Determine Bacterial Biofilm Eradication:

Determination of Minimum Bactericidal Concentrations (MBC) and Minimum Biofilm Eradication Concentrations (MBEC) using the Calgary Biofilm Device

Biofilm eradication experiments were performed using the Calgary Biofilm Device to determine MBC/MBEC values for various compounds of interest (Innovotech, product code: 19111).[7] The Calgary device (96-well plate with lid containing 96 total pegs to establish biofilms; 1 peg/well) was inoculated with 125 μL of a mid-log phase culture diluted 1,000-fold in tryptic soy broth with 0.5% glucose (TSBG) to establish bacterial biofilms after incubation at 37 °C for 24 hours. The lid of the Calgary device was then removed, washed and transferred

to another 96-well plate containing 2-fold serial dilutions of the test compounds (the "challenge plate"). The total volume of media with compound in each well in the challenge plate was 150 µL. The Calgary device was then incubated at 37 °C for 24 hours. The lid was then removed from the challenge plate and MBC/MBEC values were determined using different final assays. To determine **MBC values**, 20 µL of the challenge plate was transferred into a fresh 96-well plate containing 180 µL TSBG and incubated overnight at 37 °C. The MBC values were determined as the concentration giving a lack of visible bacterial growth (i.e., turbidity). For determination of **MBEC values**, the Calgary device lid (with attached pegs/treated biofilms) was transferred to a new 96-well plate containing 150 µL of fresh TSBG media in each well and incubated for 24 hours at 37 °C to allow viable biofilms to grow and disperse resulting in turbidity after the incubation period. MBEC values were determined as the lowest test concentration of a compound that resulted in eradicated biofilm (i.e., wells that had no turbidity after final incubation period). All data was recorded from three independent CBD experiments.

Note: MRSA-2, MRSA BAA-1707, *S. epidermidis* (MRSE; ATCC 35984) and *E. faecium* (VRE; ATCC 700221) were tested using these assay parameters.



D.) Minimum Fungicidal Concentration (MFC) Assay:

For determination of minimum fungicidal concentrations (MFC), fungal cells from MIC assays are centrifuged, re-suspended in fresh RPMI 1640 medium, and then plated onto PDA or YPD agar plates. The plates were incubated at 35 ºC. Colonies were counted after 24 hours for Candida spp. and 48 hours for *C. neoformans*. The minimum fungicidal concentration (MFC) was defined as the lowest concentration of test compound that killed 99.9% of fungal cells compared to the DMSO control.

E.) MTT Assay to Determine Minimum Biofilm Eradication Concentration (MBEC) in Fungal Strains:

Mature biofilms of *C. albicans* SC5314 and *C. neoformans* ATCC 66031 were formed in Corning 96-well flat-bottom plates using MTT as previously described.[8] These organisms were cultured onto PDA or YPD agar medium at 37 ^{o}C. One colony was picked from a 24-hour old culture of Candida spp. or 48-hour old culture of *C. neoformans* and added to YPD liquid medium for inoculation and cultured at 37 ^{o}C overnight. Cells were then washed with PBS (Phosphate-buffered saline (10 mM potassium phosphate, 150 mM NaCl, pH 7.0)) and standardized to OD_{600} = 1.0. Microtiter wells were then treated with 50 % FCS (Fetal calf serum) in PBS for at least 30 min at room temperature (FCS pre-treatment is not absolutely required for Candida spp.). The FCS was aspirated and microtiter wells were rinsed once with 200 µL PBS before 100 µL of the cell suspension was added to each microtiter well. The plate was then incubated statically at 37 °C for 2 hours. Non-adherent cells were then removed by aspiration and microtiter wells were washed with PBS twice to remove loosely associated cells. Biofilm growth was initiated by addition of 200 µL YNB supplemented with 0.5 % w/v glucose to each well and subsequently incubated at 37 °C for 48 hours for Candida spp. or 72 hours for *C. neoformans*. *Biofilm susceptibility was measured using following method:* The resulting cell culture was aspirated and wells were rinsed once with 200 µL PBS. Controls and compounds were diluted in YNB medium (200 µL) were added to microtiter wells. The plates were incubated at 37 °C for an additional 48 hours. *Biofilm viability was detected using MTT assay as follows:* Following incubation, the culture was aspirated and wells are rinsed twice with 200 µL PBS before 100 µL of MTT (0.5 mg/mL dissolved in PBS containing 1 % glucose) was added to each microtiter well. The plate was then incubated at 37 °C for 30 min, or longer, until dark blue/black crystals formation could be observed (usually 2 hours at most). The MTT reaction was terminated by aspiration of the solution. The crystals were then solubilized by adding 100 µL of 40% acetic acid to the microtiter wells. Killing efficacies were monitored by eye or quantitatively measured using a plate reader (absorbance at 550 nm). MBEC values were determined as the lowest compound concentration leading to 90% eradicated biofilm. All MBEC values using the MTT assay were recorded from at least three independent experiments.

F.) MRSA Persister Cell Kill Kinetics (Killing of Stationary Cultures):

An overnight culture of MRSA BAA-1707 was diluted in fresh TSBG (1:13 to 1:20 fold) and allowed to grow with shaking. Once the culture reached stationary phase (4-6 hours), test compounds were added at a final test concentration of 50 µM. The cultures were incubated with shaking at 250 rpm and aliquots were removed and plated out at different time points. Colony forming units (CFU) per milliliter data was recorded and plotted using Graphpad Prism 6.0.

G.) Haemolysis Assay:

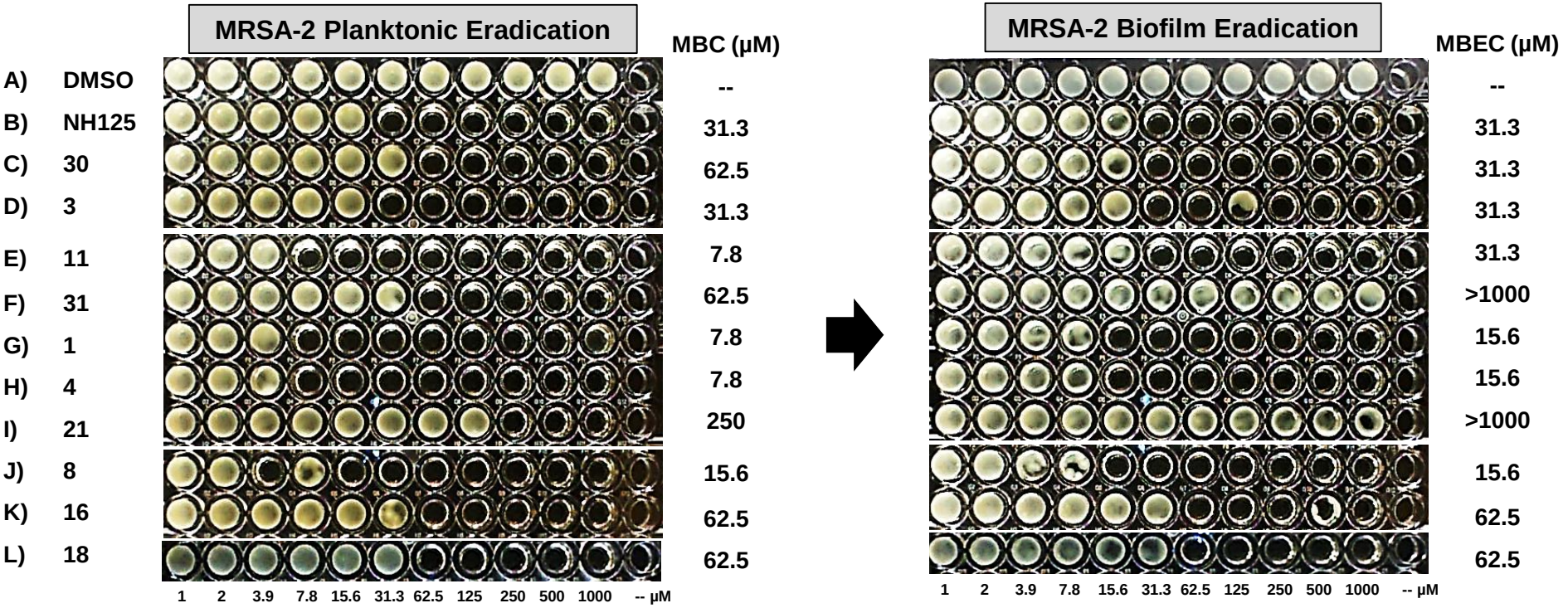
Freshly drawn human red blood cells (hRBC with ethylenediaminetetraacetic acid (EDTA) as an anticoagulant) were washed with Tris-buffered saline (0.01M Tris-base, 0.155 M sodium chloride (NaCl), pH 7.2) and centrifuged for 5 minutes at 3500 rpm. The washing was repeated three times with the buffer. In 96-well plate, the test compounds were added to the buffer. Then 50 µL of 2% of hRBCs in the buffer were added to the test plate to make the final concentrations ranging from 0.2 to 200 µM of each test compound. The plate was then incubated for 1 hour at 37 °C. After incubation, the plate was centrifuged for 5 minutes at 3500 rpm and then 80 µL of the supernatant was transferred to another 96-well plate and the Optical Density (OD) was read at 405 nm. DMSO served as our negative control (0% haemolysis) and Triton X served as our positive control (100% haemolysis). The HC_{50} (concentration of test compound required to lyse red blood cells by 50%) was calculated by plotting the dose-response curve (not shown) with Graphpad Prism 6.0. All data were obtained from three independent haemolysis experiments (presented in Supporting Table 2, page S13).

4.) Literature References:

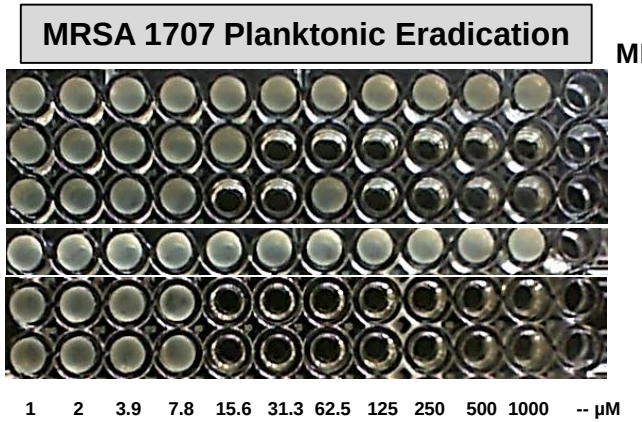
1. *J. Org. Chem.*, 2009, ***74***, 1971-1976.
2. *Syn. Commun.*, 2012, ***42***, 114-121.
3. *Adv. Synth. Catal.*, 2016, ***358***, 597-609.
4. *Polymer Degrad. Stability*, 2007, ***92***, 1753-1762.
5. a.) *Bioorg. Med. Chem. Lett.*, 2016, ***26***, 1029-1038.; b.) *Catal. Sci. Technol.*, 2011, ***1***, 1512-1525.
6. Clinical and Laboratory Standards Institute. 2009. *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard, 8th edition (M7-M8)*, Clinical and Laboratory Standard, Wayne, PA.
7. *Angew. Chem. Int. Ed.*, 2015, ***54***, 14819-14823.
8. *Methods Mol. Biol.*, 2016, ***1356***, 183-197.

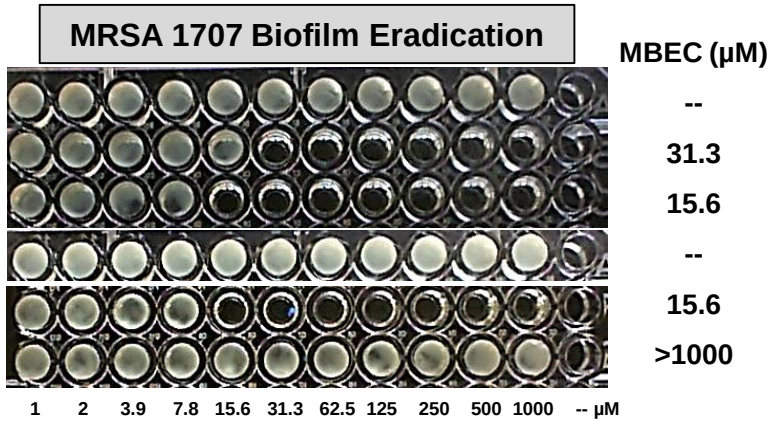
5.) Supporting Images of Biological Experiments:

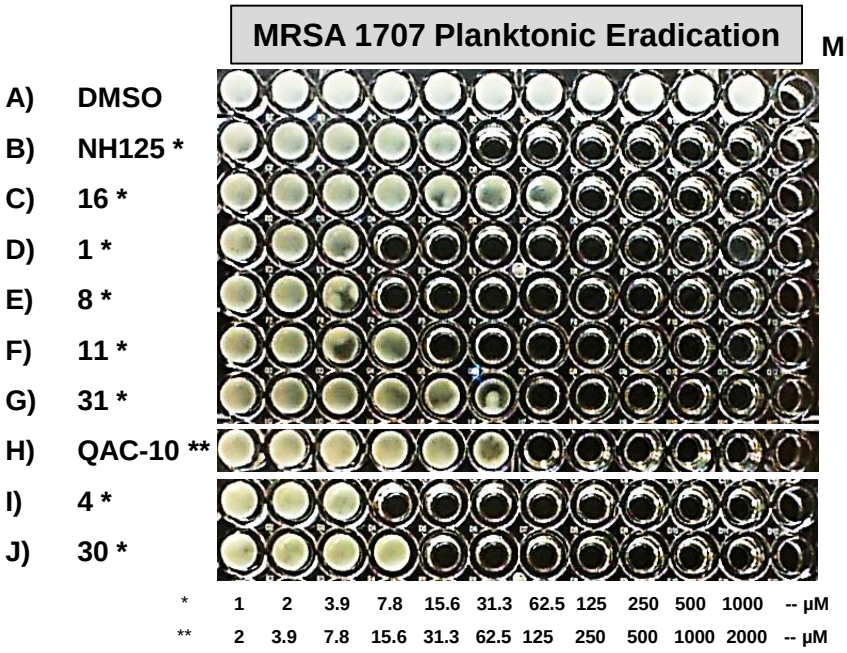
MRSA-2 Biofilm Eradication (CBD Assay)

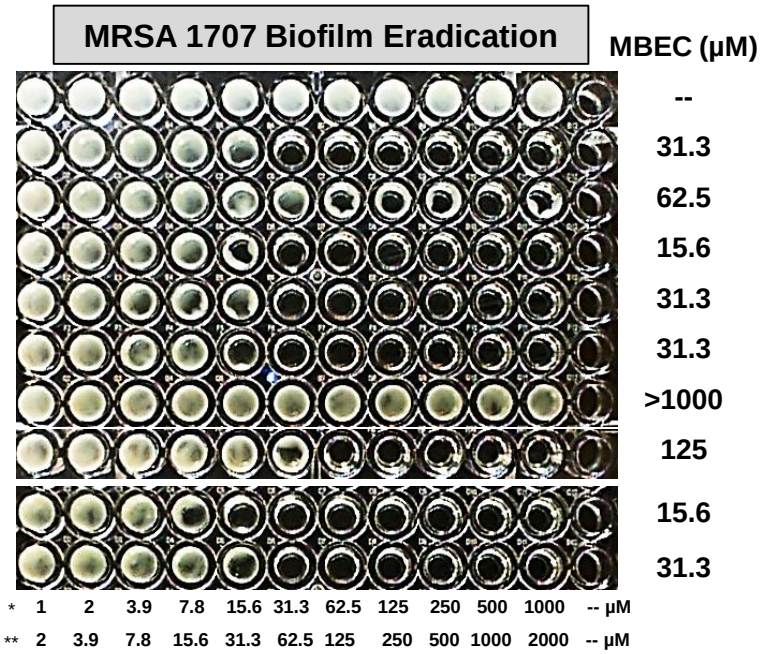


MRSA BAA-1707 Biofilm Eradication (CBD Assay)

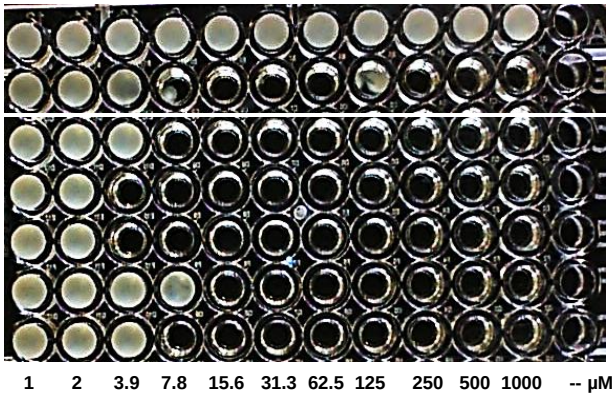




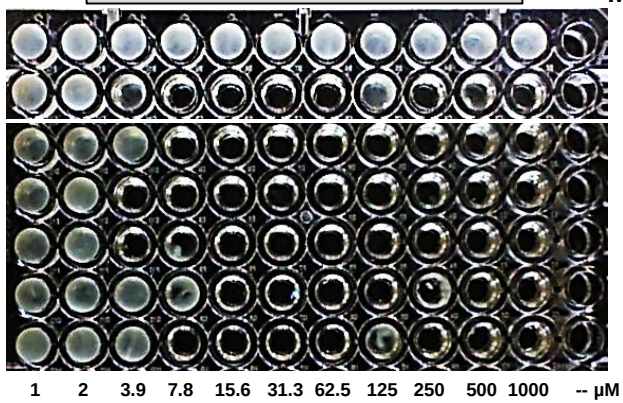




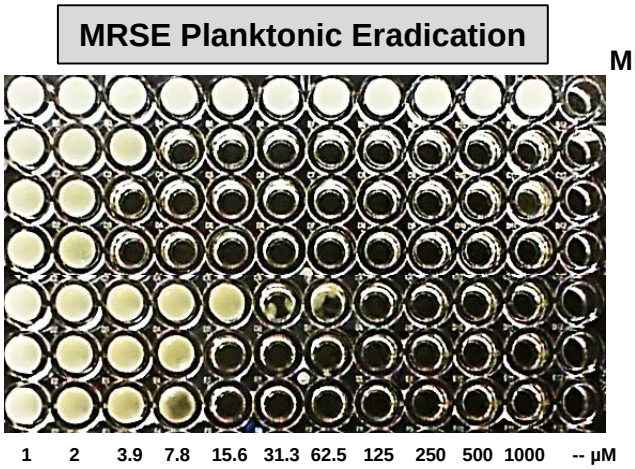
S. epidermidis (MRSE 35984) Biofilm Eradication (CBD Assay)



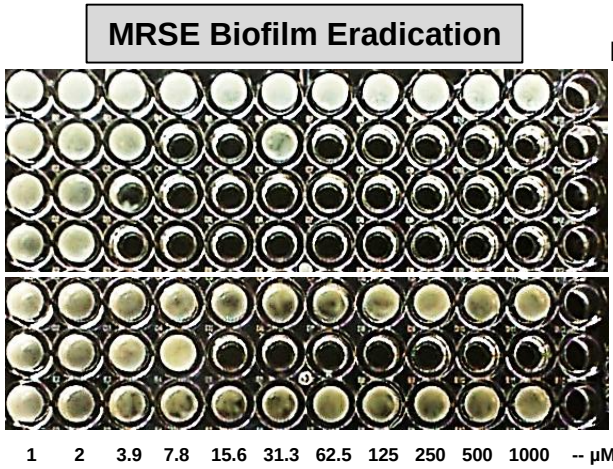
	MBC (µM)
A) DMSO	--
B) NH125	15.6
C) 18	7.8
D) 8	3.9
E) 11	3.9
F) 16	15.6
G) 31	7.8



MBEC (µM)
--
7.8
7.8
3.9
3.9
15.6
7.8

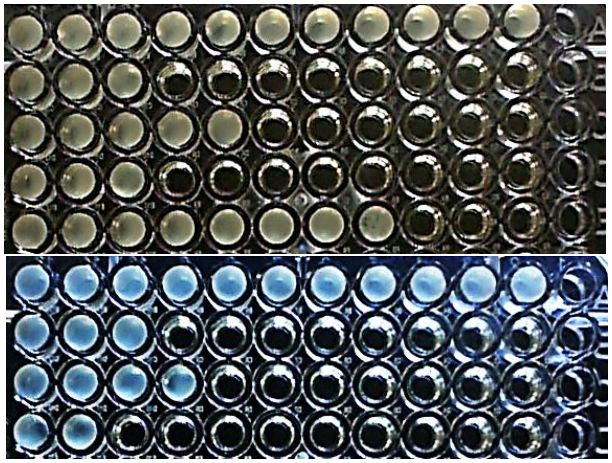


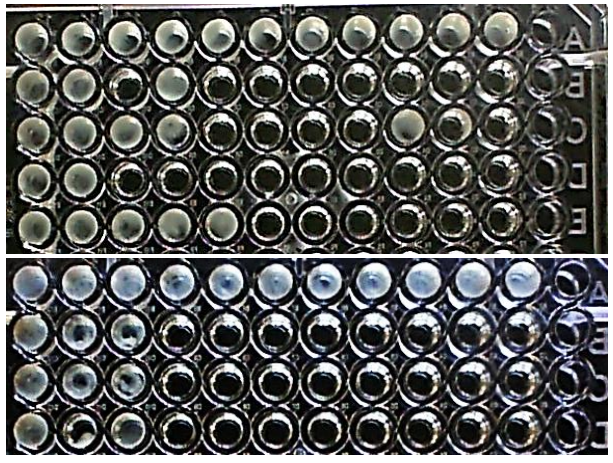
	MBC (µM)
A) DMSO	--
B) NH125	7.8
C) 1	3.9
D) 4	3.9
E) Daptomycin	31.3
F) BAC-16	15.6
G) BAC-12	15.6

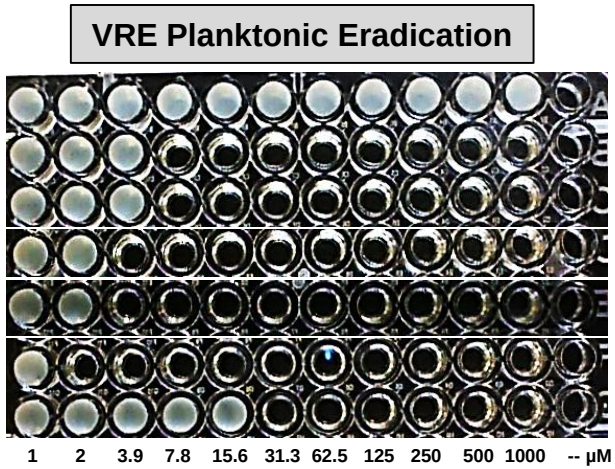


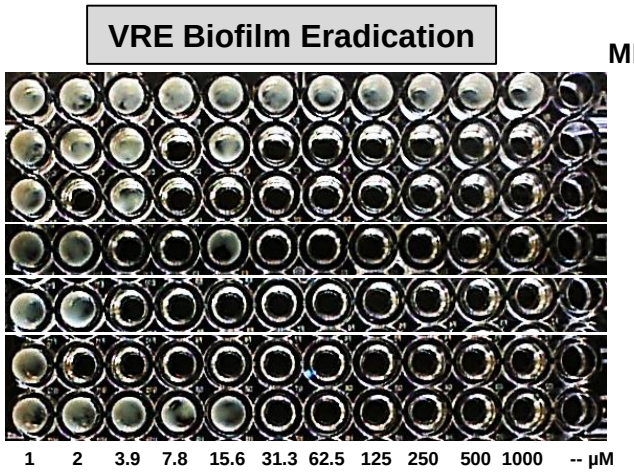
MBEC (µM)
--
7.8
7.8
3.9
>2000
15.6
>2000

E. faecium (VRE 700221) Biofilm Eradication (CBD Assay)





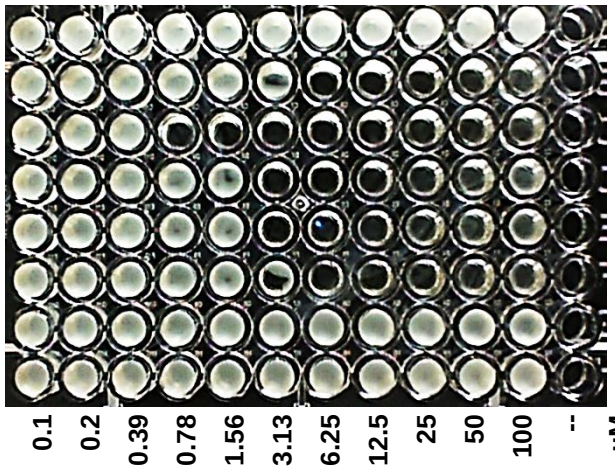




Growth Inhibition (MIC Assay) against MRSA-2

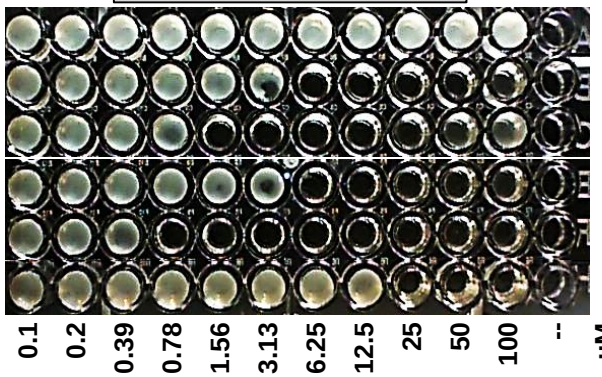
MIC against MRSA-2

		MIC (μM)
A)	DMSO	--
B)	NH125	6.25
C)	8	0.78
D)	25	3.13
E)	26	3.13
F)	27	6.25
G)	29	>100
H)	28	>100



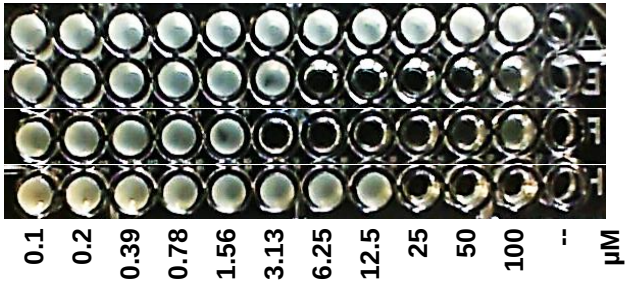
MIC against MRSA-2

		MIC (μM)
A)	DMSO	--
B)	NH125	6.25
C)	11	1.56
D)	23	6.25
E)	8	0.78
F)	31	25



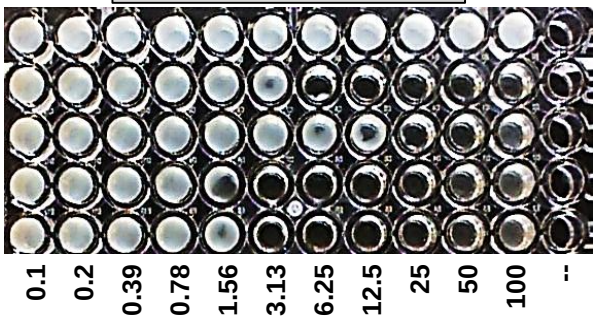
MIC against MRSA-2

		MIC (μM)
A)	DMSO	--
B)	NH125	6.25
C)	24	3.13
D)	31	25



MIC against MRSA-2

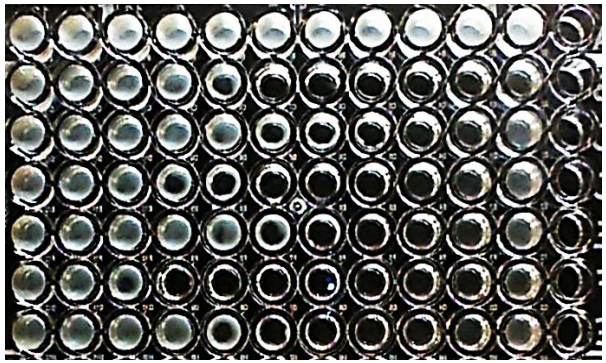
		MIC (μM)
A)	DMSO	--
B)	NH125	6.25
C)	21	25
D)	1	3.13
E)	30	3.13



Growth Inhibition (MIC Assay) against MRSE 35984

MIC against MRSE

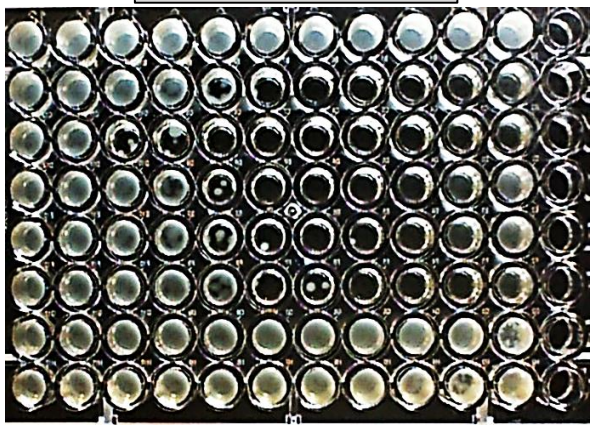
		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	20	12.5
D)	16	3.13
E)	13	6.25
F)	18	1.56
G)	12	3.13



0.1 0.2 0.39 0.78 1.56 3.13 6.25 12.5 25 50 100 -- μM

MIC against MRSE

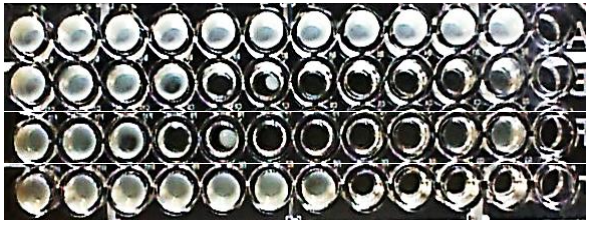
		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	8	1.56
D)	25	3.13
E)	26	6.25
F)	27	6.25
G)	29	>100
H)	28	>100



0.1 0.2 0.39 0.78 1.56 3.13 6.25 12.5 25 50 100 -- μM

MIC against MRSE

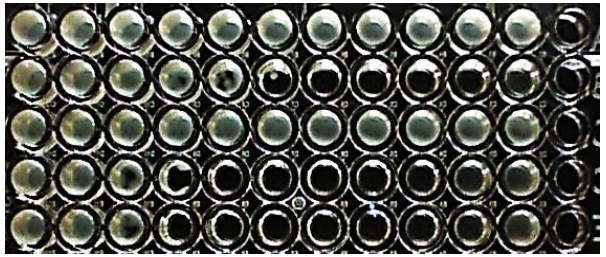
		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	24	3.13
D)	31	12.5



0.1 0.2 0.39 0.78 1.56 3.13 6.25 12.5 25 50 100 -- μM

MIC against MRSE

		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	21	>100
D)	1	0.78
E)	30	0.78

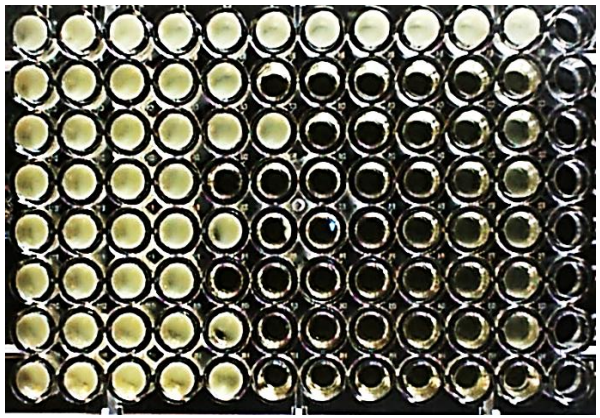


0.1 0.2 0.39 0.78 1.56 3.13 6.25 12.5 25 50 100 -- μM

Growth Inhibition (MIC Assay) against VRE 700221

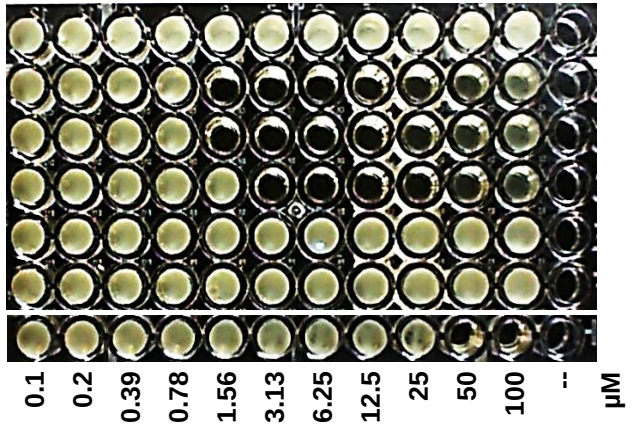
MIC against VRE

		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	20	6.25
D)	16	1.56
E)	13	3.13
F)	18	1.56
G)	12	3.13
H)	8	3.13



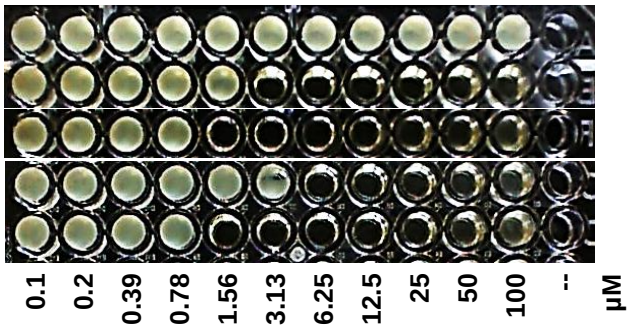
MIC against VRE

		MIC (μM)
A)	DMSO	--
B)	25	1.56
C)	26	1.56
D)	27	3.13
E)	29	>100
F)	28	>100
G)	31	50



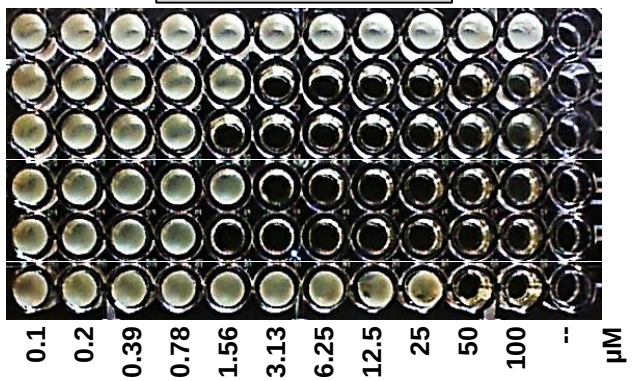
MIC against VRE

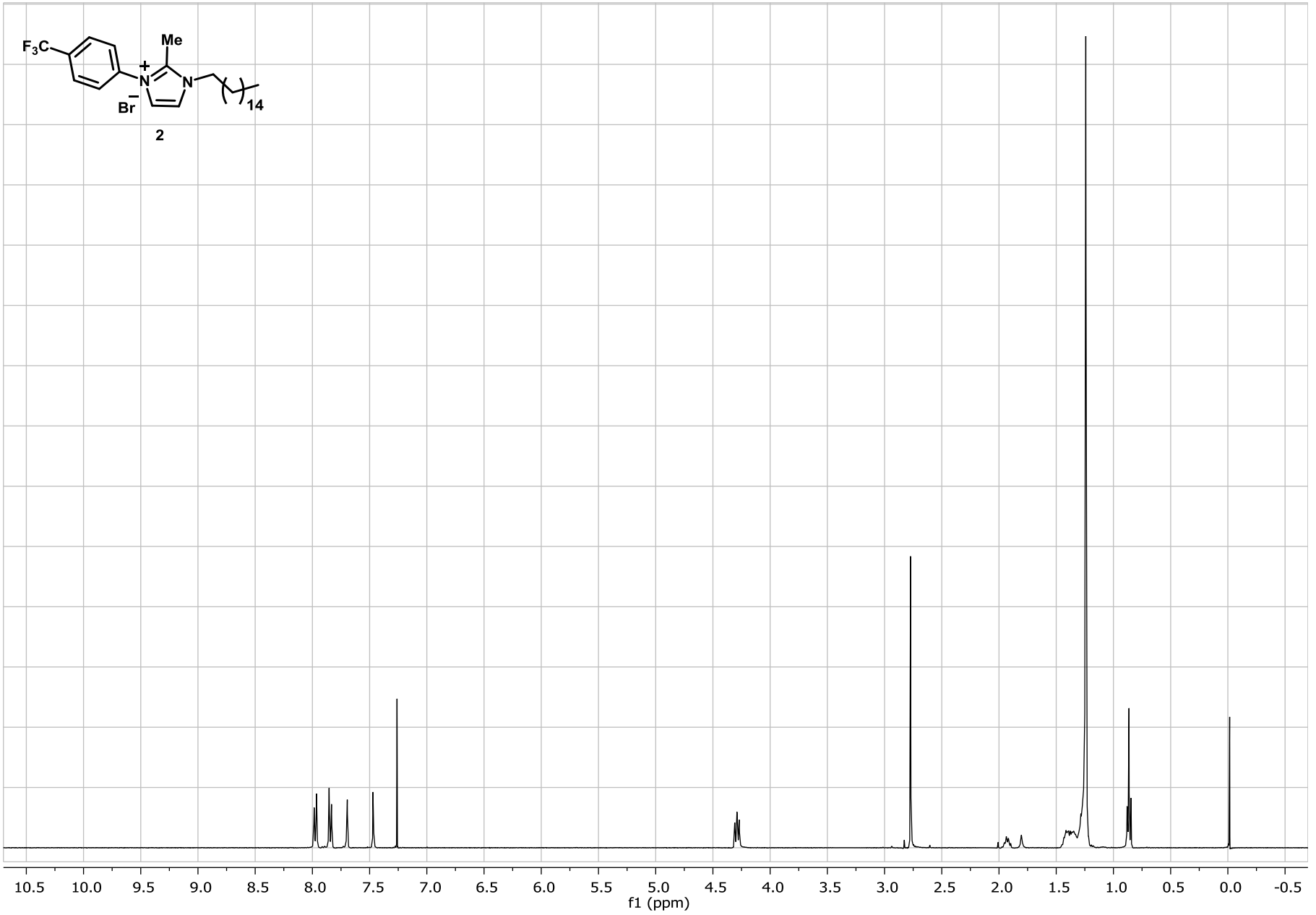
		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	24	1.56
D)	21	6.25
E)	1	3.13



MIC against VRE

		MIC (μM)
A)	DMSO	--
B)	NH125	3.13
C)	11	1.56
D)	23	3.13
E)	8	1.56
F)	31	50

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Me
N
N
Br
14
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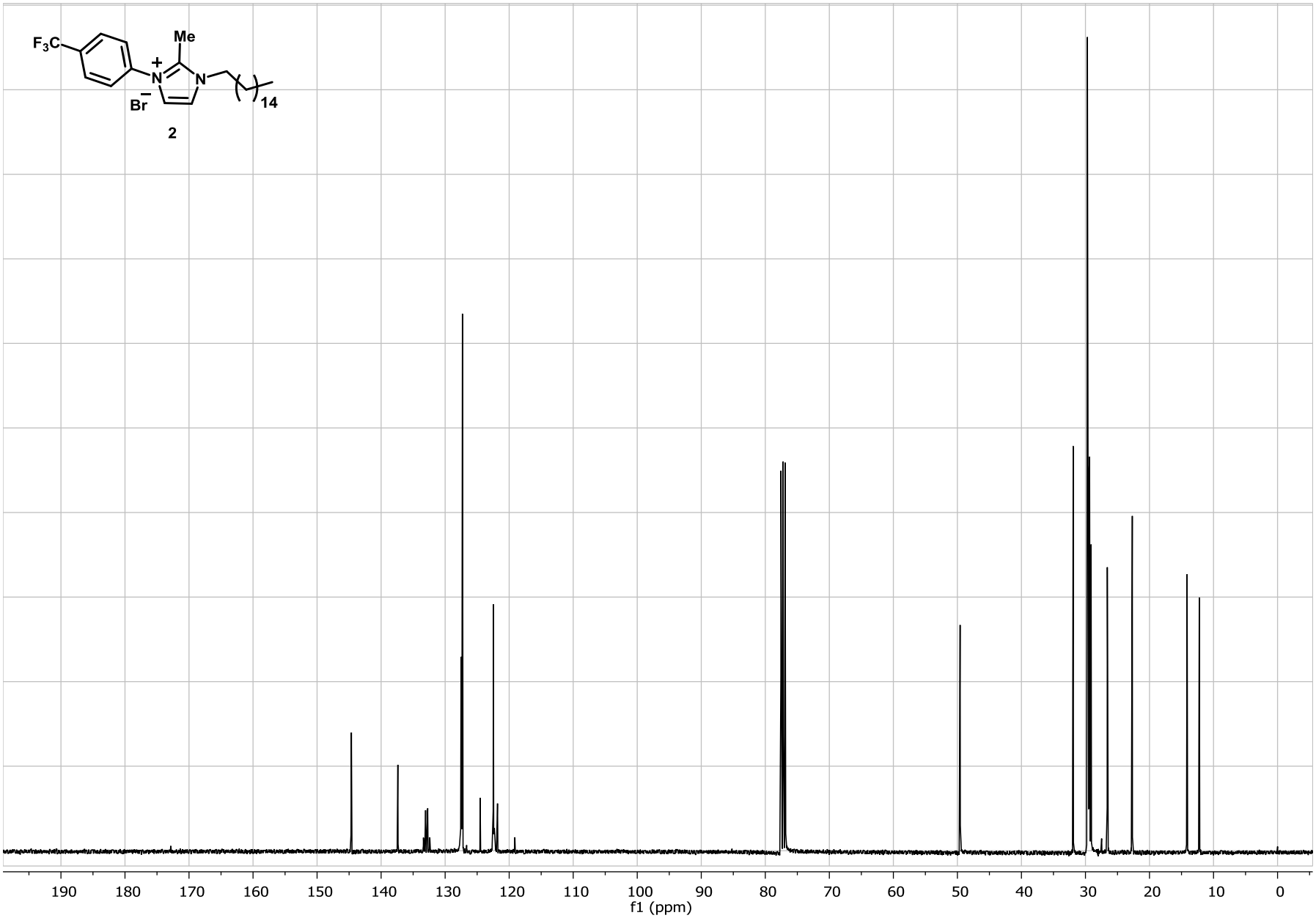
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

NMR 1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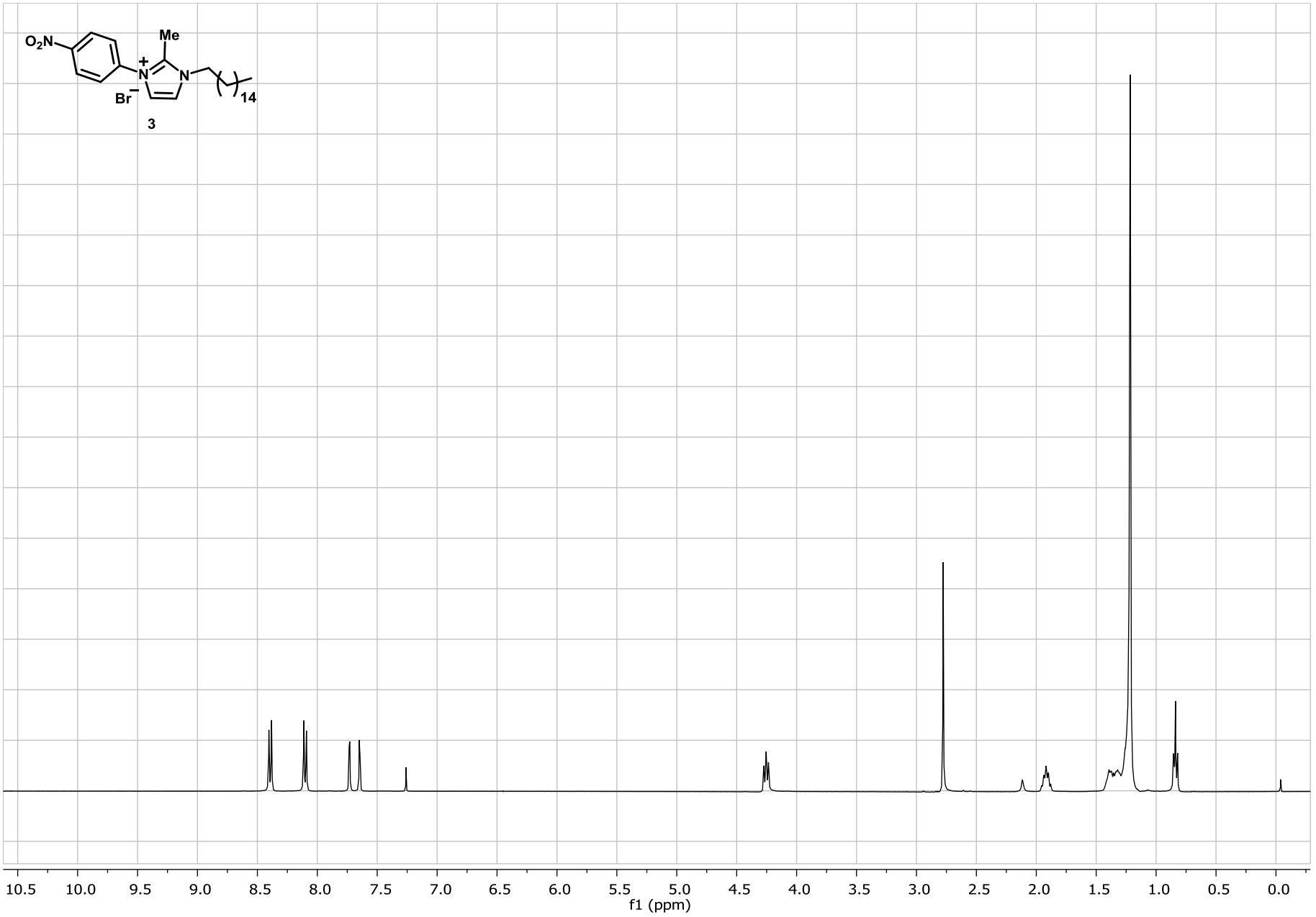
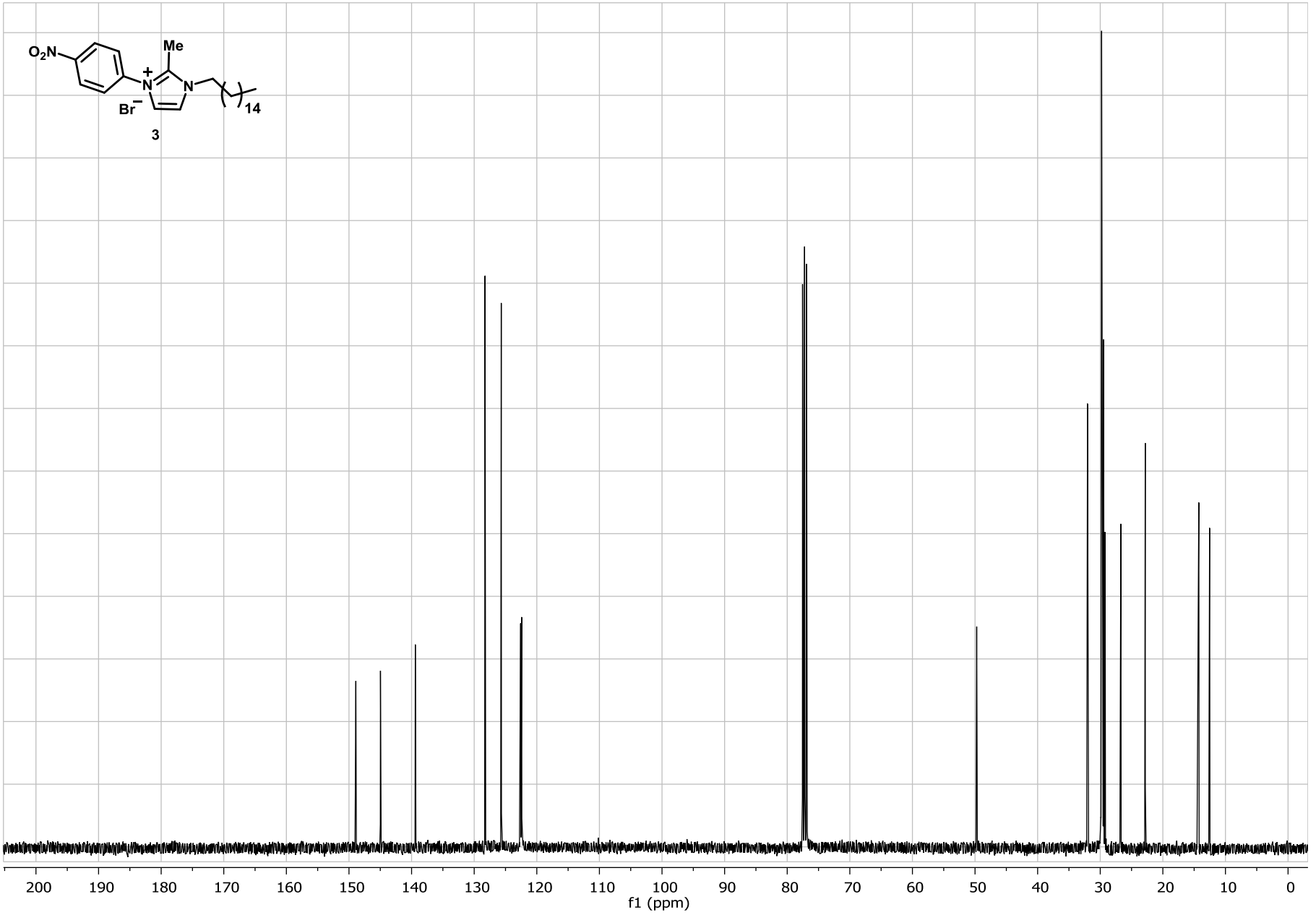
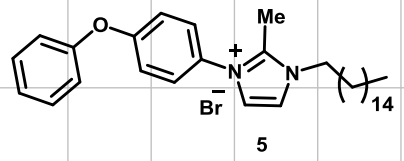
Me
N
N
Br
14
2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

NMR 2

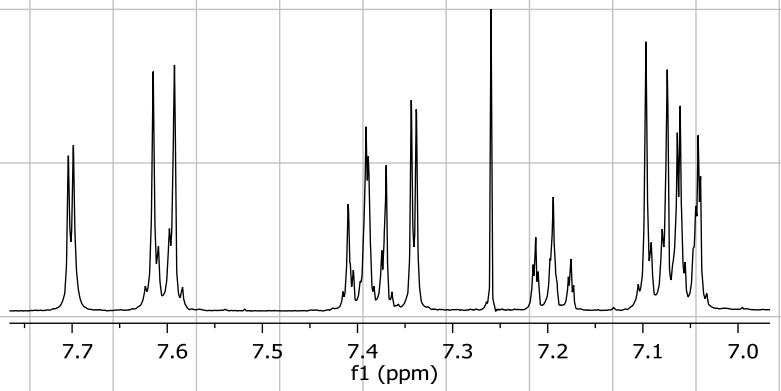

O2N
Me
N
+
N
Br
−
14
3
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

NMR 3


O2N
Me
N
N
Br
14
3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
O
N
N
Br
14

5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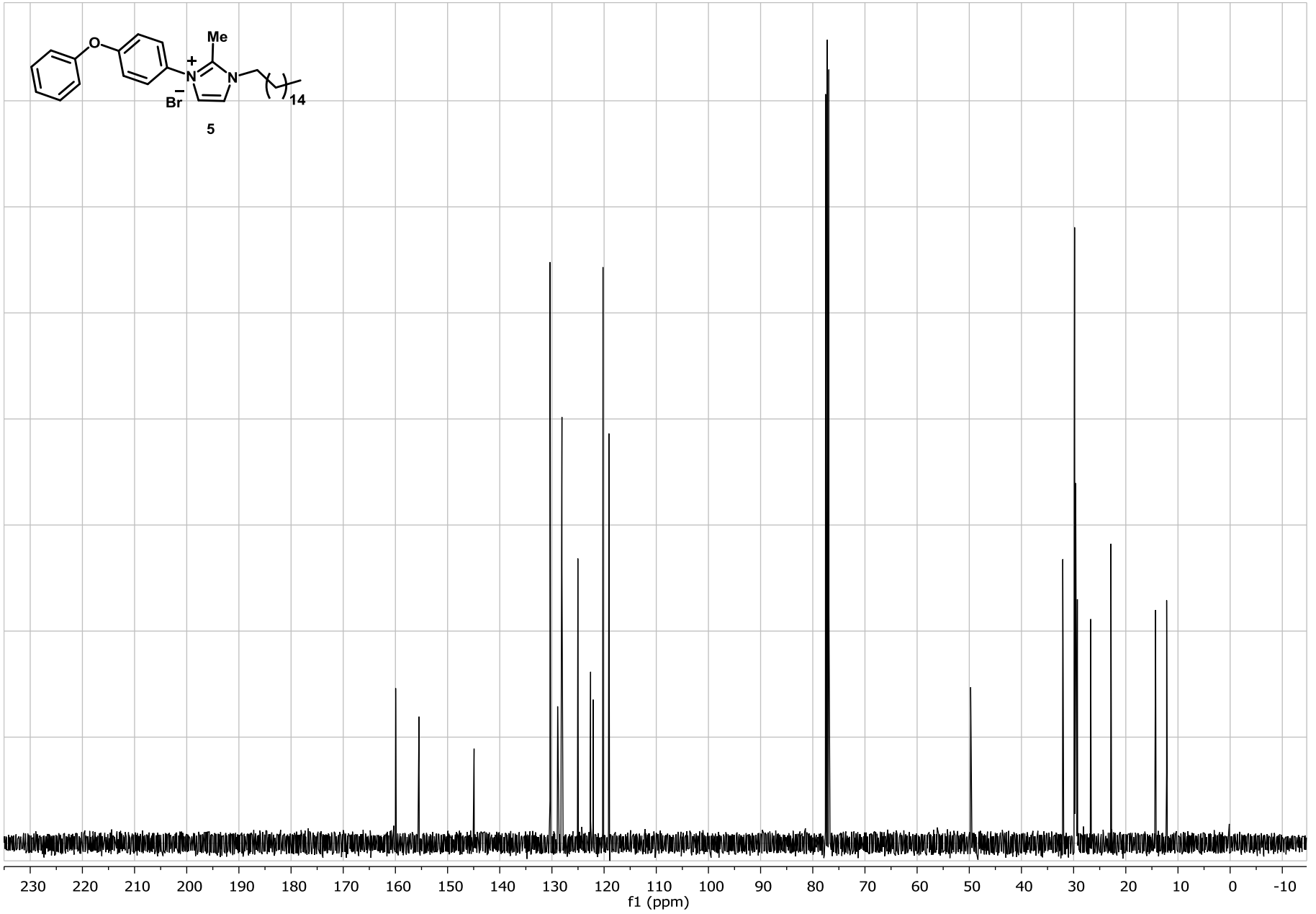
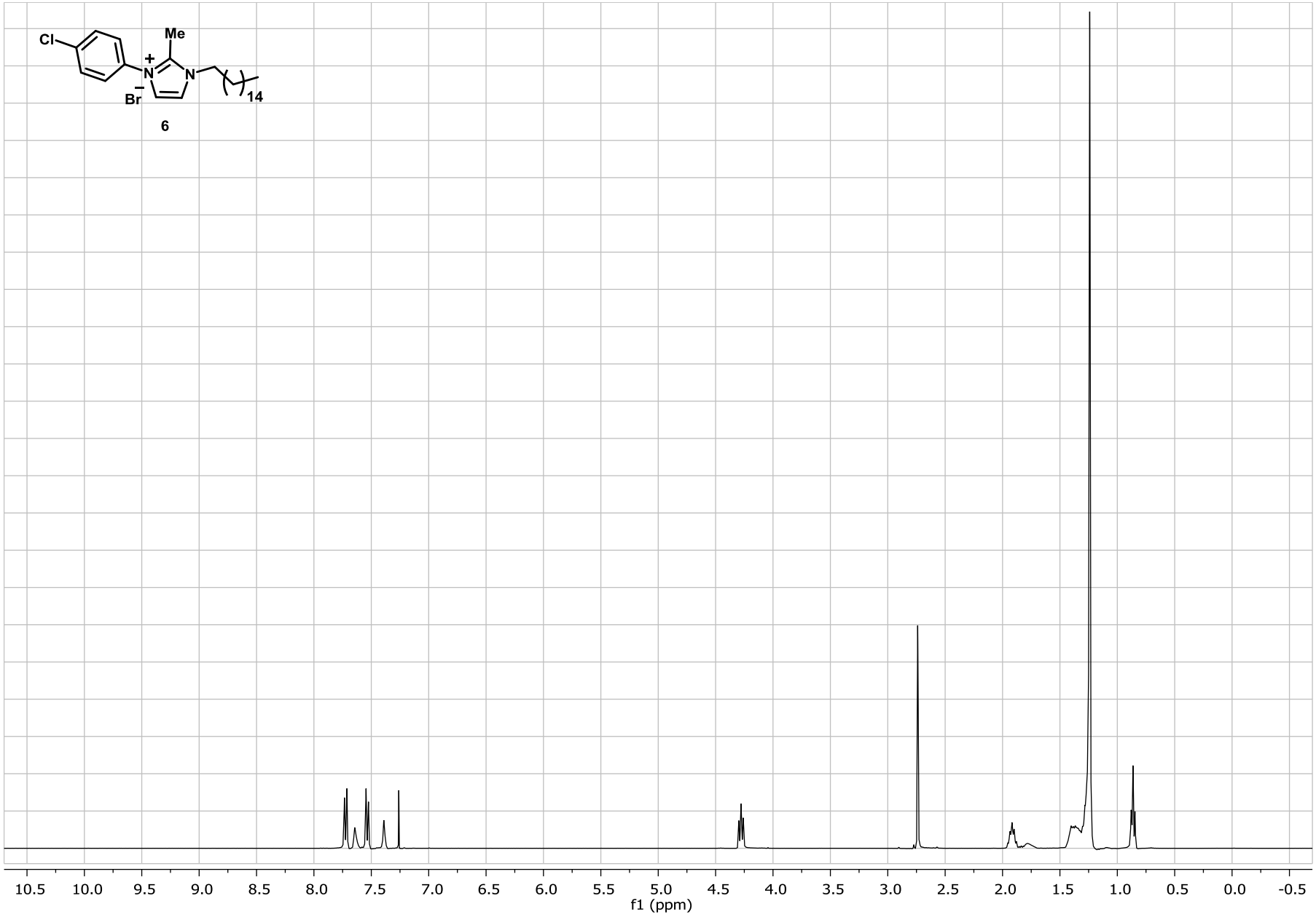
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)

10.5
10.0
9.5
9.0
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
0.0
f1 (ppm)


Me
O
N
N
Br
14
5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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Me
N
N
Br
14
6
10.5
10.0
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9.0
8.5
8.0
7.5
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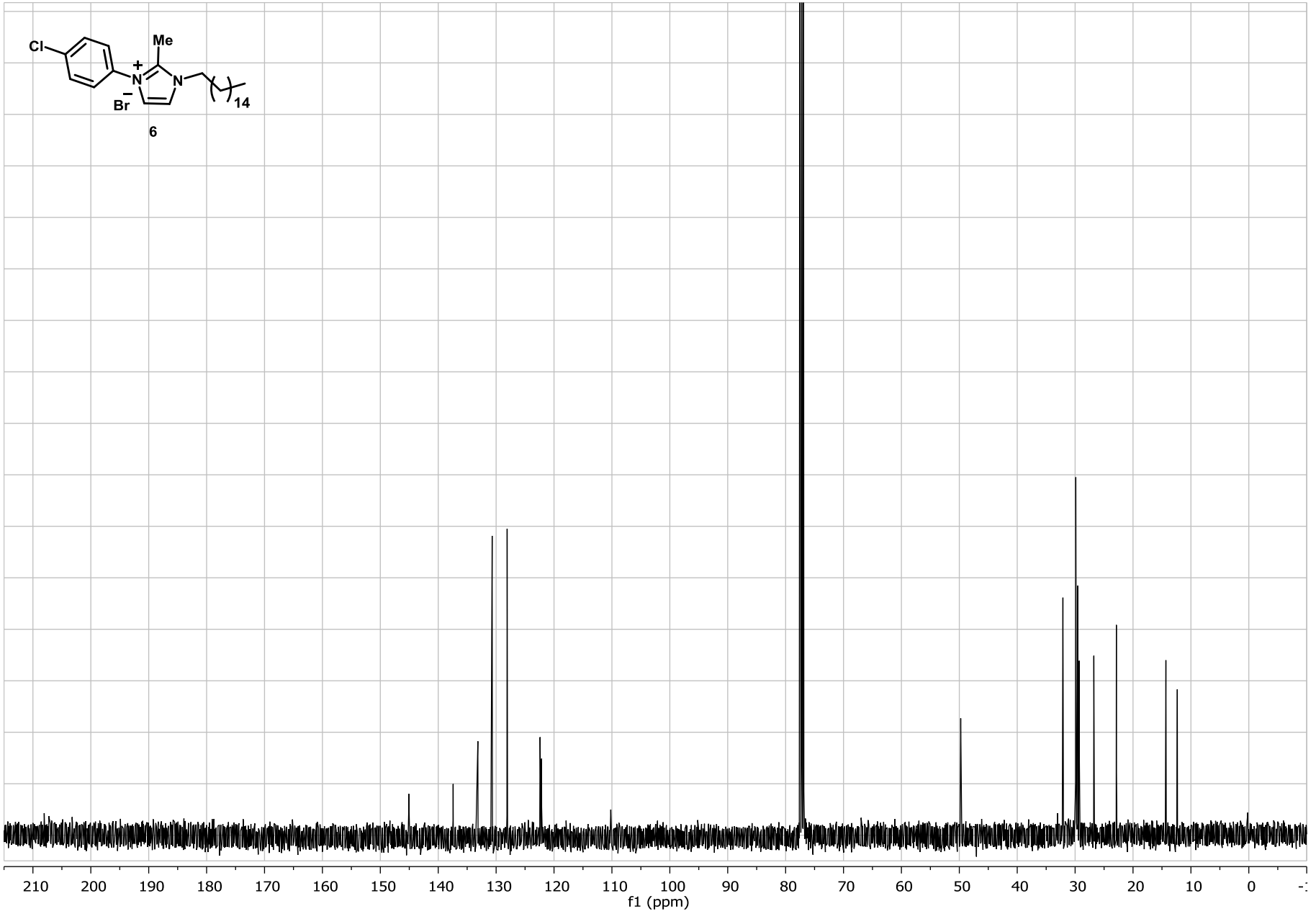
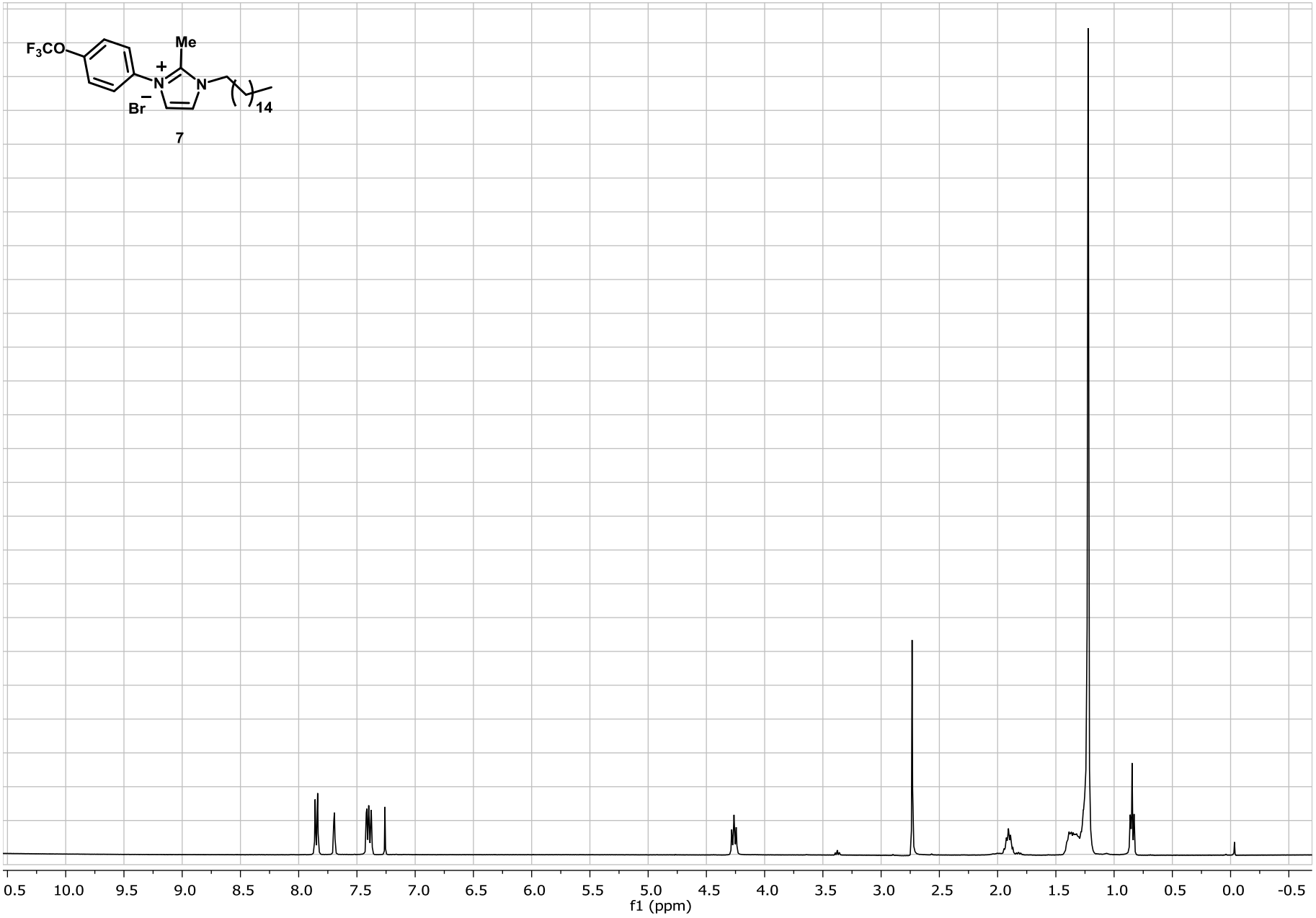
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Cl
Me
N
N
Br
14
6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F3CO
Me
N
N
Br
14
7
0.5
10.0
9.5
9.0
8.5
8.0
7.5
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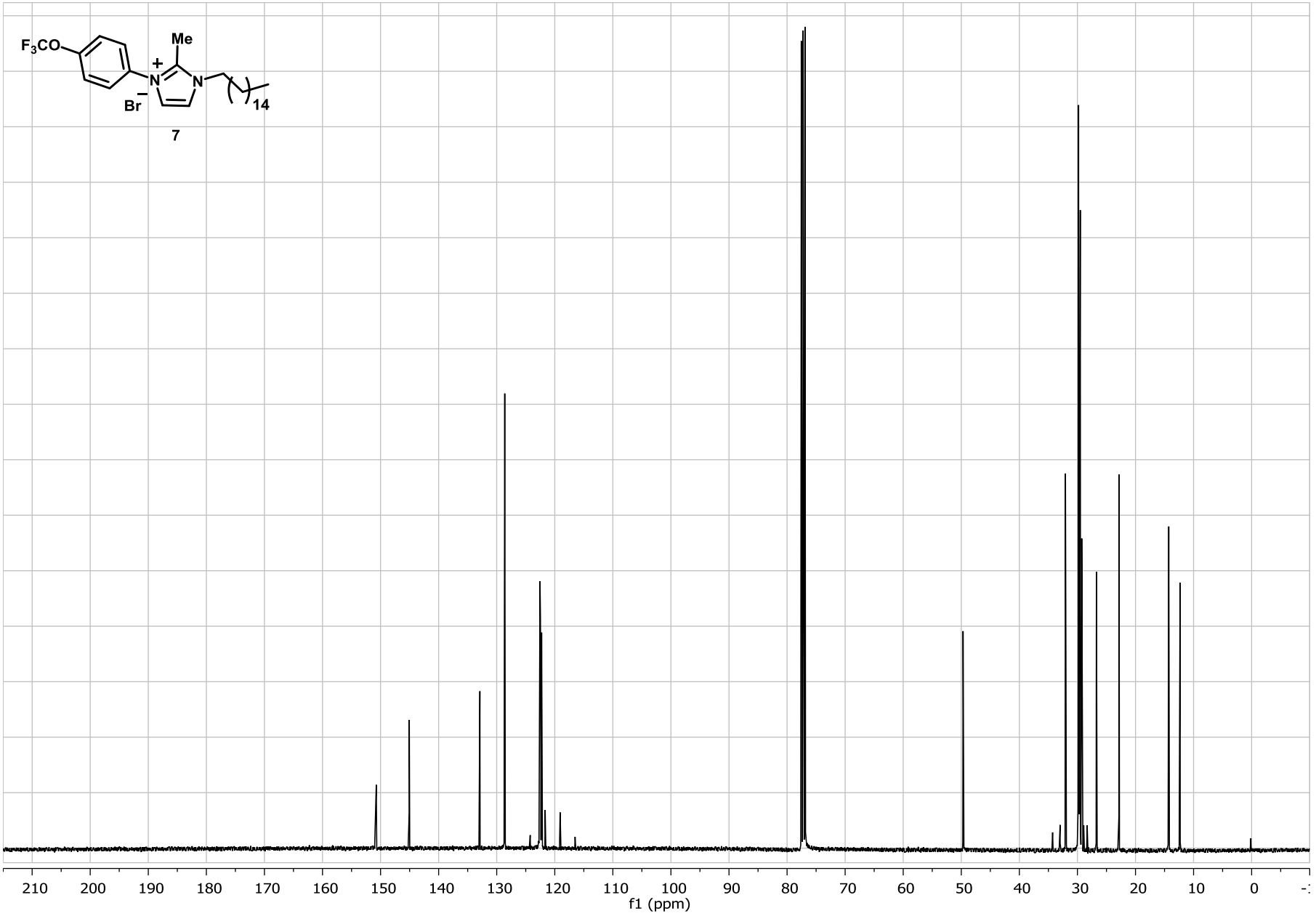
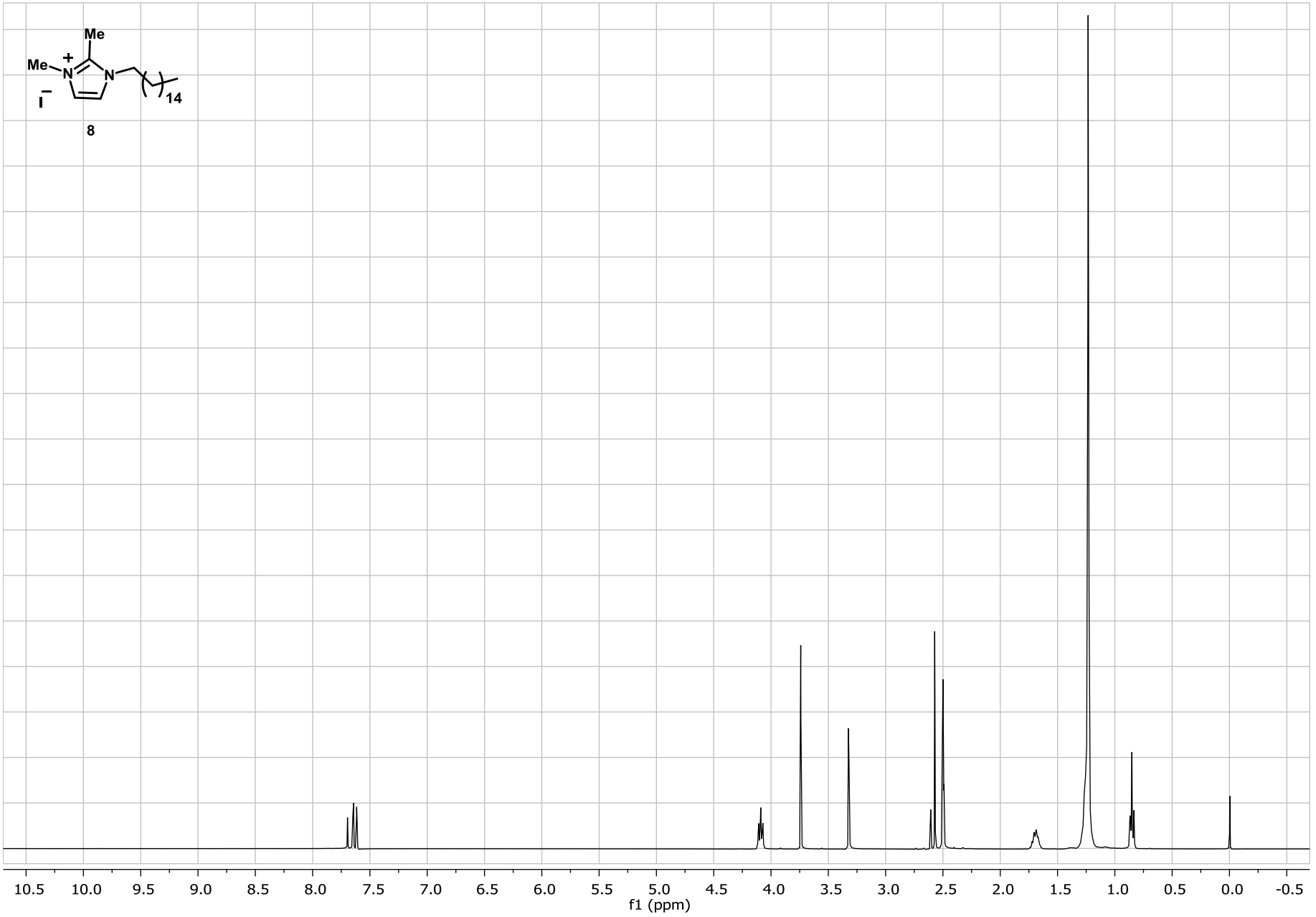
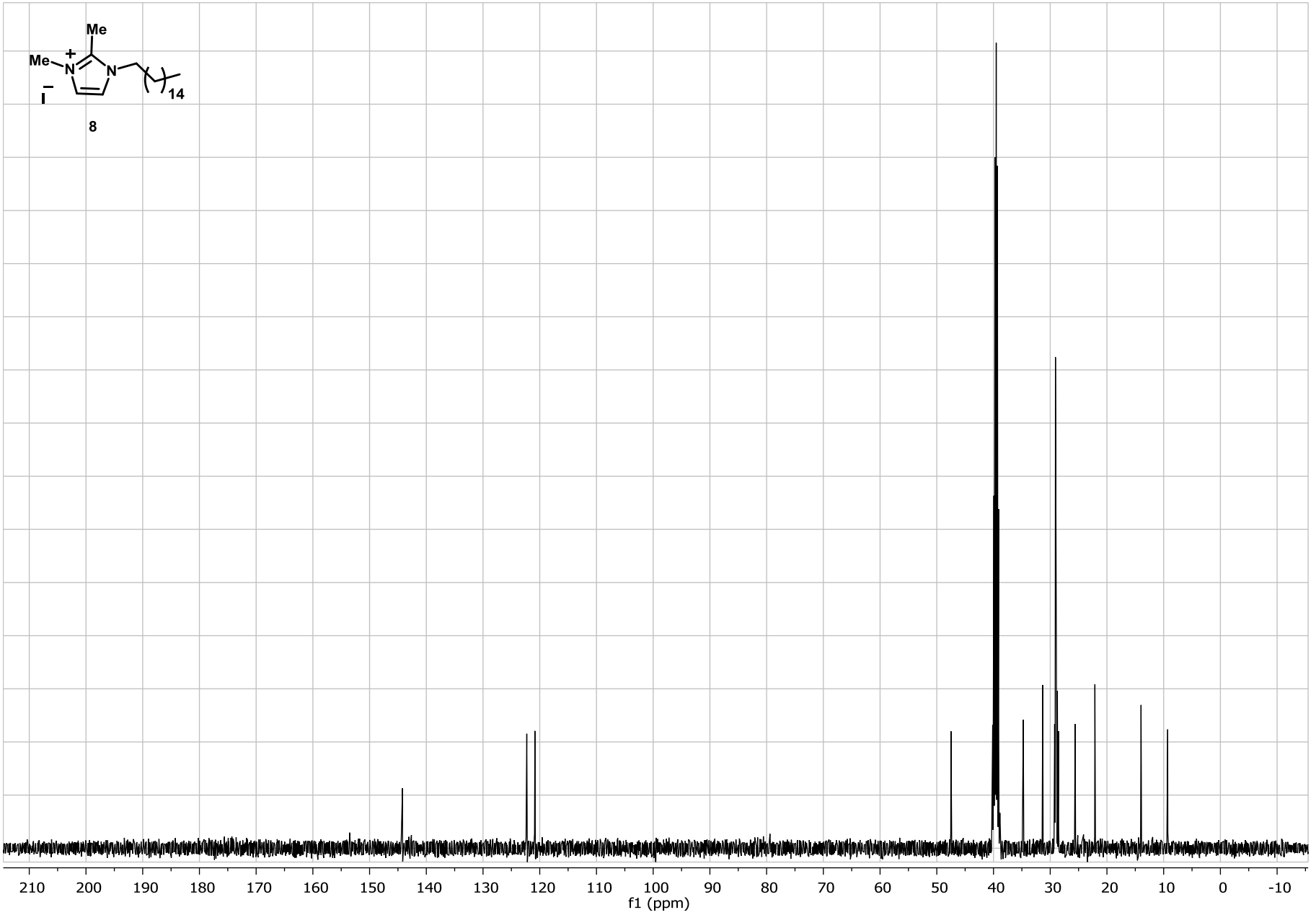
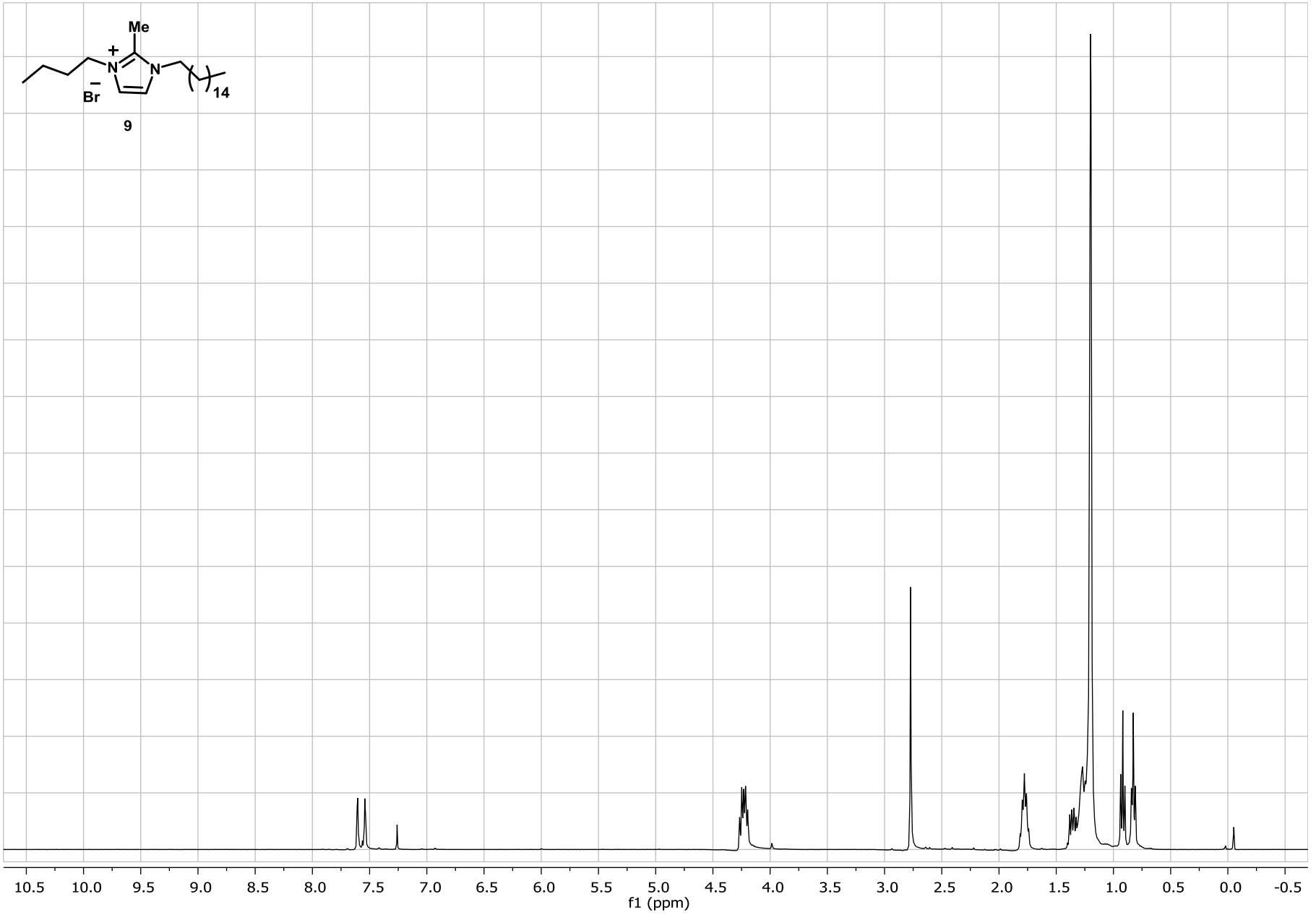
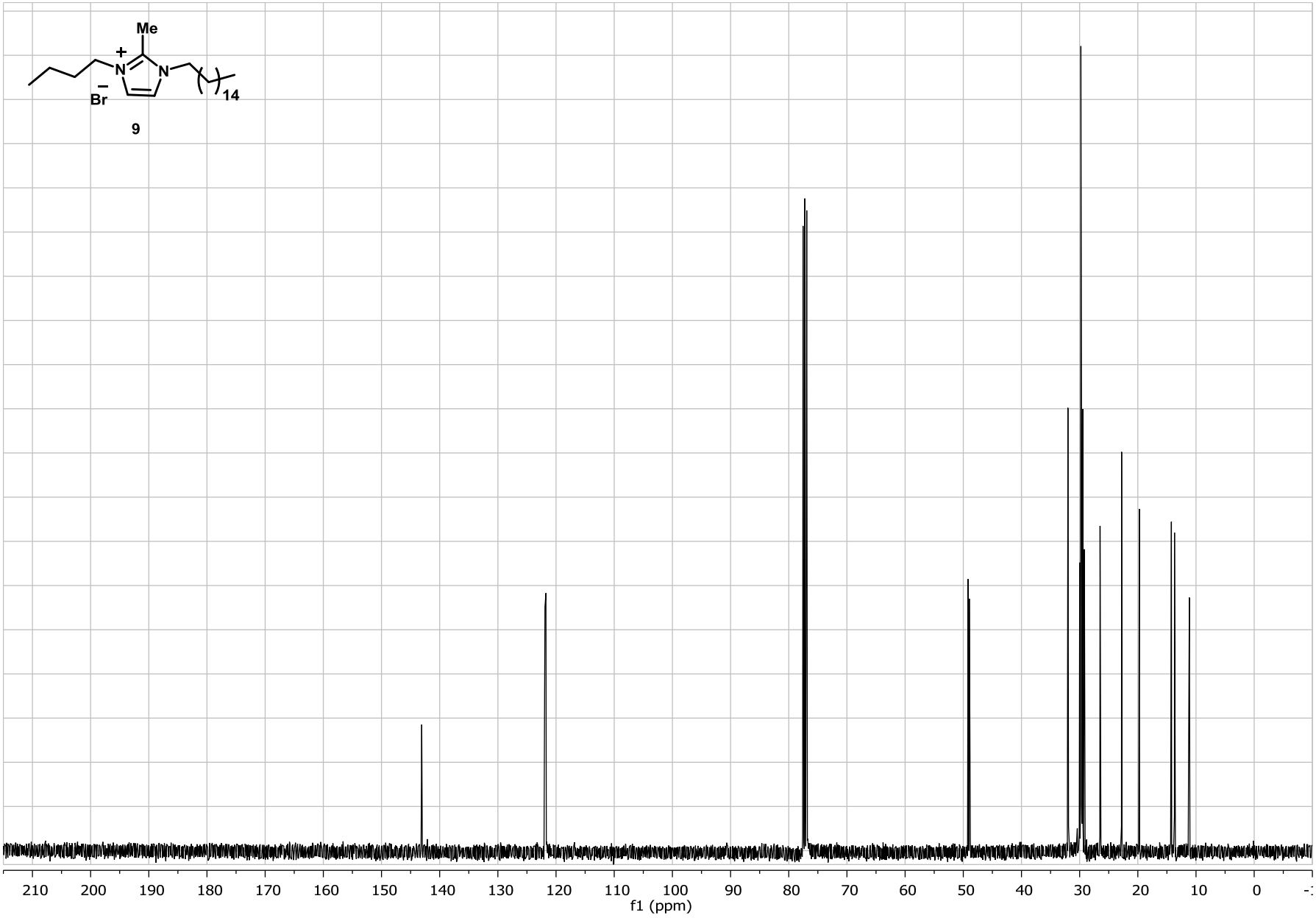
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

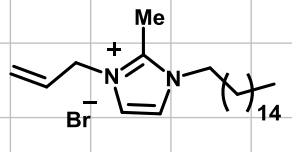

F3CO
Me
N
N
Br
14
7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
Me
N
+
N
I
−
14
8
10.5
10.0
9.5
9.0
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
0.0
-0.5
f1 (ppm)


Me
Me
N
+
N
14
I
−
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

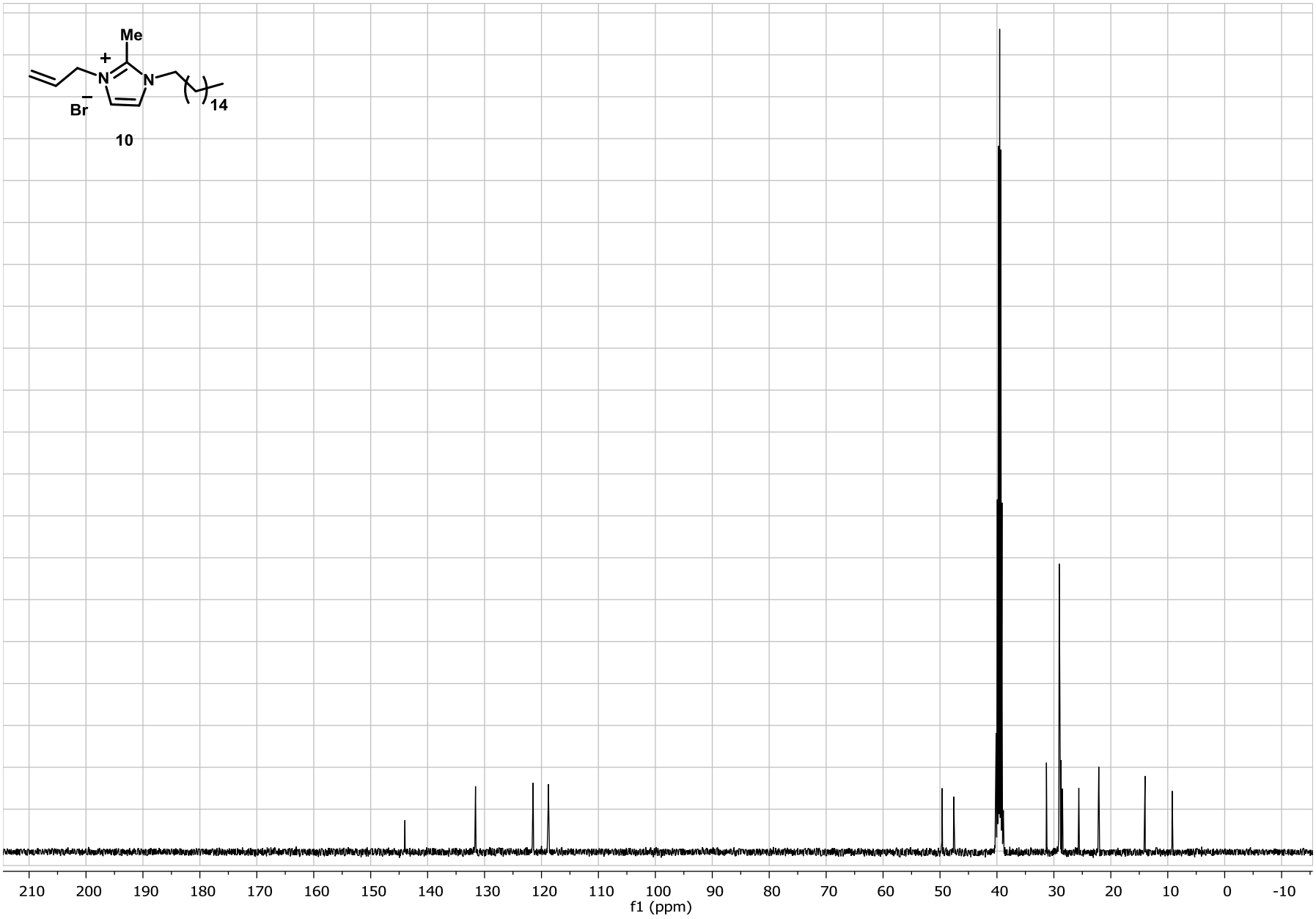

Me
N
N
Br
14
9
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

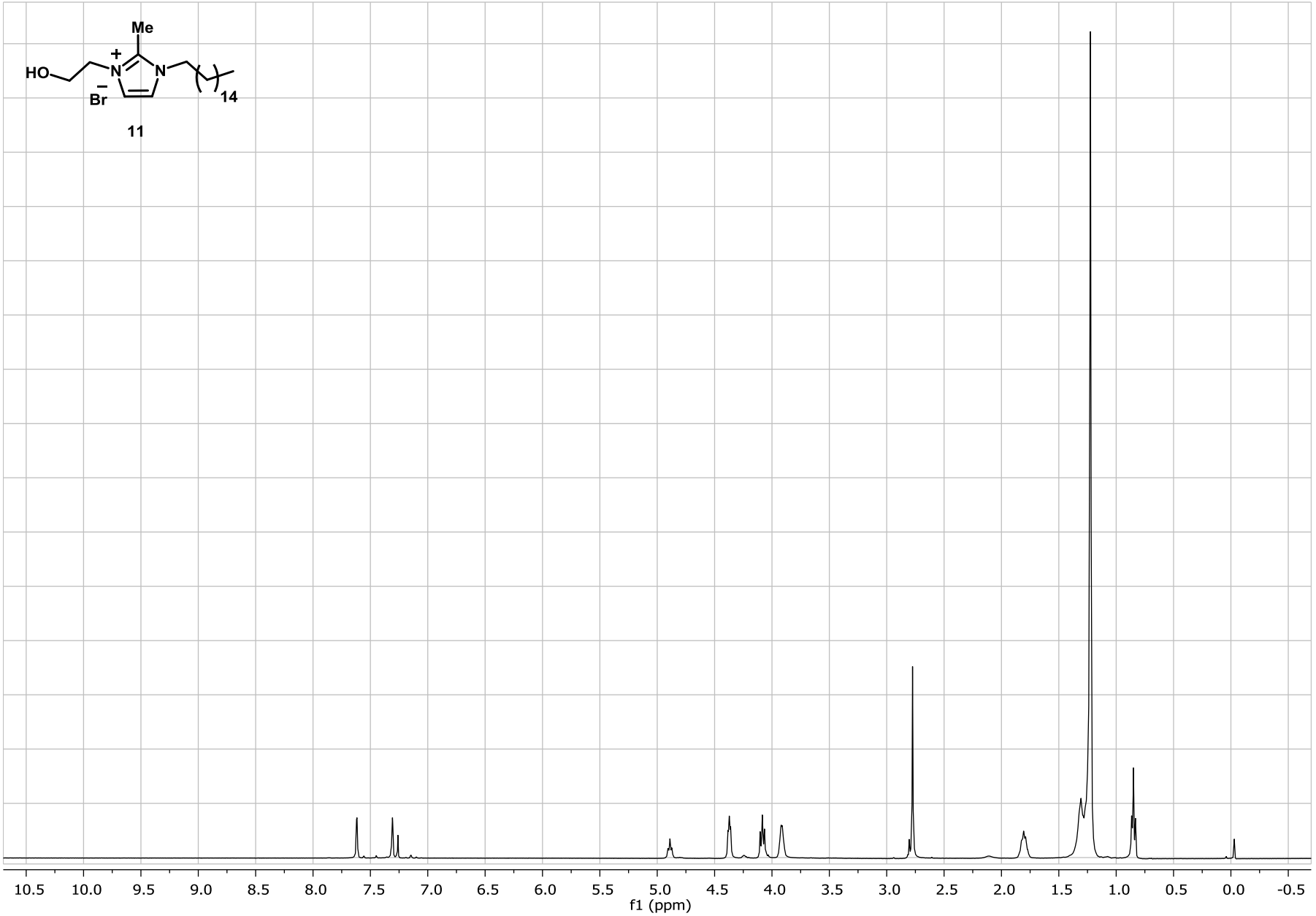

Me
N
N
Br
14
9
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

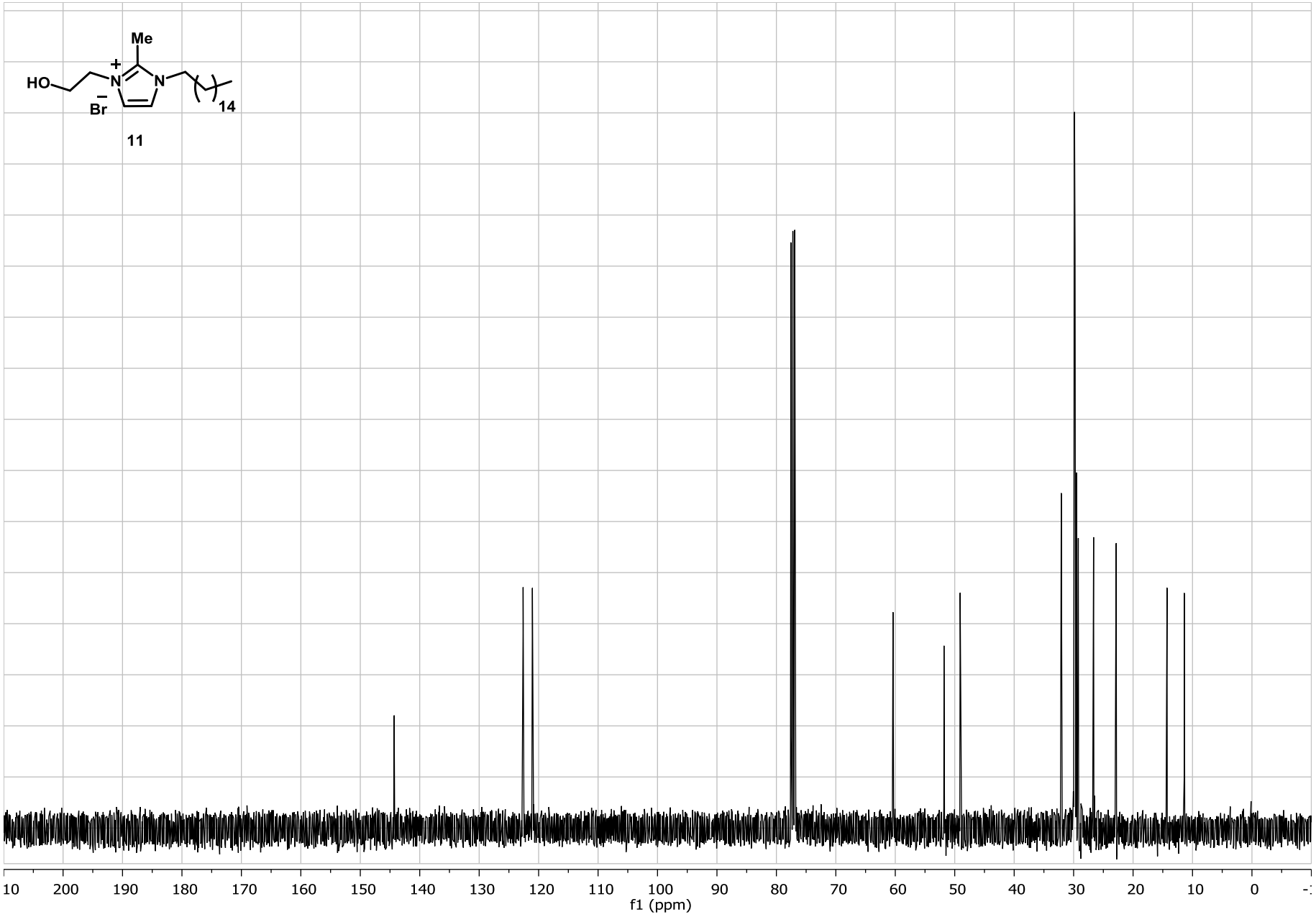

Me
N
N
Br
14

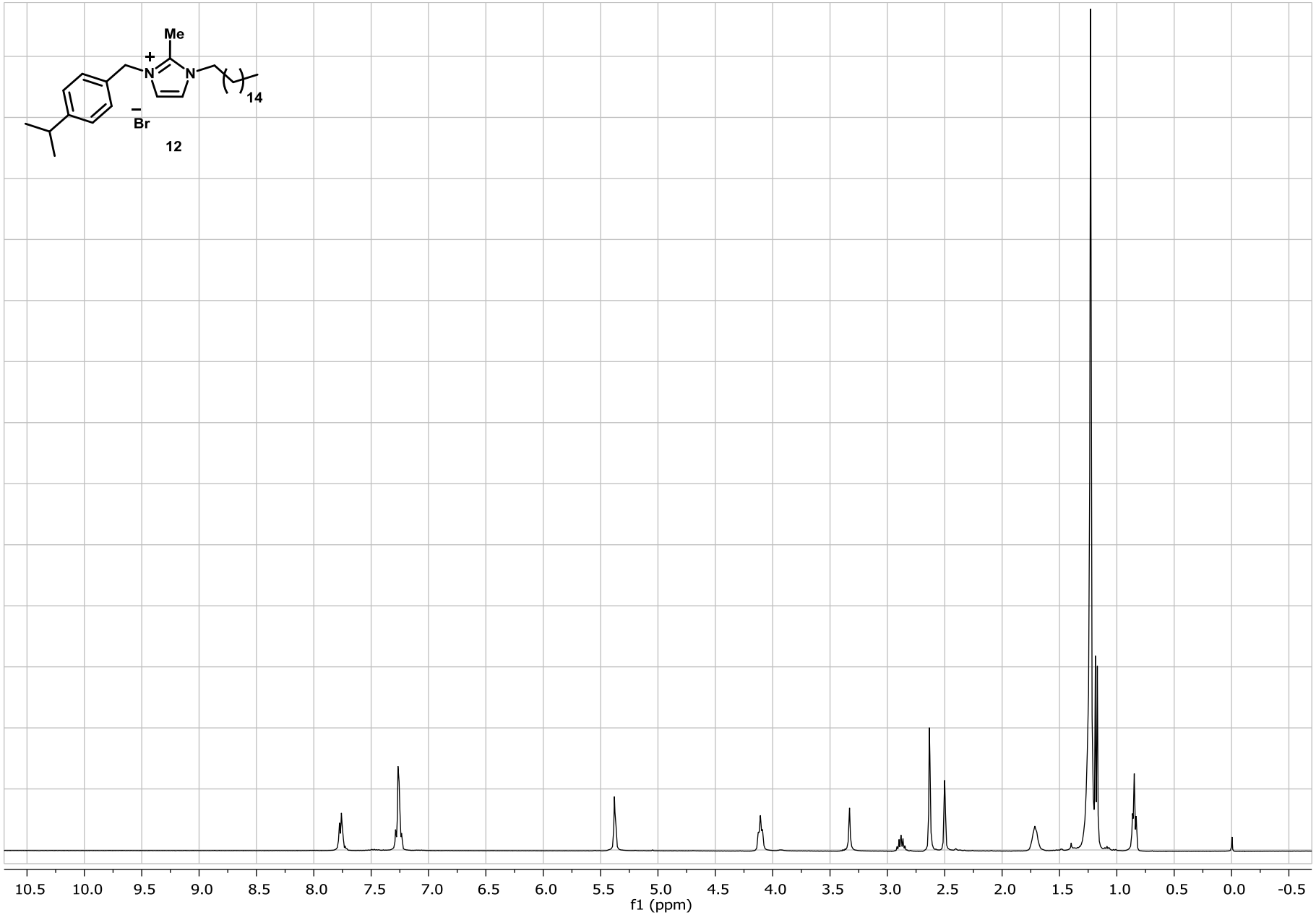
10

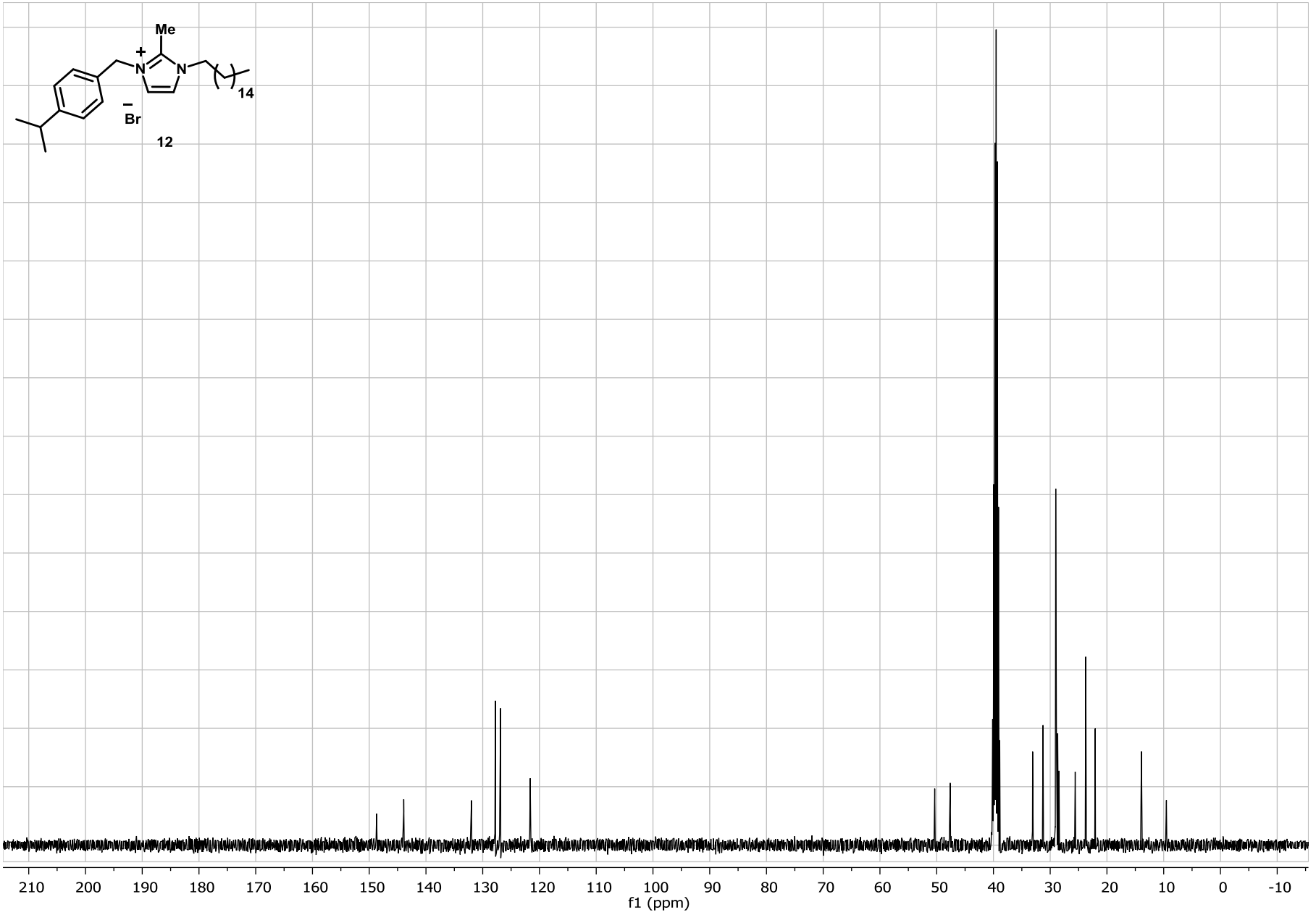
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

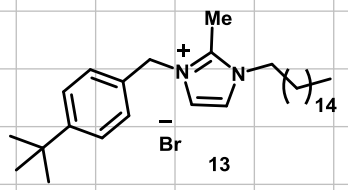

Me
+
N
N
Br
−
14
10
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
HO
N
N
Br
14
11
10.5
10.0
9.5
9.0
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
0.0
-0.5
f1 (ppm)


Me
HO
N
N
Br
14
11
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

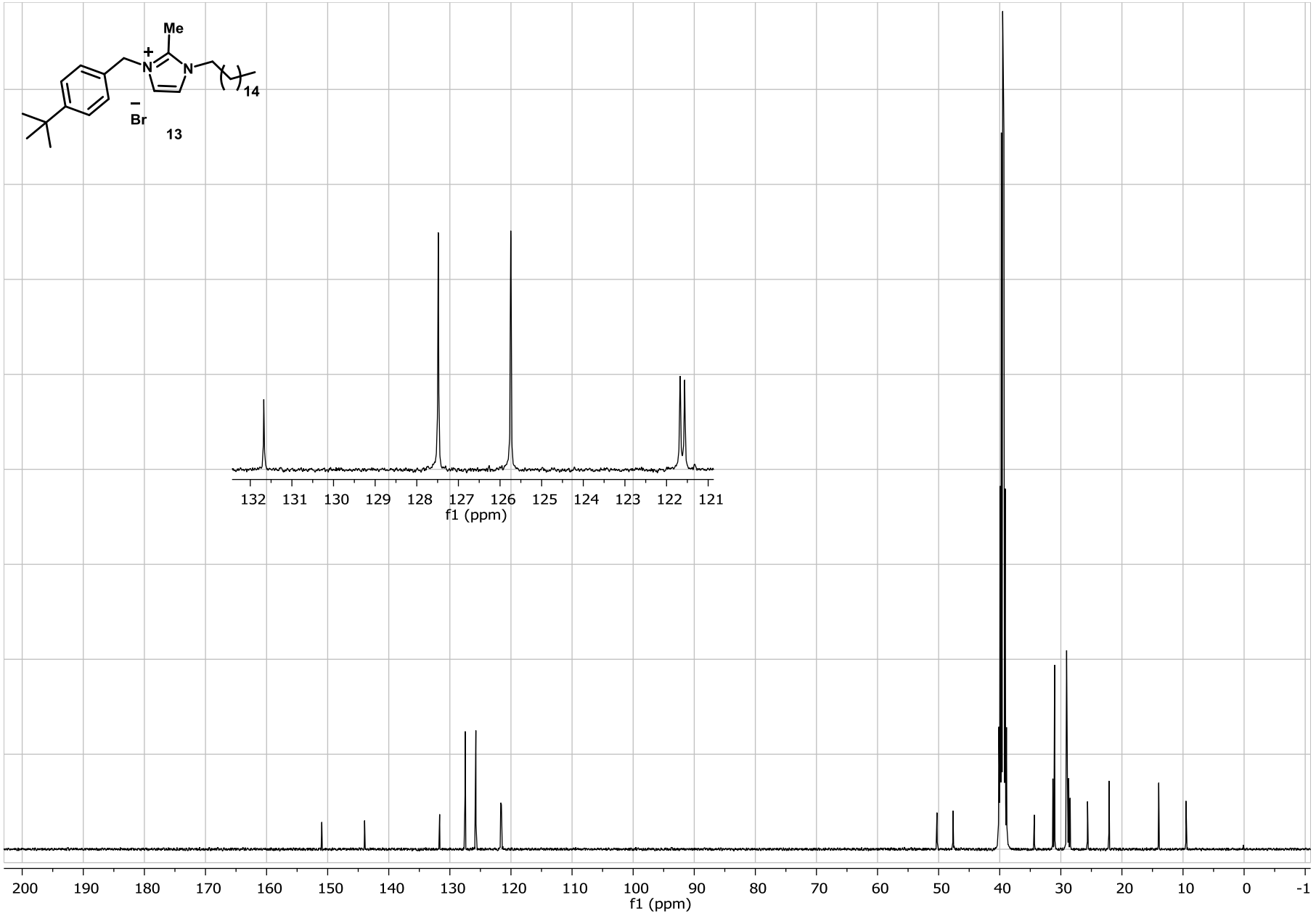

Me
N
N
14
Br
12
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

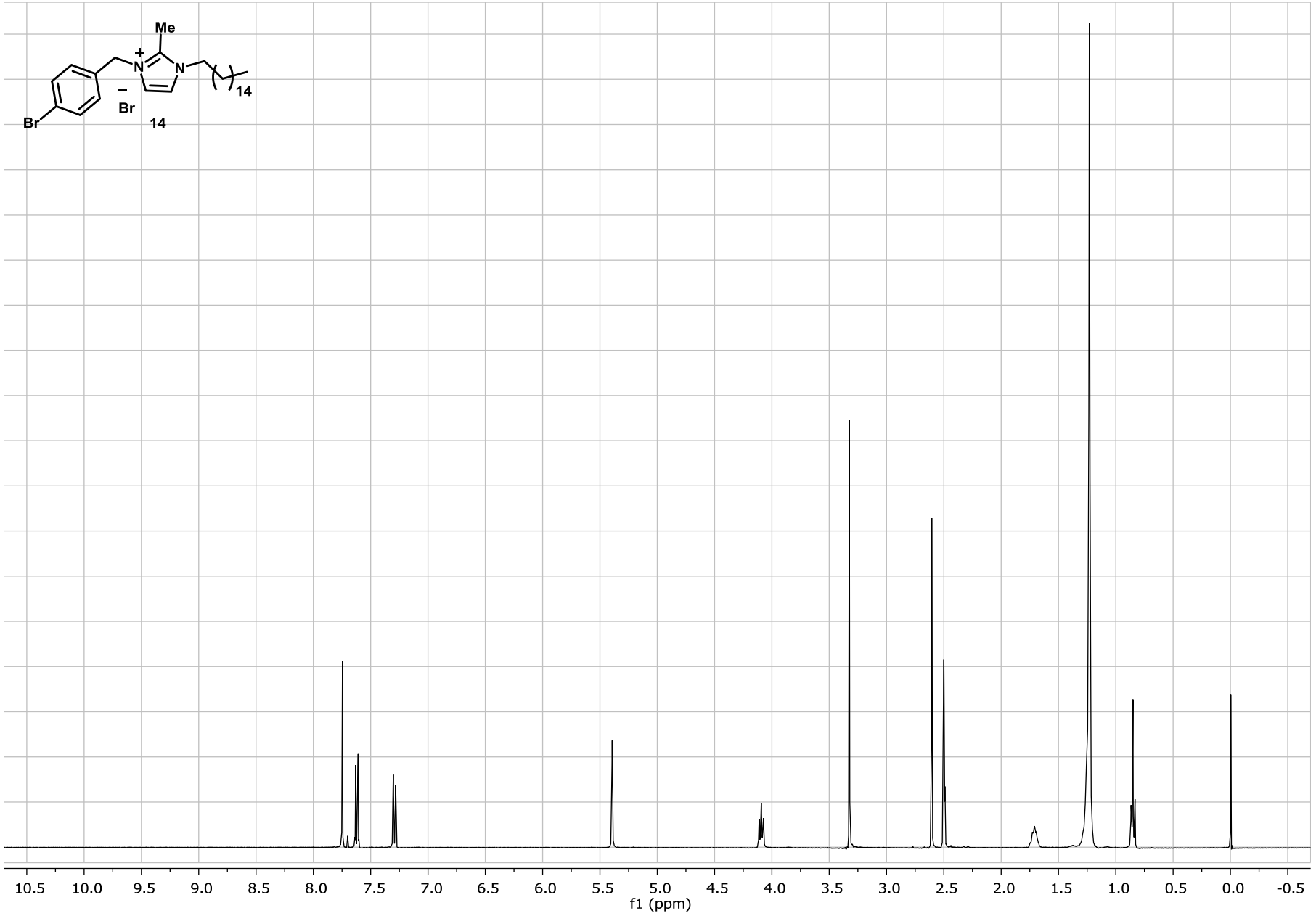

Me
N
N
14
Br
12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

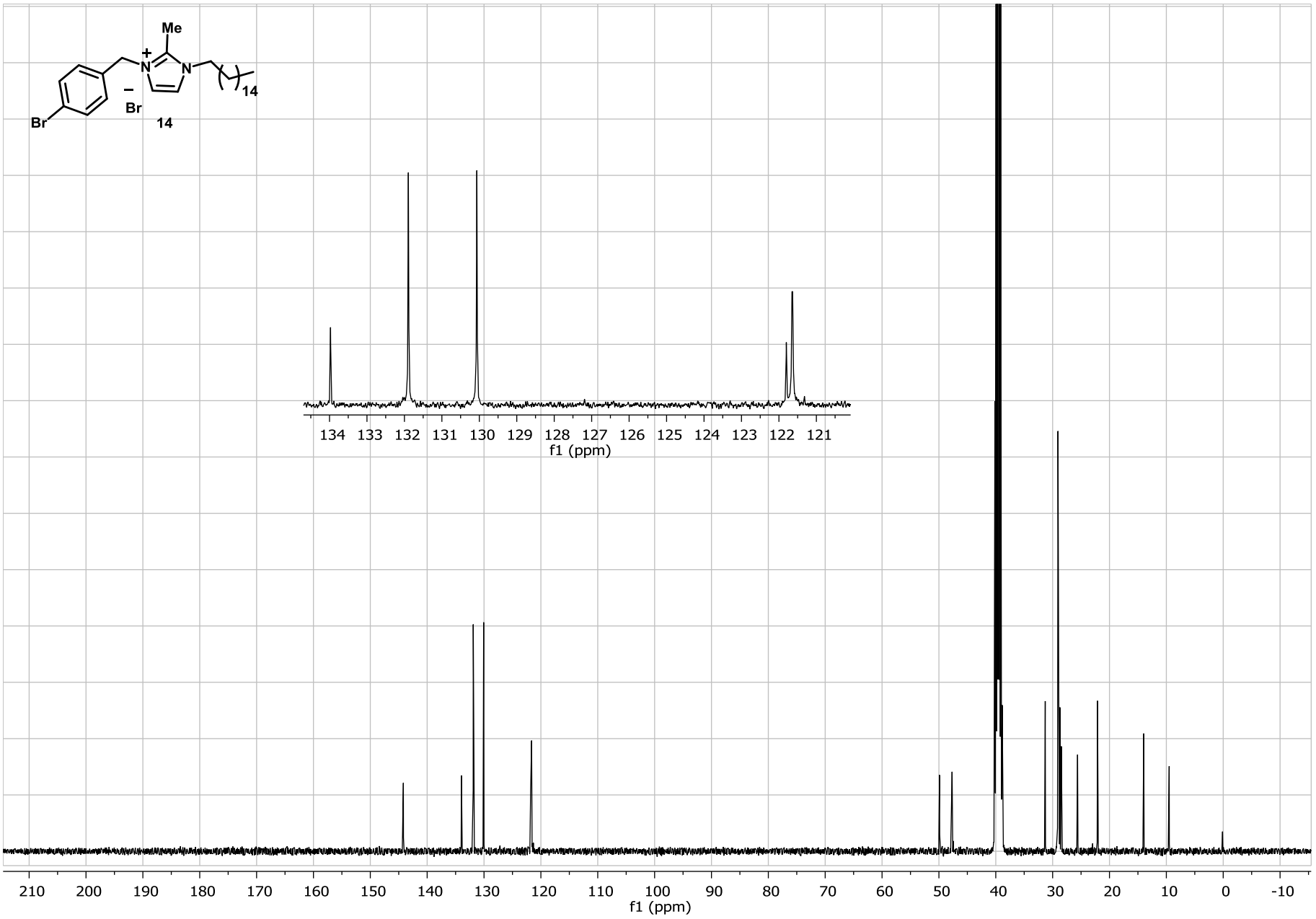

Me
N
N
14
Br

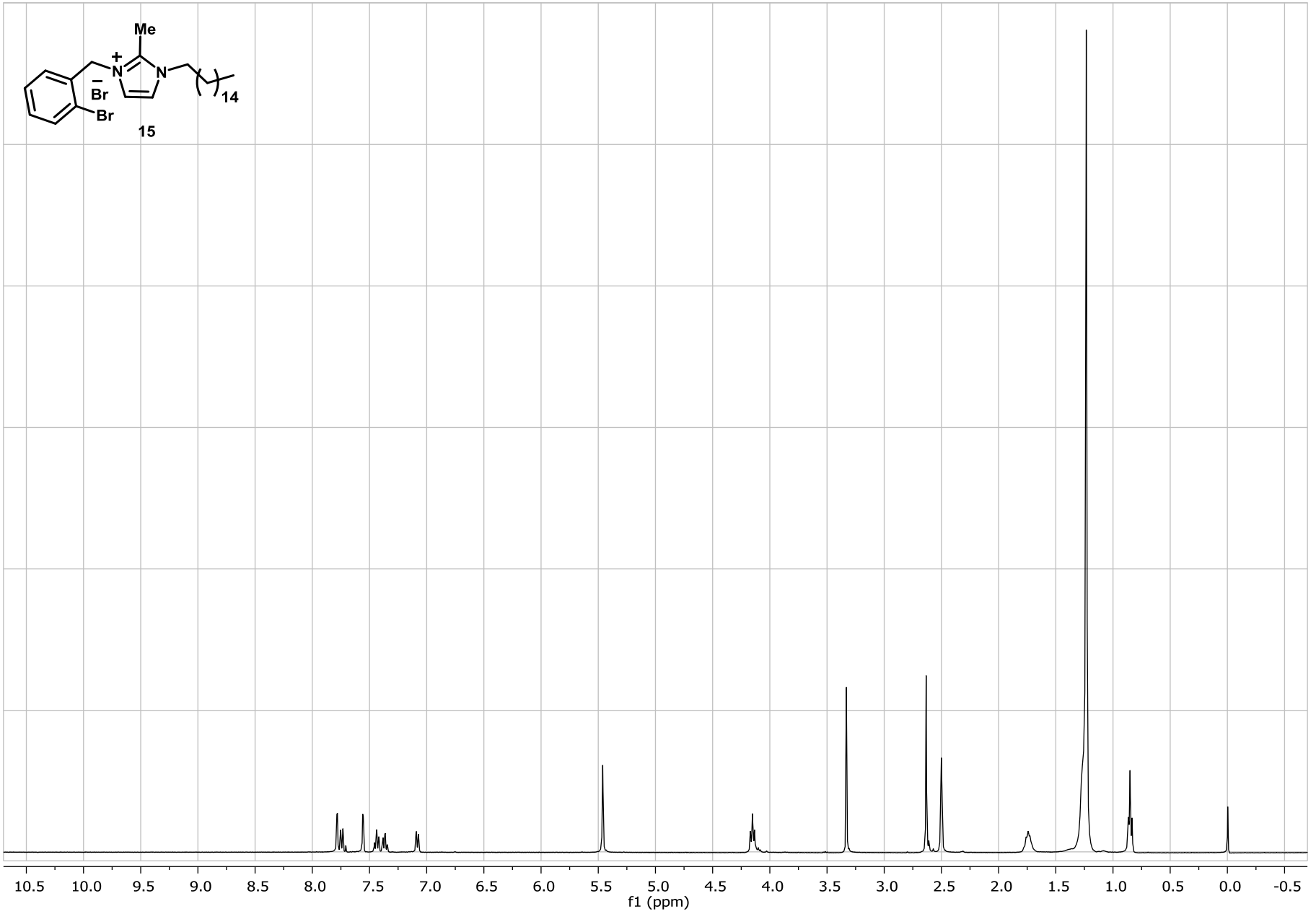
13

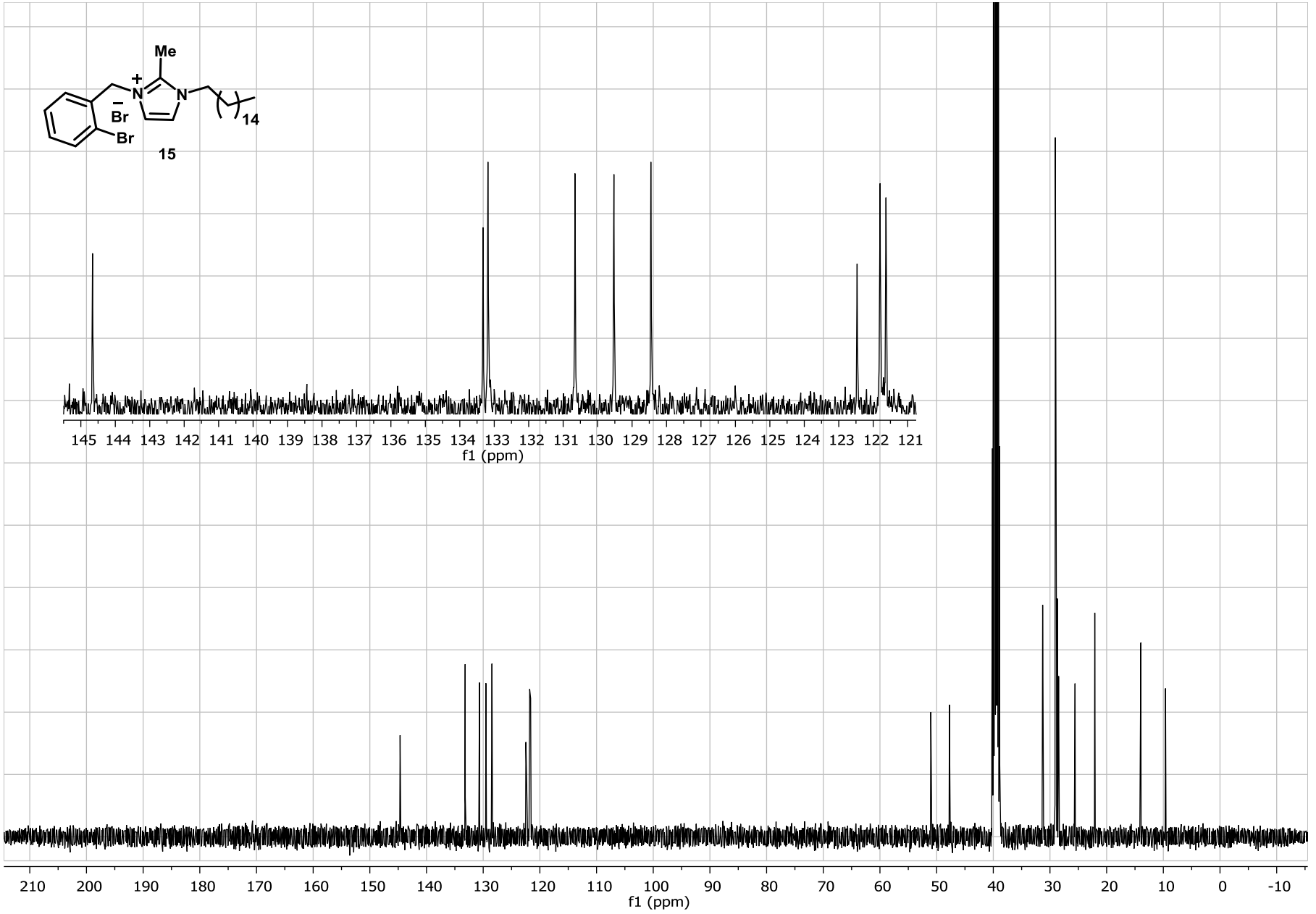
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

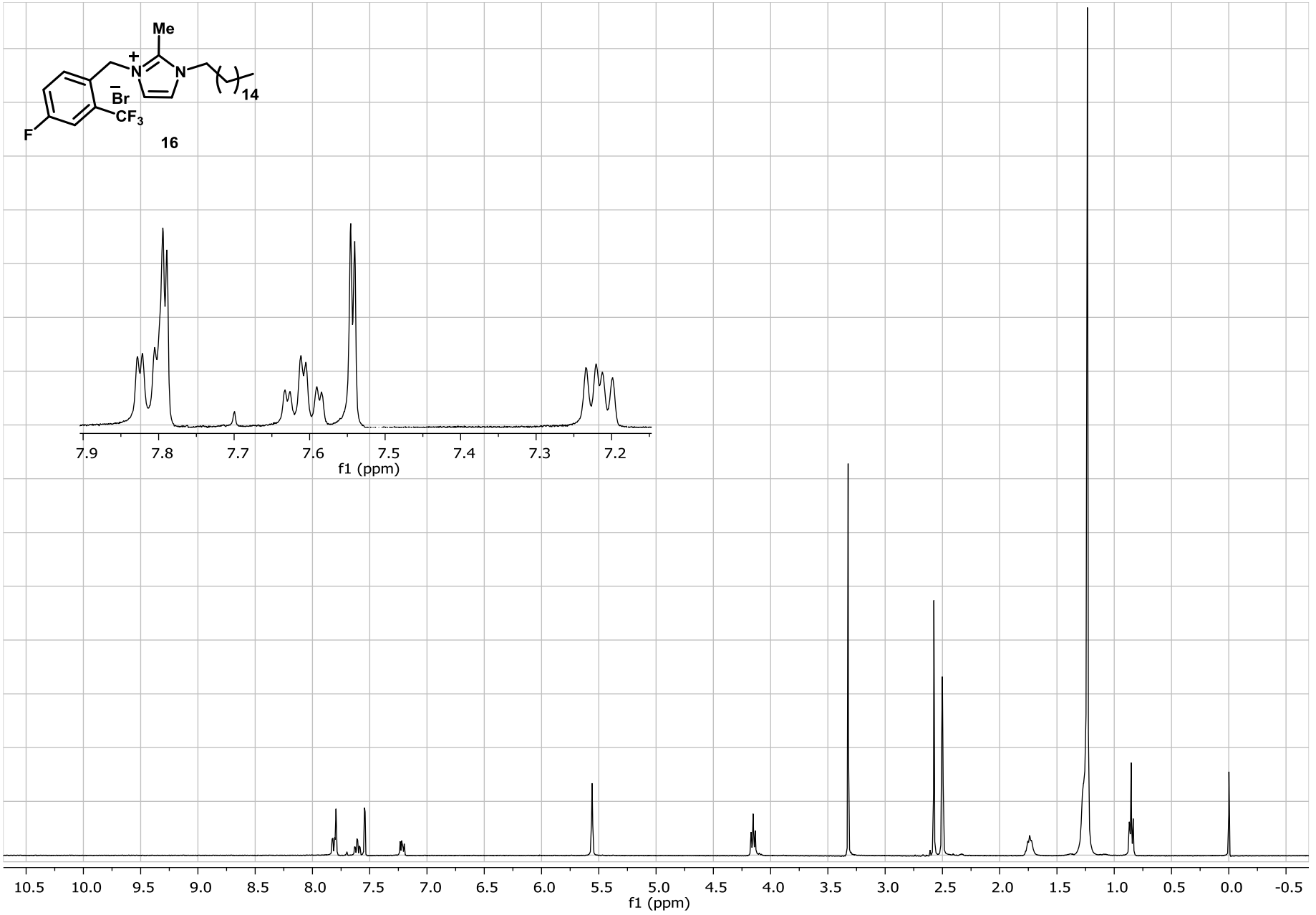

Me
N
N
14
Br
13
132 131 130 129 128 127 126 125 124 123 122 121
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

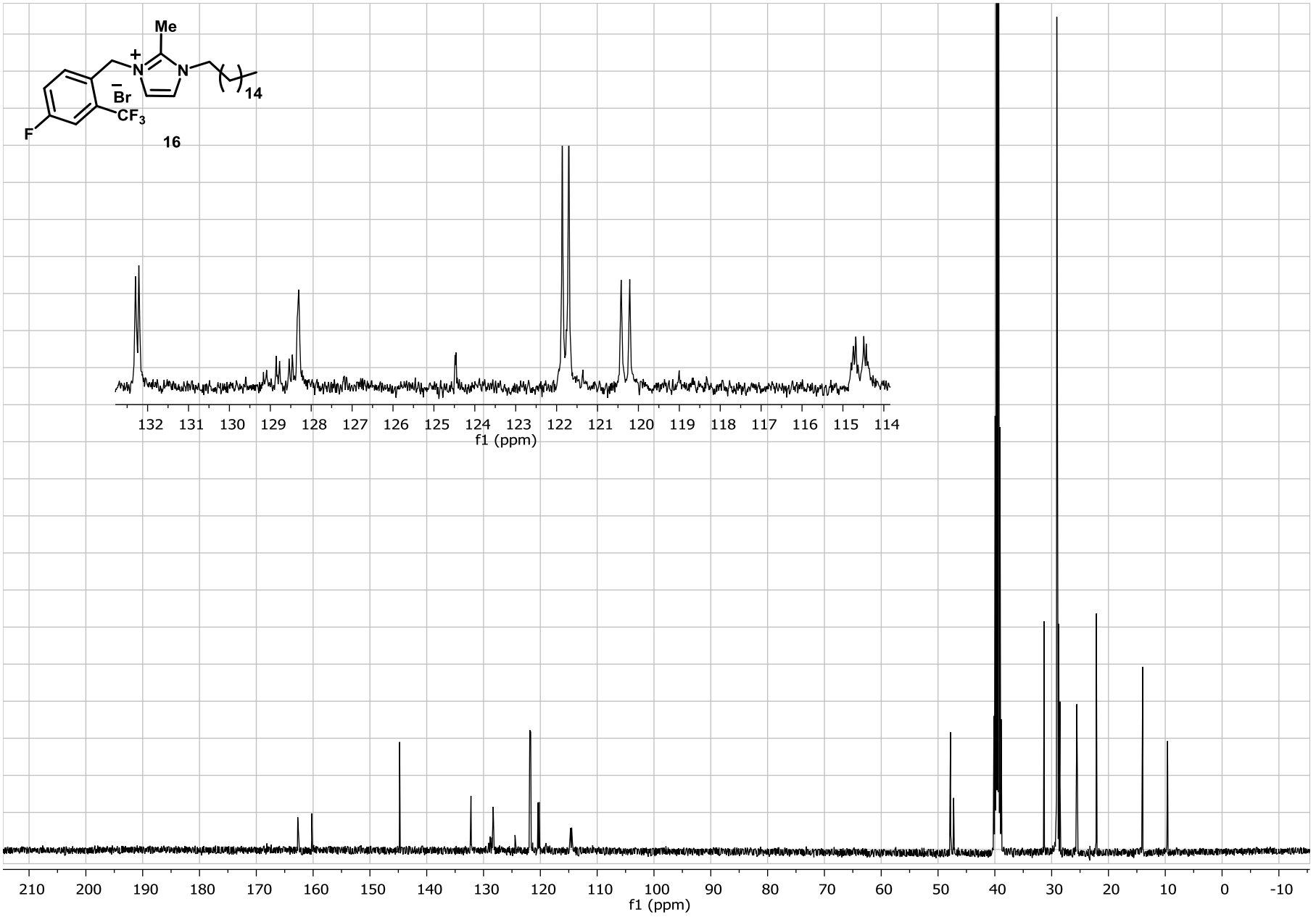

Me
N
N
14
Br
Br
14
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

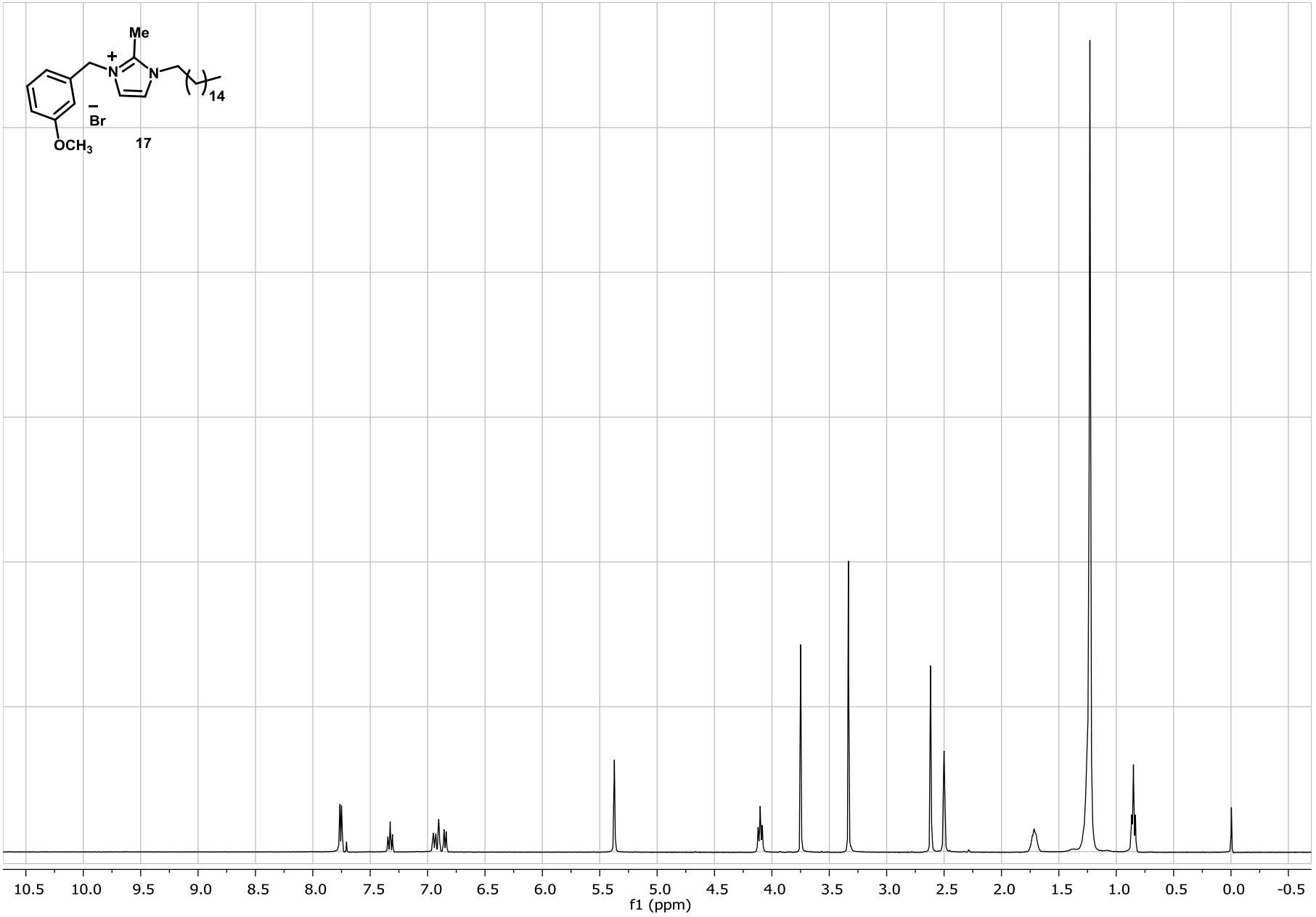

Me
N
N
14
Br
Br
14
134 133 132 131 130 129 128 127 126 125 124 123 122 121
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

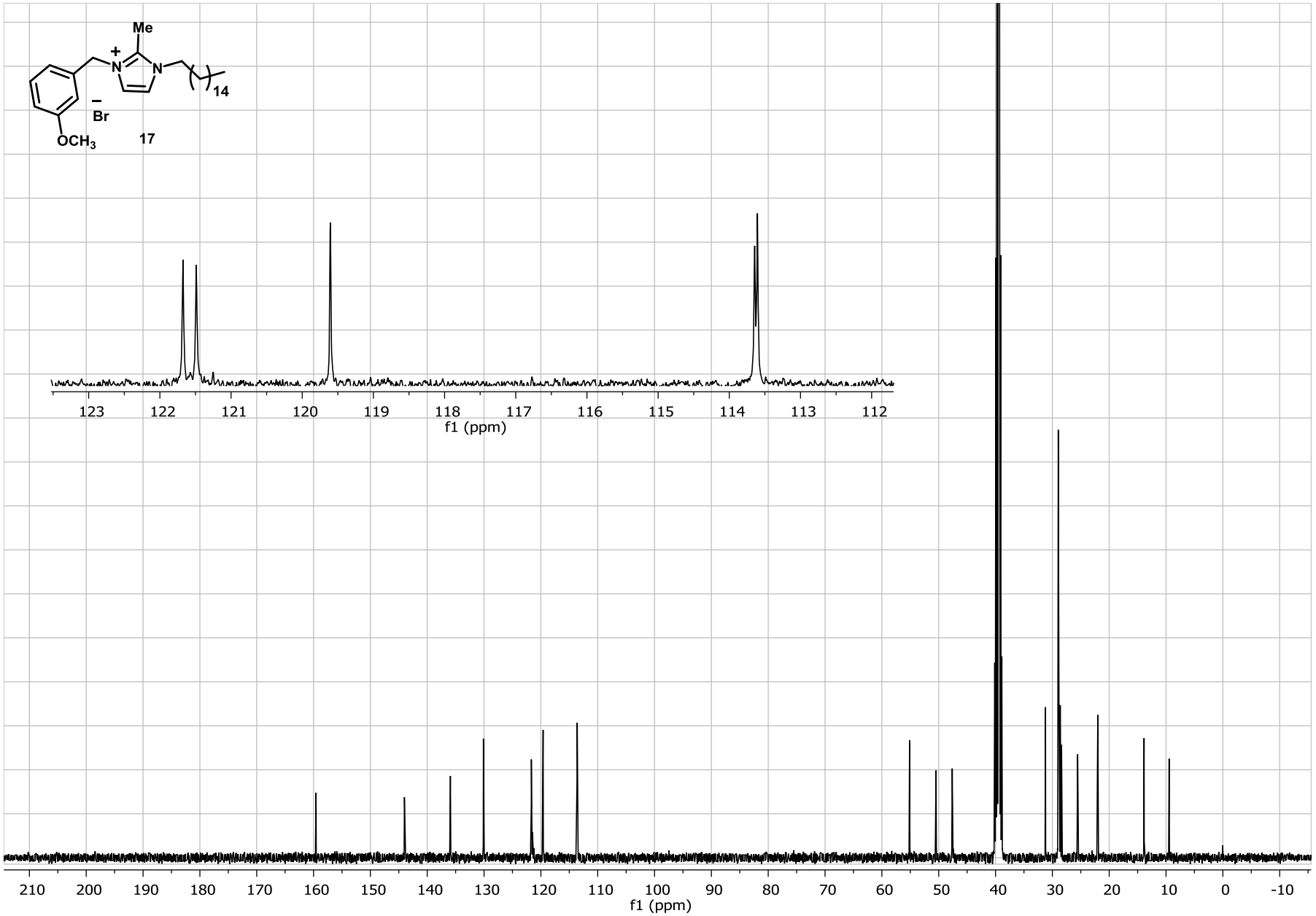

Me
N
N
Br
Br
14
15
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

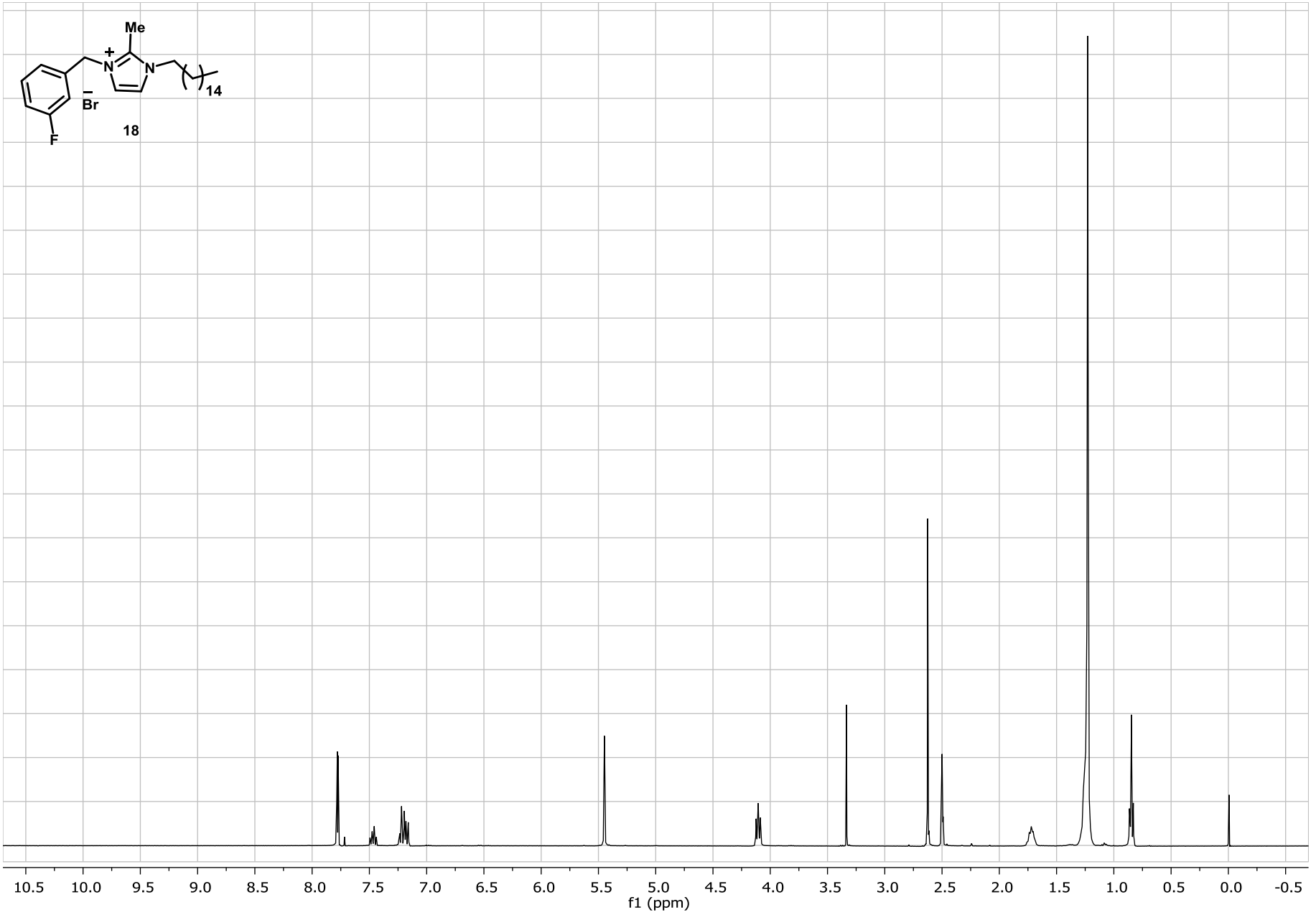

Me
Br
Br
14
15
145 144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

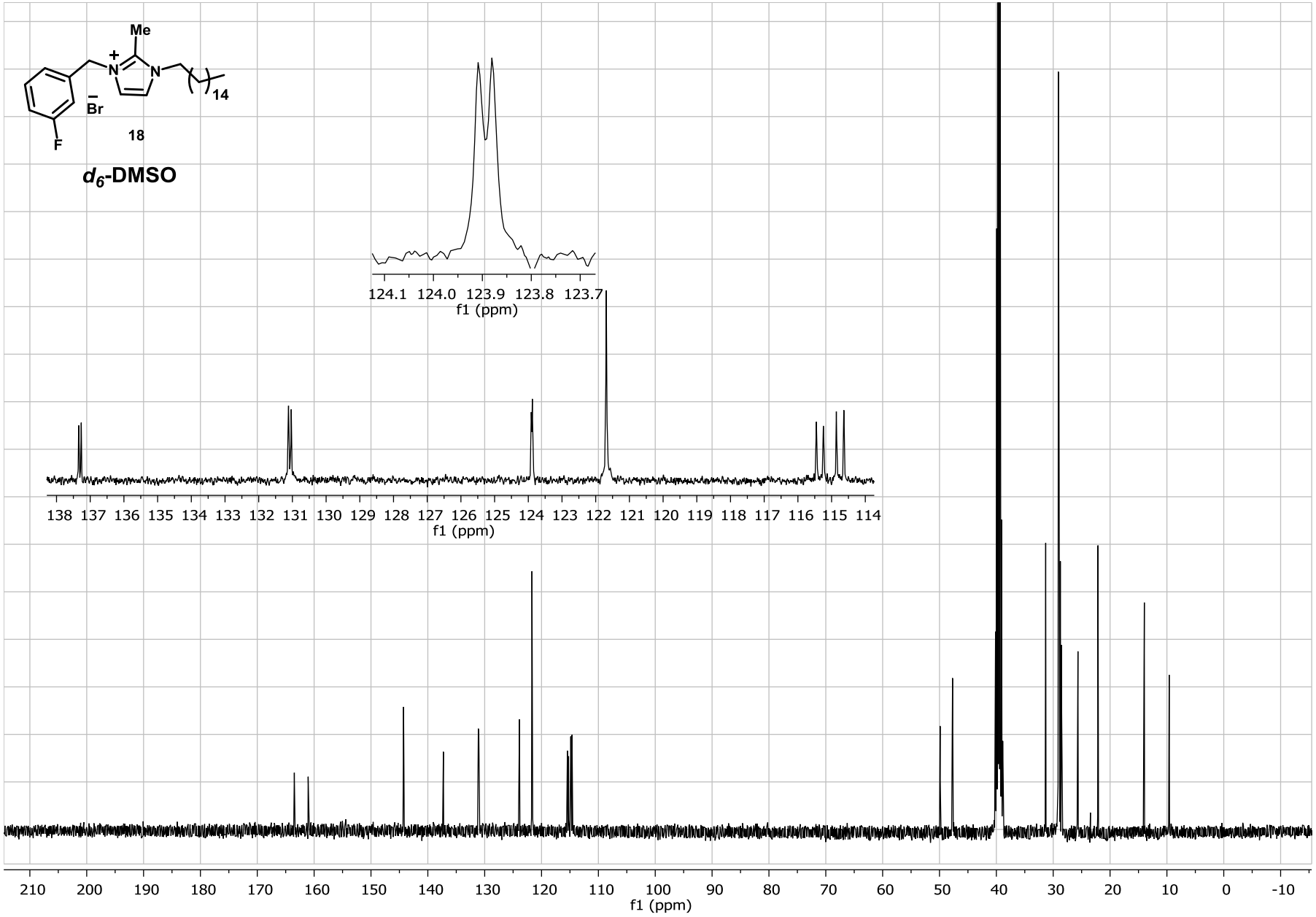

Me
Br
CF3
F
14
16
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

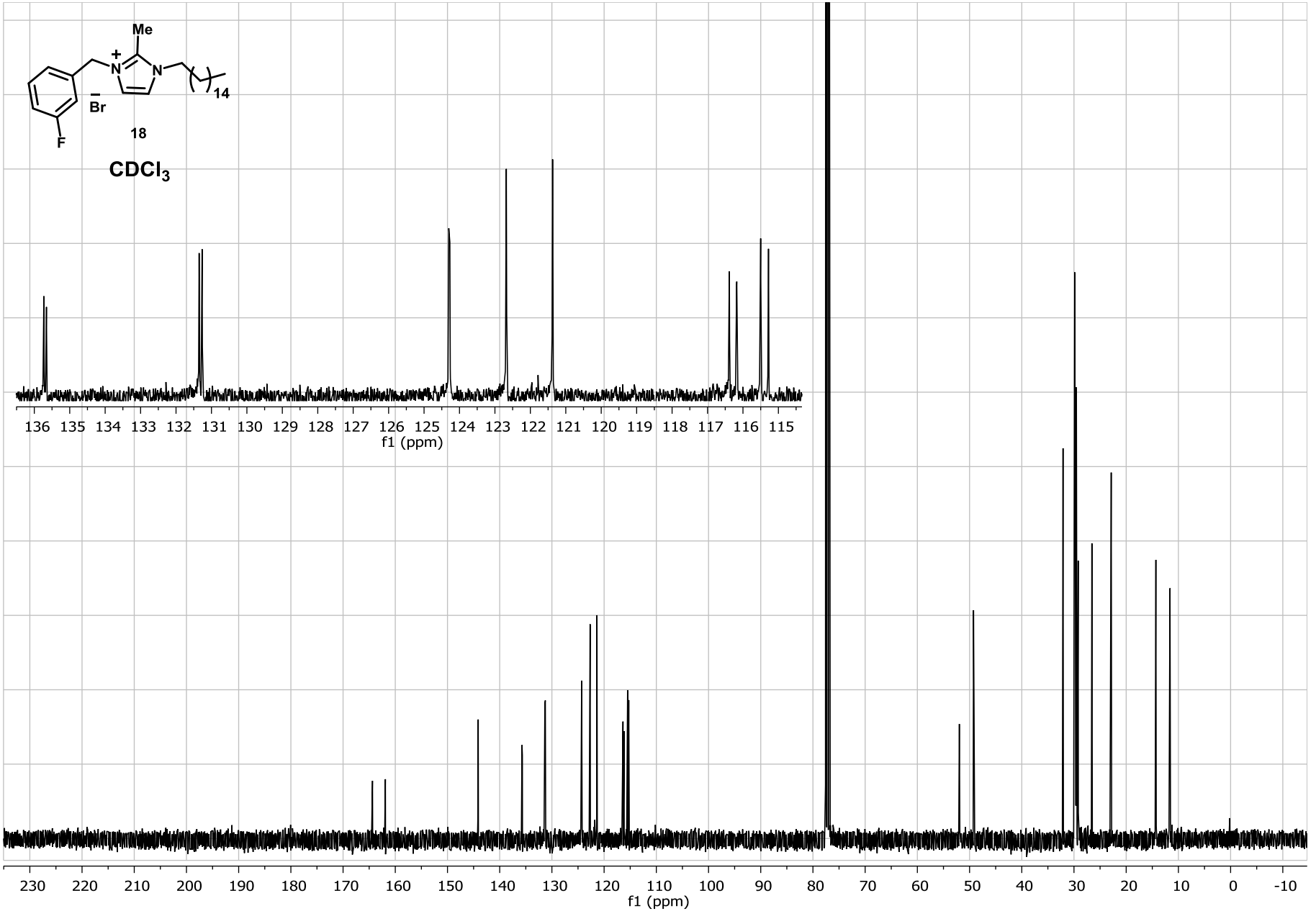

Me
N
N
14
Br
CF3
F
16
132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

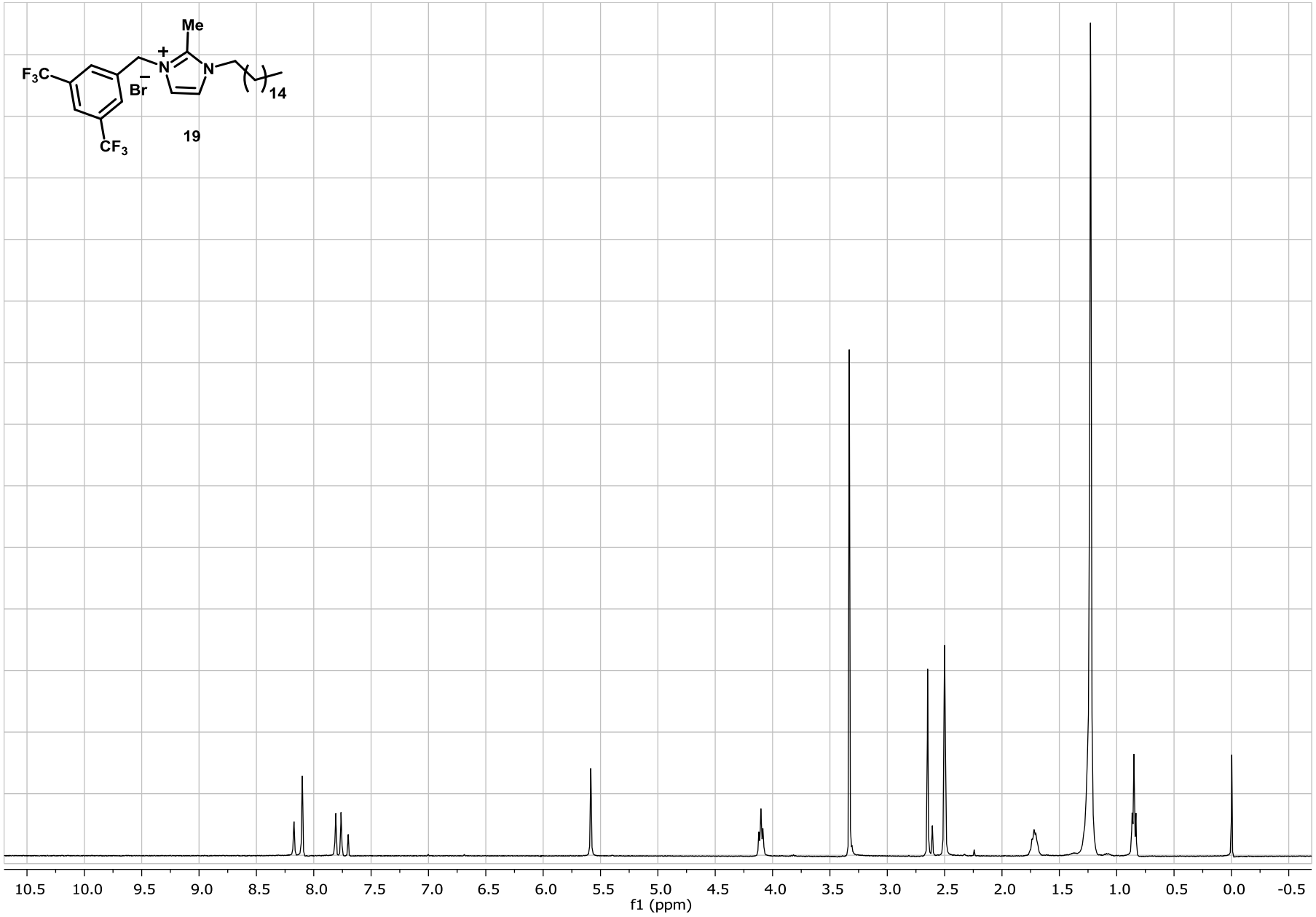

Me
N
N
14
Br
OCH3
17
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

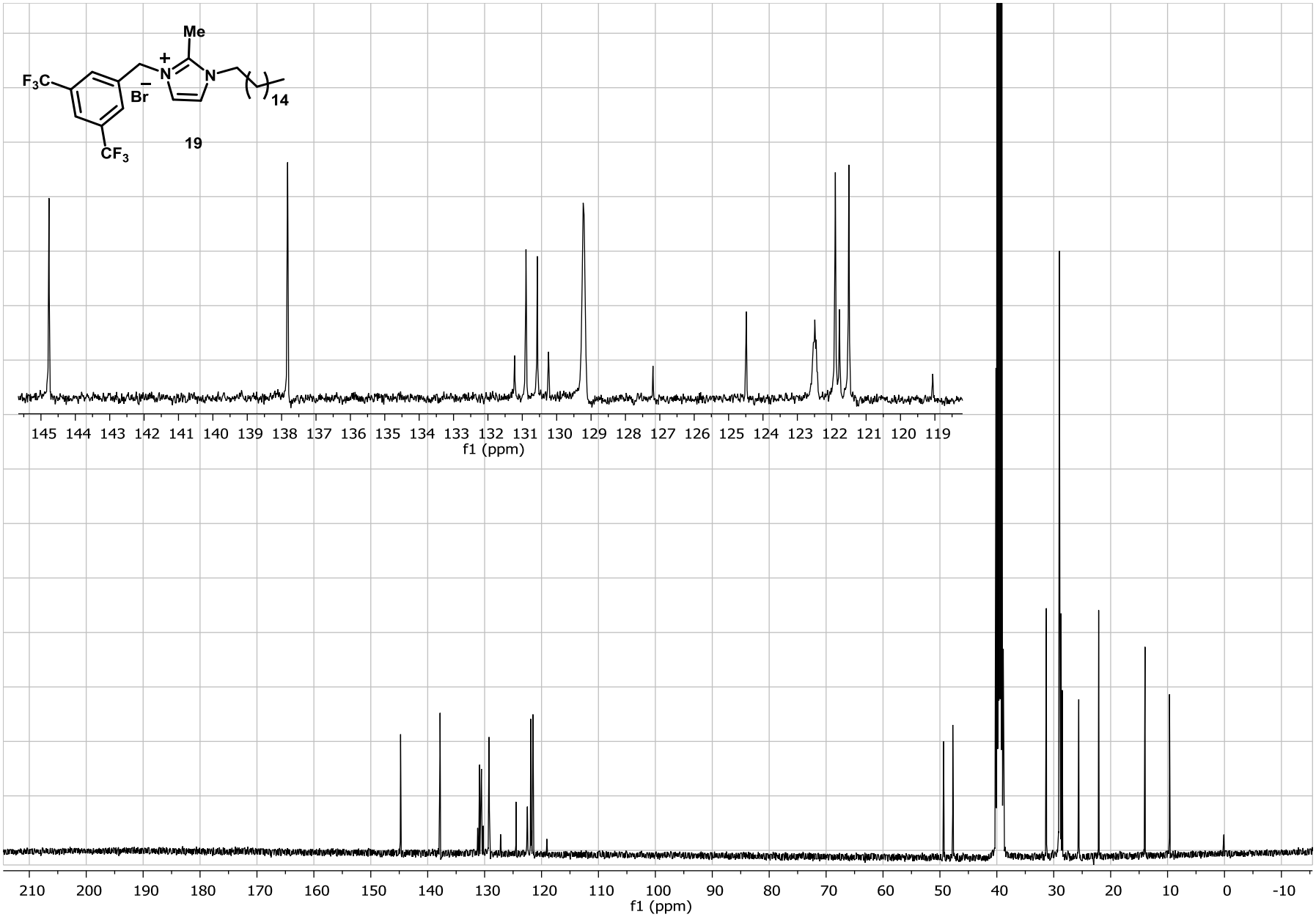

Me
N
N
14
Br
OCH3
17
123
122
121
120
119
118
117
116
115
114
113
112
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

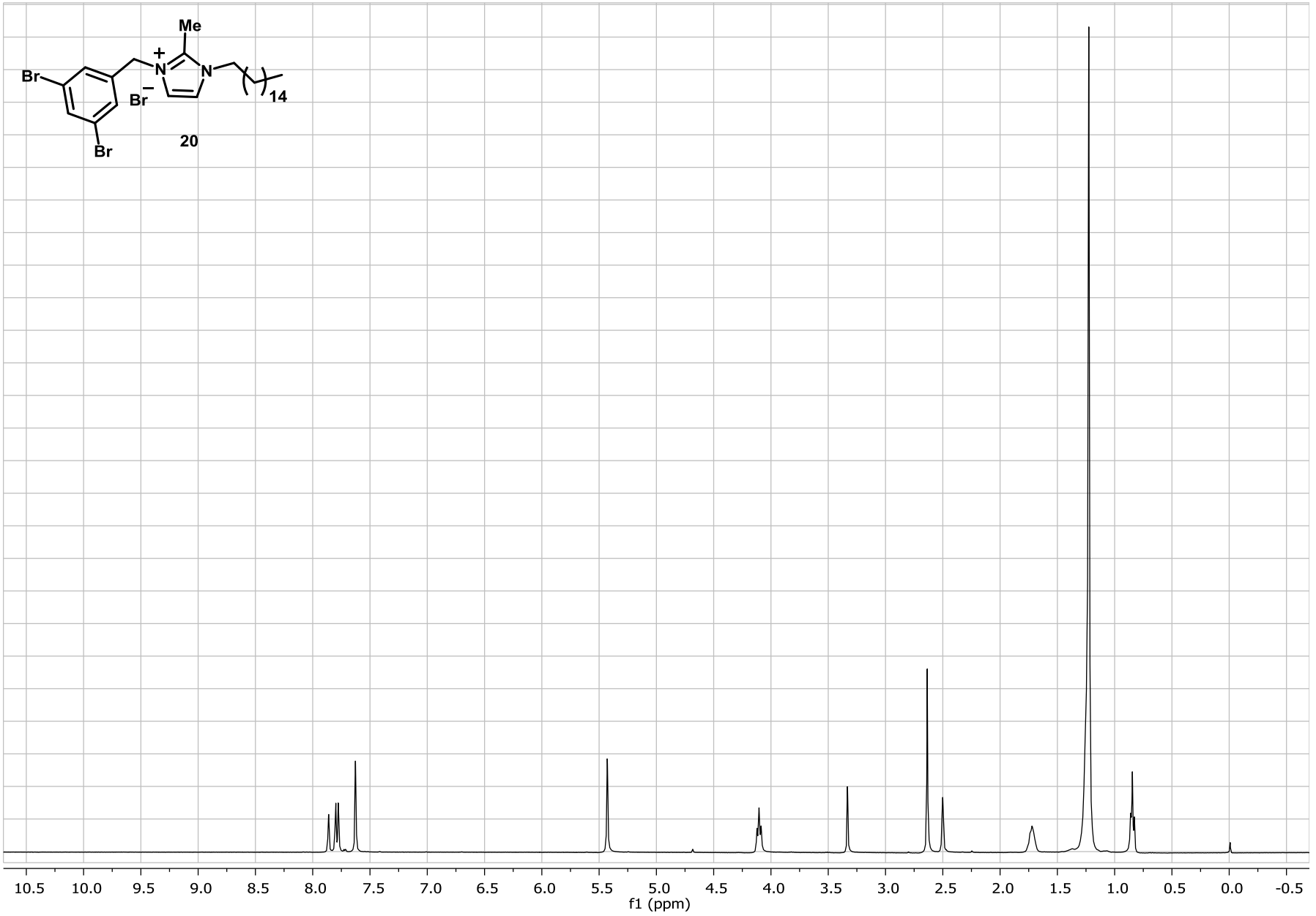

Me
N
N
14
Br
F
18
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

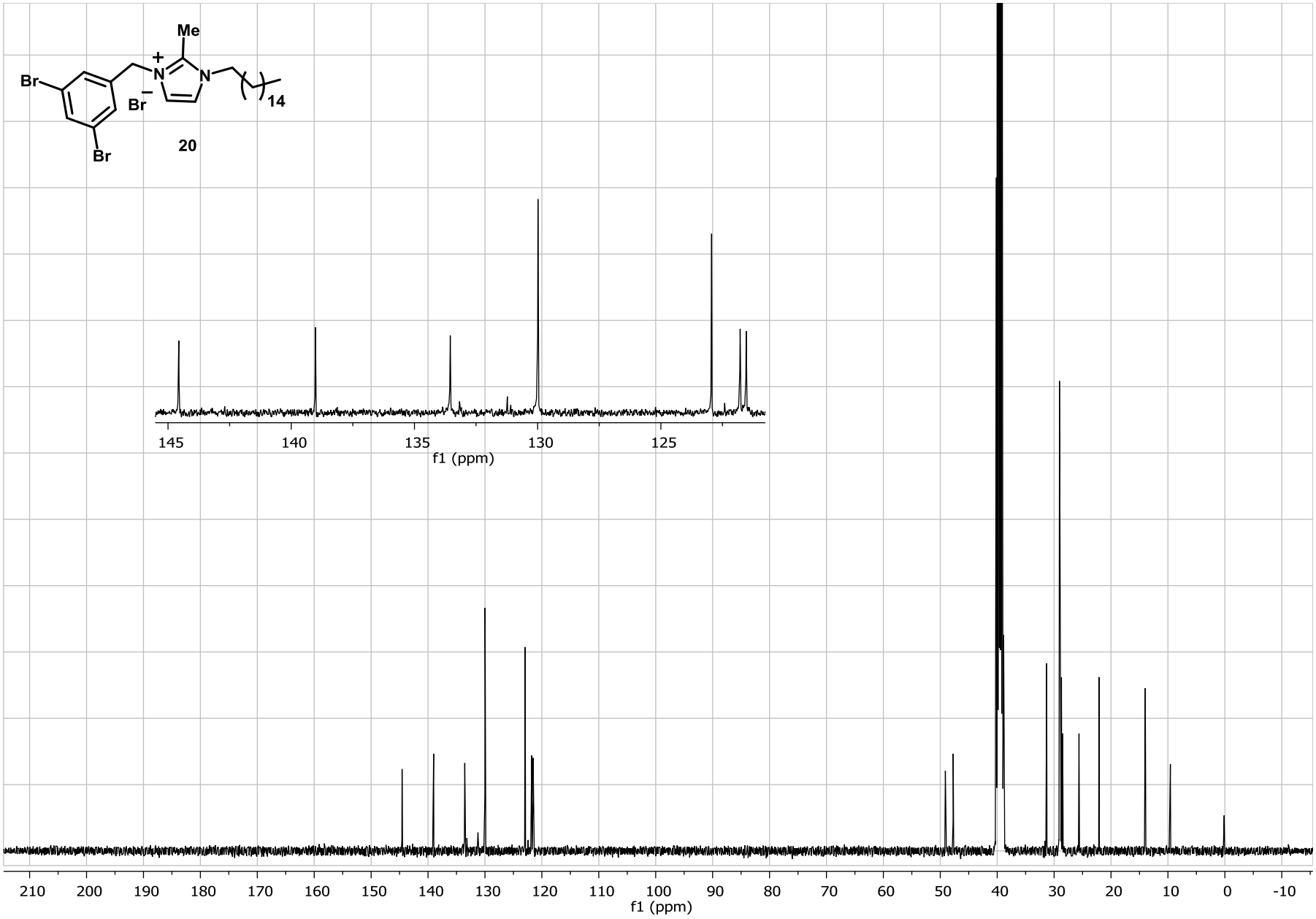

Me
N
N
14
Br
F
18
d_6-DMSO
124.1 124.0 123.9 123.8 123.7
f1 (ppm)
138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

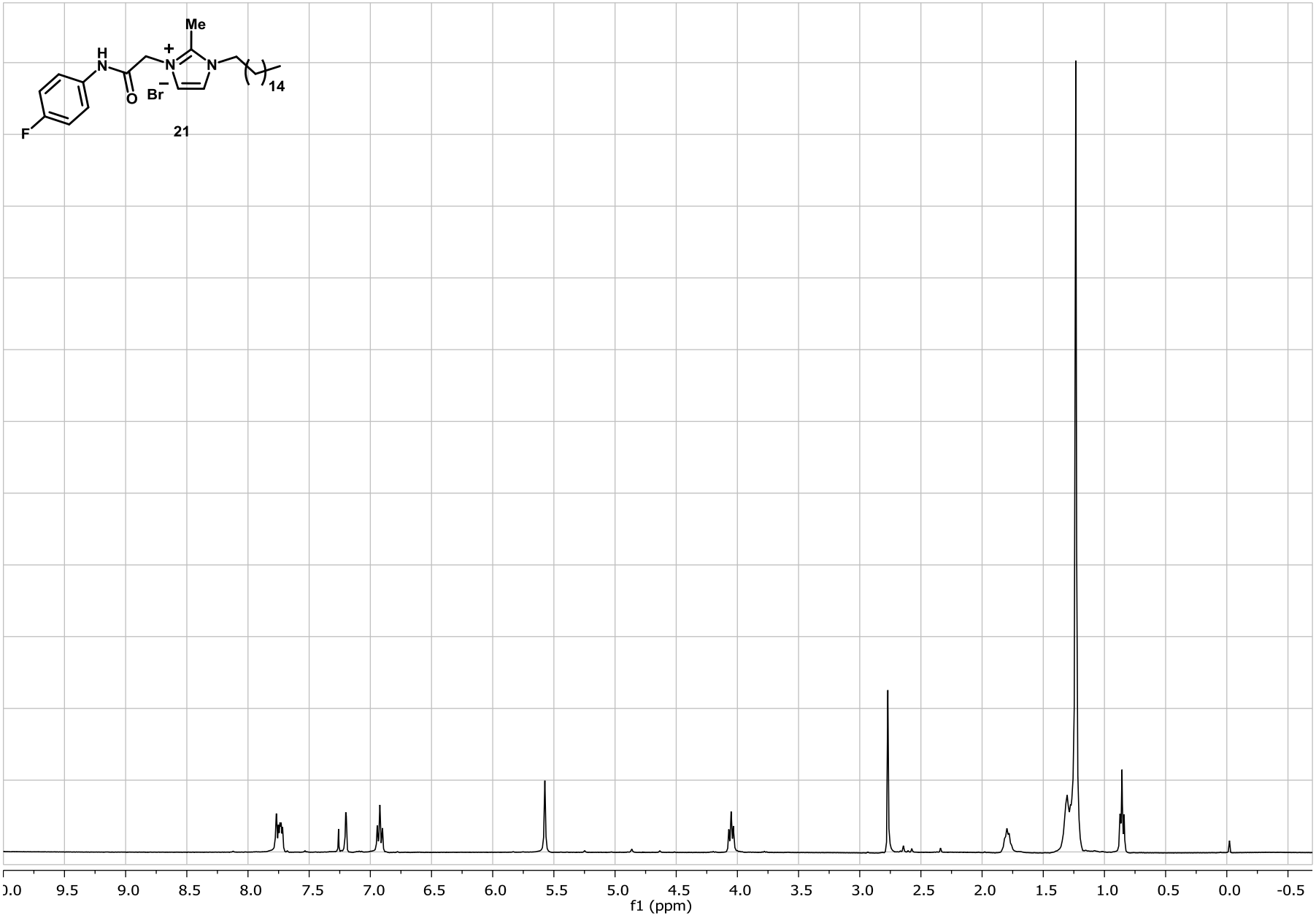

Me
N
N
14
Br
F
18
CDCl3
136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

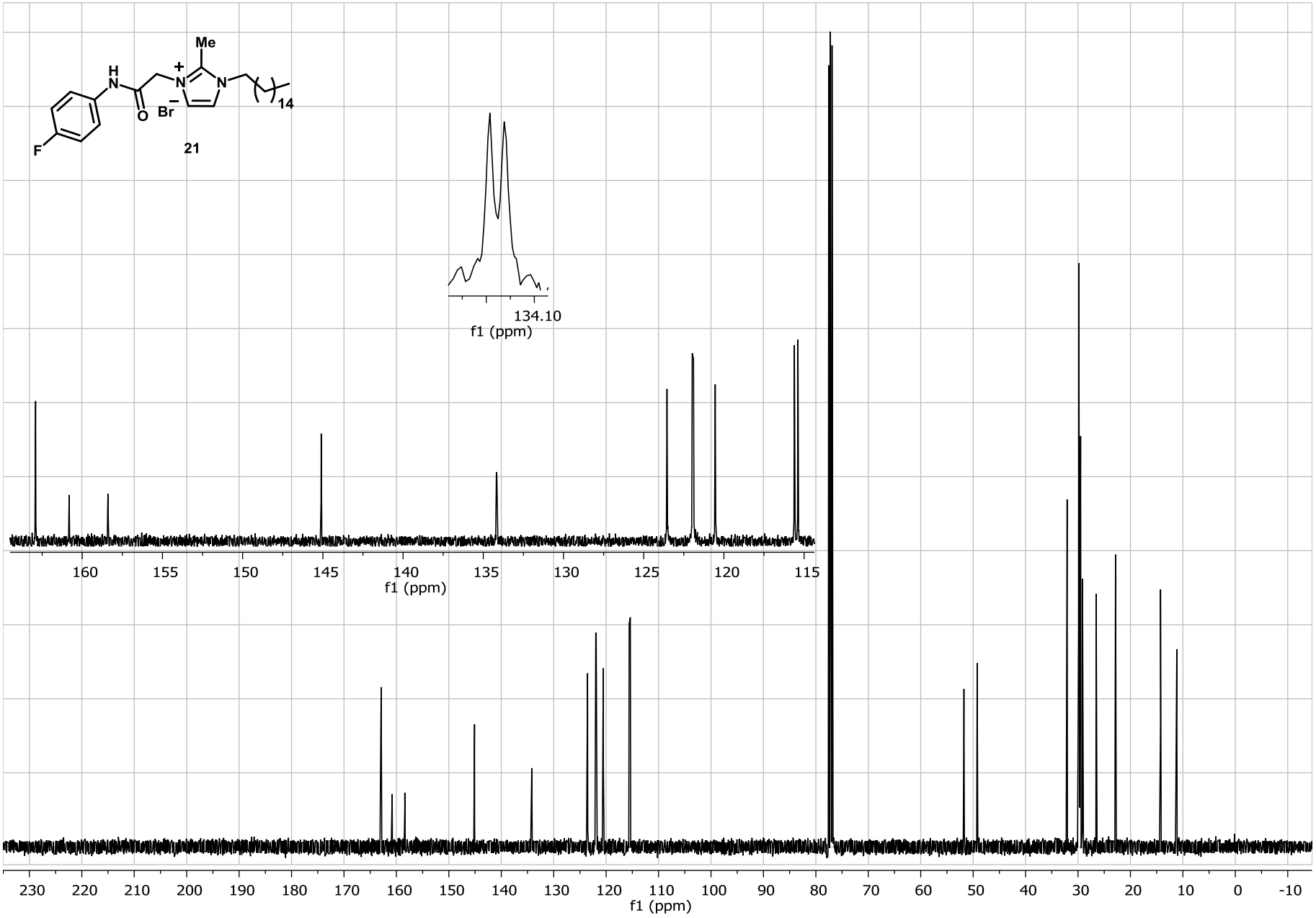

Me
F3C
Br
14
CF3
19
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

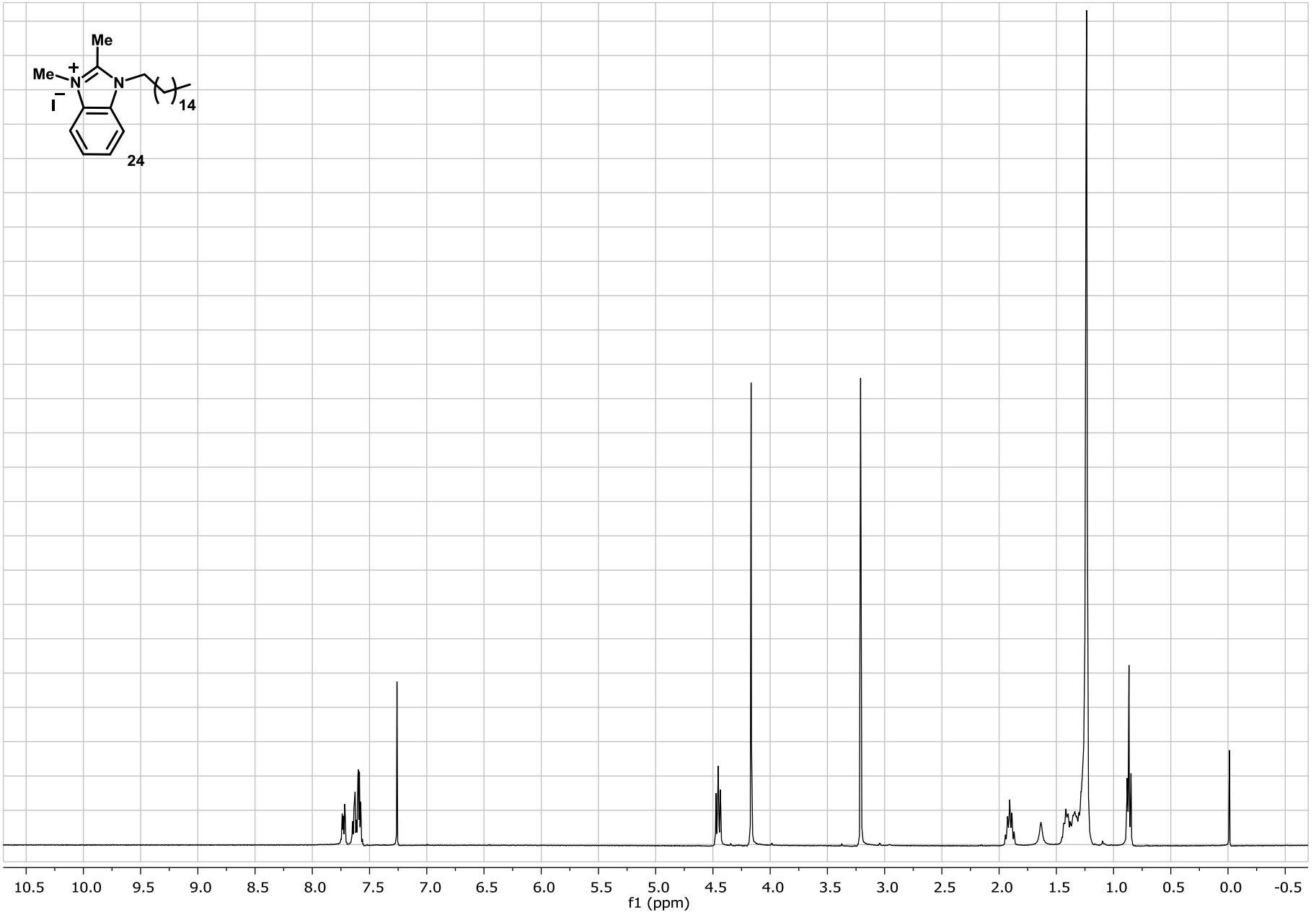

Me
F3C
Br
N
N
14
CF3
19
145 144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

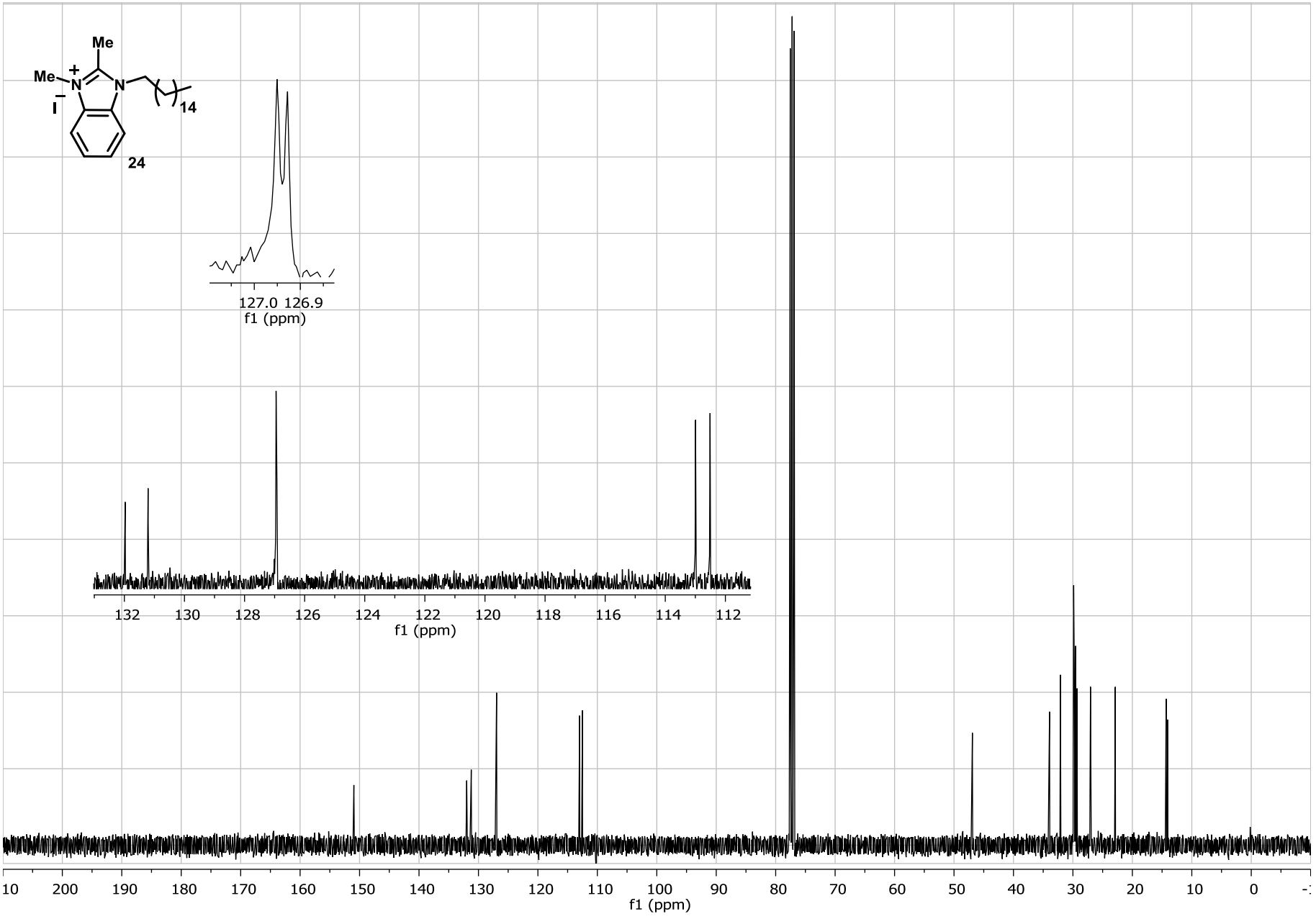

Me
Br
Br
Br
14
20
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

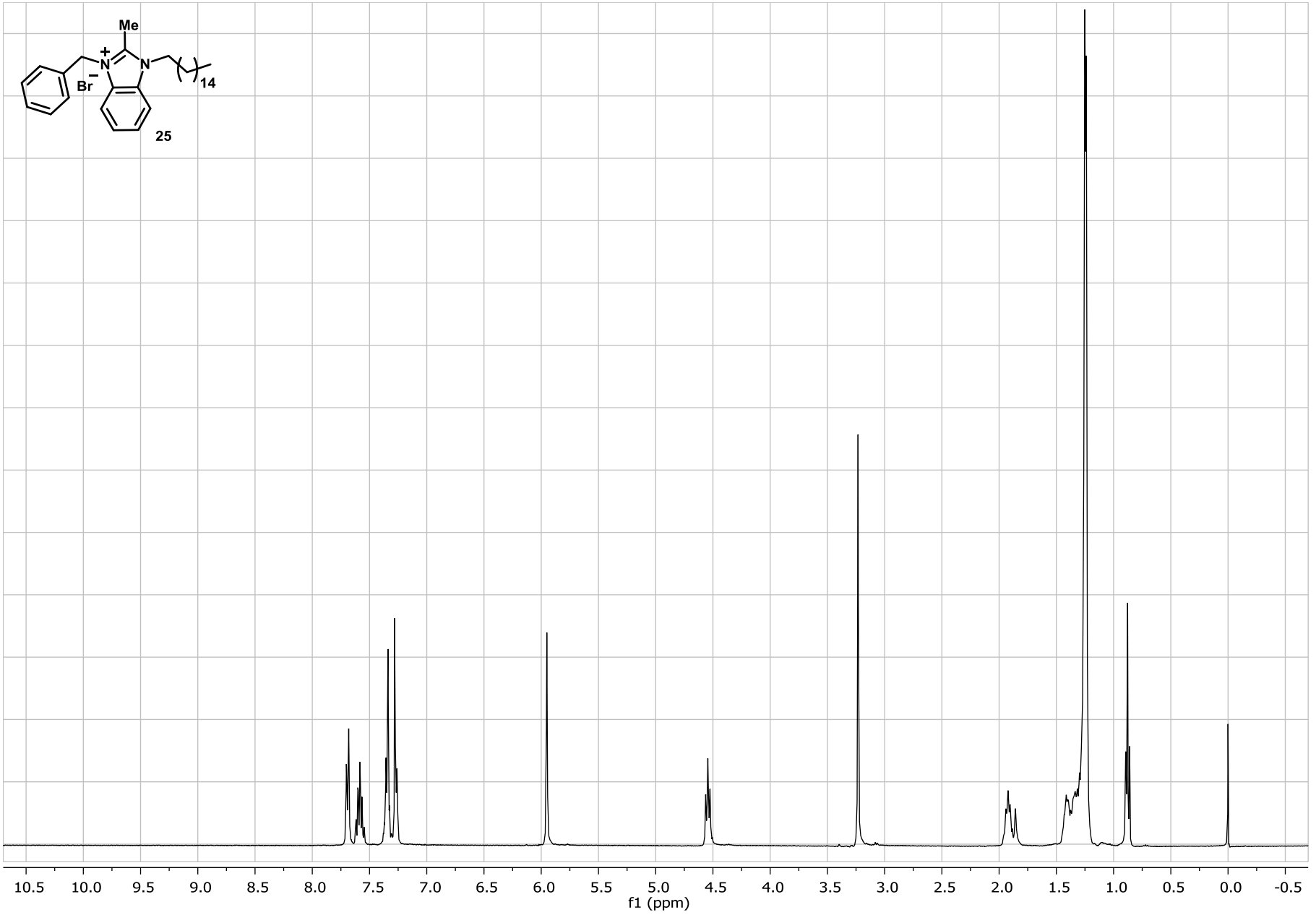

Me
Br
Br
Br
14
20
145
140
135
130
125
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

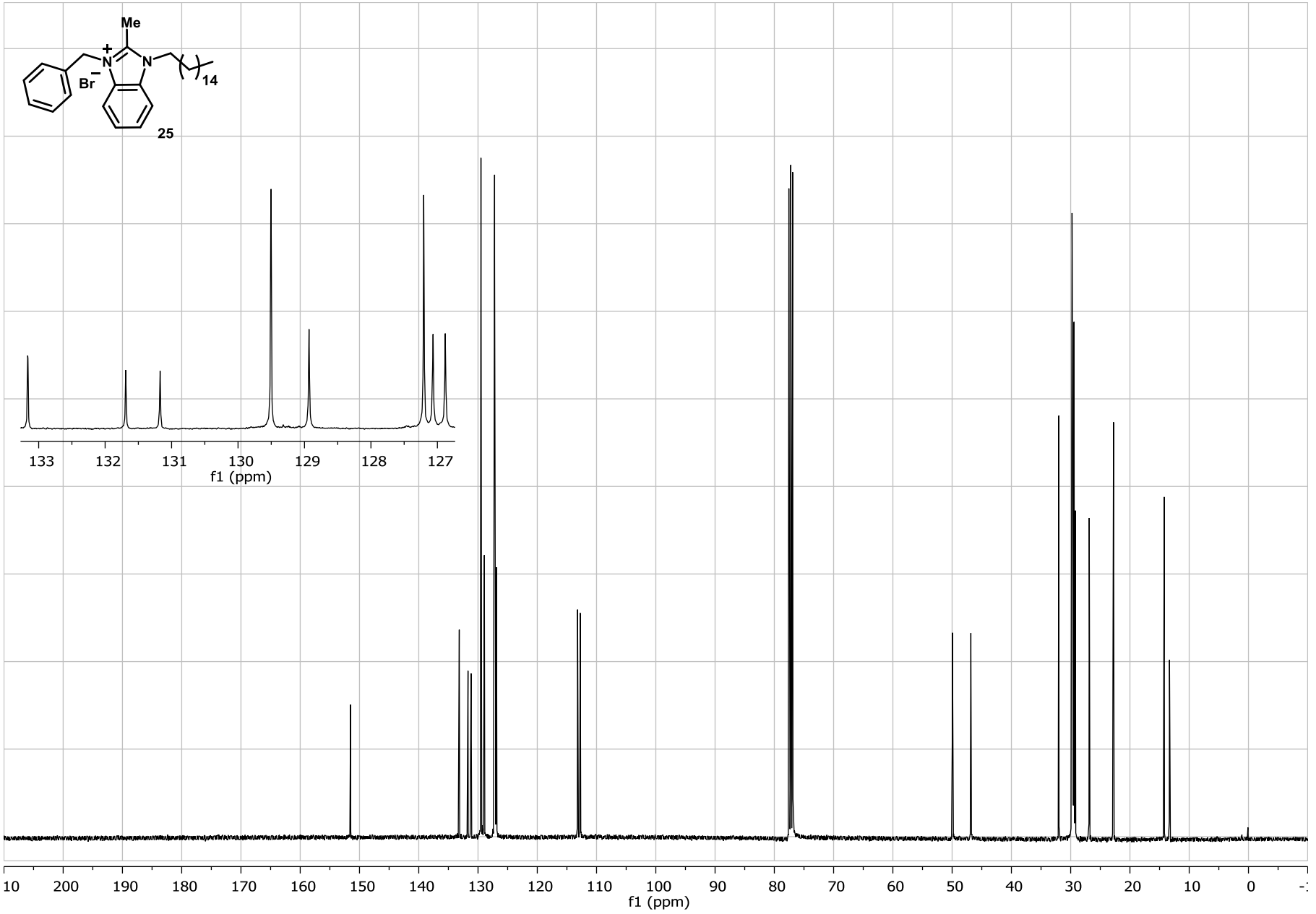

Me
H
N
O
Br
+
N
N
14
F
21
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

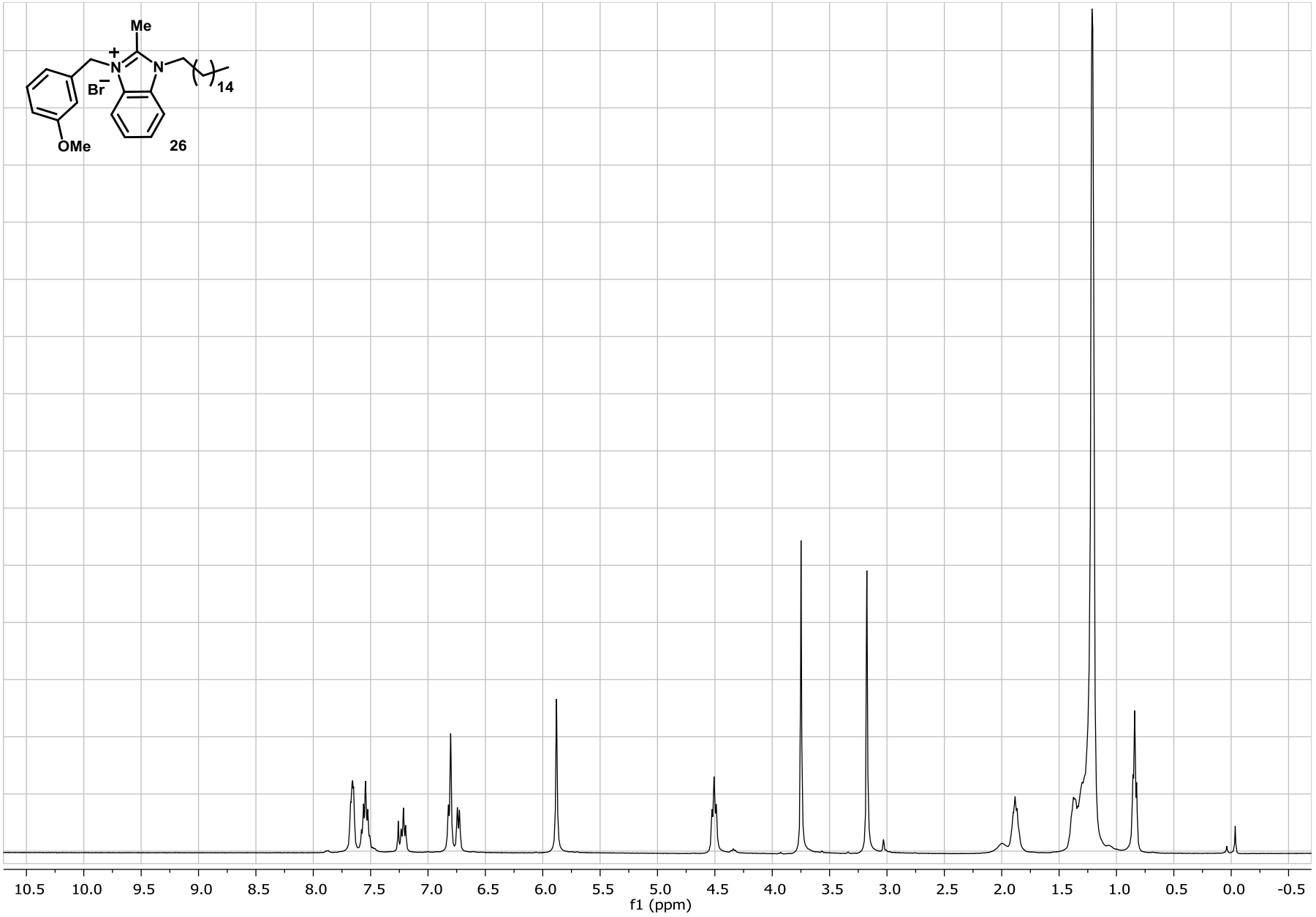

Me
H
N
+
N
N
O
Br
−
14
F
21
134.10
f1 (ppm)
160
155
150
145
140
135
130
125
120
115
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

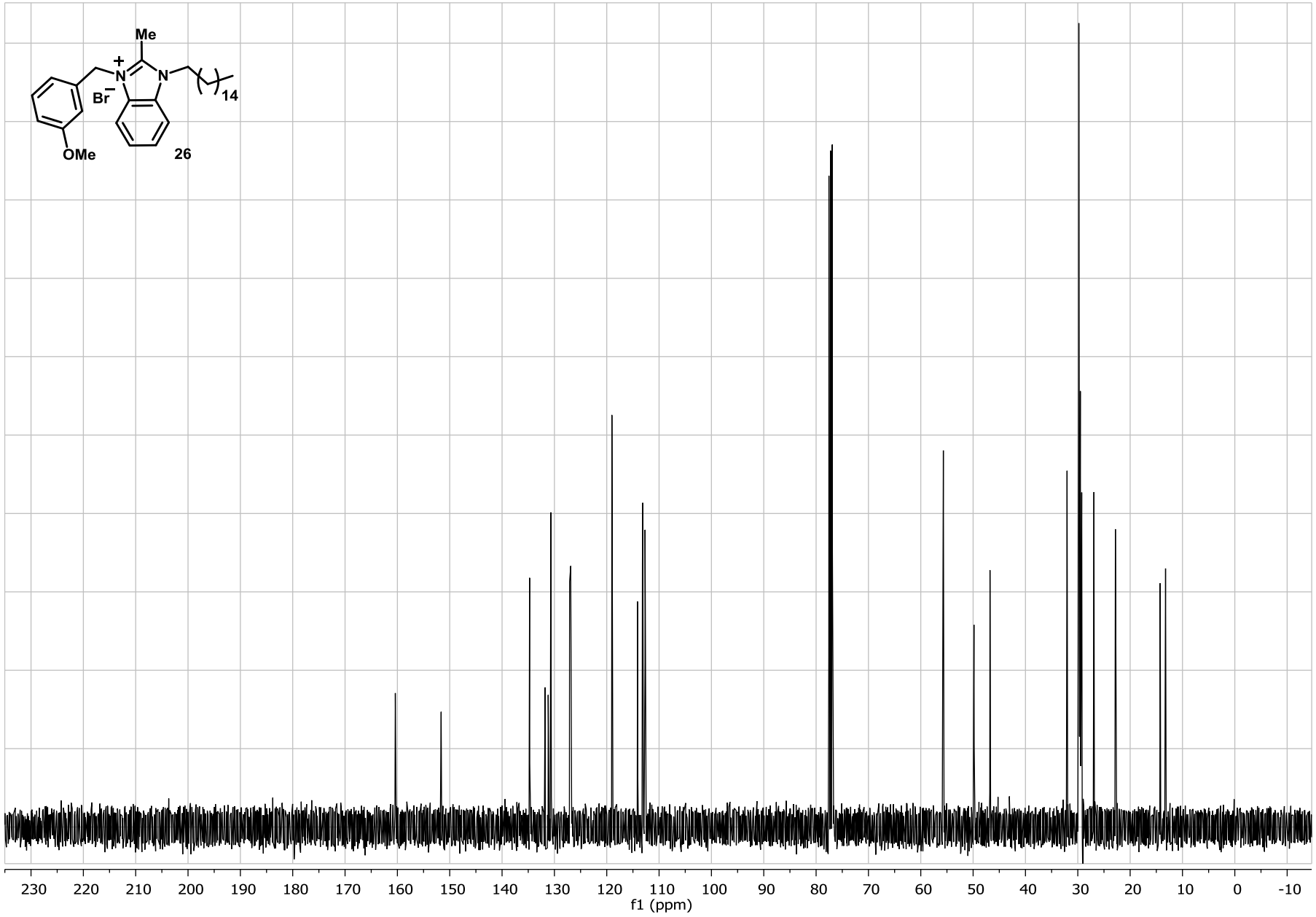

Me
Me
N
+
N
I
−
14
24
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

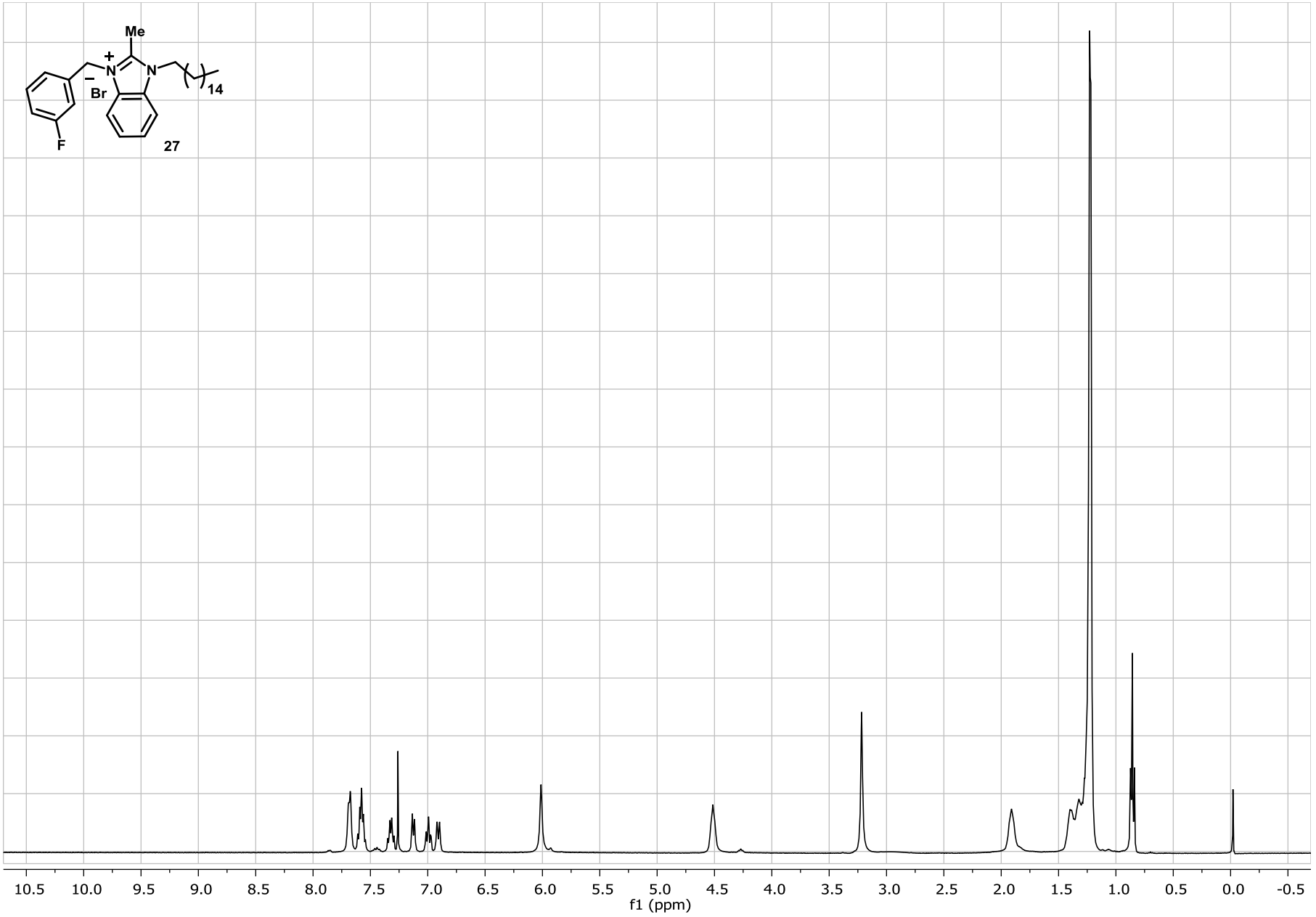

Me
Me
N
N
I
14
24
127.0 126.9
f1 (ppm)
132 130 128 126 124 122 120 118 116 114 112
f1 (ppm)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

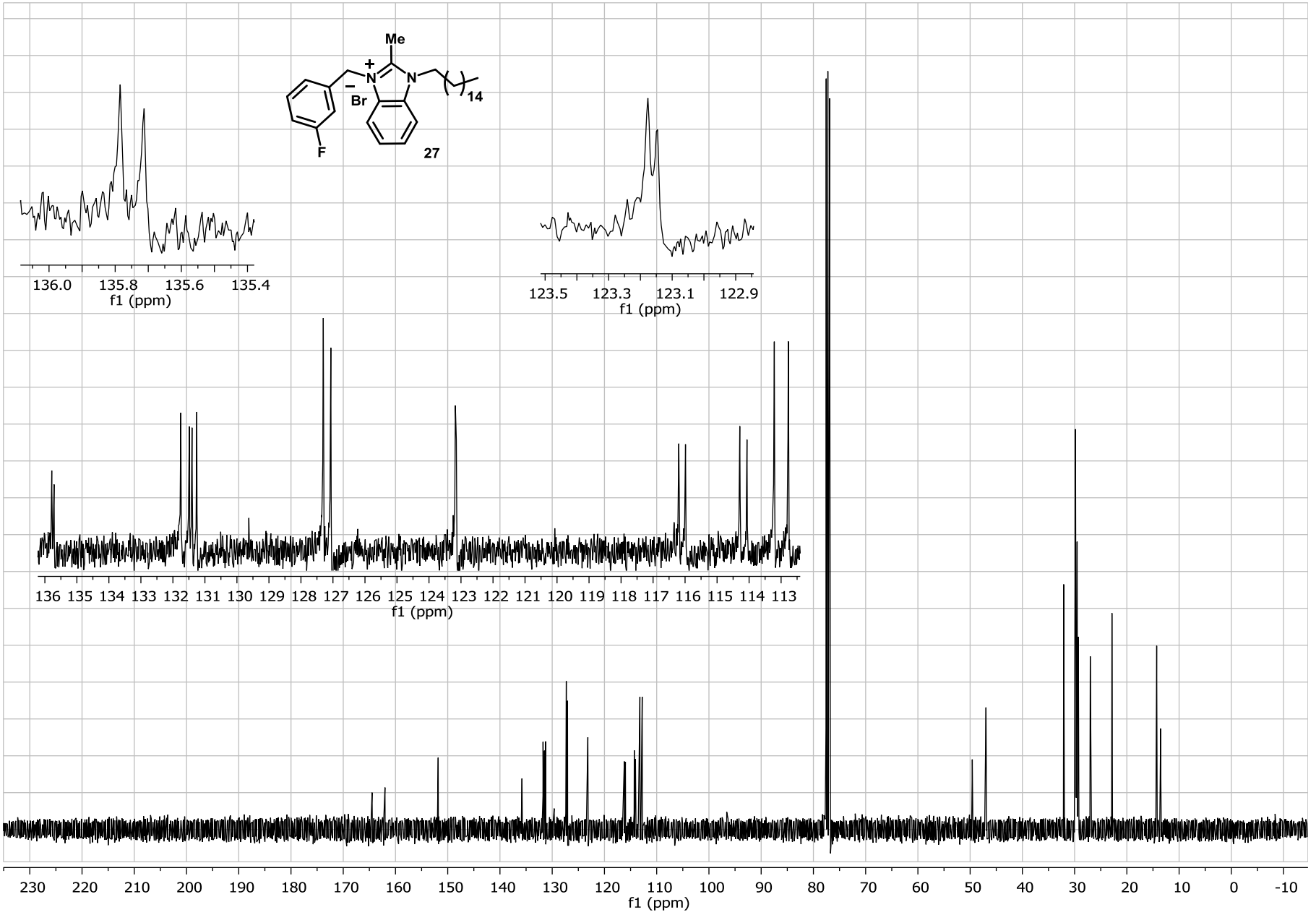

Me
N
N
Br
14
25
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

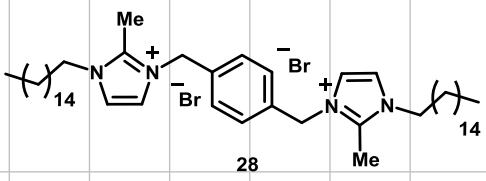

Me
Br
14
25
133
132
131
130
129
128
127
f1 (ppm)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
N
N
Br
14
OMe
26
10.5
10.0
9.5
9.0
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
0.0
-0.5
f1 (ppm)

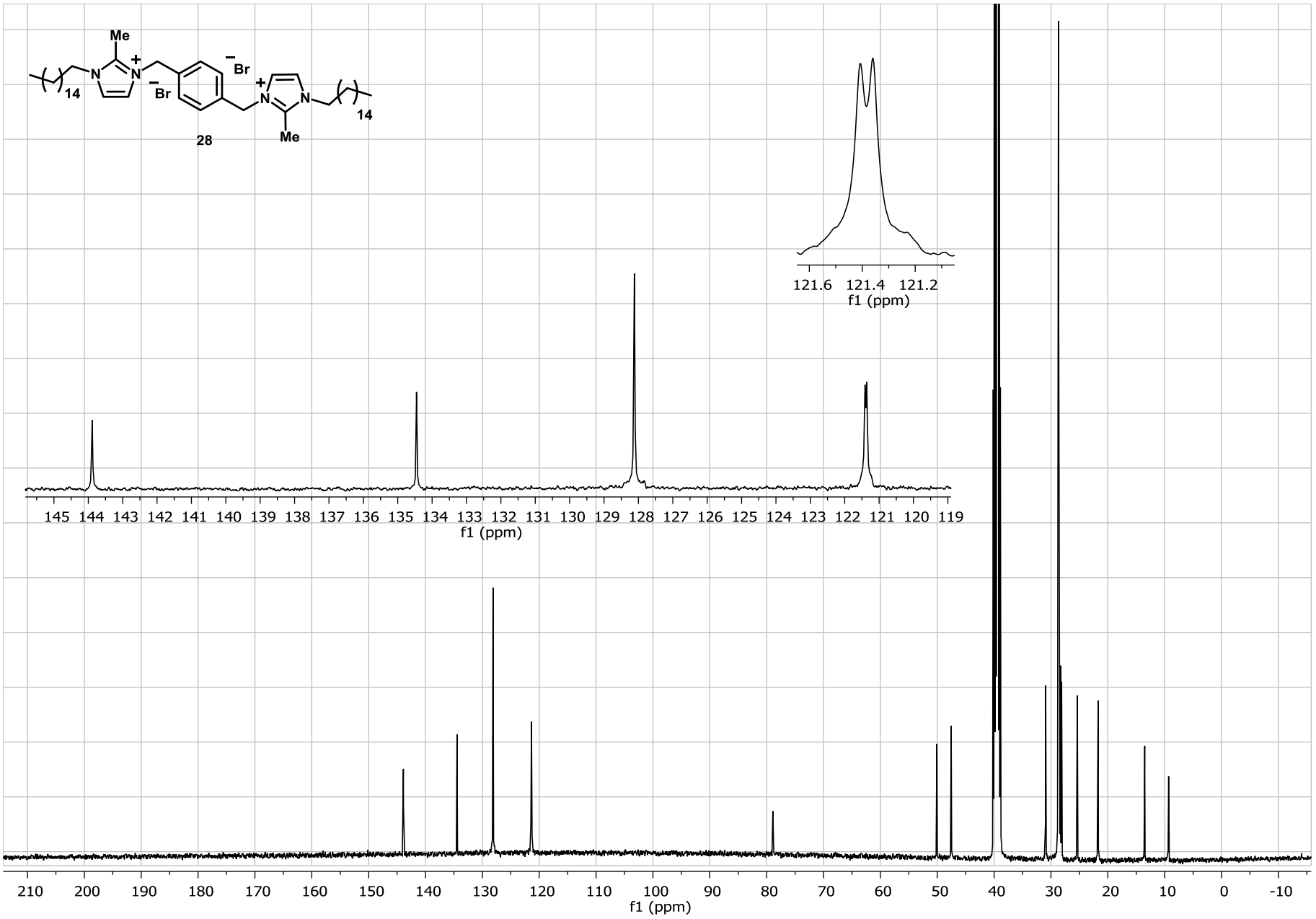

Me
N
N
Br
14
OMe
26
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

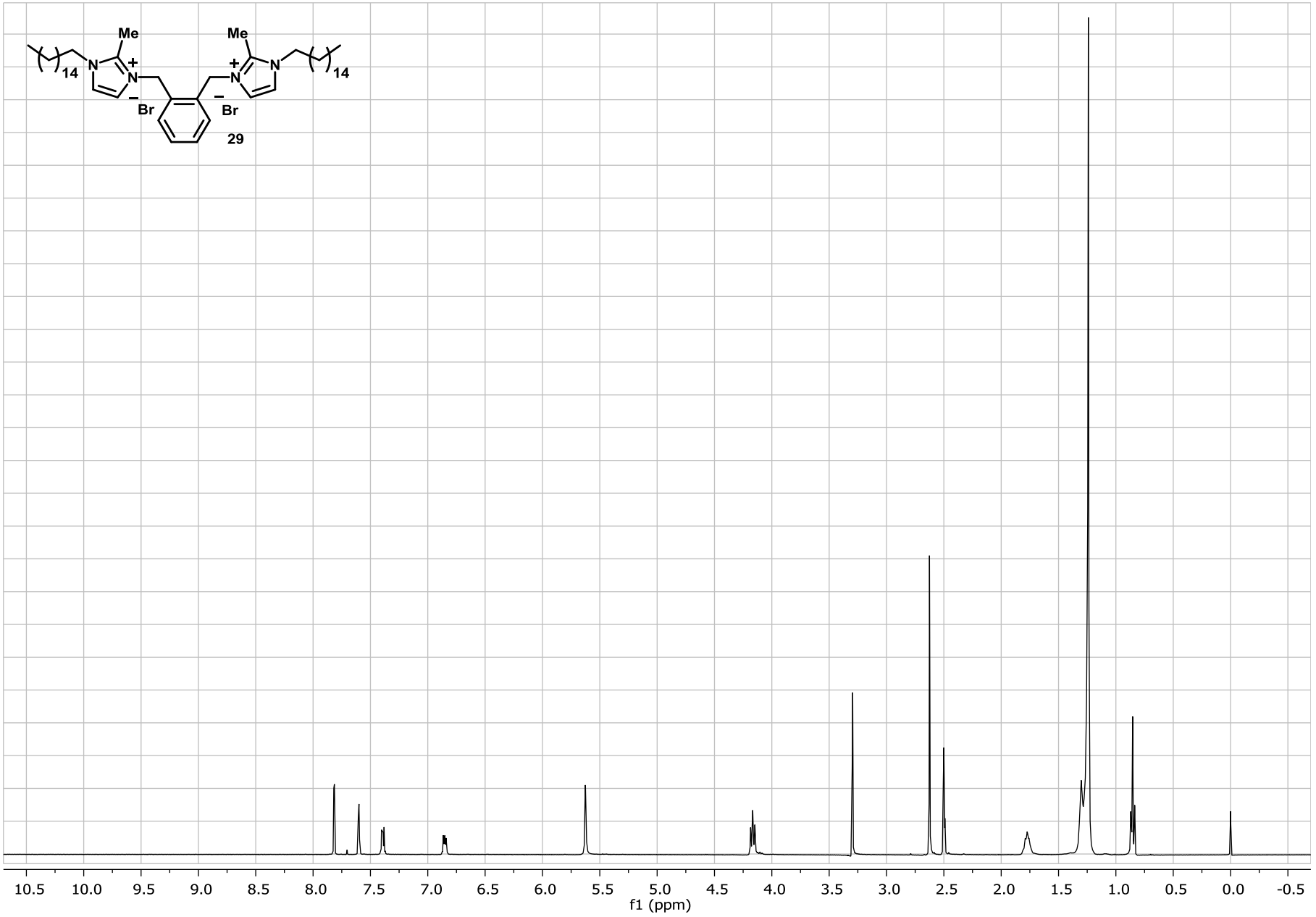

Me
N
N
Br
14
F
27
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

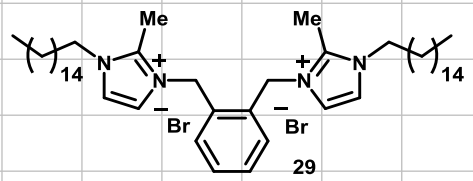

Me
Br
F
14
27
136.0 135.8 135.6 135.4
f1 (ppm)
123.5 123.3 123.1 122.9
f1 (ppm)
136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
14
Br
Br
28
Me
14

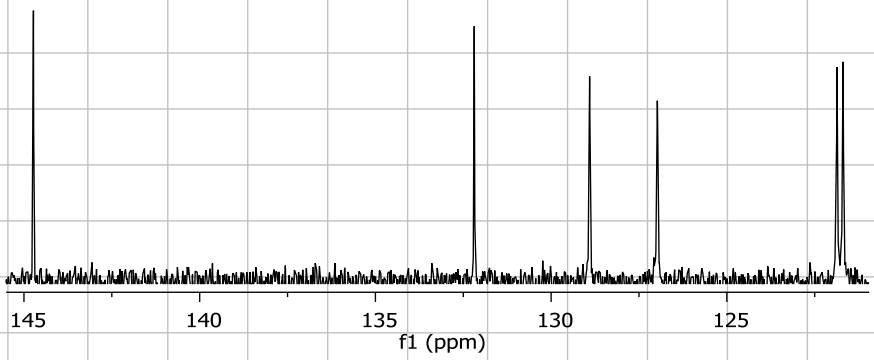
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Me
14
Br
Br
28
Me
14
121.6 121.4 121.2
f1 (ppm)
145 144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

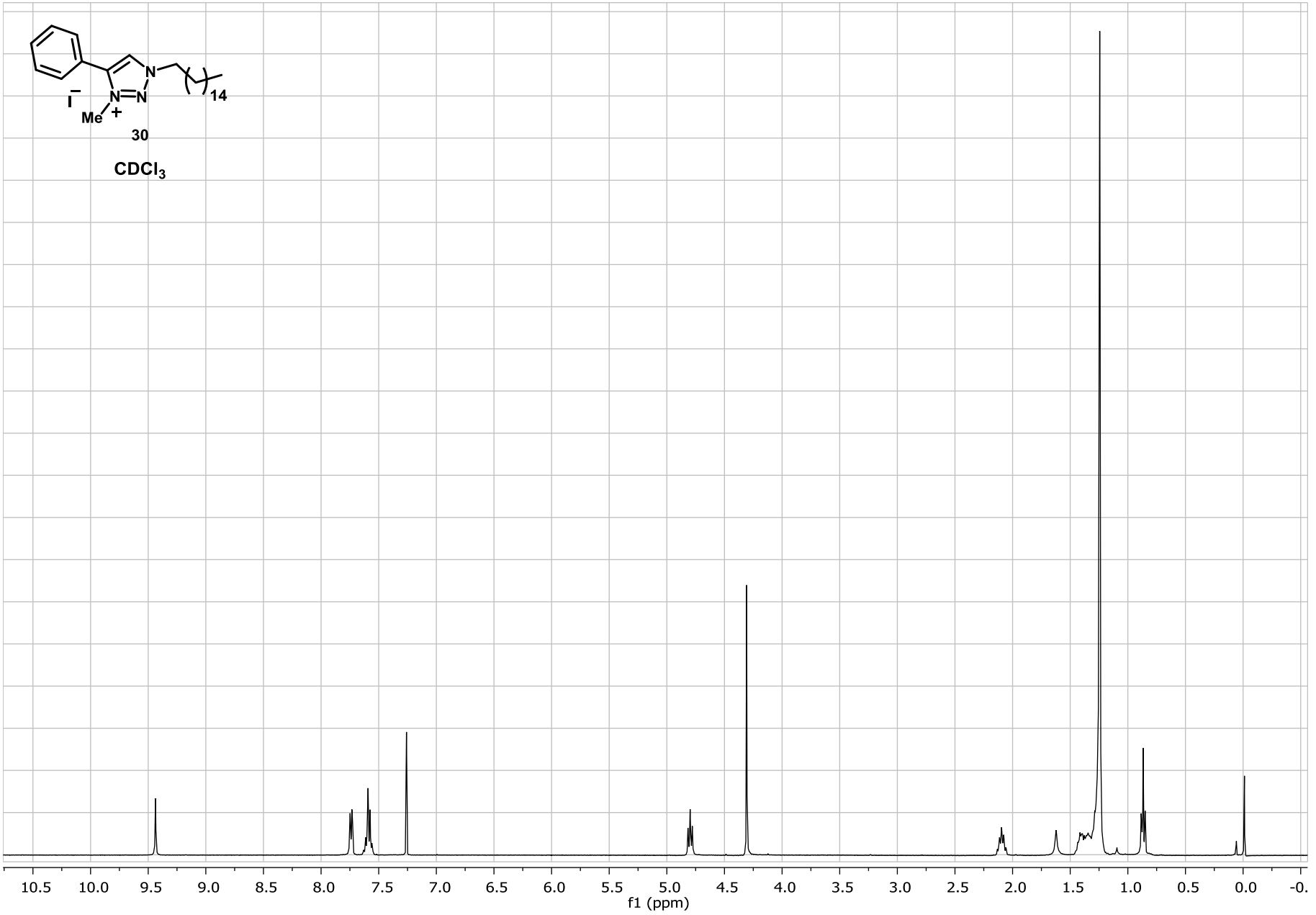

Me
Me
14
14
Br
Br
29
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

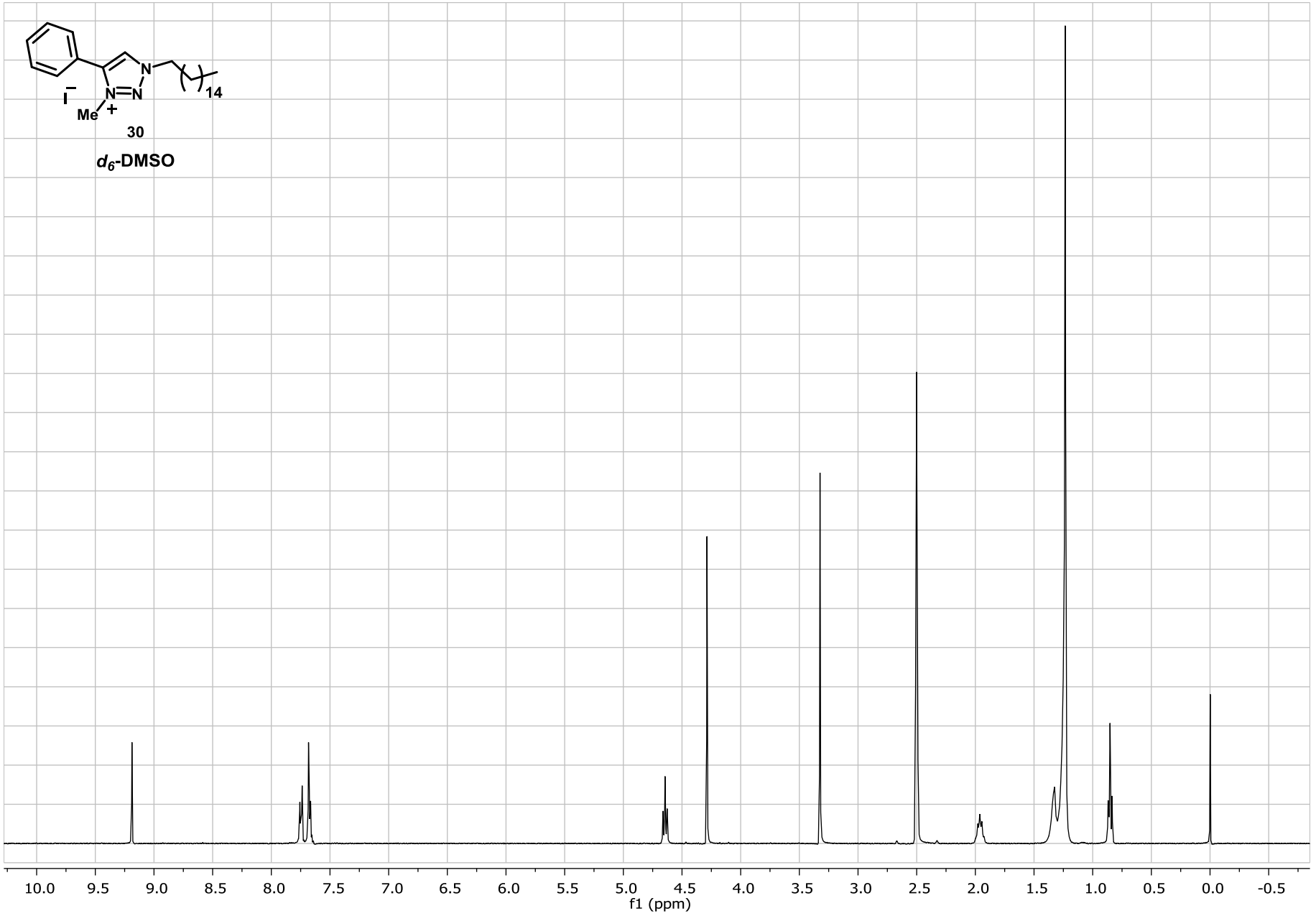

Me
Me
14
14
N
N
N
N
Br
Br

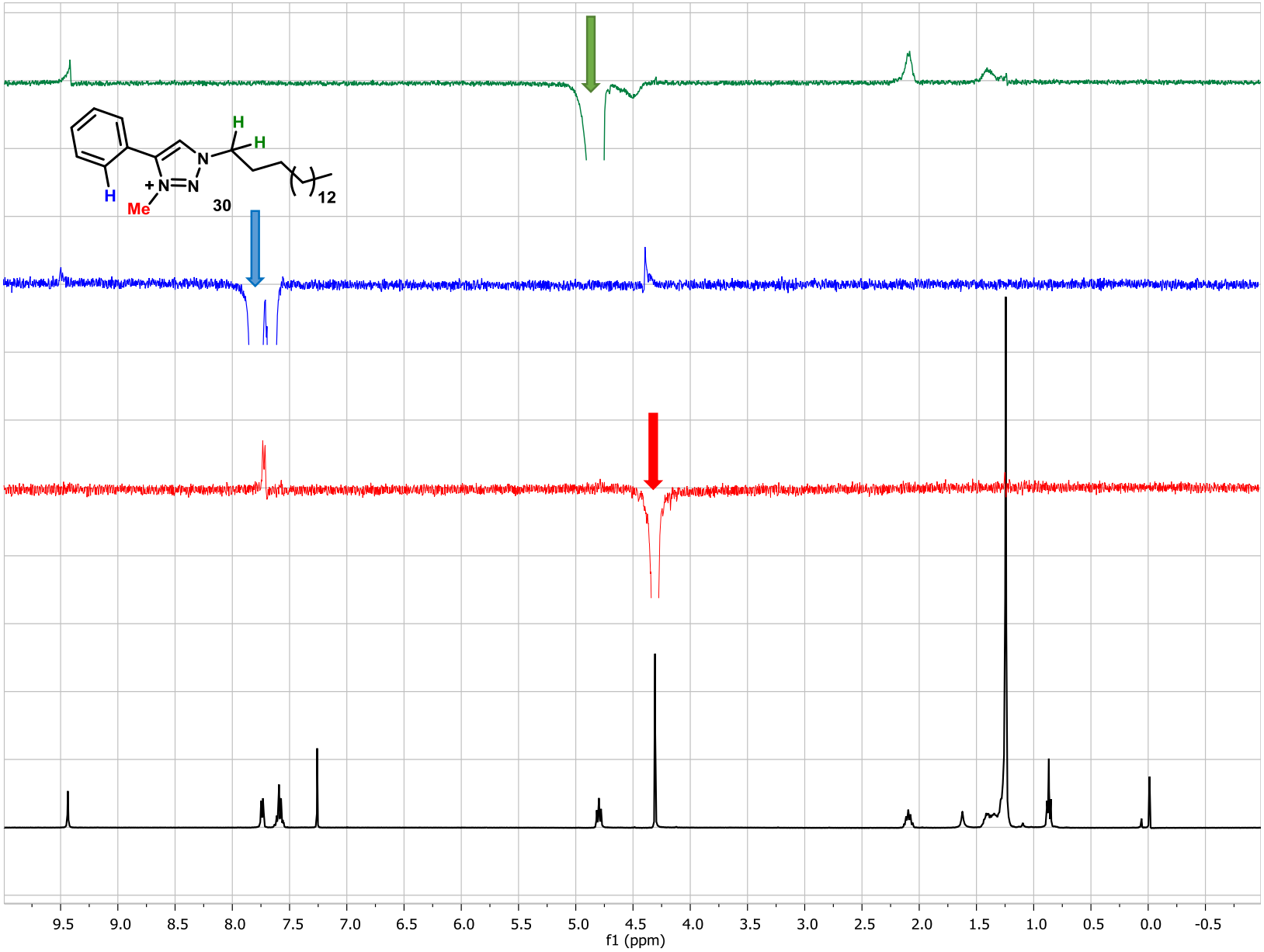
29

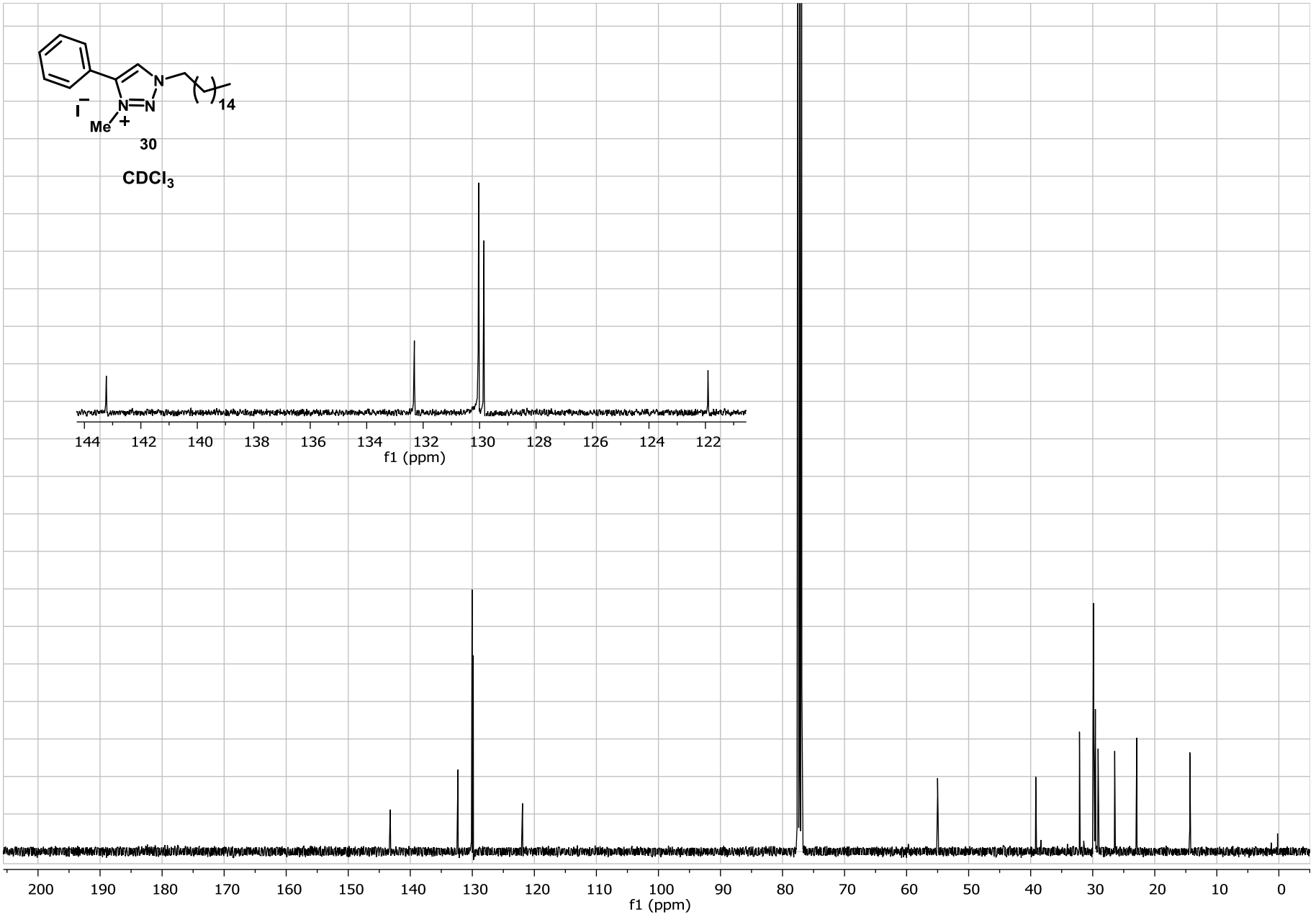

145
140
135
130
125
f1 (ppm)

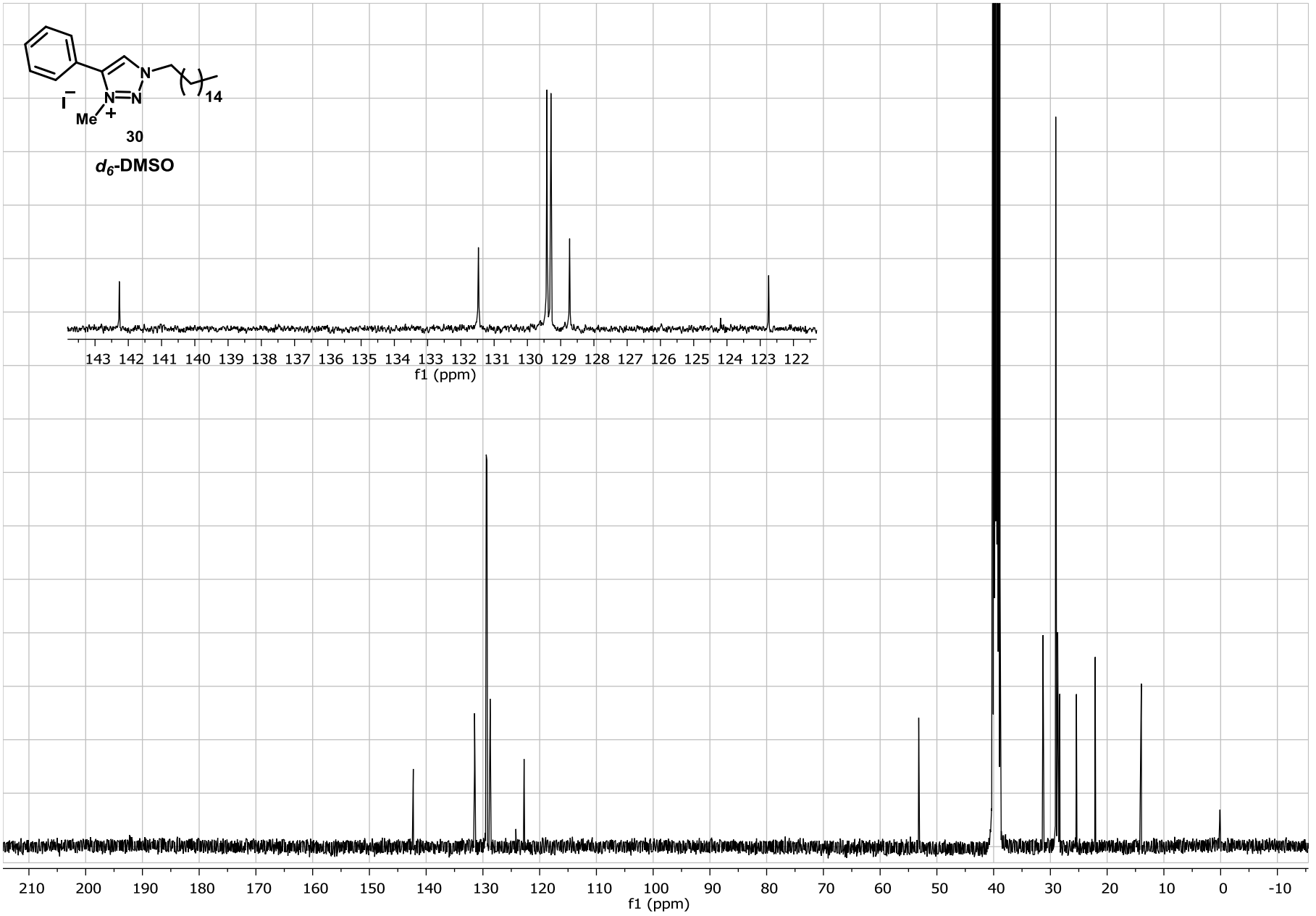
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

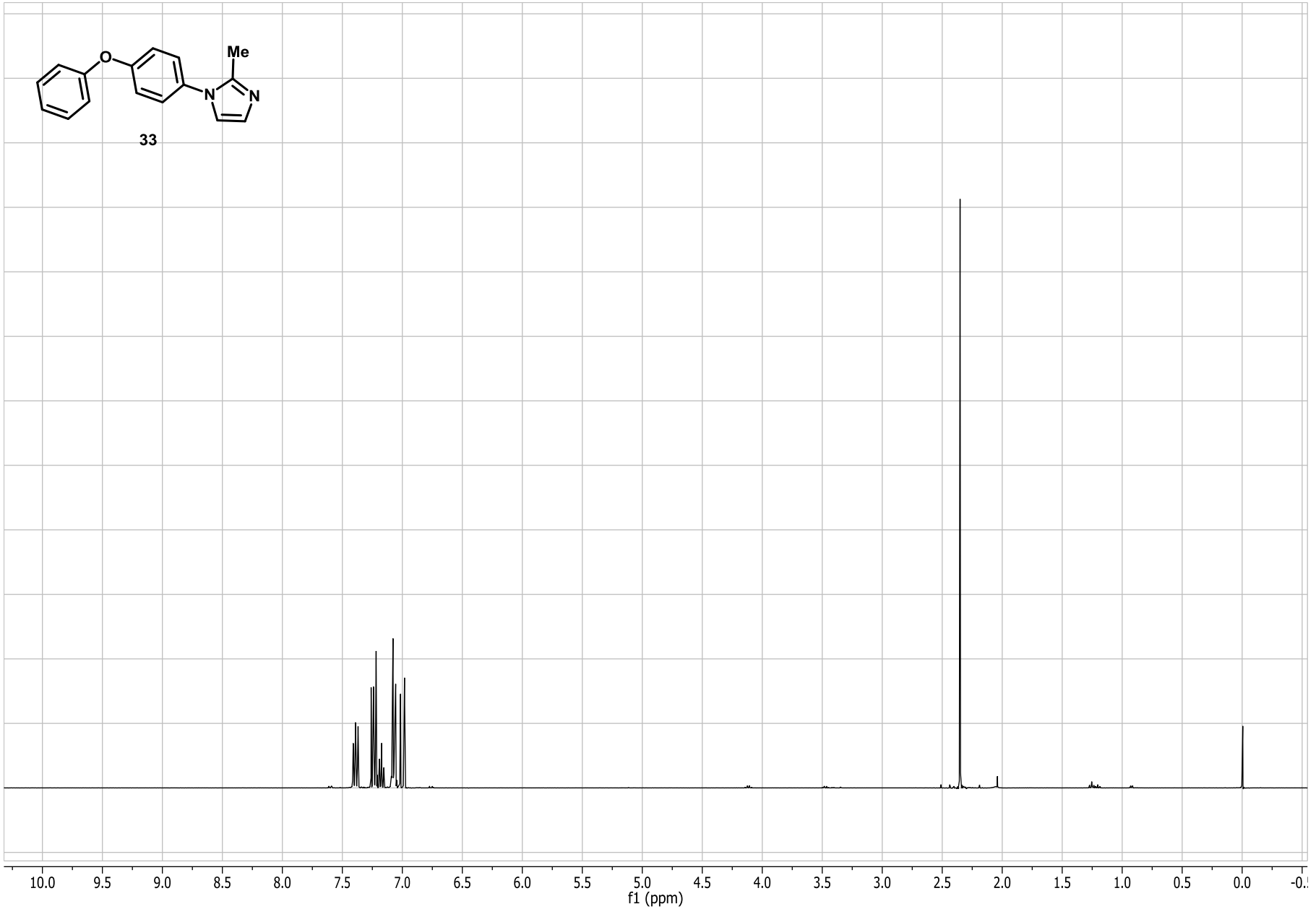

I⁻
Me
N
N
N
14
30
CDCl3
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)

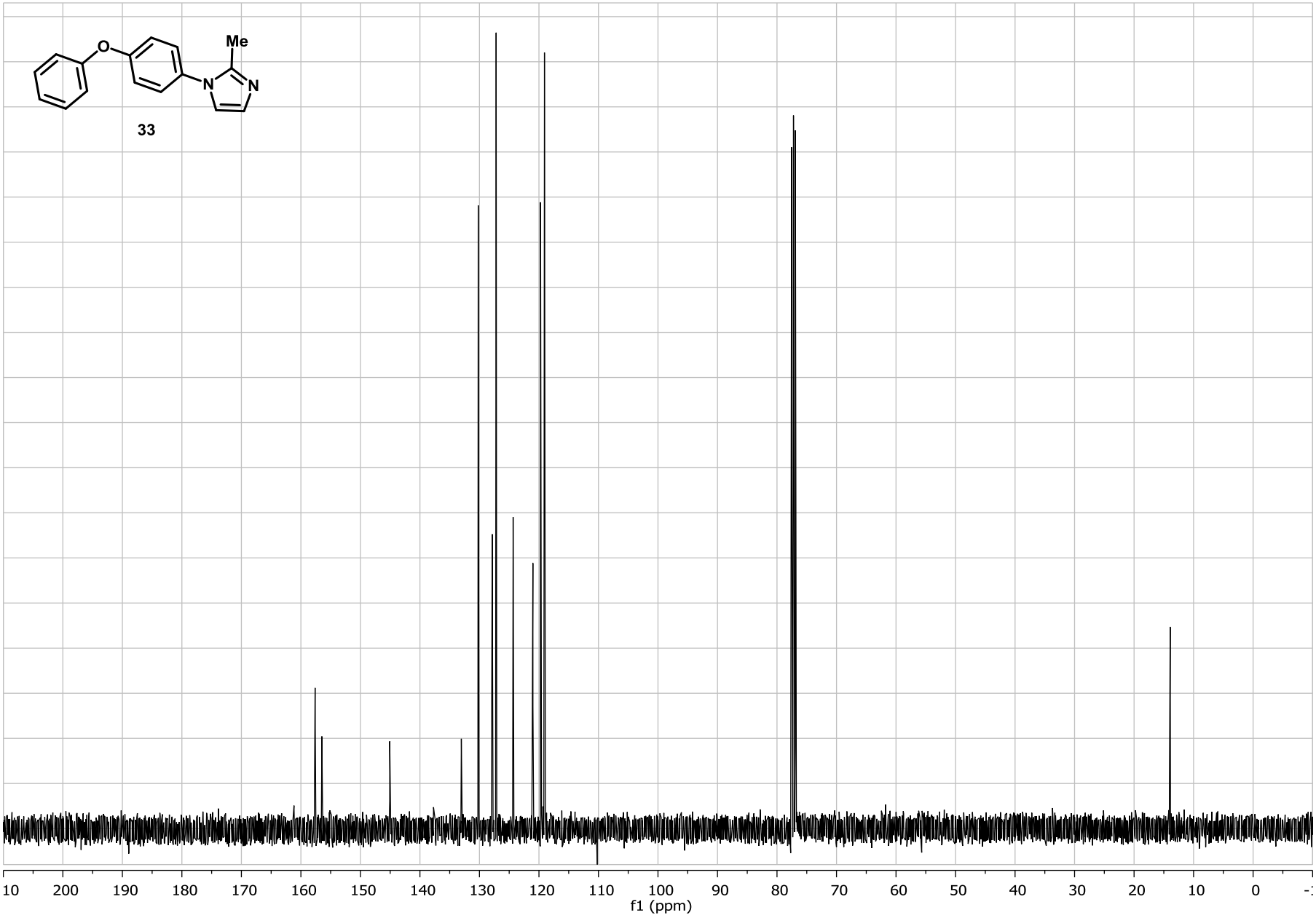

30
d_6-DMSO
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

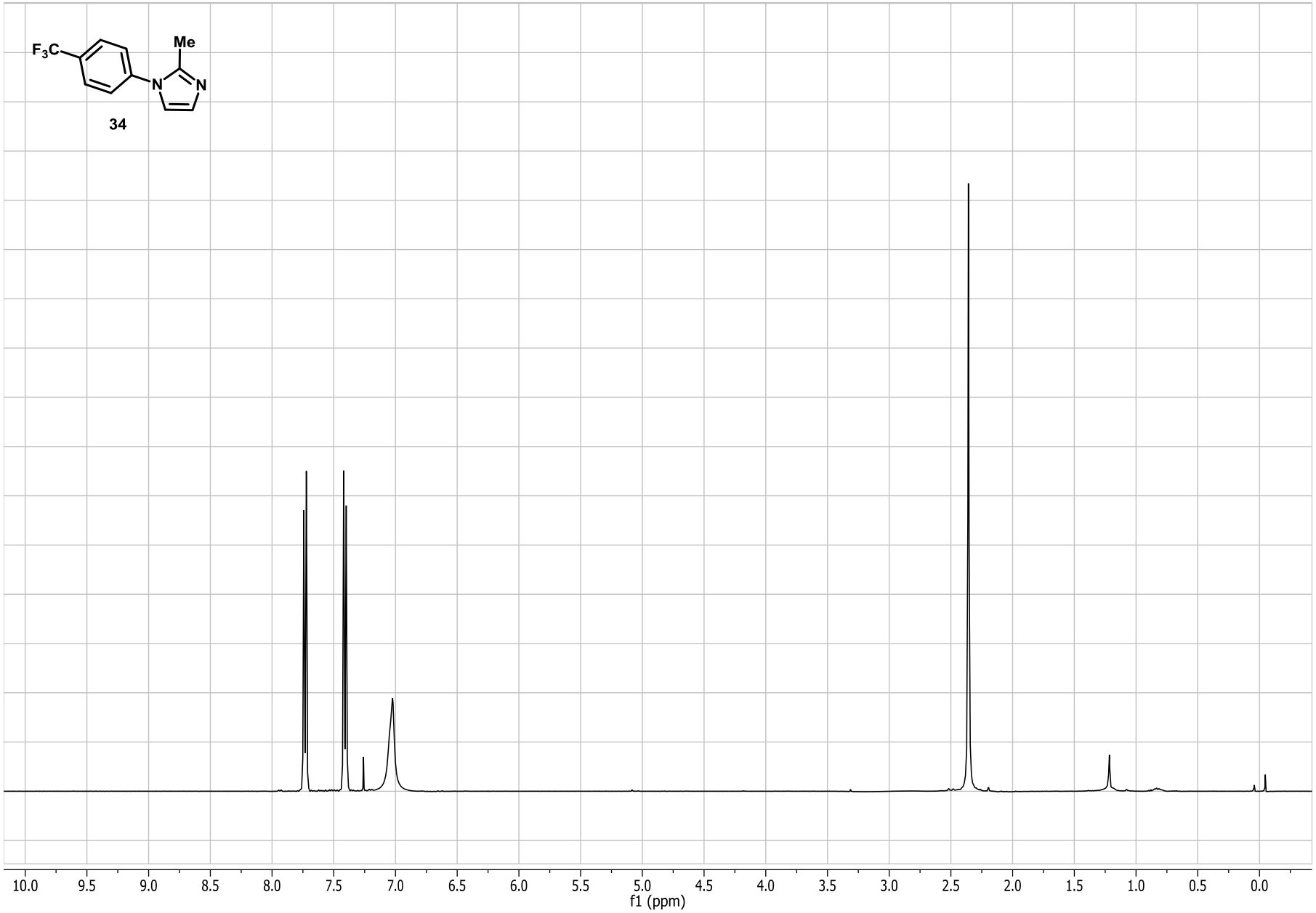

H
H
N
+N=N
H
Me
30
12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

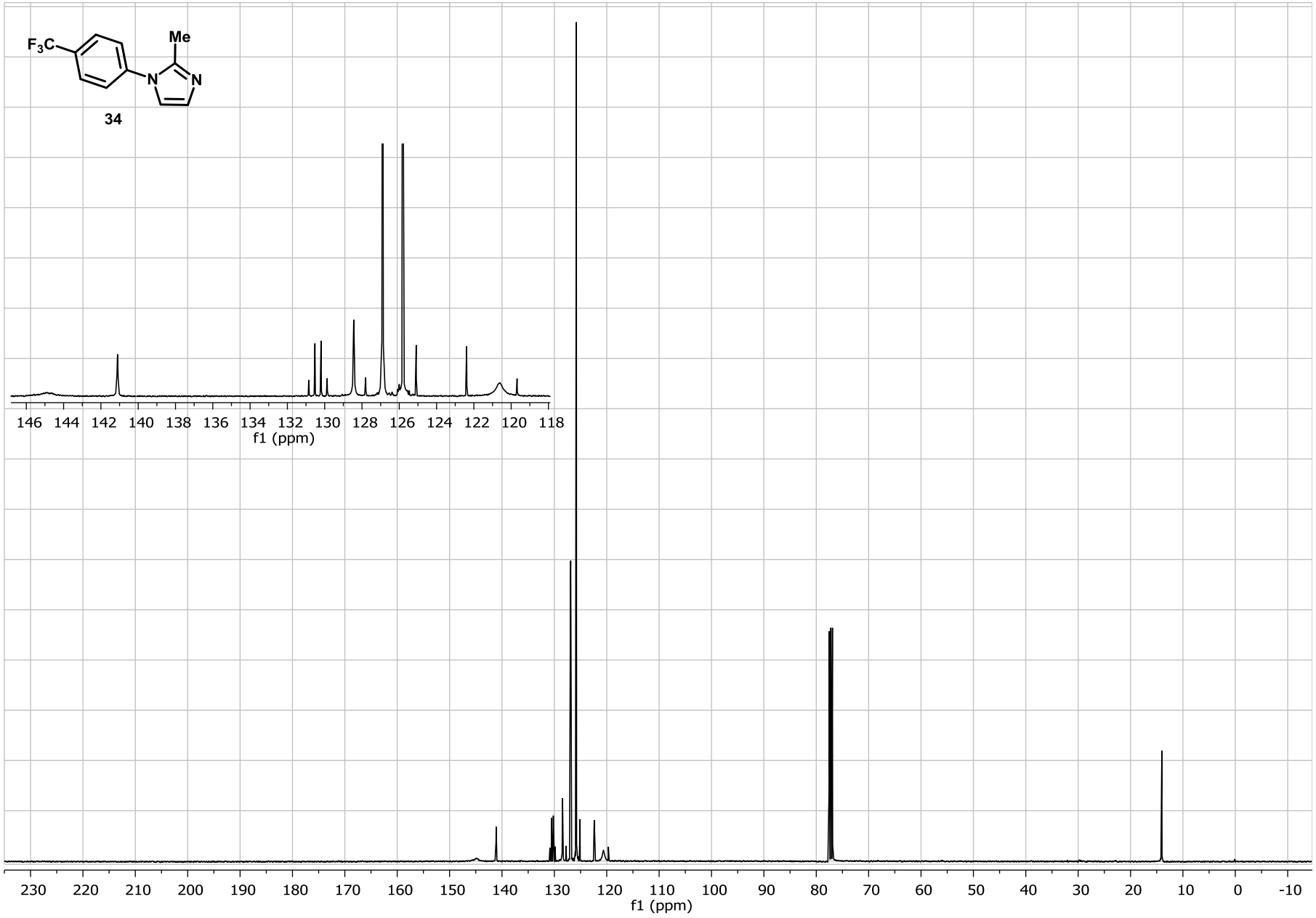

I⁻
N
N=N
Me +
14
30
CDCl3
144 142 140 138 136 134 132 130 128 126 124 122
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

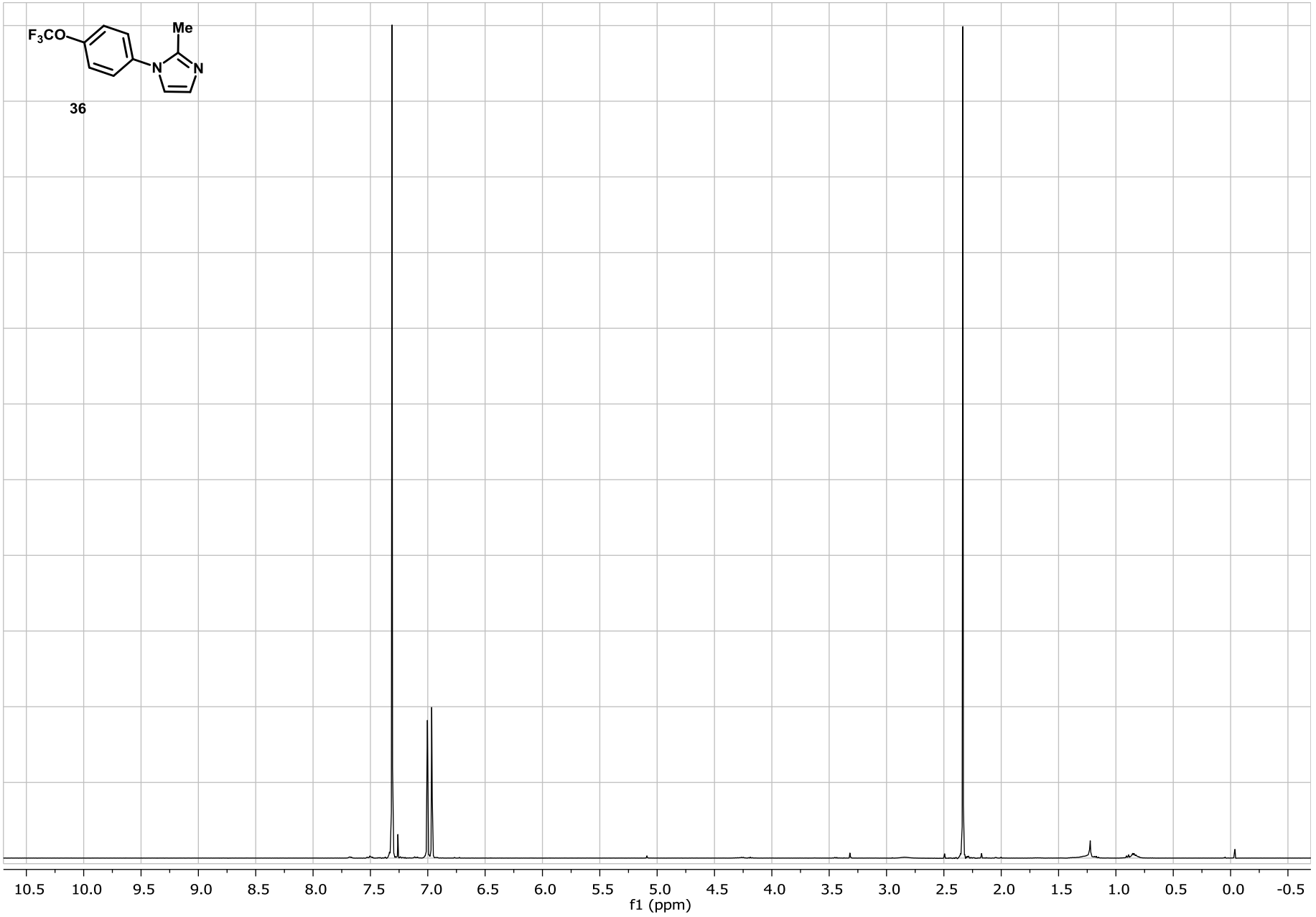

I⁻
N
N=N
Me
+
14
30
d6-DMSO
143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

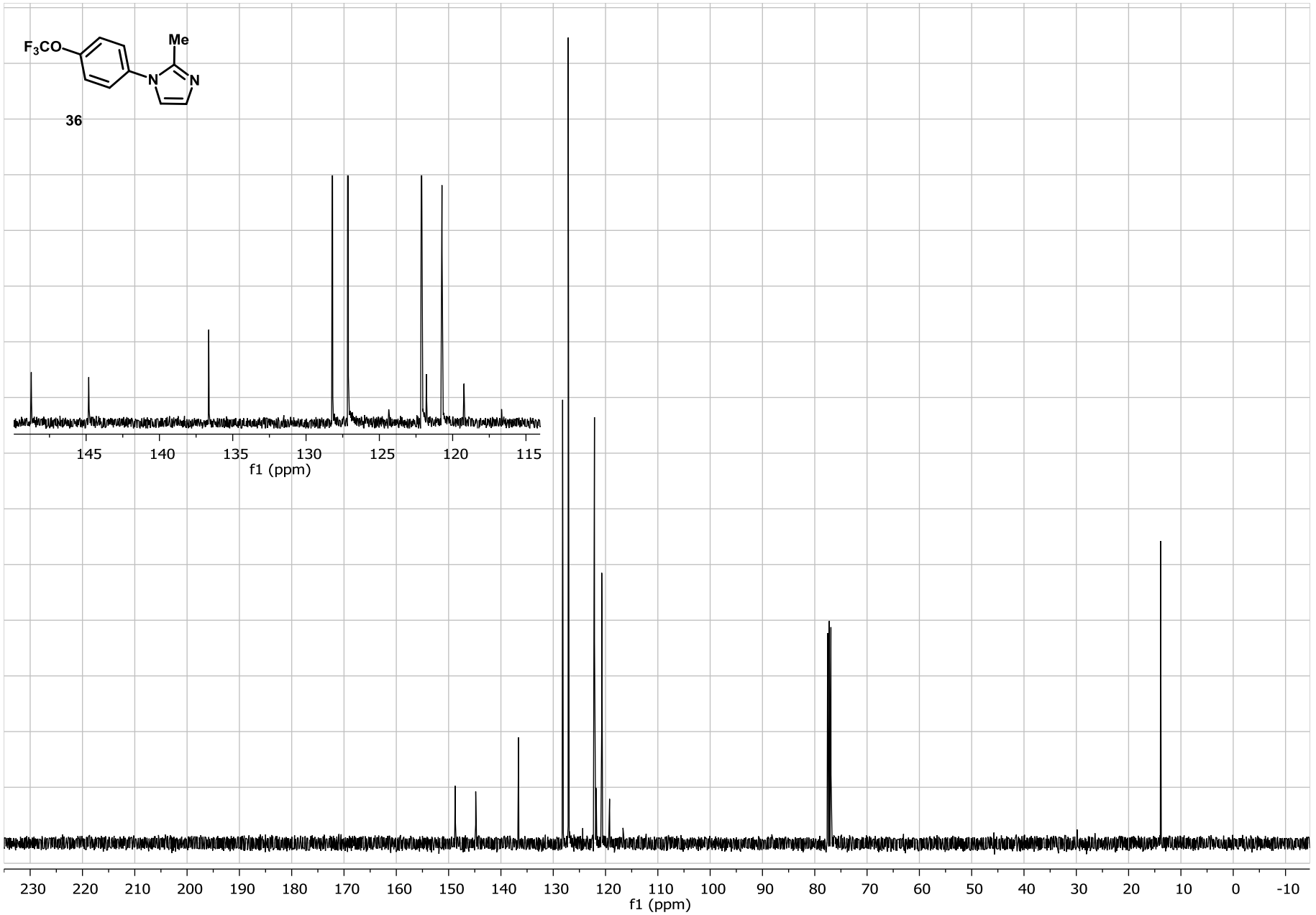

Me
O
N
N
33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Me
O
N
N
33
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F3C
Me
N
N
34
10.0
9.5
9.0
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
0.0
f1 (ppm)


F3C
Me
N
N
34
146 144 142 140 138 136 134 132 130 128 126 124 122 120 118
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3CO
Me
N
N
36
10.5
10.0
9.5
9.0
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
0.0
-0.5
f1 (ppm)


F3CO
Me
N
N
36
145
140
135
130
125
120
115
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)