Electronic Supplementary Information for

Methoxy-substituted isoTQEN family for enhanced fluorescence response toward zinc ion

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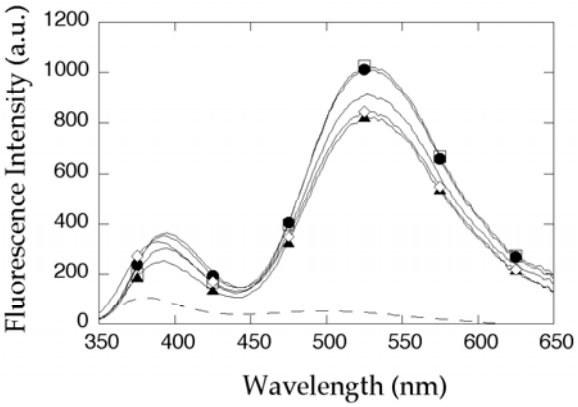

Figure S1. Fluorescence spectra of 7-MeO-1-isoTQEN in DMF/H_2O (1:1) at 25 °C in the absence (broken lines) and presence (solid lines) of 1 equivalent of Zn^{2+}. Spectra with marks contain 10 equivalent of TPEN recorded 5 min (filled circles), 1

day (open squares), 10 days (filled triangles) and 1 month (open diamonds) after addition of TPEN into 7-MeO-1-isoTQEN-Zn complex.

Experimental

1-Hydroxymethyl-6-methoxyisoquinoline (2). To the ethanol solution (45 mL) of 6-methoxy-1-isoquinolinecarboxaldehyde[1] (**1**) (828 mg, 4.42 mmol) was added $NaBH_4$ (169 mg, 4.47 mmol) and stirred for 2 h at room temperature. After addition of water, the organic material was extracted with dichloromethane, dried, and evaporated to give brown solid. Yield, 761 mg (4.02 mmol, 91%).

^{1}H NMR ($CDCl_3$): δ 8.37 (d, *J* = 5.9 Hz, 1H), 7.82 (d, *J* = 10.2 Hz, 1H), 7.49 (d, *J* = 5.9 Hz, 1H), 7.23 (dd, *J* = 2.5, 10.2 Hz, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 5.18 (s, 2H), 3.95 (s, 3H) (Figure S2).

^{13}C NMR ($CDCl_3$): δ 160.8, 156.8, 141.0, 138.0, 124.9, 120.5, 120.2, 119.6, 105.0, 61.2, 55.4 (Figure S3).

1-Chloromethyl-6-methoxyisoquinoline (3). To the dichloromethane solution (38 mL) of 1-hydroxymethyl-6-methoxyisoquinoline (**2**) (709 mg, 3.75 mmol) was added thionyl chloride (0.46 mL, 6.40 mmol) and stirred for 1.5 h at room temperature. After addition of saturated aqueous $NaHCO_3$, the organic material was extracted with dichloromethane, dried, and evaporated to give brown solid. Yield, 463 mg (2.23 mmol, 59%).

^{1}H NMR ($CDCl_3$): δ 8.40 (d, *J* = 5.7 Hz, 1H), 8.15 (d, *J* = 9.2 Hz, 1H), 7.55 (d, *J* = 5.7 Hz, 1H), 7.29 (dd, *J* = 2.6, 9.2 Hz, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 5.09 (s, 2H), 3.96 (s, 3H) (Figure S4).

^{13}C NMR ($CDCl_3$): δ 160.8, 155.1, 142.5, 138.8, 126.8, 122.1, 121.0, 120.8, 104.9, 55.5, 45.0 (Figure S5).

[Zn(6-MeO-1-isoTQEN)]$(ClO_4)_2$·$CHCl_3$. In an chloroform suspension of 6-MeO-1-isoTQEN was added equimolar amount of $Zn(ClO_4)_2$·$6H_2O$ in methanol, and the solution was kept at room temperature afforded white powder. Yield, 94%.

^{1}H NMR (DMF-d_7): δ 8.34 (br., 4H), 8.18 (d, *J* = 8.9 Hz, 4H), 7.85 (d, *J* = 5.7 Hz, 4H), 7.51 (s, 4H), 7.33 (d, *J* = 8.9 Hz, 4H), 5.10 (d, *J* = 17.3 Hz, 4H), 4.82 (d, *J* = 17.3 Hz, 4H), 3.99 (s, 12H), 3.39 (s, 4H) (Figure S8).

^{13}C NMR (DMF-d_7): δ 167.5, 161.8, 145.9, 144.8, 132.3, 127.5, 126.5, 111.2, 62.7, 61.2, 59.9 (Figure S9).

Anal. calcd for $C_{47}H_{45}N_6O_{12}Cl_5Zn$ ([Zn(6-MeO-1-isoTQEN)]$(ClO_4)_2$·$CHCl_3$): H 4.02, C 50.02, N 4.02; found: H 4.19, C 49.79, N 7.85.

1-Hydroxymethyl-7-methoxyisoquinoline (5). To the ethanol solution (11 mL) of 7-methoxy-1-isoquinolinecarboxaldehyde[1] (**4**) (140 mg, 0.747 mmol) was added $NaBH_4$ (26.3 mg, 0.695 mmol) and stirred for 1 h at room temperature. After addition of water, the organic material was extracted with dichloromethane, dried, and evaporated to give brown solid. Yield, 109 mg (0.576 mmol, 84%).

^{1}H NMR ($CDCl_3$): δ 8.36 (d, *J* = 5.7 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.53 (d, *J* = 5.7 Hz, 1H), 7.37 (dd, *J* = 2.4, 8.7 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 1H), 5.17 (s, 2H), 3.96 (s, 3H) (Figure S10).

^{13}C NMR ($CDCl_3$): δ 158.6, 155.6, 138.6, 131.4, 128.9, 126.0, 123.3, 120.0, 100.9, 61.4, 55.5 (Figure S11).

1-Chloromethyl-7-methoxyisoquinoline (6). To the dichloromethane solution (20 mL) of 1-hydroxymethyl-7-methoxyisoquinoline (**5**) (154 mg, 0.813 mmol) was added thionyl chloride (0.10 mL, 1.39 mmol) and stirred for 1.5 at room temperature. After addition of saturated aqueous $NaHCO_3$, the organic material was extracted with dichloromethane, dried, and evaporated to give brown solid, which was further purified by silica gel column chromatography (eluent: ethyl acetate/dichloromethane = 1/7). Yield, 115 mg (0.553 mmol, 68%).

^{1}H NMR ($CDCl_3$): δ 8.38 (d, *J* = 5.4 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 5.4 Hz, 1H), 7.46 (d, *J* = 2.4 Hz, 1H), 7.38 (dd, *J* = 2.4, 8.7 Hz, 1H), 5.13 (s, 2H), 4.00 (s, 3H) (Figure S12).

^{13}C NMR ($CDCl_3$): δ 158.7, 154.8, 140.0, 132.4, 129.1, 127.7, 123.6, 121.5, 102.7, 55.6, 45.4 (Figure S13).

5,6,7-Trimethoxy-1-methylisoquinoline (8). To the 5 mL solution 3,4-dihydro-5,6,7-trimethoxy-1-methylisoquinoline[2,3] (**7**) (51.9 mg, 0.221 mmol) in bis(2-methoxyethyl)ether (diglyme) was aded 10% Pd/C (26.3 mg, 0.0247 mmol Pd) and stirred under reflux for 9 h. After removal of Pd/C by filtration, water (50 mL) was added and organic materials were extracted with chloroform. The combined organic layer was dried and evporated to give dark green oil. Yield, 43.6 mg (0.187 mmol, 85%).

^{1}H NMR ($CDCl_3$): δ 8.29 (d, *J* = 5.9 Hz, 1H), 7.71 (d, *J* = 5.9 Hz, 1H), 7.11 (s, 1H), 4.04 (s, 3H), 4.03 (s, 3H), 4.02 (s, 3H), 2.89 (s, 3H) (Figure S18).

^{13}C NMR ($CDCl_3$): δ 156.1, 153.3, 147.0, 143.7, 140.2, 127.8, 124.5, 113.3, 100.0, 61.5, 61.1, 56.0, 22.6 (Figure S19).

5,6,7-Trimethoxy-1-isoquinolinecarbaldehyde (9). To the solution of 5,6,7-trimethoxy-1-methylisoquinoline (**8**) (59.8 mg, 0.256 mmol) in 1,4-dioxane (7 mL) was added selenium dioxide (34.7 mg, 0.313 mmol) at 50 °C, and the mixture was refluxed for 1 h. After the removal of insoluble material, the filtrate was evaporated to give reddish solid. Yield, 53.6 mg (0.217 mmol, 85%).

^{1}H NMR ($CDCl_3$): δ 10.36 (s, 1H), 8.65 (d, *J* = 5.7 Hz, 1H), 8.57 (s, 1H), 8.12 (d, *J* = 5.4 Hz, 1H), 4.079 (s, 3H), 4.076 (s, 3H), 4.04 (s, 3H) (Figure S20).

^{13}C NMR ($CDCl_3$): δ 196.2, 156.5, 147.4, 146.5, 144.1, 141.0, 129.8, 124.0, 119.6, 99.7, 61.7, 61.2, 56.3 (Figure S21).

1-Hydroxymethyl-,5,6,7-trimethoxyisoquinoline (10). To the ethanol solution (4 mL) of 5,6,7-trimethoxy-1-quinolinecarboxaldehyde (**9**) (40.3 mg, 0.163 mmol) was added $NaBH_4$ (10.8 mg, 0.285 mmol) and stirred for 2 h at room temperature. After addition of water, the organic material was extracted with dichloromethane, dried, and evaporated to give brown solid. Yield, 25.6 mg (0.103 mmol, 63%).

^{1}H NMR ($CDCl_3$): δ 8.36 (d, *J* = 5.9 Hz, 1H), 7.80 (d, *J* = 5.9 Hz, 1H), 6.87 (s, 1H), 5.12 (s, 2H), 4.06 (s, 3H), 4.02 (s, 3H), 4.01 (s, 3H) (Figure S22).

^{13}C NMR ($CDCl_3$): δ 154.9, 154.0, 147.3, 144.1, 138.8, 128.0, 121.9, 114.4, 97.4, 77.2, 61.6, 61.5, 61.2, 56.1 (Figure S23).

1-Chloromethyl-5,6,7-trimethoxyisoquinoline (11). To the dichloromethane solution (5 mL) of 1-hydroxymethyl-5,6,7-trimethoxyisoquinoline (**10**) (102 mg, 0.408 mmol) was added thionyl chloride (0.053 mL, 0.737 mmol) and stirred for 1 day at room temperature. After addition of saturated aqueous $NaHCO_3$, the organic

material was extracted with dichloromethane, dried, and evaporated to give brown solid in quantitative yield.

^{1}H NMR ($CDCl_3$): δ 8.37 (d, *J* = 5.7 Hz, 1H), 7.85 (d, *J* = 5.7 Hz, 1H), 7.26 (s, 1H), 5.10 (s, 2H), 4.054 (s, 3H), 4.050 (s, 3H), 4.03 (s, 3H) (Figure S24).

^{13}C NMR ($CDCl_3$): δ 154.0, 153.1, 147.2, 144.0, 140.3, 129.0, 123.7, 115.9, 99.3, 77.2, 61.6, 61.2, 56.1 (Figure S25).

[Zn(triMeO-1-isoTQEN)]$(ClO_4)_2 \cdot 1.5H_2O$. In an chloroform solution of triMeO-1-isoTQEN was added equimolar amount of $Zn(ClO_4)_2 \cdot 6H_2O$ in methanol, and the solution was kept at 4 °C temperature under ether diffusion condition afforded white powder. Yield, 45%.

Anal. calcd for $C_{54}H_{63}Cl_2N_6O_{21.5}Zn$ ([Zn(triMeO-1-isoTQEN)]$(ClO_4)_2 \cdot 1.5H_2O$): H 4.97, C 50.81, N 6.58; found: H 4.72, C 50.47, N 6.56.

^{1}H NMR (acetate, CD_3OD): δ 8.03 (d, *J* = 6.0 Hz, 4H), 7.92 (br., 4H), 7.33 (s, 4H), 5.18 (d, *J* = 17.9 Hz, 4H), 4.73 (d, *J* = 17.9 Hz, 4H), 4.08 (s, 12H), 4.05 (s, 12H), 4.02 (s, 12H), 3.48 (s, 4H), 1.92 (s, 6H) (Figure S28).

^{13}C NMR (acetate, CD_3OD): δ 180.1, 157.1, 155.0, 148.3, 147.3, 137.4, 130.5, 124.7, 118.6, 100.2, 62.3, 61.8, 60.8, 58.9, 56.9, 24.1 (Figure S29).

References

(1) French, F. A.; Blanz, Jr., E. J.; DoAmaral, J. R.; French, D. A. *J. Med. Chem.* **1970**, *13*, 1117-1124

(2) Cushman, M.; Nagarathnam, D.; Gopal, D.; He, H.-M.; Lin, C. M.; Hamel, E. *J. Med. Chem.* **1992**, *35*, 2293-2306.

(3) Hara, H.; Tsunashima, A.; Shinoki, H.; Akiba, T.; Hoshino, O.; Umezawa, B. *Chem. Pharm. Bull.* **1986**, *34*, 66-70.

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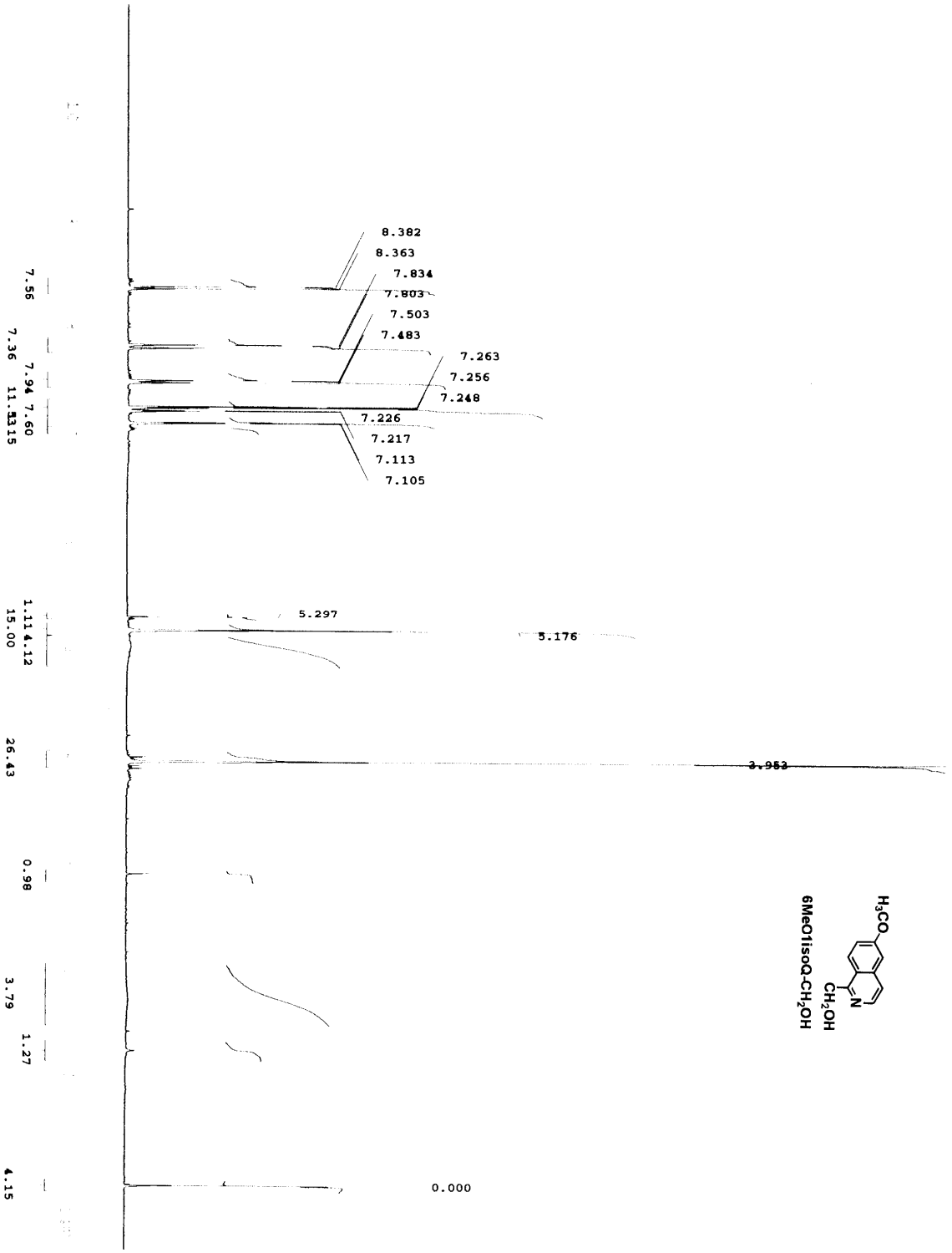

Figure S2. ^{1}H NMR spectrum of **2**.

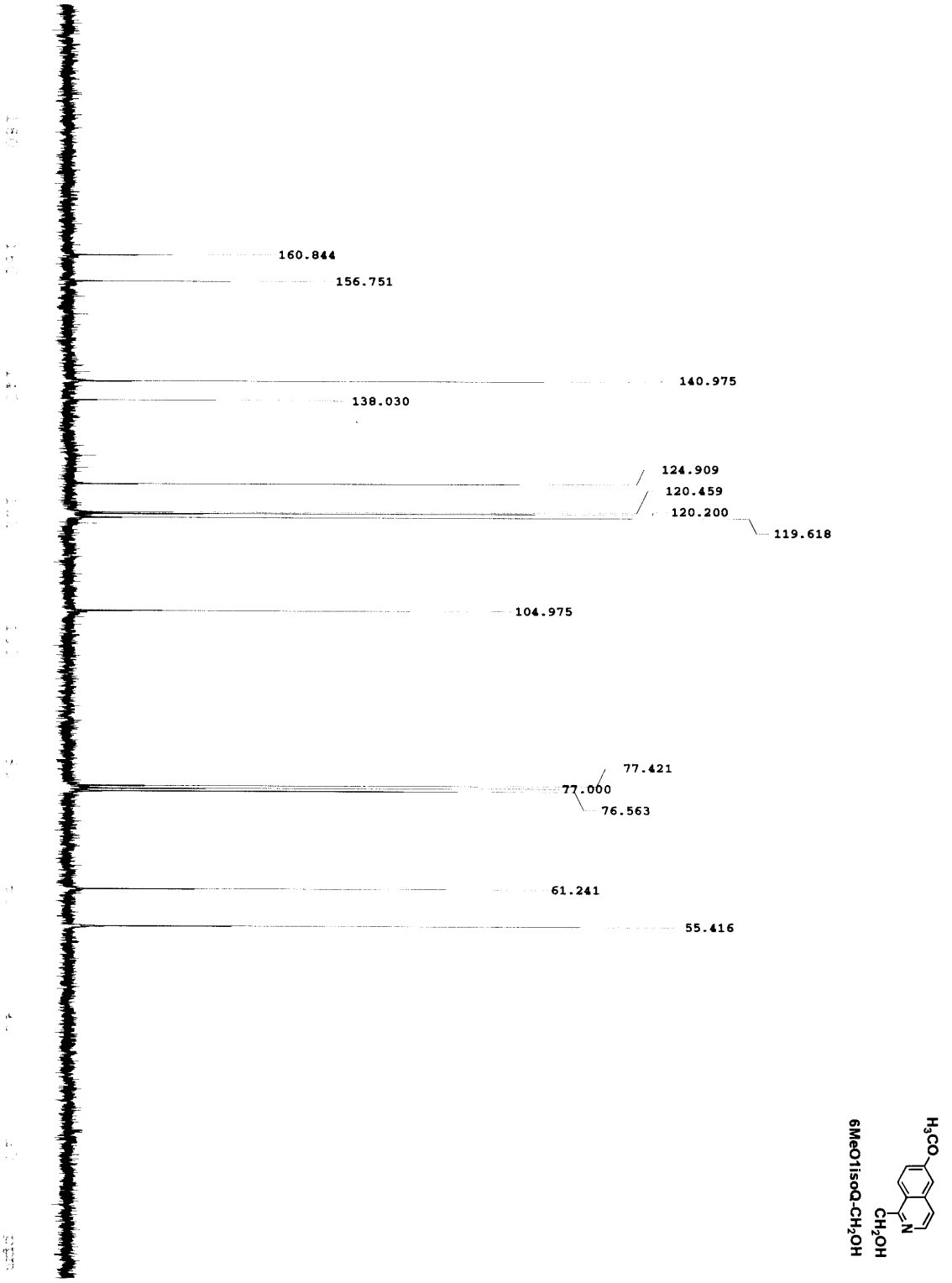

Figure S3. ^{13}C NMR spectrum of **2**.

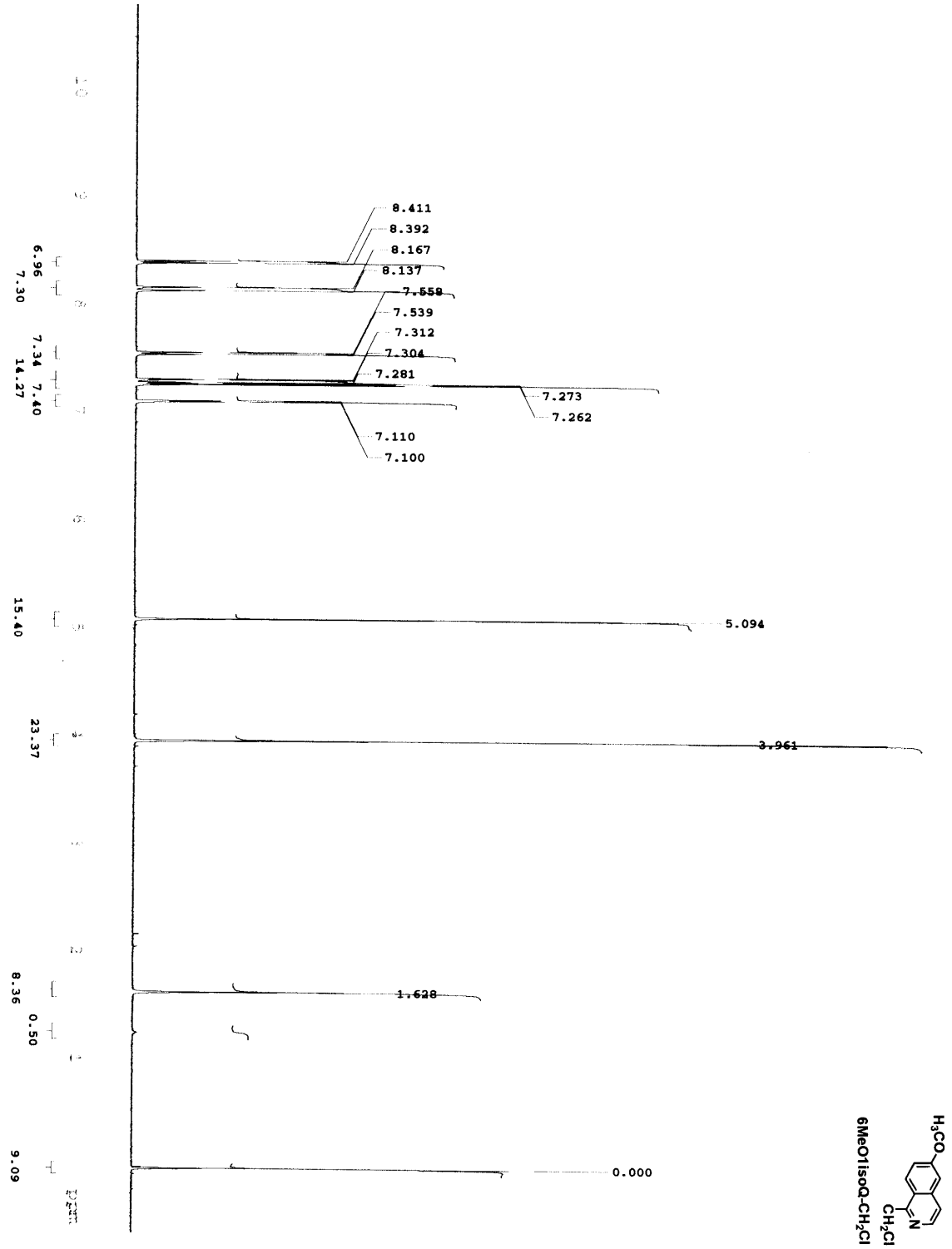

Figure S4. ^{1}H NMR spectrum of **3**.

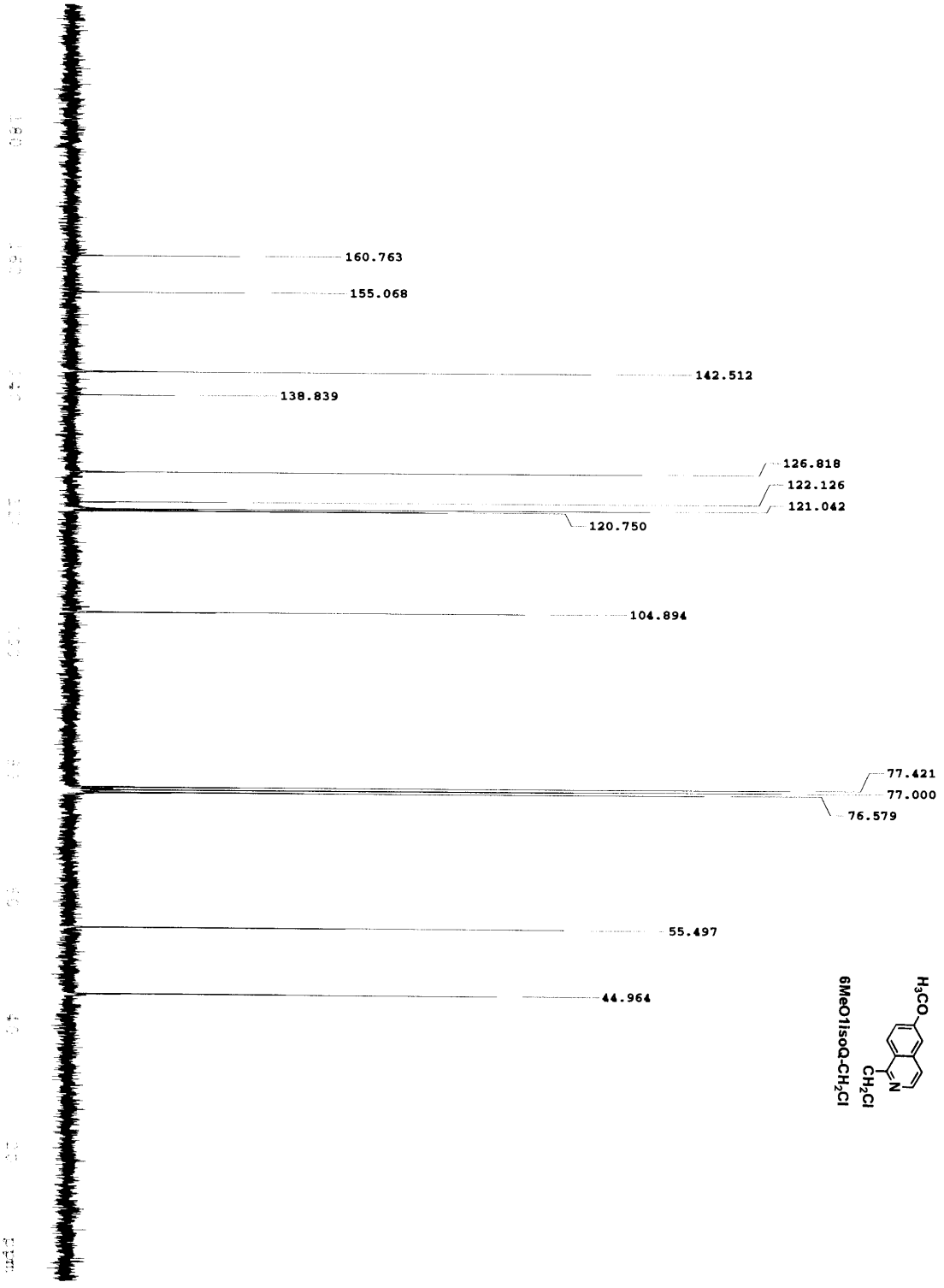

Figure S5. ^{13}C NMR spectrum of **3**.

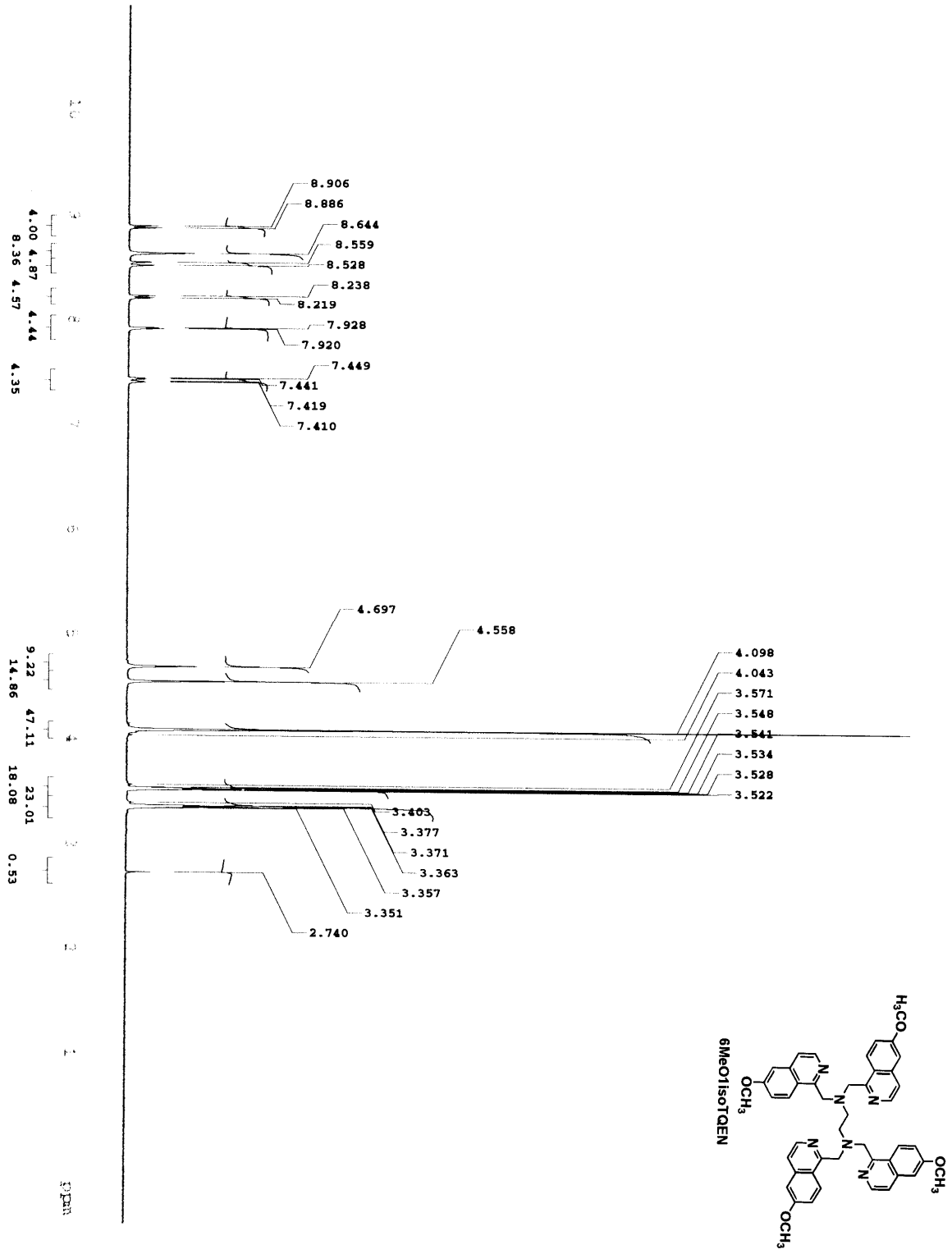

Figure S6. ^{1}H NMR spectrum of 6-MeO-1-isoTQEN.

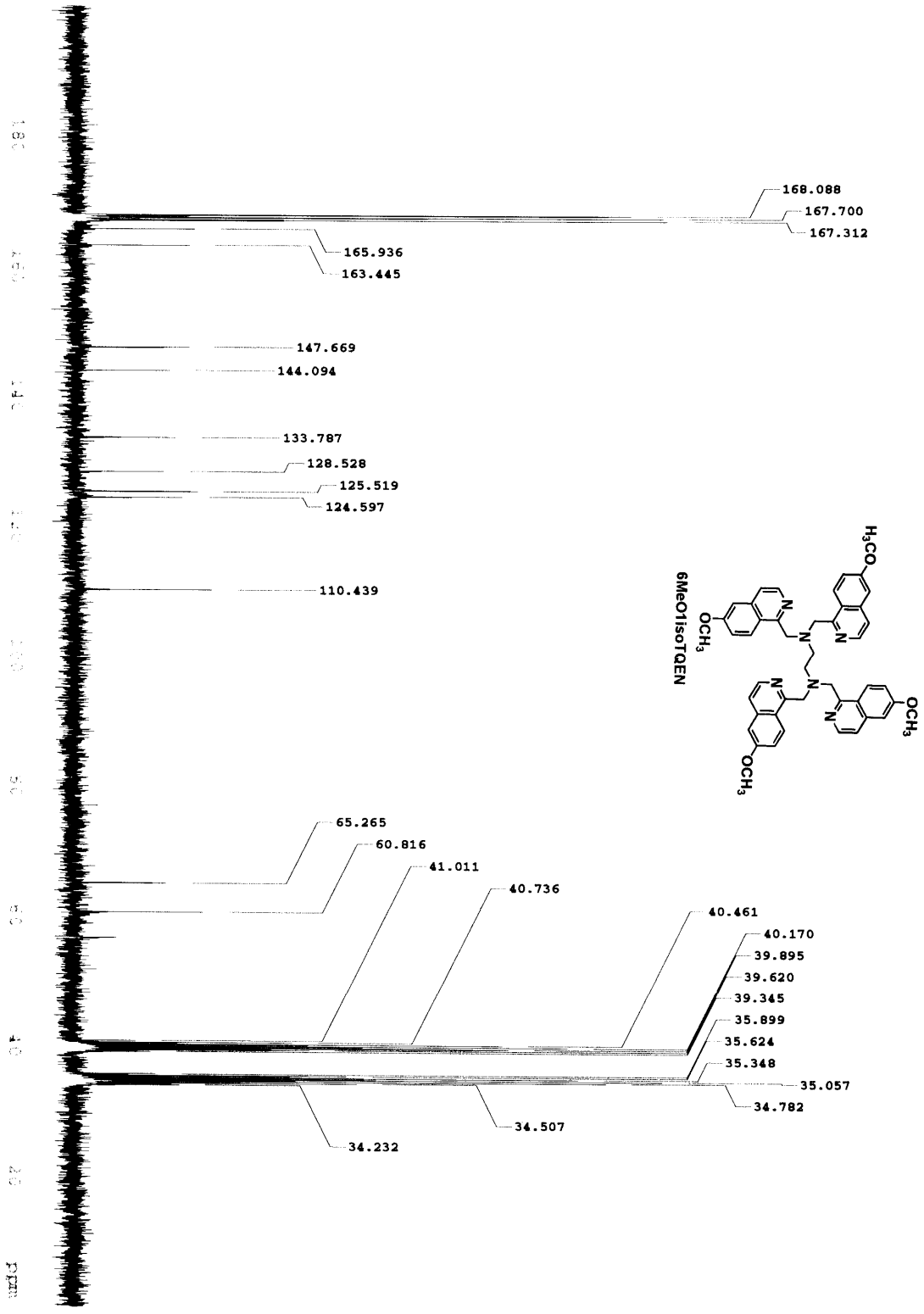

Figure S7. ^{13}C NMR spectrum of 6-MeO-1-isoTQEN.

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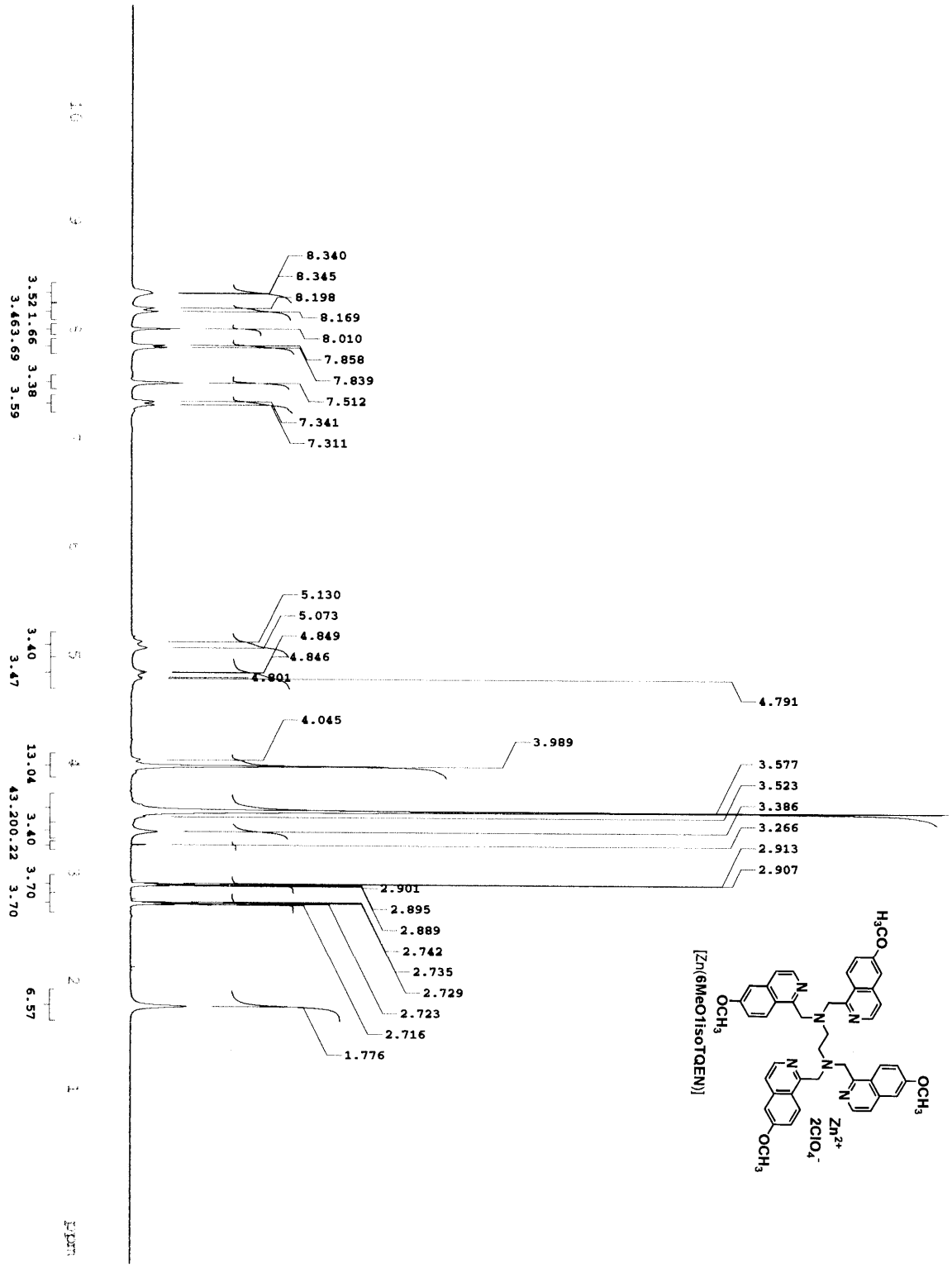

Figure S8. ^{1}H NMR spectrum of [Zn(6-MeO-1-isoTQEN)]$(ClO_4)_2$.

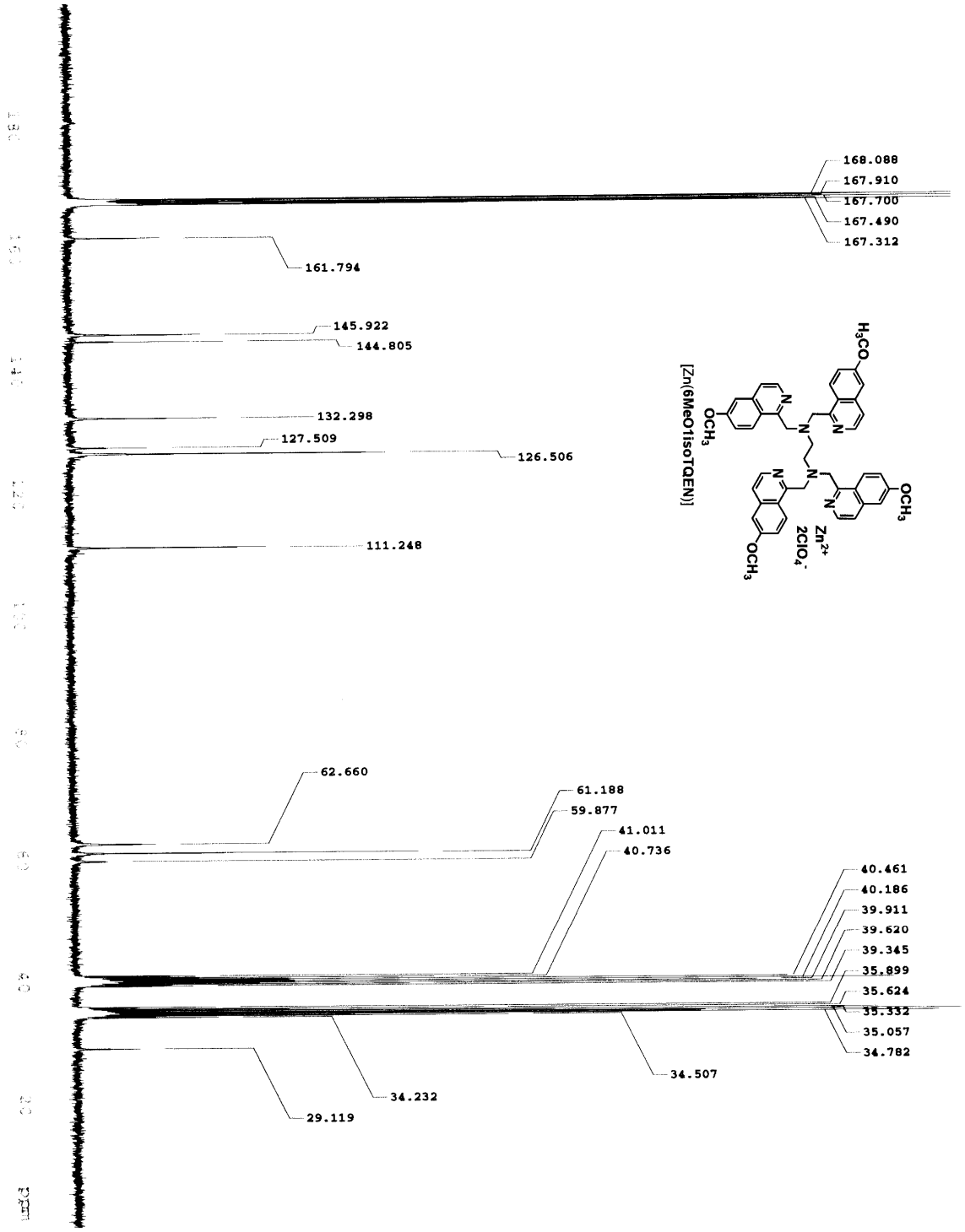

Figure S9. ^{13}C NMR spectrum of $[Zn(6\text{-MeO-1-isoTQEN})](ClO_4)_2$.

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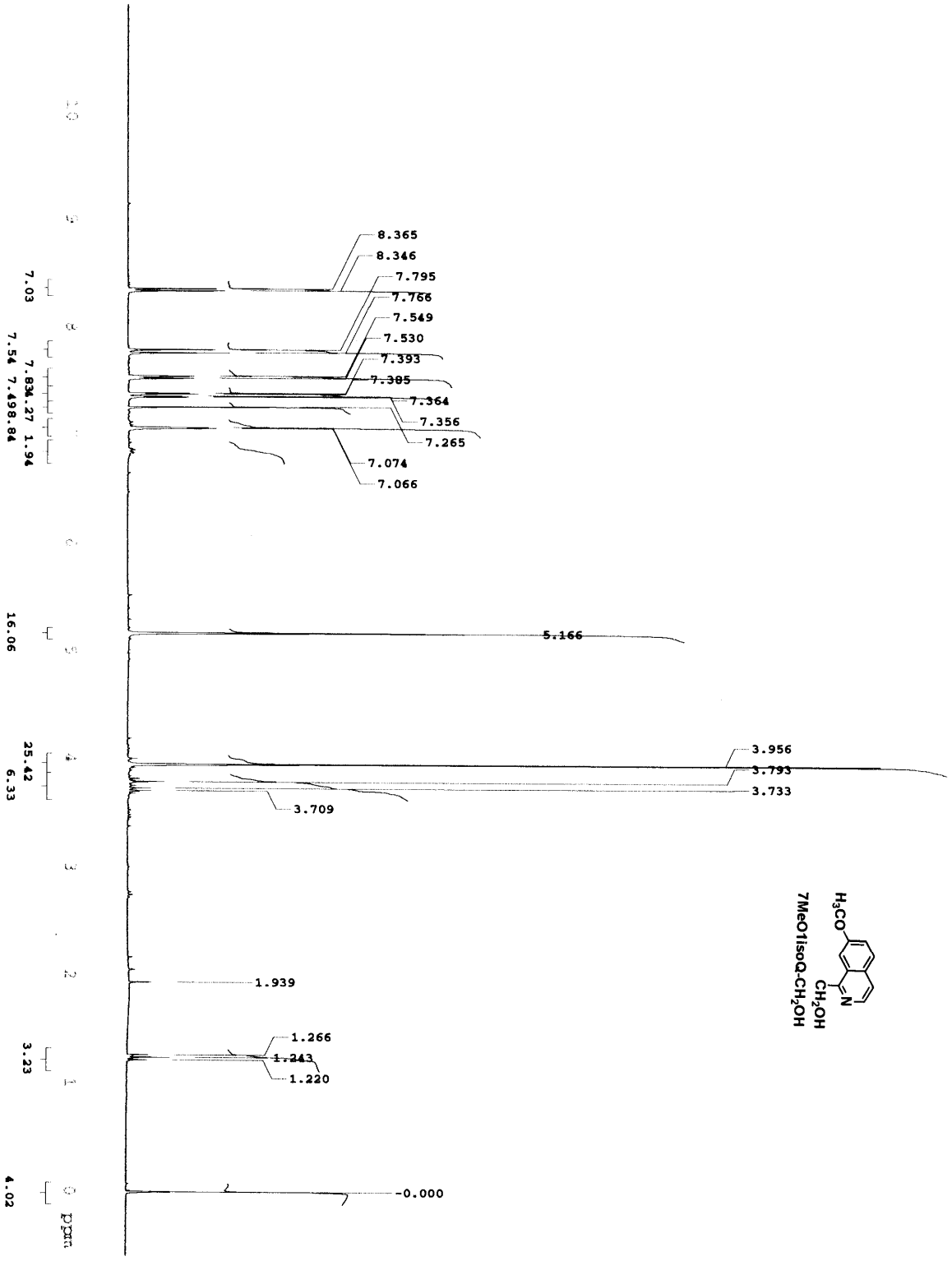

Figure S10. ^{1}H NMR spectrum of **5**.

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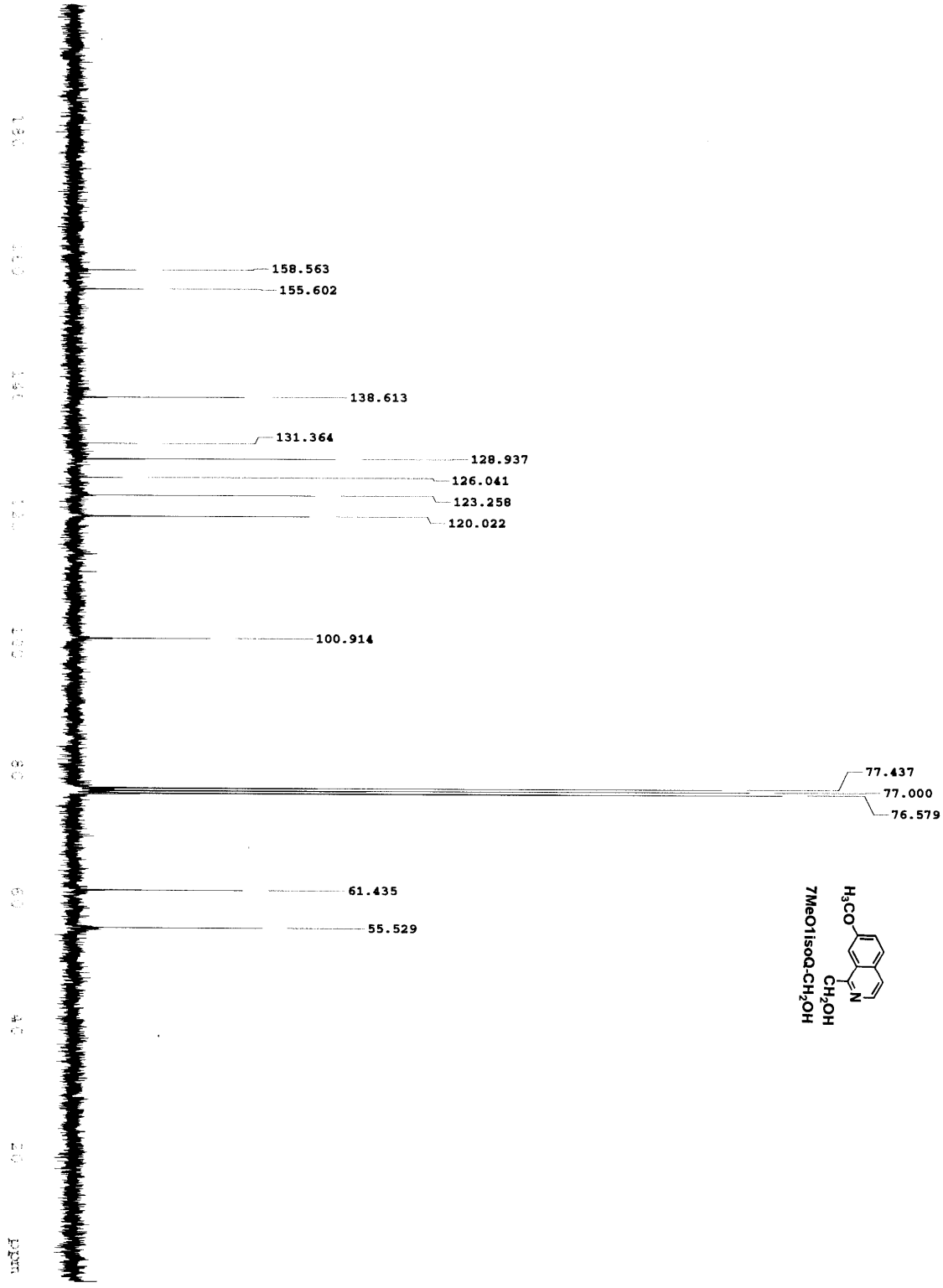

Figure S11. ^{13}C NMR spectrum of **5**.

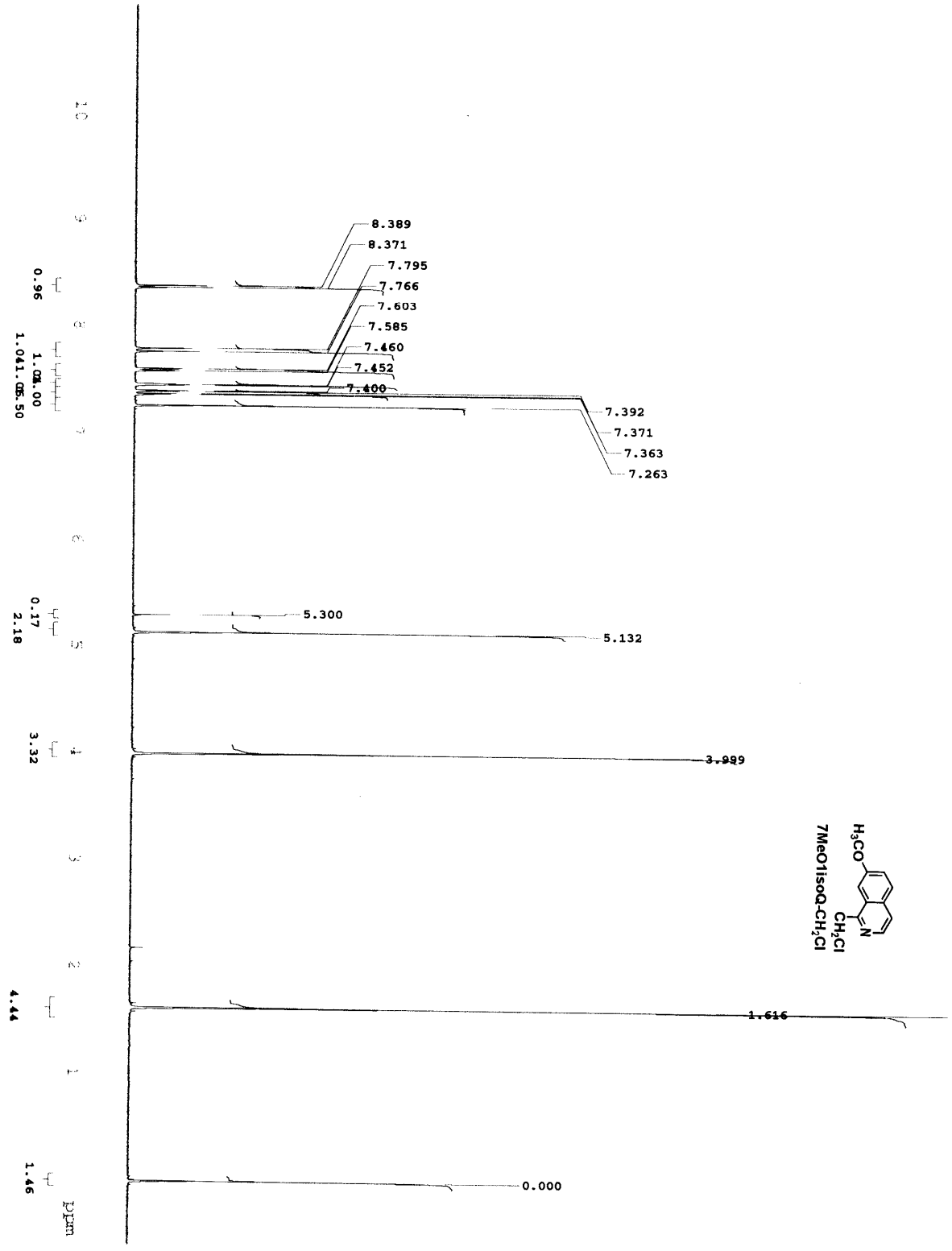

Figure S12. ^{1}H NMR spectrum of **6**.

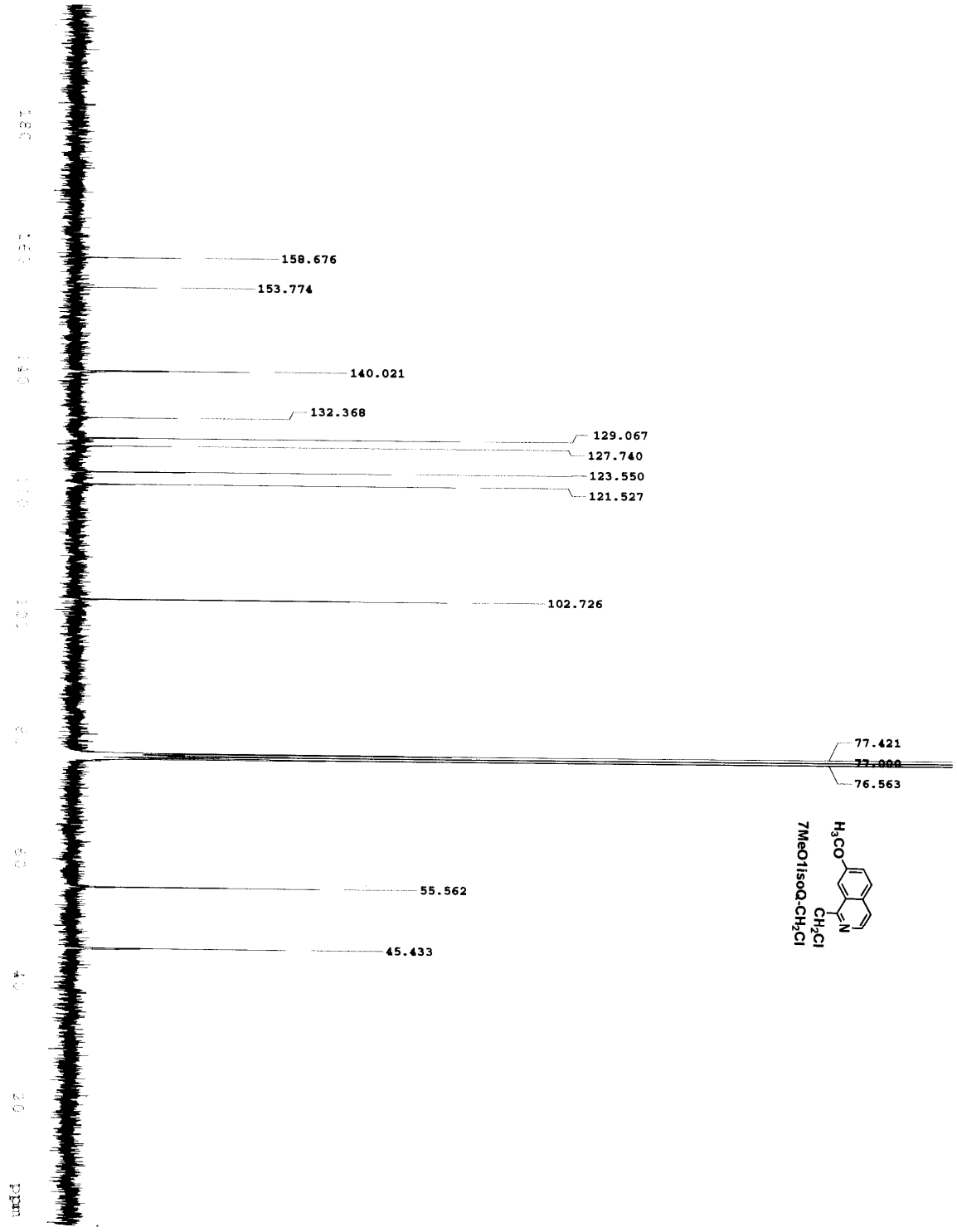

Figure S13. ^{13}C NMR spectrum of **6**.

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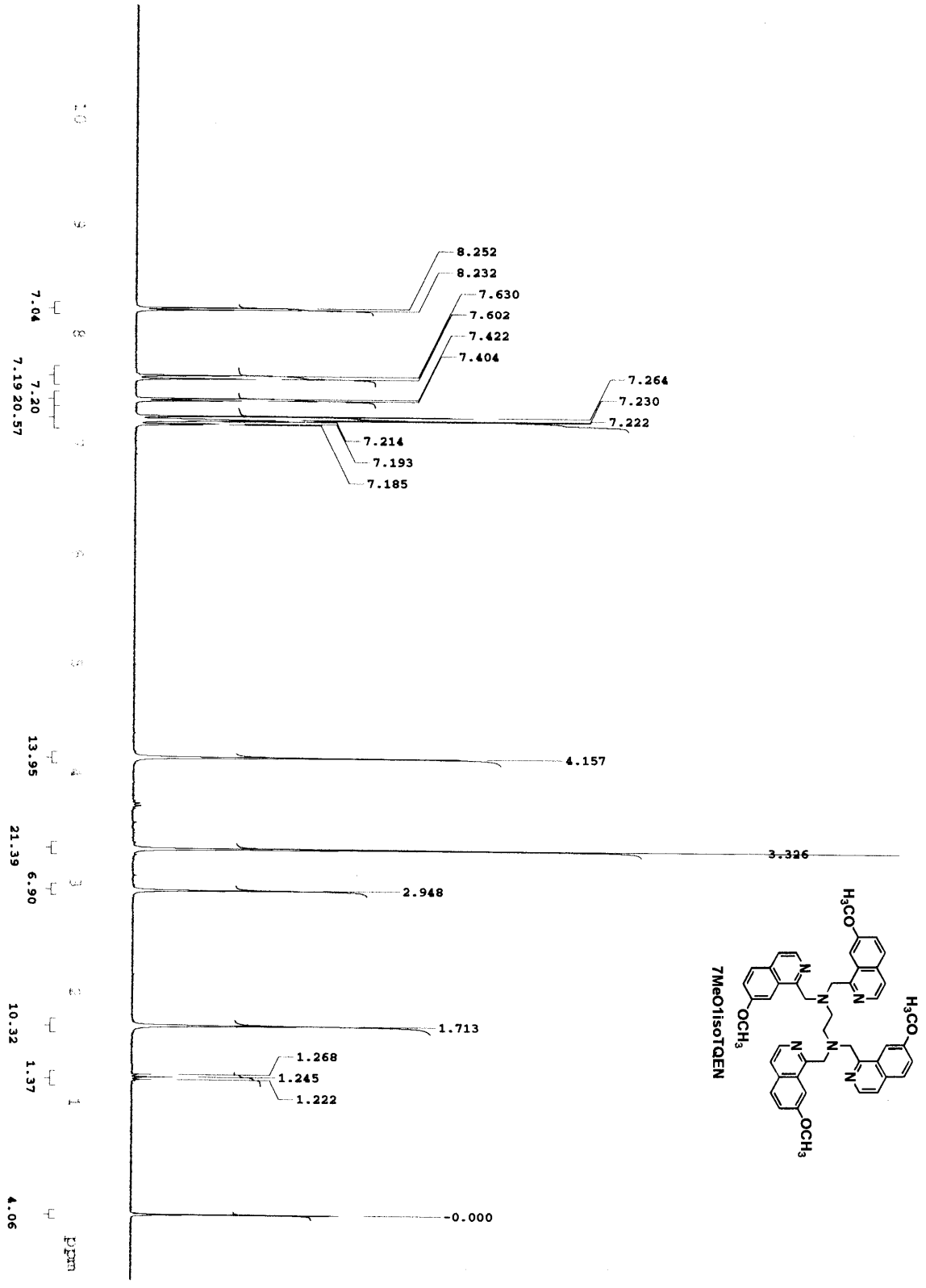

Figure S14. ^{13}C NMR spectrum of 7-MeO-1-isoTQEN.

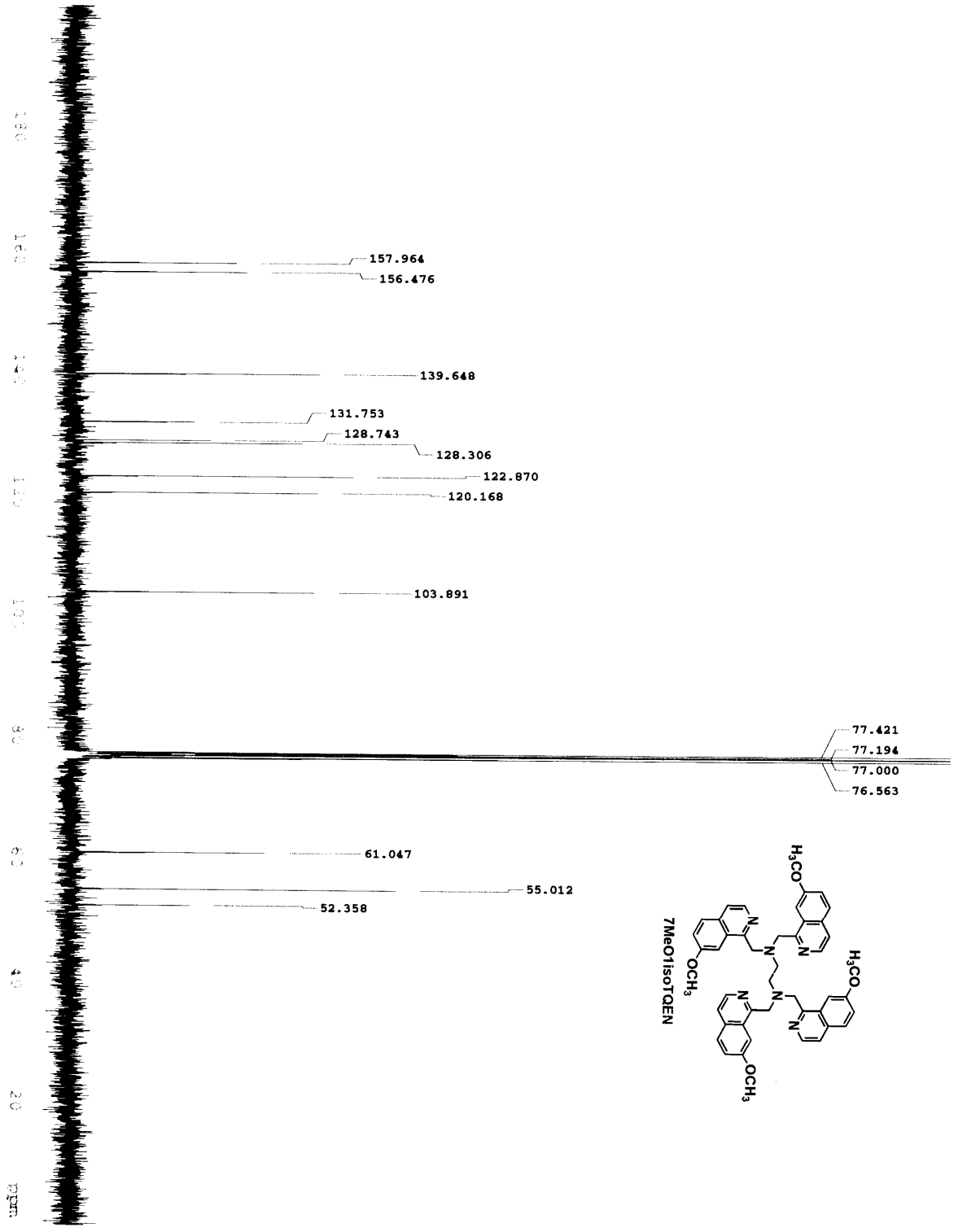

Figure S15. ^{13}C NMR spectrum of 7-MeO-1-isoTQEN.

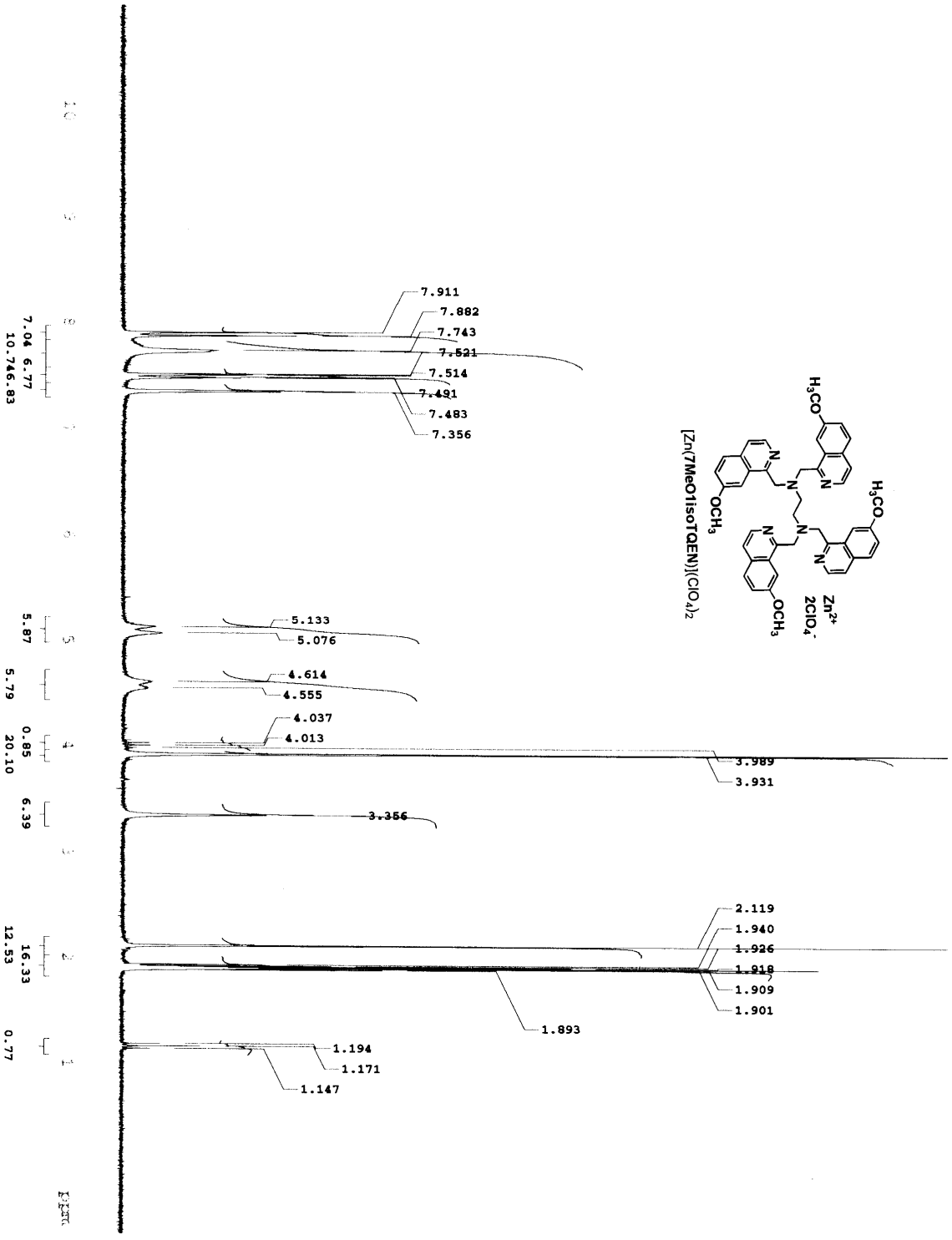

Figure S16. ^{13}C NMR spectrum of [Zn(7-MeO-1-isoTQEN)]$(ClO_4)_2$.

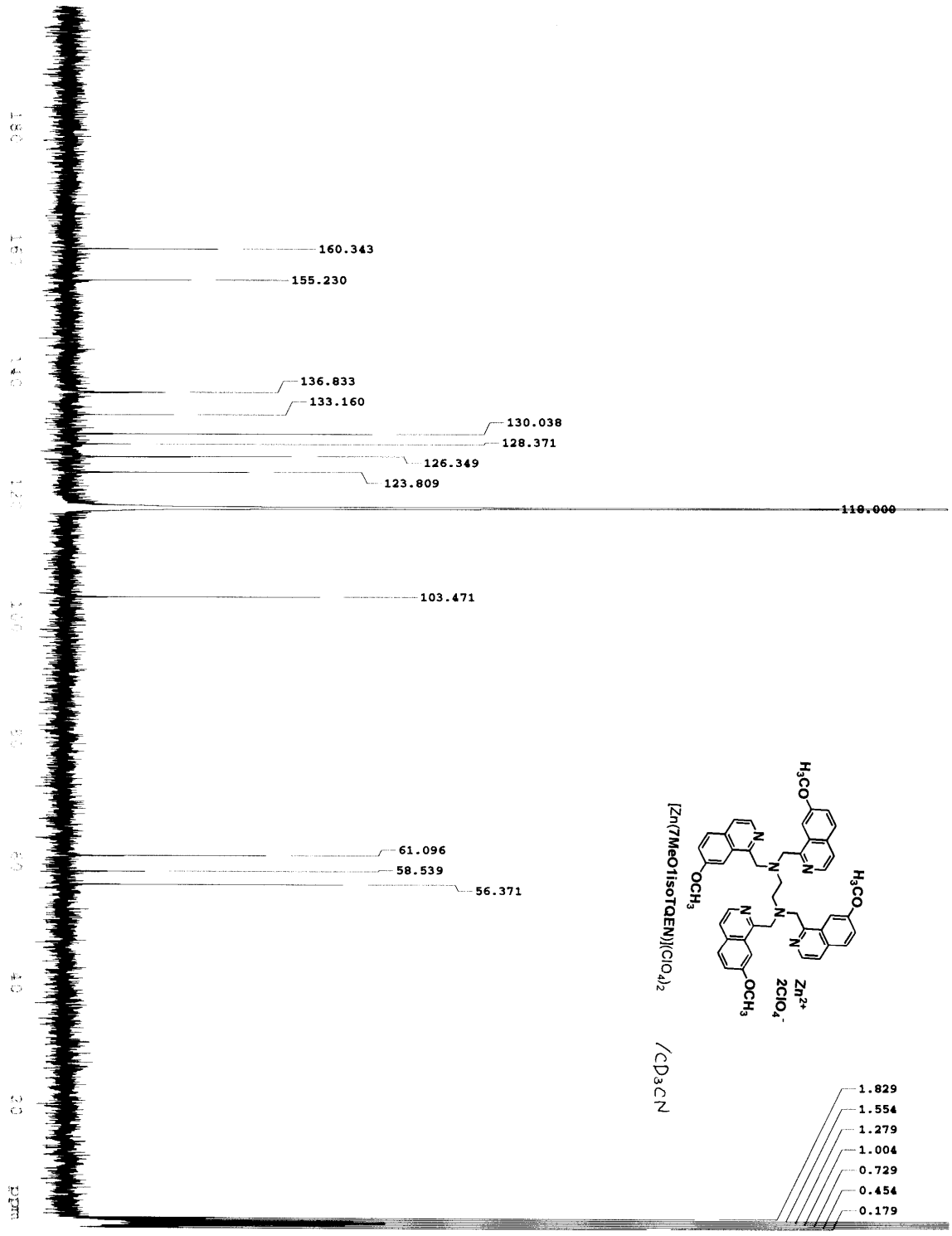

Figure S17. ^{13}C NMR spectrum of [Zn(7-MeO-1-isoTQEN)]$(ClO_4)_2$.

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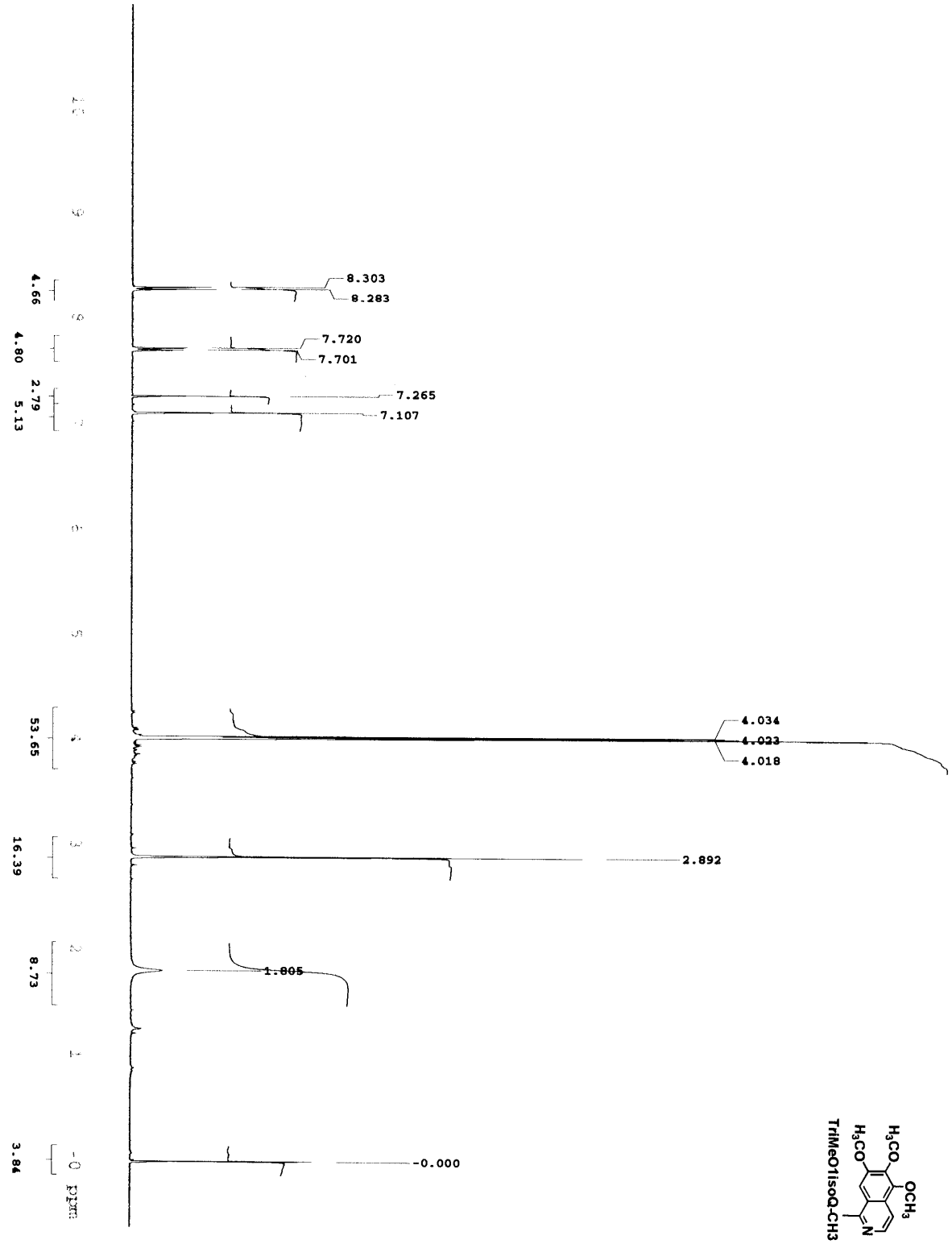

Figure S18. ^{1}H NMR spectrum of **8**.

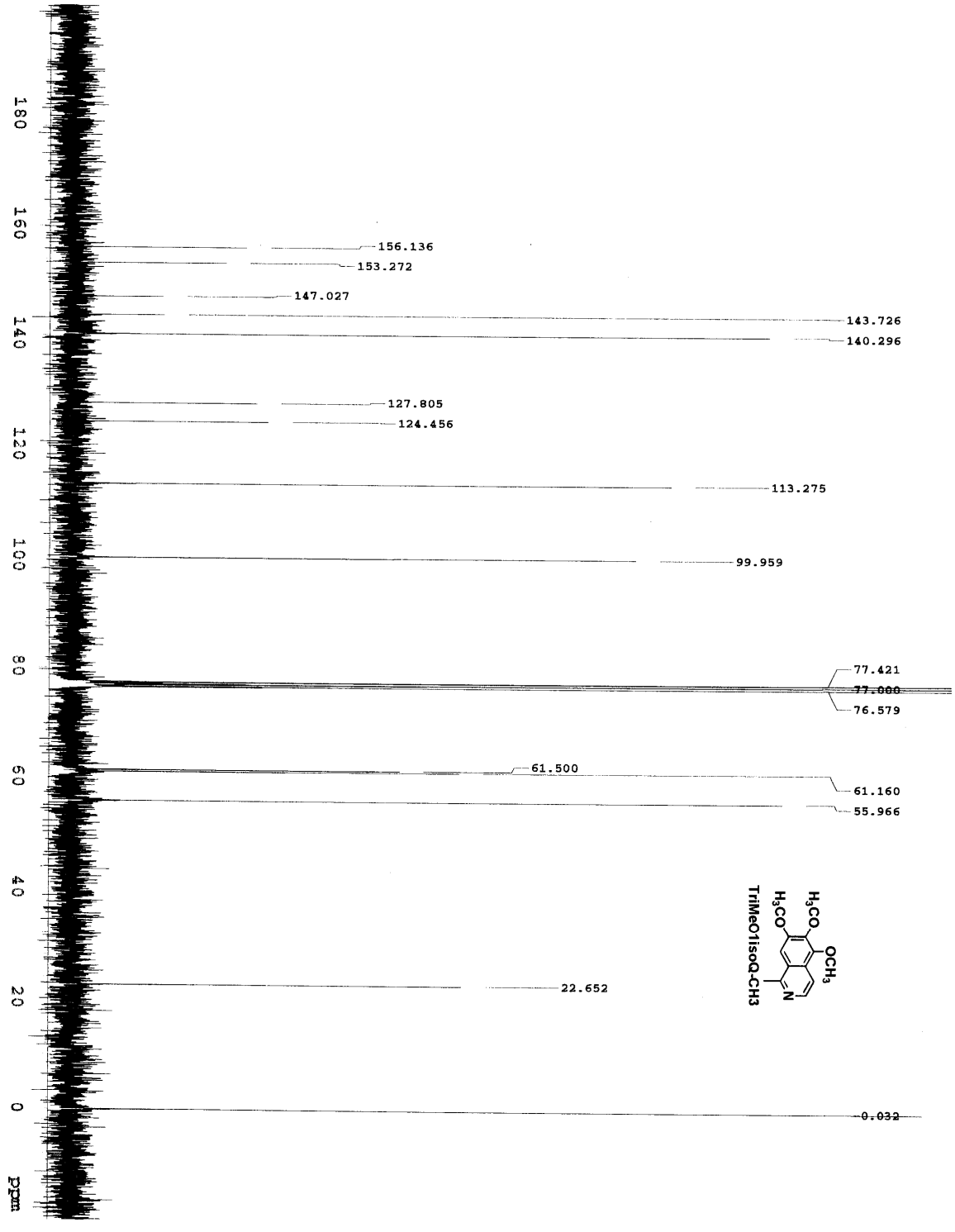

Figure S19. ^{13}C NMR spectrum of **8**.

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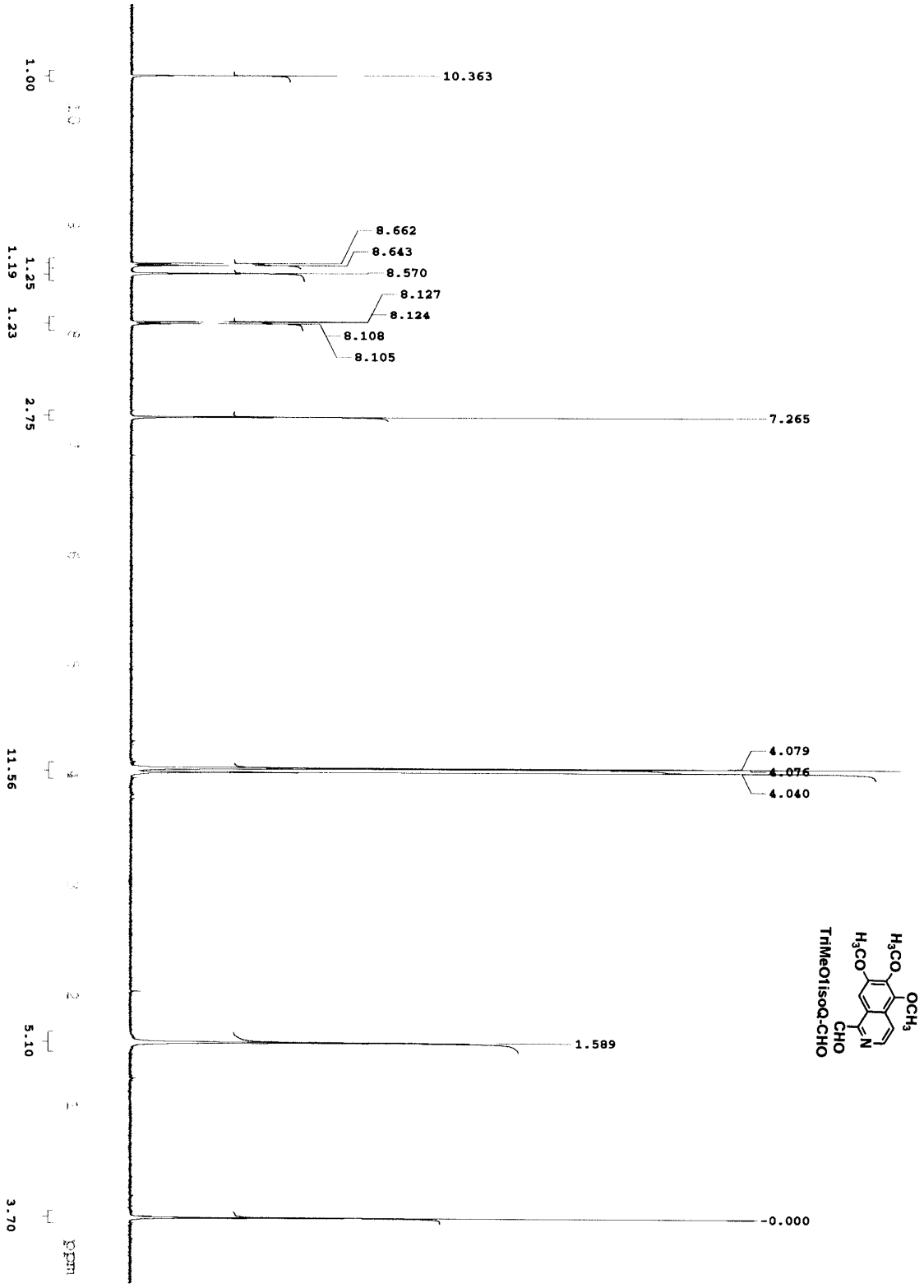

Figure S20. ^{1}H NMR spectrum of **9**.

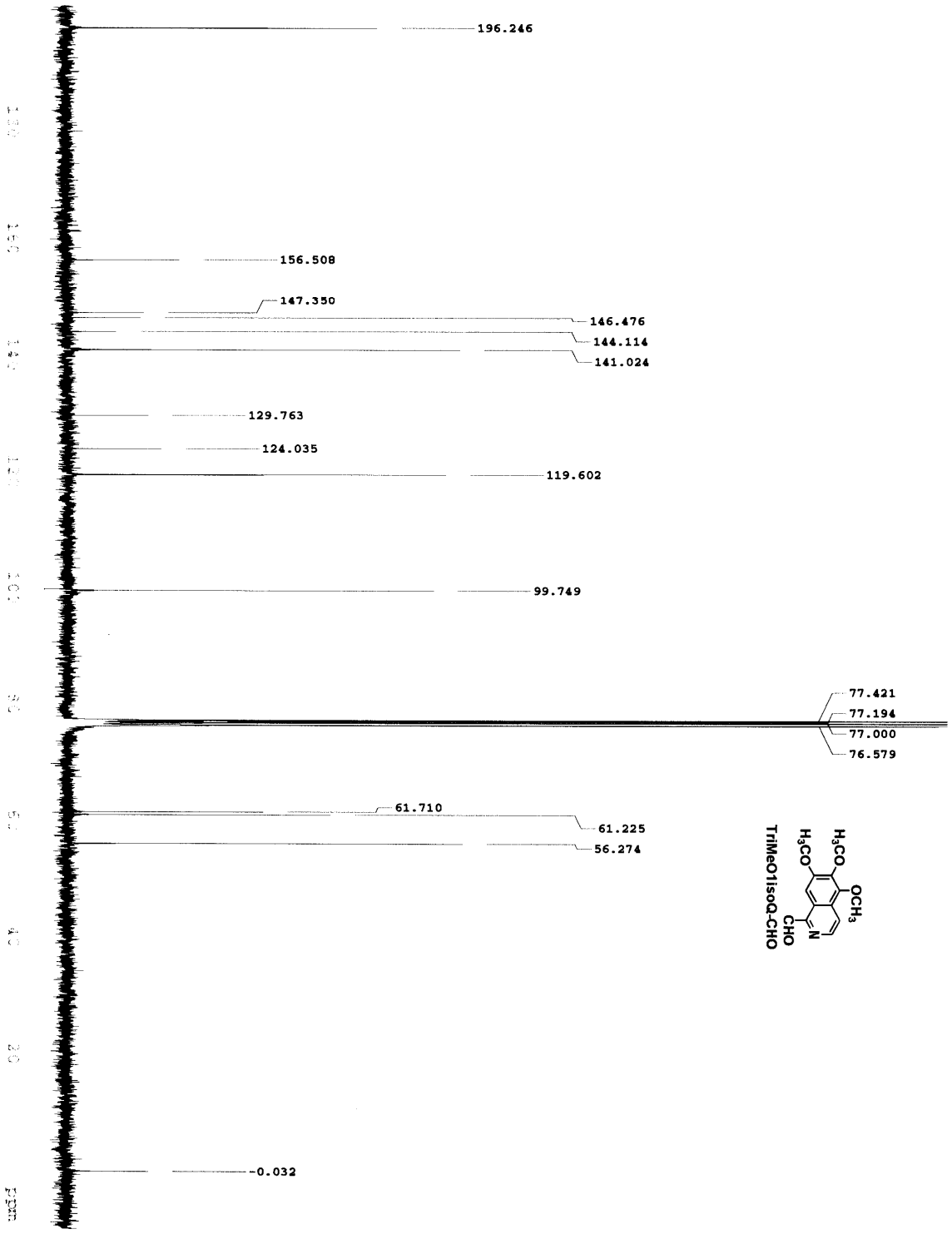

Figure S21. ^{13}C NMR spectrum of **9**.

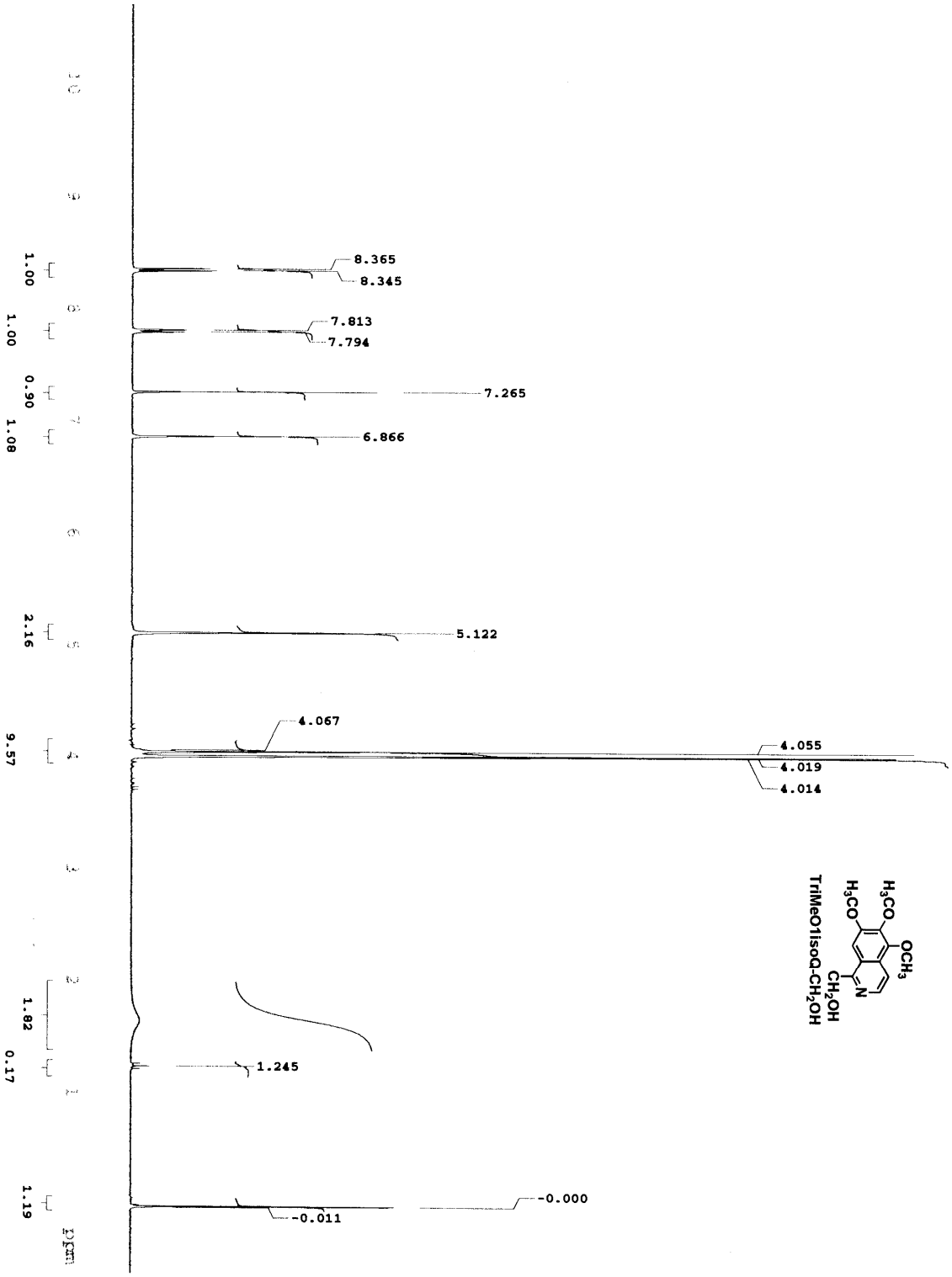

Figure S22. ^{1}H NMR spectrum of **10**.

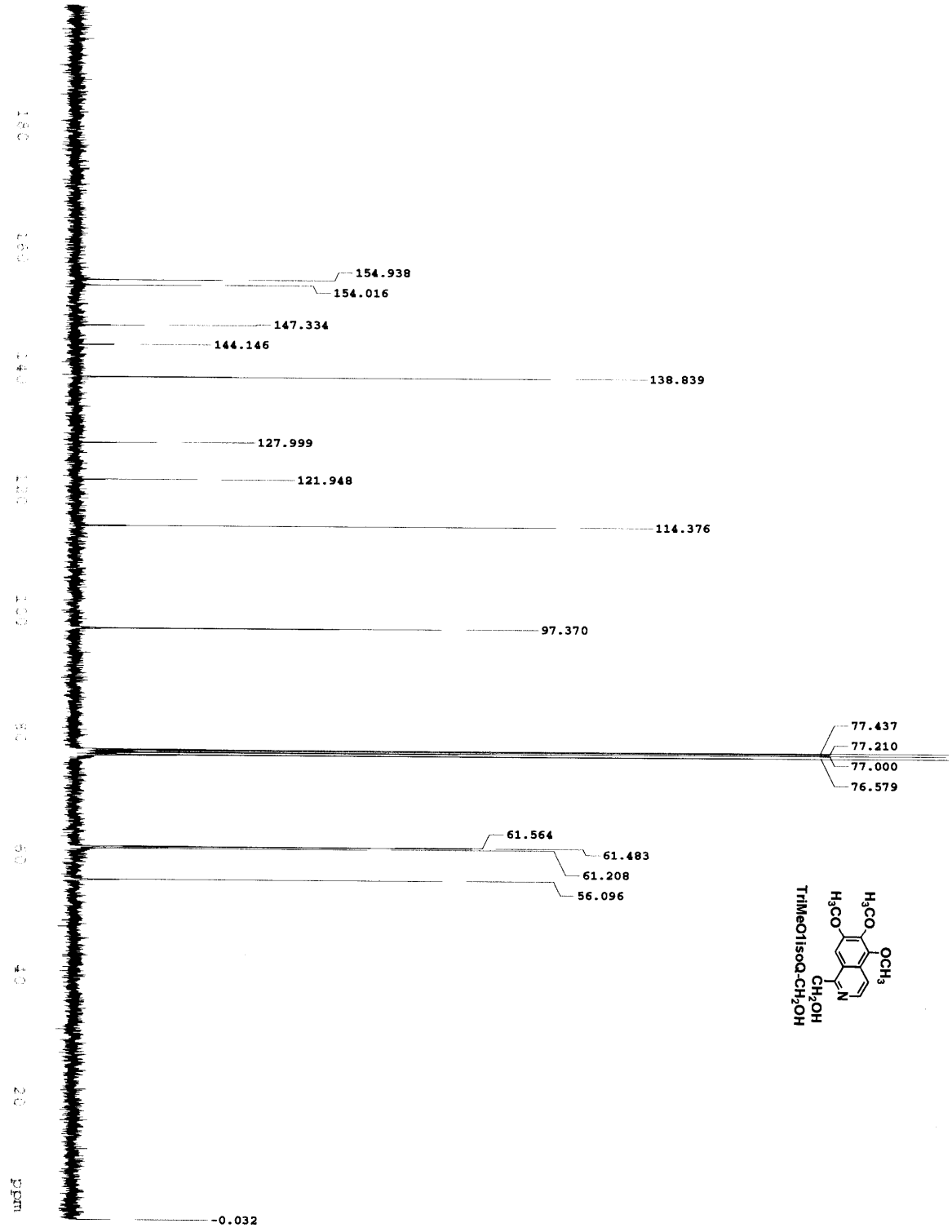

Figure S23. ^{13}C NMR spectrum of **10**.

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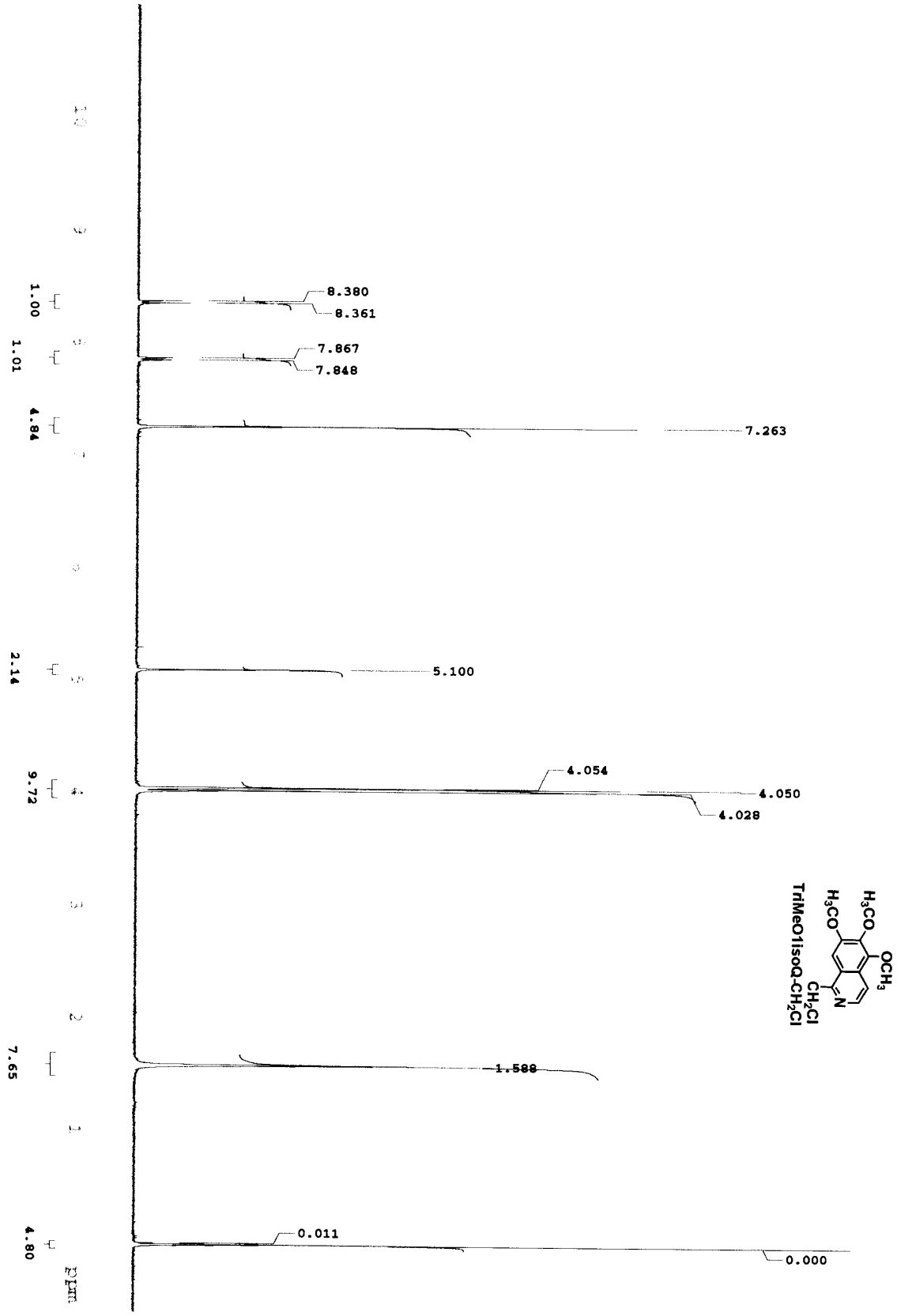

Figure S24. ^{1}H NMR spectrum of **11**.

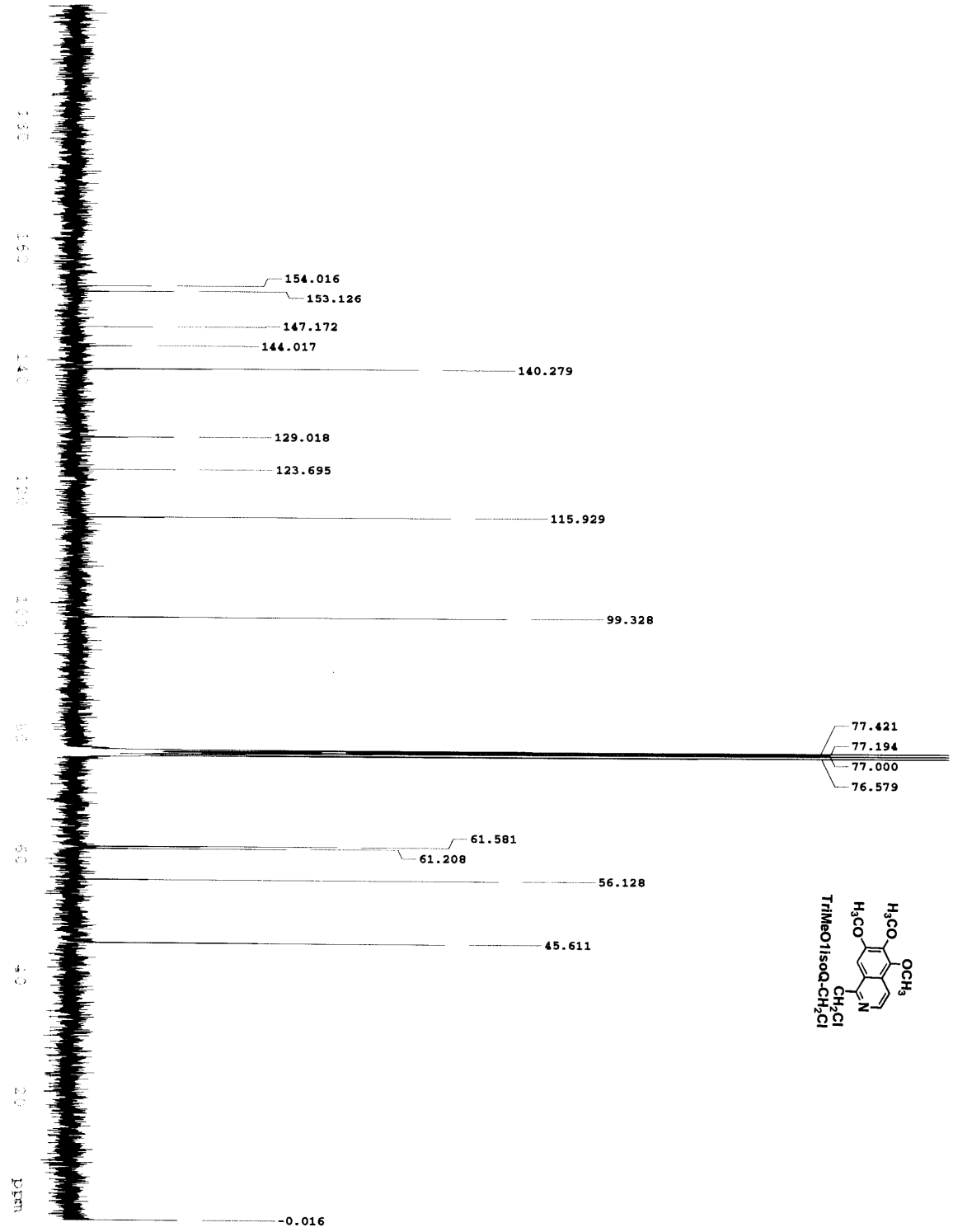

Figure S25. ^{13}C NMR spectrum of **11**.

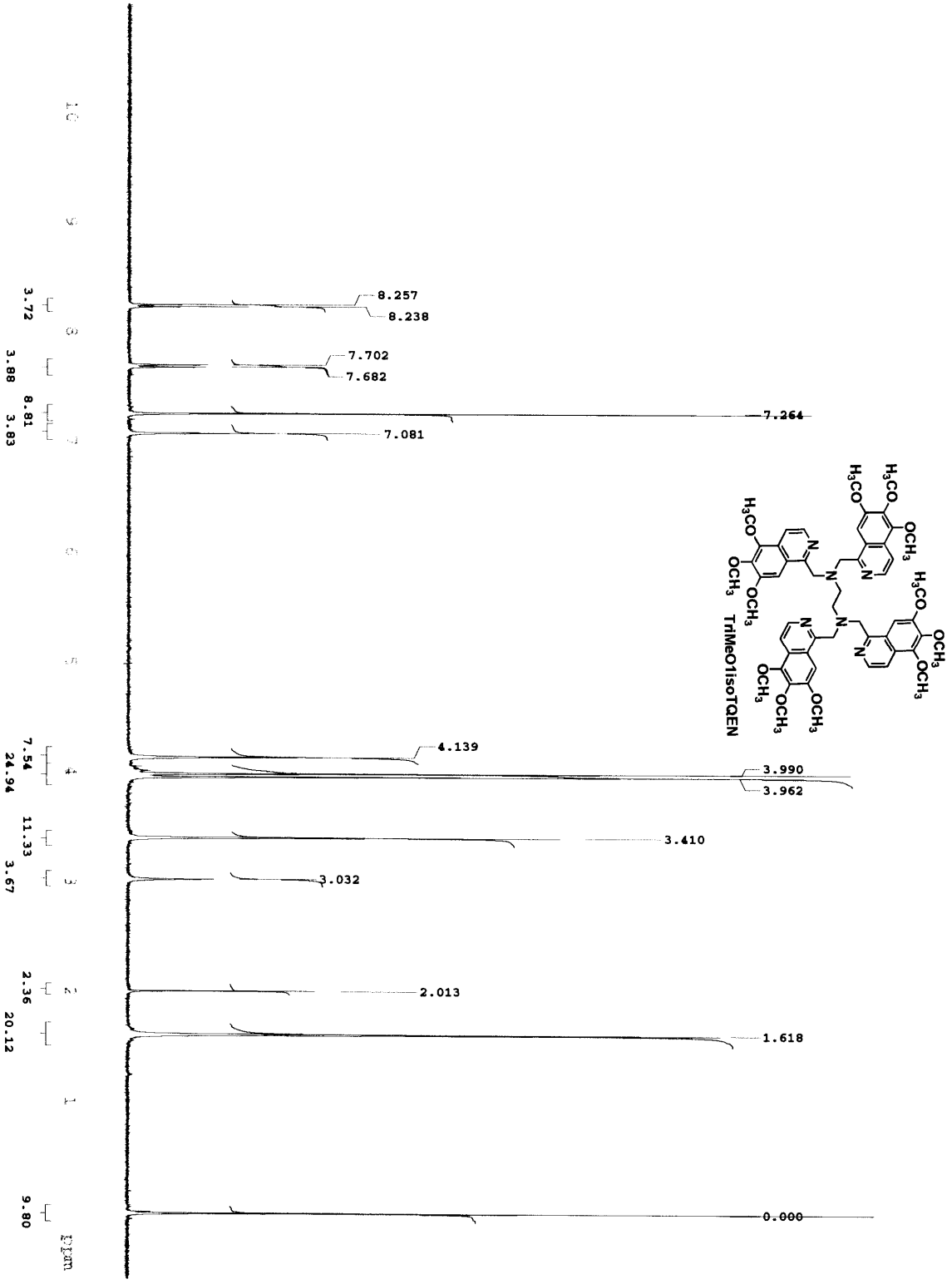

Figure S26. ^{1}H NMR spectrum of triMeO-1-isoTQEN.

Supplementary Material (ESI) for Dalton Transactions

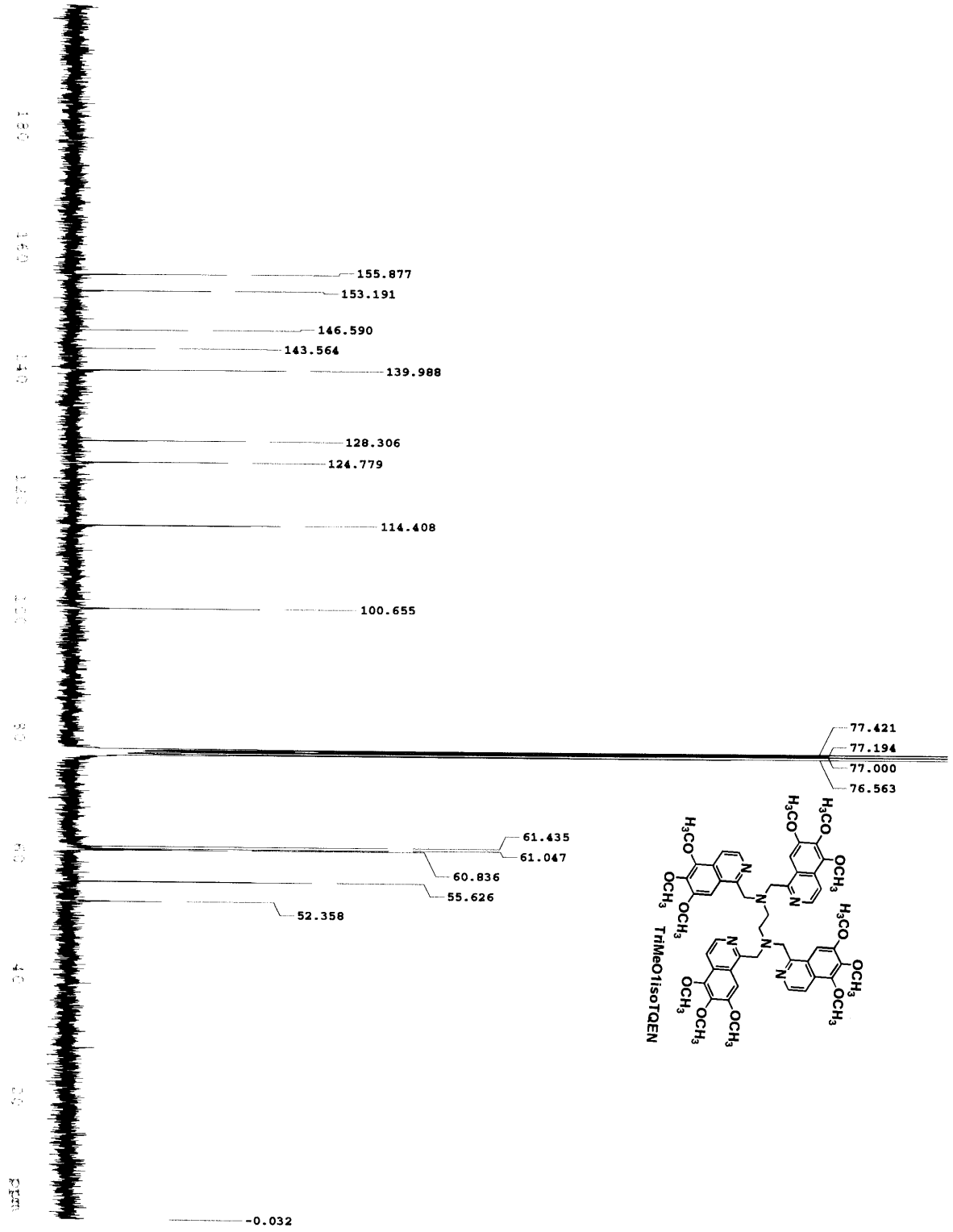

Figure S27. ^{13}C NMR spectrum of triMeO-1-isoTQEN.

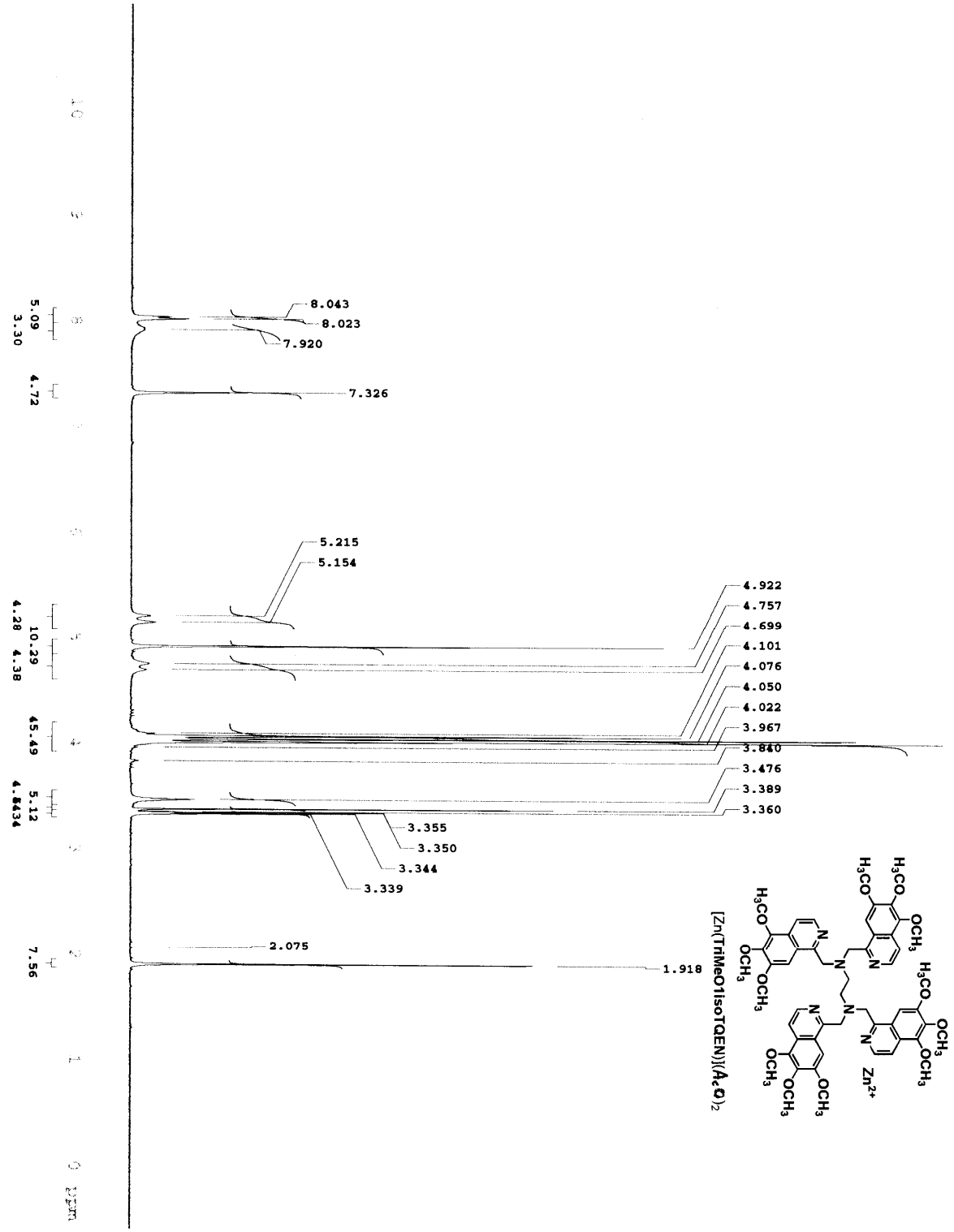

Figure S28. ^{1}H NMR spectrum of [Zn(triMeO-1-isoTQEN)](CH$_3$COO)$_2$.

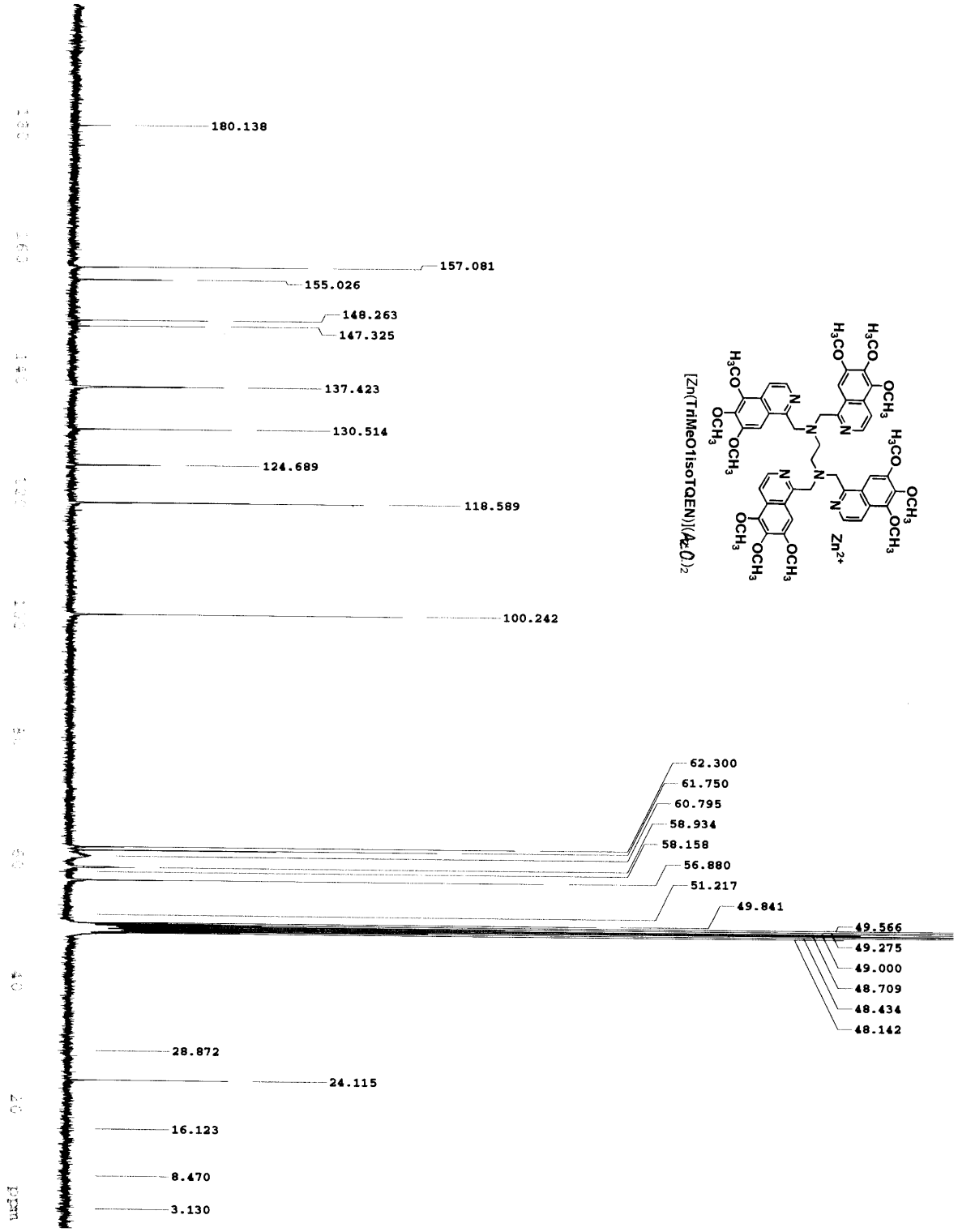

Figure S29. ^{13}C NMR spectrum of [Zn(triMeO-1-isoTQEN)]$(CH_3COO)_2$.