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Galvinoxyl-Inspired Dinitronyl Nitroxide: Structural, Magnetic, and Theoretical Studies

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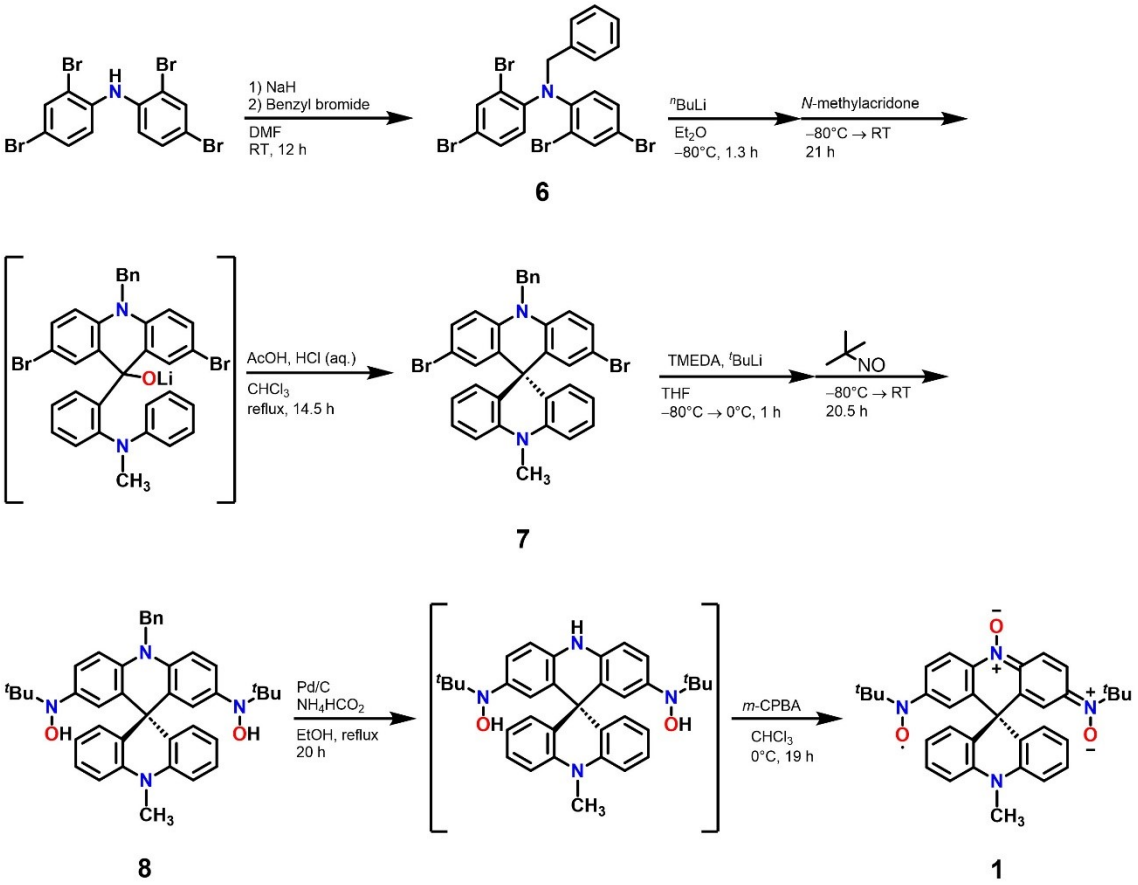
Materials and Methods.

Bis(2,4-dibromophenyl)amine and *N*-methyl-9(10*H*)acridone were prepared by the reported procedure in refs. S1 and S2, respectively. Anhydrous tetrahydrofuran (THF) and *N*,*N*-dimethylformamide (DMF) solvents were used after distillation from Na/benzophenone under an N_2 gas and dried over a molecular sieve (4A), respectively. Anhydrous diethyl ether was purchased from KANTO Chemical Co., Inc. and used without further purification. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) experiments were performed on JNM-ECZ400S (JEOL). The chemical shifts (given in ppm) were measured versus a reference peak of tetramethylsilane (TMS). Infrared (IR) spectra were obtained on an FT/IR-4600 spectrometer (JASCO) including a diamond attenuated total reflectance (ATR) method. The spectral data are listed as major peaks in wavenumber (cm^{-1}), recorded in a spectral window of 4000–400 cm^{-1}. Mass spectra (MS) were recorded on electrospray ionization (ESI) mode using a JMS-T100 AccuTOF (JEOL) spectrometer. The specimen was dissolved in methanol. Electronic spectra (UV-Vis) were obtained on a V-650 spectrometer (JASCO). Electron spin resonance (ESR) spectra were recorded on a EMXnano X-band (9.31 GHz) spectrometer (Bruker). The ESR spectra were recorded at room temperature (rt) after the sample solution in toluene was thoroughly purged with the N_2 gas.

Synthesis



Scheme S1. Synthetic approach for **1**

Synthesis of *N*-benzyl-bis(2,4-dibromophenyl)amine (6). Compound 55 wt.% NaH in paraffin liquid (2.76 g, 69.3 mmol) and bis(2,4-dibromophenyl)amine (30.55 g, 62.7 mmol) were dissolved in dry DMF solution (300 mL), and then the mixture was stirred at rt for 1 h. After benzyl bromide (8.1 mL, 68 mmol) was added, the mixture was stirred for 12 h. The reaction solution was quenched with water. The crude product purified by the recrystallization using THF to afford the clear brown crystals **6**. The yield is 17.45 g (46.2 mmol, 75%). Mp. 150–152 °C. ^{1}H NMR ($CDCl_3$, Fig. S3a): δ 7.71 (d, J = 2.3 Hz, 2H), 7.44 (d, J = 6.8 Hz, 2H), 7.28–7.17 (m, 5H), 6.80 (d, J = 8.2 Hz, 2H), and 4.75 (s, 2H). ^{13}C NMR ($CDCl_3$, Fig. S3b): δ 145.78, 136.82, 136.68, 130.95, 128.49, 127.43, 127.30, 126.27, 121.87, 117.23, and 56.67. HRMS (ESI+): m/z calcd. for $C_{19}H_{13}Br_4N$ $[M]^+$: 574.7741, found: 574.7755. IR (ATR): 1465, 1060, 730, 694, 867, 812, 713, 539, 462, and 439 cm^{-1}. UV-Vis (ethanol) λ_{max}/nm (log ε) 290 (4.2).

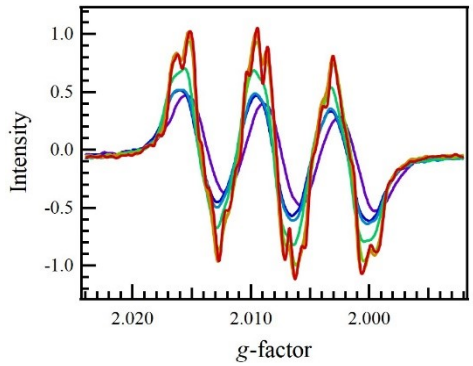
Synthesis of 10-benzyl-10'-methyl-2,7-dibromo-9,9'(10*H*,10'*H*)spirobiacridine (7). Under an Ar gas, **7** (2.881 g, 5.01 mmol) was dissolved in dehydrated diethyl ether (70 mL). After the 1.6 M *n*-butyllithium in *n*-hexane solution (7.0 mL, 11 mmol) was slowly poured at −80 °C, the mixture was stirred for 1.3 h. *N*-Methyl-9(10*H*)acridone (1.079 g, 5.15 mmol) was added to the above solution. The reaction mixture was stirred for 2 h and warmed to 0 °C with stirring for 17 h. After heating to rt, the solution was stirred for 3 h. The mixture was quenched with the saturated $NaHCO_3$ aqueous solution. The organic layer was extracted by $CHCl_3$, and the layer was washed with brine. The combined organic layer was dried over anhydrous $MgSO_4$, and the filtrate was concentrated under reduced pressure. The obtained crude was used in the next reaction without isolation and purification. The crude was dissolved in $CHCl_3$ (20 mL), and then acetic acid (40 mL) and 37% HCl aq. (6 mL) were poured into the $CHCl_3$ solution. The reaction mixture was refluxed for 15 h. After cooling to rt, the mixture was quenched with the 40% NaOH aq. The organic portion was extracted with $CHCl_3$ and washed by brine. After the organic layer was separated and dried over anhydrous $MgSO_4$, the filtrate was concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (eluted with 1/3 $CHCl_3$/*n*-hexane) to afford colourless powder **7** (1.507 g, 2.47 mmol, 49%). Mp. 289–292 °C. ^{1}H NMR ($CDCl_3$, Fig. S4a): δ 7.41 (t, J = 7.3 Hz, 2H), 7.34 (d, J = 7.3 Hz, 2H), 7.29 (d, J = 7.3 Hz, 1H), 7.20 (td, J = 8.2 Hz, J' = 1.4 Hz, 2H), 7.04 (dd, J = 8.7 Hz, J' = 2.3 Hz, 2H), 7.02–7.00 (m, 4H), 6.90 (dd, J = 7.8 Hz, J' = 1.4 Hz. 2H), 6.80 (td, J = 7.3 Hz, J' = 1.4 Hz, 2H), 6.62 (d, J = 8.7 Hz, 2H), 5.19 (s, 2H), and 3.56 (s, 3H). ^{13}C NMR ($CDCl_3$, Fig. S4b): δ 139.12, 137.25, 136.12, 134.33, 134.10, 131.89, 131.75, 130.41, 129.18, 127.72, 127.49, 125.88, 120.69, 114.60, 113.38, 112.51, 51.65, 47.36, and 33.67. HRMS (ESI+): *m*/*z* calcd. for $C_{33}H_{24}Br_2N_2$ $[M]^+$: 608.0286, found: 608.0287. (ATR): 1469, 1353, 1259, 1218, 877, 795, 746, 718, 655, and 538 cm^{-1}. UV-Vis (ethanol) λ_{max}/nm (log ε) 242 (4.4).

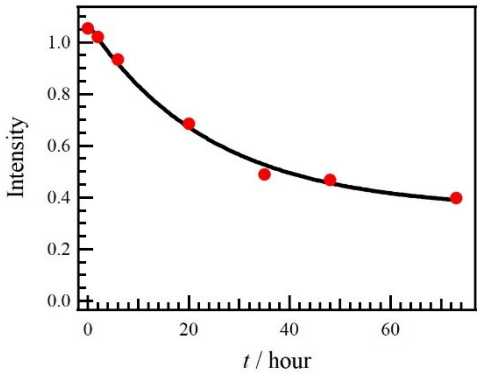
Synthesis of 10-benzyl-2,7-bis(*N*-*tert*-butyl hydroxylamino)-10'-methyl-9,9'(10*H*,10'*H*)spirobiacridine (8). After **7** (1.221 g, 2.01 mmol) was dissolved in dehydrated THF (20 mL) under the Ar gas, *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA, 1.5 mL, 10 mmol) was poured into the mixture. The 1.6 M *tert*-butyllithium in *n*-pentane solution (5.5 mL, 8.9 mmol) was slowly added to the mixture at −80 °C. The reaction temperature was warmed to 0 °C, and then the mixture was stirred for 1 h. The dehydrated THF (10 mL) solution with 2-methyl-2-nitrosopropane (0.6992 g, 8.03 mmol) was added dropwise at −80 °C, and the mixture was stirred for 18 h. After the reaction temperature was to be 0 °C, the mixture was stirred for 1 h, and then the mixture was warmed to rt and stirred for 2 h. The reaction mixture was quenched with saturated NH_4Cl aqueous solution. The organic portion was extracted with $CHCl_3$ and washed with brine. After the organic layer was separated and dried over anhydrous $MgSO_4$, the filtrate was concentrated under reduced pressure. Colourless powder **8** was obtained by recrystallization from the THF solution. The yield was 645.2

mg (1.03 mmol, 51%). Mp. 181 °C (decomp.). ^{1}H NMR (DMSO-d_6, Fig. S5a): δ 7.92 (s, 2H), 7.40 (t, J = 7.8 Hz, 2H), 7.33–7.27 (m, 3H), 7.14–7.05 (m, 4H), 6.91 (dd, J = 8.7 Hz, J' = 2.3 Hz, 2H), 6.81–6.68 (m, 6H), 6.62 (d, J = 2.3 Hz, 2H), 5.25 (s, 2H), 3.49 (s, 3H), and 0.76 (s, 18H). ^{13}C NMR (DMSO-d_6, Fig. S5b): δ 142.97, 138.81, 137.78, 134.91, 132.96, 131.11, 129.51, 128.76, 127.80, 126.94, 126.81, 126.04, 123.29, 119.86, 112.37, 111.35, 58.99, 49.74, 46.85, 33.61, and 25.59. HRMS (ESI+): m/z calcd. for $C_{41}H_{44}N_4O_2$ $[M]^+$: 624.3464, found: 624.3451. IR (ATR): 639, 716, 728, 742, 1202, 1263, 1356, 1427, 1455, and 1473 cm^{-1}. UV-Vis (ethanol) λ_{max}/nm (log ε) 217 (4.8).

Synthesis of 2,7-bis(*N*-*tert*-butyl-*N*-oxylamino)-10'-methyl-9,9'(10*H*,10'*H*)spirobiacridin-10-oxyl (1). Compound **8** (310 mg, 0.49 mmol), palladium 10% on carbon wetted with ca. 55% water (220 mg), and ammonium formate (1.28 g, 20.3 mmol) were dissolved in ethanol (10 mL) under the Ar gas. The mixture was refluxed for 20 h and filtered through celite. The organic portion was extracted with CH_2Cl_2 and washed with water. After the organic layer was separated and dried over anhydrous $MgSO_4$, the filtrate was concentrated under reduced pressure. The deprotected hydroxylamine was rapidly oxidized in the air during this reaction step, and thus we have done the next reaction without the isolation of **1**. The purple crude product was dissolved in $CHCl_3$ (10 mL). The *m*-chloroperbenzoic acid (*m*-CPBA) with 35% water (550 mg, 2.25 mmol) in $CHCl_3$ (15 mL) solution was added dropwise to the above solution at 0 °C. The combined solution was stirred for 19 h keeping the temperature of 0 °C, and then the mixture was passed through a short column (activated alumina) with $CHCl_3$ for removal of the residue derived from *m*-CPBA. The red solution was purified by column chromatography on SiO_2 (eluted with $CHCl_3$/MeOH = 20/1) and then HPLC (Japan Analytical Industry 1H+1H GPC columns; a flow rate 3.5 mL min^{-1}). Recrystallization from CH_2Cl_2 and *n*-hexane in a refrigerator gave dark-red platelet crystals, which were collected on a filter. The yield was 30.9 mg (0.057 mmol, 12%). Mp. 168 °C (decomp.). HRMS (ESI+): m/z calcd. for $C_{34}H_5N_4O_3$ $[M]^+$: 547.2709, found 547.2727. IR (ATR): 2929, 2629, 1590, 1472, 1354, 1267, 1179, 1055, 877, and 746 cm^{-1}. UV-Vis (ethanol) λ_{max}/nm (log ε) 486 (4.15).

a)





b)

Fig. S1. (a) ESR spectra after 0 h (red), 2 h (yellow), 6 h (light green), 20 h (green), 35 h (sky blue), 48 h (blue), and 73 h (purple). (b) Time dependence of the maximum ESR intensities (I) in the central peaks (red circles). The black solid line represents the fitting curve, $I = I_0 + A*\exp(-t/\tau)$; I_0 = 0.35(4), A = 0.72(3), and τ = 25(3) hour.

Single Crystal X-ray Diffractions

X-ray diffraction data of **1** was collected on a Rigaku VariMax Dual (Mo Kα radiation: λ = 0.71073 Å). The selected crystallographic data are given in Table S1. The X-ray data analysis was carried out using the SHELXT[S3] and SHELXL[S4] operated with the Olex2 interface.[S5] Numerical absorption correction was used. All the hydrogen atoms were reined as "riding". The thermal displacement parameters of the non-hydrogen atoms were refined anisotropy. The contribution of the disordered solvent was removed using the SQUEEZE option from PLATON operated with the Olex2 interface.[S5] The estimated total solvent-accessible void space was 668.4 Å^3 per the unit cell (20.4%) and 72 electrons per formula unit. The squeeze electron count correlates with the electron density of 1.7 CH_2Cl_2 molecules of unit cell (71 electrons). The CCDC number of **1** is 2256749.

Table S1. Selected crystallographic data for **1**.

Formula	$C_{68}H_{70}N_8O_6$
Fw	1095.32
T/K	93
Crystal System	Triclinic
Space group	$P\bar{1}$
a/Å	14.8226(3)
b/Å	14.8446(4)
c/Å	16.5115(5)
α/°	79.798(2)
β/°	72.410(2)
γ/°	71.824(2)
V/Å^3	3276.64(16)
Z	2
d_{calc}/g cm^{-3}	1.110
μ(Mo Kα)/ mm^{-1}	0.72
$R(F)^a$ ($I > 2\sigma(I)$)	0.0607
$R_w(F^2)^b$ (all data)	0.1549
Goodness of fit	1.042
No. unique reflns	20563

^{a} $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. ^{b} $R_w = [\Sigma w|F_o^2 - F_c^2|^2/\Sigma w(F_o^2)^2]^{1/2}$.

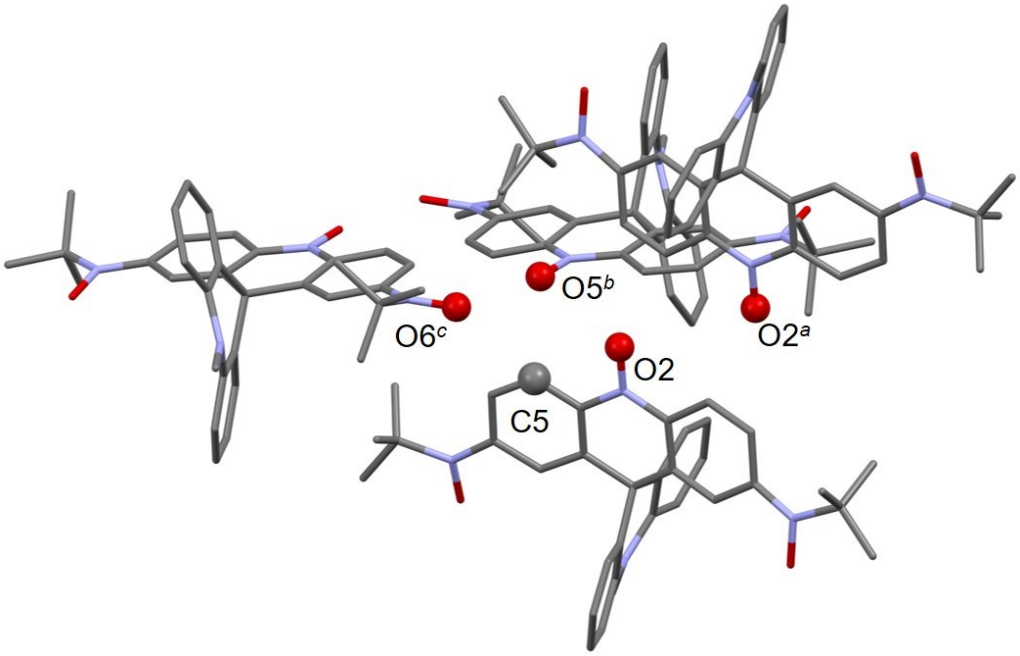


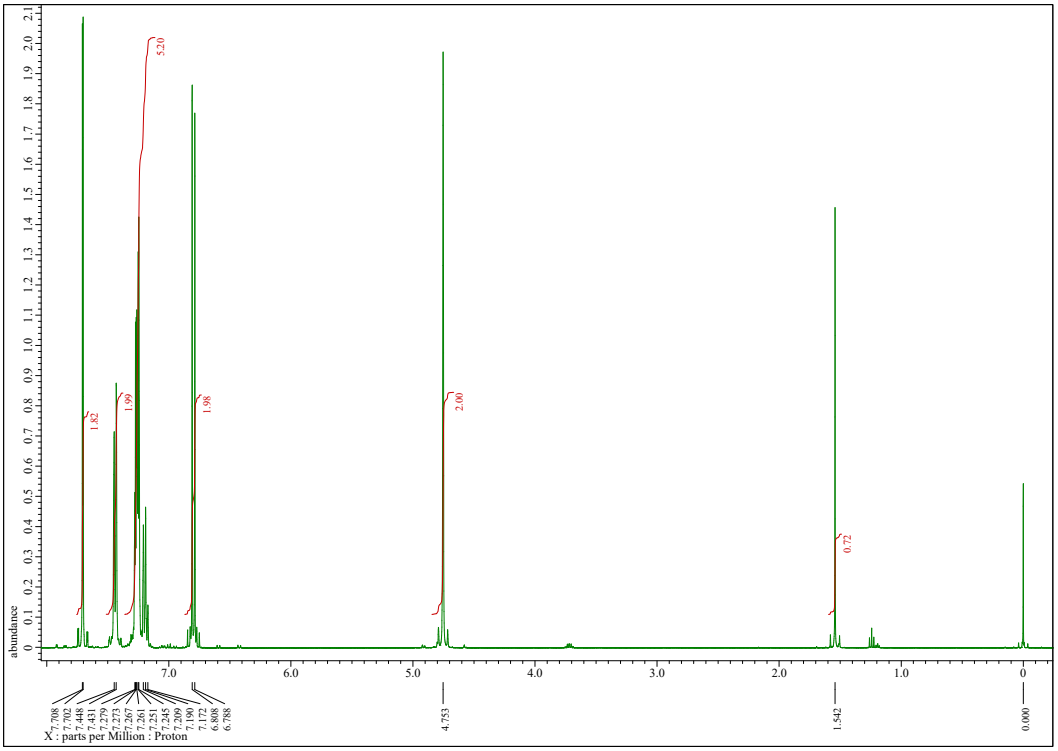
Fig. S2. Intermolecular contacts. The symmetry codes of *a*, *b*, and *c* are (2−*x*, 3−*y*, 1−*z*), (*x*, −1+*y*, *z*), and (2−*x*, 4−*y*, −*z*), respectively. O2···O5, 4.007(3) Å; O5···O6, 4.055(3) Å; O6···O2, 4.330(2) Å; O2···C5, 2.700(2) Å; O5···C5, 3.058(3) Å; O6···C5, 3.237(2) Å.

Magnetic measurements

The dc magnetic susceptibility of polycrystalline specimens of **1** in a gelatine capsule was measured on a MPMS-XL7AC SQUID magnetometer (QuantumDesign) equipped with a 7 T coil in a temperature range of 2–350 K. The magnetic data were corrected using diamagnetic blank data of the sample holder measured. The diamagnetic contribution of the sample itself was estimated from Pascal's constants.[S6]

Theoretical calculations

The DFT calculations of **1** was performed on the Gaussian09 program.[S7] The energies of the quartet and doublet states were calculated at the UB3LYP/6-311G+(2d,p) level. The structural parameters were given from the crystallographic data.



(a)

(b)

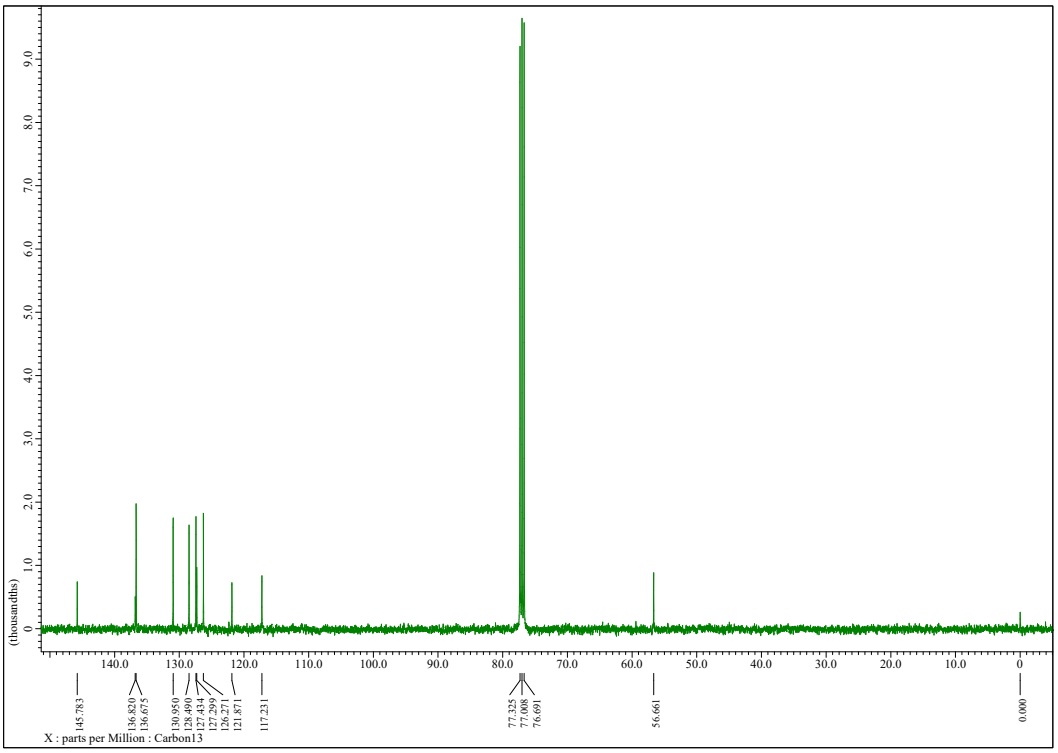
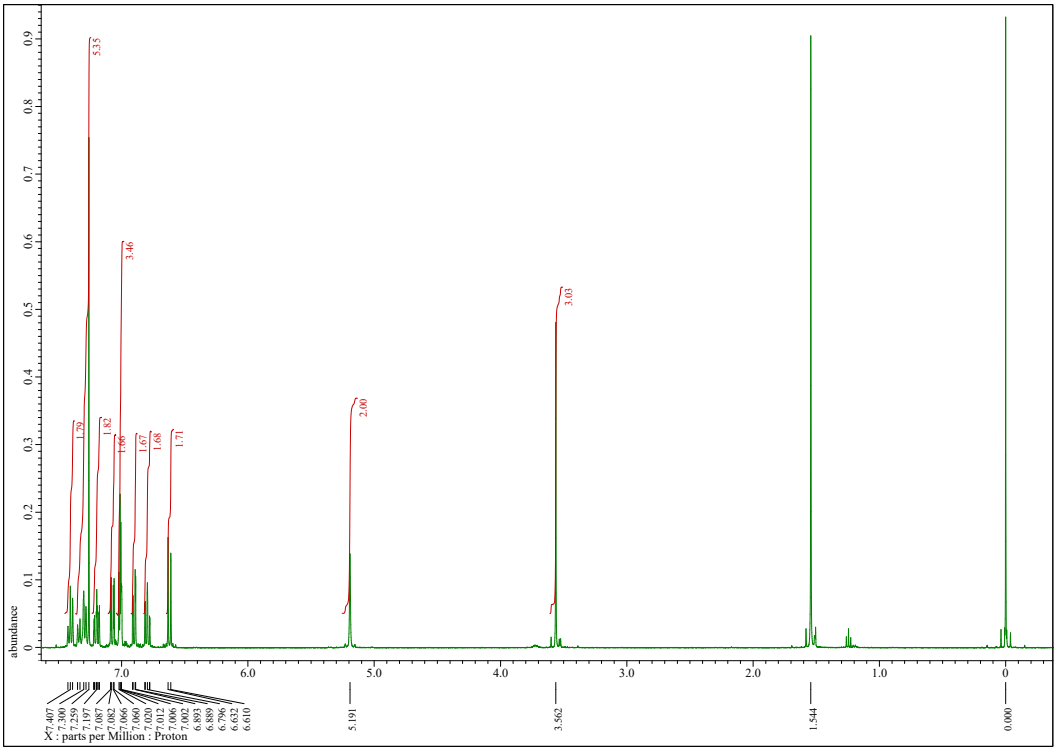


Fig. S3. (a) ^{1}H and (b) ^{13}C NMR spectra for **6**.



(a)

(b)

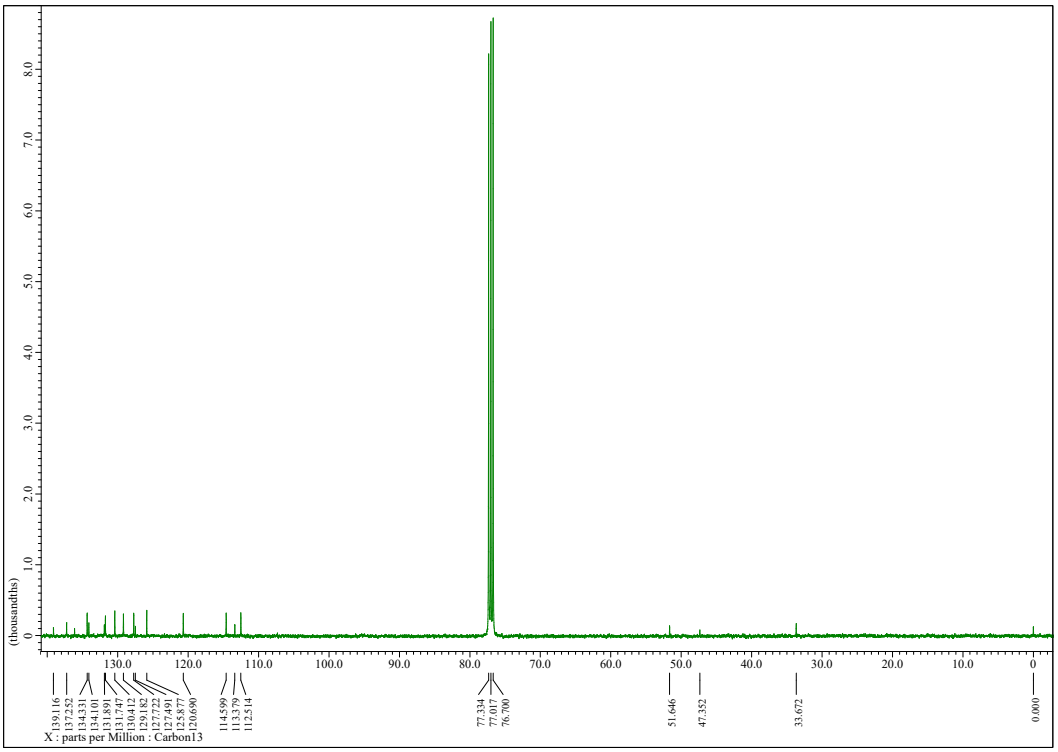
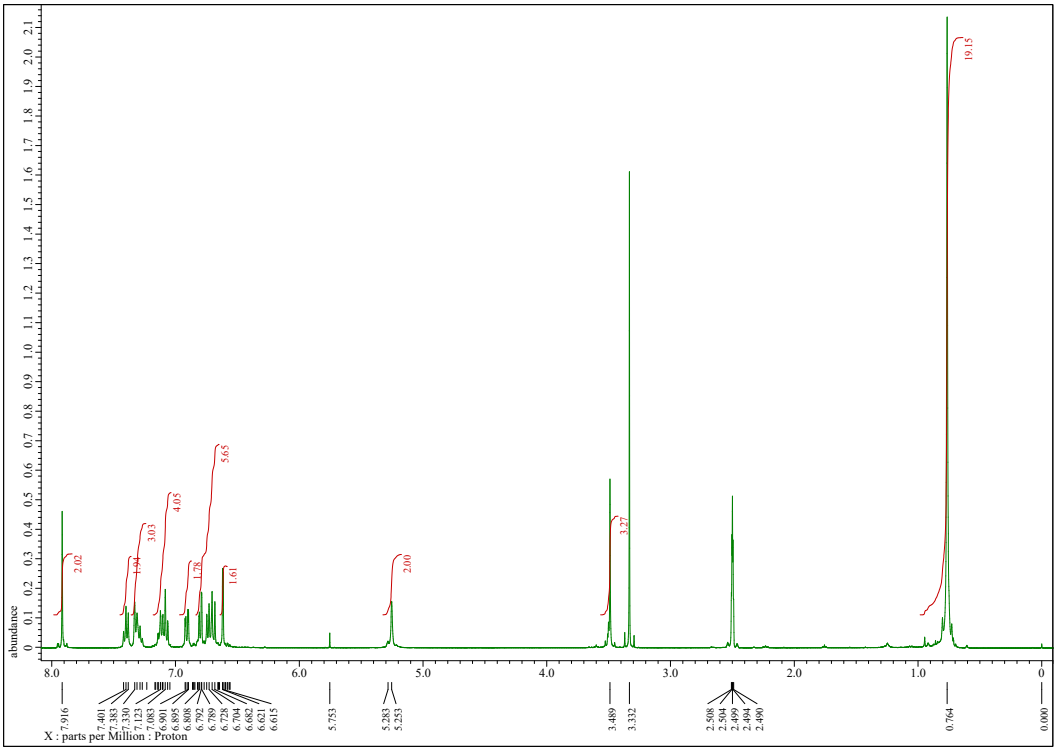


Fig. S4. (a) ^{1}H and (b) ^{13}C NMR spectra for **7**.

(a)



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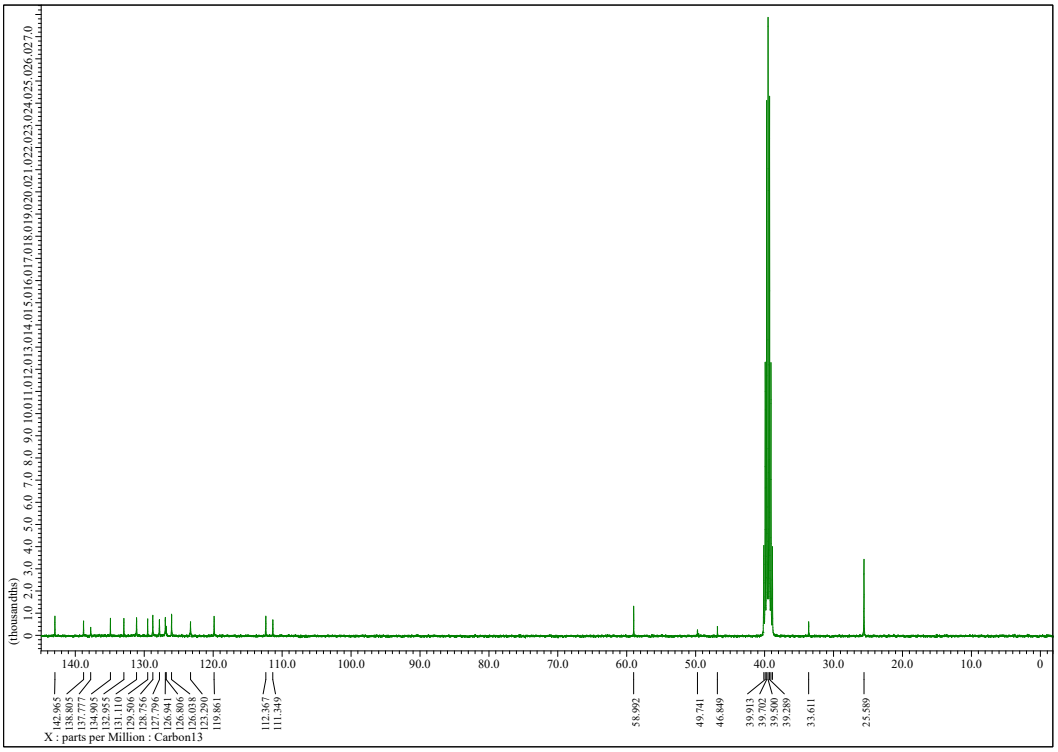

Fig. S5. (a) ^{1}H and (b) ^{13}C NMR spectra for **8**.

References

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