Electronic Supporting Information

Valorization of 2,5-Furandicarboxylic Acid. Diels-Alder Reactions with Benzyne

*Eric M. Serum, Sermadurai Selvakumar, Nicholas Zimmermann, and Mukund P. Sibi**

Department of Chemistry and Biochemistry, North Dakota State University, Fargo, North Dakota, USA,

E-mail: mukund.sibi@ndsu.edu

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1. General Methods

Unless otherwise stated, all commercially procured materials were used as received without further purification. Melting points were determined on a REACH Devices RD-MP digital melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Bruker Avance 400 MHz instrument and processed with Topspin software. Infrared spectra were recorded with a Nicolet™ iS™ 10 Fourier transform infrared spectrometer using a diamond sample plate for attenuated total reflectance and processed using Omnic; the FTIR figures were prepared using Origin Pro. High resolution mass spectra were recorded on Waters Synapt G2-Si high definition mass spectrometer and were processed using MassLynx. Unless otherwise stated, all reactions were stirred magnetically by polytetrafluoroethylene coated magnetic spin-bars. All mention of silica gel refers to Sorbtech standard grade silica gel: 230-400 mesh.

2. Discussion of Metrics

Theoretical yields have been calculated in terms of the limiting reagent throughout this work.

Equation S 1

$$Theoretical\ Yield = 1\ Molar\ Equivalent = 1\ equiv$$

Yields have been calculated only with respect to the limiting reagent and are reported as percentages.

Equation S 2

$$Yield = \frac{equiv\ product}{Theoretical\ Yield} \times 100$$

Atom economy (AE)[1] and Environmental impact factor (E-factor) are readily calculated for comparison as outlined by Roschanger *et al.*[2] Calculation of AE is only the first step to quantification of a process' greenness. It merely extends the calculation of theoretical yield to include consideration of atoms which do not become incorporated into the product.

We have calculated atom economy with molecular weight *(MW)* in grams/mol (g/mol), the optimum number is 100% which indicates that every atom of reagent and substrate gets incorporated into the product.

Equation S 3

$$AE = \frac{MW_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} \times 100$$

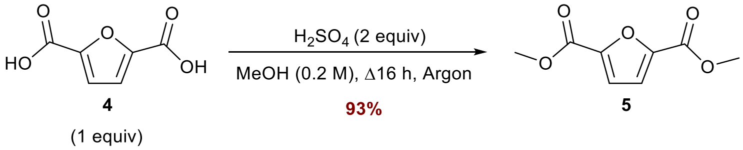
Calculation of E-factor can become onerous, and is extremely subject to change with variation of process variables and assumptions such as solvent recovery. Sheldon describes the use of simple E-factor (sEF),[3] which excludes the accounting for the water and solvent of a system. The optimum value for any E-factor is zero (0), as such, it provides an extensional value as a metric by combining elements of the yield and atom economy.

We have calculated sEF with mass *(m)* in grams (g).

Equation S 4

$$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)}$$

3. Synthesis of Dimethyl-2,5-furandicarboxylate **5**



Scheme S 1 Synthesis of **5**

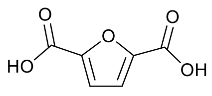
A 2 L single necked round bottom flask was charged with 2,5-furandicarboxylic acid (FDCA) **4** (55.88 g of 80% purity from AVA Biochem, 286 mmol, 1 equiv) The black-flecked tan solid was suspended in methanol (1.34 L, HPLC grade from Fisher Scientific). The brown methanolic suspension was stirred vigorously as concentrated sulfuric acid (30 mL of 18 M, 563 mmol, 2 equiv) was slowly added through a funnel; the color of the methanolic solution became black by the completion of the addition. The mixture was stirred beneath a Friedrichs condenser and the headspace was flushed with argon. The reaction was heated to a gentle reflux using a heating mantle/variac beneath an argon balloon; all the observable solid dissolved upon heating and the reflux continued for 16 h.

Upon cooling, the dark solution was concentrated to approximately one half its volume by rotary evaporation under vacuum. The acidic solution was diluted to a volume of nearly 2 L by charging the flask with crushed ice concurrently with vigorous shaking; a powdery-tan precipitate was observed. Once the ice thawed, the mixture was separated by suction filtration using a 2 L filter flask and a 9 cm ceramic Buchner funnel. The first filtrate (1900 mL) was orange in color and was discarded. The filter-cake was rinsed with deionized water (600 mL which was amber in color), pressed dry, chopped and spread on paper to air-dry.

The brown solid (53.63 g) gave a pure NMR spectrum, however the sample was an incomplete solution in $CDCl_3$. Fine brown particulate was observed to separate from a light-yellow solution upon standing. The crude product was dissolved in 250 mL of dichloromethane and gravity filtered through a column of silica gel with 500 mL of dichloromethane. The silica gel retained all the black color, and most of the orange; the eluted solution was faintly amber in color.

The dichloromethane solution was concentrated by rotary evaporation under vacuum, and the yellow solid residue was recrystallized from 2-propanol and separated by suction filtration to afford flaky white dimethyl-2,5-furandicarboxylate (46.3 g, 252 mmol, 88% yield) as crop one (melting point mp = 110-113 °C). The 350 mL of 2-propanolic liquor was concentrated to afford a second crop (2.26 g, 12.3 mmol, 5% yield, mp = 109-113 °C) of faintly yellow flaky solid.

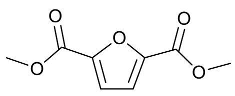
Diacid **4** was purchased from AVA Biochem as an 80% pure tan solid.



4

^{1}H NMR (400 MHz, DMSO d_6) δ 13.59 (br s,1 H), 7.28 (s,1 H)
^{13}C NMR (101 MHz, DMSO d_6) δ 159.0, 147.1, 118.4
FTIR (Neat) cm^{-1} 3150, 2994, 2640, 2560, 1690, 1571, 1521, 1417, 1264, 1222, 1186, 1161, 1039, 960, 847, 761, 583, 524, 486

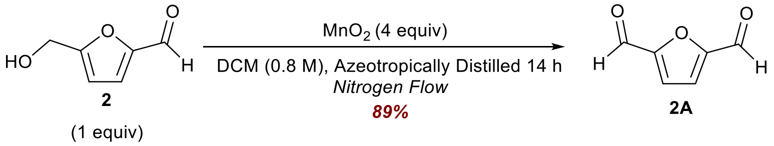
Diene **5** was prepared as described above.



5

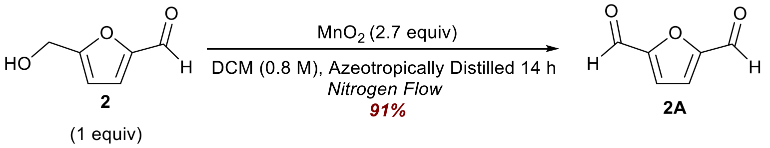
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 1 H), 3.92 (s, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 146.8, 118.6, 52.5
FTIR (Neat) cm^{-1} 3117, 3018, 2965, 1718, 1582, 1514, 1464, 1433, 1378, 1309, 1271, 1235, 1190, 1160, 1131, 1029, 985, 921, 835, 797, 764, 613, 480, 426

4. Synthesis 2,5-Diformylfuran **2A**



Scheme S 2 Synthesis of **2A**

To a 1.0L 24/40 Florence flask was added 5-(hydroxymethyl)furfural **2** (32.73 g of 95% from AVA Biochem, 247 mmol, 1 equiv), and dichloromethane (300 mL). The flask was secured by three fingered clamp over a spinning hotplate. PTFE tape was used to seal the joints throughout. A Claisen adapter was installed above of the Florence flask. A pressure equalizing-jointed solid addition auger was affixed to the direct neck with nitrogen inflow. A heavier than water Dean-Stark trap was affixed to the side neck below a West condenser plumbed with cool flowing tap water and ending in a gas flow adapter leading to a bubbler. The dichloromethane solution was a deep orange color. The solution was heated to distillation by direct heating from the hot plate under positive nitrogen pressure flowing through the addition auger and out the condenser. The trap was half-filled with distillate, the heat was killed, and upon cessation of reflux, the solid addition auger was charged with manganese dioxide (97 g, 88% active electrolytically precipitated from Acros Organics, 0.982 mmol, 4 equiv). The mixture was heated to distillation and the oxidizer was added in portions over the course of 6 h. Each addition of oxidizer was directly followed by the evolution of wet distillate. The unified reaction mixture was distilled for 12 h, then diluted while still hot with ethyl acetate (100 mL). The hot mixture was suction filtered through a finely fritted glass Buchner funnel half charged with silica gel. The mixture crystallized upon contacting the filter flask; ethyl acetate was used to rinse the filter pad free of obvious crystallized product (filtrate volume was 550 mL). The mixture was concentrated by rotary evaporation to remove dichloromethane, diluted to form a complete solution with ethyl acetate, then filtered through a fresh pad a silica gel to isolate the bright yellow solution from trace manganese oxides which had slipped past the first filtration (volume of the filtrate was 300 mL). The complete yellow solution was concentrated by rotary evaporation to afford yellow solid which was chopped and spread on paper to air dry overnight. The mass of the solid residue was 27.1 g (89% yield, mp =114 -116 °C).



Scheme S 3 Synthesis of **2A** with improved sEF

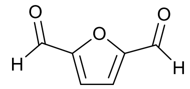
A 1 L Florence flask was charged with 5-(hydroxymethyl)furfural HMF (32.43 g of from AVA biochem 95% pure, 244 mmol, 1 equiv), and dichloromethane (300 mL). The apparatus was setup as described above and the solid addition auger was charged with manganese dioxide (66 g, 88% Active electrolytically precipitated from Acros Organics, 668 mmol, 2.73 equiv). The mixture formed a complete solution which was amber orange in color when the reflux began. Circa half the MnO_2 had been added in continuous fashion over in 40 minutes. The addition was complete in 2.5 h and the distillation was killed. The addition auger and the Claisen adapter were removed, the condenser was replaced and the mixture was refluxed overnight under positive nitrogen pressure. Following 14 h of reaction time, the heat was killed.

The mixture was isolated by suction filtration once it had cooled, and the solid residue was packed into an extraction thimble and continuously extracted in a Gregor extractor with dichloromethane. The yellow filtrate was concentrated by rotary evaporation under vacuum and proton NMR indicated that there was residual HMF in the yellow solid product. The next morning, the yellow extracts from the Gregor extractor were combined with the concentrated filtrate and the sum was concentrated to again afford a yellow solid. The combined yellow solid was recrystallized from isopropyl alcohol (circa 200 mL) by boiling the mixture in an oil bath with stirring until all the solid dissolved to form a red solution, followed by slow cooling above the bath and finally in an ice bath to afford off white crystalline solid. The mixture was separated by suction filtration over a 5 cm Buchner funnel and the residue was washed with cold isopropanol. The yellow color could in this fashion be completely removed from the filter cake which was pressed over suction, chopped and spread on paper to air dry overnight (crop one). The red isopropanol filtrate was concentrated in vacuo and chilled. The crystalline precipitate which formed was isolated by suction filtration and was rinsed heavily with isopropanol, pressed over suction, chopped and spread on paper to air dry overnight (crop two). The red filtrate was again concentrated to a red oil which gave some small amount of crystalline solid upon extended storage in the freezer. That oily mixture was taken up in acetone and adsorbed onto silica gel followed by flash chromatography with ethyl acetate and hexanes. The fractions containing 2,5-diformylfuran DFF were combined and concentrated to form a gooey yellow crystalline solid which wept oil when chopped and spread on paper to air dry overnight, that solid was returned to the flask used to concentrate it and diluted with a bit of diethyl ether. The ether dissolved the yellow oil and left behind clean DFF.

Not trusting the purity to a simple trituration, the mixture was boiled and most of the DFF dissolved. The addition of isopropanol did not crash out anything. isopropanol was added until a complete solution formed. The hot solution was diluted with a squirt from a hexane wash bottle just to see what would happen; the surface instantly clouded but could be dissipated by swirling. Crystalline solid precipitated as the reaction mixture was allowed to cool from near 40 °C to 26 °C. The cooled mixture rich in crystalline solid was chilled in an ice bath and subsequently separated by suction filtration through a 3 cm Buchner funnel followed by washing with cold isopropanol to clear away the yellow color and presumably many of the impurities. The filter cake was pressed dry, chopped and spread on paper overnight to allow final escape of residual isopropanol (crop three).

Crop one: 24.4 g off white crystalline solid (80.5 %) 114-116 °C
Crop two: 0.9 g of off white crystalline solid (3.0 %) mp = 115-118 °C
Crop three: 2.3 g of off white crystalline solid (7.6%) mp = 116-117 °C

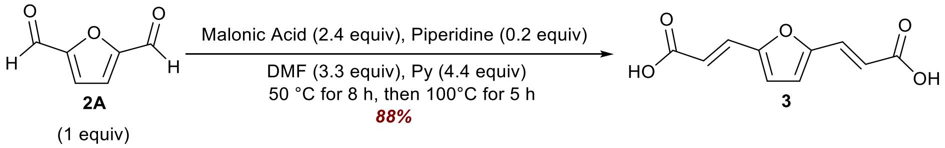
Combined 91% yield overall.



2A

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s,1 H), 7.33 (s,1 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3, 154.3, 119.4
FTIR (Neat) cm^{-1} 3123, 2874, 2748, 1665, 1562, 1510, 1409, 1264, 1237, 1171, 1021, 976, 957, 825, 795, 528

5. Synthesis (2E,2'E)-3,3'-(Furan-2,5-diyl)diacrylic acid **3**



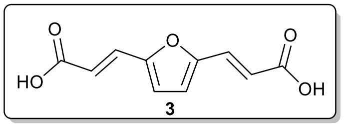
Scheme S 4 Synthesis of **3**

A 500 mL single necked round bottomed flask was charged with 2,5-diformylfuran (52.5 g, 423 mmol, 1 equiv), malonic acid (106.1 g, 1,019 mmol, 2.4 equiv), piperidine (8.2 mL, 83 mmol, 0.2 equiv), pyridine (150 mL, 1,862 mmol, 4.4 equiv), and a large PTFE coated magnetic spinbar. The mixture became a viscous syrup with yellow solid residue; the combination of materials was slightly exothermic (the temperature of the outer flask walls rose from 20 to 33 °C). The mixture was lowered into a preheated (50 °C) oil bath. A dark solution formed and bubbled vigorously (bubbles were orange). The viscosity of the mixture was too great to allow bubbles formed from carbon dioxide evolution to burst. In order to avoid effervescence, the mixture was raised from the oil bath and diluted with dry N,N-dimethylformamide (108 mL, 1,395 mmol, 3.3 equiv). The diluted mixture was lowered into the warm bath again, whereupon bubbles formed and cleanly burst as the reaction mixture was stirred magnetically.

The flask and bath were wrapped in aluminum foil and stirred at 50 °C for 8 h beneath a tall West condenser plumbed with running cool water and positive pressure (nitrogen). The mixture was a dark solution without apparent gas evolution. The bath temperature was increased to 100 °C and stirring continued for 5 h. The reaction mixture was allowed to cool, the stir bar was pulled, and the mixture was concentrated by rotary evaporation to a golden solid which coated the inner walls of the flask. The mixture was diluted with deionized water then acidified by the careful addition of concentrated sulfuric acid (50 mL, 944 mmol, 2.2 equiv); the mixture lost much of its golden color. The light-yellow solution and tan residue were transferred to a 2 L beaker and diluted to a total volume of 1 L. The mixture was stirred magnetically and heated to 60 °C. The mixture was allowed to concentrate and slowly warm for 11.5 h open in a well-ventilated fume hood to facilitate the hydrolysis any residual DMF and the neutralization of all nitrogenous bases. The temperature of the mixture was 83 °C and the volume was 600 mL. The mixture was stirred as it was allowed to cool to room temperature then chilled on an ice bath. The tan residue was isolated by suction filtration through a finely fritted glass Buchner funnel above a 2 L filter flask. The filtrate was a clear amber solution. The residue was powdery tan solid which was washed heavily with ice cold deionized water. As the filtrate was diluted, it became turbid. The first 2 L of filtrate were discarded (turbid orange solution) and another 1 L of cold water was used to rinse the residue (that filtrate was very lightly yellow). The residue was rinsed with ethyl acetate (250 mL) and the resulting filtrate was dark brown.

The residue was pressed dry on the filter, chopped and spread on paper then onto aluminum foil to airdry overnight. The light tan powdery residue was identified as (2E,2'E)-3,3'-(furan-2,5-diyl)diacrylic acid: 77.94 g, 88% yield.

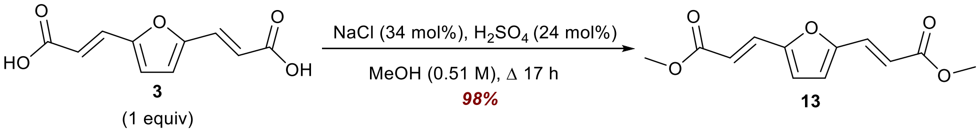
Diacid **3** was prepared as described above



3

^{1}H NMR (400 MHz, DMSO d$_6$) δ 12.49 (br s,1 H), 7.38 (d, *J*=15.77 Hz, 1 H), 7.03 (s,1 H), 6.38 (d, *J*=15.77 Hz, 1 H)
^{13}C NMR (101 MHz, DMSO d$_6$) δ 167.6, 152.5, 130.4, 118.9, 118.0
FTIR (Neat) cm^{-1} 2979, 2840, 2661, 2530, 1656, 1625, 1549, 1425, 1275, 1232, 1199, 1162, 1017, 965, 892, 798, 740, 661, 570, 539

6. Synthesis Dimethyl 3,3'-(Furan-2,5-diyl)(2E,2'E)-diacrylate **13**



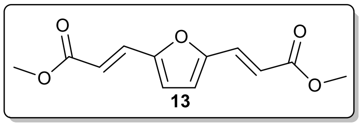
Scheme S 5 Synthesis of **13**

A 500 mL two-necked flask was charged with (2E,2'E)-3,3'-(furan-2,5-diyl)diacrylic acid **3** (31.82 g, 153 mmol, 1 equiv) and methanol (300 mL, HPLC grade from Fisher Scientific), and the mixture formed a chalky yellow suspension. The flask was fitted beneath a Graham condenser sealed with a drying tube charged with indicated Drierite. The flask was lowered into a room temperature oil bath and stirred magnetically with vigor. Sodium chloride (3 g, 51 mmol, 0.34 equiv) was added as a granular crystalline solid through the side neck—*for the purpose of decreasing the solubility of the diester product in the methanolic reaction mixture.* A polypropylene syringe was used to add concentrated sulfuric acid (2 mL, 37 mmol, 0.24 equiv) also through the side neck which was then sealed with a yellow cap-plug.

The reaction mixture was refluxed beneath the drying tube for a total of 19 hours. Within 30 minutes of refluxing, the slurry had lost much of its yellow color and appeared as a chalky slurry. The nature of the solid residue was also observed to change to a slurry of crystalline solid. When the reaction mixture was lifted from the oil bath and allowed to cool without stirring, crystalline solid was observed to precipitate from the yellow liquor. That crystalline solid trapped much of the color from the liquor and appeared darkly amber. The mixture was reheated to reflux, the solid dispersed and the color dissolved. The mixture was allowed to slowly cool with vigorous stirring to retard the agglomeration of particles in the precipitate which might have otherwise captured the colored impurities. Off-white settled from a yellow liquor upon cessation of stirring.

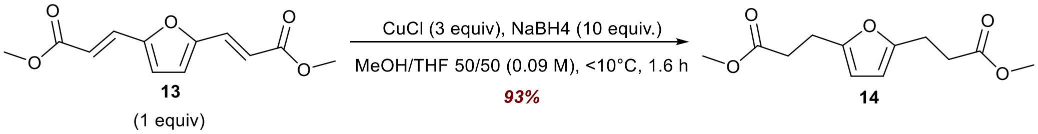
The reaction mixture was stored in the freezer overnight along with a 500 mL wash bottle of isopropyl alcohol. Some colorless crystalline solid was observed to have grown into the liquor which then appeared orange in color. The off-white solid was isolated by suction filtration through a Buchner funnel (ceramic, 9 cm, qualitative filter paper), pressed free of orange liquor then rinsed free of color with cold isopropyl alcohol. The filter-cake was sucked free of washing solvent, chopped, and spread on paper to air dry overnight. The powdery solid was identified as dimethyl 3,3'-(furan-2,5-diyl)(2E,2'E)-diacrylate **13** (35.22 g, 153 mmol, 98% isolated yield, mp = 169 °C) and was used without further purification.

Diene **13** was prepared as described above.



^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 (d, *J*=15.73 Hz, 1 H), 6.63 (s, 1 H), 6.40 (d, *J*=15.73 Hz, 1 H), 3.78 (s, 3 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 167.2, 152.5, 130.4, 117.7, 116.9, 51.9
FTIR (Neat) cm^{-1} 2966, 1719, 1633, 1553, 1505, 1434, 1386, 1302, 1238, 1163, 958, 858, 791, 659

7.Synthesis Dimethyl 3,3'-(Furan-2,5-diyl)dipropionate **14**



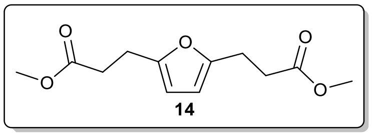
Scheme S 6 Synthesis of **14**

Following a modification of Narisada *et. al*,[4] to a 500 mL Erlenmeyer flask was added dimethyl 3,3'-(furan-2,5-diyl)(2E,2'E)-diacrylate **13** (4.21 g, 17.8 mmol, 1 equiv) and tetrahydrofuran (100 mL of HPLC grade from Macron); the mixture was stirred to afford a turbid faintly amber solution which was diluted with methanol (100 mL, HPLC grade from Fisher Scientific). Copper(I) chloride (5.39 g of 97% extra pure from Acros Organics, 52.8 mmol, 2.96 equiv) was stirred in and the reaction mixture (gray slurry) which was submerged in an ice bath and its temperature was monitored by internal digital thermometer. Sodium borohydride (6.93 g, 183 mmol, 10.3 equiv) was measured into a polystyrene weigh boat and added bit by bit to the reaction mixture at such a rate that the temperature never rose above 10 °C. Upon the first addition of sodium borohydride to the cuprous reaction slurry, the color shifted from greenish gray to light brown.

Approximately ½ the borohydride was added within the first hour of the reaction and the mixture became opaque and black with no observable particulate. The addition of the second ½ of the borohydride took place in similar portions as the first, but with more latent time between each addition so that its completion took 104 min. The mixture was stirred as the ice bath thawed and warmed to room temperature (11 h). The mixture was quenched with silica gel and allowed to settle open to the air. The solution above the dark solid which settled to the bottom of the flask was light blue in color. The light blue solution was isolated by suction filtration through a 3 cm pad of silica gel packed into a 9 cm ceramic Buchner funnel above a 1 L filter flask, the residue was black. The filter cake was rinsed heavily with dichloromethane; the filtrate was slightly turbid and pale blue. The filtrate was transferred to a 1.0 L recovery flask and concentrated by rotary evaporation to afford wet looking pale blue solid. The residue was partitioned between concentrated ammonium chloride (200 mL) and dichloromethane (200 mL); the aqueous phase was deeply blue. The dichloromethane phase appeared colorless, was isolated, and the blue aqueous phase was extracted two more times with 100 mL of dichloromethane. The dichloromethane extracts were combined, backwashed three times with 150 mL of distilled water and once with 150 mL of saturated sodium chloride.

The dichloromethane solution was isolated, dried (Na$_2$SO$_4$), and concentrated to a faintly yellow oil by rotary evaporation under vacuum. That residual oil was passed through a microcolumn (monster pipet packed with silica gel) and rinsed with circa 5 mL of dichloromethane into a tared 20 dram sample vial. The silica gel plug held the faint yellow color and the nearly colorless eluate was concentrated by nitrogen stream then vacuum drying to constant mass to afford dimethyl 3,3'-(furanyl-2,5-dipropionate) **14** as a very faintly yellow oil (3.97 g, 17.8 mmol, 93% yield). The light oil was clearly contaminated with a small amount of over-reduced side products; however, these did not interfere with the isolation clean products in the later reaction sequence.

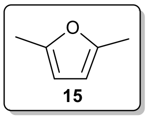
Diene **14** was prepared as described above.



14

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.85 (s, 1 H), 3.65 (s, 3 H), 2.87 (t, *J*=7.64 Hz, 2 H), 2.59 (t, *J*=7.64 Hz, 2 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 173.1, 152.9, 105.9, 51.8, 32.7, 23.6
FTIR (Neat) cm^{-1} 2956, 2915, 1729, 1601, 1516, 1439, 1354, 1292, 1197, 1148, 1040, 980, 826, 748, 583

8. Diene **15** (2,5-dimethylfuran) was purchased from Acros Organics.

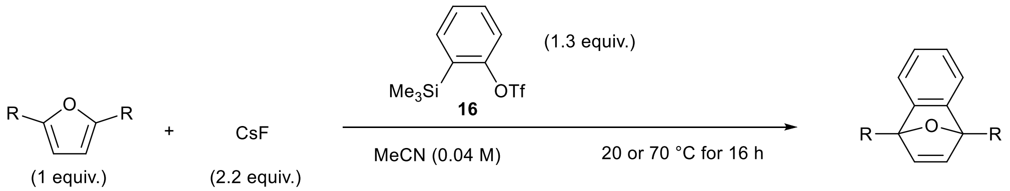


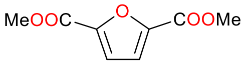
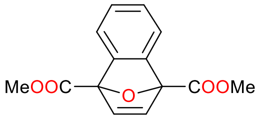
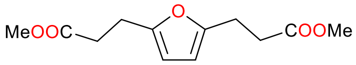
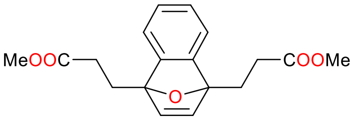
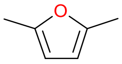
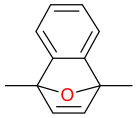
15

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.84 (s, 1 H), 2.26 (s, 3 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 150.3, 106.1, 13.6
FTIR (Neat) cm^{-1} 3500, 2989, 2937, 1712, 1617, 1360, 1163, 951

9. Diels Alder Reactions

Table S 1 Desilylation of **16:** Exploring the Relationship Between Temperature and Benzyne Trapping by Furan Diene Substrates



Entry	*Substrate*	*Product*	*Yield (%)[a] 20 °C*	*Yield (%)[a] 70 °C*
1	 **5**	 **8**	38	84
2	 **14**	 **17**	97	--
3	 **15**	 **18**	97	--

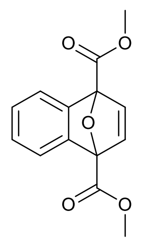
[a] *Isolated yield*

General procedure

To a vigorously stirred solution of furan substrate (2.0 mmol) and cesium fluoride (4.4 mmol) in acetonitrile (24 mL) was added a solution of trimethylsilylphenyl-2-triflate (2.6 mmol) in acetonitrile (24 mL) dropwise by syringe pump over 16 hours at given temperature (20 or 70 °C). After completion of the reaction, the mixture was diluted with diethyl ether (100 mL) and water (50 mL). The biphasic mixture was extracted with diethyl ether (30 mL x 3) and the combined organic phases were dried over anhydrous sodium sulfate. Solvent was evaporated under vacuum and the residue was purified by column chromatography using (10:1) hexane/ethyl acetate as eluent.

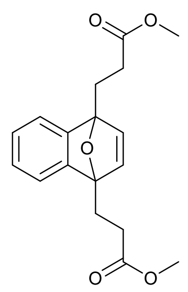
Discussion of Results: Table S1

The method of benzyne generation was developed following the procedures of Shi *et al.*[5] and the results—*specifically Entry 3 of this table*—are in agreement with the results recently reported by Medina *et al.*[6]



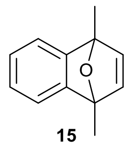
8

H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J*=3.00, 5.24 Hz, 1 H), 7.15 (s, 1 H), 7.07 (dd, *J*=3.00, 5.24 Hz, 1 H), 3.99 (s, 3 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 146.3, 143.2, 126.2, 120.5, 90.4, 53.1
FTIR (Neat) cm^{-1} 3645, 3467, 3096, 3013, 2957, 2853, 1764, 1738, 1603, 1439, 1364, 1321, 1268, 1202, 1144, 1109, 1054, 966, 922, 805, 760, 694, 640, 552
HRMS Calculated for $C_{14}H_{12}O_5Na$: 283.0583, Found: 283.0577



17

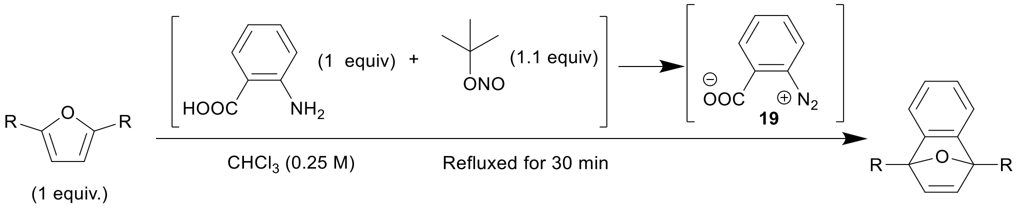
H NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, *J*=2.96, 5.12 Hz, 1 H), 6.97 (dd, *J*=2.98, 5.14 Hz, 1 H), 6.74 (s, 1 H), 3.70 (s, 3 H), 2.79–2.50 (m, 4 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 151.6, 145.9, 125.0, 118.9, 91.2, 51.8, 29.5, 24.4
FTIR (Neat) cm^{-1} 3354, 3069, 2951, 2849, 1732, 1437, 1321, 1265, 1169, 1088, 1023, 938, 886, 758, 695, 567
HRMS Calculated for $C_{18}H_{20}O_5Na$: 339.1208, Found: 339.1209

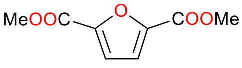
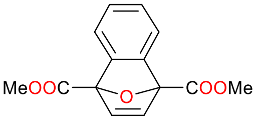


15

H NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J*=3.00, 5.08 Hz, 1 H), 6.98 (dd, *J*=2.96, 5.12 Hz, 1 H), 6.79 (s, 1 H), 1.91 (s, 3 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 146.8, 124.7, 118.3, 88.6, 15.3
FTIR (Neat) cm^{-1} 3070, 2980, 2933, 2865, 1566, 1451, 1383, 1344, 1299, 1235, 1140, 1077, 1034, 1004, 888, 856, 767, 746, 694, 648, 605, 511, 433

Table S 2 Thermolysis of **19** generated *in situ*: Trapping in Chloroform



Entry	***Substrate***		***Isolated Yield (%)***
1	 **5**	 **8**	50, 44

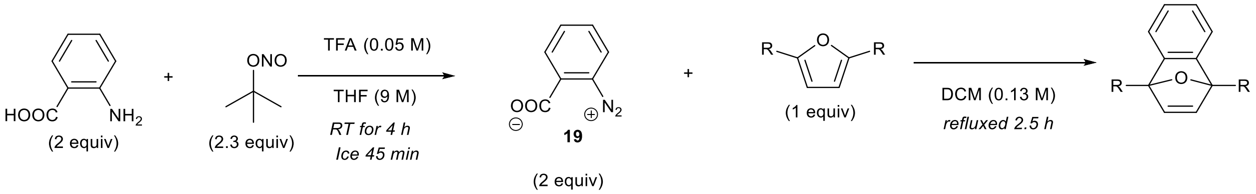
General procedure: Thermolysis of **19** generated *in situ*: Trapping in Chloroform

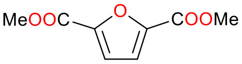
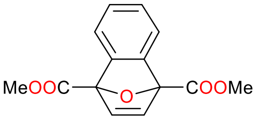
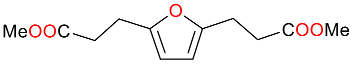
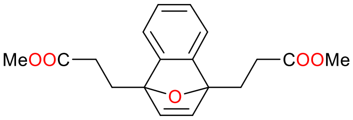
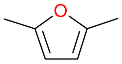
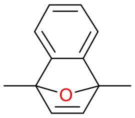
A 50 mL single necked RBF was charged with furan-substrate (2 mmol, 1 equiv), a spin-bar, anthranilic acid (2 mmol, 1.0 equiv) and chloroform (8 mL). To that stirring mixture (above an oil bath preheated to 65 °C) was added t-butylnitrite (0.3 mL, 90%, 2.2 mmol, 1.1 equiv) and after 5 minutes, the brick red reaction slurry was affixed to a tall West condenser outfitted with a mineral oil bubbler and lowered into the oil bath to reflux for 30 min. The reaction mixture was pulled from the oil bath and worked up as described above.

Discussion of Results: Table S2

t-Butyl nitrite was used in this experiment due to the established reactivity of benzyne with alcohols[7] and more importantly the reaction between **19** and oxidizable alcohols[8]. The results compared favorably with a 65% yield of 7-oxabenzonorbornadiene reported by Friedman and Logullo[9] given the decrease in yield expected by combination of anthranilic acid, nitrite, and furan in a single shot. This method advantageously avoids the isolation of **19** and displays significant improvement in the AE of a thermolysis approach over the desilylation method explored in Table S1.

Table S 3 Partially Isolated **19**: Thermolysis and Trapping Substrate Screening



Entry	***Substrate***	***Product***	***Isolated Yield (%)***
1	 **5**	 **8**	84
2	**5**	**8**	85[a]
3	**5**	**8**	67[b], 72[b]
4	 **14**	 **17**	77
5	**14**	**17**	76[b]
6	 **15**	 **18**	68
7	**15**	**18**	63[b], 74[b]

[a] Partially isolated **19** was suspended in ice cold dichloromethane (35 mL) and added in 35 portions over 3 h to a 1,4-dioxane solution of furan-substrate (3.3 mmol, 0.33 M); each portion addition took less than 2 minutes and the DCM was allowed to boil away following each addition. Residual **5** was isolated (8%).

[b] TFA concentration in the preparation of **19** was increased to 0.19 M and the prereaction time was shortened to 2.5 h

*Benzenediazonium-2-carboxylate is known to be shock sensitive and may be easily detonated when dry. Strangely, there is also a greater danger of detonation when a slurry of **19** has been allowed to settle and especially when the diazotization mixture is stored in a freezer. Both factors seem to facilitate crystallization of the inner salt and lead to solvent exclusion with concomitant enhanced sensitivity. Do not use metal spatulas at any time. Disposable polyethylene transfer pipets were extremely useful for agitation and transfer of the slurry.*

General Procedure: Partially Isolated **19** Thermolysis and Trapping Substrate Screening

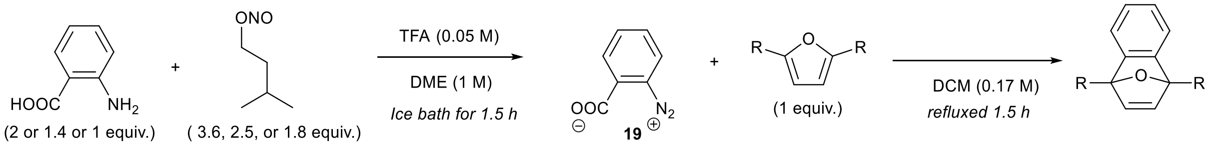
Following a modified Organic Syntheses procedure[10] and similar to those recently reported by the Lautens group,[11] a 20 Dram vial was charged with anthranilic acid (0.9069 g, 6.6 mmol, 2 equiv), 7 mL of HPLC grade tetrahydrofuran (0.94 M solution) and the mixture was stirred. A complete solution formed rapidly. Trifluoroacetic acid was added (0.2 mL of a solution of 1.87 M solution [1 mL TFA dissolved in 7 mL of HPLC grade THF]) to prepare a 0.053 M solution; no change in appearance was observed. The mixture was placed into a room temperature water bath and t-BuONO (1.0 mL, 90 %, 7.57 mmol, 2.3 equiv) was added dropwise by syringe. The mixture formed a cream-colored suspension, then thickened and turned brick red.

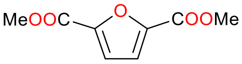
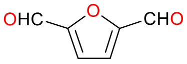
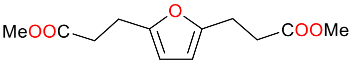
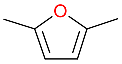
The mixture was stirred at room temperature. The diazotization mixture had certainly begun to lose its red color on the walls of the flask within 3 h. The diazotization mixture had lost all of its red color and had become tan within 4 h. A Pasteur pipet was used to free the solid from the walls of the vial by gently taking up the slurry and jetting it into the walls. A water bath (ambient temperature) was traded for an ice bath. After 45 minutes the tan precipitate was diluted with a bit of dichloromethane, isolated by suction filtration over a Hirsch funnel, rinsed heavily with dichloromethane (circa 40 mL) and transferred to a pear-shaped flask which was calibrated with a 25 mL mark. ***The tan solid was never allowed to dry, and it was transferred to the flask with the assistance of a dichloromethane wash bottle.*** Furan substrate (3.3 mmol, 1 equiv) was added and the reaction volume was brought up to 25 mL with dichloromethane. The flask was fitted with a short West condenser and lowered into an oil bath (48 °C). The mixture was refluxed for 2.5 h and then adsorbed onto silica gel and purified by flash chromatography.

Discussion of Results: Table S3

This method led to improved yields over those observed in Table S3, but at the cost of atom economy which is now similar to those observed in Table S1. These results indicated the role of acid in the timely conversion of anthranilic acid into **19**. They also show the decreasing trend in electron rich 7-oxabenzonorbornadiene yield when benzyne super stoichiometry is employed. It was subsequently observed that dilution of the diazotization mixture led to incomplete washing of the acid and nitrite solution from the partially isolated **19.** It must also be noted that over-washing with dichloromethane in the washing leads to loss of **19** to the extent that if one doubles the washing volume, one cuts the yield by approximately 40%.

Table S 4 Partially Isolated **19** Thermolysis: Substrate Screen Exploring the Relationship Between Stoichiometry and Reaction Outcome



Entry	***Substrate***	***1.0 equiv Yield (%)[a]***	***1.4 equiv Yield (%)[a]***	***2.0 equiv Yield (%)[a]***
1	 **5**	42[b]	80	94, 91[c]
2	 **2A**	--	0[d]	--
3	 **14**	56	84, 80,	91
4	 **15**	70[e]	85	67

[a] *Isolated yield corrected by subtracting the 7-oxabenzonorbornadieneoxide based on proton NMR*

[b] *Uncorrected was 68%*

[c] *1 equiv was 98 mmol*

[d] *2,5-diformylfuran was recovered (0.24 equiv)*

[e] *1 equiv 34 mmol*

*Benzenediazonium-2-carboxylate is known to be shock sensitive and may be easily detonated when dry. Strangely, there is also a greater danger of detonation when a slurry of **19** has been allowed to settle and especially when the diazotization mixture is stored in a freezer. Both factors seem to facilitate crystallization of the inner salt and lead to solvent exclusion with concomitant enhanced sensitivity. Do not use metal spatulas at any time. Disposable polyethylene transfer pipets were extremely useful for agitation and transfer of the slurry.*

General Procedure

To a 6-dram sample vial was added anthranilic acid (4.9 mmol from Sigma Aldrich, 2, 1.5, or 1 equiv), 1,2-dimethoxyethane (5 mL, stabilized with BHT from Acros Organics), and the mixture was stirred to form a colorless solution. Trifluoroacetic acid (0.02 mL from Sigma Aldrich, 0.26 mmol) was added in two drops to the 1,2-dimethoxyethane solution with no apparent change. While stirring vigorously at room temperature, ice cold isopentyl nitrite (1.2 mL, of 99% from TCI as light yellow solution, 8.8 mmol, 3.6, 2.7, or 1.8 equiv) was added rapidly and the reaction mixture quickly became turbid yellow and then transitioned to a brick red slurry; The reaction mixture was capped and stirred vigorously at room temperature for 90 minutes as the red color dissipated; room temperature stirring was required as the triazene is stable at ice bath temperatures. Periodically a rubber policeman was used to liberate the precipitate which clung to the walls of the vial. The reaction mixture was composed of cream colored solid and light orange solution at the completion of 90 minutes, and it was submerged in an ice bath.

A 50 mL single necked round bottomed flask was calibrated to 19 mL with dichloromethane and charged with substrate (4.9, 3.5, or 2.45 mmol depending on the entry). The ice-cold benzenediazonium-2-carboxylate slurry separated by pouring it into a 15 mL medium fritted glass Buchner funnel and careful application of suction by water aspirator. The filtrate was deeply red, and the residue was cream colored solid stained with orange solution. The mixture was never allowed to dry. The stir bar was pulled, rinsed with dichloromethane and added to the calibrated flask charged with substrate. The filter-cake was dispersed in dichloromethane and stirred up with a rubber policeman repeatedly followed by careful suction; the total volume of the filtrate was circa 25 mL.

The cream-colored dichloromethane slurry was transferred to the calibrated substrate flask with the aid of a plastic funnel and a stream of dichloromethane from a wash bottle. The reaction mixture was diluted to the calibration mark and affixed to a West condenser plumbed with cold flowing tap water. The reaction flask was lowered into a preheated oil bath (50 °C) and allowed to reflux for 90 minutes.

The reaction mixture was concentrated by rotary evaporation and purified by flash chromatography using ethyl acetate and hexanes as elution solvent. The eluate fractions containing the 7-oxabenzonorbornadiene could be easily identified by staining the thin layer chromatography thin layer chromatography slide with potassium permanganate. The fractions containing the product were combined, concentrated by rotary evaporation and vacuum dried.

Discussion of Results: Table S4

The 1.4 equivalent results appeared in Table 2 of the manuscript. The use of isopentyl nitrite as opposed to t-butyl nitrite was made since the reaction of anthranilic acid and isopentyl nitrite is faster. Therefore, the latent time before the reaction was minimized, thereby significantly decreasing the time spent with shock sensitive material on the bench.

Reaction Diene **13** with Benzyne Generated by Thermolysis**.**

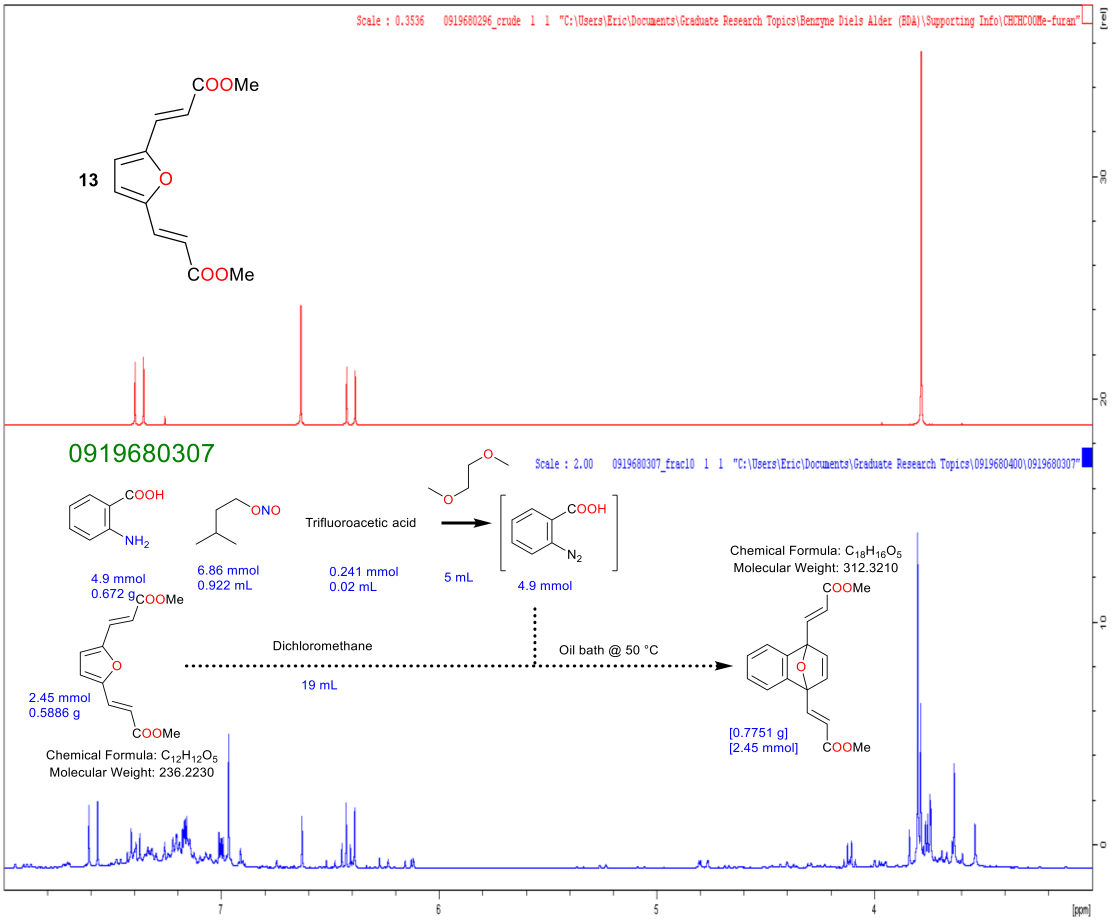
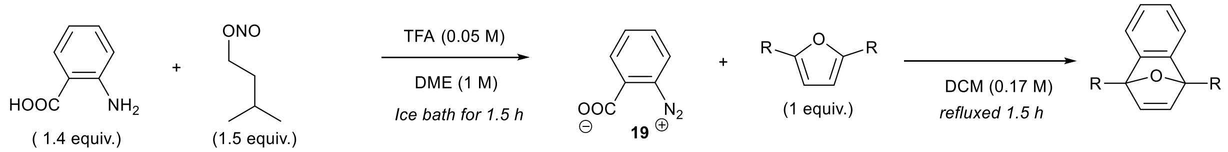
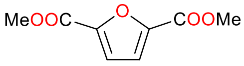
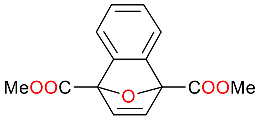
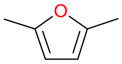
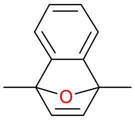


Fig. S 1 Diels-Alder Reaction Between Benzyne and Diene **13**

Following the general procedure described in Table 2, and Table S4, diene **13** was used employed as benzyne trapping agent. The reaction mixtures typically become so red as to appear black, however this preparation was a lighter red color and solid precipitated upon cooling. This indicated that the excess benzyne was consumed. That solid was relatively insoluble in acetone. The material was partially purified by flash chromatography; the center fraction of the major eluate peak was analyzed by ^{1}HNMR. Some residual starting material was detected, which indicated that a side reaction engaging benzyne and the first adduct was proceeding faster than the Diels-Alder reaction with tetraene **13**. Some 7-oxabenzonorbornadiene was detected, which was likely a consequence of benzyne depletion.

Table S 5 Isolated **19**: Thermolysis and Trapping Single Shot with Limited Excess Nitrite



Entry	*Substrate*	*Product*	*1.4 equiv Yield (%)*[a]
1	 **5**	 **8**	74, 76
2	 **15**	 **18**	73, 72

[a] *isolated yield*

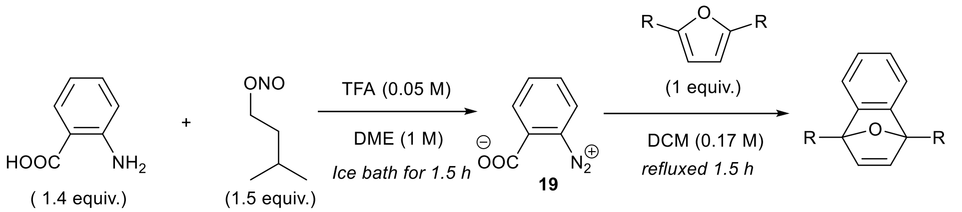
General Procedure

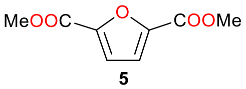
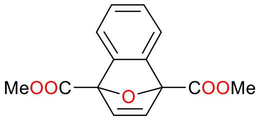
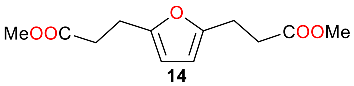
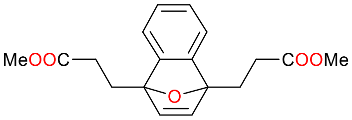
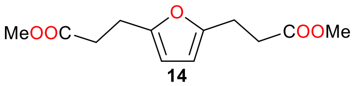
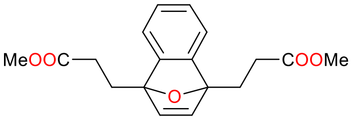
Same as for Table S4 but with only a very slight excess of isopentylnitrite (1.5 equiv) in relation to the anthranilic acid added (1.4 equiv).

Discussion of Results: Table S5

An attempt to mitigate the oxidation of the Diels-Alder adducts by using less excess diazotizing reagent led to decreased yields of 7-oxabenzonorbornadienes.

Table S 6 Crude Preparation of **19** Added Directly to Diene Solution



Entry	***Substrate***	***Product***	***Isolated Yield (%)***
1	 **5**	 **8**	56
2	 **14**	 **17**	55
3[a]	 **14**	 **17**	74

[a] *diazotization mixture added directly to furan-substrate with no isolation in small shots over the course of the reaction.*

General Procedure

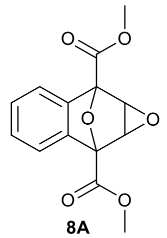
Same as for Table S4 but with no purification of **19** by partial isolation the diazotization mixture was added directly to the flask containing dichloromethane and furan (**5, 14**) either in a single shot (Entries 1, 2: Table S5) or in many small shots (0.5 mL of slurry per 5 min).

Discussion of Results: Table S6

When considering the results of Table S1 and Table S5, it is not surprising that yields in the low 50's were observed for adducts **8** and **17**. Astonishingly, note the beneficial effect of adding portions of the crude diazotization slurry to the refluxing furan-dichloromethane solution as observed in Entry 3:Table S6. This implies that the dangers of handling **19** could be largely mitigated while not even partially isolating **19**. If a method for safely adding aliquots of **19** slurry on large scale could be devised the facility of this technology could make the kilogram synthesis of these adducts feasible.

10. Identification Dimethyl 3,4-epoxy-7-oxabenzynorbornadiene-1,4-dicarboxylate

It was during this portion—*specifically when excess nitrite reagent was employed as in Table S4, entry 1*—of the study when we encountered the nitrite catalyzed aerobic oxidation[12] of 7-oxabenzonorbornadienes which we are currently investigating. The determining factor in the oxidation of the adduct seemed to be extent of coelution with residual nitrites in the flash chromatographic separation; 7-oxanorbornadiene was disproportionately affected and the rate of oxidation was not uniform between the preparations at different stoichiometry's.

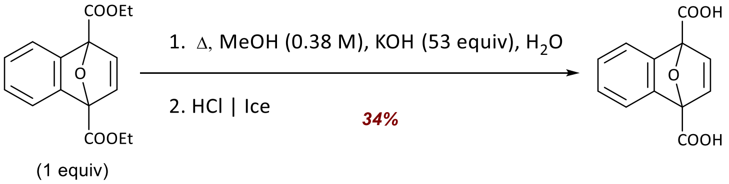


8A

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.53 (dd, *J*=3.04, 5.40 Hz, 1 H), 7.28 (dd, *J*=3.04, 5.40 Hz, 1 H), 3.98 (s, 3 H), 3.91 (s, 1 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 166.5, 142.9, 128.3, 121.5, 84.9, 57.4, 53.3
HRMS Calculated for $C_{14}H_{12}O_6Na$: 299.0532, Found: 299.0554

11. Synthesis 7-Oxabenzonorbornadiene-1,4-dicarboxylic acid

In order to further characterize this new class of electron-deficient 7-oxabenzonorbornadienes, and to evaluate the likelihood that they would survive polyester or nylon synthesis, we subjected an analog of **8** (diethyl 7-oxabenzonorbornadiene-1,4-dicarboxylate) to harsh-alkaline hydrolysis.

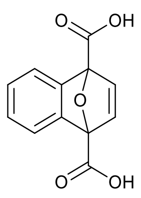


Scheme S 7 Hydrolysis of Diethyl 7-Oxabenzonorbornadiene-1,4-dicarboyxlate

A light-yellow oil, diethyl 7-oxabenzonorbornadiene-1,4-dicarboxylate (0.3355 g, 1.164 mmol 1 equiv) was diluted with methanol (3 mL), and the mixture was warmed by submersion in a 65 °C oil bath. A solution of KOH (3.5 g, 62.5 mmol, 54 equiv) in water (2.5 mL) was prepared and diluted to 7 mL with MeOH. The alkaline solution was added dropwise by Pasteur pipette into the stirring methanolic solution of diethyl 7-oxabenzonorbornadiene-1,4-dicarboxylate and the reaction mixture turned from light yellow to dark orange with the first drop's contact. That mixture was stirred on the oil bath for 2 h and was then allowed to cool to room temperature.

Wet ice (100 mL) was combined with concentrated hydrochloric acid (6 mL) and the alkaline mixture was dripped into that acidic mixture with vigorous stirring provided by a glass rod. A light-yellow solution developed. The methanol and all of the water was removed by rotary evaporation to leave a white solid residue. That mixture was digested in boiling dichloromethane and when all the DCM had escaped, the mixture was digested in warm ethyl acetate. Once the mixture had cooled to room temperature, it was gravity filtered through a plug of cotton and stored in a 250 mL Erlenmeyer flask with a little bit of sodium sulfate.

The ethyl acetate was concentrated by rotary evaporation under vacuum to afford a light brown oil which smelled faintly of acetic acid and was observed to crystallize upon standing. The white solid was determined to have a mass of 0.2969 g. The mixture was triturated under diethyl ether and the ether was pipetted away and deposited on a watch glass. Upon drying, the brown ether solution had clearly deposited some crystalline material onto the watch glass. The residual light brown solid was flushed with nitrogen stream until the ether smell had dissipated. The mass of residual solid was 0.0918 g, 34%.

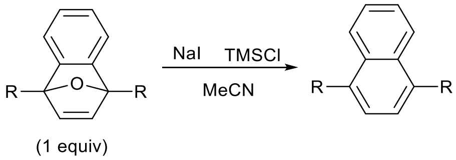


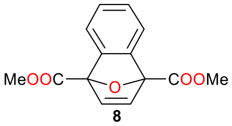
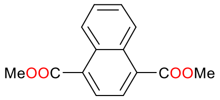
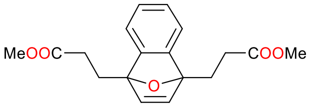
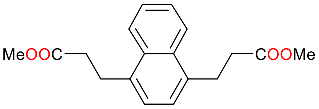
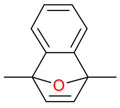
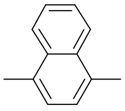
8B

^{1}H NMR (400 MHz, DMSO d$_6$) δ 7.36 (dd, *J*=3.02, 5.18 Hz, 1 H), 7.23 (s, 1 H), 7.08 (dd, *J*=3.02, 5.18 Hz, 1 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 168.1, 147.3, 143.8, 125.7, 119.9, 89.7
FTIR (Neat) cm^{-1} 3458, 3079, 1916, 1732, 1449, 1357, 1254, 1205, 1155, 1080, 1007, 837, 756, 635, 443

12. Deoxyaromatization

Table S 7 Naphthalenes from 7-Oxabenzonorbornadienes: Trimethylsilyl Iodide Mediated Deoxyaromatization

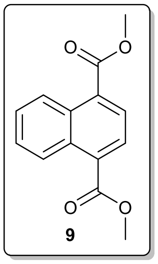


Entry	***Substrate***	***Product***	***Method***	***Temp (°C)***	***Isolated Yield (%)***
1	 **8**	 **9**	A	70	25
2	 **17**	 **20**	A	20	98
3	 **18**	 **21**	B	20	92

General Procedure for the Deoxy-aromatization of 1,4-Disubstituted-7-oxabenzonorbornadienes A
To a solution of 7-oxabenzonorbornadiene substrate (0.58 mmol) in acetonitrile (50 mL) was added sodium iodide (2.9 mmol) at room temperature (circa 23 °C). The mixture was chilled on an ice bath under argon and trimethylsilyl chloride (2.9 mmol) was slowly added to the mixture and stirred as it was allowed to warm to room temperature. The stirring continued for 24 h and if the reaction was completed as observed by TLC then the mixture was partitioned between saturated sodium bisulfate and chloroform followed by two extractions of the aqueous phase with chloroform. The organic extracts were combined and dried (anhydrous sodium sulfate) followed by flash chromatography using Sorbtech 230 X 400 mesh amorphous silica gel as the stationary phase and 95 / 5 hexanes / ethyl acetate as the mobile phase. If the reaction was uncompleted at room temperature, then the mixture was refluxed overnight prior to extraction and chromatography

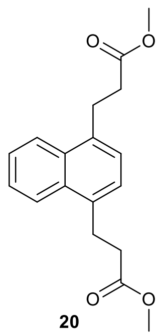
General Procedure for the Deoxy-aromatization of 1,4-Disubstituted-7-oxabenzonorbornadienes B
To the 1,4-disubstituted-7-oxabenzonorbornadiene (0.87 mmol) in acetonitrile (6 mL) was added sodium iodide (2.604 mmol) at room temperature (circa 23 °C). The mixture was chilled on an ice bath under argon and trimethylsilyl chloride (2.623 mmol) was slowly added to the mixture and stirred as it was allowed to warm to room temperature. The stirring continued for 24 h and if the reaction was completed as observed by TLC then the mixture was purified by flash chromatography using Sorbtech 230 X 400 mesh amorphous silica gel as the stationary phase and 95 / 5 hexanes / ethyl acetate as the mobile phase.

Discussion of Results: Table S7
This procedure was adapted from the report of Jung and Koreeda.[13] It is a convenient method on the small scale, but with restrictively low AE to the extent that even with high yields, use of this method for preparation of multigram quantities of material is infeasible.



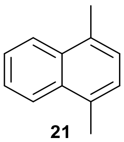
9

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.82 (dd, *J*=3.38, 6.66 Hz, 1 H), 8.09 (s,1 H), 7.63 (dd, *J*=3.36, 6.68 Hz, 1 H), 4.03 (s, 3 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 167.7, 131.8, 131.5, 128.1, 127.9, 126.1, 52.6
FTIR (Neat) cm^{-1} 2992, 2944, 2841, 1712, 1580, 1516, 1459, 1432, 1281, 1243, 1198, 1126, 1035, 1013, 900, 816, 784, 741, 665, 569, 525



20

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (dd, J=3.30, 6.50 Hz, 1 H), 7.54 (dd, J=3.32, 6.48 Hz, 1 H), 7.27 (s, 1 H), 3.70 (s, 3 H), 3.40 (t, *J*=8.00 Hz, 2 H), 2.76 (t, *J*=8.07Hz, 2 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 173.4, 135.4, 132.0, 125.8, 125.7, 124.2, 51.7, 35.0, 28.1
FTIR (Neat) cm^{-1} 3075, 3000, 2956, 2916, 1729, 1601, 1516, 1439, 1354, 1294, 1234, 1197, 1148, 1040, 980, 920, 826, 749, 687, 583

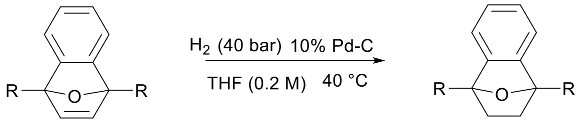


21

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (dd, *J*=3.34, 6.42 Hz, 1 H), 7.55 (dd, *J*=3.32, 6.44 Hz, 1 H), 7.23 (s, 1 H), 2.69 (s, 3 H)
^{13}C NMR (101 MHz, CDCl$_3$) δ 132.8, 132.5, 126.4, 125.5, 124.8, 19.5
FTIR (Neat) cm^{-1} 3071, 2940, 2863, 1597, 1510, 1462, 1393, 1273, 1158, 1023, 820, 749, 694, 566

13. Catalytic Hydrogenation

Table S 8 7-Oxabenzonorbornenes Synthesized by Catalytic Hydrogenation of 7-Oxabenzonorbornadienes

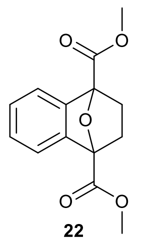


		Yield (%)[a]
8 COOMe	**22** COOMe	98[b]
17 CH_2CH_2COOMe	**23** CH_2CH_2COOMe	95
18 CH_3	**24** CH_3	98[c]

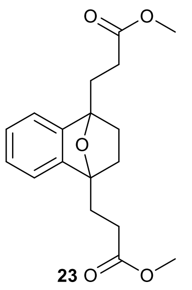
[a] *isolated yield* | [b] *89 mmol* | [c] *34 mmol*

General Procedure: Synthesis of 1,4-disubstituted-7-oxabenzonorbornenes by Flow Catalytic Hydrogenation

The H-Cube Pro was primed with HPLC-grade tetrahydrofuran at 3 mL/min with 100% hydrogen generation; the reaction chamber was set to 40 bar H_2 pressure and set to 40 °C. A 0.2 M solution of pure 1,4-disubstituted-7-oxabenzonorbornadiene in HPLC-grade tetrahydrofuran was prepared by stirring at room temperature, then eluted through a 30 mm Pd/C catalyst cartridge at a flow rate of 1 mL/min (40 °C). The eluting solution was concentrated to afford the 1,4-disubtituted-7-oxabenzonorbornene product.

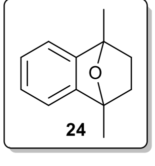

22

MP: 98–104 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J*=3.06, 5.46 Hz, 1 H), 7.27 (dd, *J*=3.06, 5.46 Hz, 1 H), 3.95 (s, 3 H), 2.48–2.37 (m, 1 H), 1.94–1.83 (m, 1 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 142.5, 127.8, 119.2, 86.3, 52.7, 32.2
FTIR (Neat) cm^{-1} 2956, 1755, 1451, 1430, 1351, 1321, 1268, 1225, 1169, 1117, 1069, 1044, 927, 897, 794, 763, 743, 658, 605
HRMS Calculated for $C_{14}H_{14}O_5Na$: 285.0739, Found: 285.0767

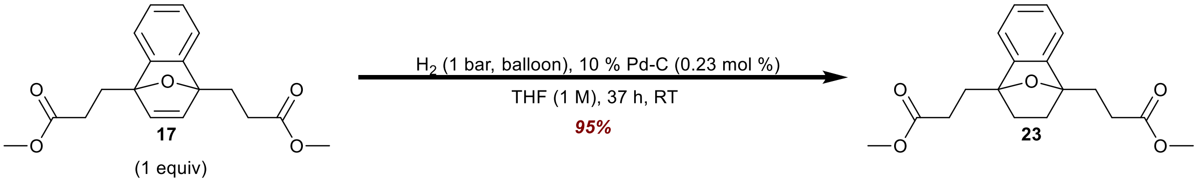

23

MP: 67 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (m, 1 H), 7.13 (m, 1 H), 3.66 (s, 3H), 2.65-2.81 (m, 4 H), 1.95–1.84 (m, 1 H), 1.48–1.37 (m, 1 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 146.8, 126.7, 118.0, 86.8, 51.7, 33.8, 29.9, 26.7
FTIR (Neat) cm^{-1} 2980, 2951, 1742, 1432, 1360, 1308, 1193, 1169, 1078, 1010, 975, 895, 863, 758, 720, 657, 618, 534, 447
HRMS Calculated for $C_{18}H_{22}O_5Na$: 341.1365, Found: 341.1394


24

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.13 (m, 2 H), 1.99–1.89 (m, 1 H), 1.83 (s, 3 H), 1.58–1.47 (m, 1 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 126.5, 117.5, 84.8, 35.7, 17.8
FTIR (Neat) cm^{-1} 3047c 2972, 2933, 2864, 1454, 1380, 1348, 1303, 1229, 1204, 1141, 1097, 1009, 901, 853, 750, 613



Scheme S 8 Batch Hydrogenation of

General Procedure for Batch Hydrogenation

Since the strained olefin did not require aggressive hydrogenation conditions, a batch hydrogenation was prepared which used minute quantities of catalyst.

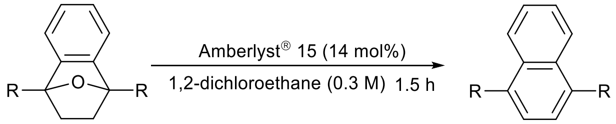
A round bottom flask was charged with substrate (between 5 and 50 mmol, 1 equiv), THF (1 M), 10% palladium on carbon (0.23 mol%) and the flask was sealed with a rubber septum. A hydrogen line was used to flush the headspace of the flask through a modified syringe/disposable needle combination. Another modified syringe/needle combination topped with a balloon was installed through the septum and kept charged with hydrogen as the reaction was stirred at room temperature for 30-40 h). The hydrogenation mixture was separated by filtering through Celite 545.

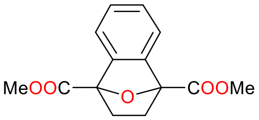
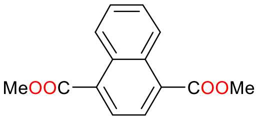
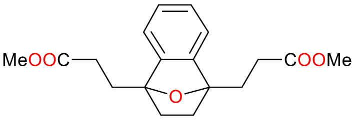
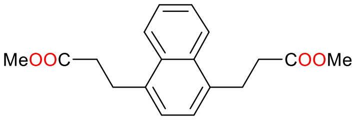
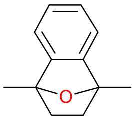
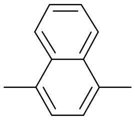
The product crystallized in the freezer upon concentration of the filtrate.

Unfortunately, crude reaction mixtures could not be subjected to direct hydrogenation. Contaminants always killed the catalyst.

14. Dehydroaromatizations

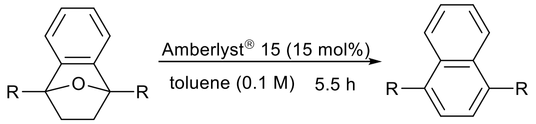
Table S 9 Naphthalenes by Dehydro-aromatization of 7-Oxabenzonorbornenes: Mediated by Amberlyst 15 and Azeotropic Distillation in Dichloromethane

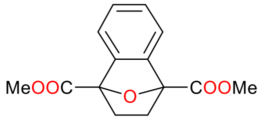
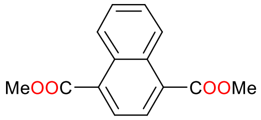
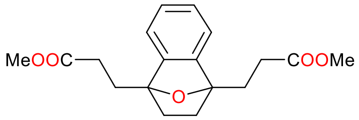
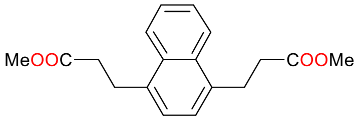
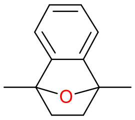
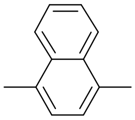


Entry	*Substrate*	*Product*	*Isolated Yield (%)*
1	 **22**	 **9**	17
2	 **23**	 **20**	97
3	 **24**	 **21**	97

General Procedure for Catalytic Dehydration: Table S9
A 5 mL single neck round bottom flask was charged with 7-oxabenzonorbornene (1 mmol, 1 equiv) which was taken up in DCE (3 mL, 0.3 M). The solution was charged with Amberlyst 15 (34 mg, 15 mol% when taking the Wt equivalent to be 4.4 equiv/kg resin and thereby making 0.227 g Amberlyst /equiv) and refluxed for 90 minutes. The mixture was separated by suction filtration, concentrated, adsorbed onto silica gel and purified by flash chromatography using ethyl acetate and hexanes. No hydrolysis products were observed in these reaction mixtures.

Table S 10 Naphthalenes by Dehydro-aromatization of 7-Oxabenzonorbornenes: Mediated by Amberlyst 15 and Azeotropic Distillation in Toluene



Entry	*Substrate*	*Product*	*Isolated Yield (%)*
1	 **22**	 **9**	37[a]
2	 **23**	 **20**	79
3	 **24**	 **21**	97

[a] 49 % recovered starting material

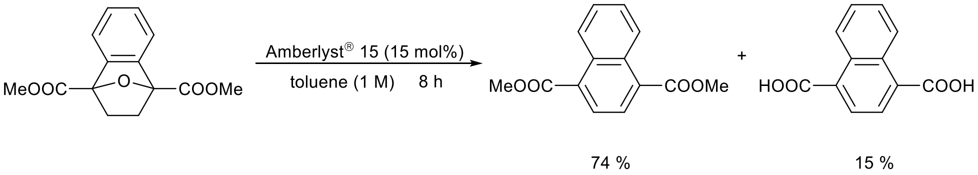
General Procedure for Catalytic Dehydration: Table S10

Same as the procedure described in Table S8, but with toluene substituted as the solvent (0.1 M) and the reaction time extended to 5.5 h.

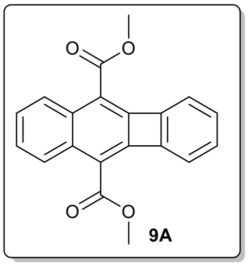
Discussion of Results: Table S9

The low conversion and incomplete mass balance in Entry 1 compared with the yield of naphthalene **18** indicates that this reaction setup is not sufficiently removing the water extruded in this reaction and that some hydrolysis of ester moieties is occurring. Hydrolysis can be considered as the rationalization as to why naphthalene **17** suffered by extended, harsher reaction time.

The dehydration reaction of **22** from Table S9 was scaled up to 40 mmol, and 74% of **9** was isolated.



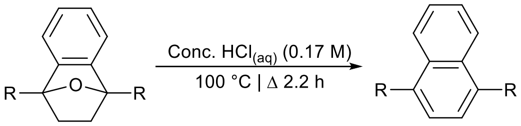
A small amount (~75 mg, 0.236 mmol, ~0.5% yield) of dimethyl benzo[b]biphenylene-1,4-dicarboxylate was isolated from that reaction mixture, presumably from the acid catalyzed dehydration of the [2+2] cycloadduct of and benzyne which was not completely isolated in the previous workups.

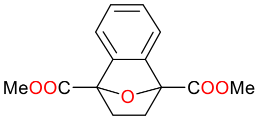
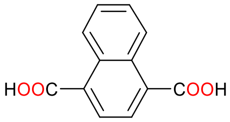
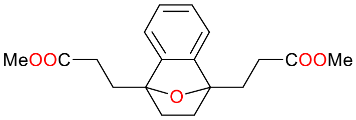
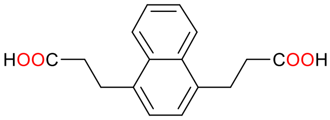
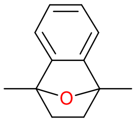
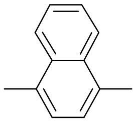


9A

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (dd, *J*=6.36 Hz, *J*=3.44 Hz, 1 H), 7.39 (dd, *J*=6.36 Hz, *J*=3.44 Hz 1 H), 7.11 (dd, *J*=5.78 Hz, *J*=3.82 Hz 2 H), 3.98 (s,3 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 151.7, 150.6, 132.4, 131.9, 127.6, 126.8, 122.0, 116.9, 52.07
FTIR (Neat) cm^{-1} 2982, 1723, 1438, 1361, 1303, 1193, 1167, 1080, 983, 897, 866, 761, 619
HRMS Calculated for $C_{20}H_{14}O_4Na$: 341.0790, Found: 341.0791

Table S 11 Naphthalenes by Dehydro-aromatization of 7-Oxabenzonorbornenes: Mediated by Concentrated Hydrochloric Acid$_{(aq)}$

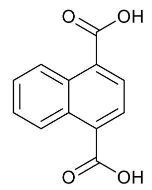


Entry	*Substrate*	*Product*	*Yield (%)*
1	 **22**	 **10**	91
2	 **23**	 **12**	72
3	 **24**	 **21**	84

General Procedure One-Pot 12 M Hydrochloric Acid Mediated Dehydroaromatization/Hydrolysis

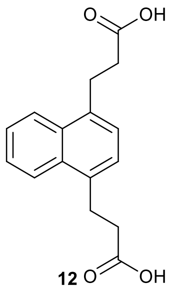
A 50 mL single necked RBF was charged with 1,4-disubstituted-7-oxabenzonorbornene (2.012 mmol, 1 equiv), concentrated hydrochloric acid (12 mL) and the mixture was heated in a 100 °C oil bath beneath a West condenser and an empty balloon (to contain the evolved HCl). The mixture was stirred magnetically for 2.2 h then pulled from the oil bath and allowed to cool.

In the case of carboxylic acid products (**10** and **12**), the mixture was chilled on ice, then isolated by suction filtration, rinsed with ice cold water, pressed, chopped and spread on paper to air dry. In the case of naphthalene **18** the condenser was washed with dichloromethane and the reaction was observed to partition between dichloromethane solution (bottom) and a cloudy acidic aqueous solution. The mixture was further diluted with dichloromethane which was isolated from the acid with a separatory funnel. The dichloromethane solution was washed with water three times and then once with saturated sodium chloride before drying (Na_2SO_4). The dry solution was concentrated and adsorbed onto silica gel then purified by flash chromatography using hexanes and ethyl acetate as eluents.



10

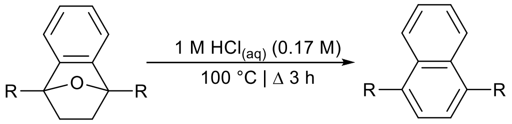
^{1}H NMR (400 MHz, DMSO d$_6$) δ 13.43 (br s, 1 H), 8.79 (dd, *J*=3.36, 6.68 Hz, 1 H), 8.10 (s, 1 H), 7.70 (dd, *J*=3.53, 6.81 Hz, 1 H)
^{13}C NMR (101 MHz, DMSO d$_6$) δ 168.4, 132.2, 130.7, 127.8, 127.5, 125.9
FTIR (Neat) cm^{-1} 2960, 2808, 2629, 2558, 1679, 1582, 1518, 1463, 1415, 1282, 1258, 1199, 1125, 1024, 883, 769, 718, 613, 454

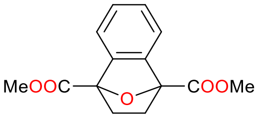
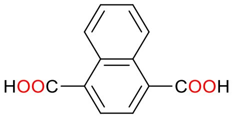
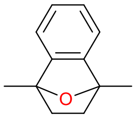
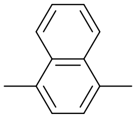


12

^{1}H NMR (400 MHz, DMSO d$_6$) δ 12.18 (br s,1 H), 8.08 (dd, *J*=3.32, 6.48 Hz, 1 H), 7.57 (dd, *J*=3.28, 6.48 Hz, 1 H), 7.29 (s, 1 H), 3.27 (t, *J*=7.68 Hz, 2 H), 2.62 (t, *J*=7.68 Hz, 2 H)
^{13}C NMR (101 MHz, DMSO d$_6$) δ 173.8, 135.3, 131.5, 125.8, 125.4, 124. 2, 34.6, 27.4
FTIR (Neat) cm^{-1} 3080, 2918, 2630, 2559, 1871, 1697, 1604, 1518, 1428, 1408, 1365, 1301, 1205, 967, 840, 741, 673, 543

Table S 12 Naphthalenes by Dehydro-aromatization of 7-Oxabenzonorbornenes: Mediated by 1M Hydrochloric Acid$_{(aq)}$



Entry	*Substrate*	*Product*	*Yield (%)*
1			3[a]
2			82[b]

[a] *In entry 1 the isolate was 65% the expected mass and was comprised of 7-oxabenzonorbornyl-1,4-dicarboxylic acid (91%) and 1-methylcarboxy-7-oxabenzonorbornyl-4-carboxylic acid (5%) and 1,4-naphthalenedicarboxylic acid by ^{1}H NMR*

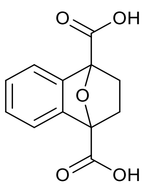
[b] *isolated yield*

Procedure for Table S11, entry 1

A 25 mL single necked 24/40 round bottomed flask was charged with 1,4-dimethyl-7-oxabenzonorbornene (0.4634 g, 1.664 mmol, 1 equiv), and 1.0 M HCl (10 mL). The mixture was refluxed in a 105 °C oil bath (preheated). The solid 7-oxabenzonorbornene was observed to melt within 15 minutes, and a dark solid residue was observed floating around by 2.5 h into the reaction. Some dichloromethane was added to cause the mixture to break up a bit at reaction time = 2.25 h. The addition of DCM caused the mixture to disperse. When the mixture was observed around reaction time = 2.67 h, there was off white solid precipitate coating the upper walls of the flask so more DCM was added to disperse the mixture. The mixture was pulled from the oil bath following 3 h of reflux, allowed to cool, then the solid was isolated by suction filtration. The filter cake was pressed dry, dried on the filter, then chopped and spread on paper to air dry. The residue was a gray-white powder. The mass of the residue was 0.237 mg, 65% of the theoretical mass following 36 h of drying. A bit of the solid residue was dissolved in deuterated DMSO and analyzed by proton and ^{13}C NMR. The proton NMR indicated that there was mixture of 1,4-dicarboxy-7-oxabenzonorbornene (91 mol%), 1,4-naphthalene dicarboxylate (4 mol%), and 1-methoxycarbonyl-4-carboxy-7-oxabenzonorbornene (5 mol%).

Procedure for Table S11, entry 2

Same as for entry 1, but with 7-oxabenzonorbornene substituted as the substrate. The product never solidified, and was isolated by liquid/liquid extraction with dichloromethane. ^{1}H NMR of the concentrated isolate was pure naphthalene **21.**



22A

^{1}H NMR (400 MHz, DMSO d$_6$) δ 7.45 (dd, *J*=3.04, 5.44 Hz, 1 H), 7.29 (dd, *J*=3.06, 5.42 Hz, 1 H), 2.34–2.19 (m, 1 H), 1.75–1.59 (m, 1 H)

^{13}C NMR (101 MHz, DMSO d$_6$) δ 169.8, 143.3, 127.5, 118.9, 85.5, 31.7

FTIR (Neat) cm^{-1} 3486, 3078, 2215, 1925, 1733, 1681, 1481, 1460, 1410, 1365, 1329, 1281, 1215, 1181, 1121, 1064, 1030, 1013, 951, 889, 838, 761, 737, 698, 600, 574, 515, 449, 429

15. Calculation of Atom Economy and simple E-factor

From Page S4, Section 3, Synthesis of Dimethyl-2,5-furandicarboxylate 5

In this case we include methanol as part of the raw materials since it is also a reagent:

Equation S 5
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{184.15}{(156.09+98.07\times2+32.04\times5)} = 36\%$$

Equation S 6
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(1061.3+55.2-48.6)}{48.6} = 22.0$$

From Page S5, Section 4, Synthesis 2,5-Diformylfuran 2A

In this case we excluded dichloromethane as solvent:

Equation S 7
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{124.9}{(126.11+86.94\times4)} = 26\%$$

Equation S 8
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(32.7+97-27.1)}{27.1} = 3.8$$

From Page S6, Section 4, Synthesis 2,5-Diformylfuran 2A

Be employing azeotropic distillation and adding the manganese oxide slowly, less oxidant is required since less is lost to deactivation which corresponds with and improvement in the AE.

Equation S 9
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{124.10}{(126.11+86.94\times2.7)} = 34\%$$

Equation S 10
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(32.4+66-27.6)}{27.6} = 2.5$$

From Page S7, Section 5, Synthesis (2E,2'E)-3,3'-(Furan-2,5-diyl)diacrylic acid 3

If we exclude pyridine and N,N-dimethylformamide as solvents:

Equation S 11
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{208.17}{(124.10+104.06\times2.4+85.15\times0.2)} = 53\%$$

If we count pyridine as a reagent:

Equation S 12
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{208.17}{(124.10+104.06\times2.4+79.10\times4+85.15\times0.2)} = 44\%$$

Equation S 13
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(52.5+106.1+8.1+-77.9)}{77.9} = 1.1$$

From Page S8, Section 6, Synthesis Dimethyl 3,3'-(Furan-2,5-diyl)(2E,2'E)-diacrylate 13

In this case we include sodium chloride and methanol as part of the raw materials since it is also a reagent:

Equation S 14
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{236.22}{(208.17+98.07\times0.24+32.04\times2+58.44\times0.34)} = 75\%$$

Equation S 15
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(31.8+228.6+3.9-35.2)}{35.2} = 6.5$$

From Page S9, Section 7, Dimethyl 3,3'-(Furan-2,5-diyl)dipropionate 14

Equation S 16
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{240.25}{(236.22+99.00\times3+37.83\times10)} = 34\%$$

Equation S 17 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(4.2+5.4+6.9-4.0)}{4.0} = 3.1$

From Page S11, Section 9, Diels Alder Reactions, Table S1

Diels-Alder Adduct **8** Table S1, entry 1

Equation s 18 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+151.90\times 2.2+298.35\times 1.3)} = 29\%$

Equation S 19 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.368+0.776+0.668-0.416)}{0.416} = 3.4$

Diels-Alder Adduct **17** Table S1, entry 2

Equation S 20 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+151.90\times 2.2+298.35\times 1.3)} = 33\%$

Equation S 21 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.480+0.776+0.668-0.613)}{0.613} = 2.1$

Diels-Alder Adduct **18** Table S1, entry 3 has been reported[6]

Equation S 22 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+151.90\times 2.2+298.35\times 1.3)} = 21\%$

Equation S 23 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.192+0.776+0.668-0.334)}{0.334} = 3.9$

From Page S13, Section 9, Diels Alder Reactions, Table S2

Diels-Alder Adduct **8** Table S2, entry 1

Equation S 24 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+137.14\times 1+103.12\times 1.1)} = 60\%$

Equation S 25 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.480+0.274+0.268-0.245)}{0.245} = 3.2$

From Page S14, Section 9, Diels Alder Reactions, Table S3

Diels-Alder Adduct **8** Table S3, entry 1

Equation S 26 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+137.14\times 1+103.12\times 1.1)} = 38\%$

Equation S 27 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.607+0.907+0.781-0.721)}{0.721} = 2.2$

Diels-Alder Adduct **17** Table S3, entry 4

Equation S 28 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+137.14\times 1+103.12\times 1.1)} = 43\%$

Equation S 29 $sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.792+0.907+0.781-0.804)}{0.804} = 2.1$

Diels-Alder Adduct **18** Table S3, entry 6

Equation S 30 $\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+137.14\times 1+103.12\times 1.1)} = 28\%$

Equation S 31 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.317+0.907+0.781-0.381)}{0.381} = 2.1$$

From Page S16, Section 9, Diels Alder Reactions, Table S4

Diels-Alder Adduct **8** was prepared by the method described in Table S4.

Table S4, entry 1, 1.0 equiv

Equation S 32 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+137.14\times1+117.15\times1.8)} = 49\%$$

Equation S 33 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.902+0.672+1.031-0.381)}{0.381} = 3.9$$

Table S4, entry 1, 1.4 equiv

Equation S 34 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+137.14\times1.4+117.15\times2.5)} = 39\%$$

Equation S 35 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.645+0.672+1.031-0.729)}{0.729} = 2.22$$

Table S4, entry 1, 2.0 equiv

Equation S 36 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+137.14\times2+117.15\times3.6)} = 30\%$$

Equation S 37 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.451+0.672+1.031-0.587)}{0.587} = 2..7$$

Diels-Alder Adduct **17** was prepared by the method described in Table S4.

Table S4, entry 3, 1.0 equiv

Equation S 38 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+137.14\times1+117.15\times1.8)} = 53\%$$

Equation S 39 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(1.177+0.672+1.031-0.868)}{0.868} = 2.3$$

Table S4, entry 3, 1.4 equiv

Equation S 40 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+137.14\times1.4+117.15\times2.5)} = 44\%$$

Equation S 41 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.841+0.672+1.031-0.908)}{0.908} = 1.8$$

Table S4, entry 3, 2.0 equiv

Equation S 42 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+137.14\times2+117.15\times3.6)} = 34\%$$

Equation S 43 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.587+0.672+1.031-0.705)}{0.705} = 2.2$$

Diels-Alder Adduct **18** was prepared by the method described in Table S4.

Table S4, entry 3, 1.0 equiv

Equation S 44 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+137.14\times1+117.15\times1.8)} = 39\%$$

Equation S 45 $$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.471+0.672+1.031-0.590)}{0.590} = 2.7$$

Table S4, entry 3, 1.4 equiv

Equation S 46
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+137.14\times1.4+117.15\times2.5)} = 30\%$$

Equation S 47
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.336+0.672+1.031-0.512)}{0.512} = 3.0$$

Table S4, entry 3, 2.0 equiv

Equation S 48
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+137.14\times2+117.15\times3.6)} = 22\%$$

Equation S 49
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.235+0.672+1.031-0.283)}{0.283} = 5.9$$

However, AE cannot justly be used to compare the results of Table S1 with those compiled in Table S4 since the consideration of **19**'s incidental waste from its preparation is included whereas the combined AE of **16**'s synthesis is ignored. To understand the limits of AE in these applications we must consider the AE of the reaction with only **19** and diene compared with **16** and diene. These are the figures appearing in the manuscript since we are trying to identify the method with the greatest potential for efficiency.

AE for Diels-Alder Adduct **8** was calculated considering only **19** as reagent.

Equation S 50
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{260.25}{(184.15+148.12*1.4)} = 66\%$$

AE for Diels-Alder Adduct **17** was calculated considering only **19** as reagent.

Equation S 51
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{316.35}{(240.25+148.12*1.4)} = 71\%$$

AE for Diels-Alder Adduct **18** was considering only **19** as reagent.

Equation S 52
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{172.23}{(96.13+148.12*1.4)} = 57\%$$

From Page S23, Section 12, Deoxyaromatization, Table S7

Naphthalene **9** Deoxygenation: Table S7, entry 1

Equation S 53
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{244.25}{(260.25+149.85\times5+108.64\times5)} = 16\%$$

Equation S 54
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.151+0.315+0.435-0.053)}{0.035} = 24.4$$

Naphthalene **20** Deoxygenation: Table S7, entry 2

Equation S 55
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{300.35}{(316.35+149.85\times5+108.64\times5)} = 19\%$$

Equation S 56
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.183+0.315+0.435-0.171)}{0.171} = 4.5$$

Naphthalene **21** Deoxygenation: Table S7, entry 3

Equation S 57
$$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material)+\sum MW(Reagents)} = \frac{156.23}{(172.23+149.85\times3+108.64\times3)} = 16\%$$

Equation S 58
$$sEF = \frac{\sum m(Raw\ Material)+\sum m(Reagents)-m(Product)}{m(Product)} = \frac{(0.150+0.282+0.390-0.125)}{0.25} = 5.6$$

From Page S23, Section 13, Catalytic Hydrogenation, Table S8

Since on a large scale, the supply of hydrogen gas may be controlled exactly, only a stoichiometric amount was used to calculate AE.

7-oxabenzonorbornene **22** by flow hydrogenation

Equation S 59 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{262.26}{(260.25+1.01\times 2)} = 100\%$$

Equation S 60 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(23.21+1.8-22.86)}{22.86} = 0.1$$

7-oxabenzonorbornene **23** by flow hydrogenation

Equation S 61 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{318.37}{(316.35+1.01\times 2)} = 100\%$$

Equation S 62 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(1.20+0.08-1.15)}{1.15} = 0.1$$

7-oxabenzonorbornene **24** by flow hydrogenation

Equation S 63 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{174.24}{(172.23+1.01\times 2)} = 100\%$$

Equation S 63 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(5.85+0.68-5.80)}{5.80} = 0.1$$

From Page S27, Section 14, Dehydroaromatization, Table S9

Naphthalene **9** by dehydration with Amberlyst

Equation S 64 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{244.25}{(262.26)} = 93\%$$

Equation S 65 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.262-0.041)}{0.041} = 5.4$$

Naphthalene **20** by dehydration with Amberlyst

Equation S 66 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{300.35}{(318.37)} = 94\%$$

Equation S 67 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.318-0.291)}{0.291} = 0.1$$

Naphthalene **21** by dehydration with Amberlyst

Equation S 68 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{156.23}{(174.24)} = 90\%$$

Equation S 69 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.174-0.151)}{0.151} = 0.2$$

From Page S28, Section 14, Dehydroaromatization, Table S10

Naphthalene **9** by dehydration with Amberlyst

Equation S 70 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.262-0.09)}{0.09} = 1.9$$

Naphthalene **20** by dehydration with Amberlyst

Equation S 71 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.318-0.237)}{0.237} = 0.3$$

Naphthalene **21** by dehydration with Amberlyst

Equation S 72 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.174-0.151)}{0.151} = 0.2$$

Naphthalene **9** by dehydration with Amberlyst

Equation S 70 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(10.48-7.23)}{7.23} = 0.4$$

From Page S30, Section 14, Dehydroaromatization, Table S11

Naphthalene **10** by dehydration with concentrated hydrochloric acid

Equation S 71 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{216.19}{(262.26)} = 83\%$$

Equation S 72 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.528 - 0.397)}{0.397} = 0.3$$

Naphthalene **12** by dehydration with concentrated hydrochloric acid

Equation S 73 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{272.3}{(318.37)} = 85\%$$

Equation S 74 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.640 - 0.394)}{0.394} = 0.6$$

Naphthalene **21** by dehydration with concentrated hydrochloric acid

Equation S 75 $$\mathrm{AE} = \frac{\mathrm{MW}_{Product}}{\sum MW(Raw\ Material) + \sum MW(Reagents)} = \frac{156.23}{(174.24)} = 90\%$$

Equation S 76 $$sEF = \frac{\sum m(Raw\ Material) + \sum m(Reagents) - m(Product)}{m(Product)} = \frac{(0.351 - 0.264)}{0.264} = 0.3$$

16. Appendix 2 FTIR, ^{1}H NMR, ^{13}C NMR

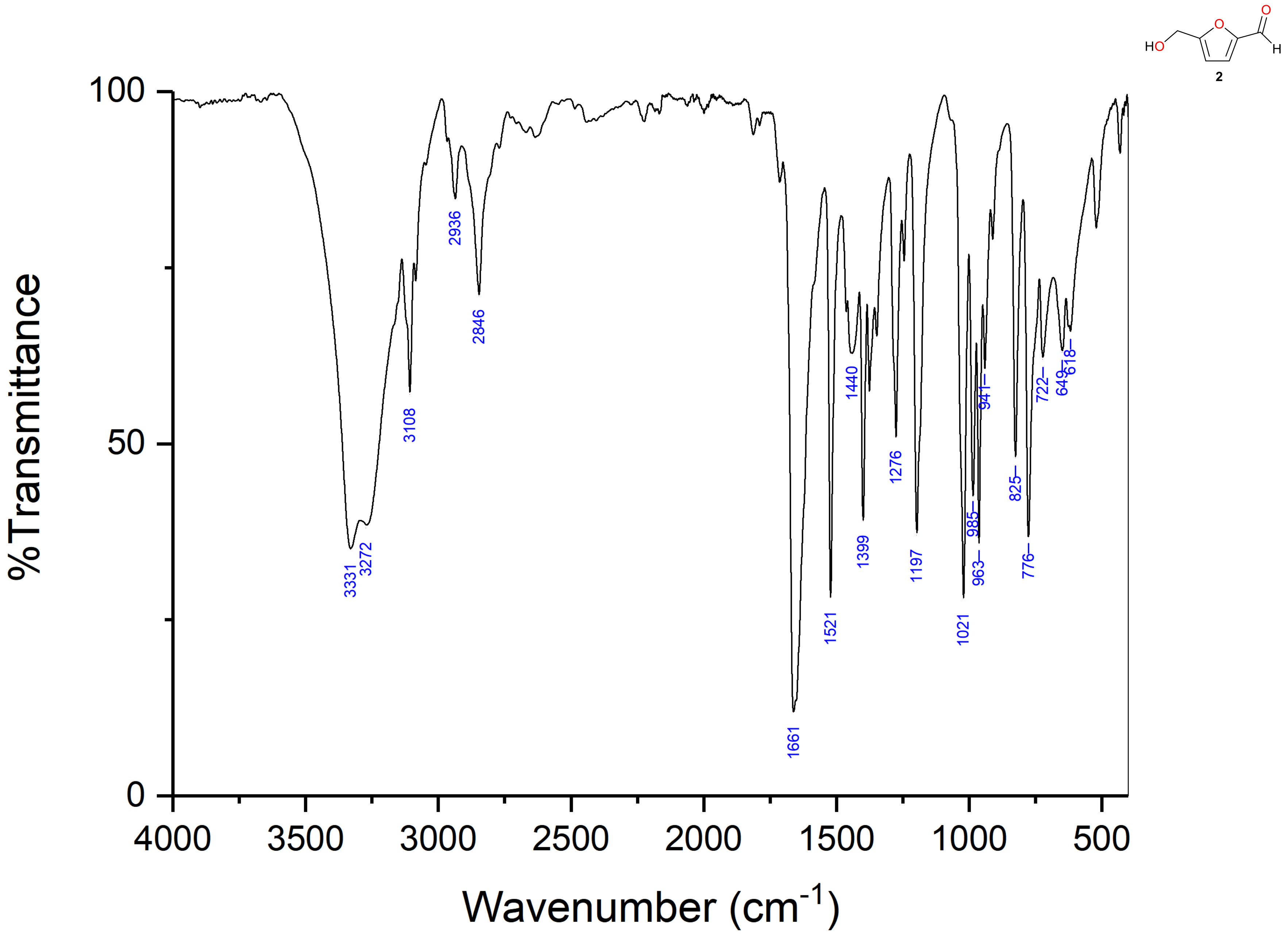
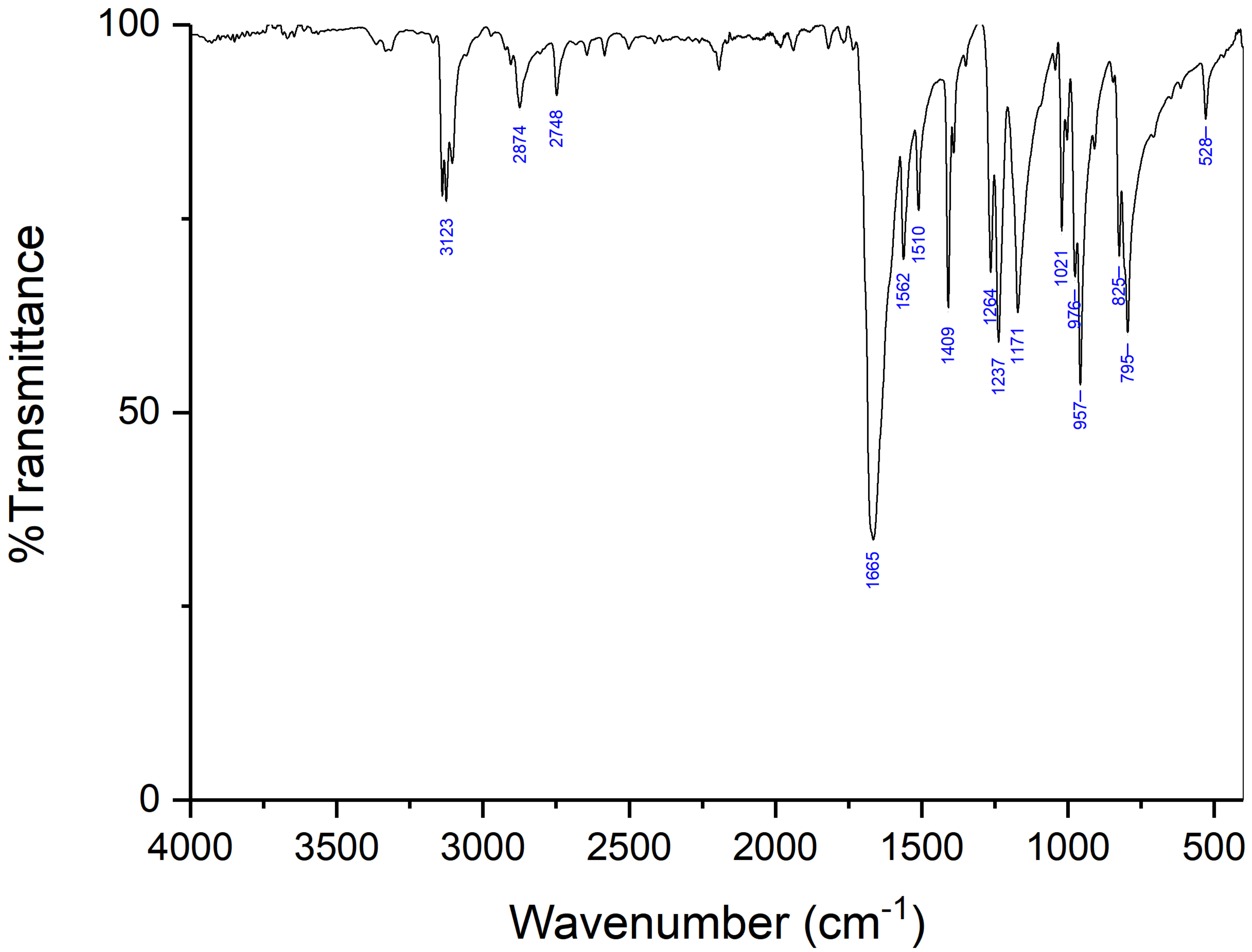
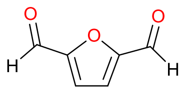


Fig. S2 5-(Hydroxymethyl)furfural **2** (Neat, FTIR)





2A

Fig. S3 2,5-Diformylfuran **2A** (Neat, FTIR)

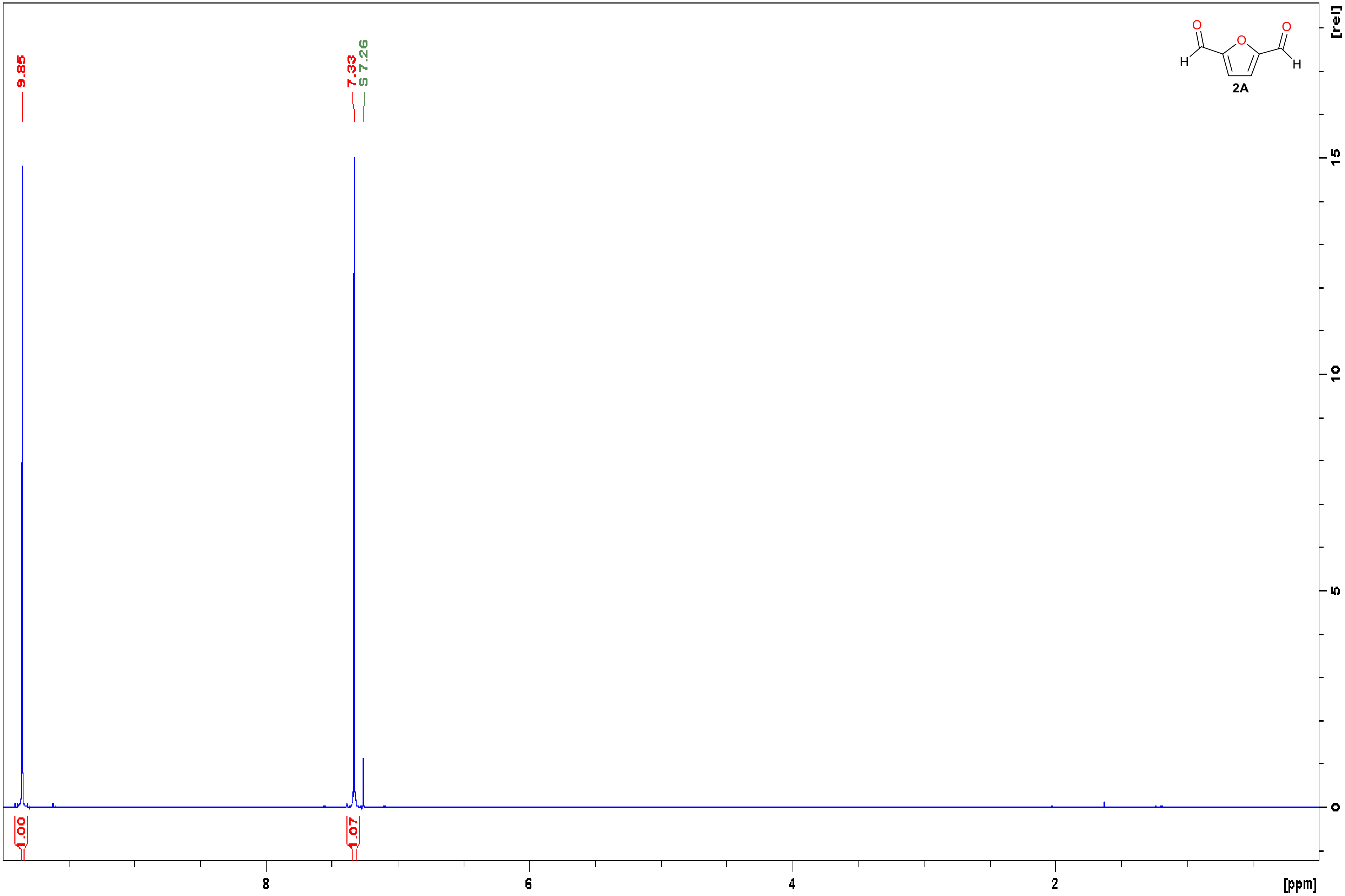


Fig. S4 2,5-Diformylfuran **2A** (CDCl$_3$, ^{1}H NMR)

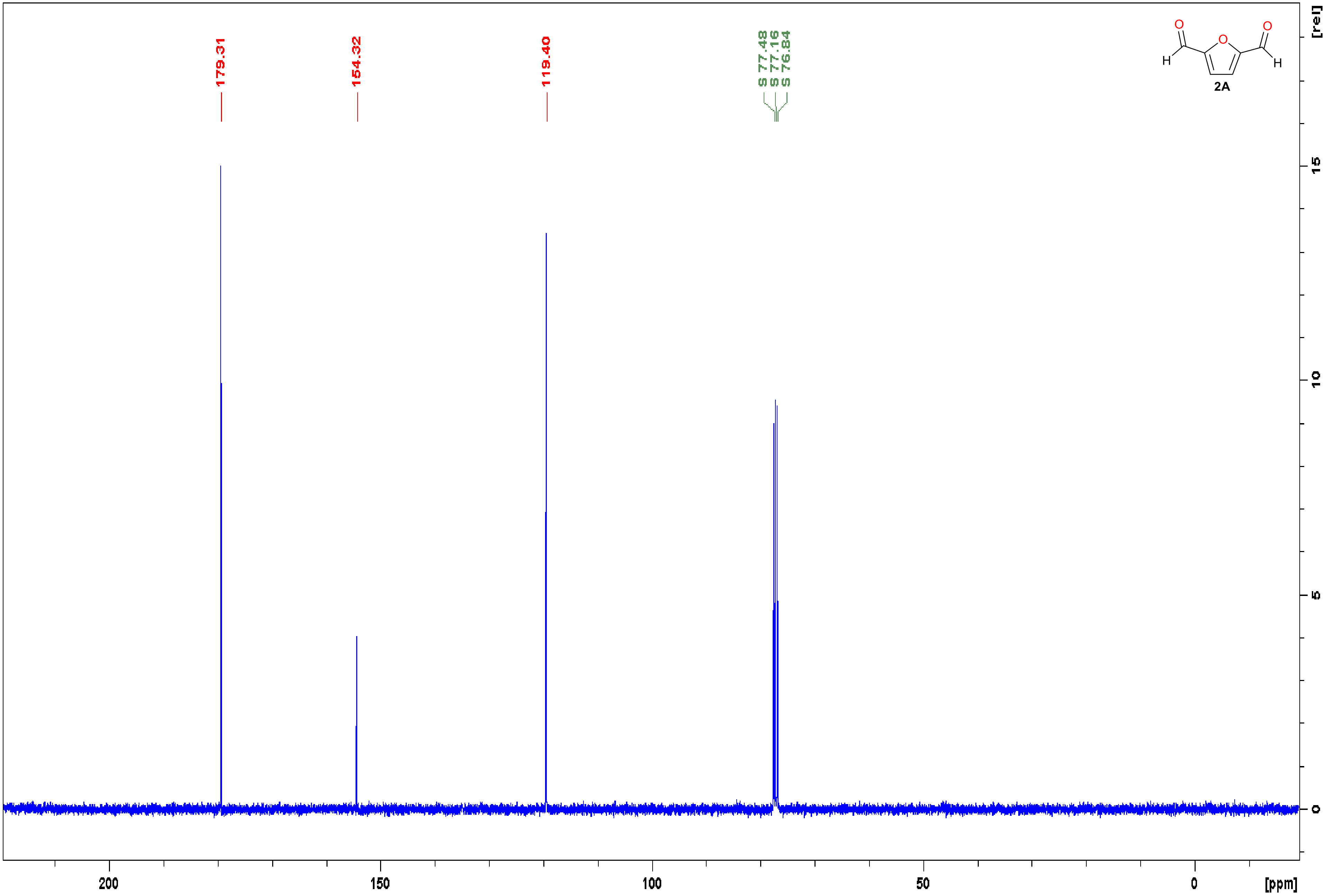


Fig. S5 2,5-Diformylfuran **2A** ($CDCl_3$, ^{13}C NMR)

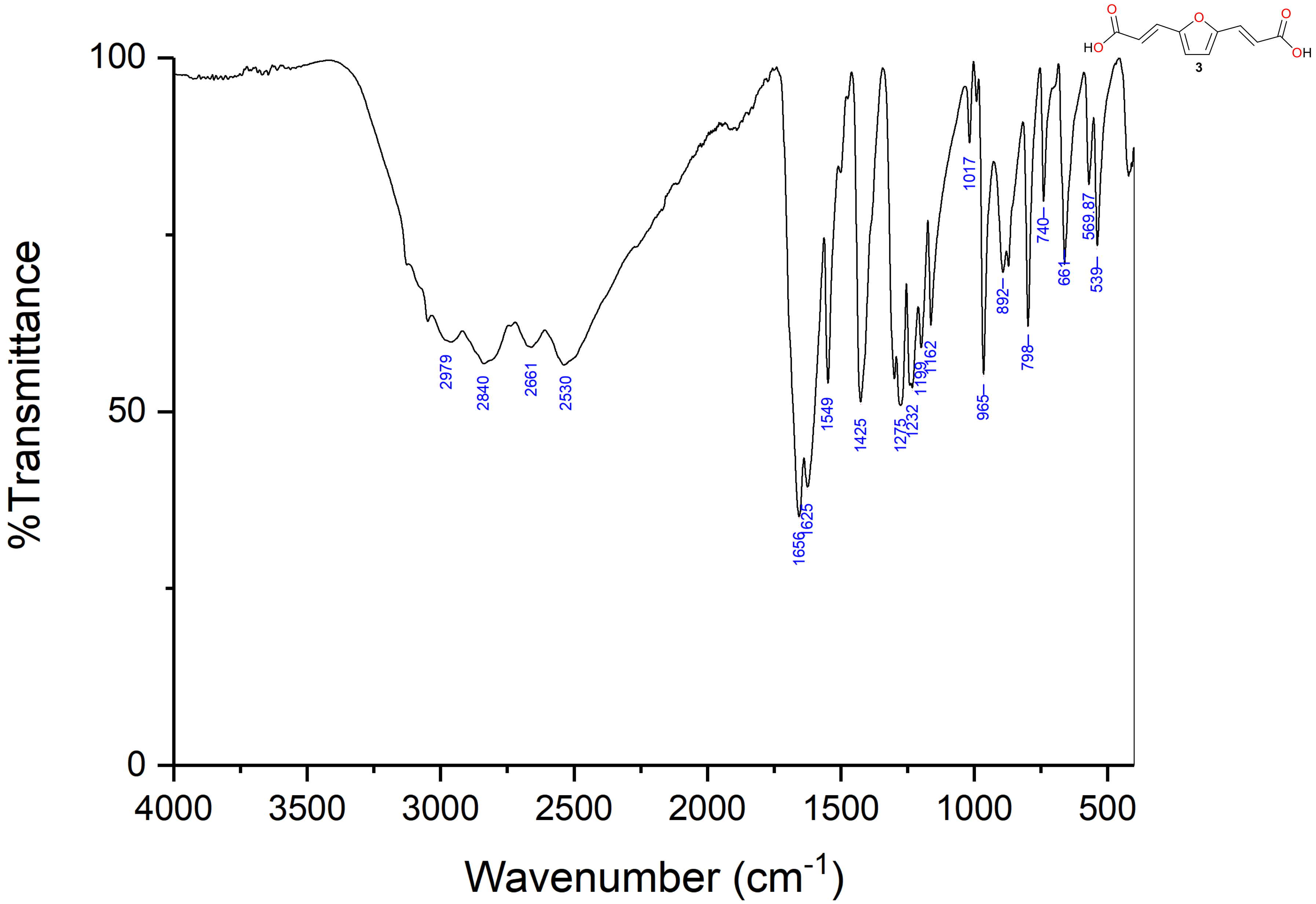


Fig. S6 (2E,2'E)-3,3'-(furan-2,5-diyl)diacrylic Acid **3** (Neat, FTIR)

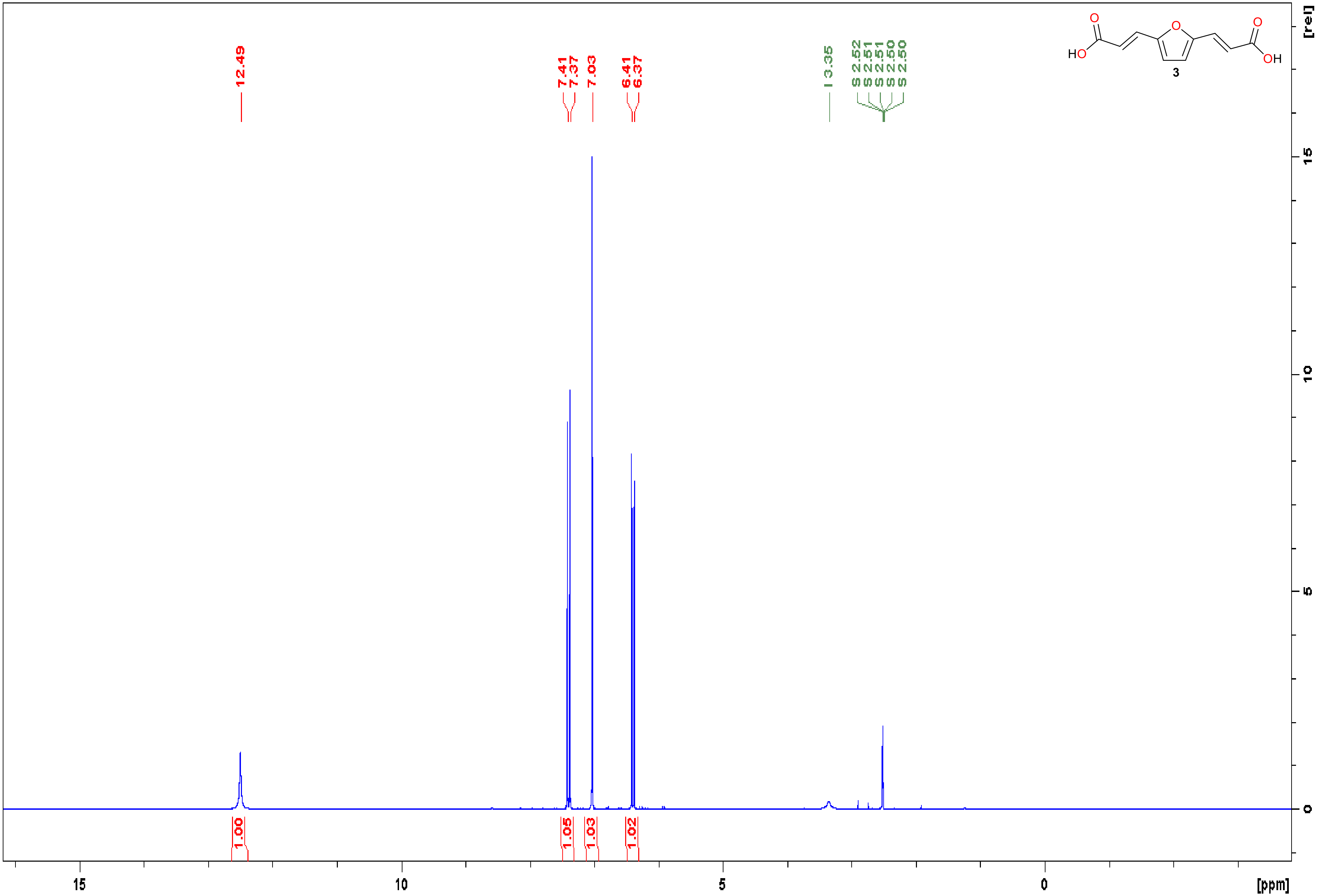


Fig. S7 (2E,2'E)-3,3'-(furan-2,5-diyl)diacrylic Acid **3** (DMSO, ^{1}H NMR)

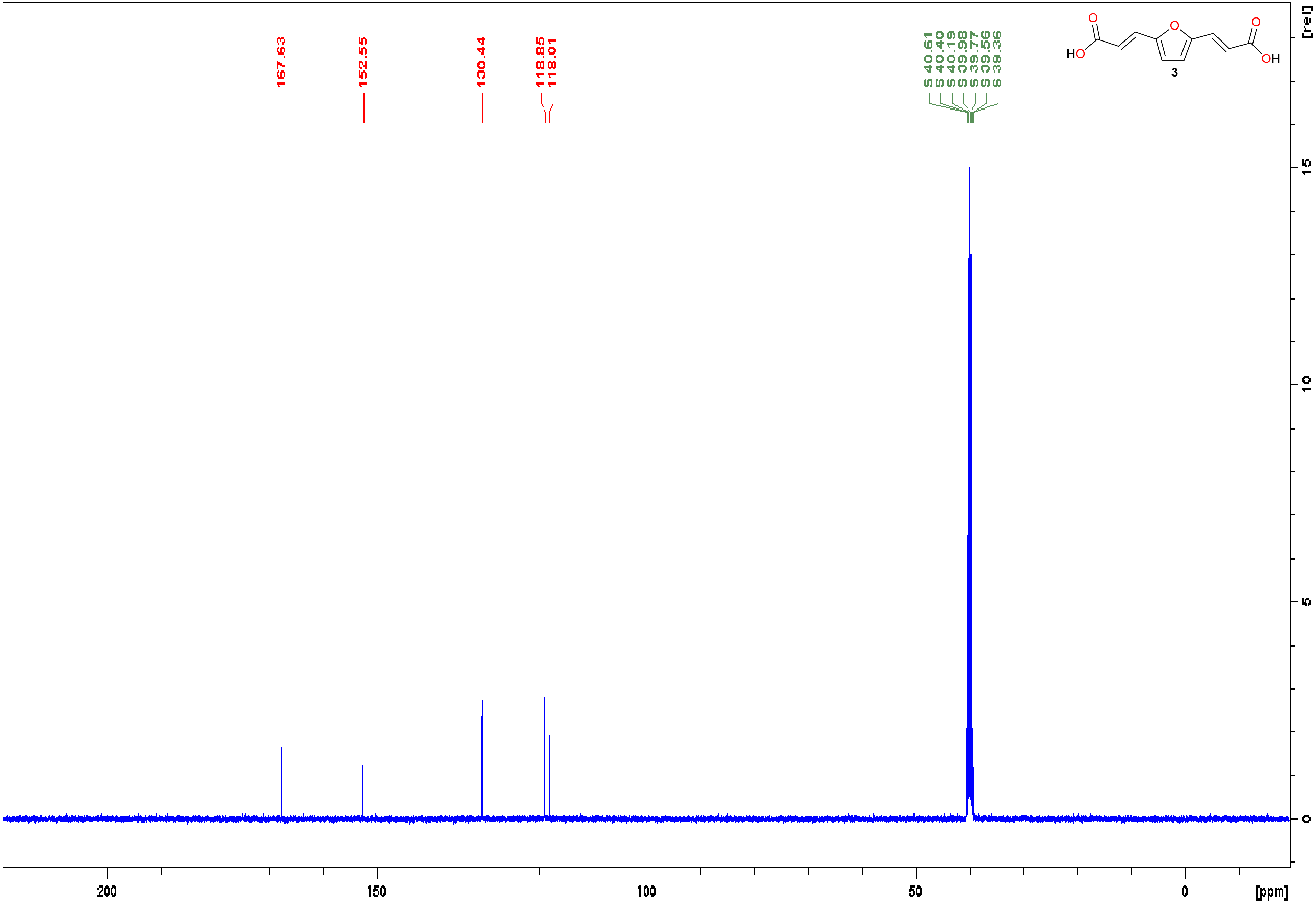


Fig S8 (2E,2'E)-3,3'-(furan-2,5-diyl)diacrylic Acid 3-Furan-2,5-diylbisacrylic Acid **3** (DMSO, ^{13}C NMR)

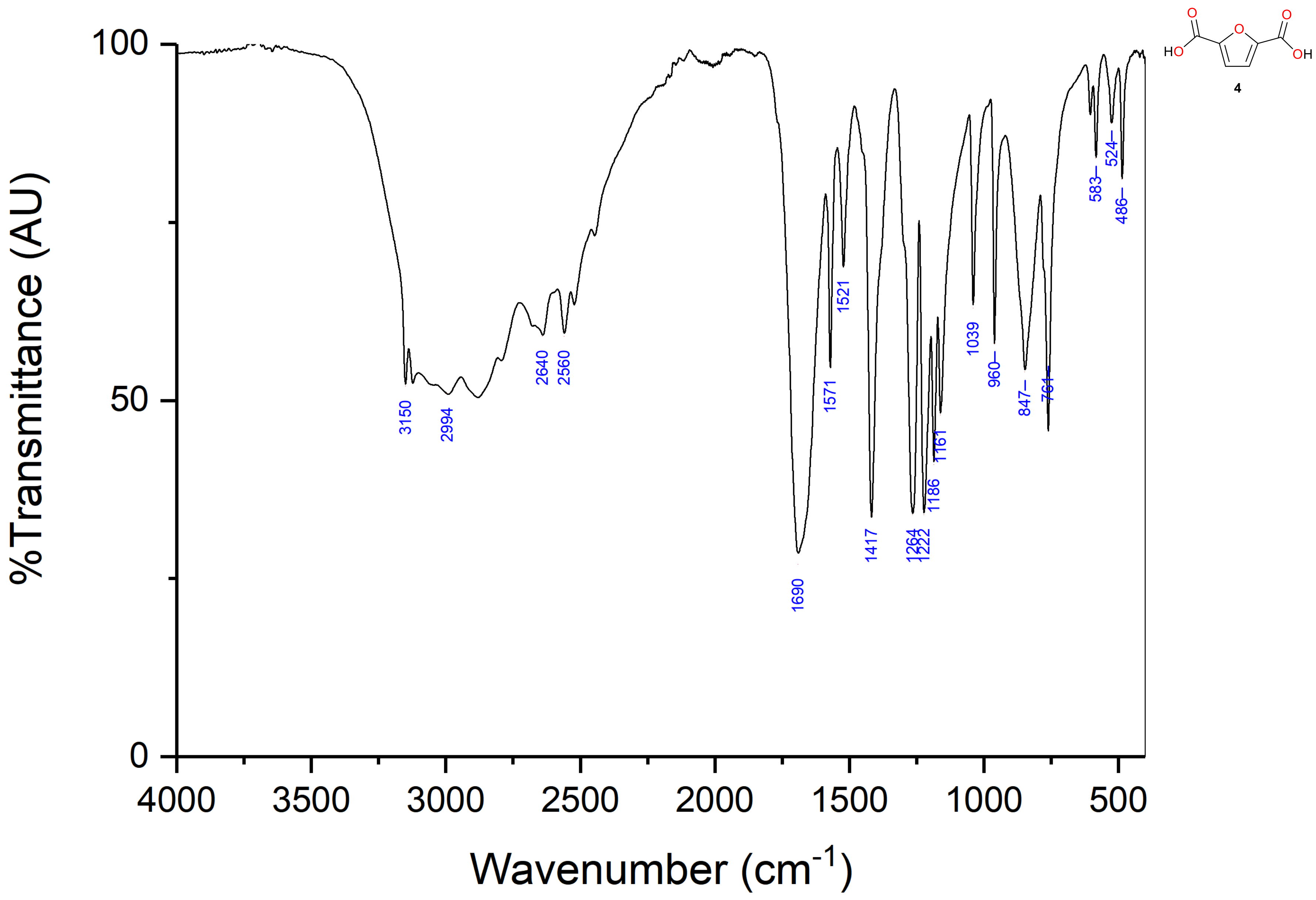


Fig. S9 2,5-Furandicarboxylic Acid **4** (Neat, FTIR)

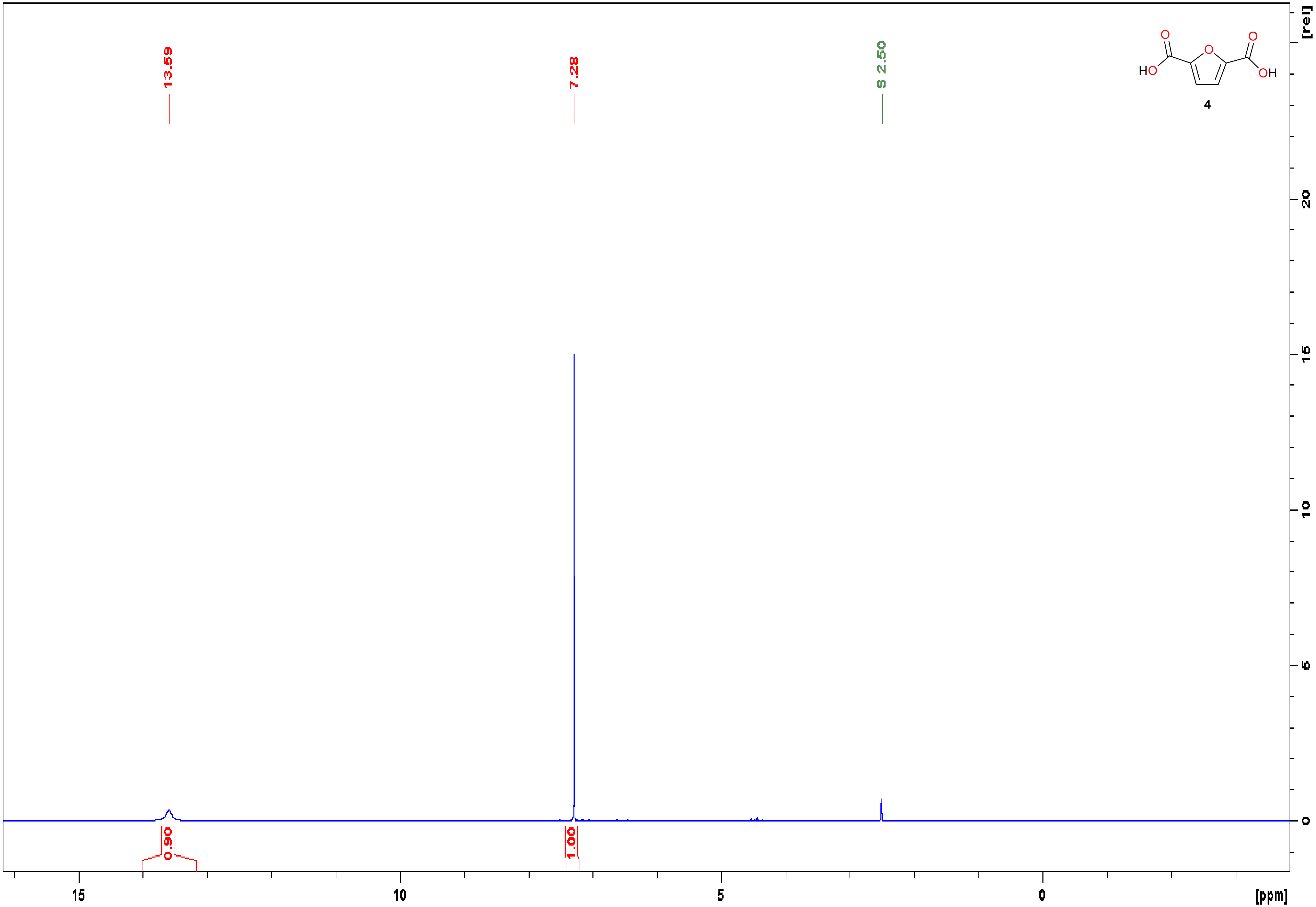


Fig. S10 2 2,5-Furandicarboxylic Acid **4** (DMSO, ^{1}H NMR)

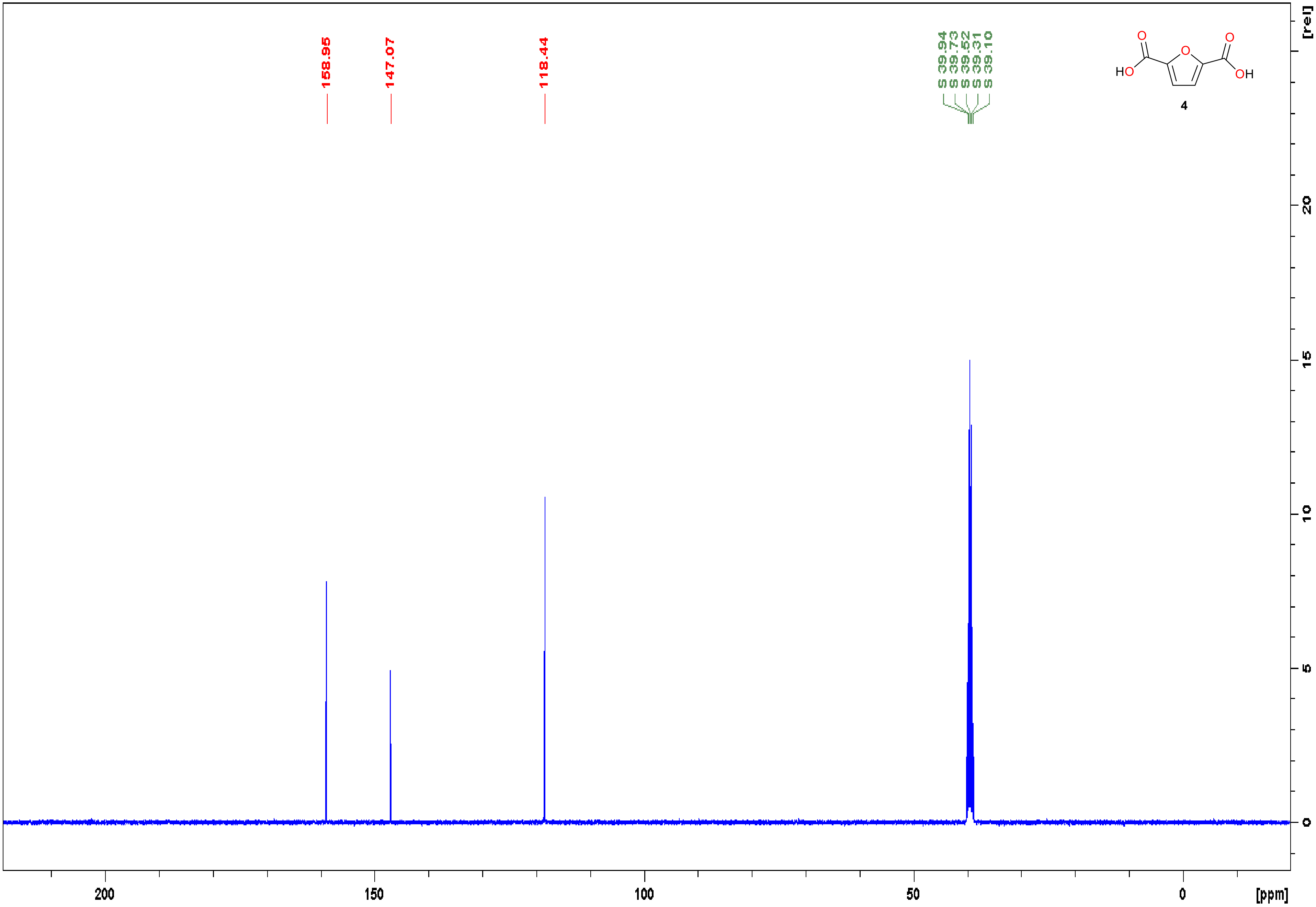


Fig. S11 2,5-Furandicarboxylic Acid **4** (DMSO, ^{13}C NMR)

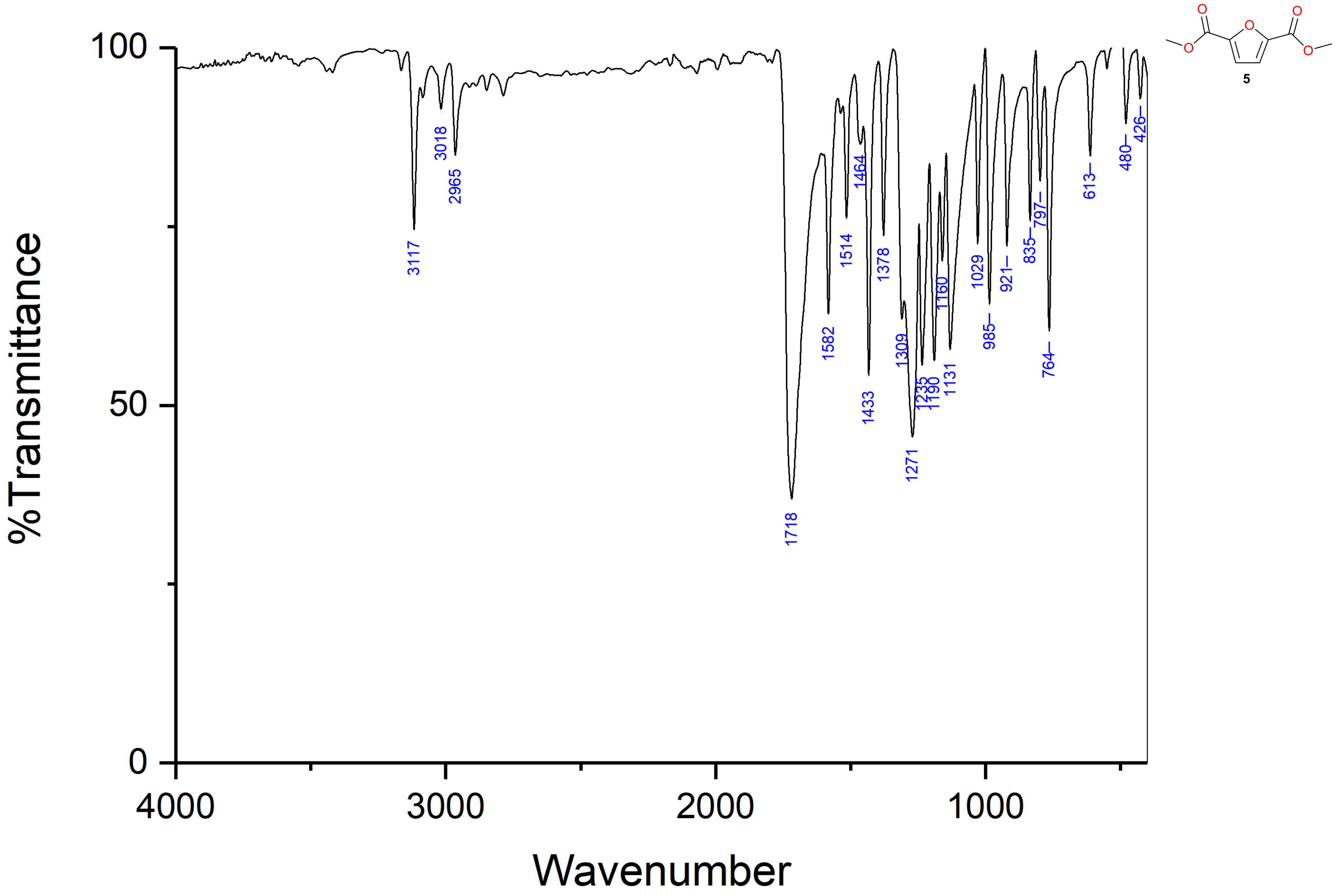


Fig. S12 Dimethyl 2,5-Furandicarboxylate **5** (Neat, FTIR)

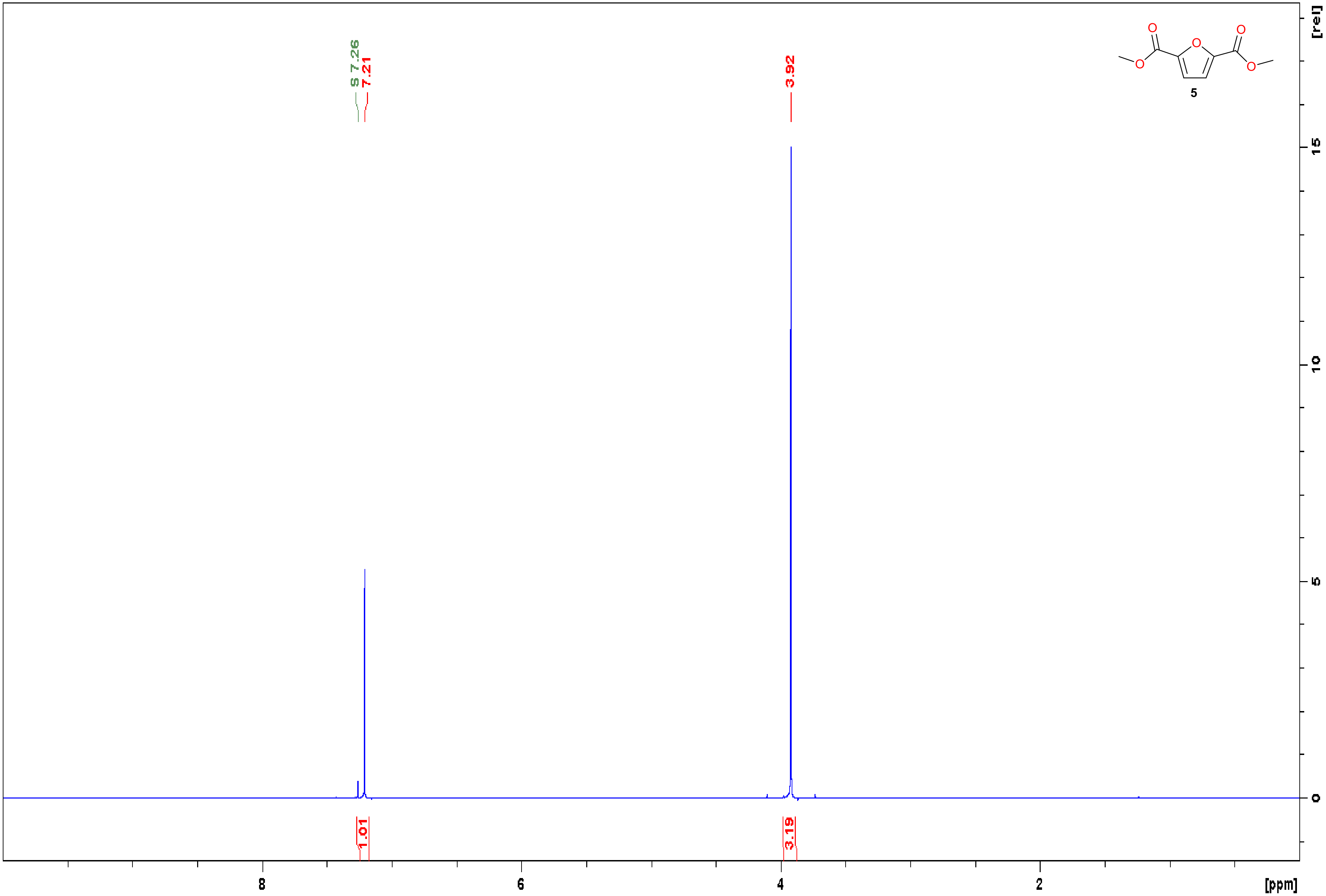


Fig. S13 Dimethyl 2,5-Furandicarboxylate **5** ($CDCl_3$, ^1H NMR)

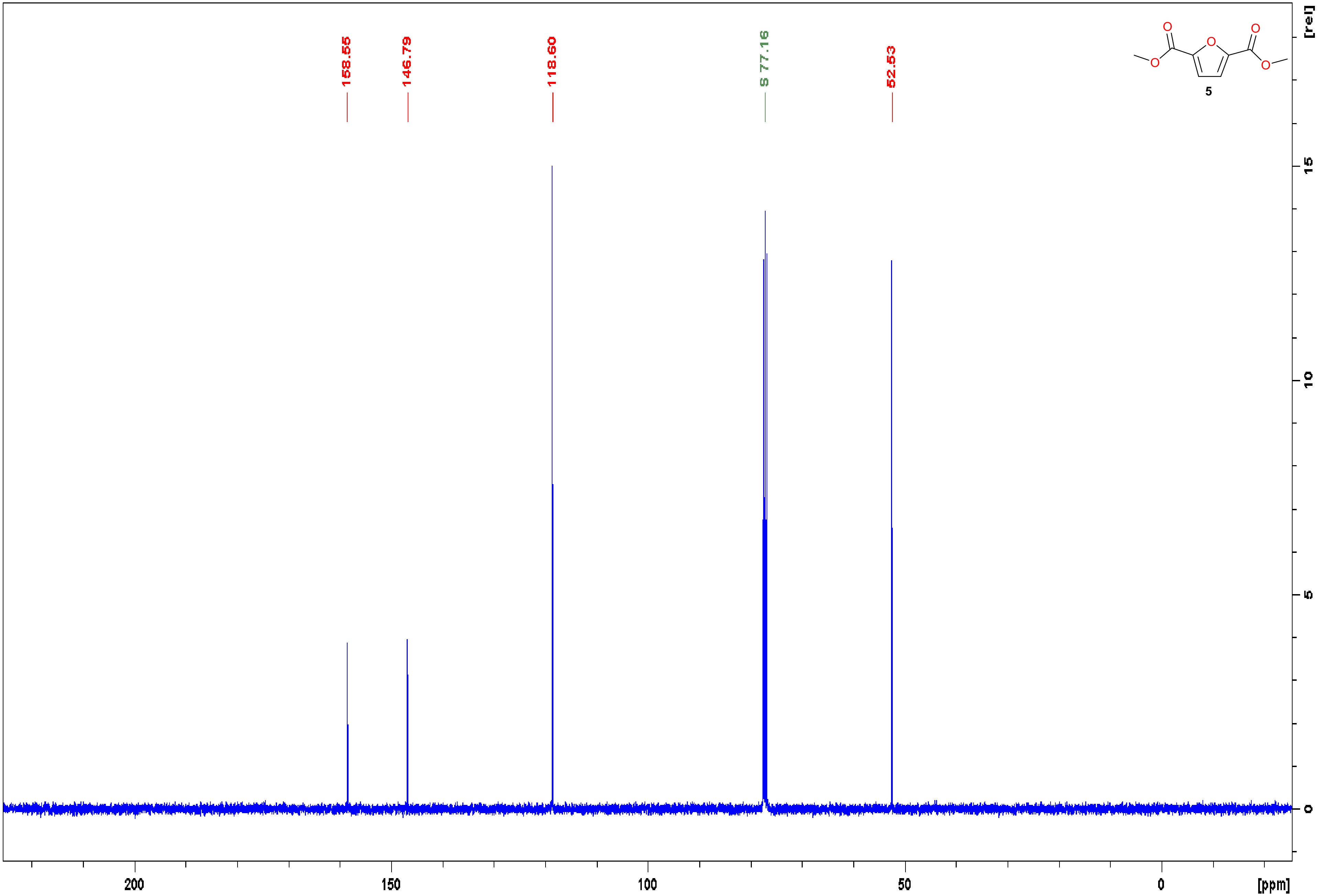


Fig. S14 Dimethyl 2,5-Furandicarboxylate **5** (CDCl$_3$, ^{13}C NMR)

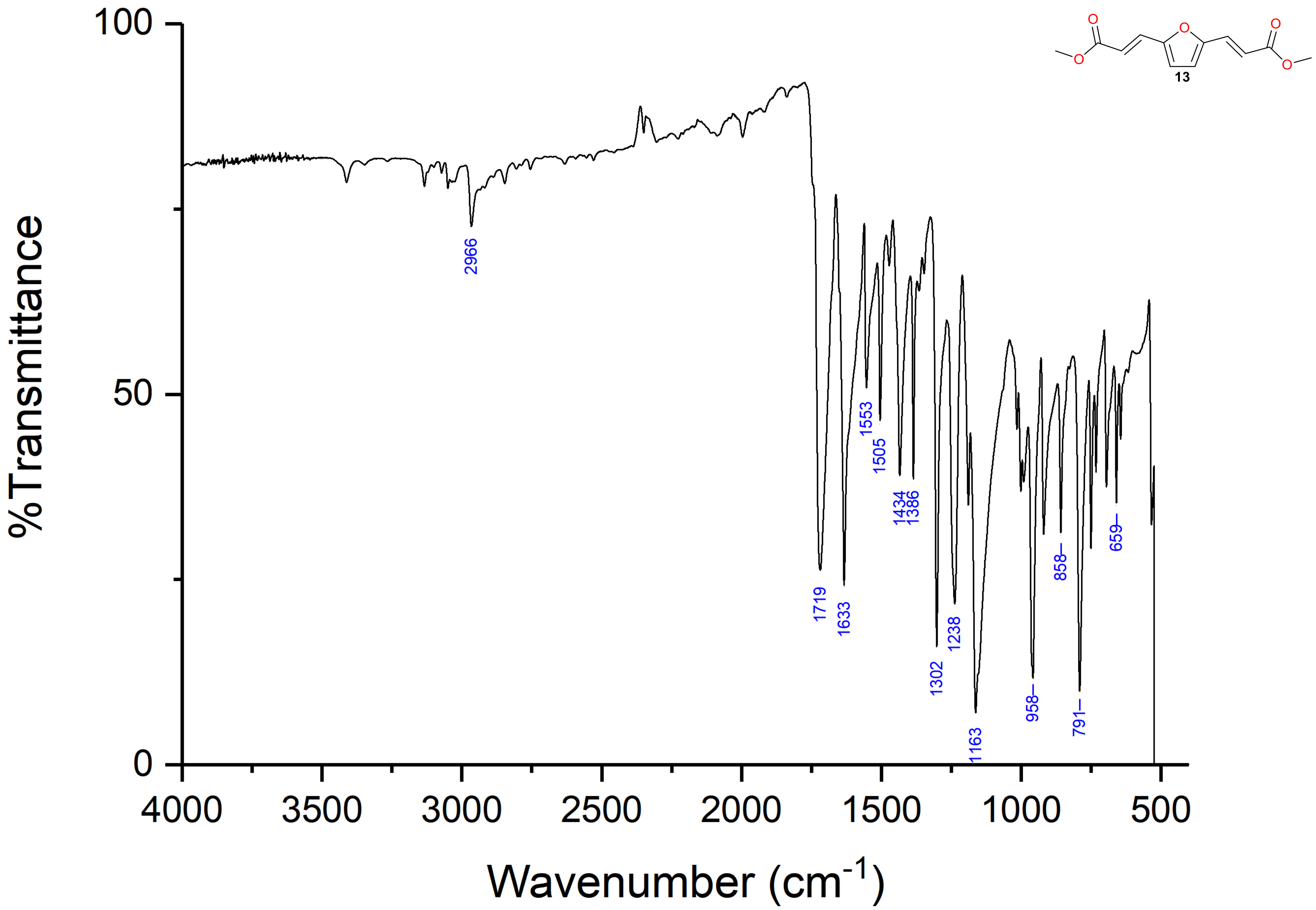


Fig. S3 Dimethyl 3,3'-(Furan-2,5-diyl)(2E,2'E)-diacrylate **13** (Neat, FTIR)

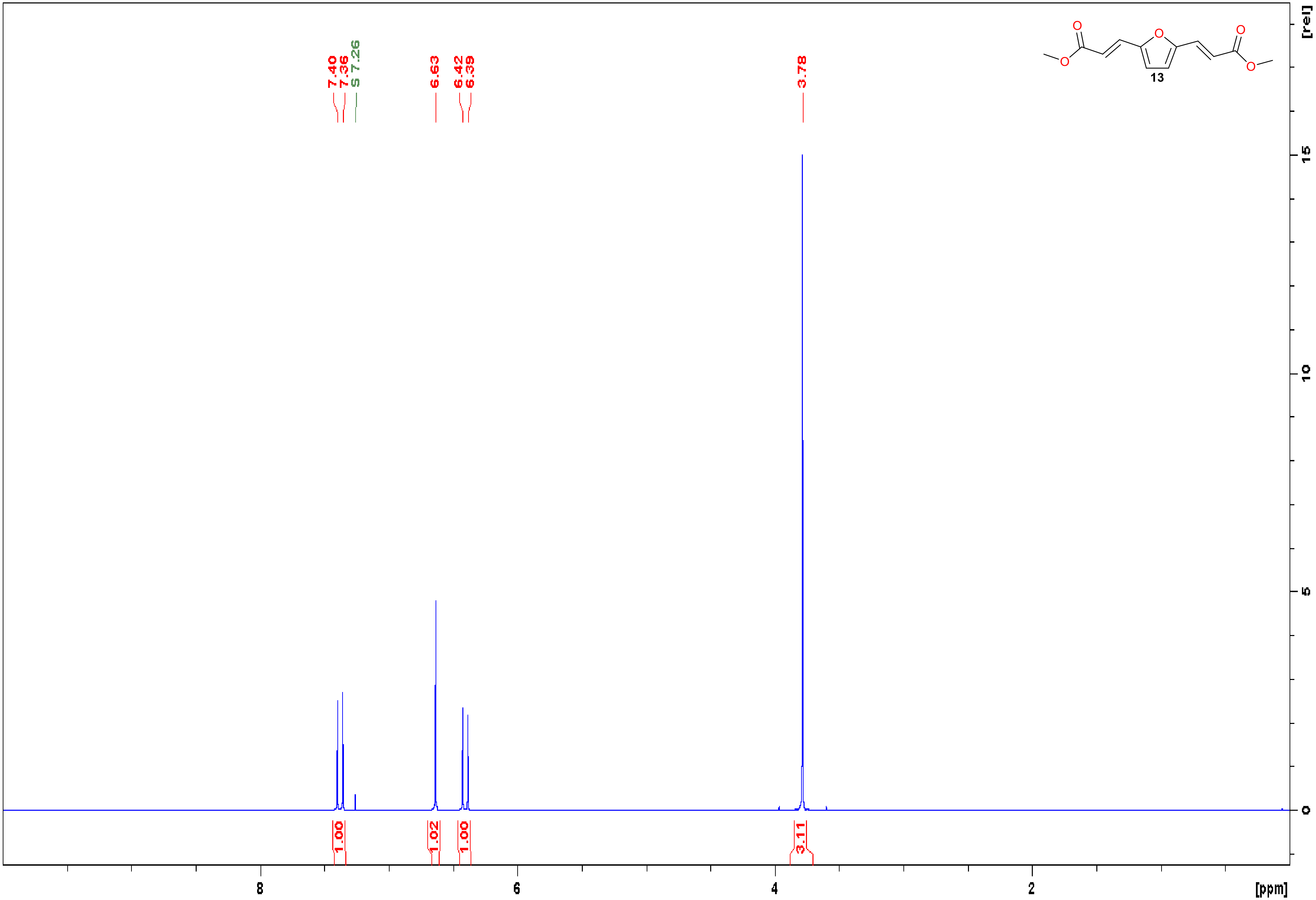


Fig. S16 Dimethyl 3,3'-(Furan-2,5-diyl)(2E,2'E)-diacrylate **13** ($CDCl_3$, ^1H NMR)

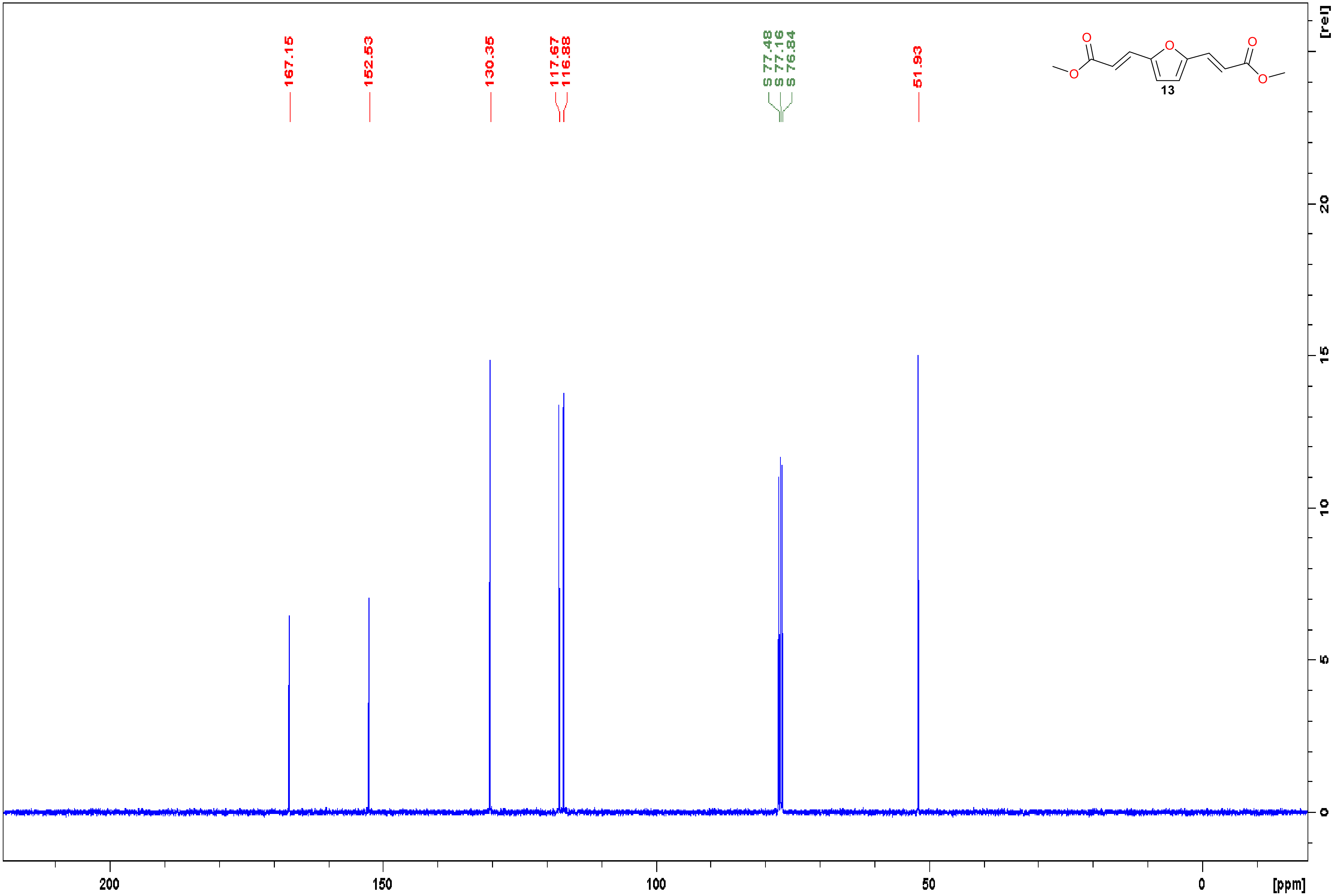


Fig. S17 Dimethyl 3,3'-(Furan-2,5-diyl)(2E,2'E)-diacrylate **13** ($CDCl_3$, ^{13}C NMR)

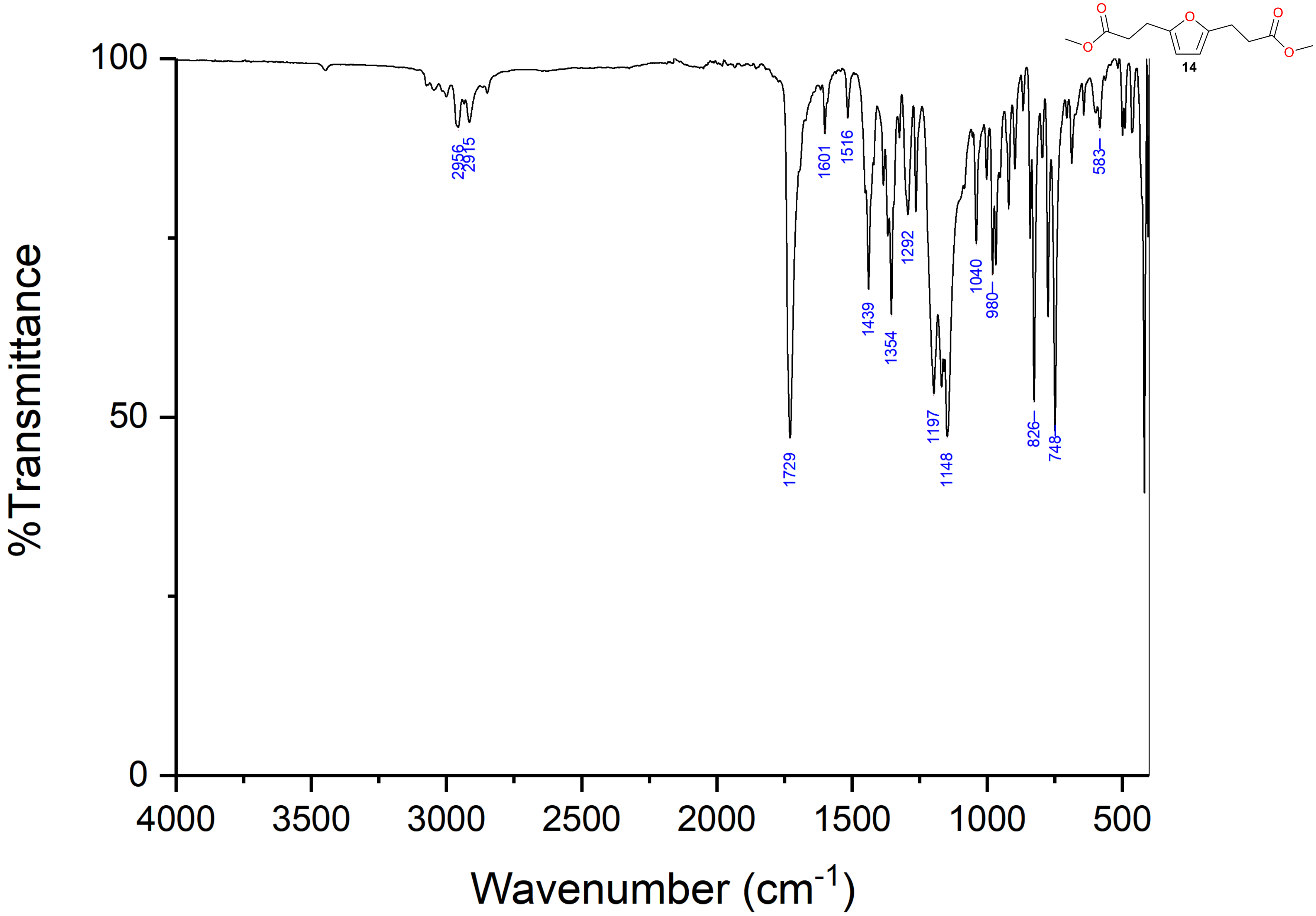


Fig. S18 Dimethyl 3,3'-(Furan-2,5-diyl)dipropionate **14** (Neat, FTIR)

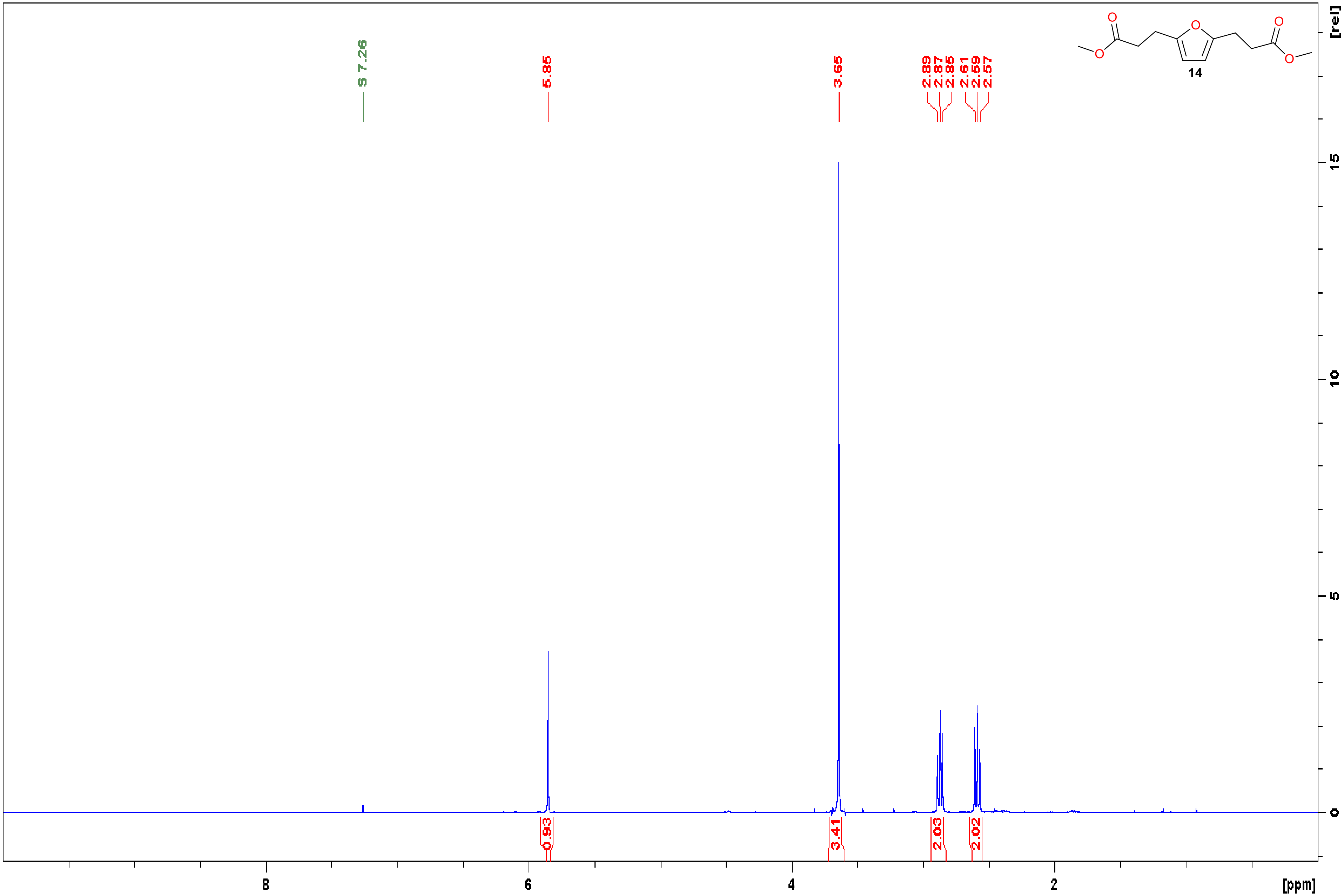


Fig. S19 Dimethyl 3,3'-(Furan-2,5-diyl)dipropionate **14** ($CDCl_3$, ^1H NMR)

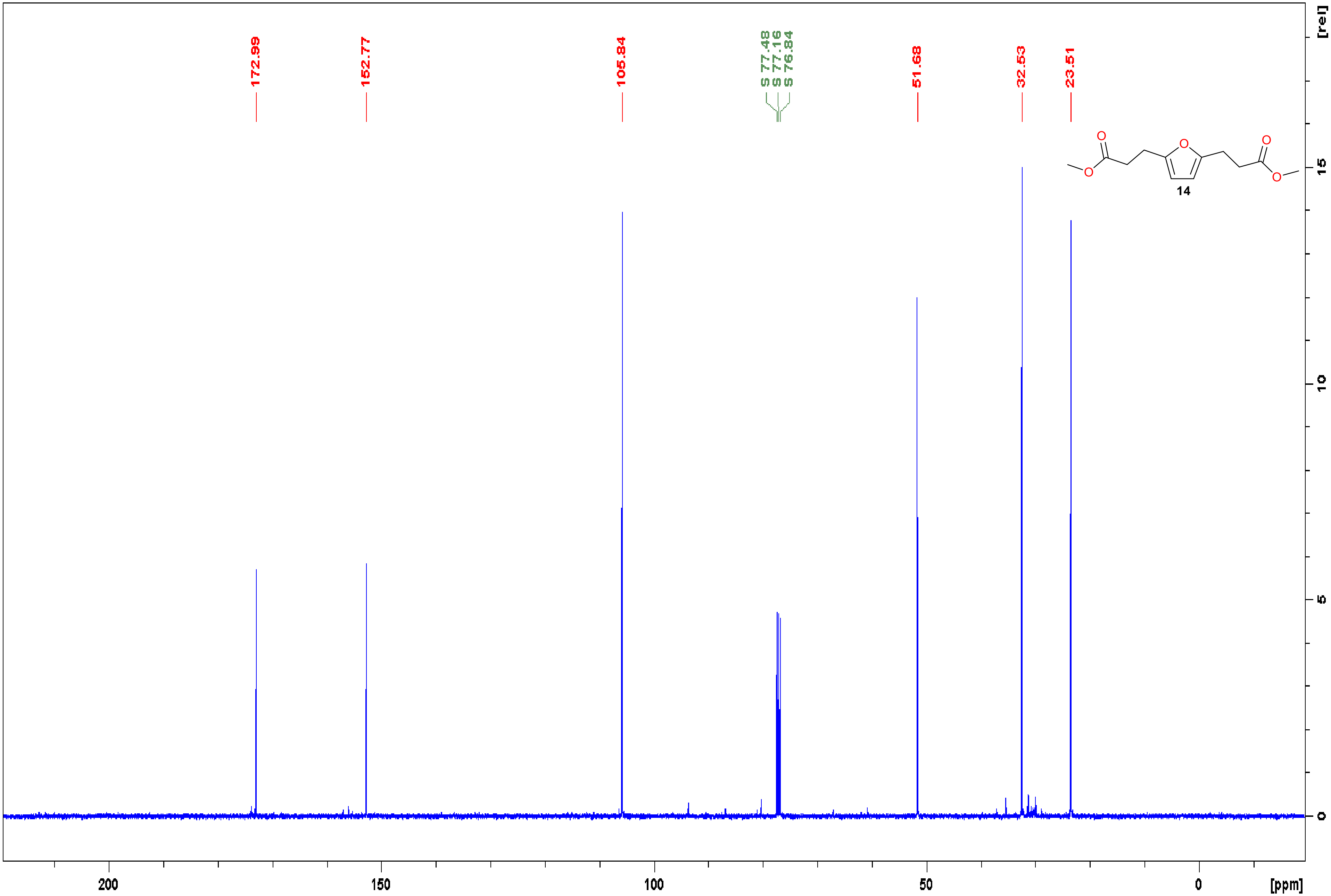


Fig. S20 Dimethyl 3,3'-(Furan-2,5-diyl)dipropionate **14** (^{13}C NMR, $CDCl_3$)

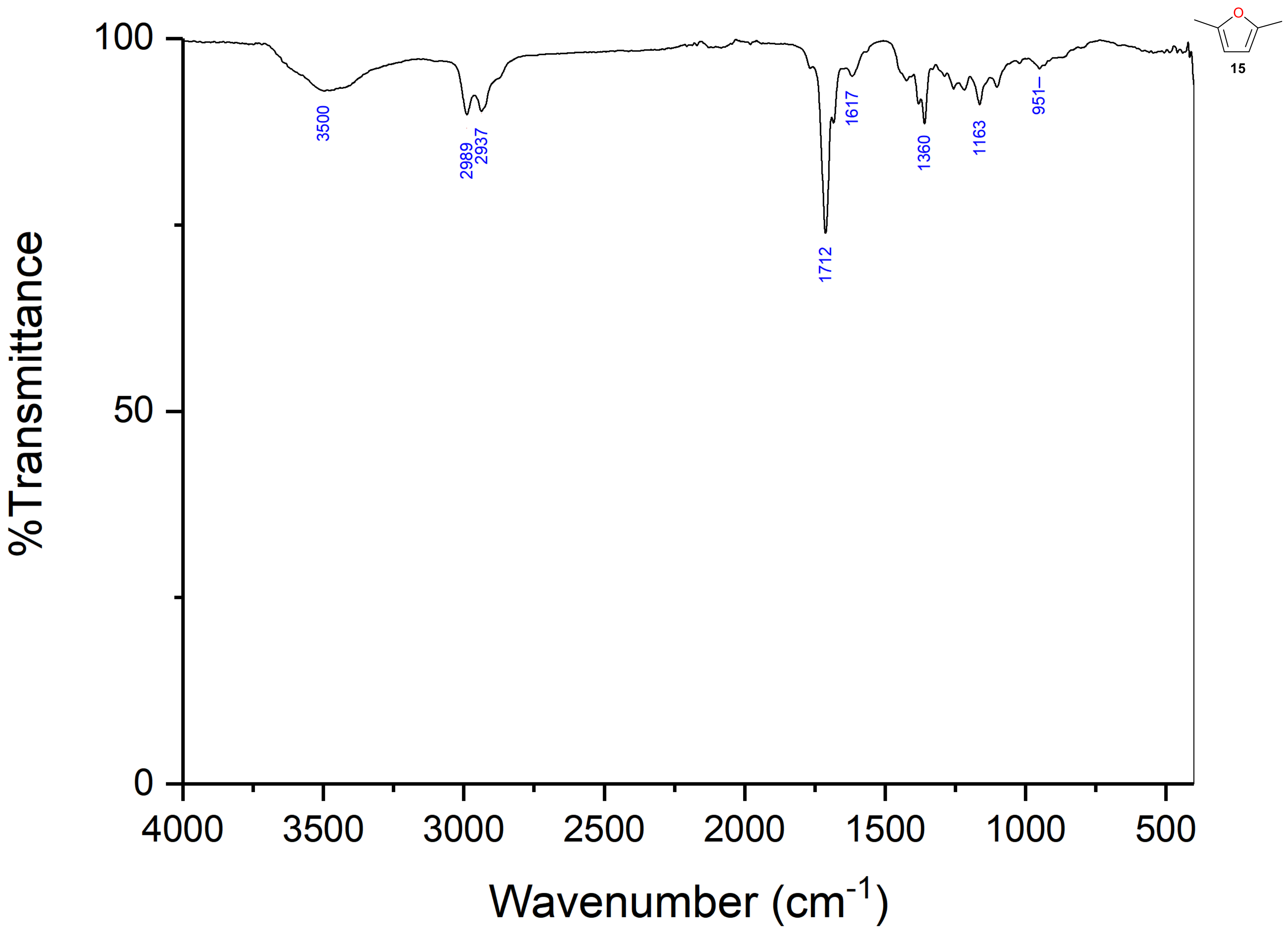


Fig. S21 2,5-Dimethylfuran **15** (FTIR, Neat)

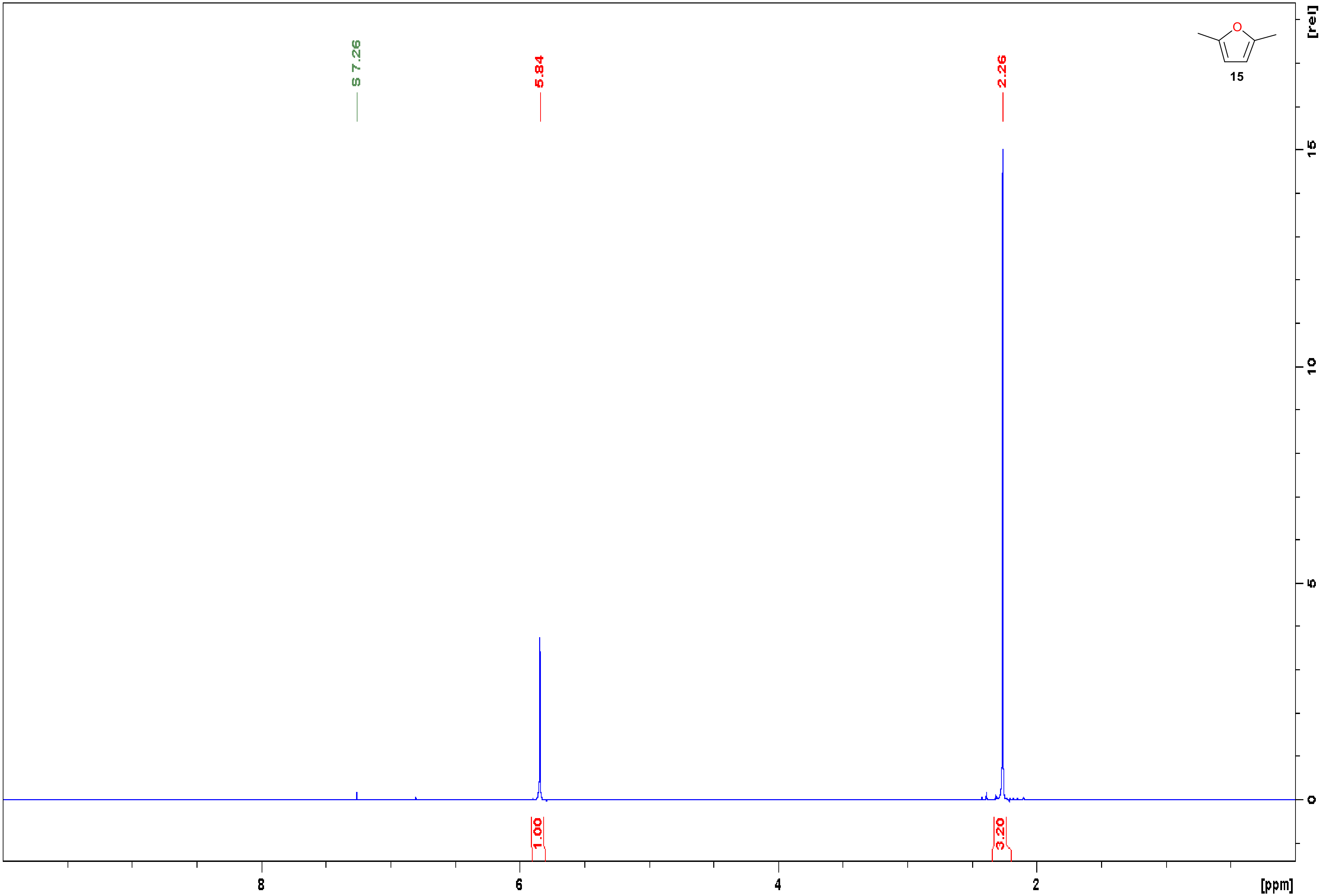


Fig. S4 2,5-Dimethylfuran **15** (^{1}H NMR, $CDCl_3$)

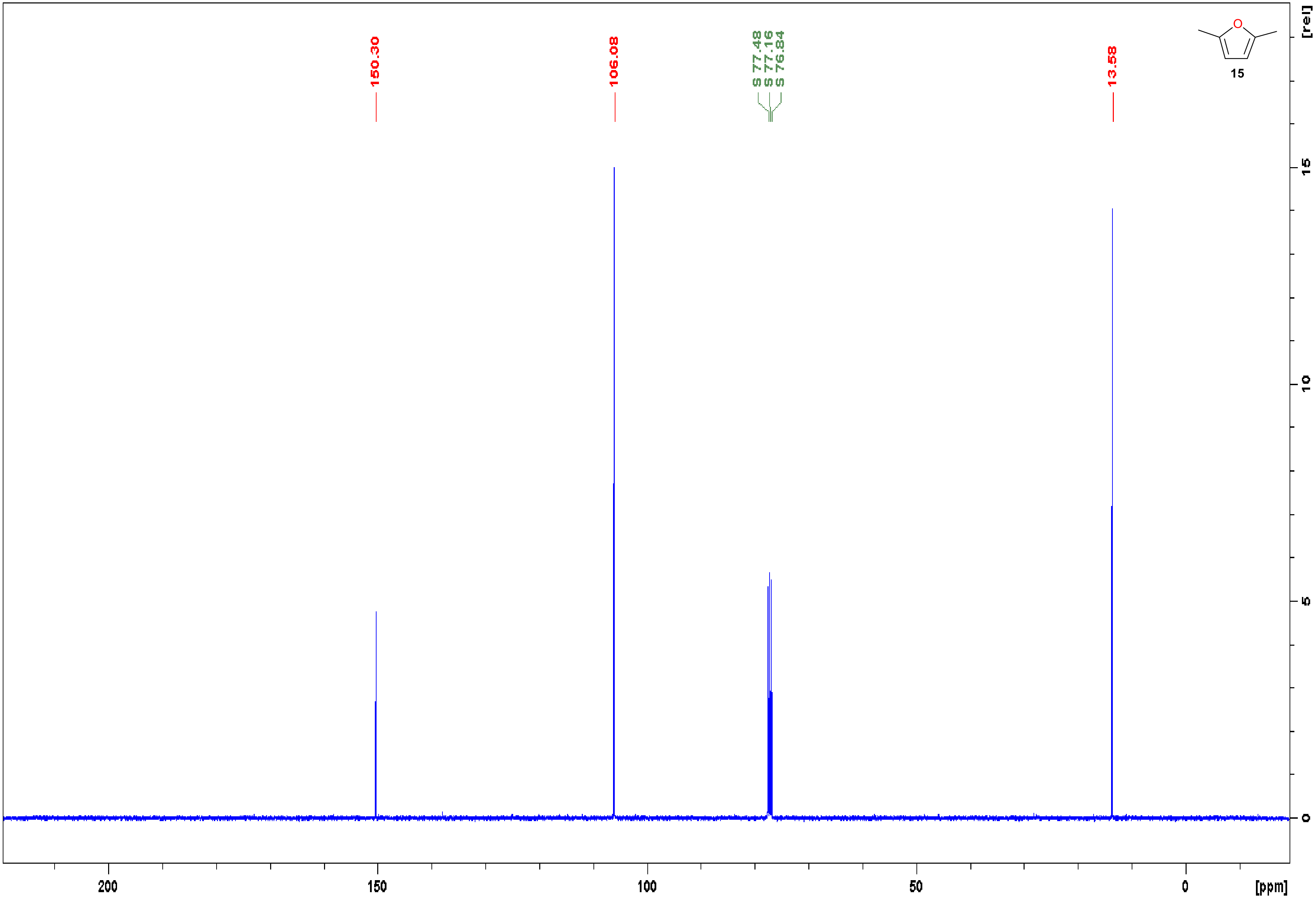


Fig. S5 2,5-Dimethylfuran **15** (^{13}C NMR, $CDCl_3$)

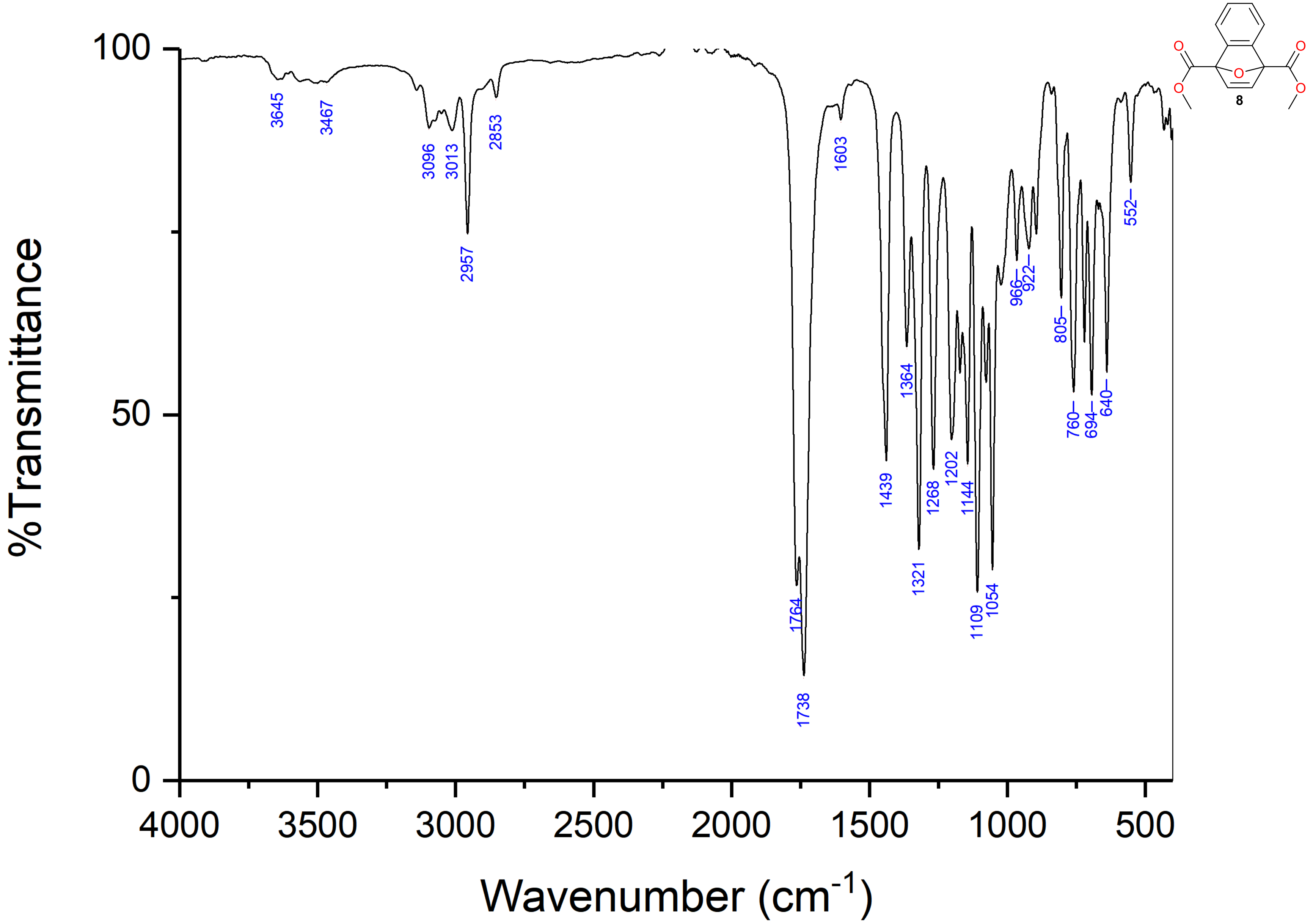


Fig. S6 Dimethyl 7-Oxabenzonorbornadienyl-1,4-dicarboxylate **8** (FTIR, Neat)

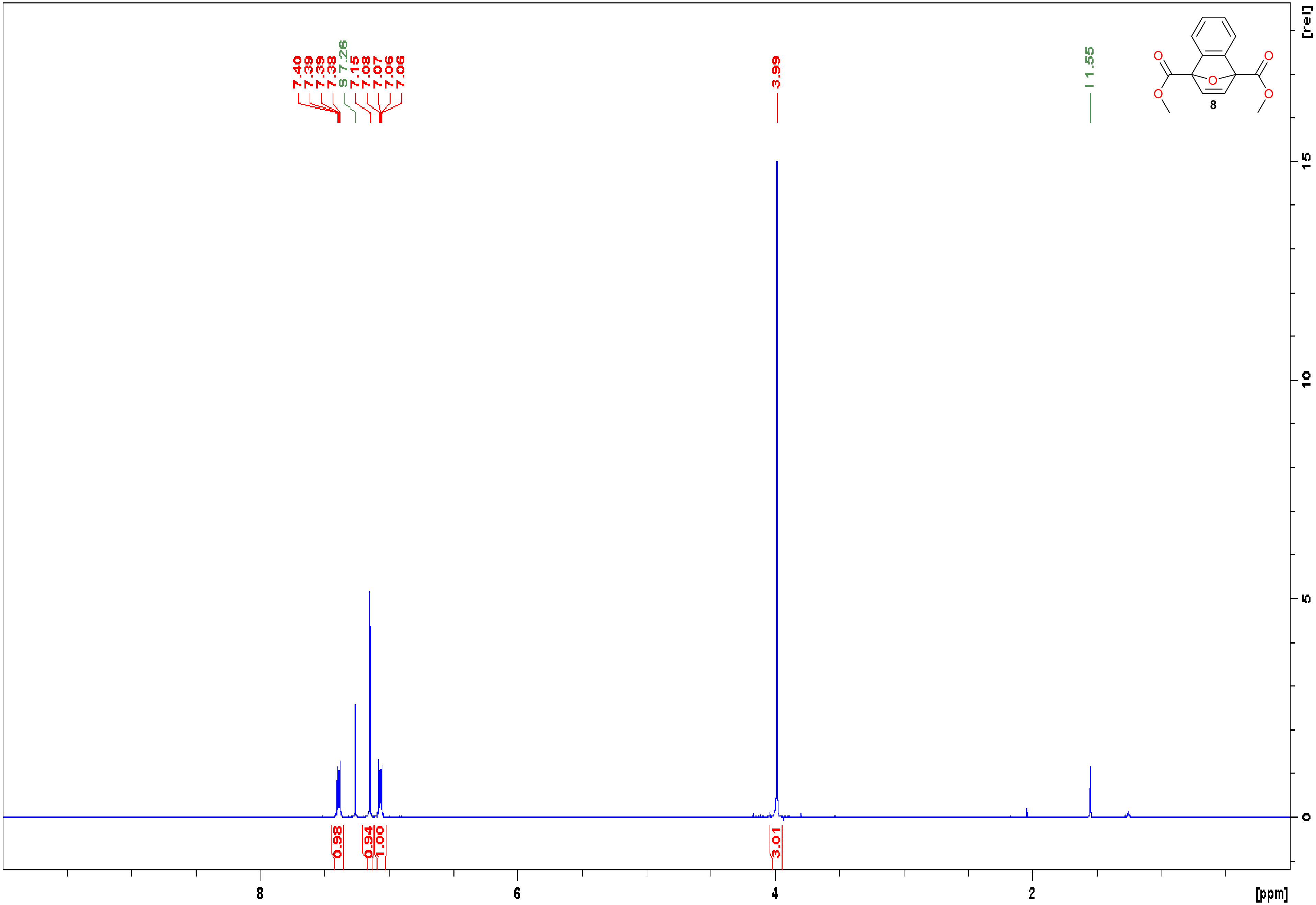


Fig.S75 Dimethyl 7-Oxabenzonorbornadieny-1,4-dicarboxylate **8** (^{1}HNMR, CDCl$_3$)

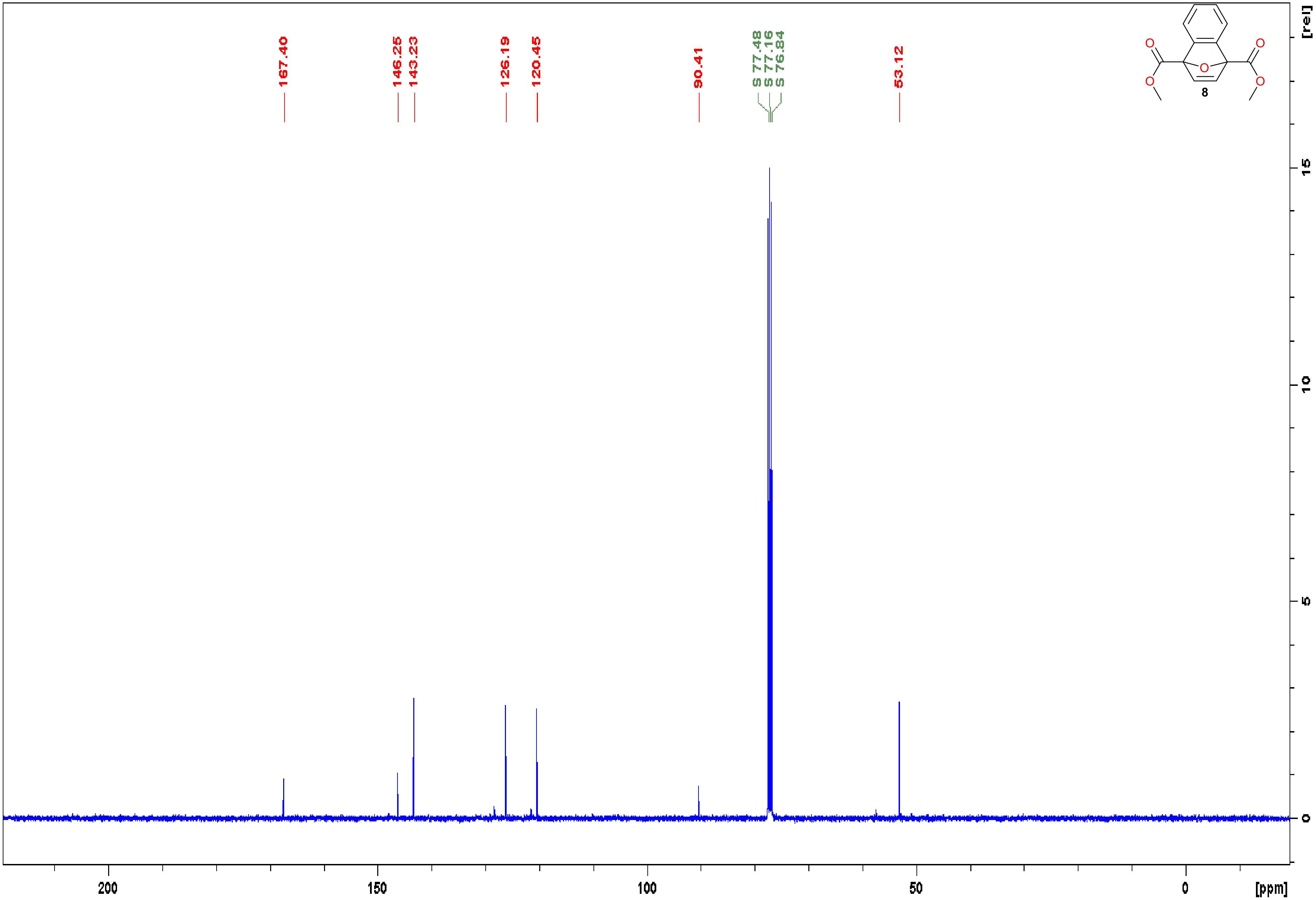


Fig. S 8 Dimethyl 7-Oxabenzonorbornadieny-1,4-dicarboxylate **8** (^{13}C NMR, CDCl$_3$)

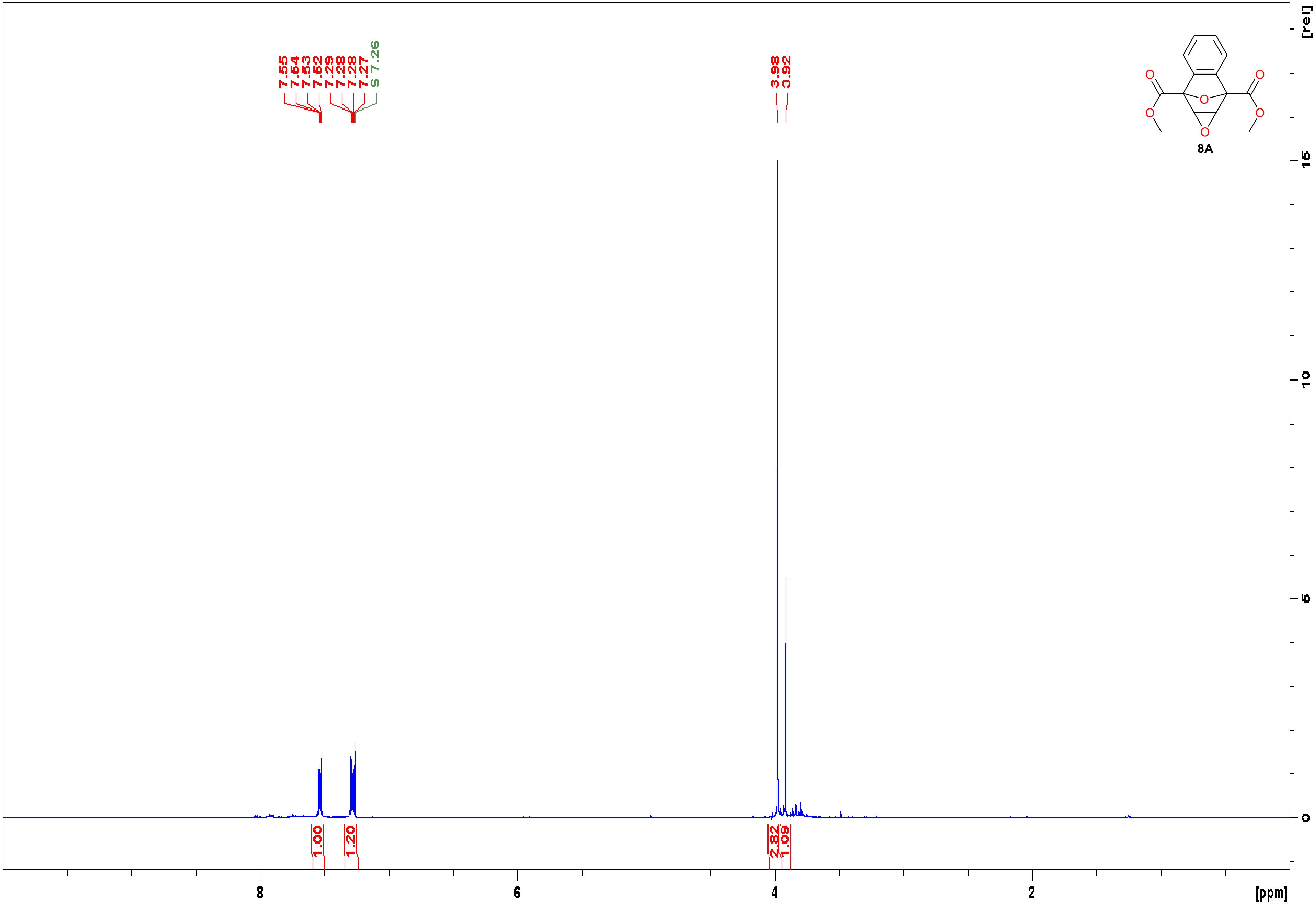


Fig. S 9 Dimethyl 3,4-epoxy-7-oxabenzynorbornadiene-1,4-dicarboxylate (^{1}H NMR, $CDCl_3$)

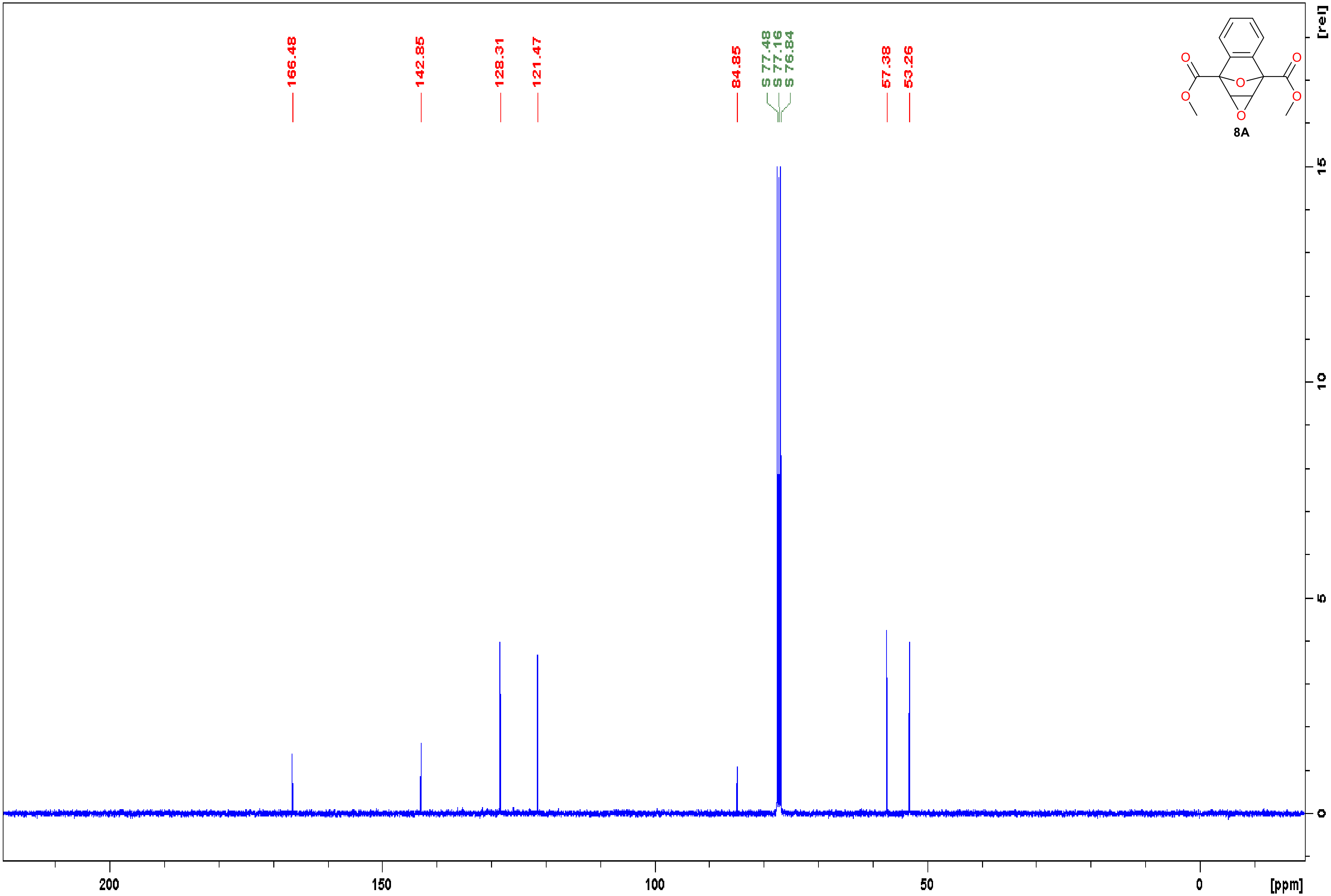


Fig. S 10 Dimethyl 3,4-epoxy-7-oxabenzynorbornadiene-1,4-dicarboxylate (^{13}C NMR, CDCl$_3$)

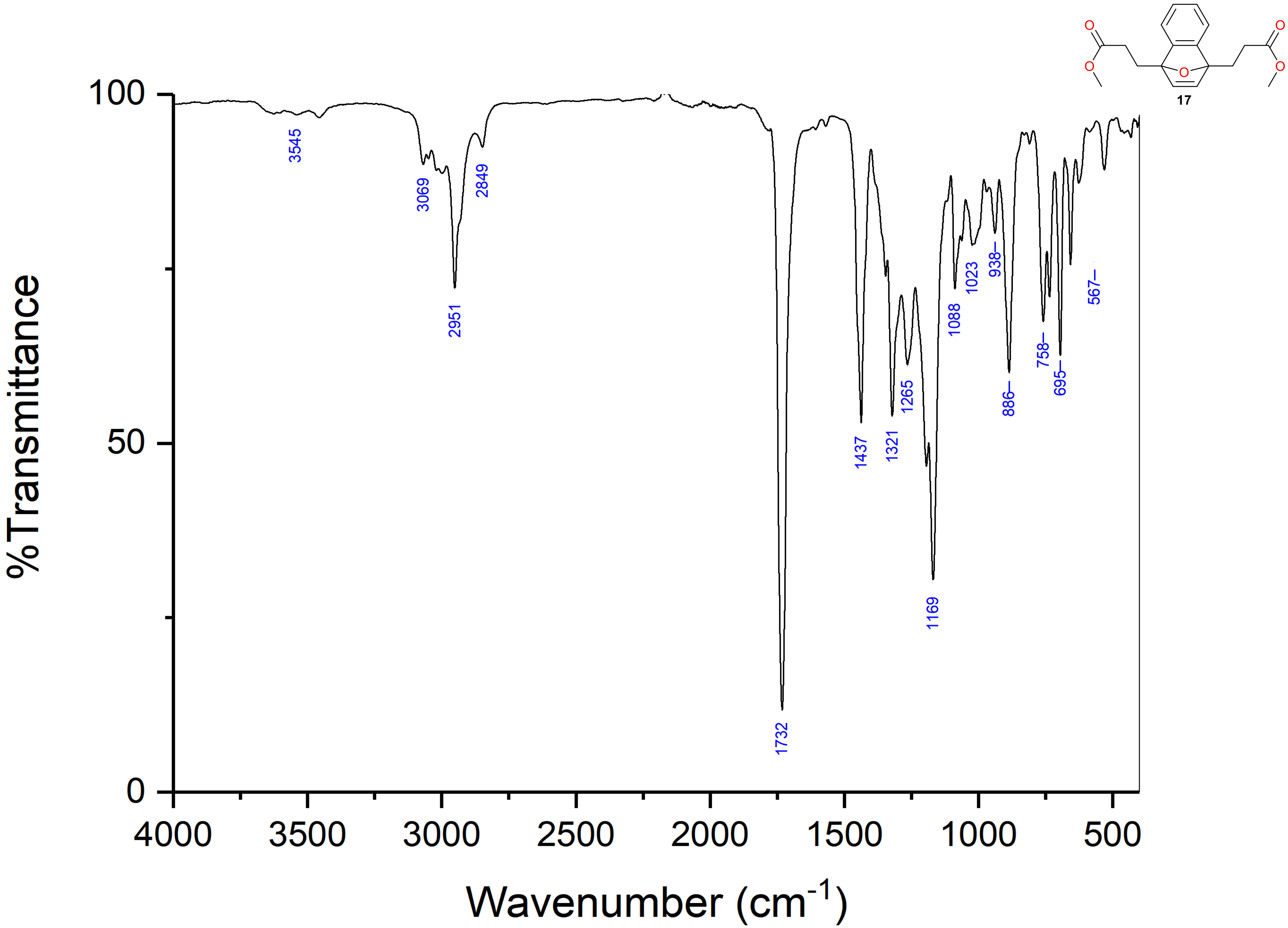


Fig. S 11 Dimethyl 3,3’(7-Oxabenzonorbornadienyl-1,4-dipropanoate) **17** (FTIR, Neat)

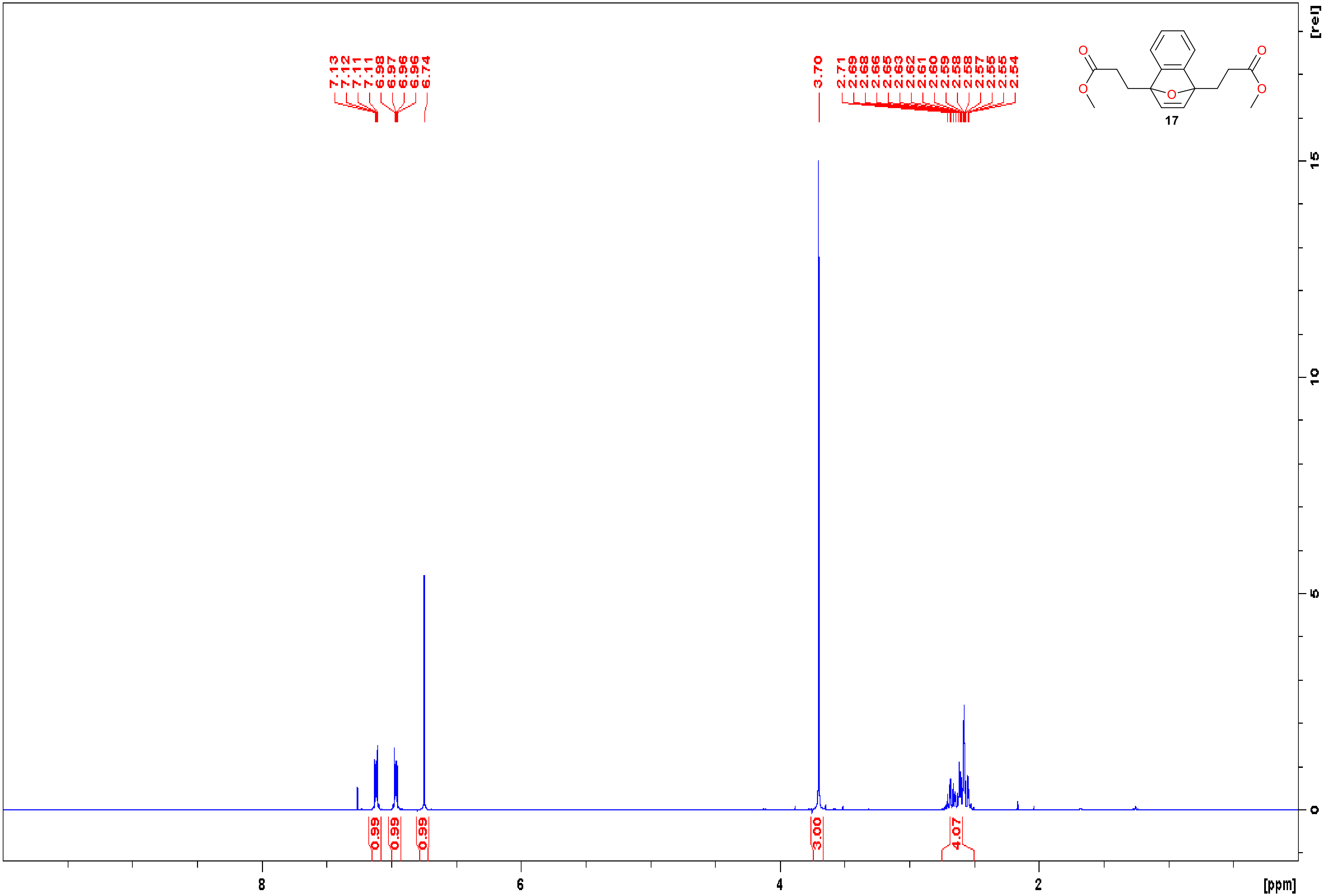


Fig. S 12 Dimethyl 3,3’(7-Oxabenzonorbornadienyl-1,4-dipropanoate) **17** (^{1}H NMR, $CDCl_3$)

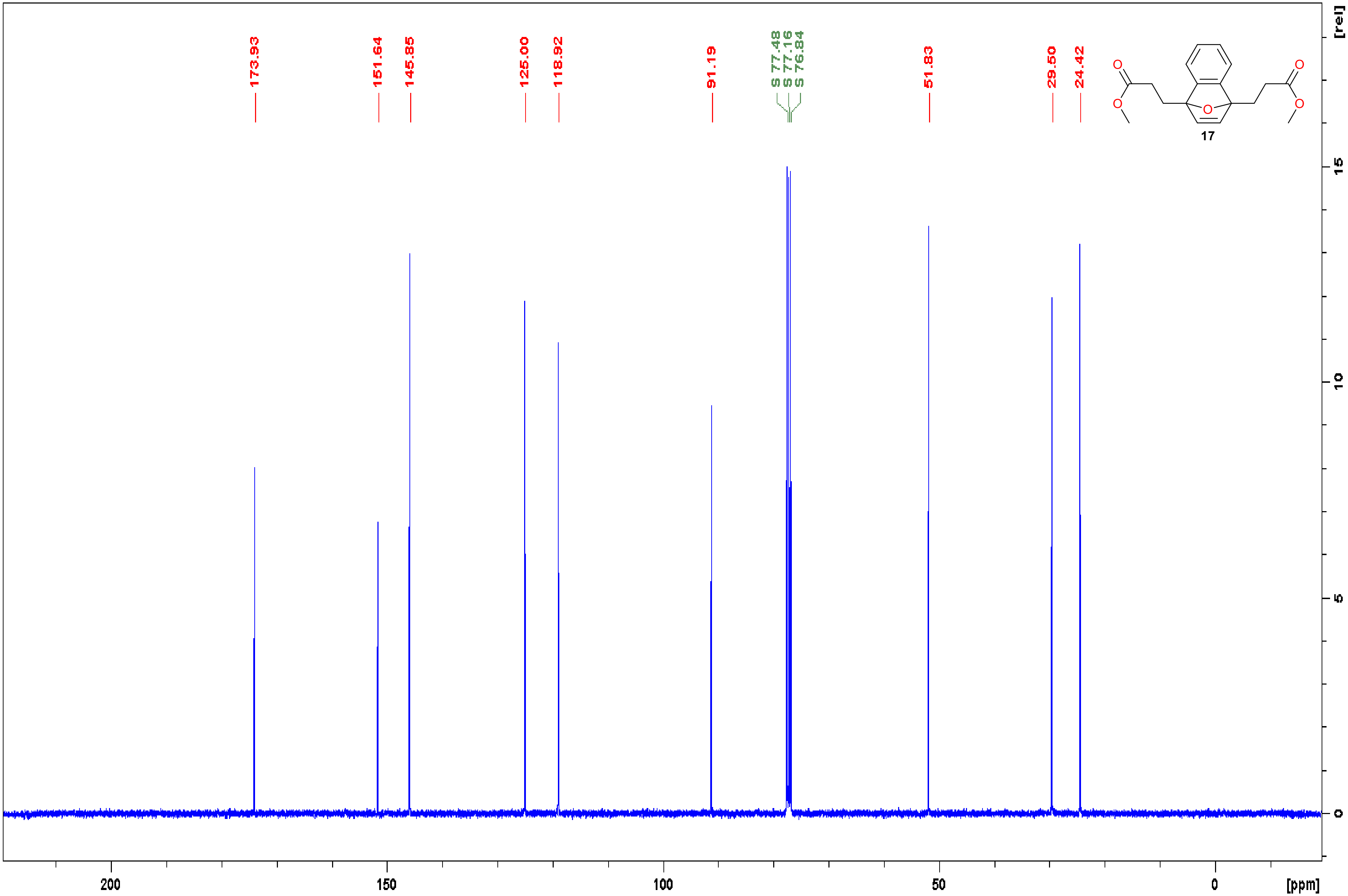


Figure S 13 Dimethyl 7-Oxabenzonorbornadien-1,4-diylbispropanoate **17** (^{13}C NMR, $CDCl_3$)

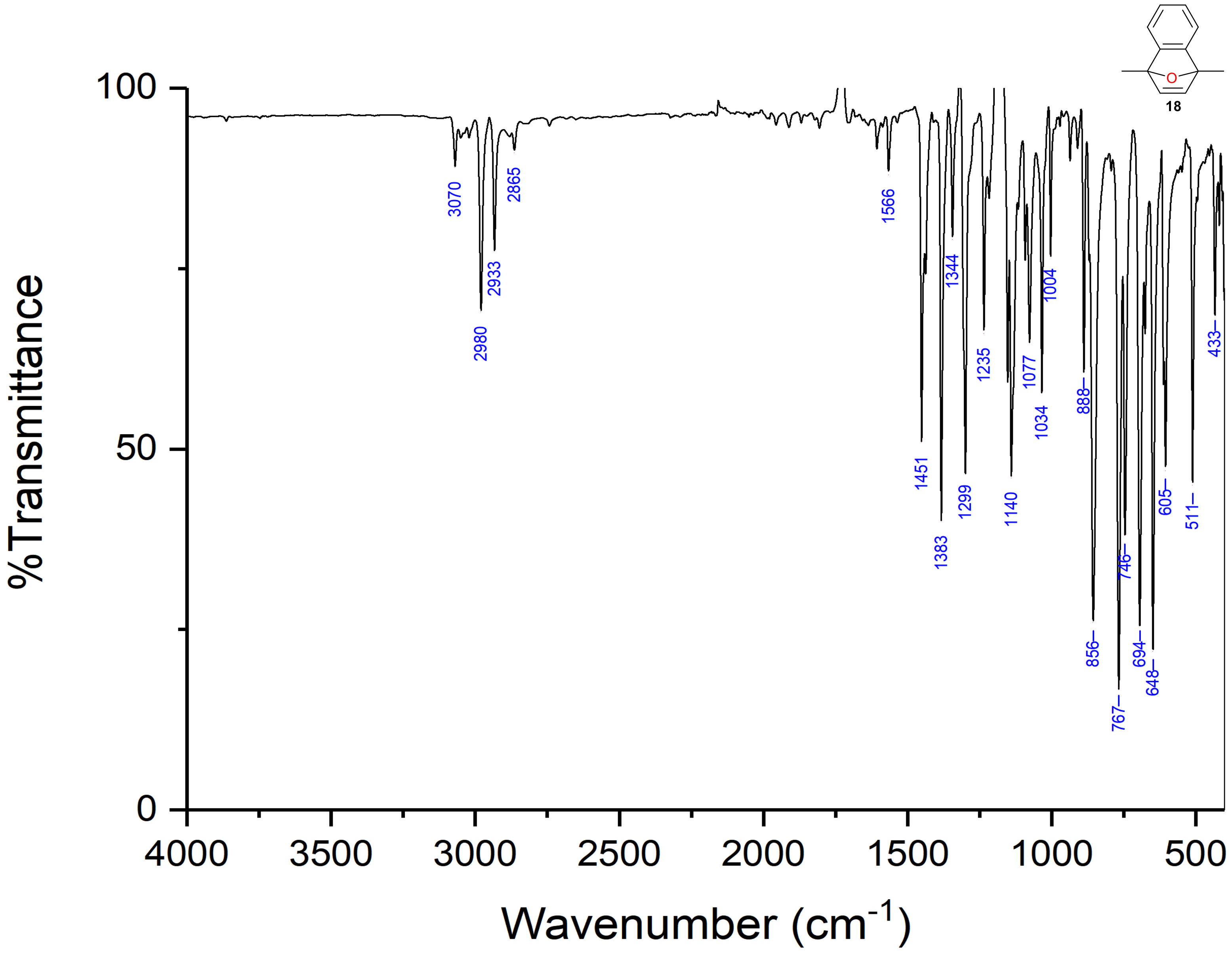


Fig. S 14 1,4-Dimethyl-7-oxabenzonorbornadiene **18** (FTIR, Neat)

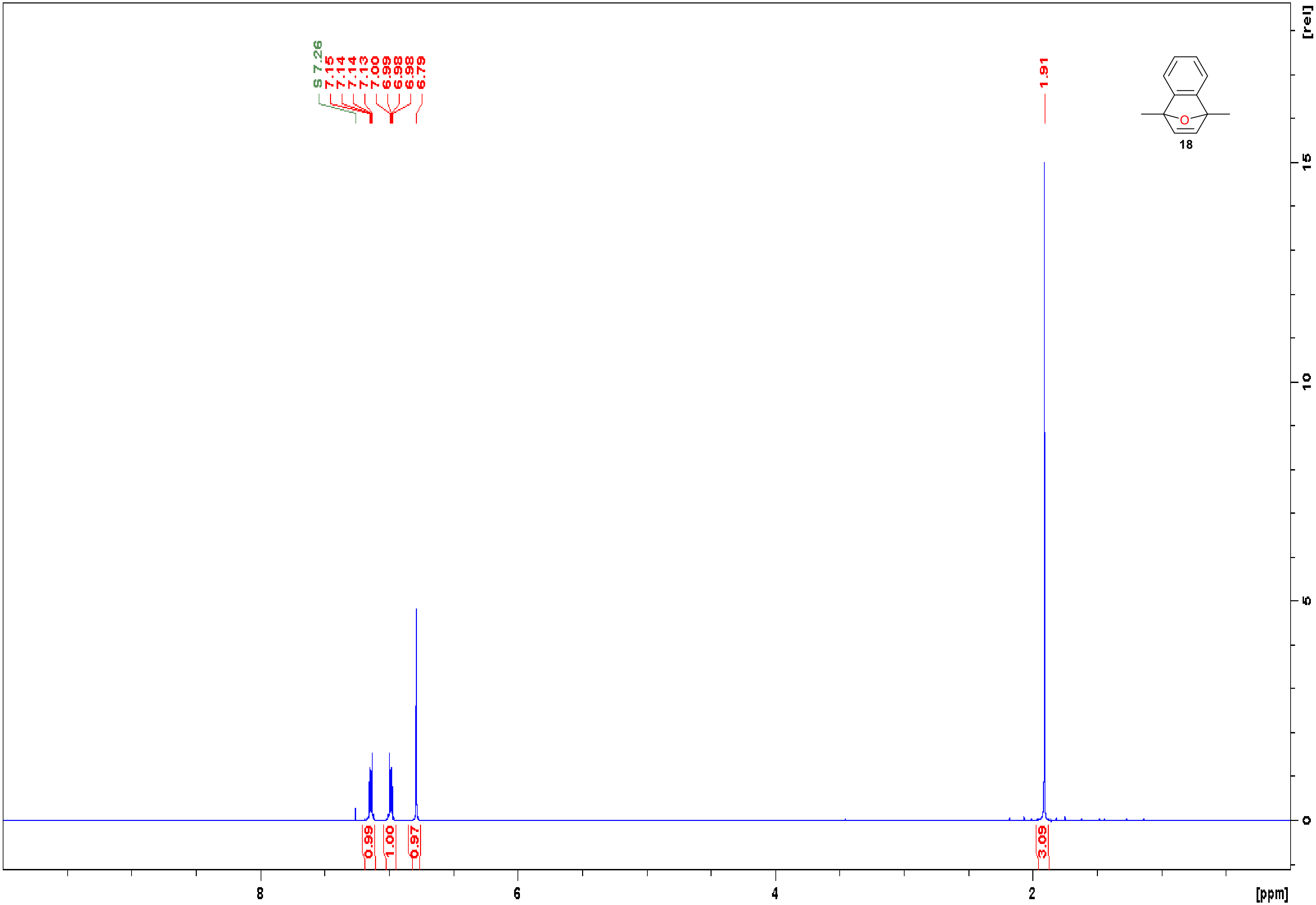


Fig. S 15 1,4-Dimethyl-7-Oxabenzonorbornadiene **18** (^{1}H NMR, (CDCl$_3$)

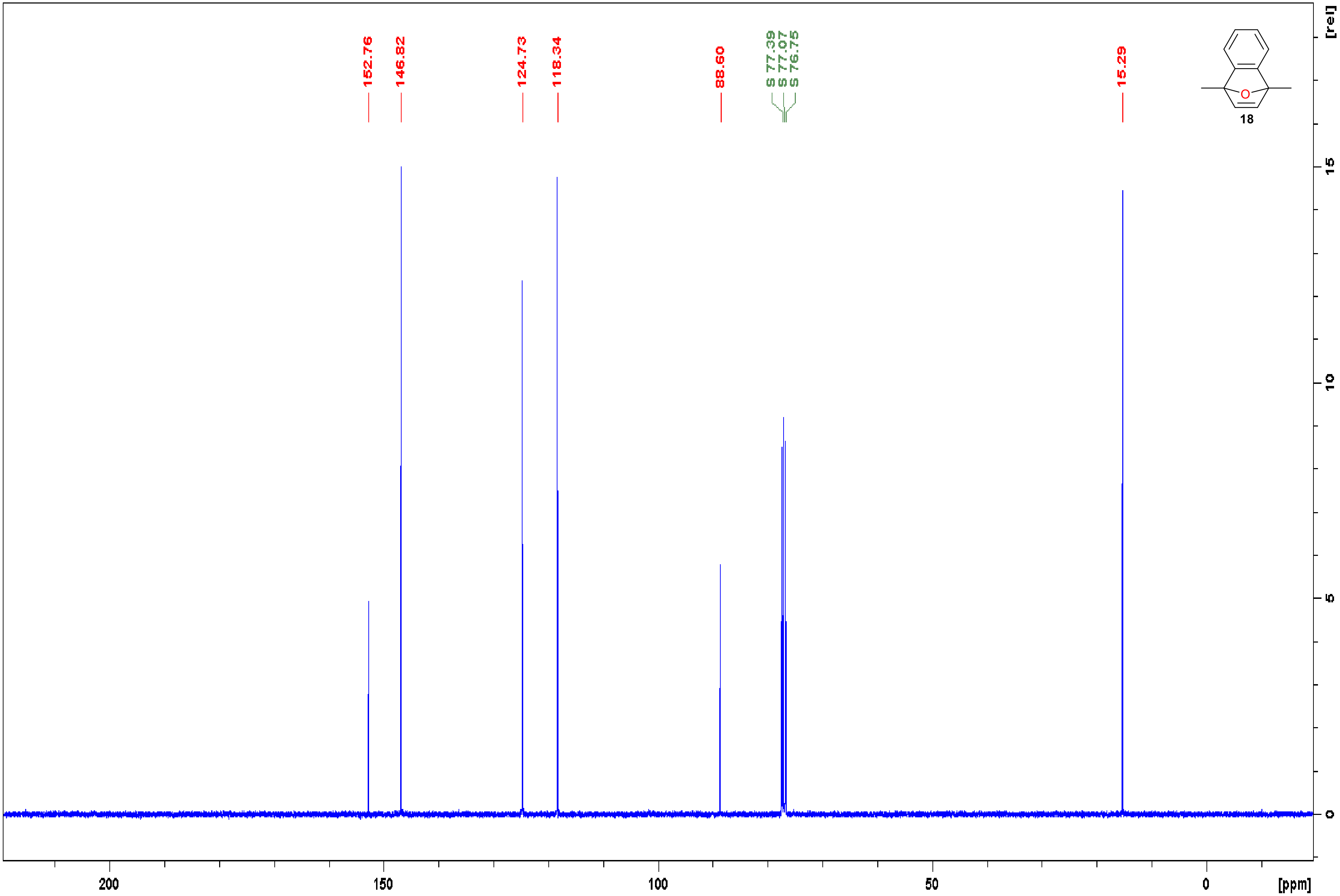


Fig. S 16 1,4-Dimethyl-7-Oxabenzonorbornadiene **18** (^{13}CNMR, $CDCl_3$)

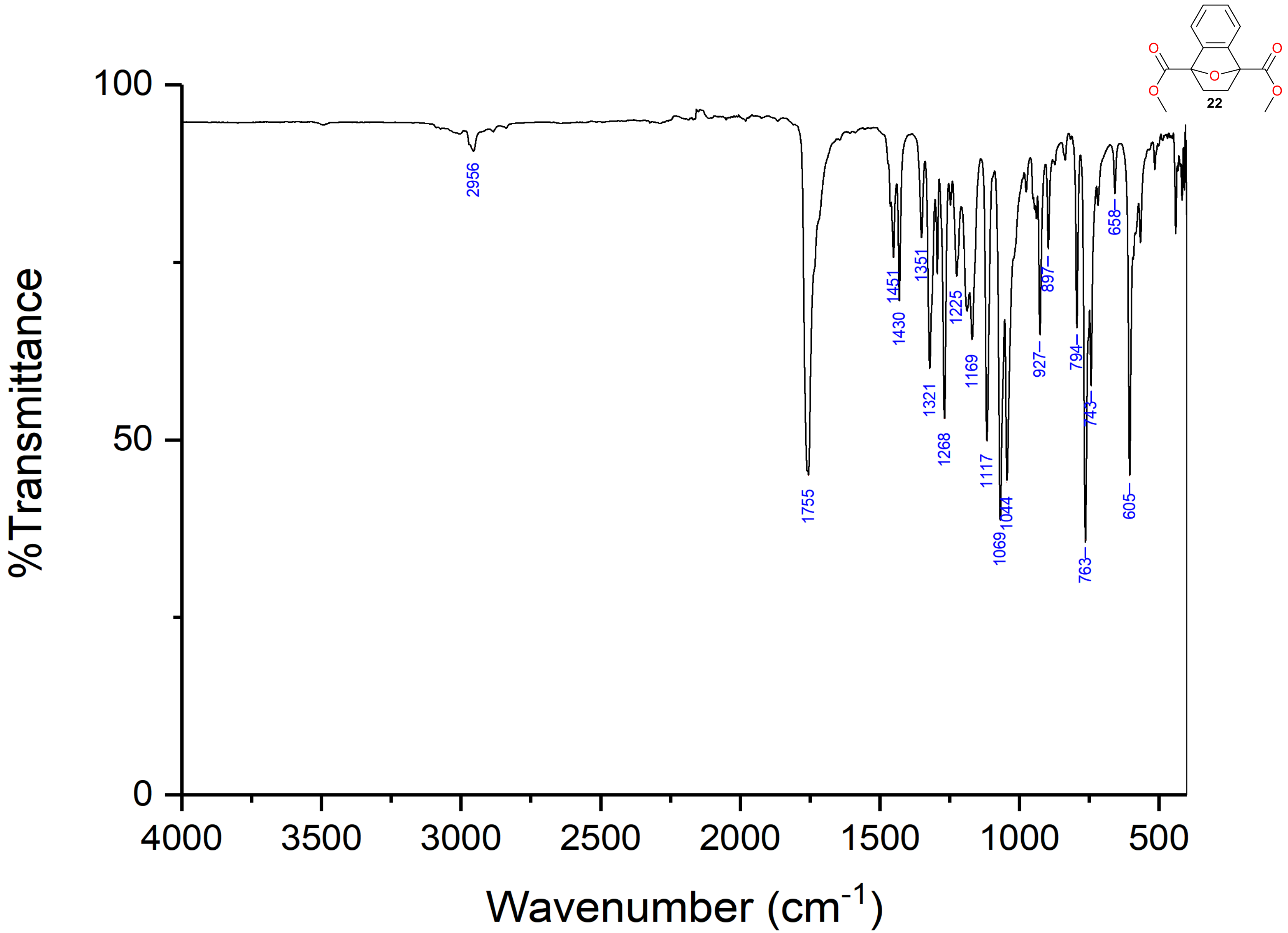


Fig. S 17 Dimethyl 7-Oxabenzonorbornyl-1,4-dicarboxylate **22** (FTIR, Neat)

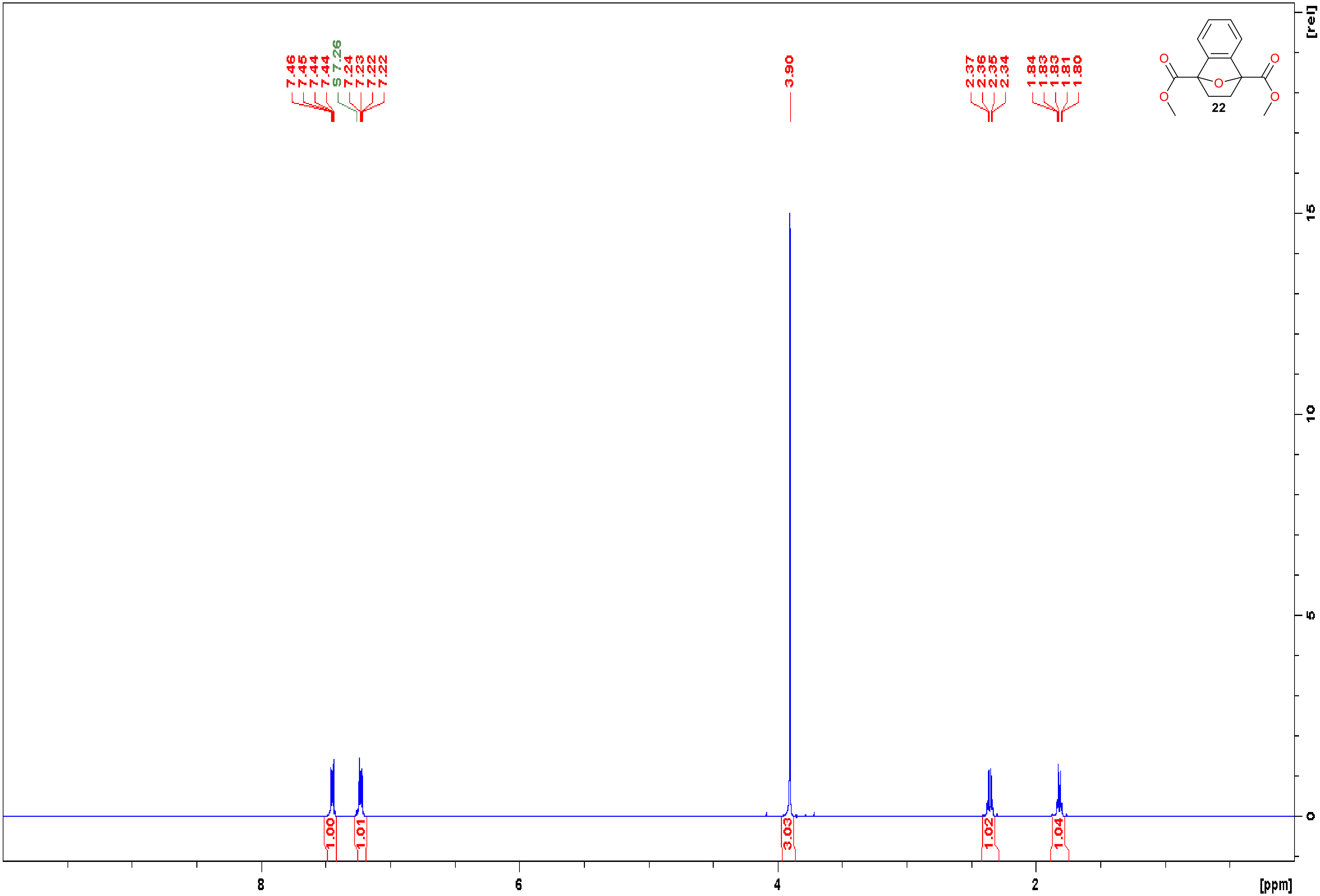


Fig. S 18 Dimethyl 7-Oxabenzonorbornyl-1,4-dicarboxylate **22** (^{1}H NMR, CDCl$_3$)

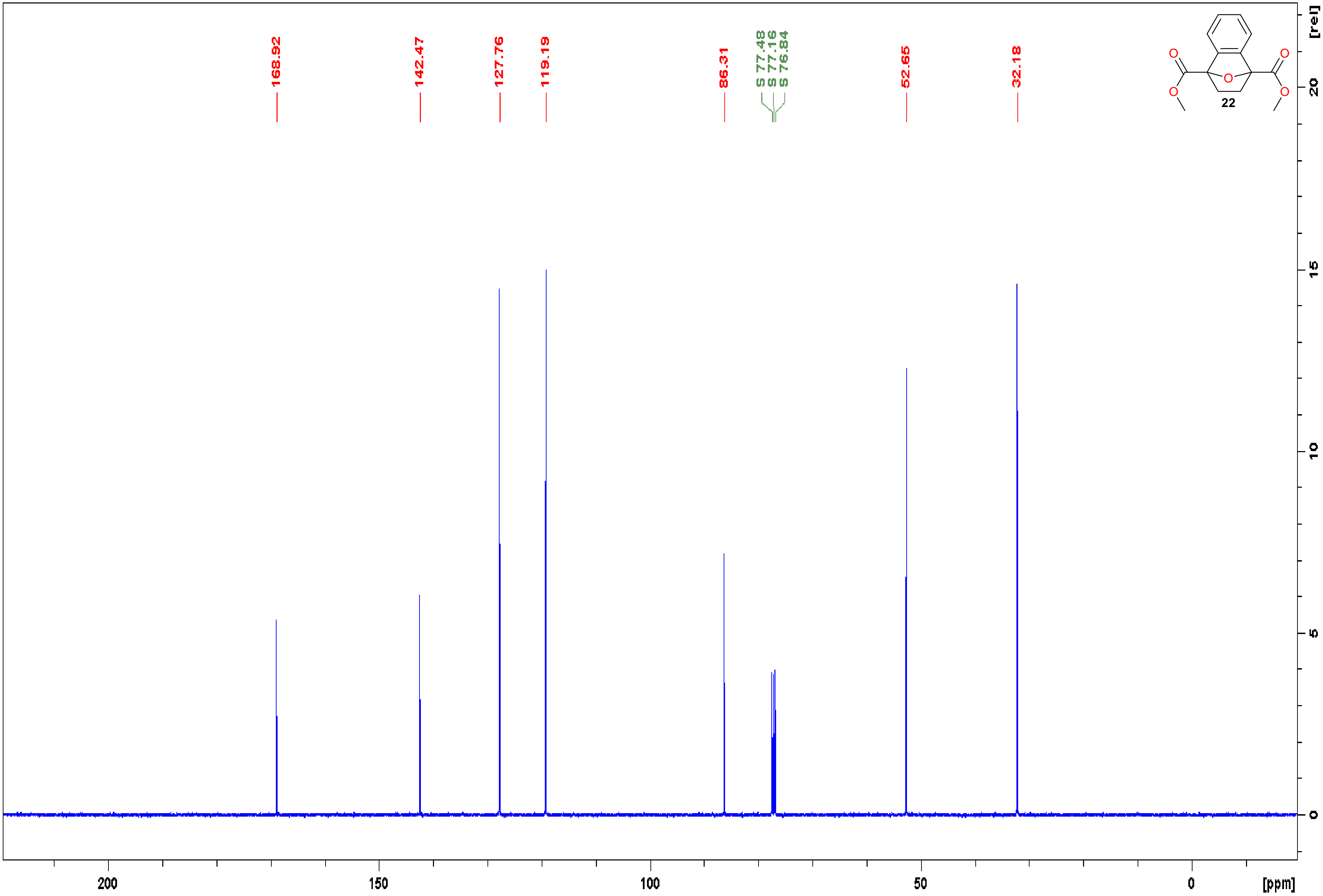
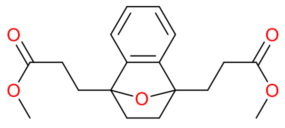


Fig. S 19 Dimethyl 7-Oxabenzonorbornyl-1,4-dicarboxylate **22** (^{13}C NMR, $CDCl_3$)



23

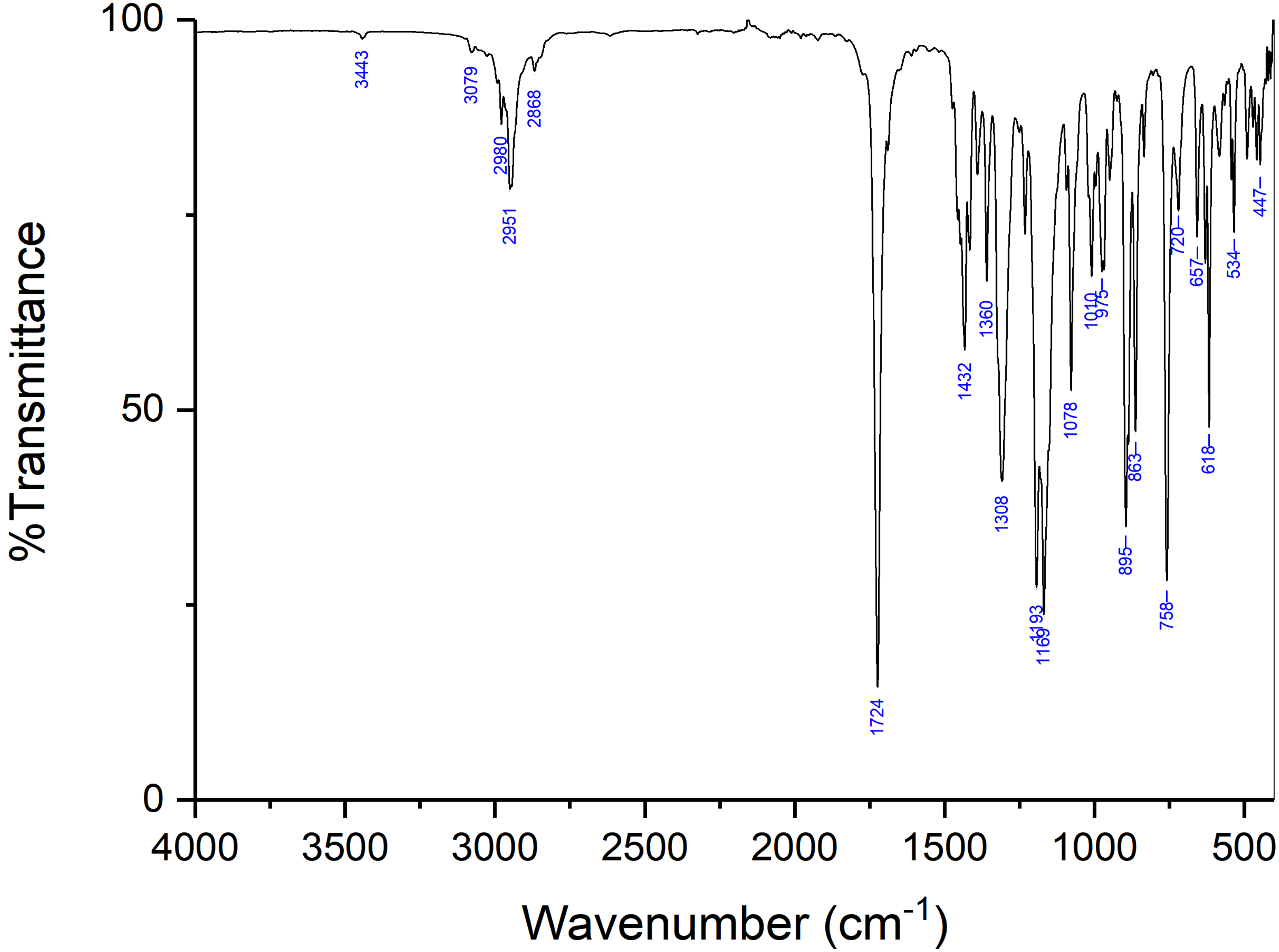


Fig. S 20 Dimethyl 3,3’(7-Oxabenzonorborn-1,4-diyl)bispropanoate **23** (FTIR, Neat)

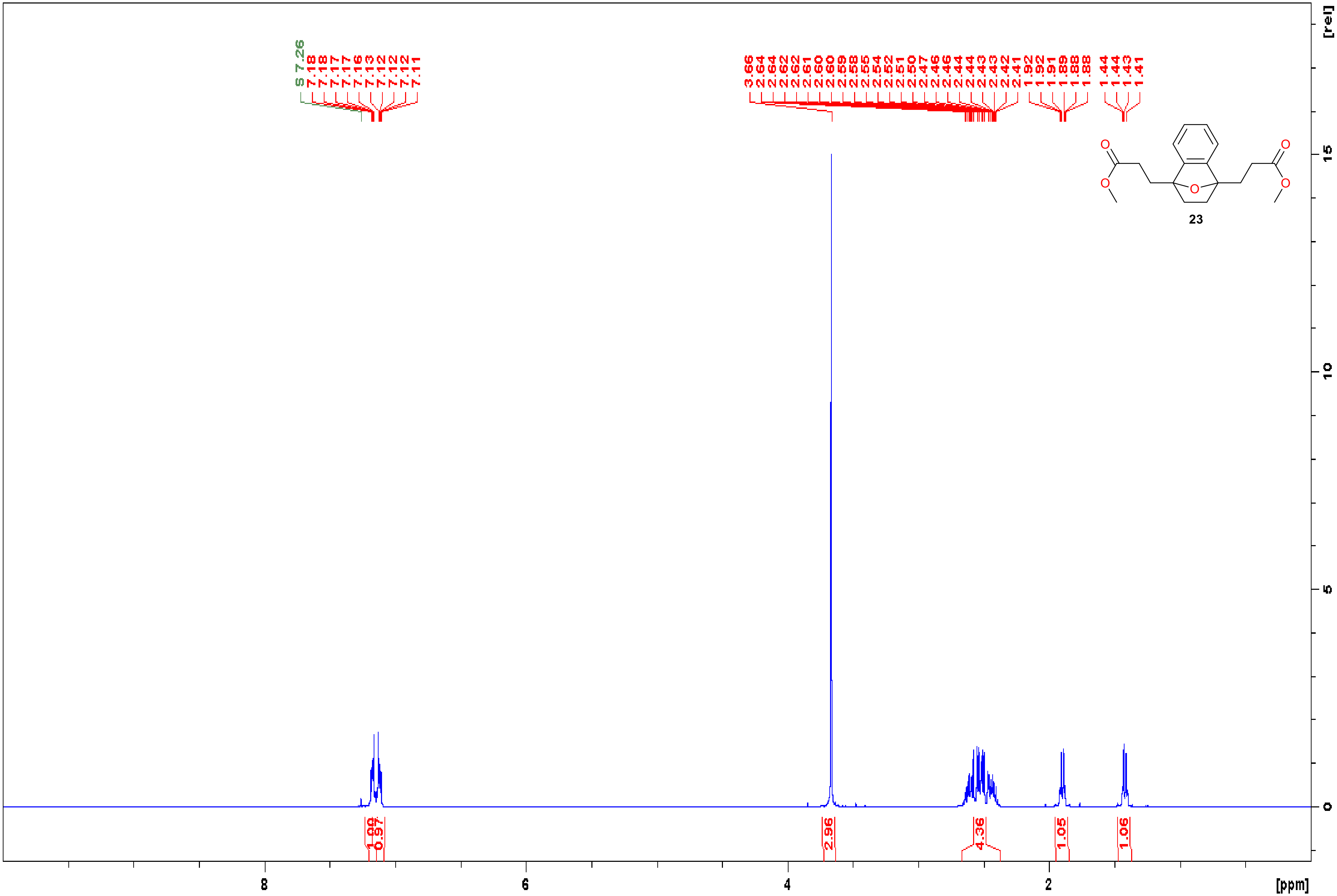


Fig. S 21 Dimethyl 3,3'(7-Oxabenzonorborn-1,4-diyl)bispropanoate (^{1}H NMR, $CDCl_3$)

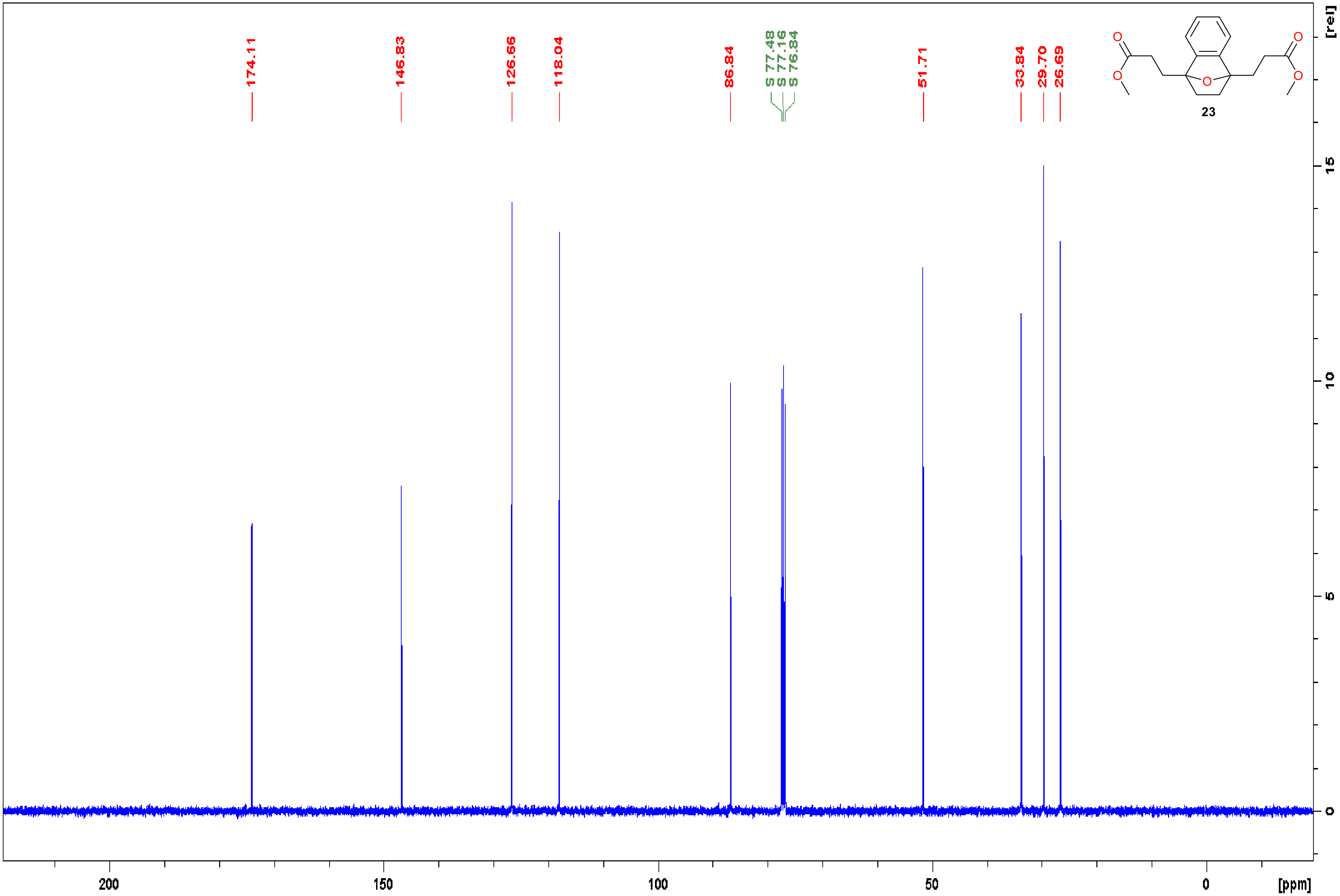


Fig. S 22 Dimethyl 3,3’(7-Oxabenzonorborn-1,4-diyl)dipropanoate **23** (^{13}C NMR, CDCl$_3$)

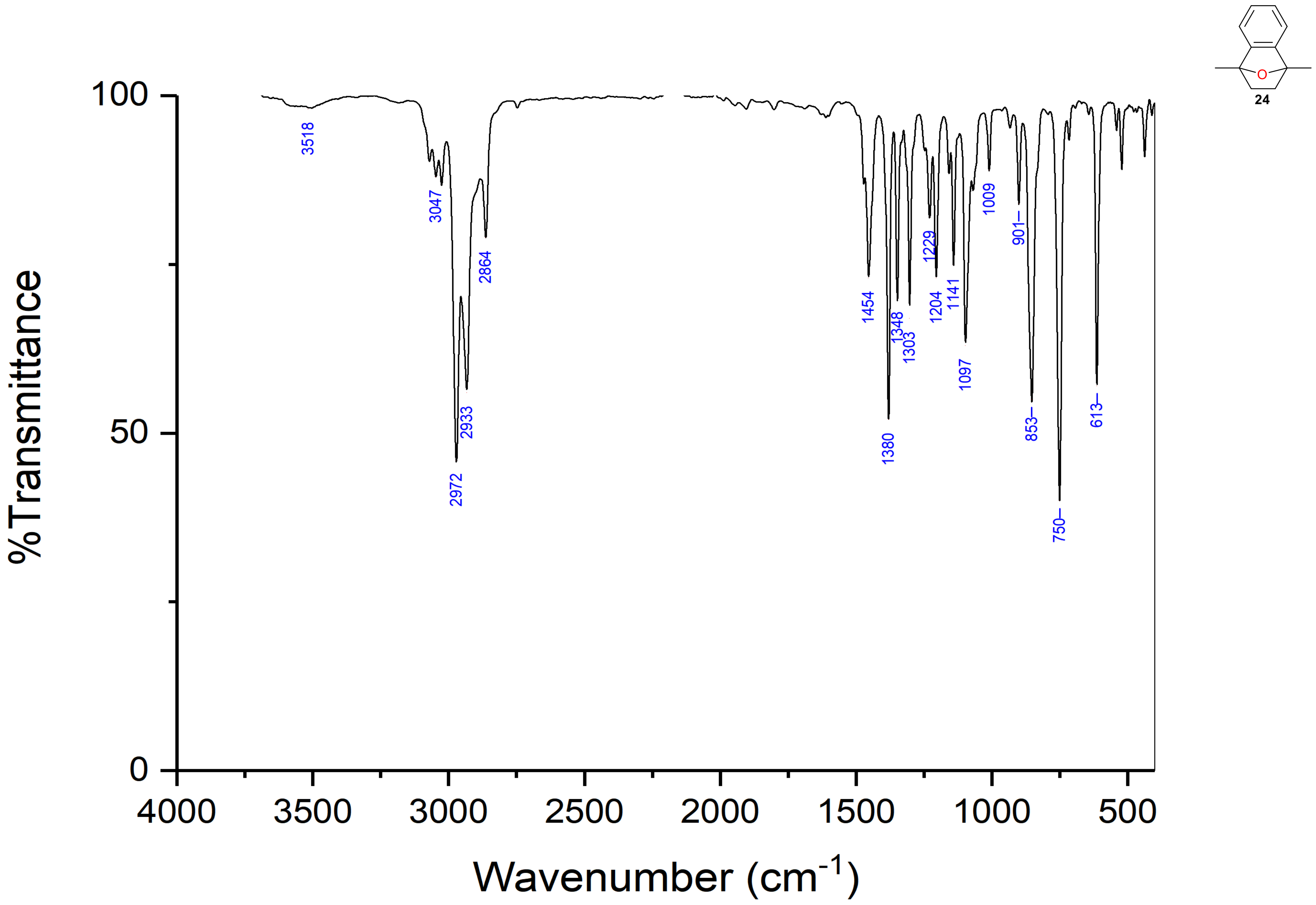


Figure S 23 1,4-Dimethyl-7-oxabenzonorbornene **24** (FTIR, Neat)

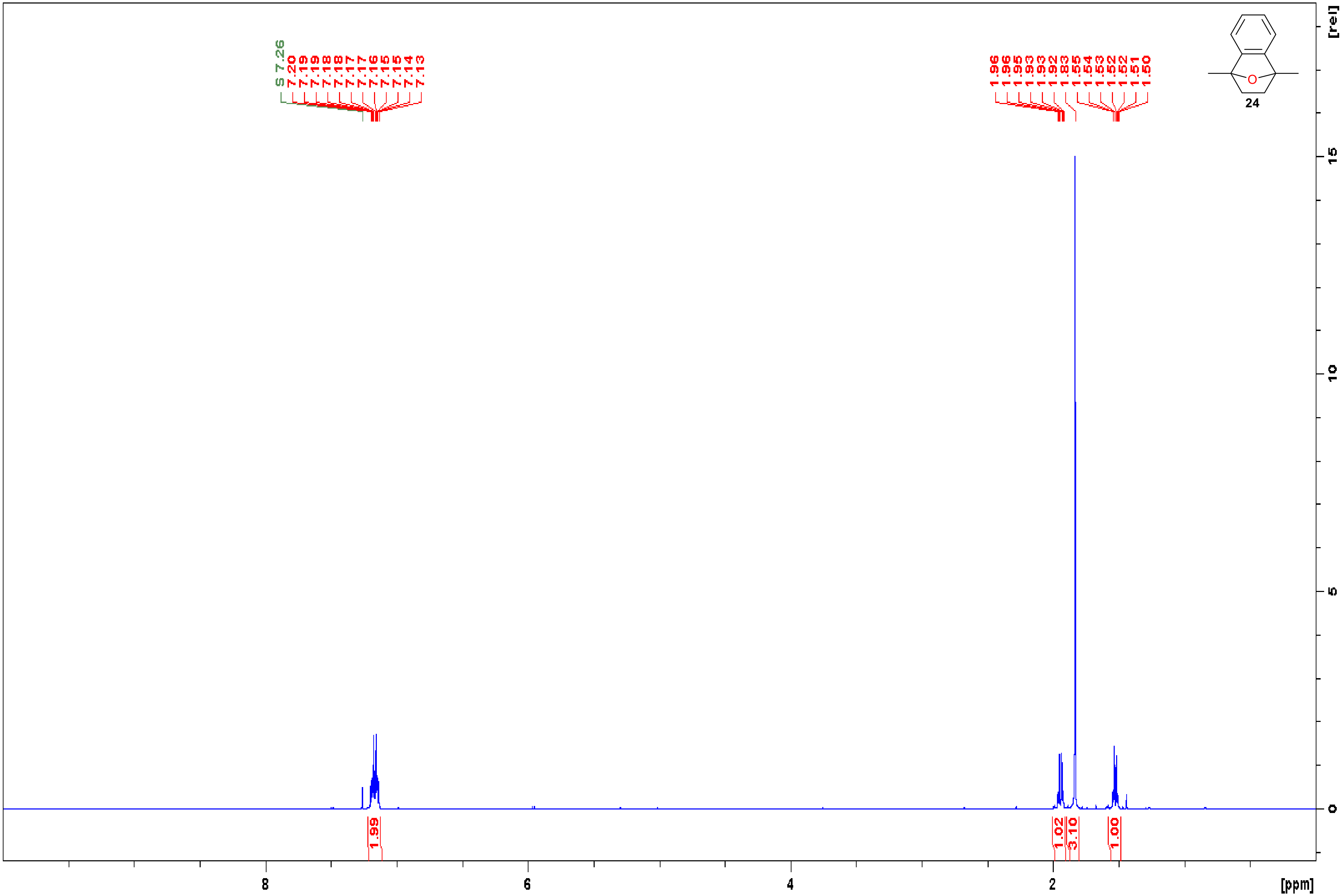


Fig. S 24 1,4-Dimethyl-7-oxabenzonorbornene **24** (^{1}H NMR, $CDCl_3$)

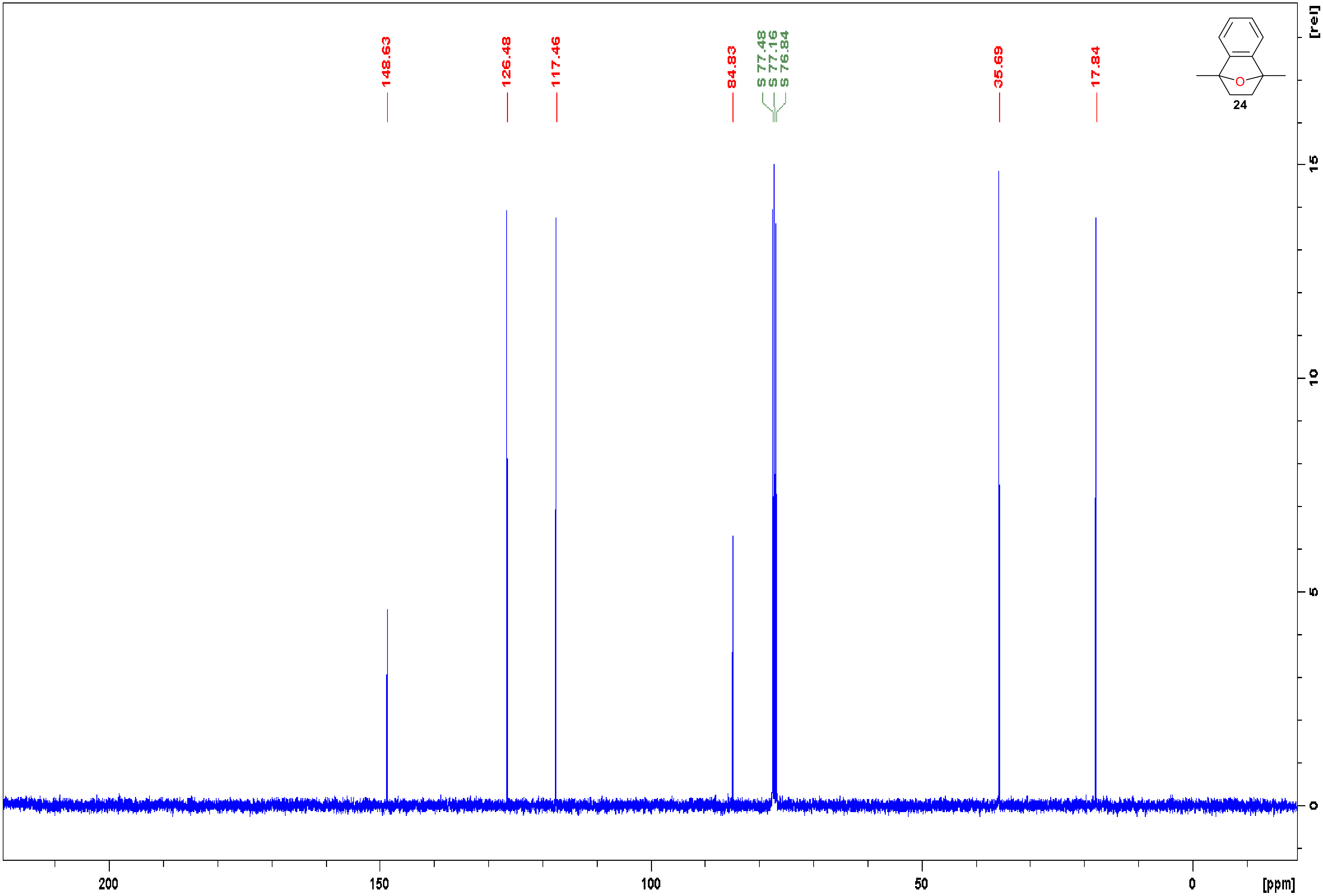


Fig.S 25 1,4-Dimethyl-7-oxabenzonorbornene **24** (^{13}C NMR, $CDCl_3$)

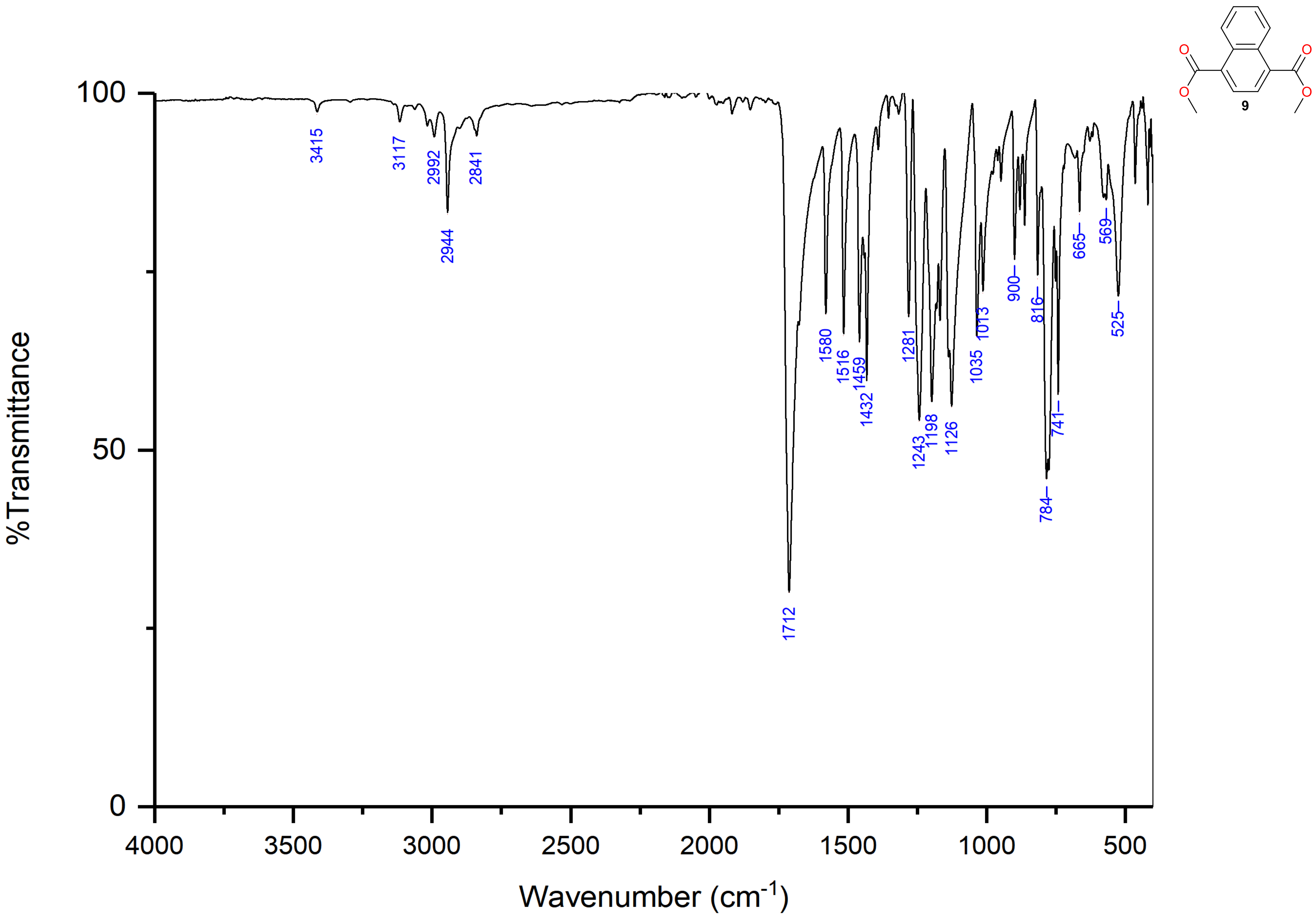


Fig. S 26 Dimethyl 1,4-Naphthalenedicarboxylate **9** (FTIR, Neat)

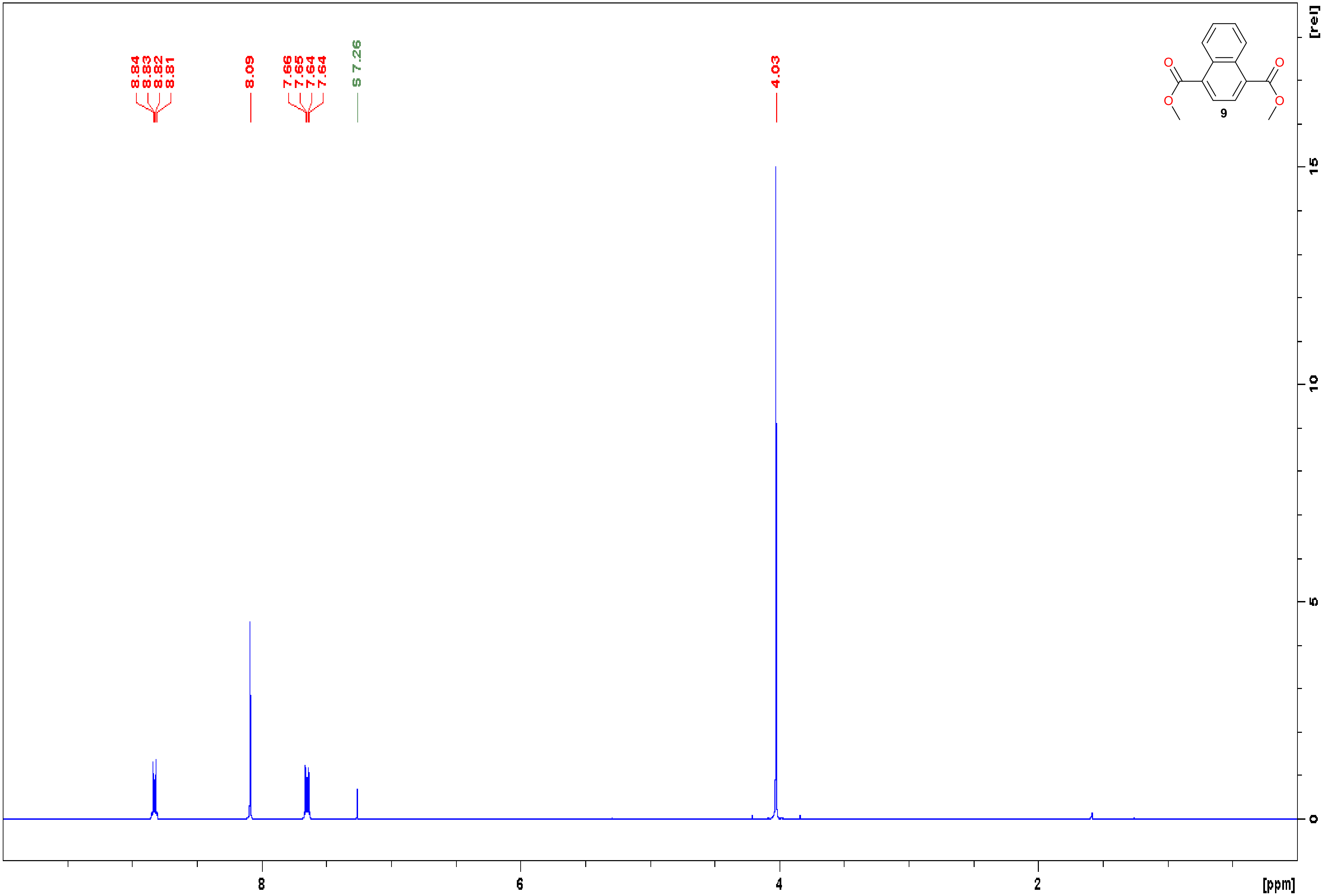


Fig. S 27 Dimethyl Naphthalene-1,4-dicarboxylate **9** (^{1}H NMR, $CDCl_3$)

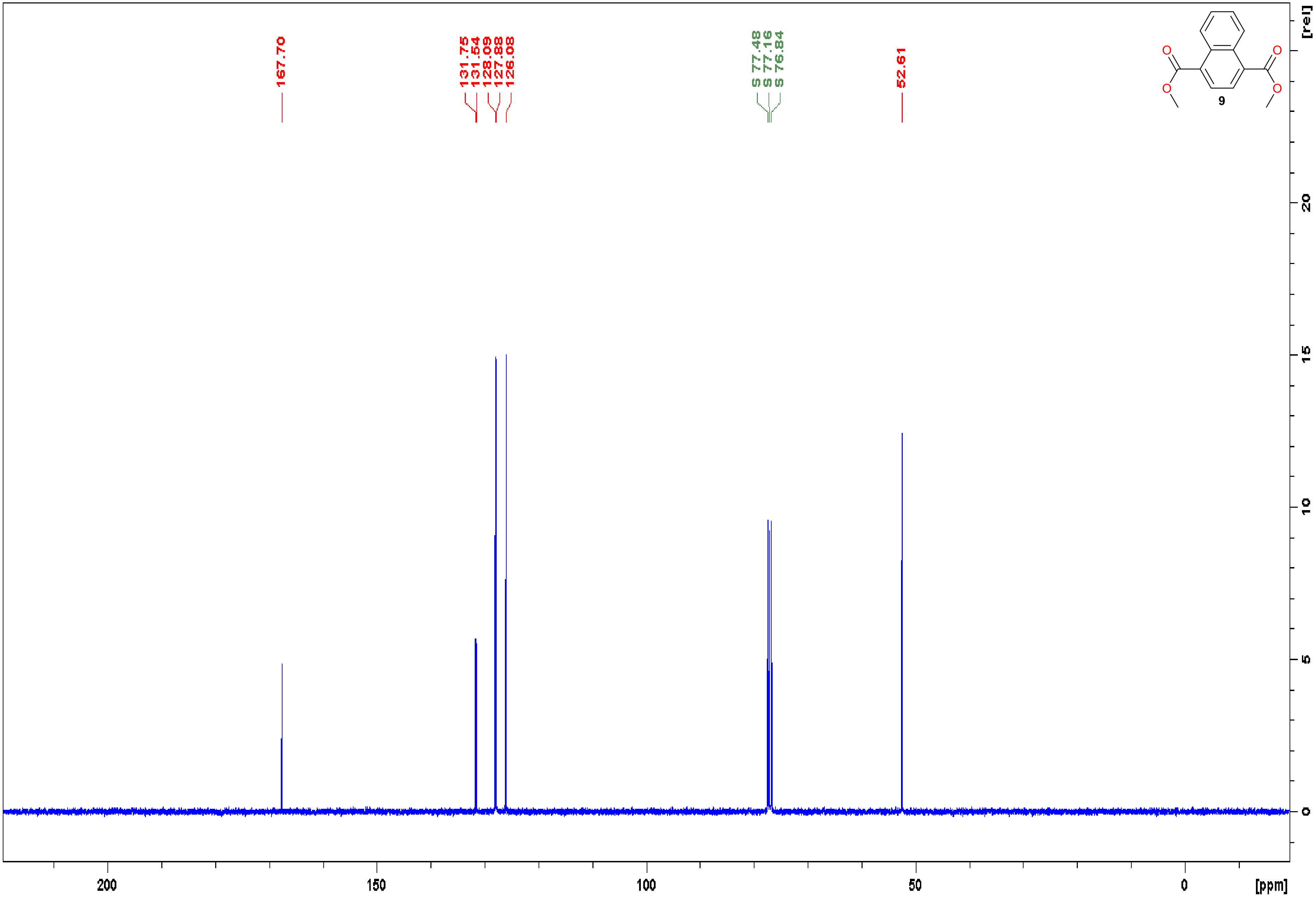


Fig. S 28 Dimethyl Naphthalene-1,4-dicarboxylate **9** (^{13}C NMR, $CDCl_3$)

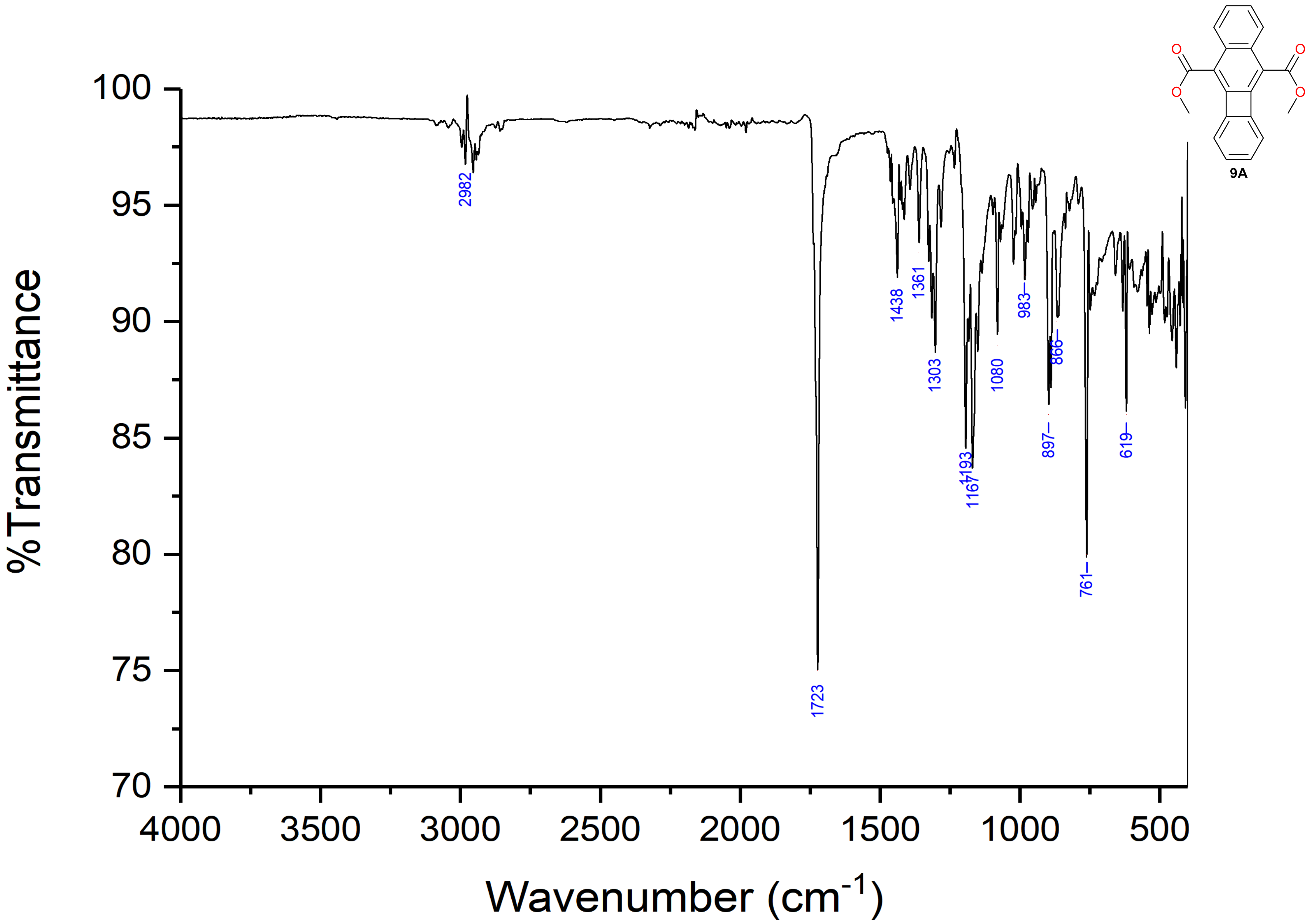


Figure S 29 Dimethyl Benzo[b]biphenylene-1,4-dicarboxylate (FTIR, Neat)

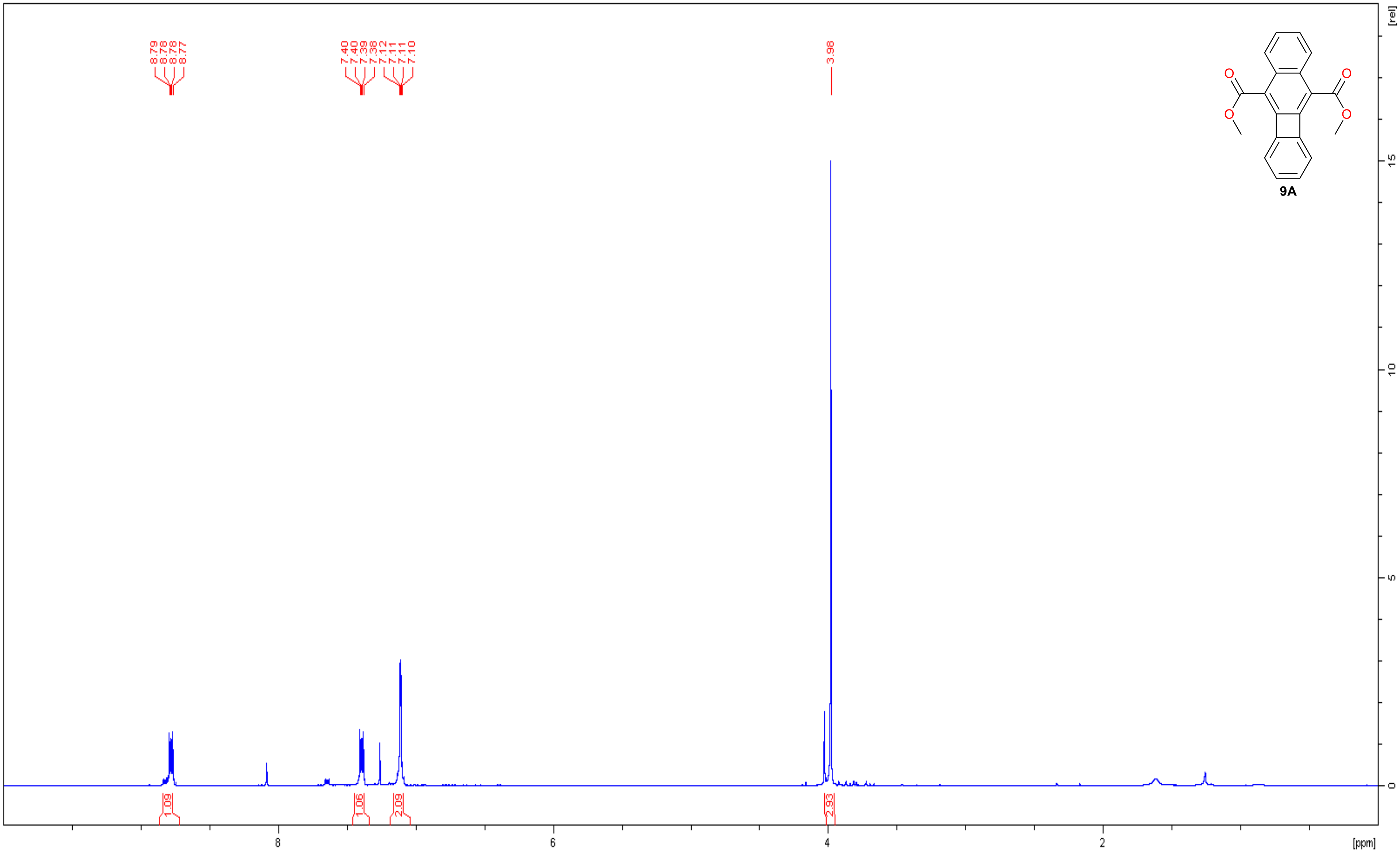


Fig.S 30 Dimethyl benzo[b]biphenylene-1,4-dicarboxylate (^{1}H NMR, CDCl$_3$)

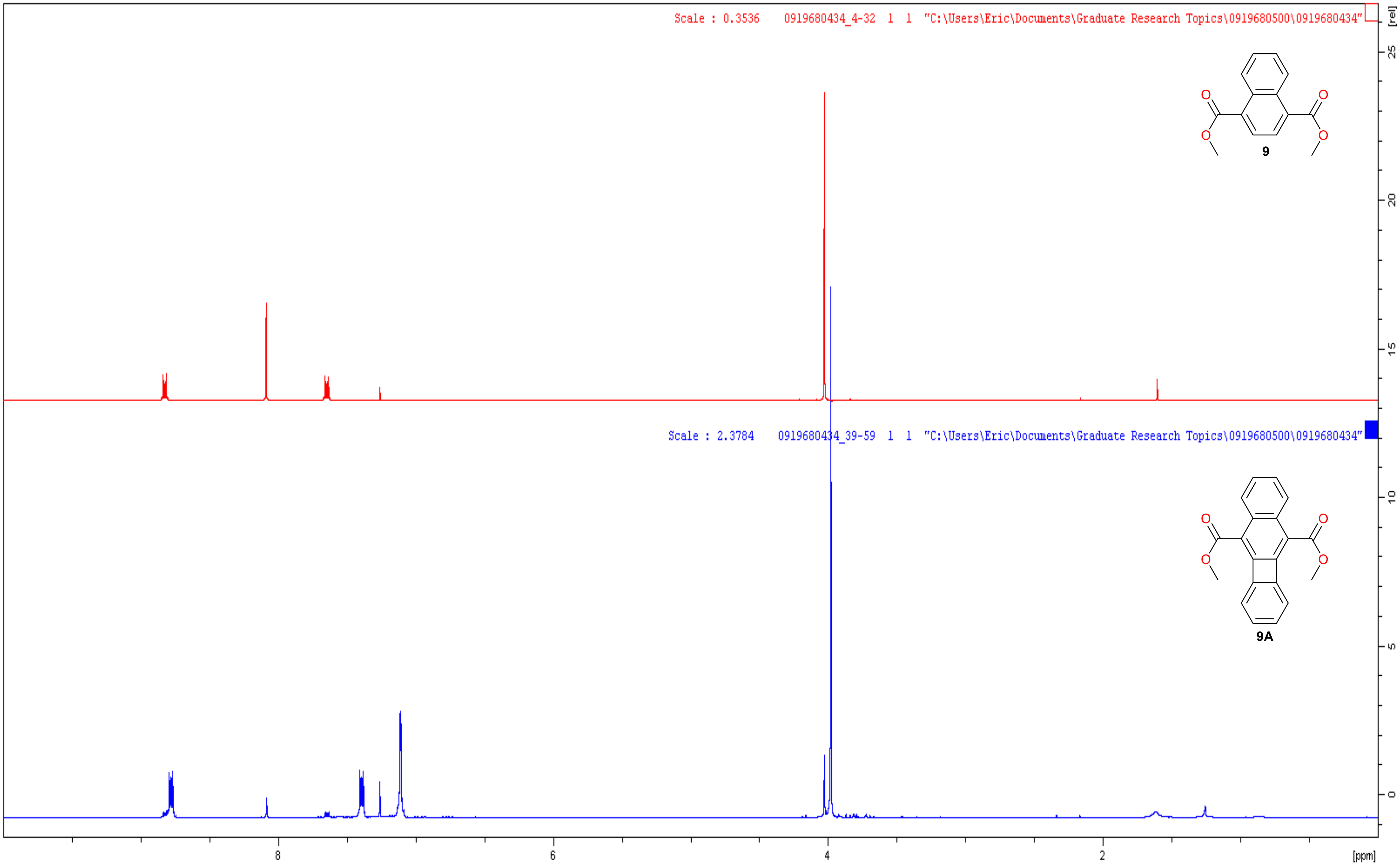


Fig.S 31 Dimethyl benzo[b]biphenylene-1,4-dicarboxylate Stacked with Dimethyl naphthalene-1,4-dicarboxylate (^{1}H NMR, $CDCl_3$)

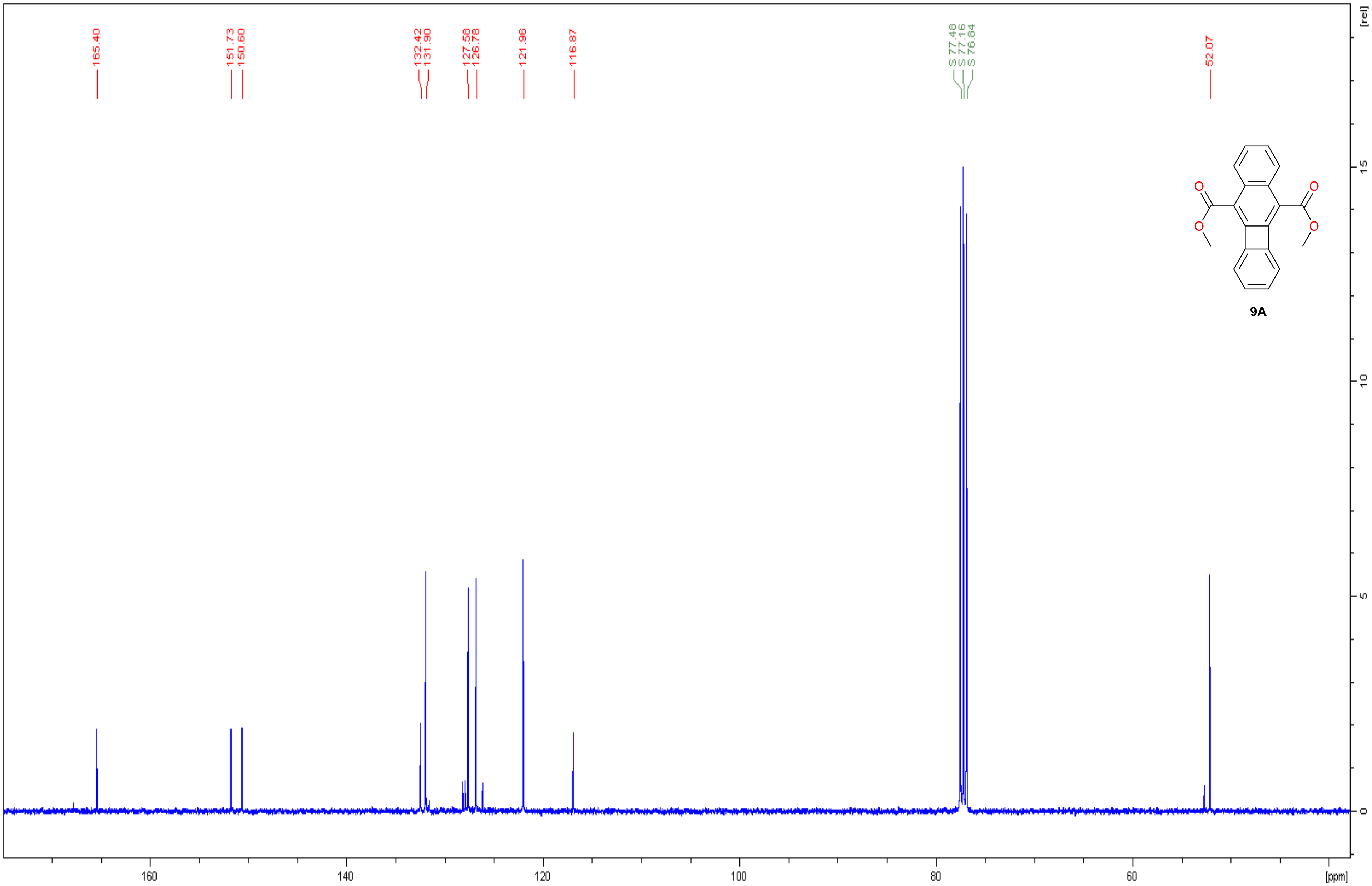


Fig. S 32 Dimethyl benzo[b]biphenylene-1,4-dicarboxylate (^{13}C NMR, $CDCl_3$)

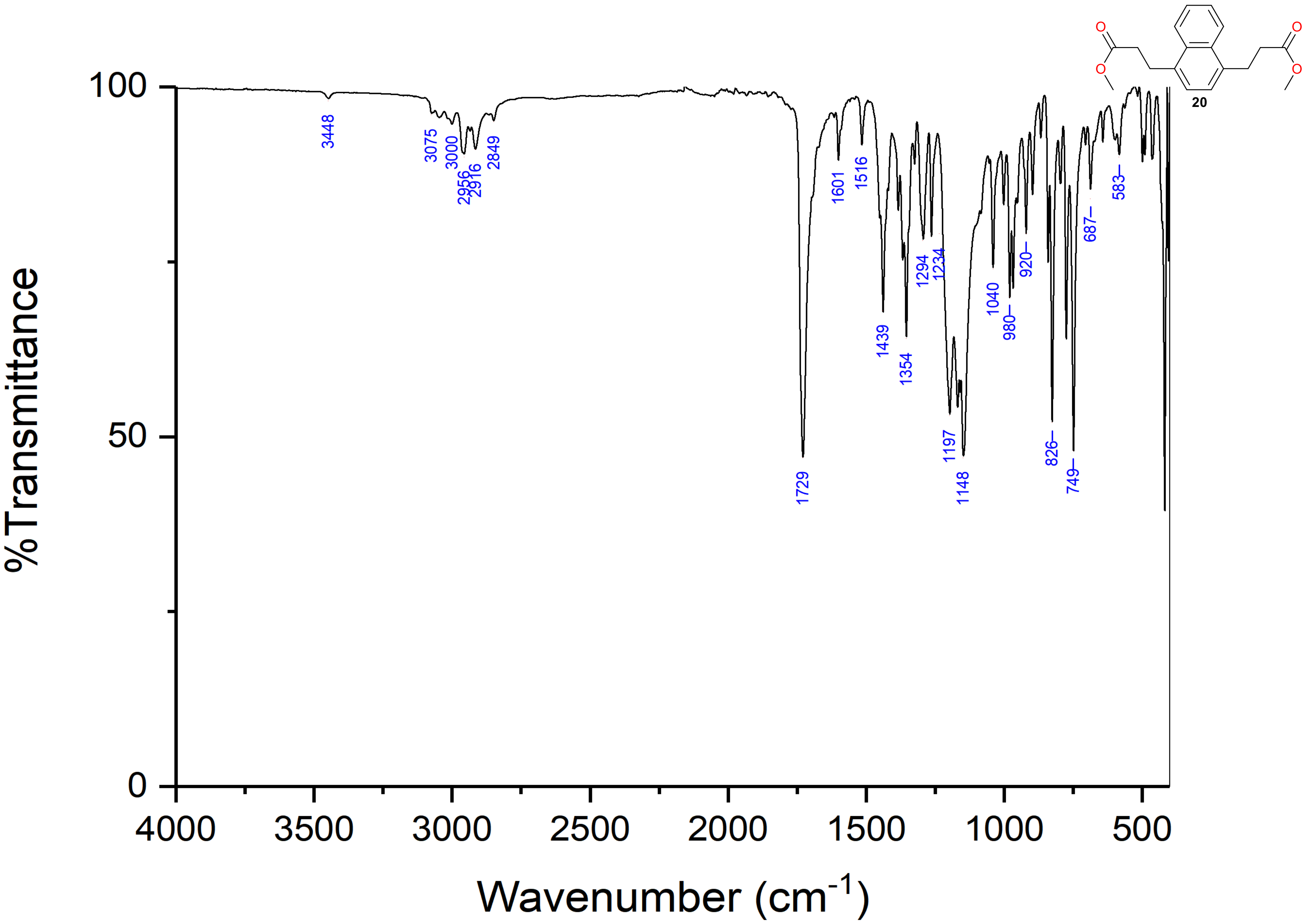


Fig. S 33 Dimethyl 3,3'-Naphthalene-1,4-diylbispropanoate **20** (FTIR, Neat)

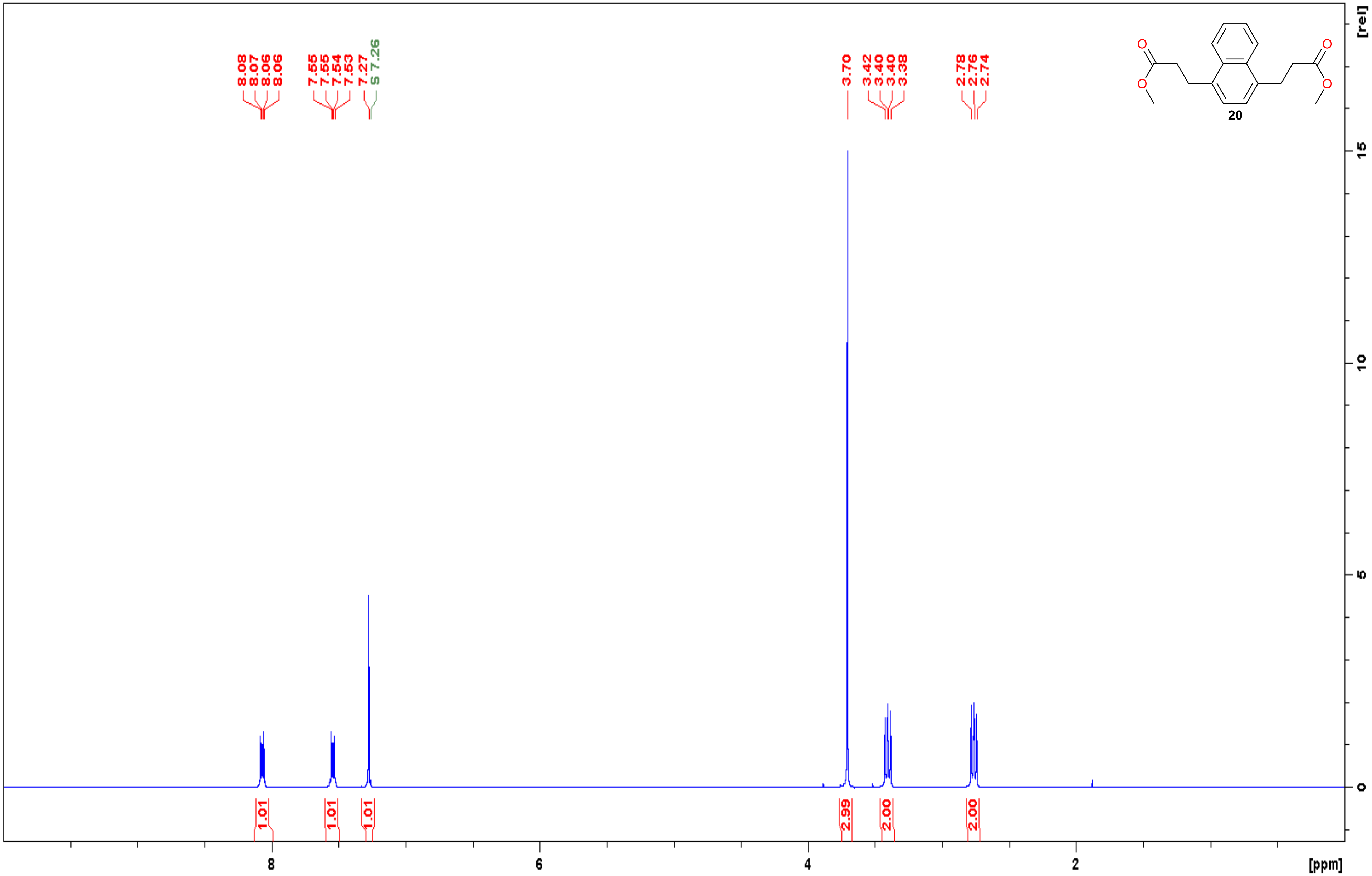


Fig. S 34 Dimethyl 3,3'-Naphthalene-1,4-diylbispropanoate **20** (^{1}H NMR, $CDCl_3$)

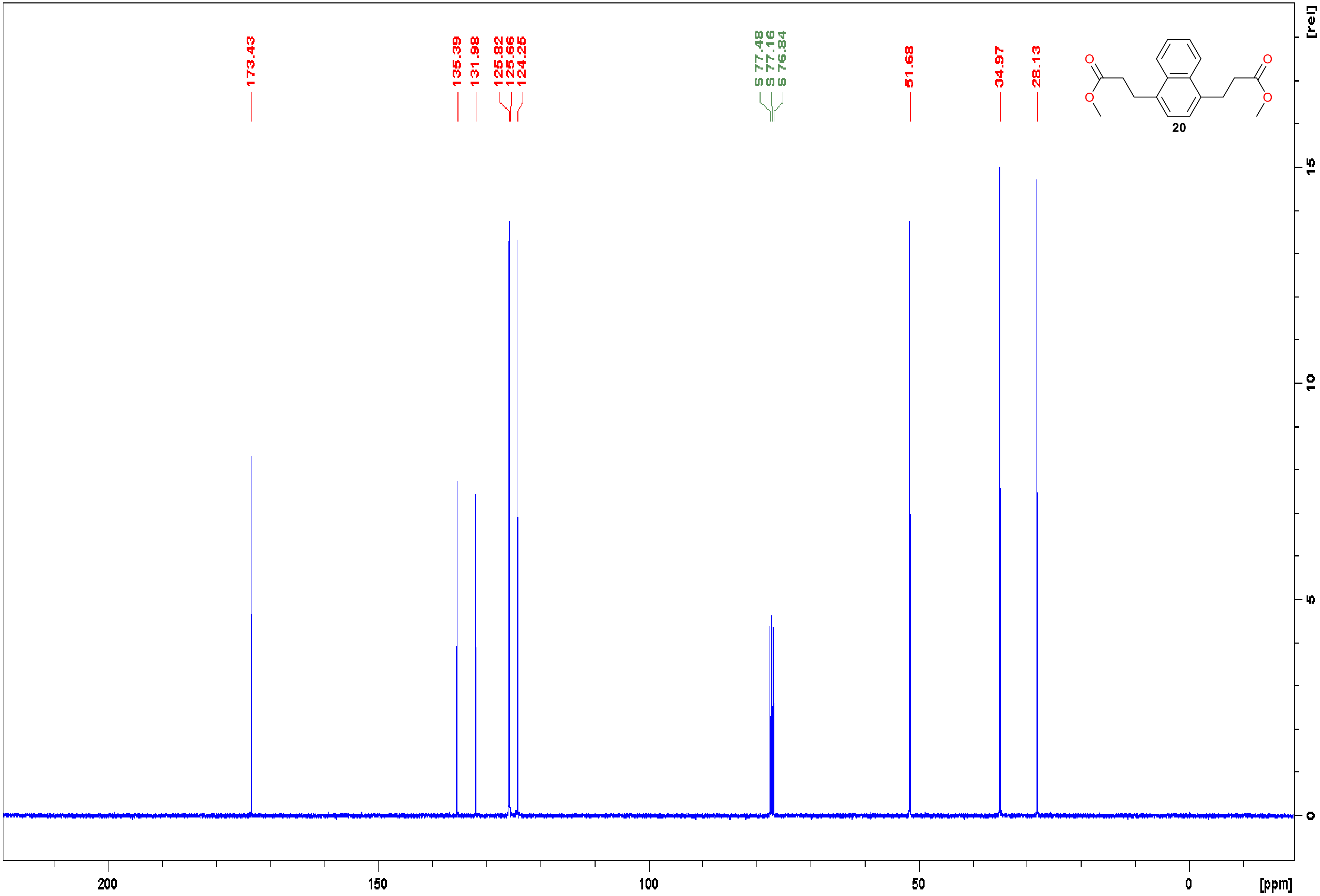


Fig. S 35 Dimethyl 3,3’-Naphthalene-1,4-diylbispropanoate **20** (^{13}C NMR, $CDCl_3$)

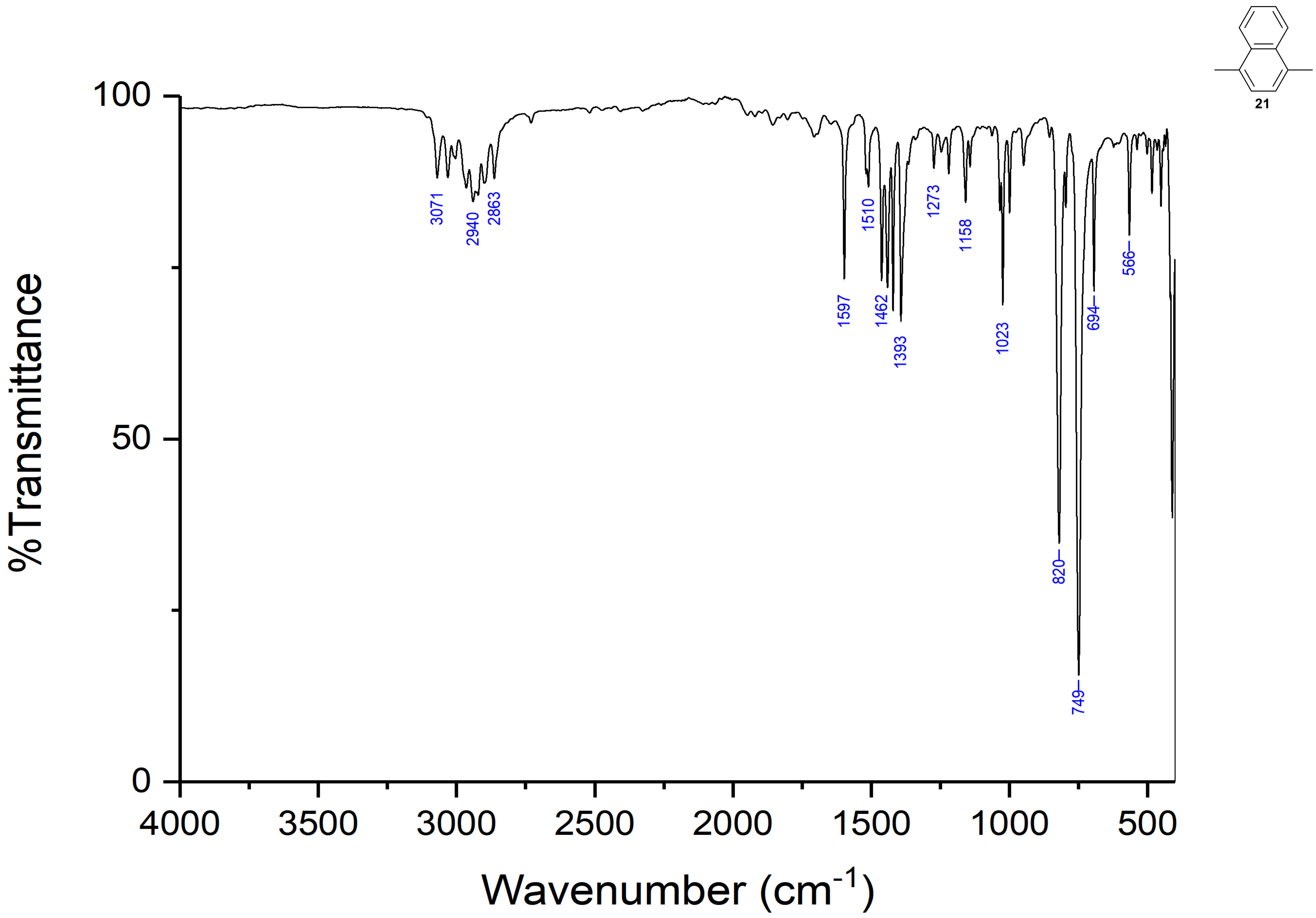


Fig.S 36 1,4-Dimethylnaphthalene **21** (FTIR, Neat)

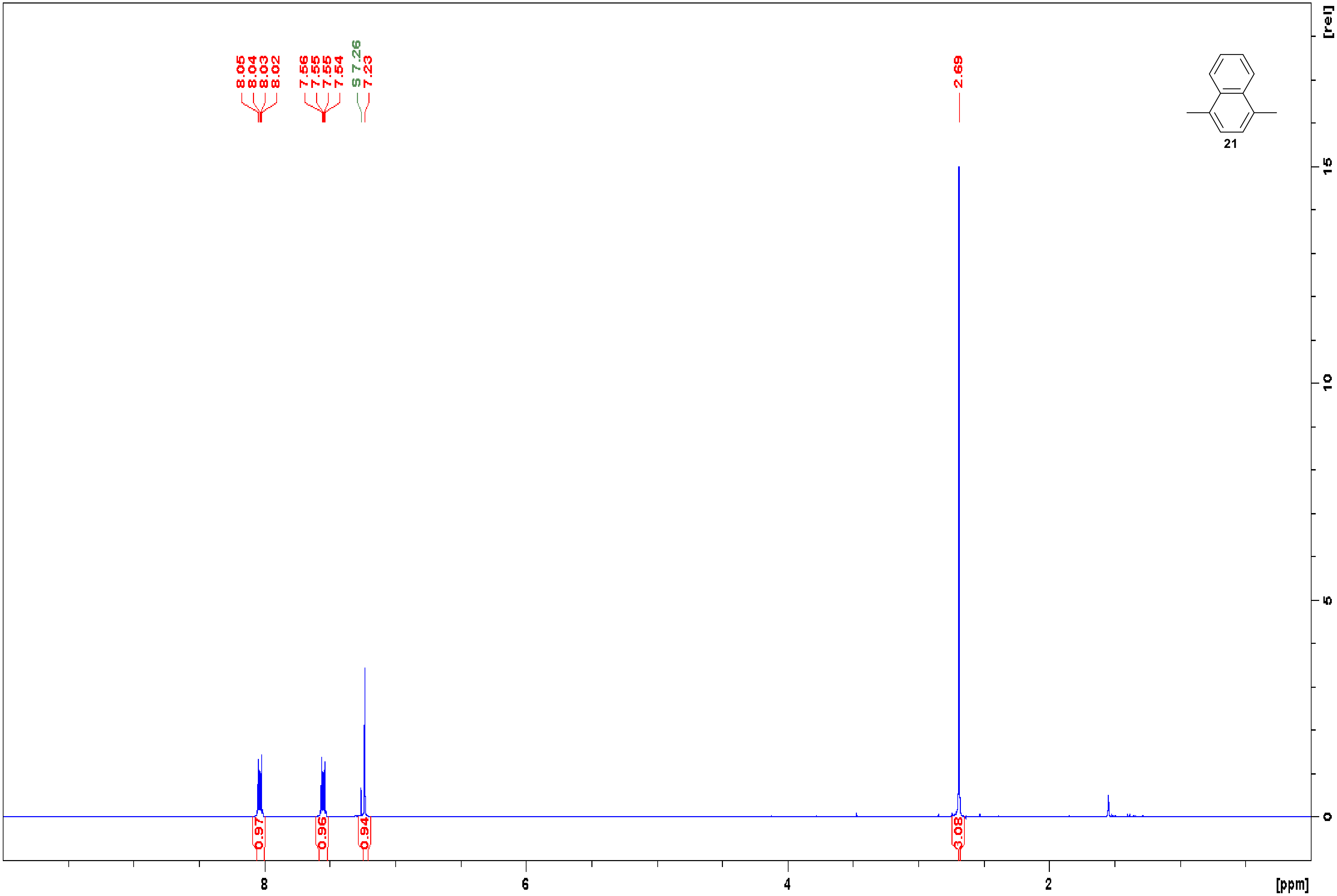


Fig. S 37 1,4-Dimethylnaphthalene **21** (^{1}H NMR, $CDCl_3$)

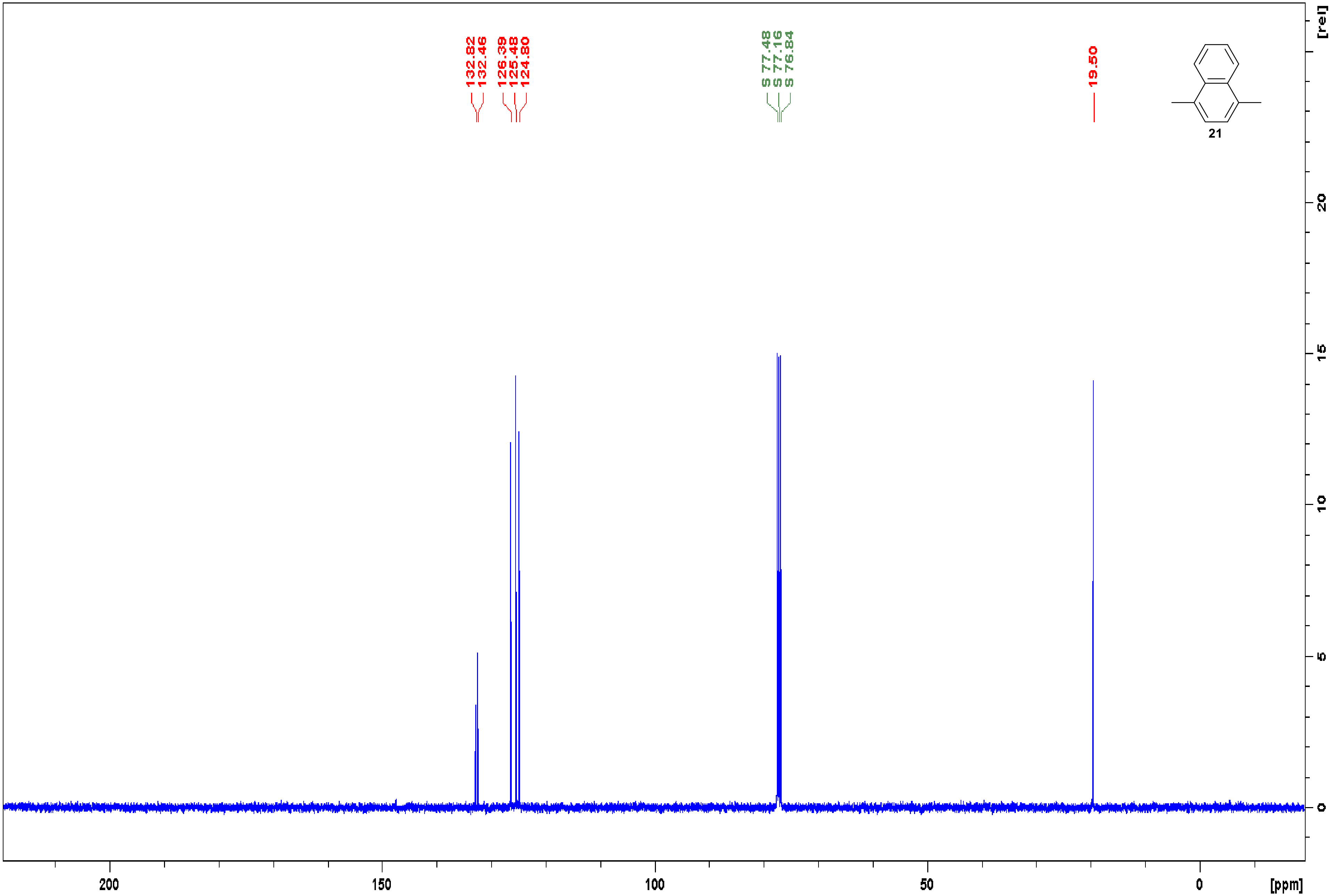


Fig. S 38 1,4-Dimethylnaphthalene **21** (^{13}C NMR, $CDCl_3$)

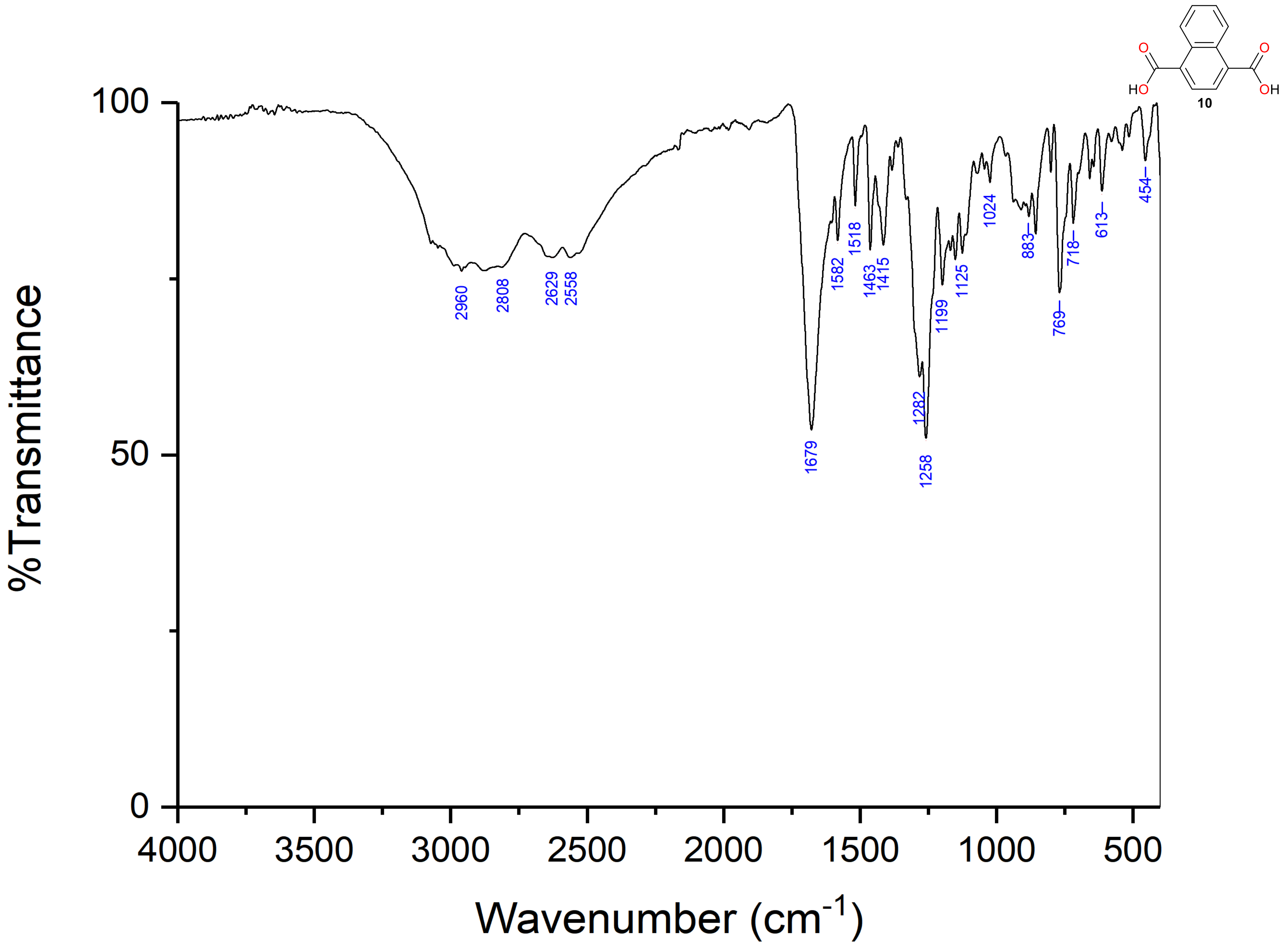


Fig. S 39 1,4-Naphthalene Dicarboxylic Acid **10** (FTIR, Neat)

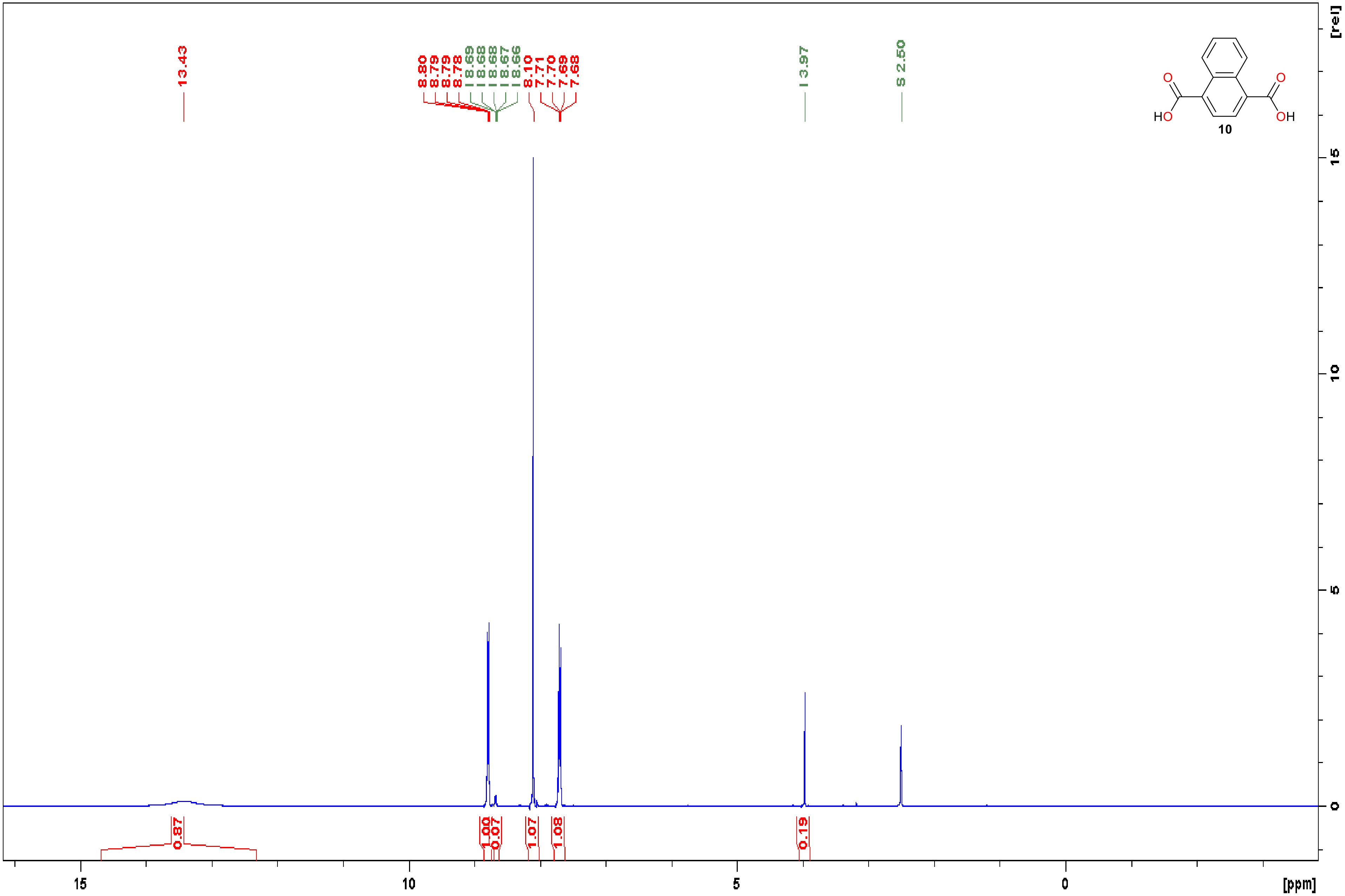


Fig. S 40 1,4-Naphthalene Dicarboxylic Acid **10** (^{1}H NMR, $CDCl_3$)

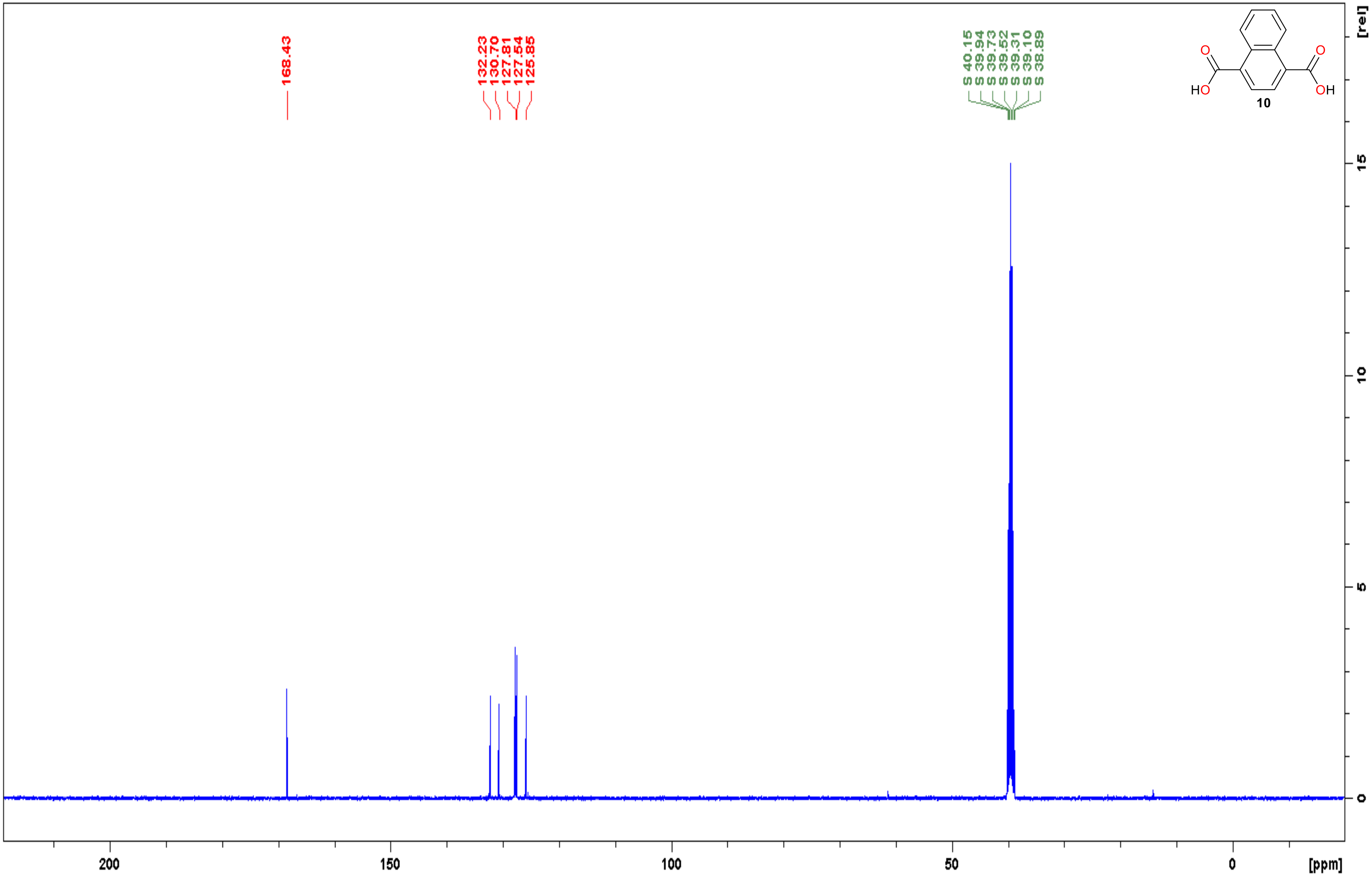


Fig. S 411,4-Naphthalene Dicarboxylic Acid **10** (^{13}C NMR, $CDCl_3$)

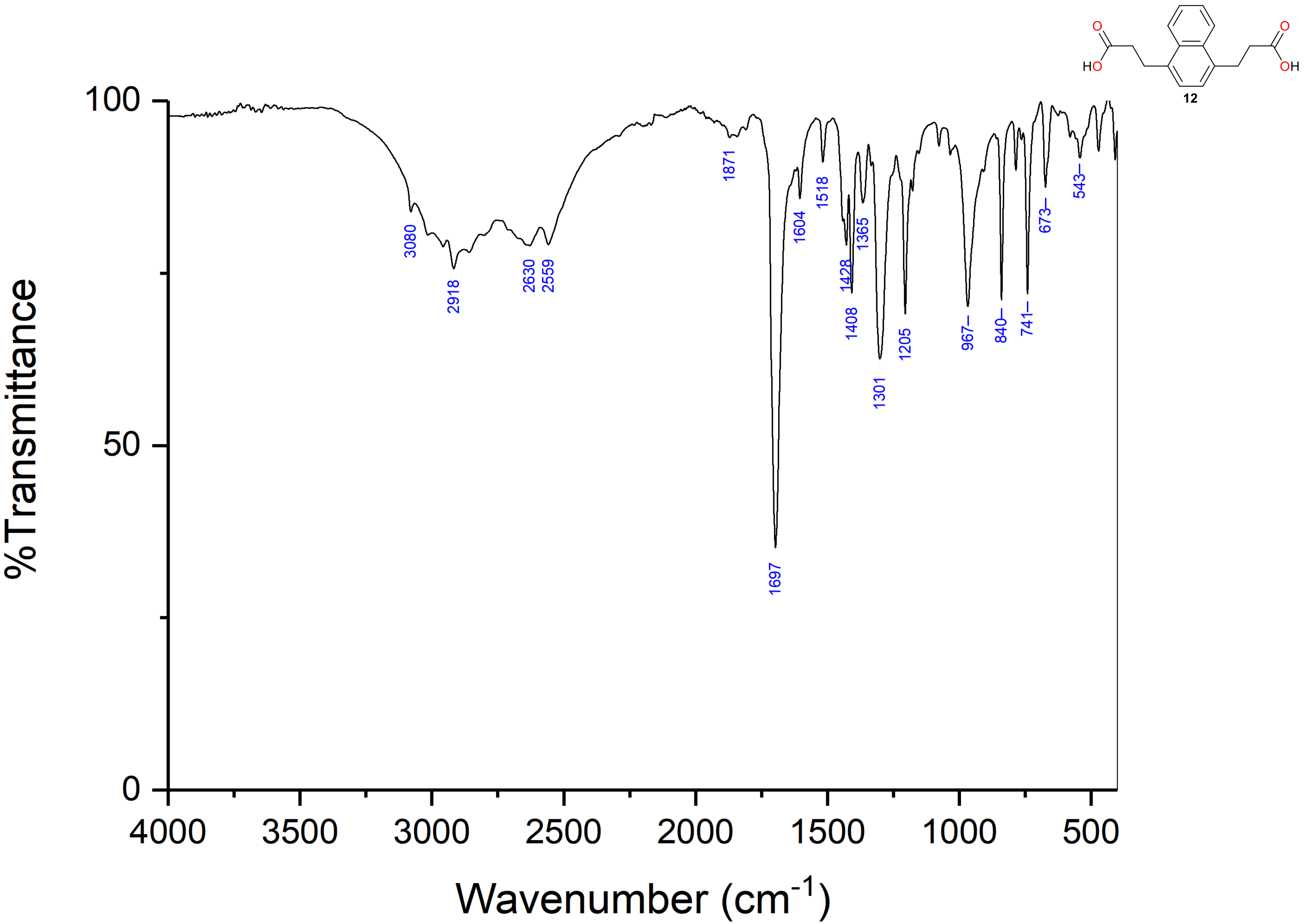


Figure S 43 3,3'-Naphthalene-1,4-diylbispropanoic Acid **12** (FTIR, Neat)

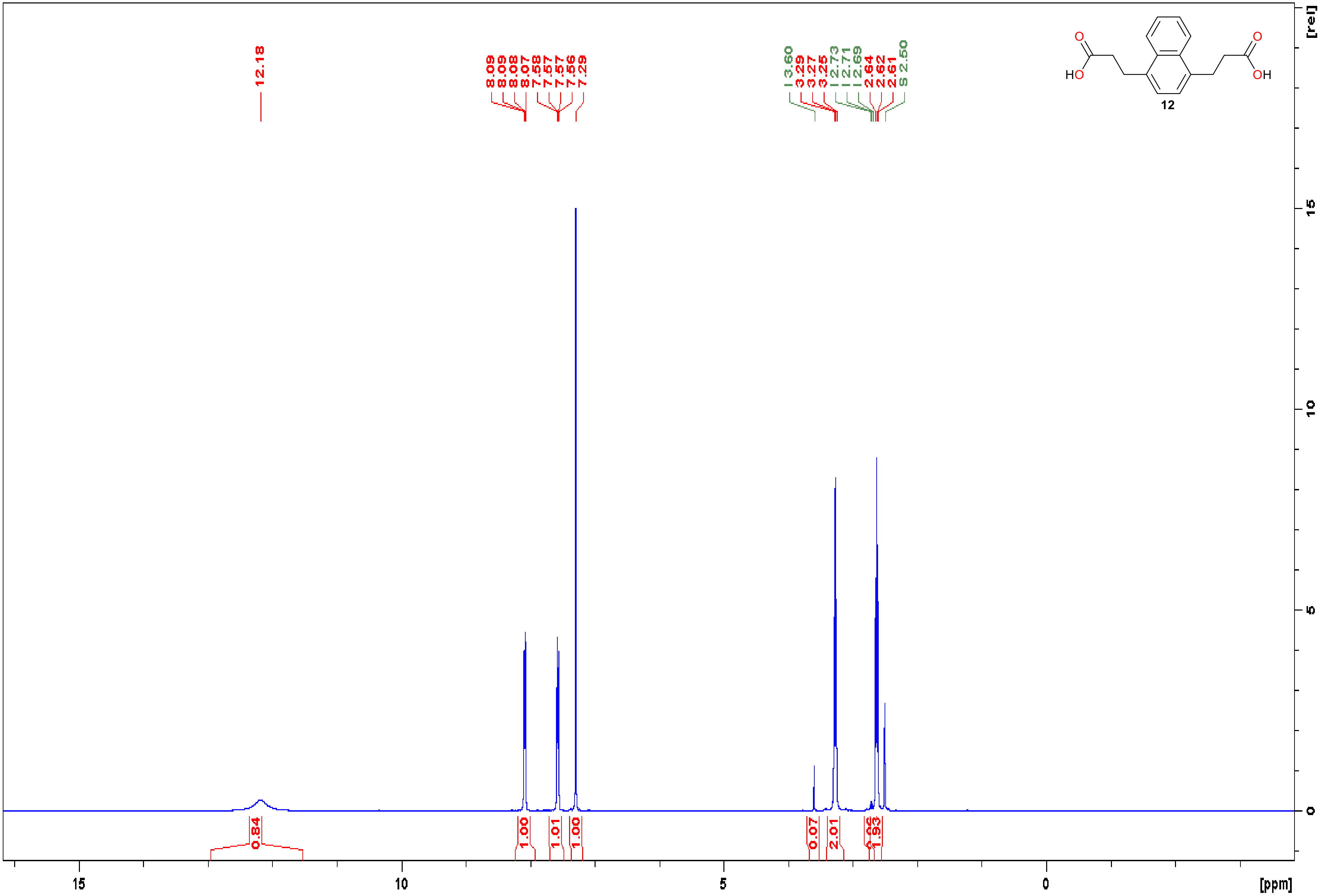


Fig. S 44 3,3’-Naphthalene-1,4-diylbispropanoic acid **12** (^{1}H NMR, DMSO)

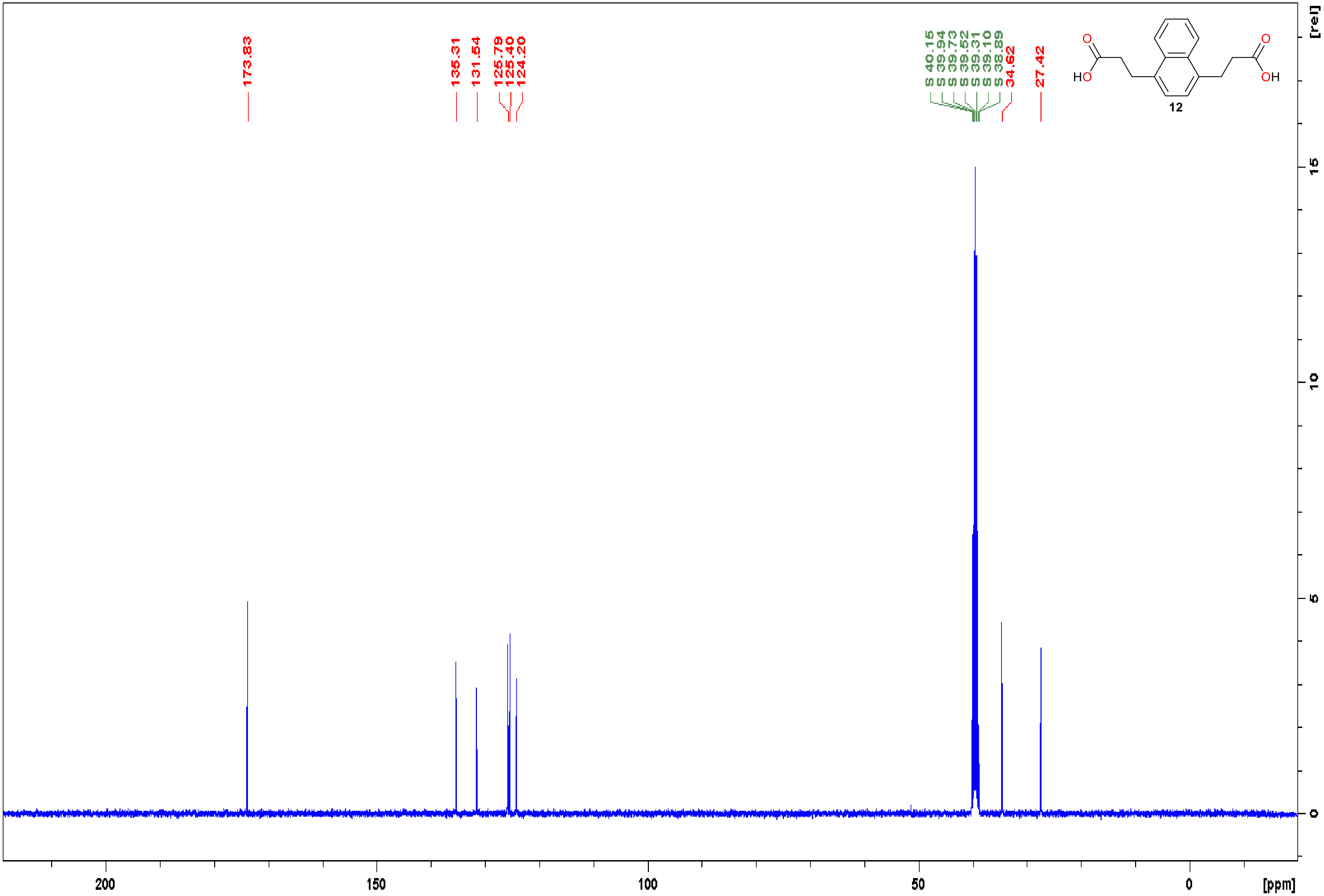


Fig. S 45 3,3'-Naphthalene-1,4-diylbispropanoic Acid **12** (^{13}C NMR, DMSO)

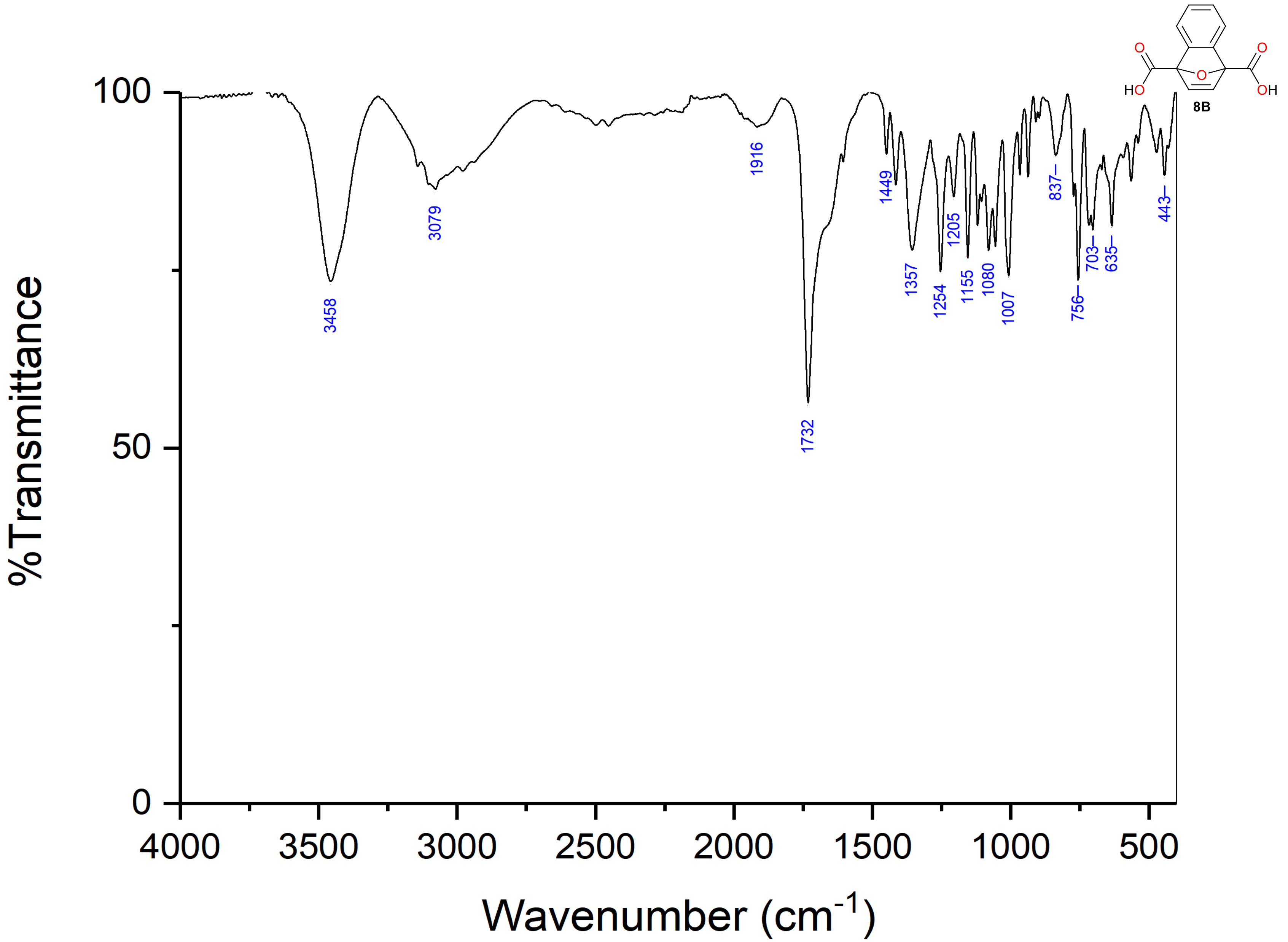


Fig. S 46 7-Oxabenzonorbornadiene-1,4-dicarboxylic Acid **8B** (FTIR, Neat)

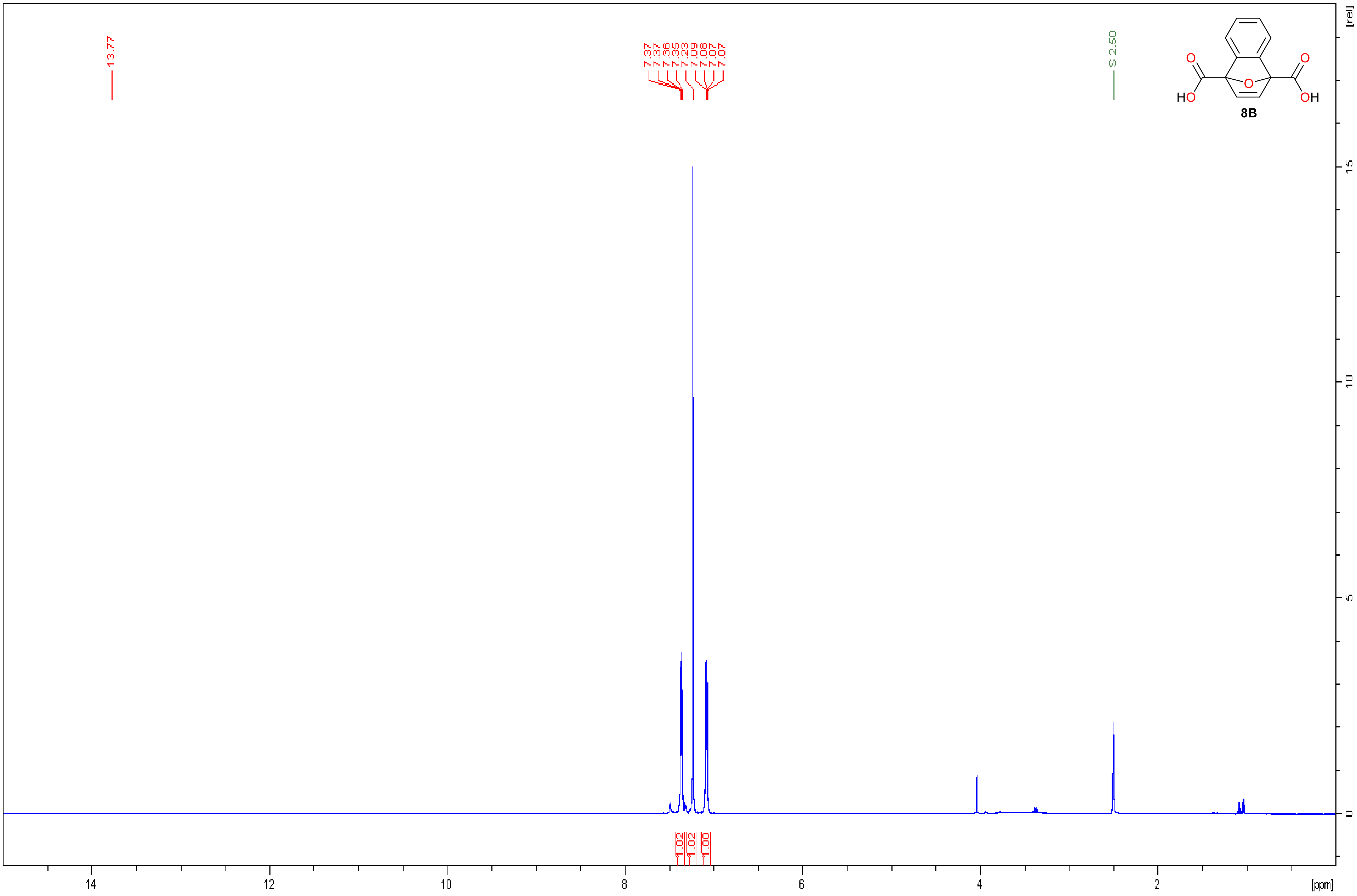


Fig. S 47 7-Oxabenzonorbornadiene-1,4-dicarboxylic Acid **8B** (^{1}H NMR, DMSO)

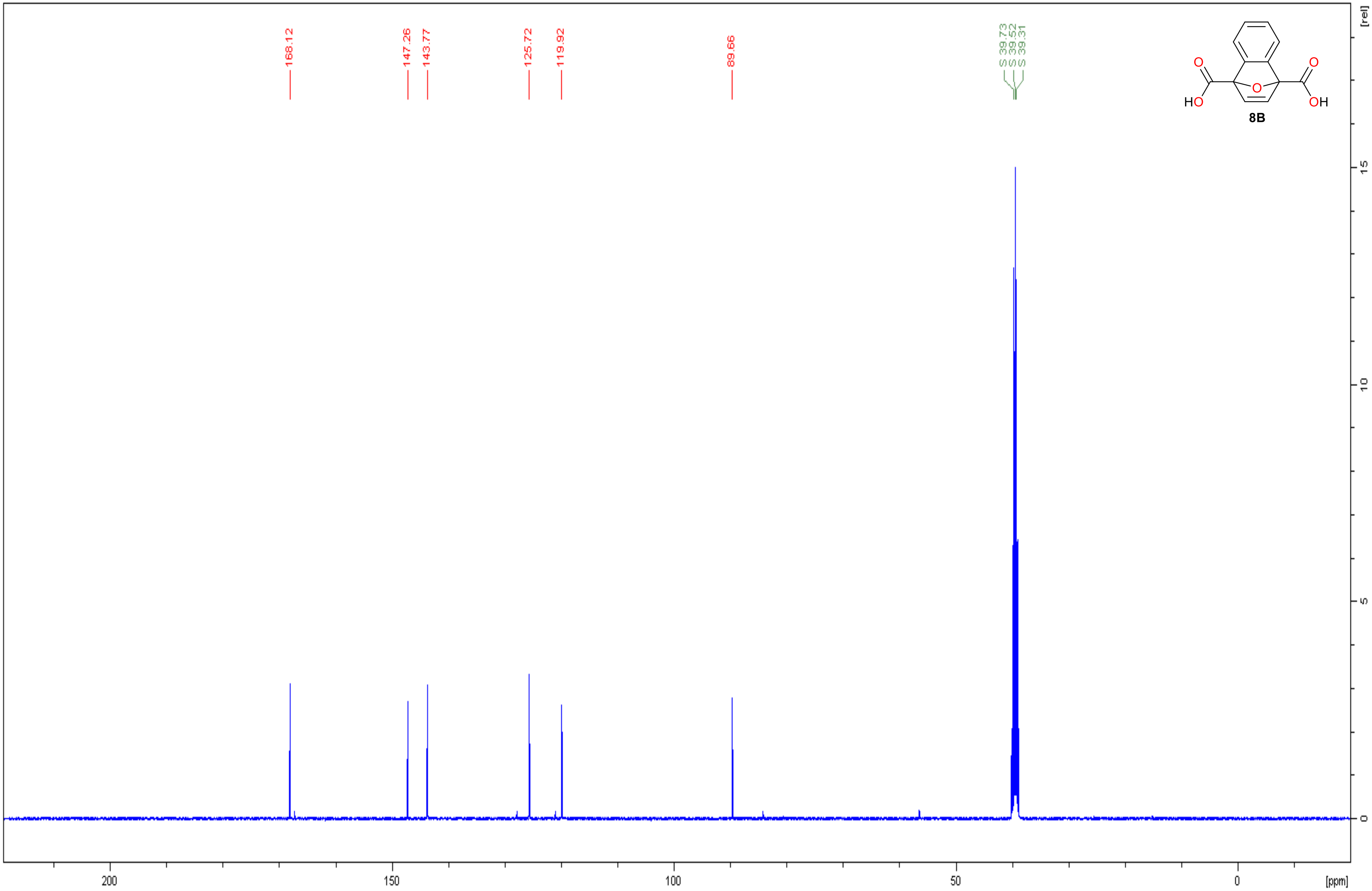


Fig. S 48 7-Oxabenzonorbornadiene-1,4-dicarboxylic Acid **8B** (^{1}H NMR, DMSO)

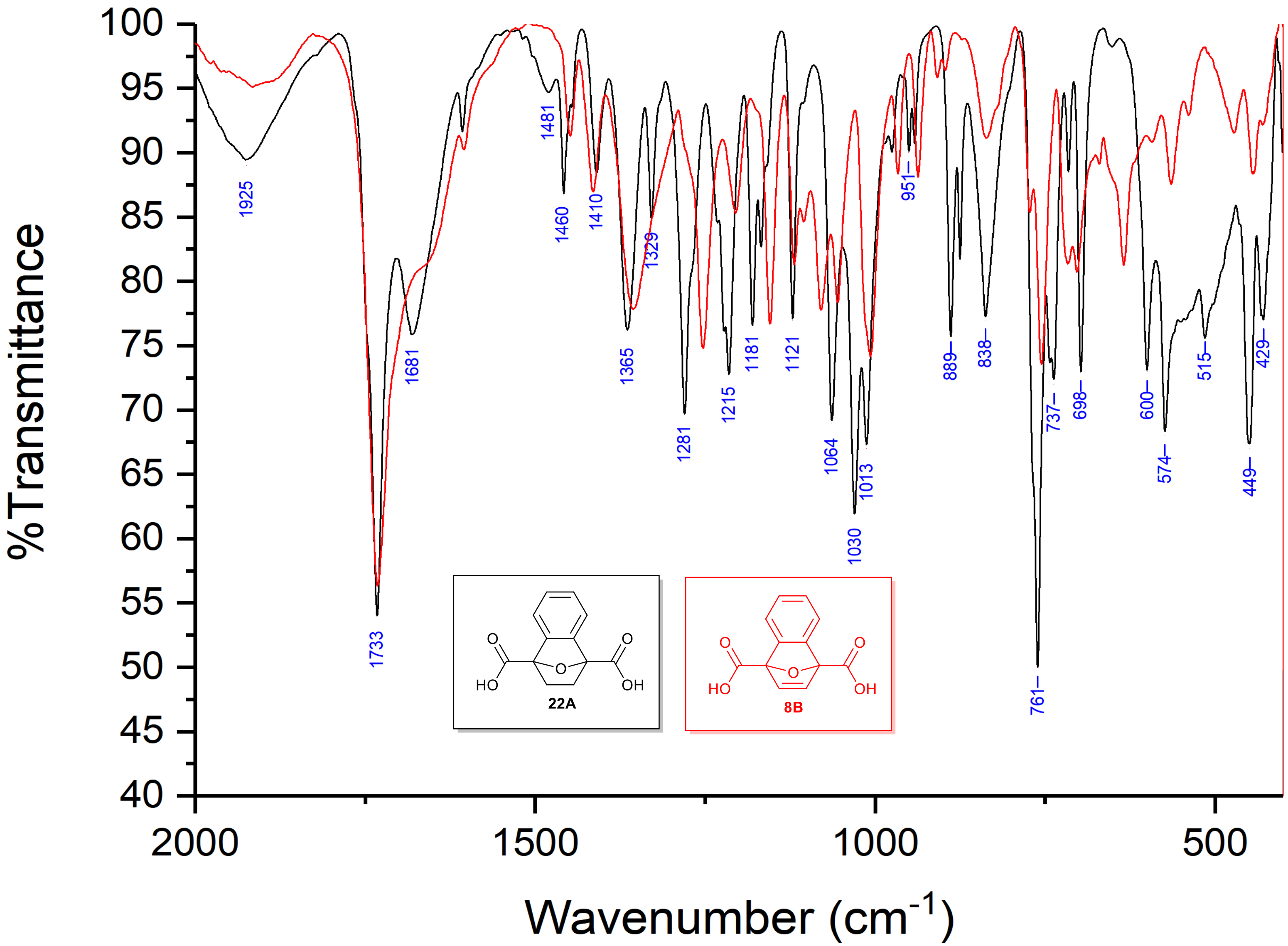


Fig. S 49 7-Oxabenzonorbornadiene-1,4-dicarboxylic Acid **8B** Overlaid with **22A** (FTIR, Neat)

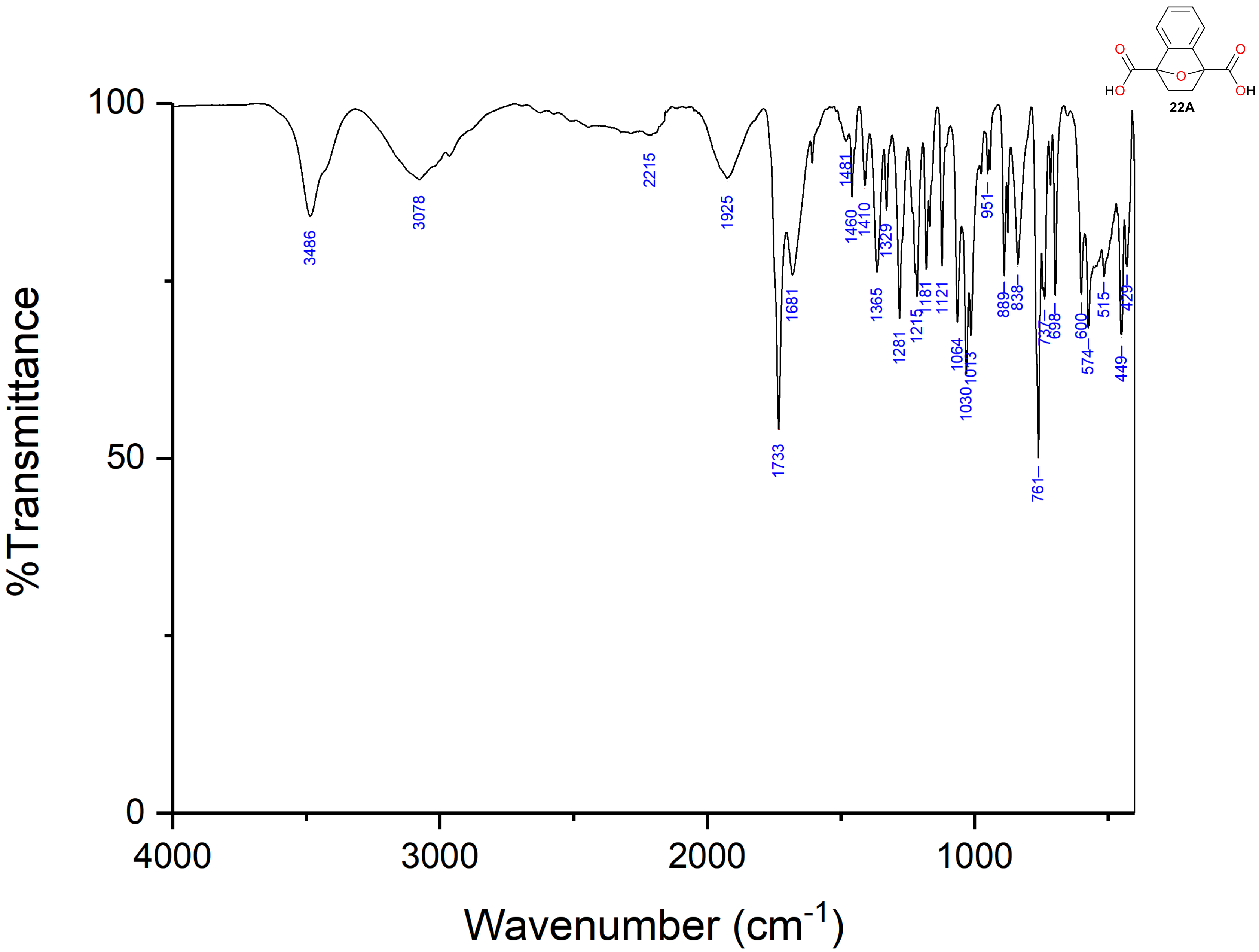


Fig. S 50 7-Oxabenzonorbornene-1,4-dicarboxylic Acid **22A** (FTIR, Neat)

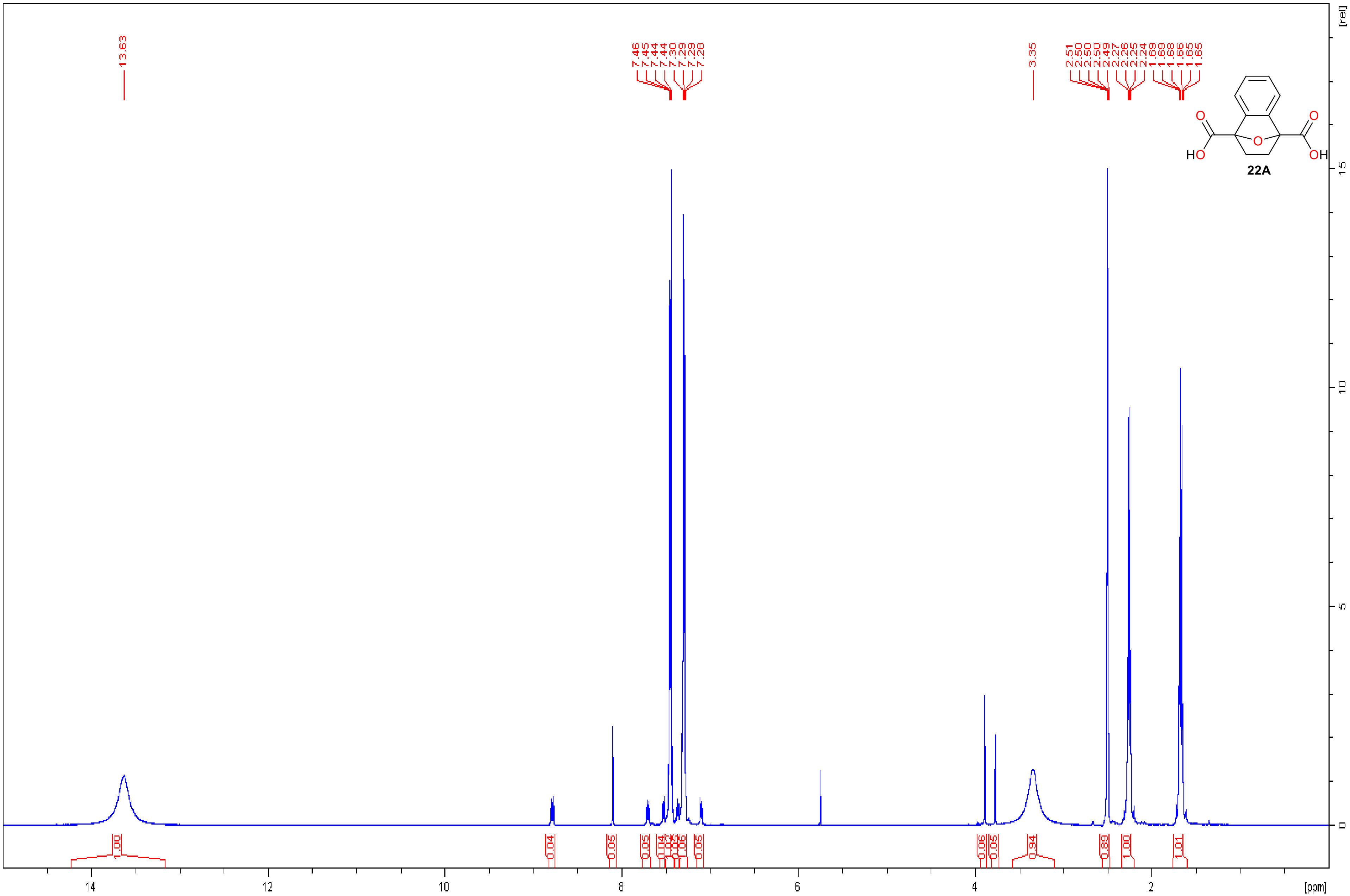


Fig. S 70 7-Oxabenzonorbornene-1,4-dicarboxylic Acid **22A** (^{1}H NMR, DMSO)

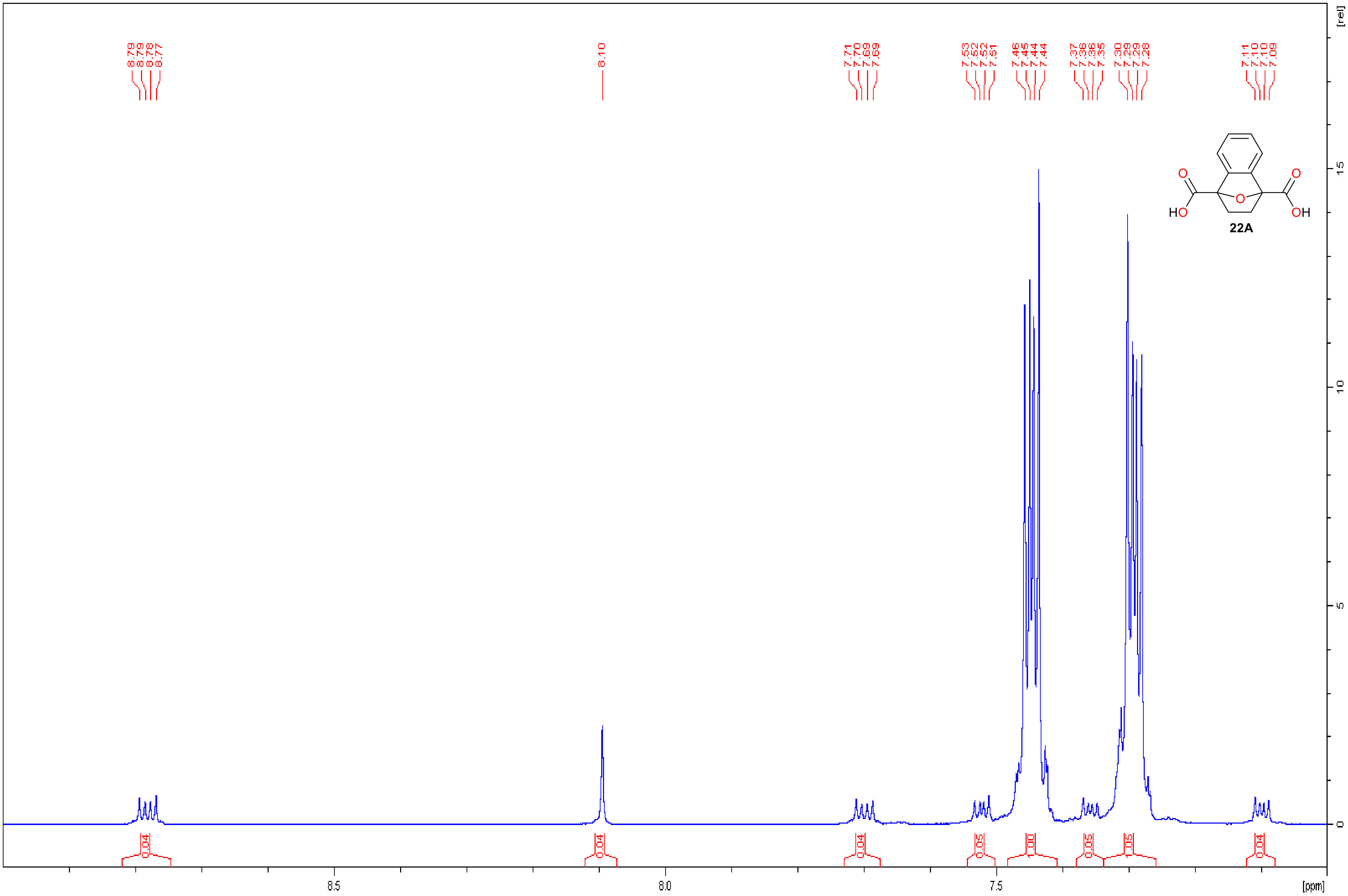


Fig. S 71 7-Oxabenzonorbornene-1,4-dicarboxylic Acid **22A** (^{1}H NMR, DMSO)

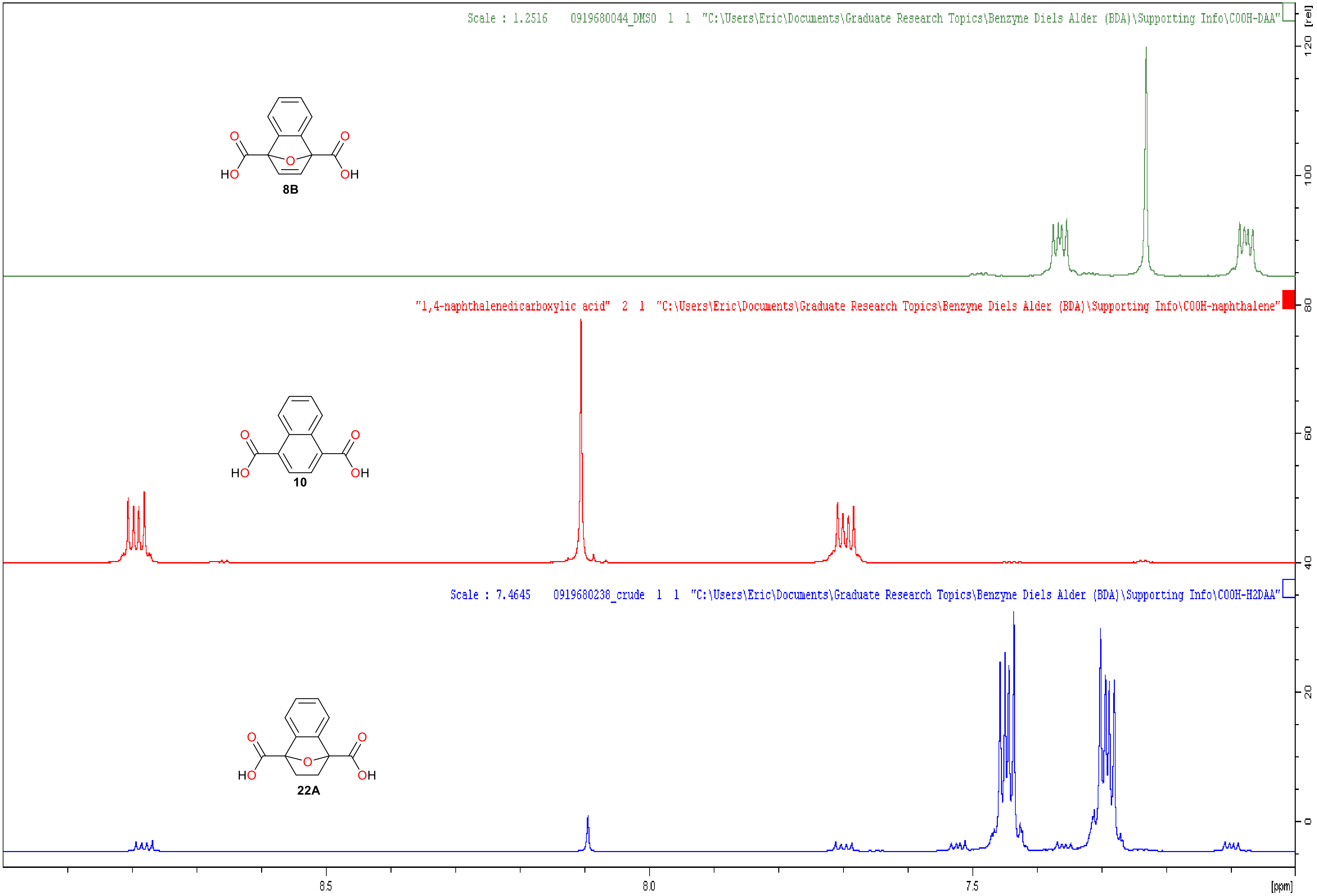


Fig. S 72 7-Oxabenzonorbornene-1,4-dicarboxylic Acid **22A** (^{1}H NMR, DMSO)

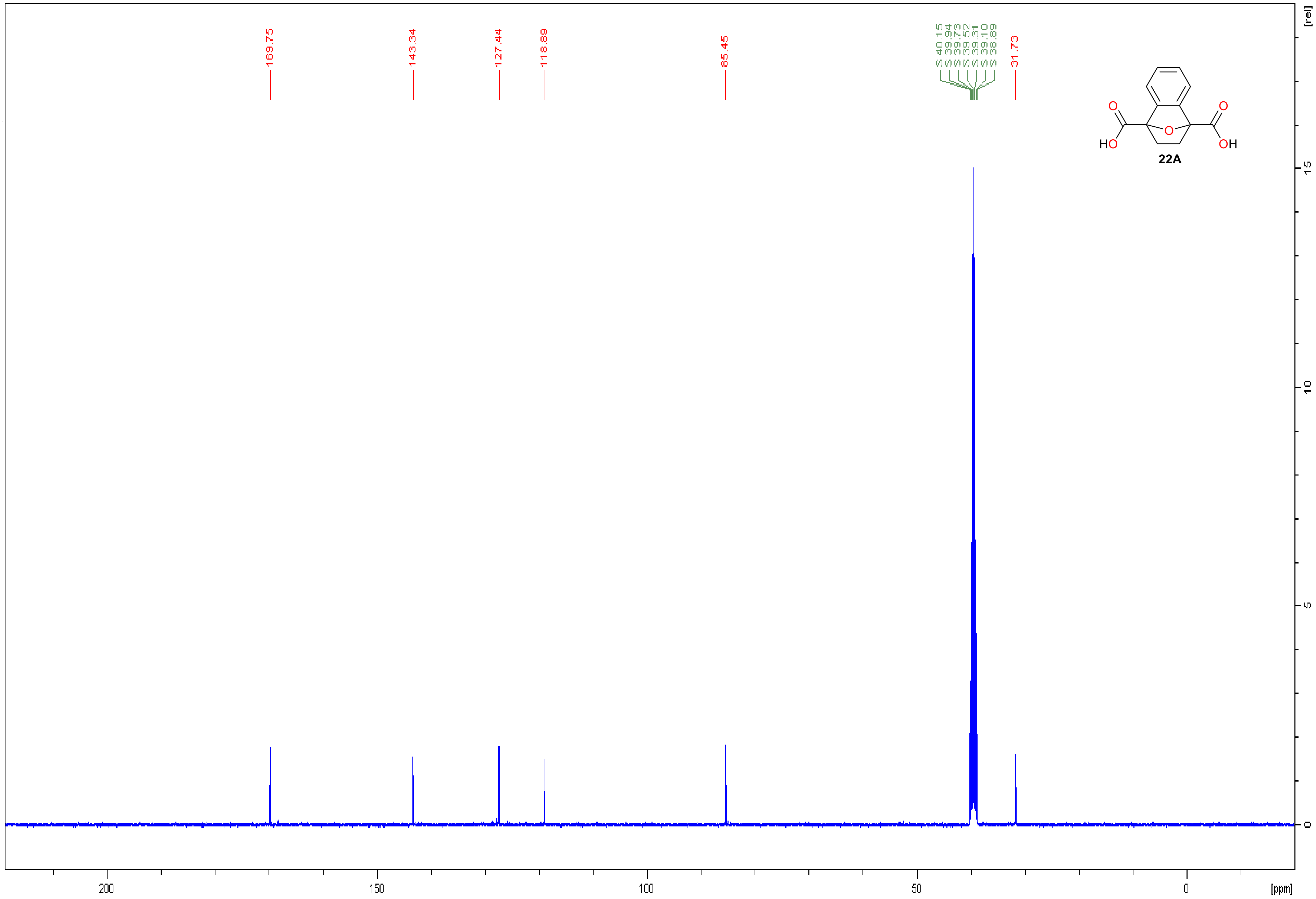


Fig. S 70 7-Oxabenzonorbornene-1,4-dicarboxylic Acid **22A** (^{13}C NMR, DMSO)