Supplementary Information for:

Synthesis of mesoionic triazolones via a formal [3+2] cycloaddition between 4-phenyl-1,2,4-triazoline-3,5-dione and alkynes

Yusuke Kuroda,*[a,b] Maya Krell,[‡a,c] Kazuma Kurokawa[‡a] and Kiyosei Takasu*[a]

[‡]These authors contributed equally

[a] Graduate School of Pharmaceutical Sciences, Kyoto University Yoshida, Sakyo-ku, Kyoto 606-8501, Japan
[b] Research Foundation ITSUU Laboratory, C1232 Kanagawa Science Park R&D Building, 3-2-1 Sakado, Takatsu-ku, Kawasaki, Kanagawa 213-0012, Japan
[c] Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences, ETH Zurich, 8093 Zurich, Switzerland

*Email: kuroday@pharm.kyoto-u.ac.jp (Y.K.) takasu.kiyosei.6r@kyoto-u.ac.jp (K.T.)

Table of Contents

1. General Considerations 1

2. Preparation of Alkynes 2

3. Azo-Yne [3+2] Reactions 6

4. X-ray Crystallographic Analysis 14

5. HOMA/HOMHED Calculations 16

6. DFT Calculations 17

7. Mechanistic Details 20

8. References 21

9. NMR Spectra 22

1. General Considerations

1.1. Solvents and Reagents

4-Phenyl-1,2,4-triazole-3,5-dione (PTAD), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) and anhydrous CH_2Cl_2 were purchased from Tokyo Chemical Industry, Oakwood Chemical and Kanto Chemical respectively and used as received. Unless otherwise noted, all other reagents were purchased from commercial suppliers and used as received.

1.2. Experimental Procedures

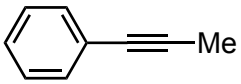
Unless otherwise noted in the experimental procedures, reactions were carried out in flame or oven-dried glassware under a positive pressure of argon in anhydrous solvents using standard Schlenk techniques. Reaction progresses were monitored using thin-layer chromatography (TLC) on Merck TLC silica gel 60 F254 (0.25 mm) plates. Visualization of the developed plates was performed under UV-light (254 nm) irradiation. Flash column chromatography was performed on Silica gel 60N (Kanto Chemical, particle size 63-210 μ m).

1.3. Analytical Instrumentation

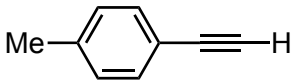
NMR data were recorded on a JEOL JNM-LA 500 spectrometers (^{1}H NMR; 500 MHz, ^{13}C NMR; 126 MHz) or a JEOL JNM ECZ 600R (^{1}H NMR; 600 MHz, ^{13}C NMR; 151 MHz) typically at 20–23 °C. ^{1}H and ^{13}C NMR spectra were referenced using the residual solvent signal (^{1}H NMR; $CDCl_3$ at 7.26 ppm, $(CD_3)_2SO$ at 2.50 ppm, ^{13}C NMR; $CDCl_3$ at 77.16 ppm, $(CD_3)_2SO$ at 39.52 ppm). NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra were obtained with SHIMADZU LCMS-IT-TOF. Melting points were determined using Yanaco micro melting point apparatus Model MP-500D.

2. Preparation of Alkynes

Following alkynes were obtained from Tokyo Chemical Industry (TCI) and used as received:

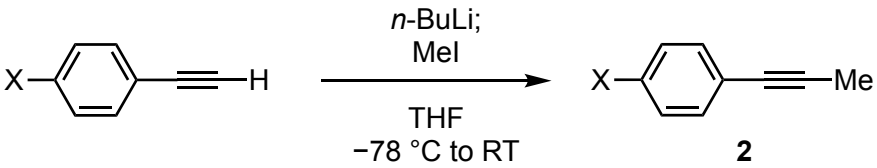


2a
(TCI)



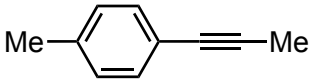
2g
(TCI)

General Procedure A



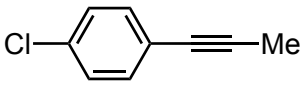
2

A round-bottom flask charged with a solution of terminal alkyne (1.0 equiv) in THF (0.33 M) was cooled to −78 °C. *n*-BuLi (1.6 M in hexane, 2.0 equiv) was added dropwise, and the resulting solution was allowed to stir for 30 min at −78 °C. To the mixture was added MeI (2.1 equiv), and the resulting mixture was warmed to room temperature. After 12 h, the reaction mixture was quenched with sat. NH_4Cl aq., and the mixture was partitioned with hexane and H_2O. The aqueous phase was extracted with hexane (× 2). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography to provide alkyne **2**.



2b

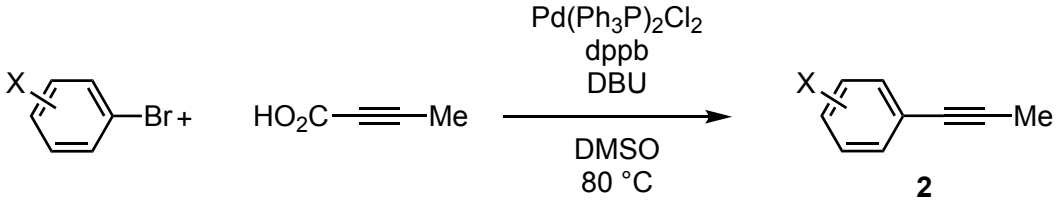
Prepared following the general procedure A using 4-thyenyltoluene (0.620 mL, 5.00 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2b** in 75% yield (489 mg) as a colorless oil. Spectral data were in full agreement with the reported literature values.[1]



2c

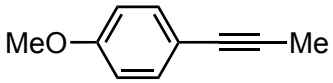
Prepared following the general procedure A using 1-chloro-4-ethynylbenzene (1.00 g, 7.32 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2c** in 82% yield (906 mg) as a colorless oil. Spectral data were in full agreement with the reported literature values.[2]

General Procedure B



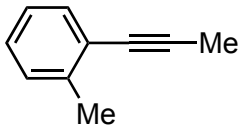
2

To a round-bottom flask containing a solution of bromoarene (1.0 equiv), 2-butynoic acid (1.2 equiv), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU 3.0 equiv) and 1,4-bis(diphenylphosphino)butane (dppb, 2 mol%) in DMSO (0.33 M) was added $Pd(Ph_3P)_2Cl_2$ (1 mol%). The flask was carefully evacuated and backfilled with argon gas three times, and the resulting mixture was then heated to 80 °C. After 2.5 h, the reaction mixture was quenched with sat. NH_4Cl aq., and the mixture was partitioned with $CHCl_3$. The aqueous phase was extracted with $CHCl_3$ (× 3). The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography to provide alkyne **2**.



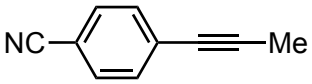
2d

Prepared following the general procedure B using 4-bromoanisole (0.370 mL, 2.80 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2d** in 86% yield (314 mg) as a colorless oil. Spectral data were in full agreement with the reported literature values.[3]



2e

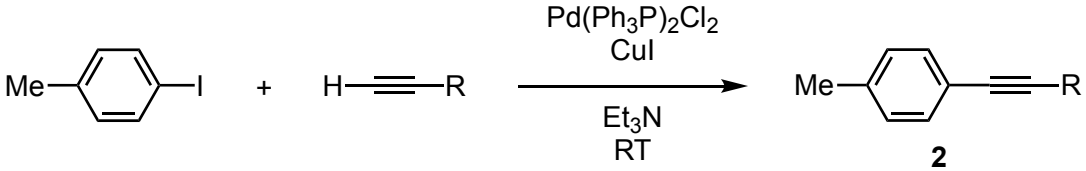
Prepared following the general procedure B using 2-bromotoluene (0.360 mL, 3.00 mmol) with the modification that the reaction was conducted at 110 °C for 3 h. Purification by column chromatography (SiO_2, hexanes) afforded **2e** in 77% yield (302 mg) as a colorless oil. Spectral data were in full agreement with the reported literature values.[4]



2f

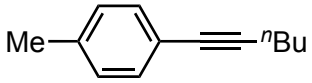
Prepared following the general procedure B using 4-bromobenzonitrile (271 mg, 1.50 mmol) with the modification that tetrabutylammonium fluoride (TBAF, 1.0 M in THF, 3.0 equiv) was used as a base instead of DBU, and the reaction was conducted at 110 °C for 2 h. Purification by column chromatography (SiO_2, hexanes) afforded **2f** in 74% yield (156 mg) as a white solid. Spectral data were in full agreement with the reported literature values.[3]

General Procedure C



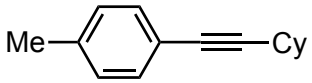
2

To a round-bottom flask containing a solution of 4-iodotoluene (1.0 equiv) and terminal alkyne (1.2 equiv) in Et_3N (0.75 M) was added $Pd(Ph_3P)_2Cl_2$ (5 mol%) and CuI (10 mol%). The flask was carefully evacuated and backfilled with argon gas three times, and the resulting mixture was stirred at room temperature. After 23 h, the reaction mixture was filtered through a pad of Celite/SiO_2, and the filter cake was rinsed with hexanes. The resulting filtrate was then concentrated and purified by column chromatography to provide alkyne **2**.



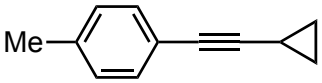
2h

Prepared following the general procedure C using 1-hexyne (0.38 mL, 3.30 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2h** in 95% yield (495 mg) as a pale-yellow oil. Spectral data were in full agreement with the reported literature values.[5]



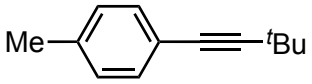
2i

Prepared following the general procedure C using cyclohexylacetylene (1.00 g, 9.24 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2i** in 82% yield (1.25 g) as a colorless oil. Spectral data were in full agreement with the reported literature values.[6]



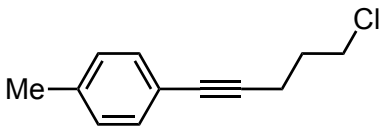
2j

Prepared following the general procedure C using cyclopropylacetylene (0.41 mL, 4.80 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2j** in 83% yield (519 mg) as a colorless oil. Spectral data were in full agreement with the reported literature values.[7]



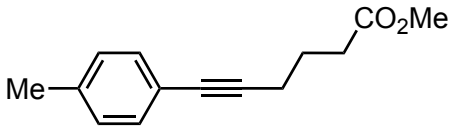
2k

Prepared following the general procedure C using 3,3-dimethyl-1-butyne (1.47 mL, 12.0 mmol). Purification by column chromatography (SiO_2, hexanes) afforded **2k** in 75% yield (1.28 g) as a colorless oil. Spectral data were in full agreement with the reported literature values.[8]



2l

Prepared following the general procedure C using 5-chloro-1-pentyne (0.63 mL, 6.0 mmol). Purification by column chromatography (SiO_2, 100/0 to 90/10hexanes/EtOAc) afforded **2l** in 69% yield (668 mg) as a pale-yellow oil. Spectral data were in full agreement with the reported literature values.[9]



2m

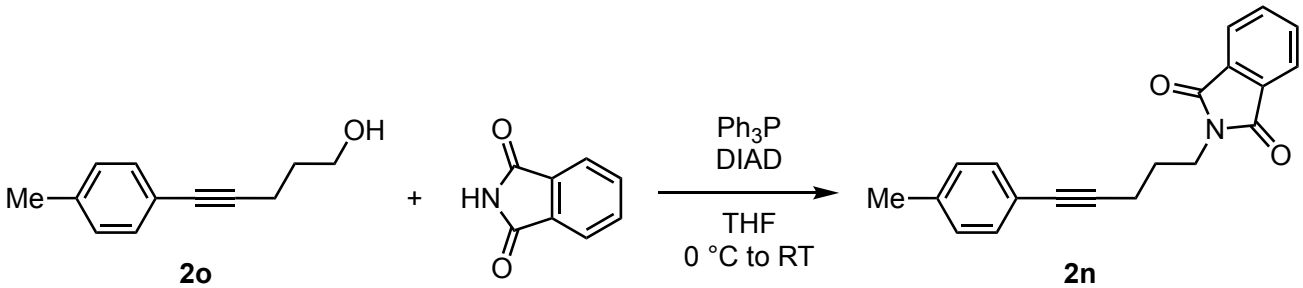
Prepared following the general procedure C using methyl 5-hexynoate (757 mg, 6.00 mmol). Purification by column chromatography (SiO_2, 95/5 to 85/15 hexanes/EtOAc) afforded **2m** in 77% yield (827 mg) as a pale-yellow oil.

R_f: 0.23 (10/1 hexanes/EtOAc, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 3.68 (s, 3H), 2.51 (t, *J* = 7.0 Hz, 2H), 2.48 (t, *J* = 7.0 Hz, 2H), 2.33 (s, 3H), 1.93 (quint, *J* = 7.0 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.8, 137.8, 131.5, 129.1, 120.7, 88.1, 81.6, 51.7, 33.0, 24.1, 21.5, 19.0;

HRMS (ESI): Calc'd for $C_{14}H_{16}O_2Na$ $[M+Na]^+$: 239.1043, found: 239.1035.



2o **2n**

To a round-bottom 50 mL flask containing a solution of **2o** (523 mg, 3.00 mmol, 1.0 equiv), phthalimide (574 mg, 3.90 mmol, 1.3 equiv) and Ph_3P (1.02 g, 3.90 mmol, 1.3 equiv) in Et_3N (10 mL) was cooled to 0 °C. Diisopropyl azodicarboxylate (1.9 M solution in toluene, 2.05 mL, 3.90 mmol, 1.3 equiv) was added dropwise over 3 min and the resulting mixture was warmed to room temperature. After 18 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 95/5 to 80/20 hexanes/EtOAc) to provide **2n** as an off-white solid (788 mg, 87%).

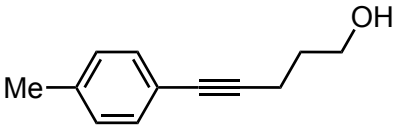
Melting Point: 113–115 °C;

R_f: 0.49 (5/1 hexanes/EtOAc, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.67 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 3.86 (t, *J* = 7.0 Hz, 2H), 2.49 (t, *J* = 7.0 Hz, 2H), 2.31 (s, 3H), 2.01 (quint, *J* = 7.0 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.5, 137.6, 134.0, 132.2, 131.5, 128.9, 123.3, 120.6, 88.0, 81.4, 37.5, 27.6, 21.5, 17.4;

HRMS (ESI): Calc'd for $C_{20}H_{17}NO_2Na$ $[M+Na]^+$: 326.1152, found: 326.1156.

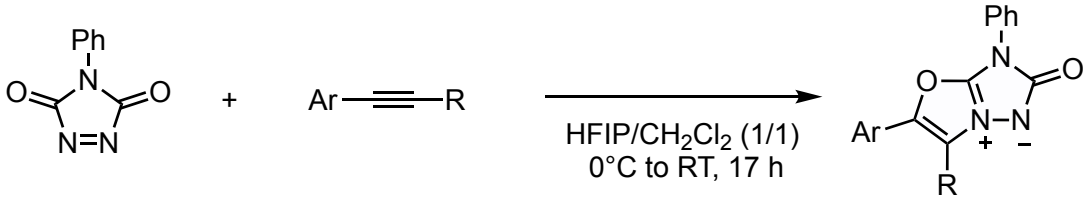


2o

Prepared following the general procedure C using 4-pentyn-1-ol (1.47 mL, 18.0 mmol). Purification by column chromatography (SiO_2, 95/5 to 85/15 hexanes/EtOAc) afforded **2o** in 90% yield (2.34 g) as a brown solid. Spectral data were in full agreement with the reported literature values.[10]

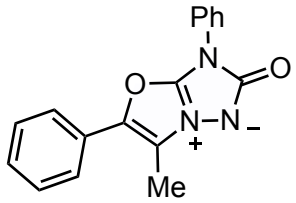
3. Azo-Yne [3+2] Reactions

3-1. General Procedure



PTAD (**1**) **2** **3**

A 4 mL scintillation vial charged with a solution of alkyne **2** (0.40 mmol) in HFIP (0.5 mL) and CH_2Cl_2 (0.5 mL) was cooled to 0 °C. PTAD (**1**) (35.0 mg, 0.20 mmol) was added, and the resulting mixture was warmed to room temperature (20–23 °C). After 17 h, the solvent was removed under reduced pressure, and the crude residue was purified by column chromatography to provide **3**.



3a

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2a** (49 μL, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 20/1 $CHCl_3$/MeOH) provided **3a** as an off-white solid (43.6 mg, 74%). A single crystal suitable for X-ray crystallographic analysis was grown by slow diffusion of hexanes into a solution of **3a** in EtOAc at room temperature.

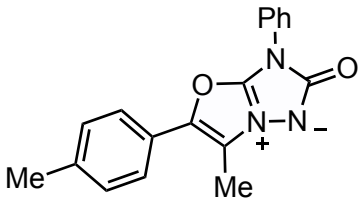
Melting Point: 165 °C (decomp.);

R_f: 0.24 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (d, J = 7.4 Hz, 2H), 7.57 (d, J = 7.4 Hz, 2H), 7.52–7.48 (m, 4H), 7.42 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 2.61 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.9, 144.9, 144.0, 132.2, 129.8, 129.6, 129.4, 128.0, 126.3, 125.5, 121.9, 119.0, 8.4;

HRMS (ESI): Calc'd for $C_{17}H_{14}N_3O_2$ $[M+H]^+$: 292.1081, found: 292.1081.



3b

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2b** (52.1 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3b** as an off-white solid (43.5 mg, 71%).

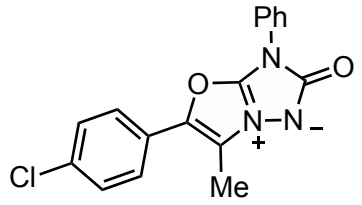
Melting Point: 155 °C (decomp.);

R_f: 0.28 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 2.60 (s, 3H), 2.42 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.8, 145.1, 143.8, 139.9, 132.4, 130.0, 129.7, 127.8, 125.5, 123.5, 121.6, 118.3, 21.5, 8.3;

HRMS (ESI): Calc'd for $C_{18}H_{16}N_3O_2$ $[M+H]^+$: 306.1237, found: 306.1234.



3c

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2c** (60.2 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3c** as an off-white solid (70.1 mg, 71%).

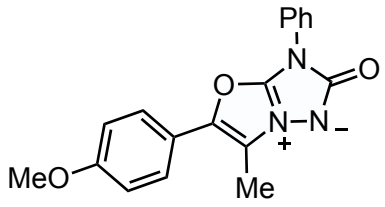
Melting Point: 148 °C (decomp.);

R_f: 0.25 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (d, J = 7.8 Hz, 2H), 7.55–7.48 (m, 6H), 7.40 (t, J = 7.8 Hz, 1H), 2.63 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.7, 144.0, 143.8, 135.6, 132.2, 129.8, 129.7, 128.0, 126.6, 124.9, 121.8, 119.5, 8.4;

HRMS (ESI): Calc'd for $C_{17}H_{13}ClN_3O_2$ $[M+H]^+$: 326.0691, found: 326.0682.



3d

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2b** (58 μL, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3d** as a white solid (57.6 mg, 89%).

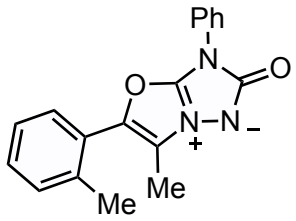
Melting Point: 154 °C (decomp.);

R_f: 0.21 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.54–7.50 (m, 4H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 3.87 (s, 3H), 2.59 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 160.7, 158.9, 145.1, 143.8, 132.6, 129.8, 127.8, 127.5, 121.7, 118.8, 117.7, 114.9, 55.6, 8.3;

HRMS (ESI): Calc'd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$: 322.1186, found: 322.1188.



3e

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2b** (52.1 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3e** as an off-white solid (40.0 mg, 65%).

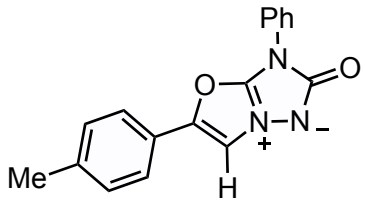
Melting Point: 169 °C (decomp.);

R_f: 0.28 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.37–7.31 (m, 4H), 2.42 (s, 3H), 2.39 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.8, 144.9, 144.3, 138.6, 132.5, 131.2, 131.1, 130.8, 129.6, 127.6, 126.4, 124.6, 121.4, 120.5, 20.3, 7.8;

HRMS (ESI): Calc'd for $C_{18}H_{16}N_3O_2$ $[M+H]^+$: 306.1237, found: 306.1237.



3g

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2g** (57 μL, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3e** as an off-white solid (40.4 mg, 69%).

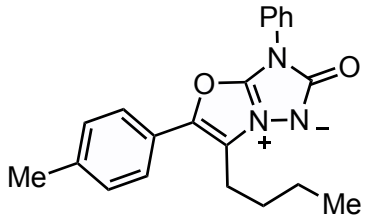
Melting Point: 195 °C (decomp.);

R_f: 0.30 (EtOAc, UV);

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.74 (s, 1H), 7.86 (d, J = 7.5 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.59 (t, J = 7.5 Hz, 2H), 7.43 (d, J = 7.5 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 2.35 (s, 3H);

^{13}C NMR (151 MHz, DMSO-d_6): δ 157.9, 148.3, 145.2, 139.1, 132.6, 129.8, 129.4, 127.3, 123.4, 123.3, 121.9, 108.5, 20.9;

HRMS (ESI): Calc'd for $C_{17}H_{14}N_3O_2$ $[M+H]^+$: 292.1081, found: 292.1083.



3h

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2h** (68.9 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3h** as an off-white solid (39.7 mg, 57%).

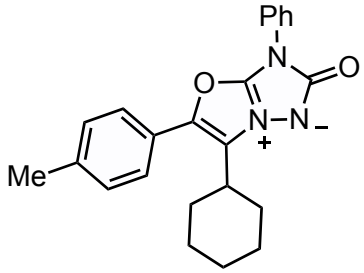
Melting Point: 119 °C (decomp.);

R_f: 0.48 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.8 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 7.8 Hz, 1H), 7.30 (d, J = 7.8 Hz, 2H), 2.95 (t, J = 7.5 Hz, 2H), 2.42 (s, 3H), 1.87 (quint, J = 7.5 Hz, 2H), 1.46 (pent, J = 7.5 Hz, 2H), 0.96 (t, J = 7.5 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.8, 144.9, 144.0, 140.1, 132.5, 130.1, 129.7, 127.8, 125.8, 123.5, 122.9, 121.8, 29.1, 22.8, 22.6, 21.5, 13.8;

HRMS (ESI): Calc'd for $C_{21}H_{22}N_3O_2$ $[M+H]^+$:348.1707, found: 348.1695.



3i

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2i** (79.3 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3i** as a white solid (60.1 mg, 80%).

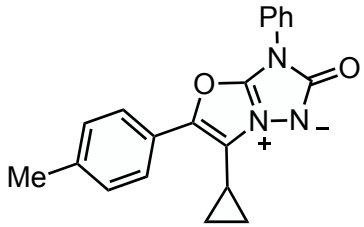
Melting Point: 186 °C (decomp.);

R_f: 0.60 (EtOAc, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 3.01 (tt, *J* = 12.5, 3.5 Hz, 1H), 2.44 (s, 3H), 2.26 (qd, *J* = 12.5, 2.9 Hz, 2H), 1.92–1.84 (m, 4H), 1.74 (d, *J* = 12.0 Hz, 1H), 1.47–1.31 (m, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.6, 144.5, 143.8, 140.3, 132.5, 130.0, 129.7, 127.7, 127.2, 126.9, 123.6, 121.8, 34.3, 29.4, 26.1, 25.2, 21.6;

HRMS (ESI): Calc'd for $C_{23}H_{24}N_3O_2$ $[M+H]^+$:374.1863, found: 374.1869.



3j

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2j** (62.6 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 25/1 $CHCl_3$/MeOH) provided **3i** as a white solid (18.6 mg, 28%).

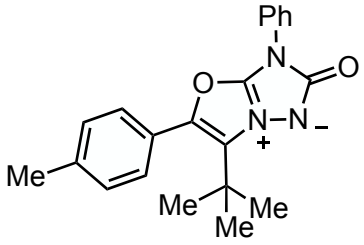
Melting Point: 157 °C (decomp.);

R_f: 0.31 (EtOAc, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 2.42 (s, 3H), 2.12–2.07 (m, 1H), 1.39 (td, *J* = 5.6, 4.4 Hz, 2H), 1.17 (td, *J* = 7.6, 5.6 Hz, 2H);

^{13}C NMR (151 MHz, DMSO-d_6): δ 157.7, 144.2, 144.1, 138.6, 132.4, 129.7, 129.4, 127.4, 125.2, 123.9, 122.7, 122.1, 20.9, 5.9, 4.4;

HRMS (ESI): Calc'd for $C_{20}H_{18}N_3O_2$ $[M+H]^+$: 332.1394, found: 332.1384



3k

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2k** (68.9 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 0/100 hexanes/EtOAc) provided **3k** as an off-white solid (46.1 mg, 66%).

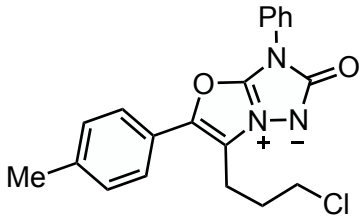
Melting Point: 196 °C (decomp.)

R_f: 0.56 (EtOAc, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83–7.81 (m, 2H), 7.47–7.43 (m, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.34–7.28 (m, 3H), 2.43 (s, 3H), 1.40 (s, 9H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.5, 144.5, 143.9, 141.7, 132.5, 131.8, 131.7, 129.6, 129.3, 127.6, 124.1, 121.8, 32.0, 28.6, 21.7;

HRMS (ESI): Calc'd for $C_{21}H_{22}N_3O_2$ $[M+H]^+$: 348.1707, found: 348.1701.



3l

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2l** (77.1 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3l** as an off-white solid (40.1 mg, 55%).

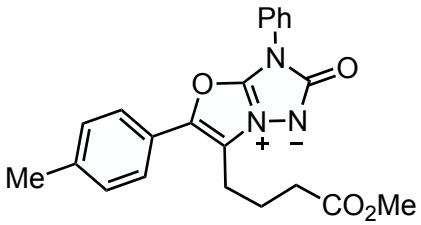
Melting Point: 120 °C (decomp.)

R_f: 0.48 (20/1 $CHCl_3$/MeOH, UV);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, J = 9.0 Hz, 2H), 7.55–7.50 (m, 4H), 7.39 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 2H), 3.68 (t, J = 5.9 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 2.46–2.40 (m, 2H), 2.43 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.8, 145.6, 144.2, 140.4, 132.4, 130.2, 129.8, 128.0, 126.0, 123.2, 121.9, 121.1, 44.1, 29.3, 21.6, 20.5;

HRMS (ESI): Calc'd for $C_{20}H_{18}ClN_3O_2Na$ $[M+Na]^+$: 390.0981, found: 390.0991.



3m

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2m** (86.5 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3m** as a yellow solid (64.4 mg, 82%).

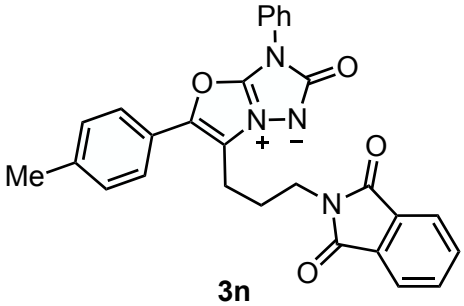
Melting Point: 125 °C (decomp.)

R_f: 0.48 (20/1 $CHCl_3$/MeOH, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.6 Hz, 2H), 7.54–7.49 (m, 4H), 7.39 (t, *J* = 7.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.66 (s, 3H), 3.05 (t, *J* = 7.5 Hz, 2H), 2.49 (t, *J* = 7.5 Hz, 2H), 2.42 (s, 3H), 2.22 (quint, *J* = 7.5 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.1, 158.7, 145.3, 143.9, 140.1, 132.3, 130.0, 129.6, 127.7, 125.7, 123.1, 121.65, 121.60, 51.7, 32.8, 22.11, 22.07, 21.4;

HRMS (ESI): Calc'd for $C_{22}H_{22}N_3O_4$ $[M+H]^+$: 392.1605, found: 392.1624.



3n

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2n** (121 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3n** as a yellow solid (74.4 mg, 78%).

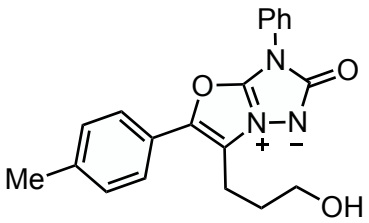
Melting Point: 190 °C (decomp.)

R_f: 0.48 (20/1 $CHCl_3$/MeOH, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.79 (m, 4H), 7.71–7.70 (m, 2H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.41–7.36 (m, 3H), 7.22 (d, *J* = 8.3 Hz, 2H), 3.82 (t, *J* = 7.3 Hz, 2H), 3.05 (t, *J* = 7.3 Hz, 2H), 2.38 (s, 3H), 2.30 (quint, *J* = 7.3 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.3, 158.7, 145.3, 144.1, 140.2, 134.1, 132.3, 131.9, 130.0, 129.7, 127.8, 125.9, 123.4, 123.1, 121.8, 121.3, 37.1, 25.7, 21.5, 20.5;

HRMS (ESI): Calc'd for $C_{28}H_{22}N_4O_4Na$ $[M+Na]^+$: 501.1533, found: 501.1526.



3o

Prepared from PTAD (**1**) (35.0 mg, 0.20 mmol) and **2o** (69.7 mg, 0.40 mmol) following the general procedure. Purification by column chromatography (SiO_2, 100/0 to 20/1 $CHCl_3$/MeOH) provided **3o** as a beige solid (36.6 mg, 52%).

Melting Point: 155 °C (decomp.)

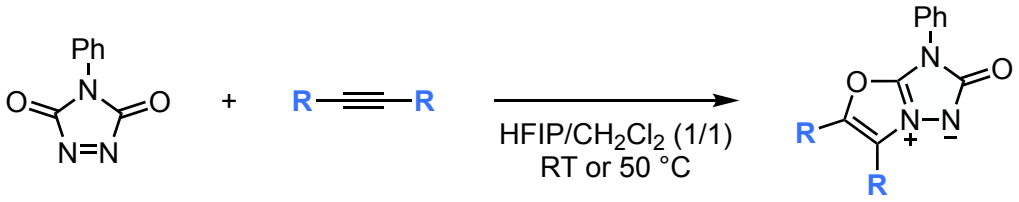
R_f: 0.41 (20/1 $CHCl_3$/MeOH, UV);

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 3.76 (t, *J* = 6.0 Hz, 2H), 3.43 (brs, 1H), 3.14 (t, *J* = 6.0 Hz, 2H), 2.42 (s, 3H), 2.11 (quint, *J* = 6.0 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.5, 145.4, 143.9, 140.2, 132.3, 130.1, 129.8, 128.0, 125.7, 123.4, 122.3, 121.9, 60.3, 30.4, 21.6, 19.1;

HRMS (ESI): Calc'd for $C_{20}H_{19}N_3O_3Na$ $[M+Na]^+$: 372.1319, found: 372.1320.

3-2. Limitations



R	temp	results
n-Pr	RT to 50 °C	recovery of alkyne (PTAD was fully consumed)
Ph	RT	complex mixtures

4. X-ray Crystallographic Analysis

Data collection and Structure solution details: Single crystal X-ray data for **3a** was collected on a Rigaku XtaLaB P200 diffractometer Cu-Kα radiation. Data collection, cell refinement, data reduction and analysis were carried out with the CrysAlisPro (Rigaku Oxford Diffraction). These structures were solved by intrinsic phasing methods with the SHELXT program and refines using SHELXL[11–13] with anisotropic displacement parameters for non-H atoms. CCDC 2292795 (for **3a**) contains the supplementary crystallographic data for this paper, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif

Table S1. Summary of crystallographic data of **3a**

Empirical formula	$C_{17}H_{14}N_3O_2$
Formula weight	292.31
Temperature/K	100
Crystal system	triclinic
Space group	P-1
a/Å	7.1044(2)
b/Å	10.0383(3)
c/Å	10.7169(3)
α/°	102.103(3)
β/°	109.324(3)
γ/°	102.128(3)
Volume/Å^3	672.07(4)
Z	2
ρ_{calc}g/cm^3	1.444
μ/mm^{-1}	0.793
F(000)	306.0
Crystal size/mm^3	0.14 × 0.06 × 0.02
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.174 to 147.38
Index ranges	-8 ≤ h ≤ 8, -12 ≤ k ≤ 12, -12 ≤ l ≤ 13
Reflections collected	13502
Independent reflections	2613 [R_{int} = 0.0385, R_{sigma} = 0.0281]
Data/restraints/parameters	2613/0/200
Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0373, wR_2 = 0.0983
Final R indexes [all data]	R_1 = 0.0404, wR_2 = 0.1004
Largest diff. peak/hole / e Å^{-3}	0.19/-0.28

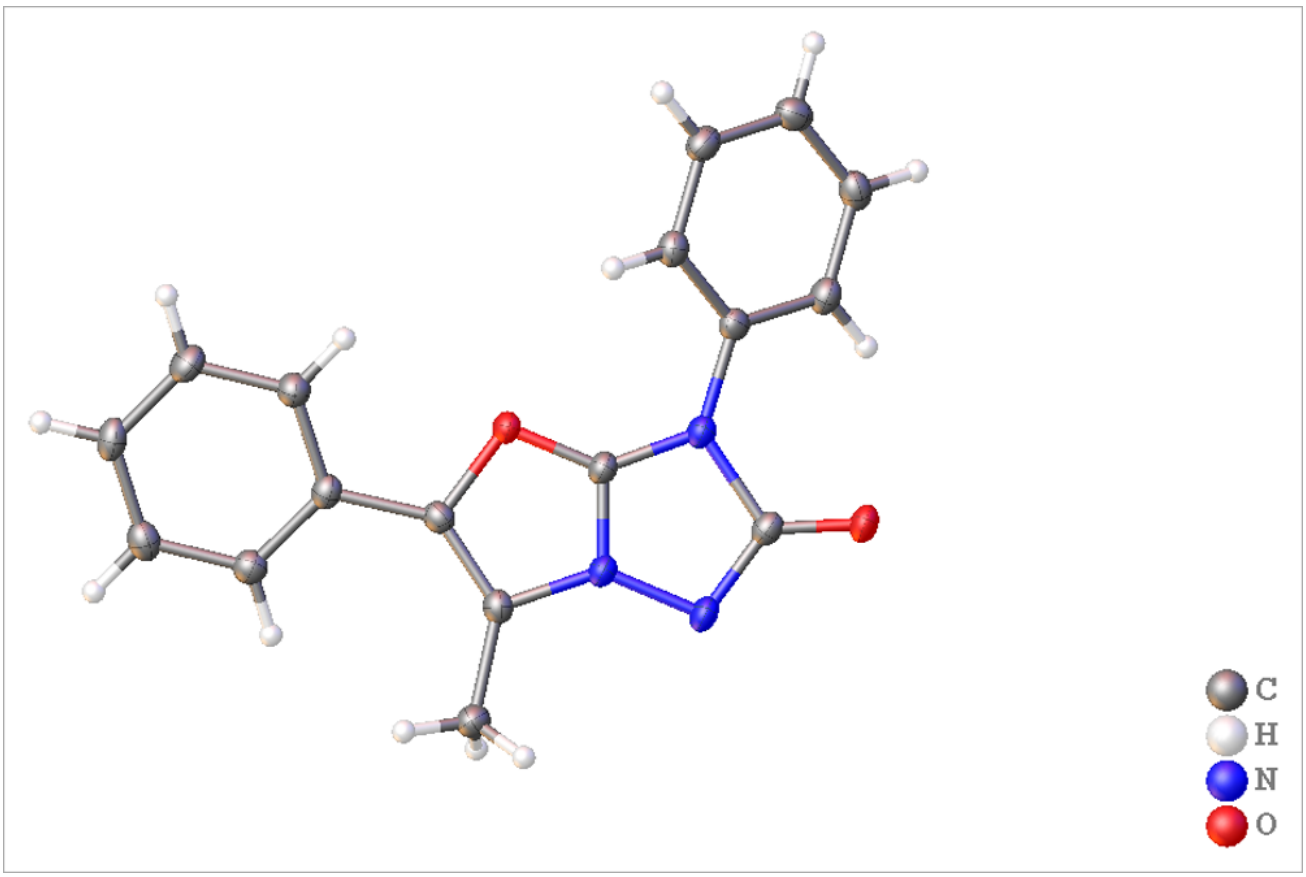


Figure S1. X-ray crystallographic structure of **3a**

5. HOMA/HOMHED Calculations

Harmonic Oscillator Model of Aromaticity (HOMA)[14] and Harmonic Oscillator Model of Aromaticity for Heterocycle Electron Delocalization (HOMHED)[15] values for **3a** were calculated from a following equation:

$$\mathrm{HOMHED(HOMA)} = 1 - \frac{1}{n}\{\alpha_{\mathrm{CC}} \sum[(R(\mathrm{CC})_{\mathrm{opt}} - R_{\mathrm{i}})]^2 + \alpha_{\mathrm{CX}} \sum[(R(\mathrm{CX})_{\mathrm{opt}} - R_{\mathrm{i}})]^2 + \alpha_{\mathrm{CY}} \sum[(R(\mathrm{CY})_{\mathrm{opt}} - R_{\mathrm{i}})]^2 + \alpha_{\mathrm{XY}} \sum[(R(\mathrm{XY})_{\mathrm{opt}} - R_{\mathrm{i}})]^2\}$$

where n is the number of bonds taken into summation, a is an empirical constant, R_{opt} is an optimal bond length, R_{i} is an experimental bond length from X-ray crystallographic structure.

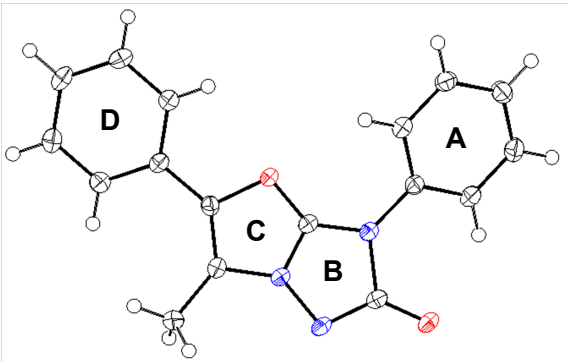
For HOMHED,

a_{CC} = 78.6, a_{CN} = 87.4, a_{CO} = 77.2, a_{NN} = 78.6, $R(\mathrm{CC})_{\mathrm{opt}}$ = 1.387 Å, $R(\mathrm{CN})_{\mathrm{opt}}$ = 1.339 Å, $R(\mathrm{CO})_{\mathrm{opt}}$ = 1.282 Å and $R(\mathrm{NN})_{\mathrm{opt}}$ = 1.311 Å were used.

For HOMA,

a_{CC} = 257.7, a_{CN} = 93.52, a_{CO} = 157.38, a_{NN} = 130.33, $R(\mathrm{CC})_{\mathrm{opt}}$ = 1.388 Å, $R(\mathrm{CN})_{\mathrm{opt}}$ = 1.334 Å, $R(\mathrm{CO})_{\mathrm{opt}}$ = 1.265 Å and $R(\mathrm{NN})_{\mathrm{opt}}$ = 1.309 Å were used.

Table S2. HOMHED and HOMA values for **3a**



Ring	HOMHED	HOMA
A	0.999	0.997
B	0.494	0.361
C	0.564	–0.043
D	0.996	0.989

6. DFT Calculations

Computational results

All the calculations were performed using Gaussian 16 program.[16,17] NICS values were calculated using the standard GIAO (GIAO=NMR) at the level of B3LYP/6-311++G(d,p) for the structure optimized at the B3LYP/6-31++G(d,p) theoretical level.

Optimized structure for 3a

O	-0.45292	-0.30253	0.03002
O	3.3325	2.48201	-0.08917
N	0.02234	1.80566	-0.02878
N	1.83407	0.63093	-0.00198
N	1.03464	2.82867	-0.07968
C	-2.91743	-0.3308	0.00789
C	-1.69272	0.45225	0.00503
C	0.51666	0.60397	0.00881
C	-1.37092	1.75265	-0.04595
C	2.72928	-0.47553	0.04276
C	2.17823	2.11111	-0.06254
C	4.0983	-0.27188	-0.04927
H	4.4687	0.72251	-0.14412
C	-2.91902	-1.60669	-0.5471
H	-2.01429	-2.00307	-0.95864
C	3.08938	-2.83948	0.21828
H	2.68948	-3.82816	0.32403
C	-4.08929	0.17754	0.55674
H	-4.08874	1.13895	1.02829
C	-4.08082	-2.35188	-0.56707
H	-4.07352	-3.33302	-0.99744
C	2.22504	-1.76257	0.17845
H	1.17118	-1.92514	0.25376
C	-5.25208	-0.56987	0.52311
H	-6.15089	-0.17018	0.94778
C	-5.25181	-1.83399	-0.0387
H	-6.15276	-2.41349	-0.05822
C	4.94888	-1.36093	-0.00717
H	6.00523	-1.19552	-0.07838
C	4.45539	-2.64581	0.12519
H	5.12344	-3.48279	0.15687

C	-2.18673	2.99544	-0.13871
H	-2.28991	3.45486	0.83806
H	-3.1669	2.78266	-0.54003
H	-1.6771	3.69871	-0.78412

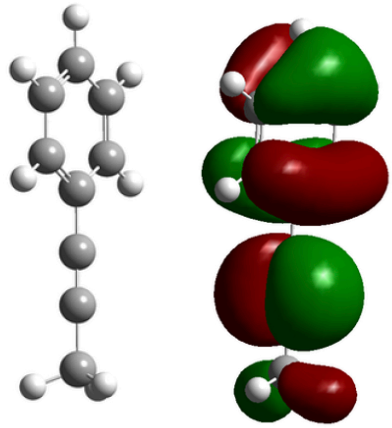
Input geometry for NICS(1) calculation of 3a

O	0.46690000	-0.32640000	-0.02410000
O	-3.29380000	2.53860000	0.05570000
N	-0.01180000	1.81700000	-0.06940000
N	-1.83290000	0.62590000	-0.00360000
N	-0.96800000	2.80480000	-0.01100000
C	2.90900000	-0.35880000	0.03200000
C	1.68010000	0.41920000	0.00390000
C	-0.50140000	0.58580000	-0.06380000
C	1.37750000	1.75620000	-0.00110000
C	-2.74650000	-0.45990000	-0.04480000
C	-2.14640000	2.13400000	0.01890000
C	-4.04660000	-0.29380000	0.45170000
H	-4.35120000	0.66960000	0.83850000
C	2.91240000	-1.66500000	0.55960000
H	1.99100000	-2.09080000	0.94220000
C	-3.23910000	-2.76250000	-0.59980000
H	-2.91980000	-3.71510000	-1.01200000
C	4.11420000	0.17530000	-0.46420000
H	4.12540000	1.16070000	-0.91720000
C	4.09160000	-2.40670000	0.59840000
H	4.07690000	-3.41210000	1.00870000
C	-2.34280000	-1.69360000	-0.57770000
H	-1.34120000	-1.81980000	-0.97490000
C	5.29260000	-0.56820000	-0.40740000
H	6.21280000	-0.14130000	-0.79500000
C	5.28810000	-1.86120000	0.12310000
H	6.20570000	-2.44030000	0.15910000
C	-4.93210000	-1.37190000	0.41220000
H	-5.93980000	-1.23940000	0.79450000
C	-4.53730000	-2.60760000	-0.10710000
H	-5.23380000	-3.44010000	-0.13050000
C	2.20300000	2.99280000	0.08330000

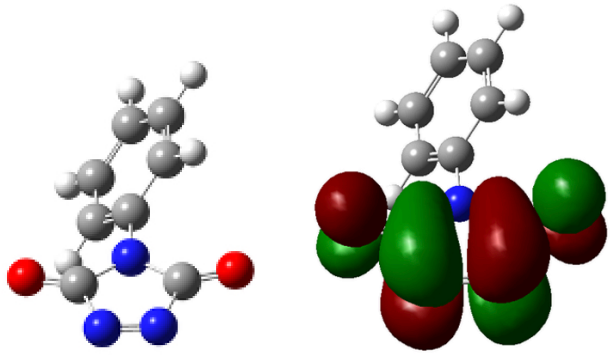
H	2.35330000	3.44230000	-0.90520000
H	3.17890000	2.77790000	0.52200000
H	1.68700000	3.73190000	0.70290000
Bq	4.10130000	-1.11410000	0.07360000
Bq	4.29740000	-0.74250000	0.98100000
Bq	3.90020000	-1.48130000	-0.83460000
Bq	0.60230000	0.85040000	-0.03090000
Bq	0.63090000	0.84130000	-1.03040000
Bq	0.57360000	0.85940000	0.96860000
Bq	-1.09210000	1.59350000	-0.02580000
Bq	-1.05330000	1.58670000	0.97340000
Bq	-1.12640000	1.60920000	-1.02510000
Bq	-3.64070000	-1.53150000	-0.07760000
Bq	-3.95480000	-1.24940000	-0.98410000
Bq	-3.32670000	-1.81370000	0.82890000

7. Mechanistic Details

We currently believe our PTAD-alkyne [3+2] cycloaddition takes place in a stepwise manner based on the following 2 reasons. First, the frontier molecular orbital analysis revealed that the calculated HOMO of alkynes and the LUMO of PTAD are mismatched to form new σ-bonds simultaneously as shown below (calculated at B3LYP/6-311++G(d,p) level of theory). Second, literature survey revealed that there are several precedents documenting the formation of vinyl cation intermediates that are stabilized by HFIP.[18]



HOMO of alkyne



LUMO of PTAD

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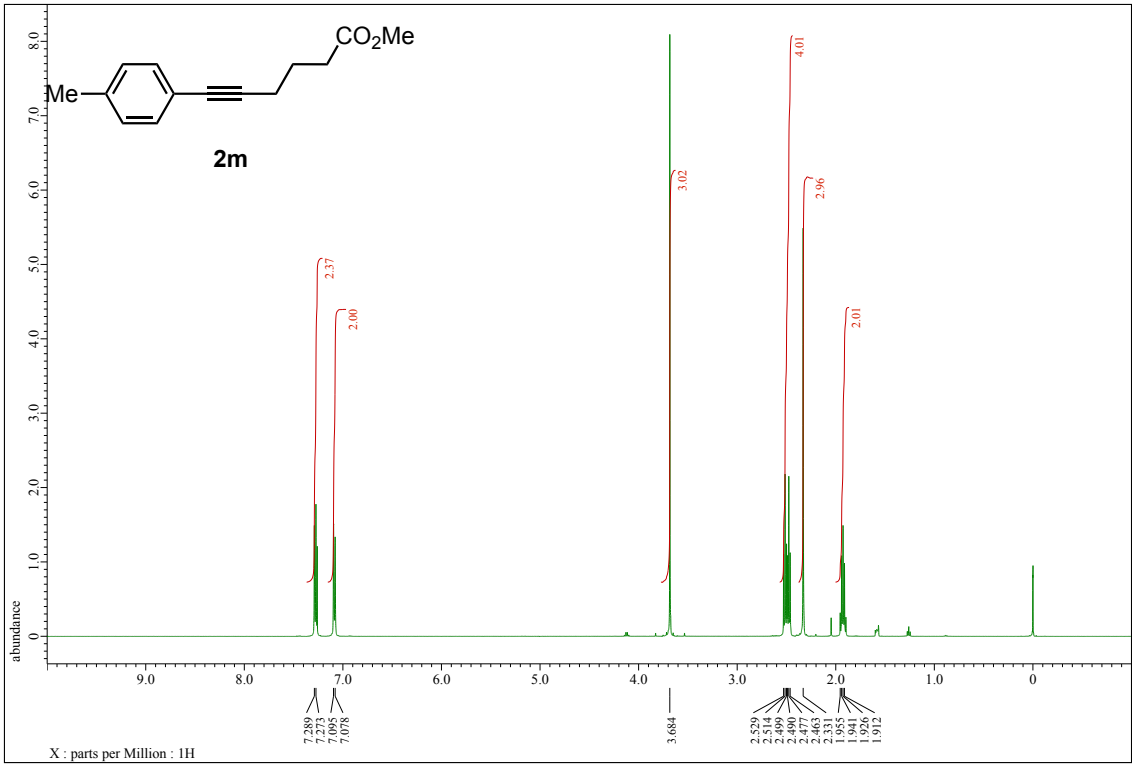
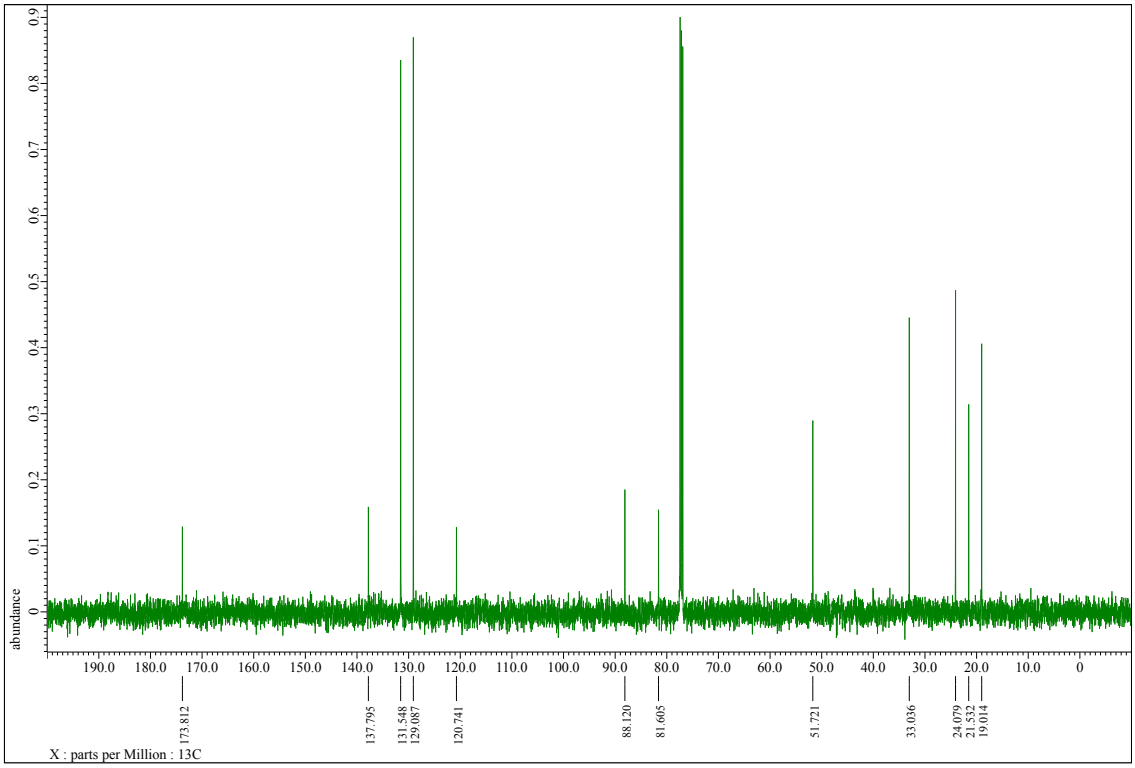
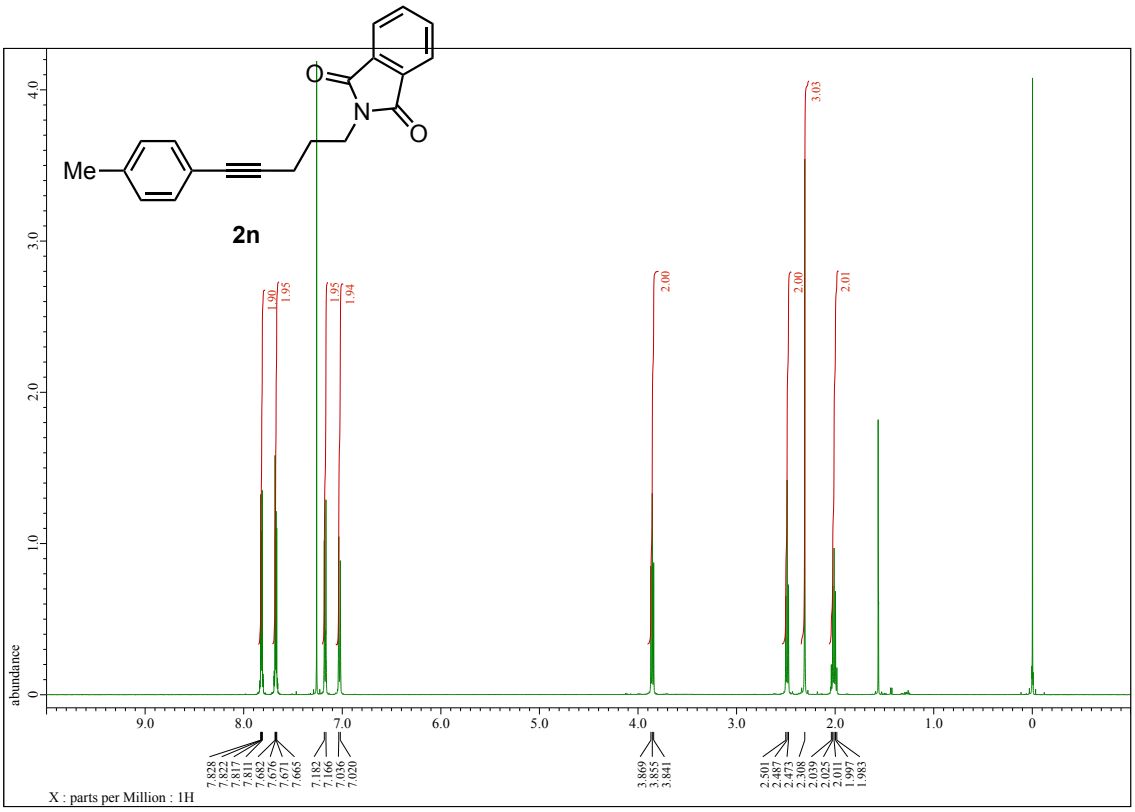
9. NMR Spectra






Me
2n
abundance
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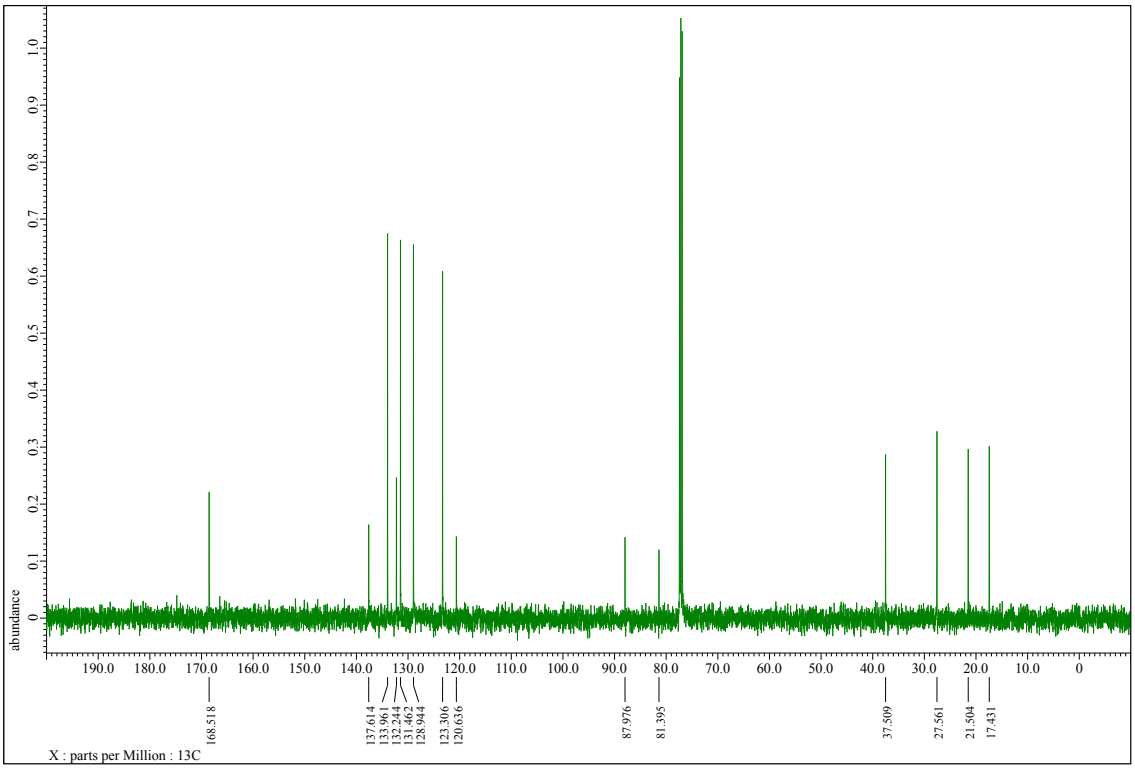
abundance
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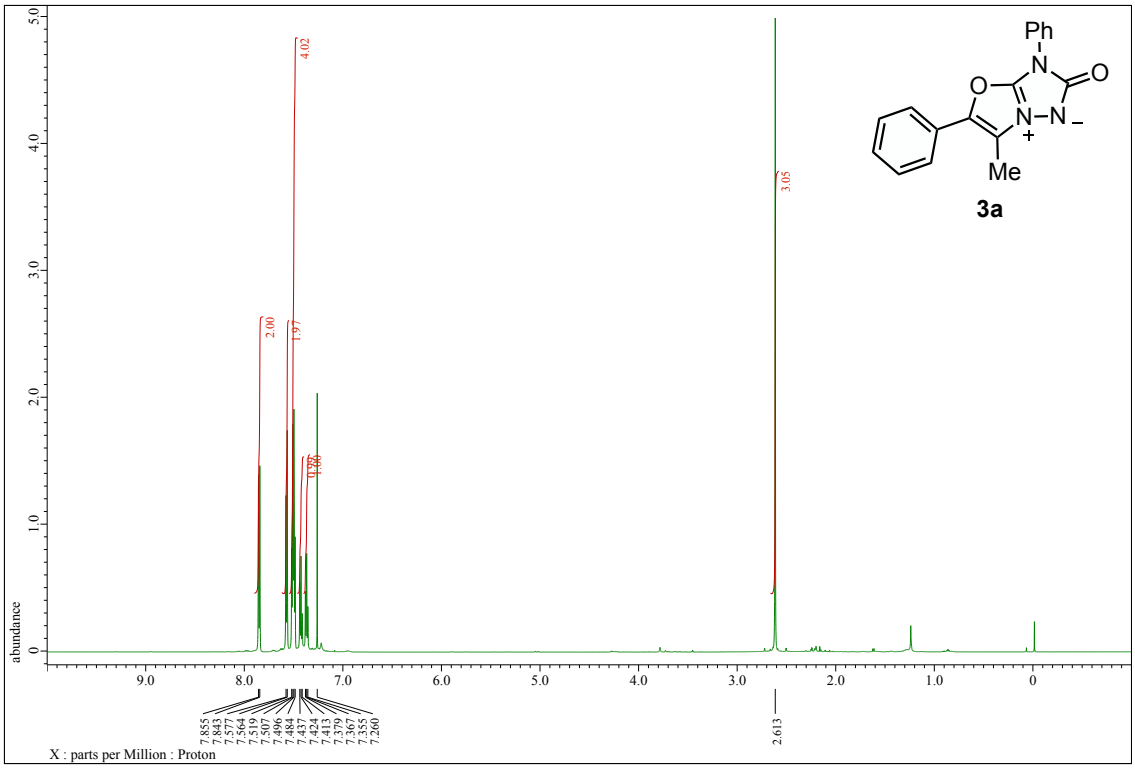
Ph
N
O
O
N–N
+
Me
3a
4.02
2.00
1.97
1.00
1.00
3.05
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.855
7.843
7.577
7.564
7.519
7.507
7.496
7.484
7.437
7.424
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7.379
7.367
7.355
7.260
2.613
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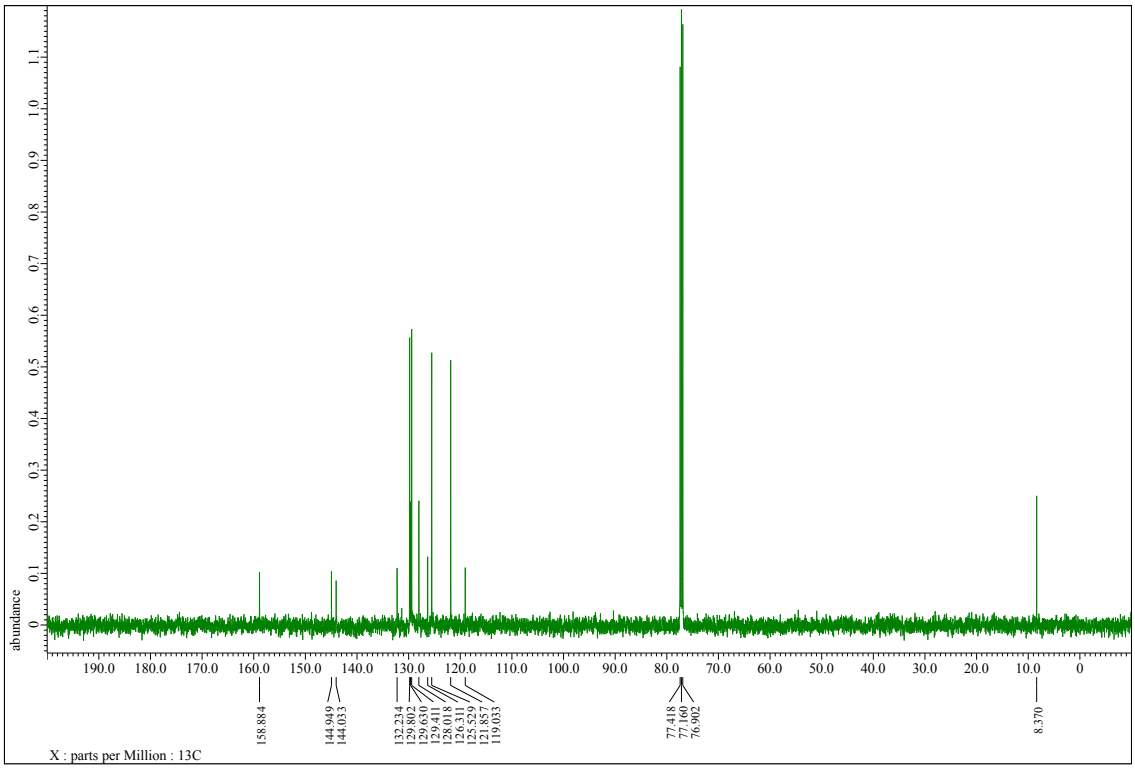
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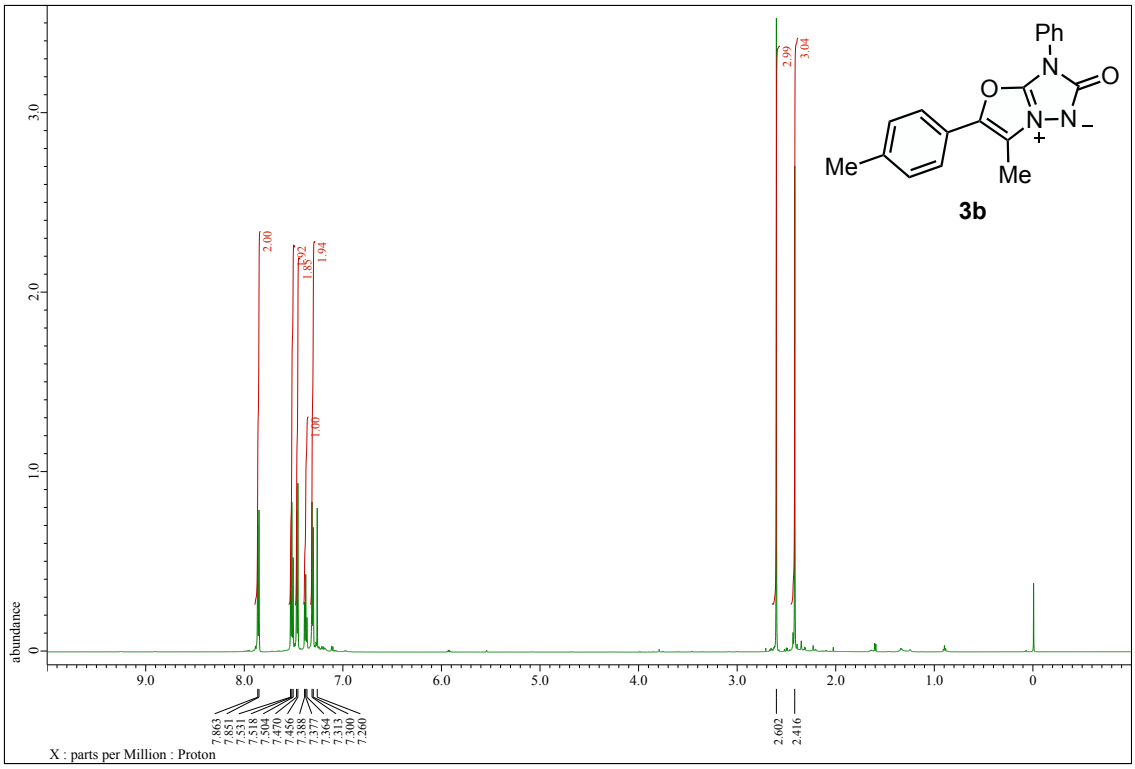
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
158.884
144.949
144.033
132.234
129.802
129.630
129.411
128.018
125.811
125.529
121.857
119.033
77.418
77.160
76.902
8.370
X : parts per Million : 13C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O
O
N–N
+
Me
Me
3b
2.99
3.04
2.00
1.92
1.85
1.94
1.00
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.863
7.851
7.531
7.518
7.504
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7.377
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2.416
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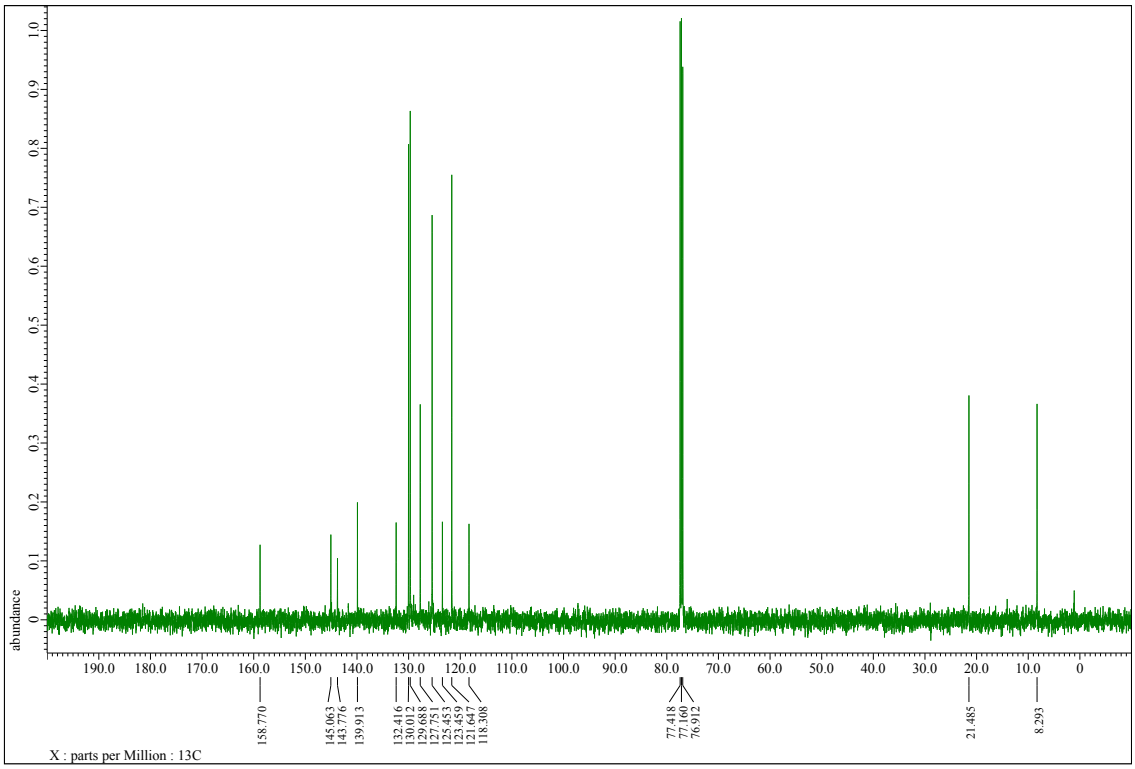
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160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
158.770
145.063
143.776
139.913
132.416
130.012
129.688
127.751
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121.647
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77.418
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76.912
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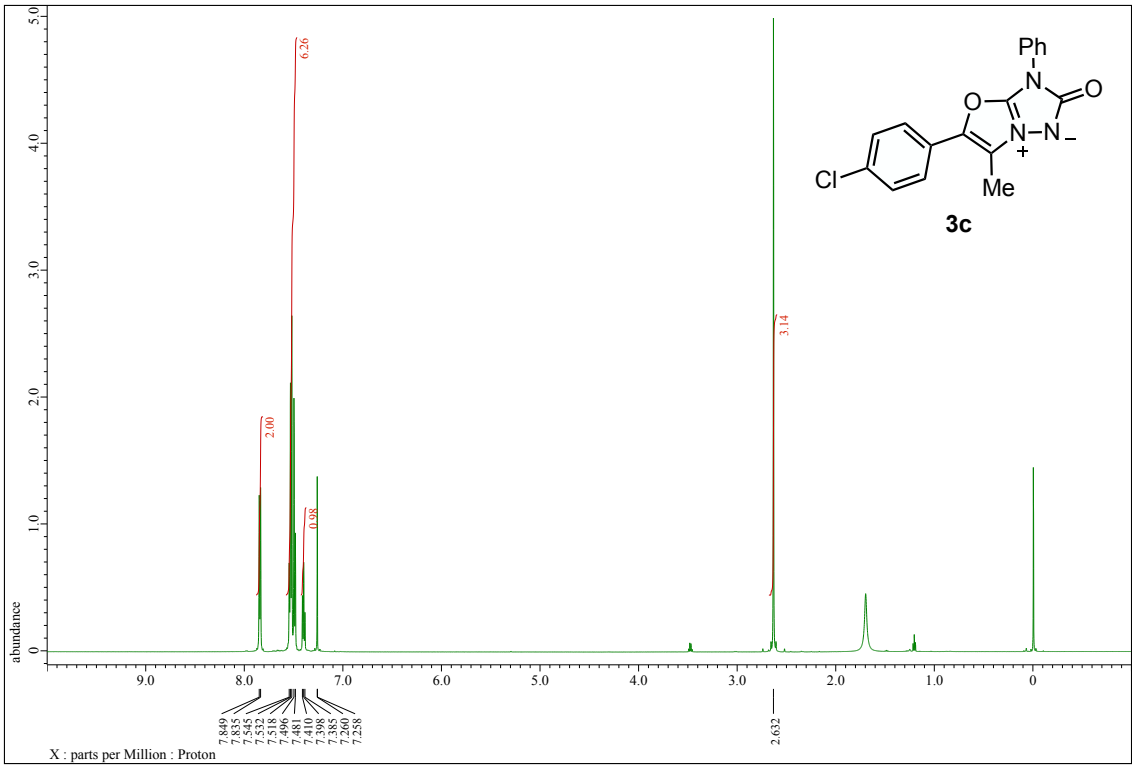
Ph
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O
O
N–N
+
Cl
Me
3c
6.26
3.14
2.00
0.98
abundance
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8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.849
7.845
7.543
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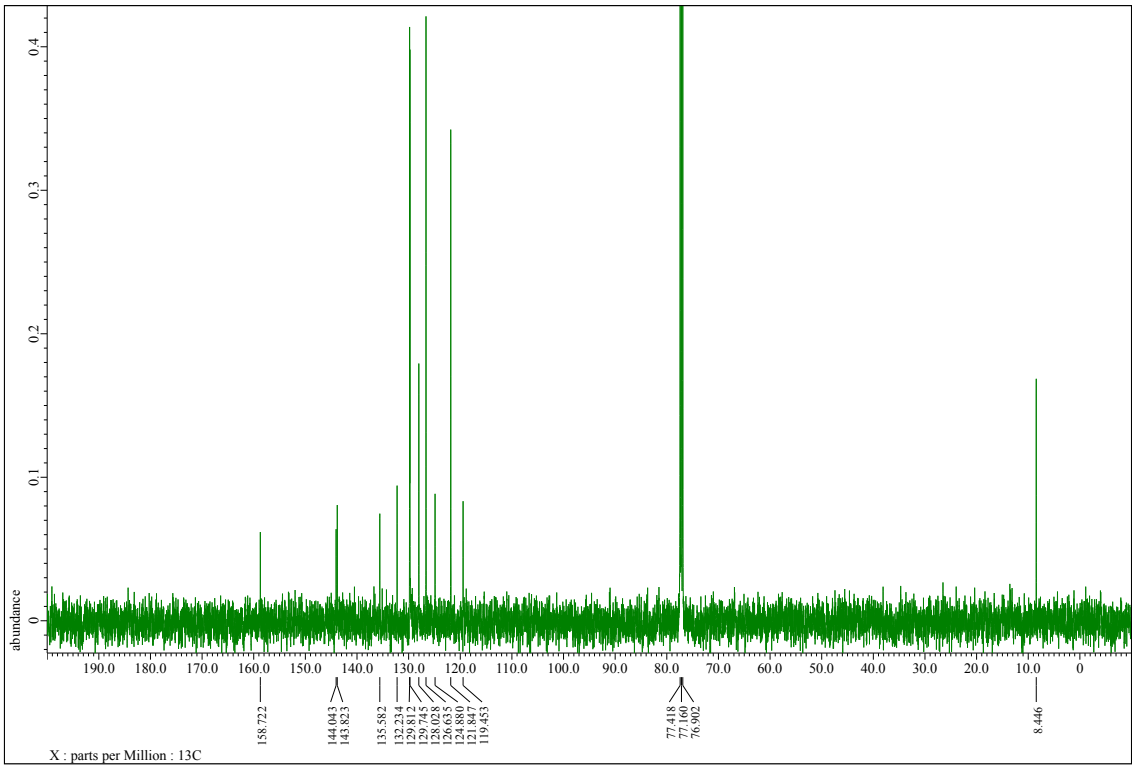
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160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
158.722
144.043
143.823
135.582
132.234
129.812
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77.160
76.902
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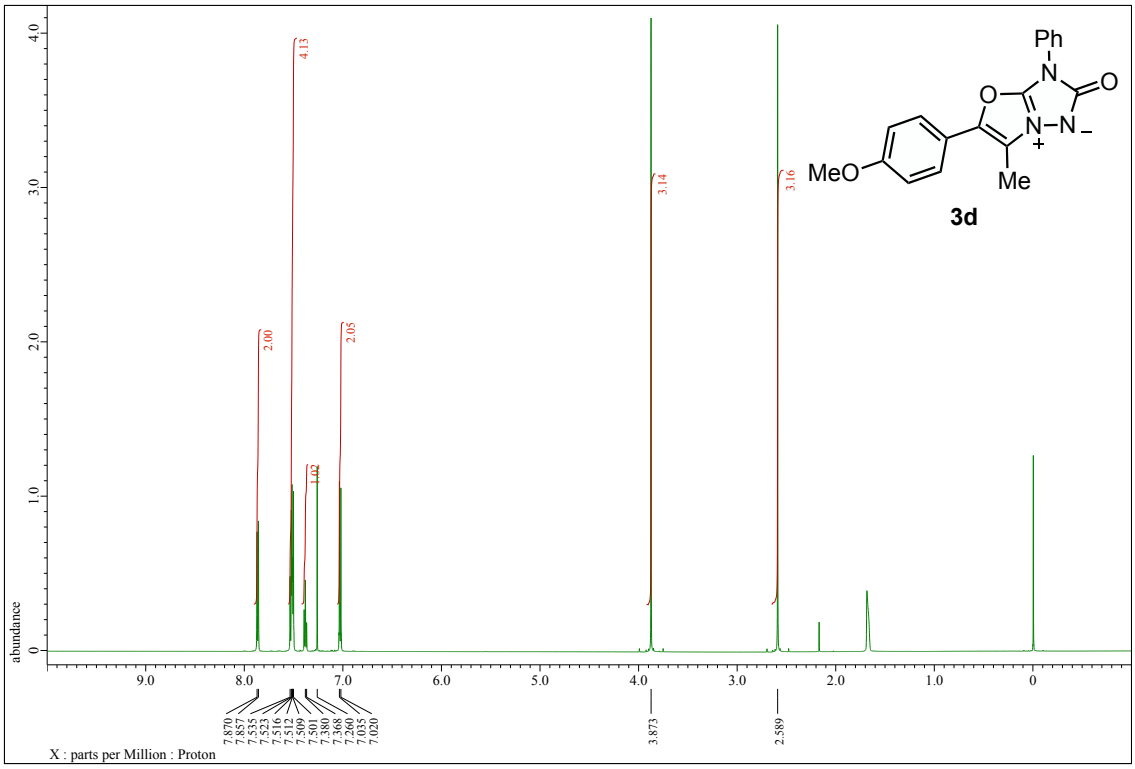
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O
N–N
+
MeO
Me
3d
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3.14
3.16
2.00
2.05
1.02
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.870
7.857
7.535
7.523
7.516
7.512
7.509
7.501
7.380
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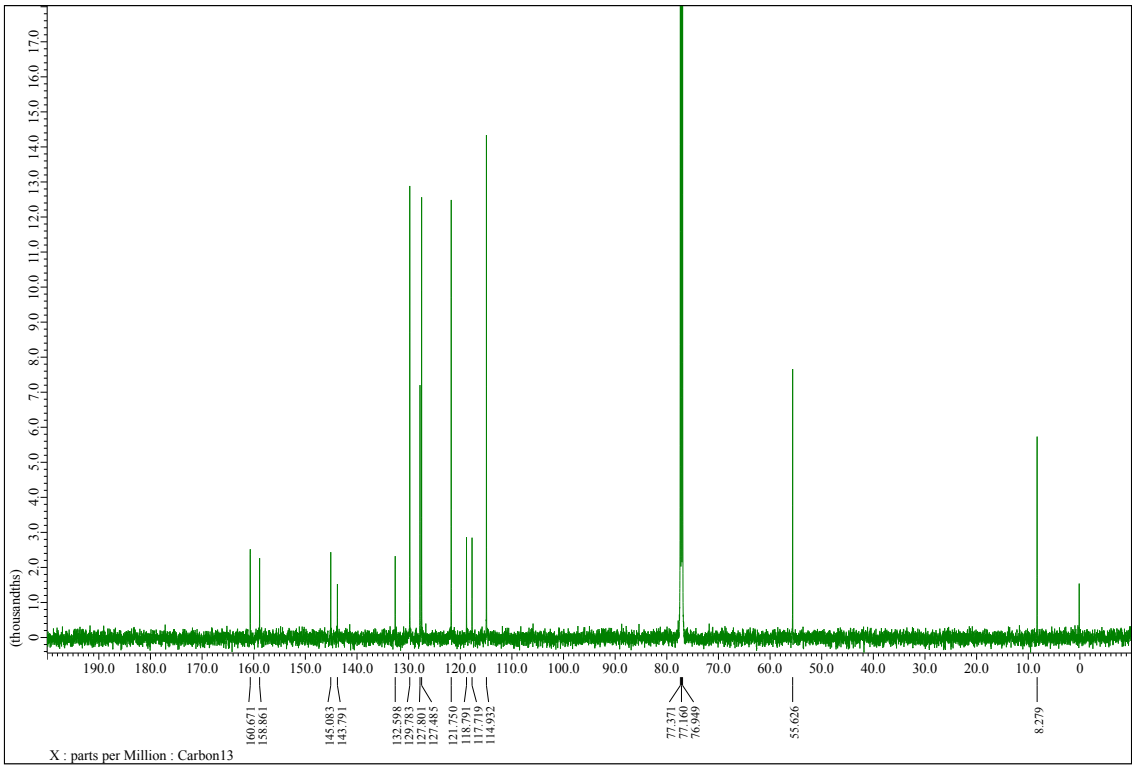
7.360
7.345
7.020
3.873
2.589
X : parts per Million : Proton


(thousandths)
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150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
160.671
158.861
145.083
143.791
132.598
129.783
127.801
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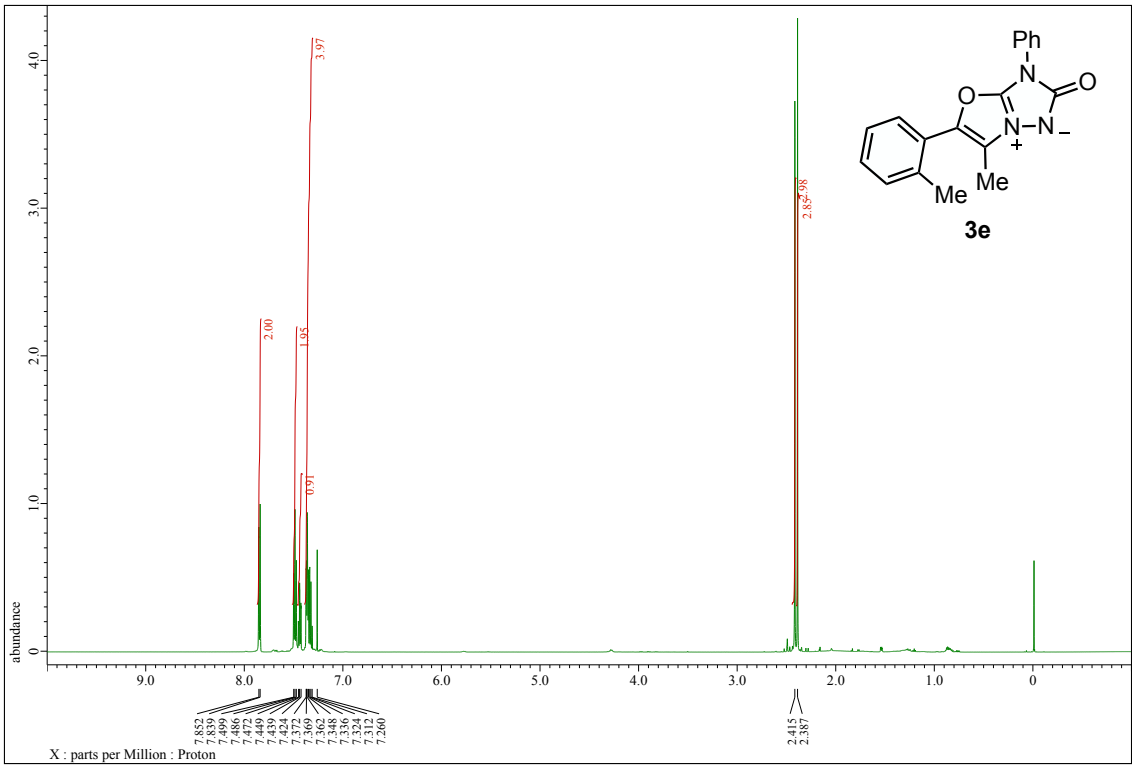
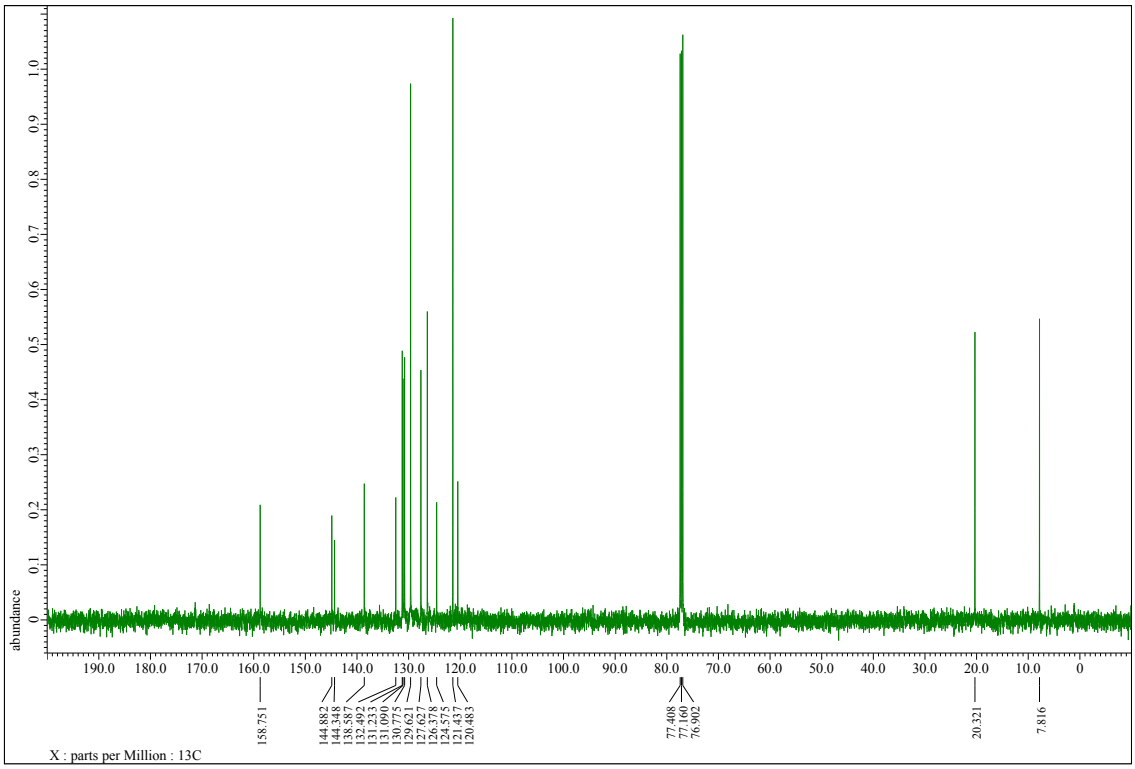
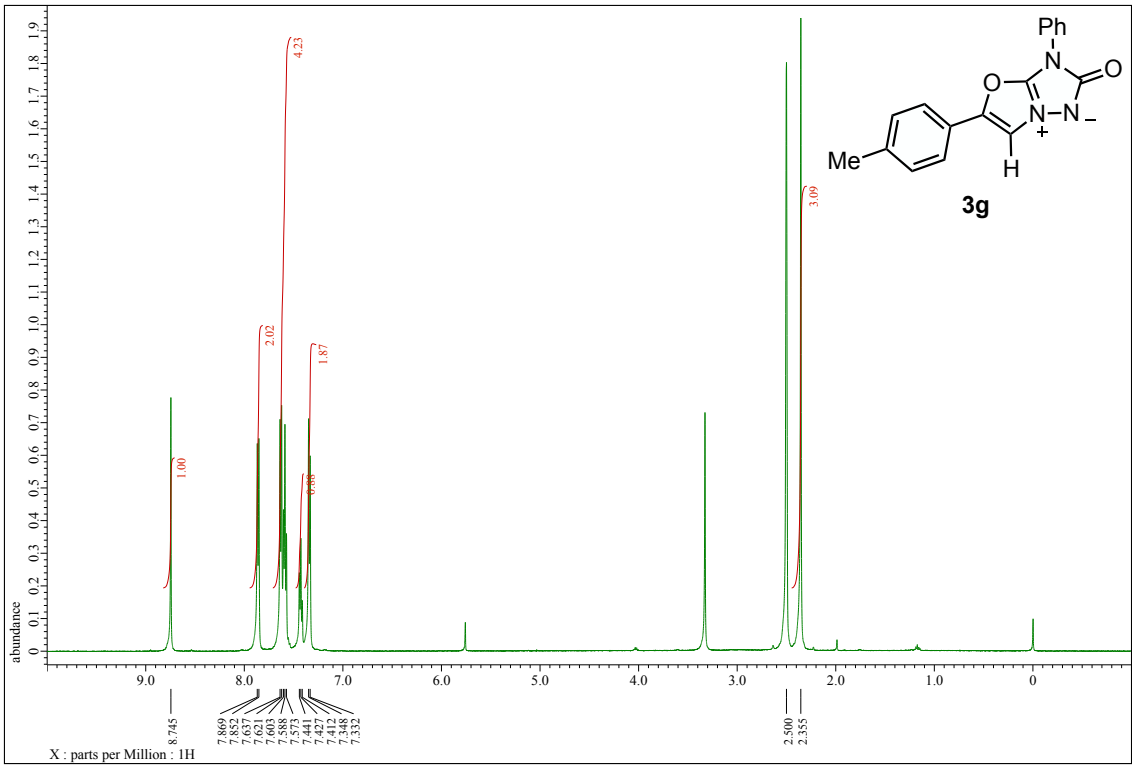

Ph
N
O
O
N–N
+
Me
Me
3e
abundance
X : parts per Million : Proton


abundance
X : parts per Million : 13C


Ph
N
O
O
N–N
+
Me
H
3g
abundance
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2.02
1.87
1.00
0.88
3.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.745
7.869
7.852
7.637
7.621
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7.448
7.332
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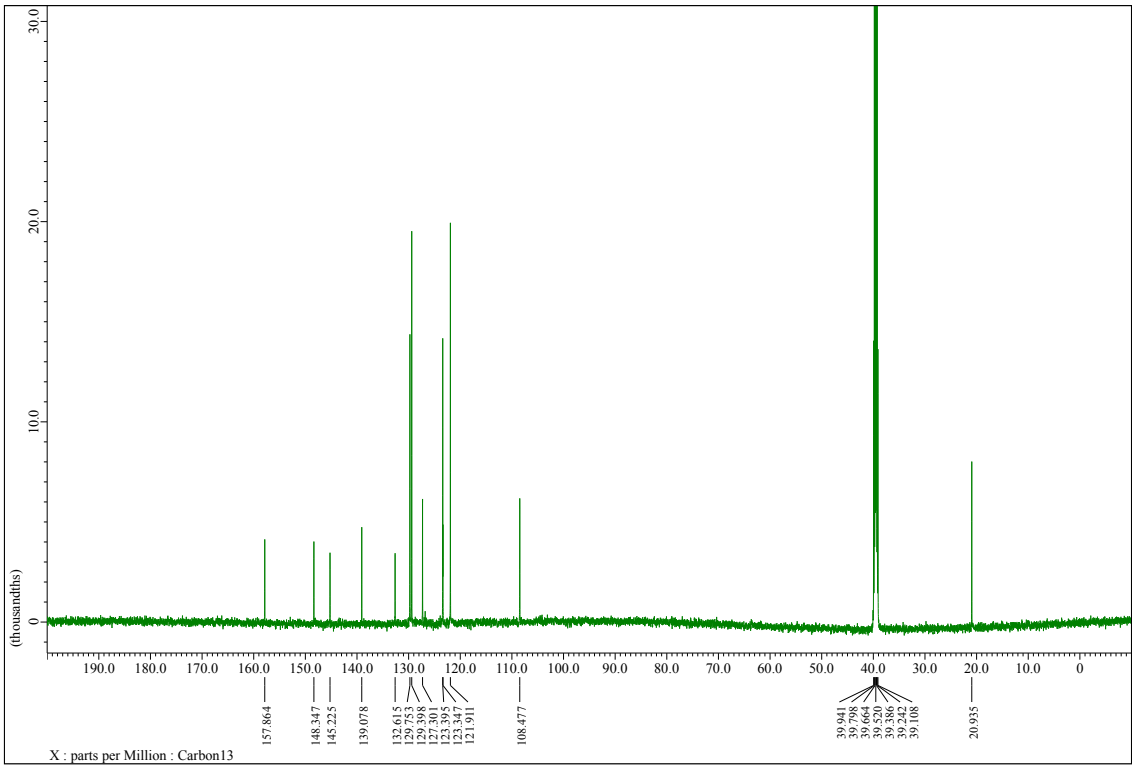
2.355
X : parts per Million : 1H


(thousandths)
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120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
157.864
148.347
145.225
139.078
132.615
129.753
129.398
127.301
123.395
123.347
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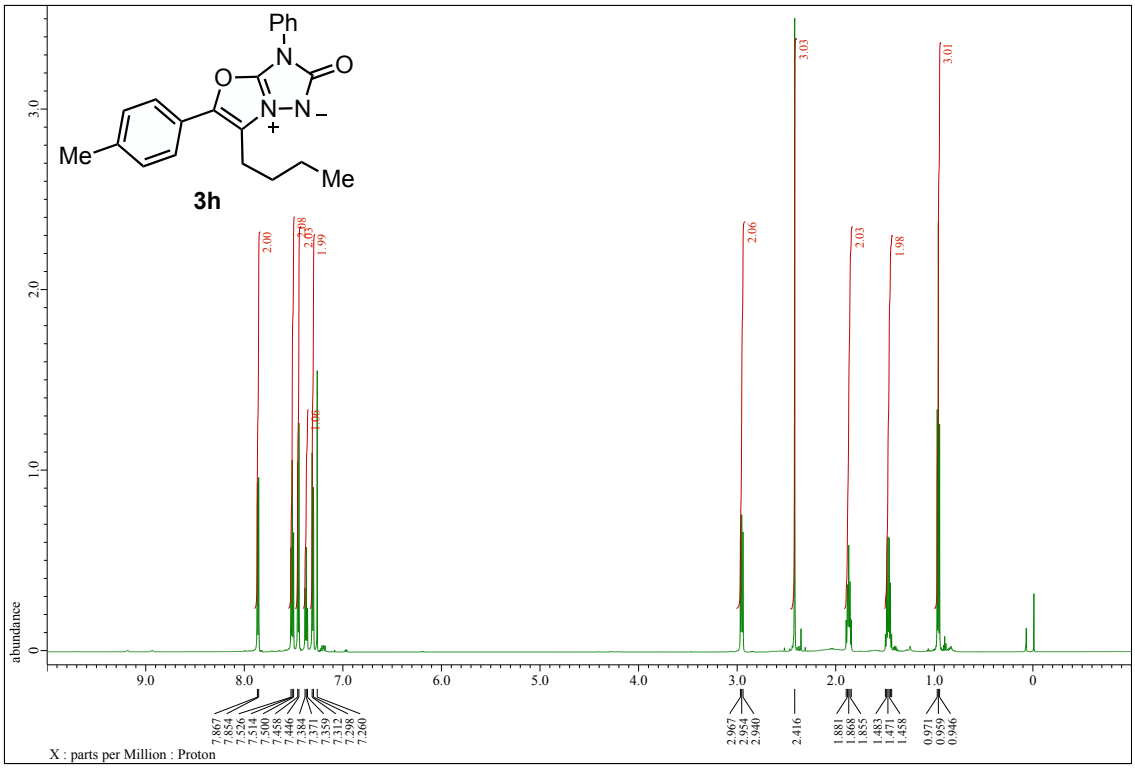
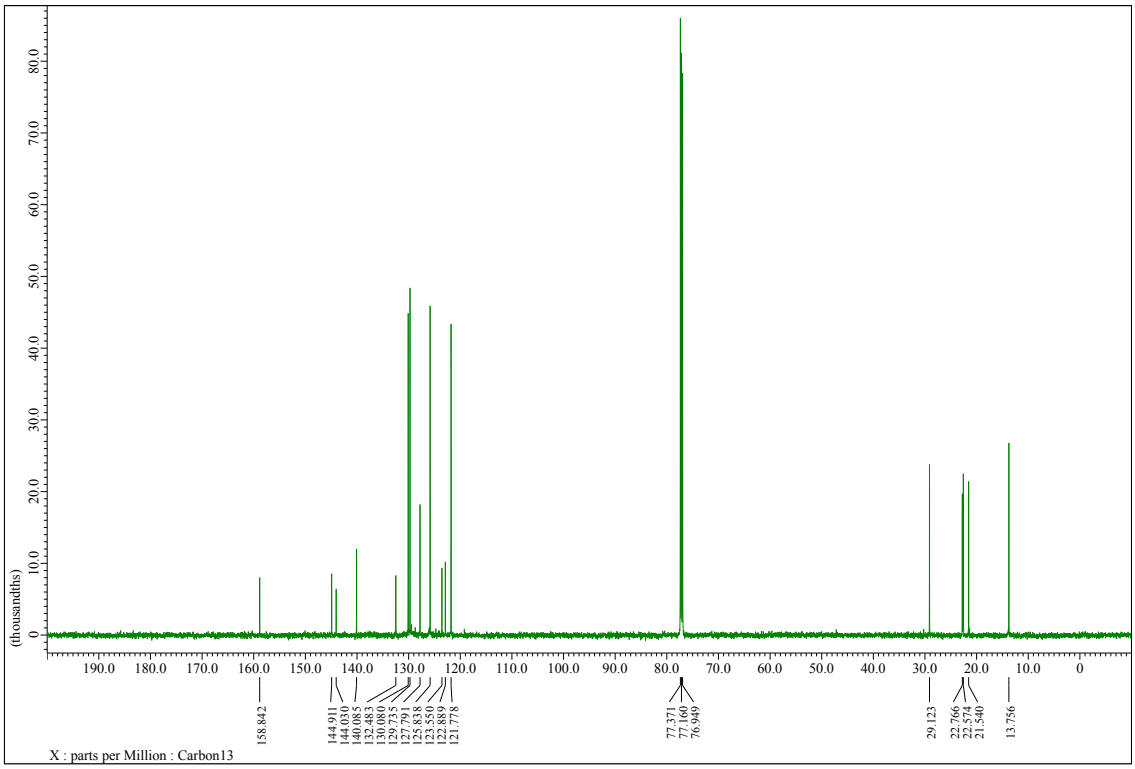

Ph
N
O
O
N–N
Me
Me
3h
abundance
X : parts per Million : Proton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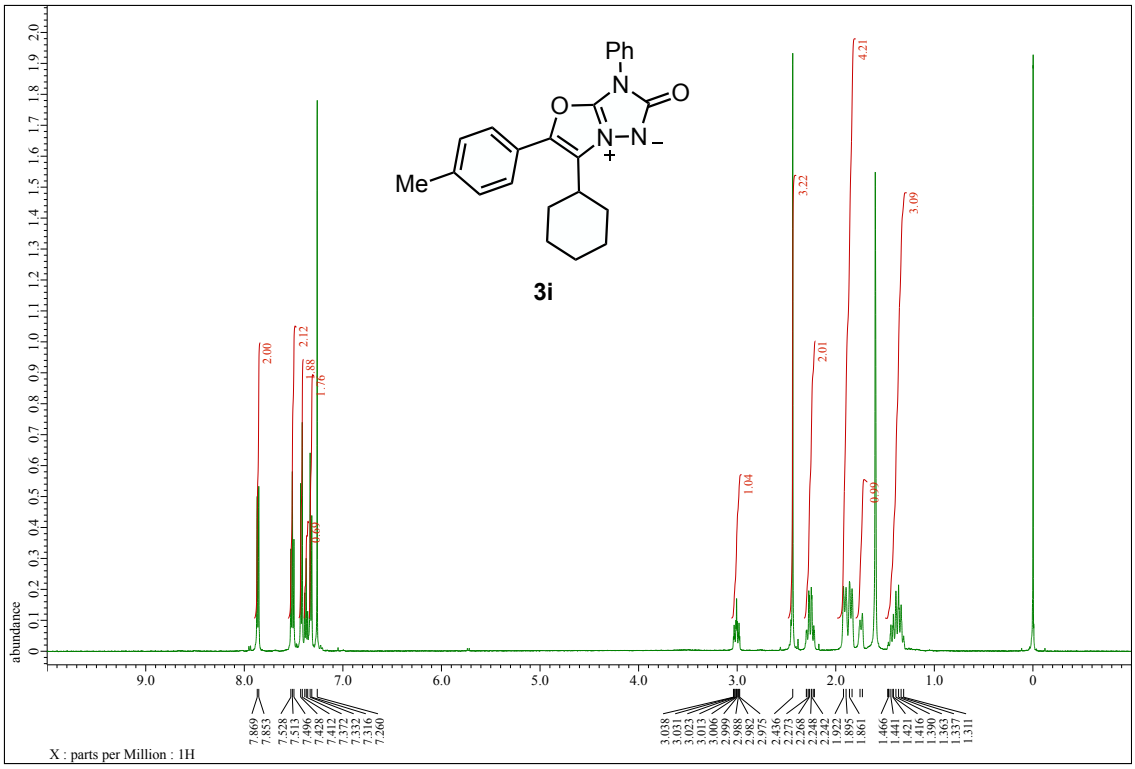
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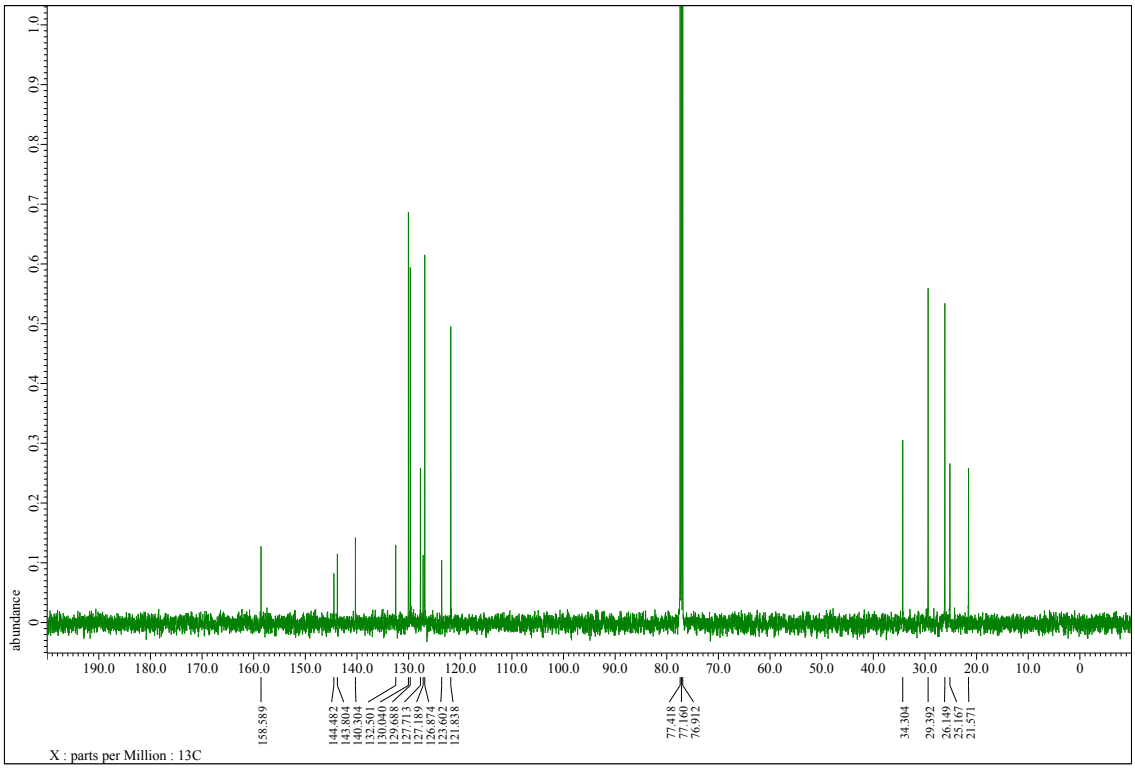
N
O
O
N–N
+
Me
3i
abundance
X : parts per Million : 1H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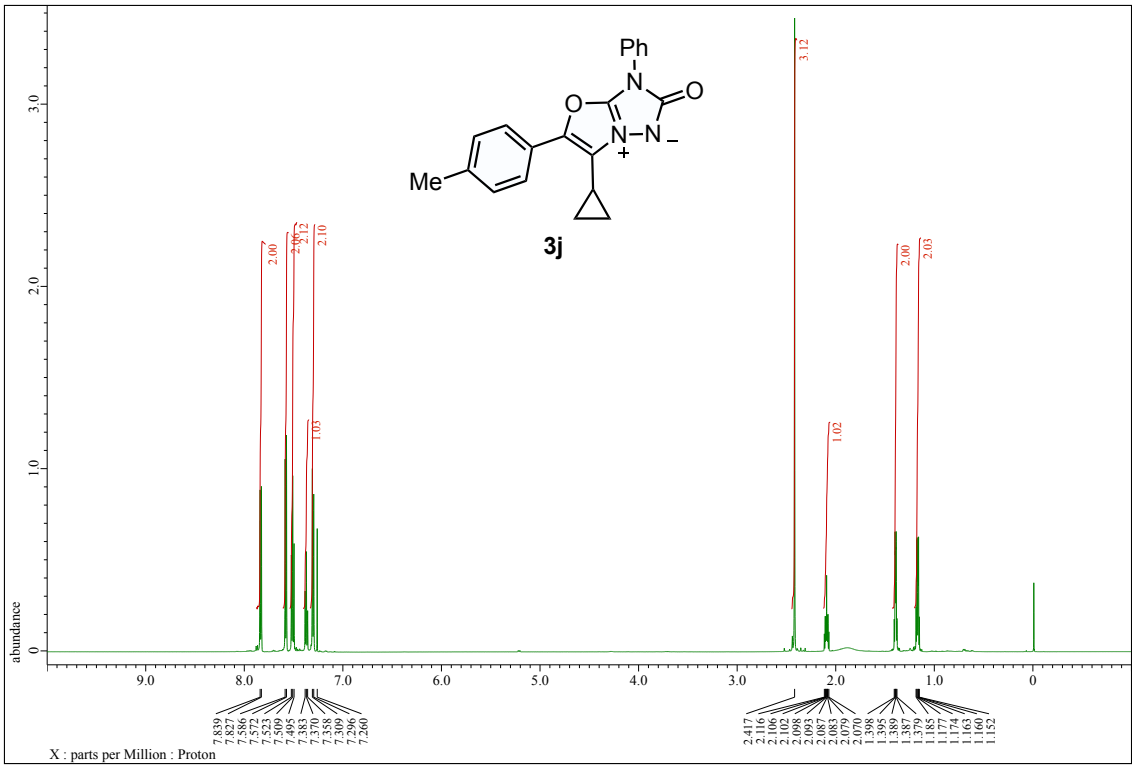
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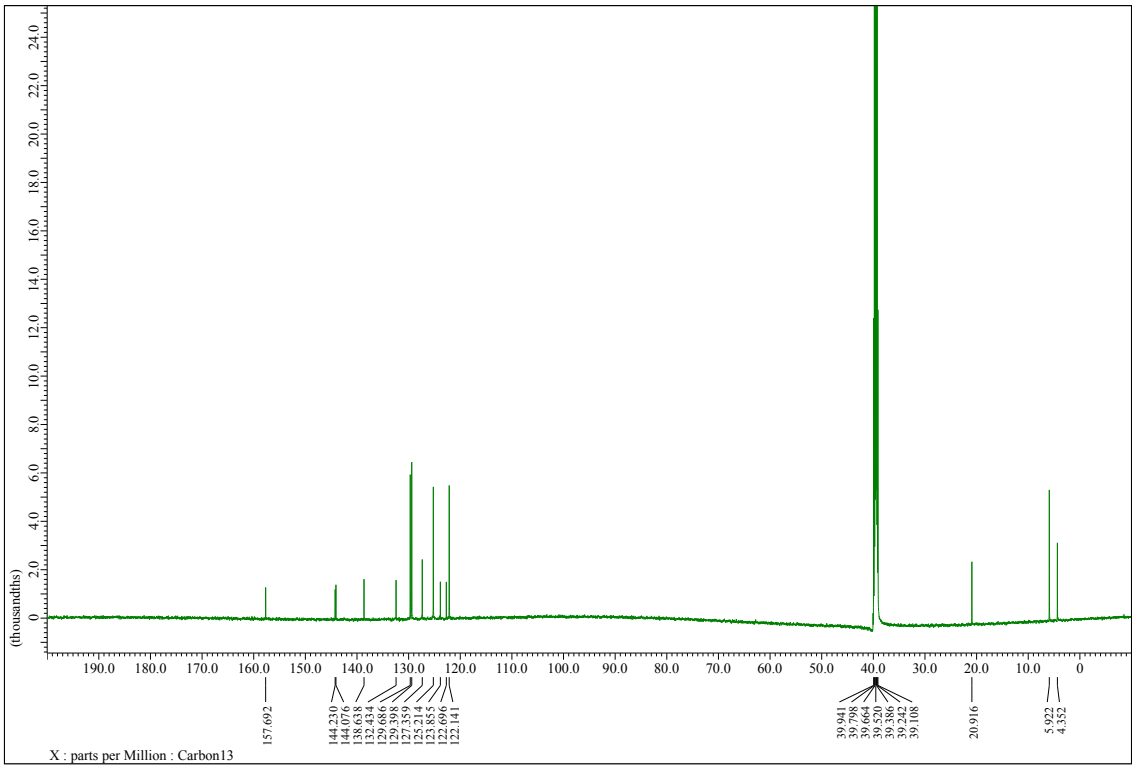
O
O
N–N
+
Me
3j
abundance
X : parts per Million : Proton


(thousandths)
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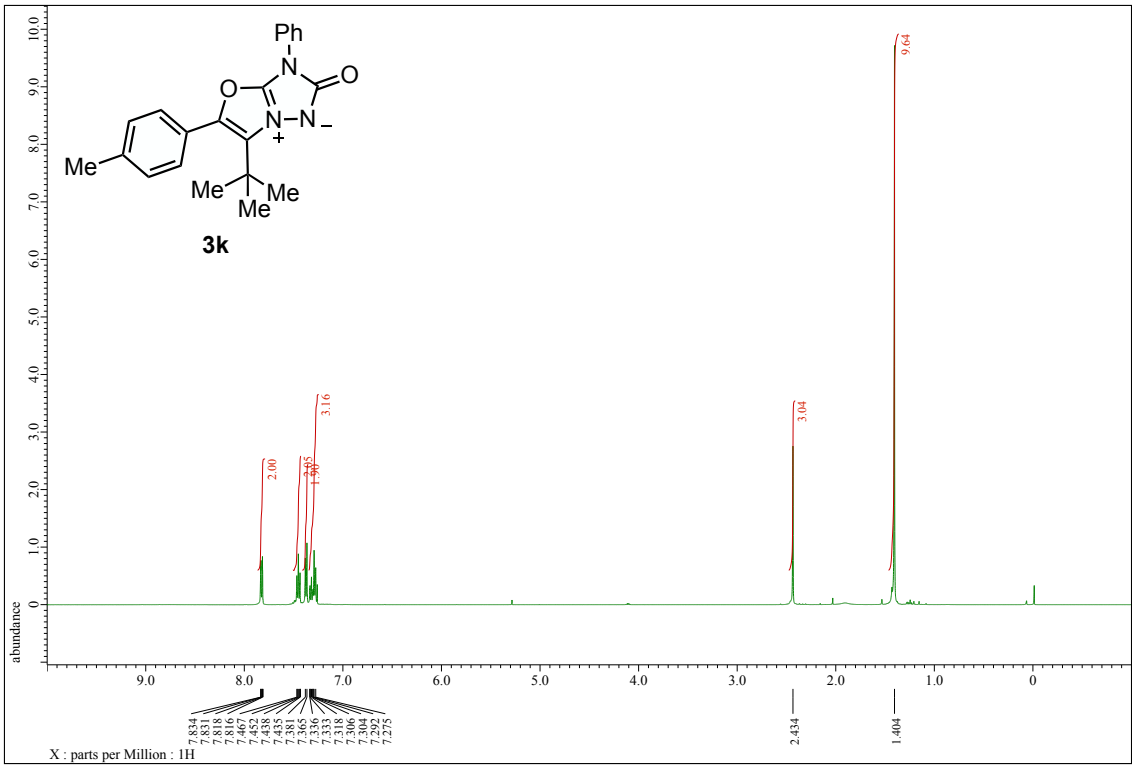
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O
O
N–N
+
Me
Me
Me
Me
3k
abundance
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3.16
3.04
2.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.834
7.831
7.818
7.816
7.467
7.452
7.438
7.435
7.383
7.365
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7.318
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7.304
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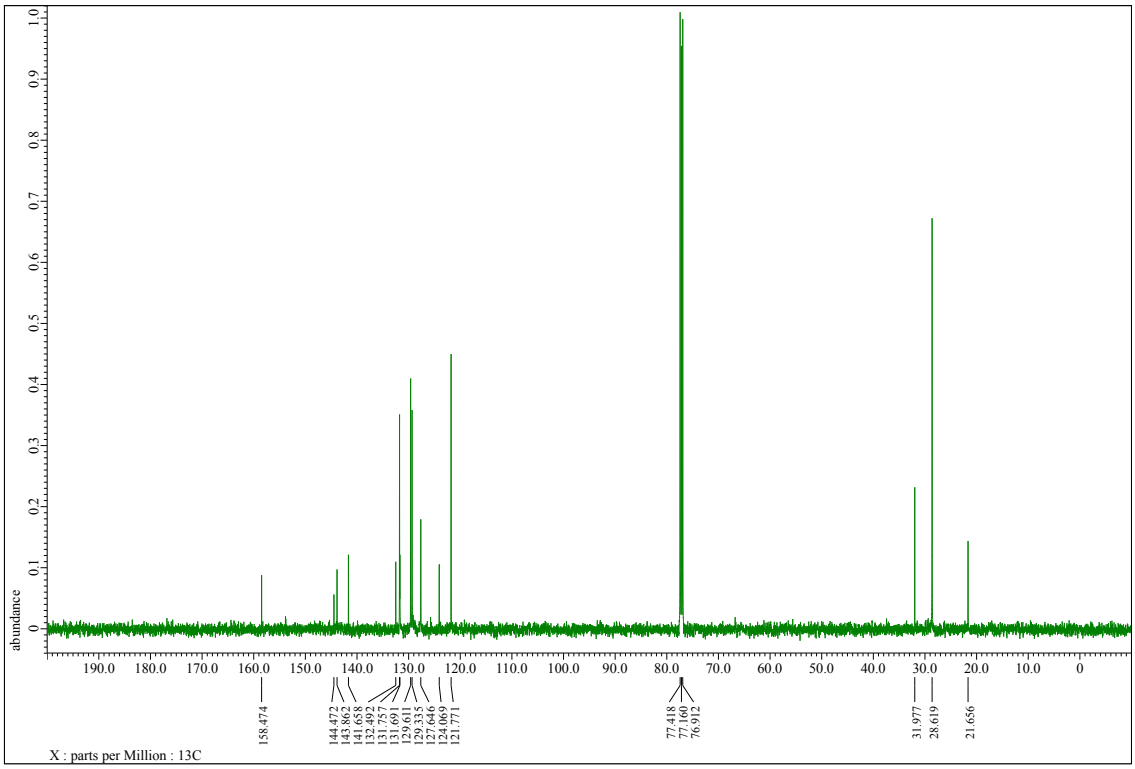
1.404
X : parts per Million : 1H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120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
158.474
144.472
143.862
141.658
132.492
131.757
131.691
129.611
129.535
127.646
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121.771
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77.160
76.912
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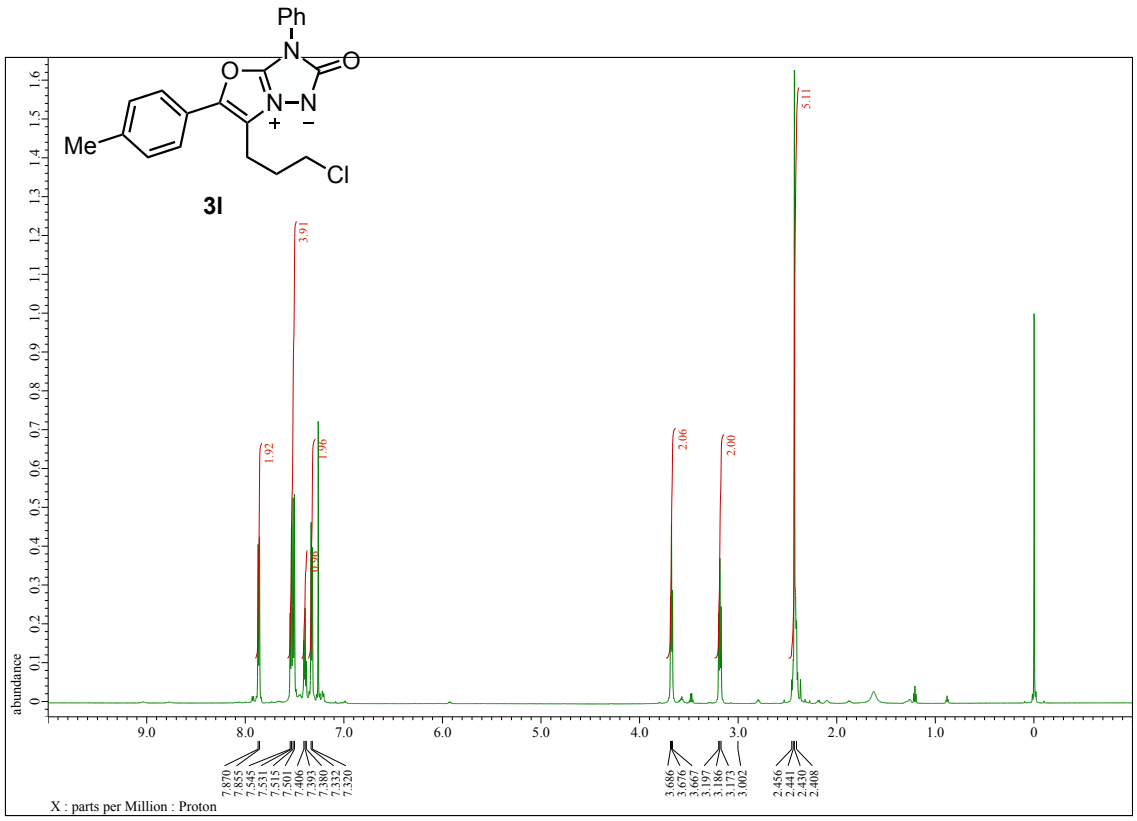
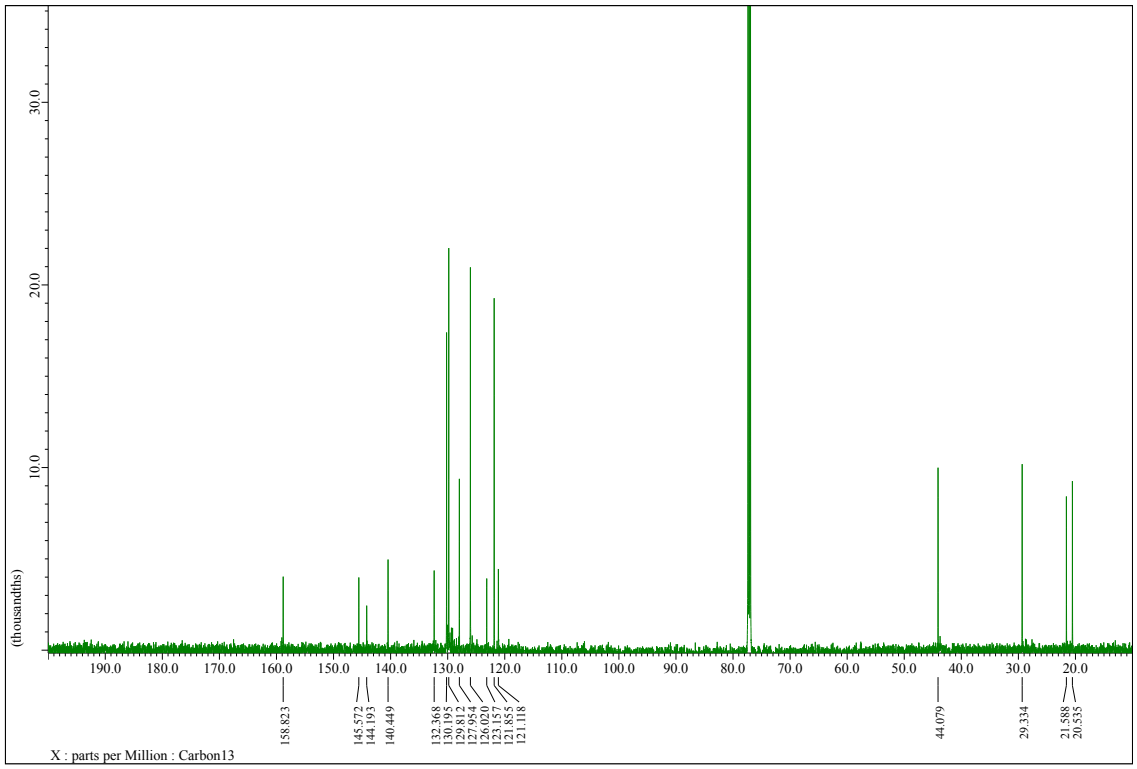
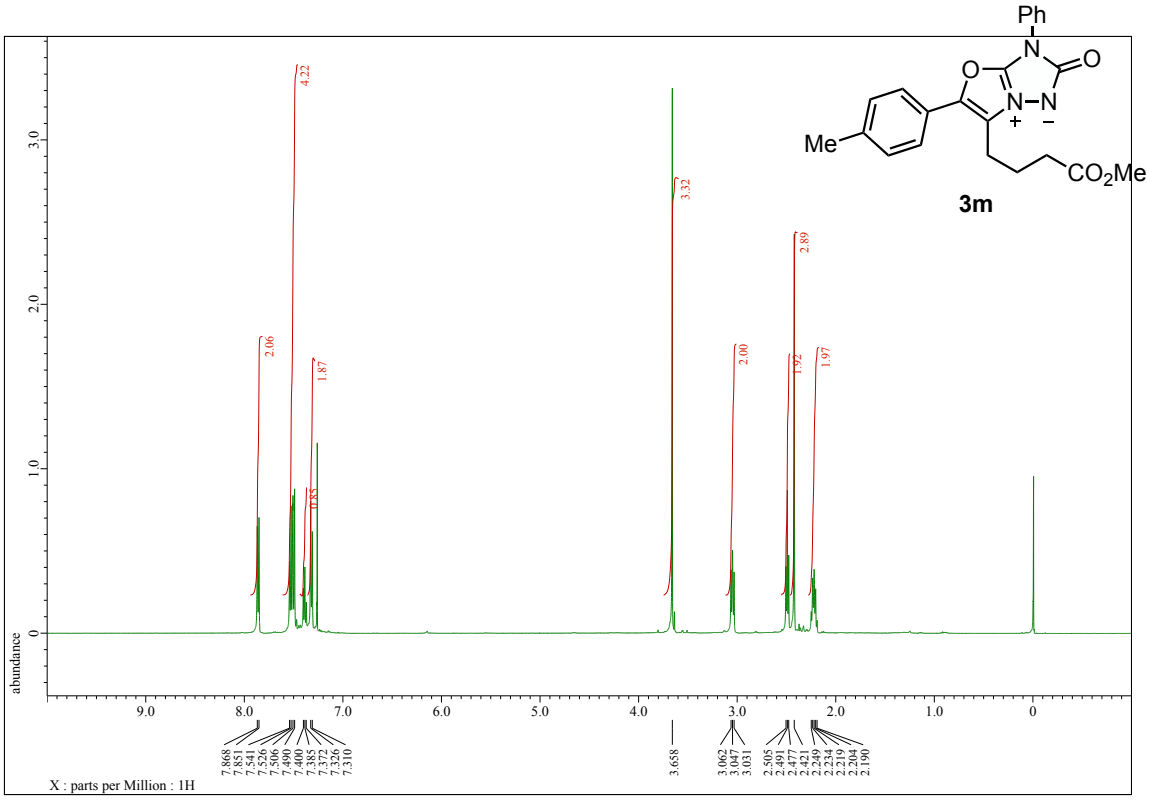
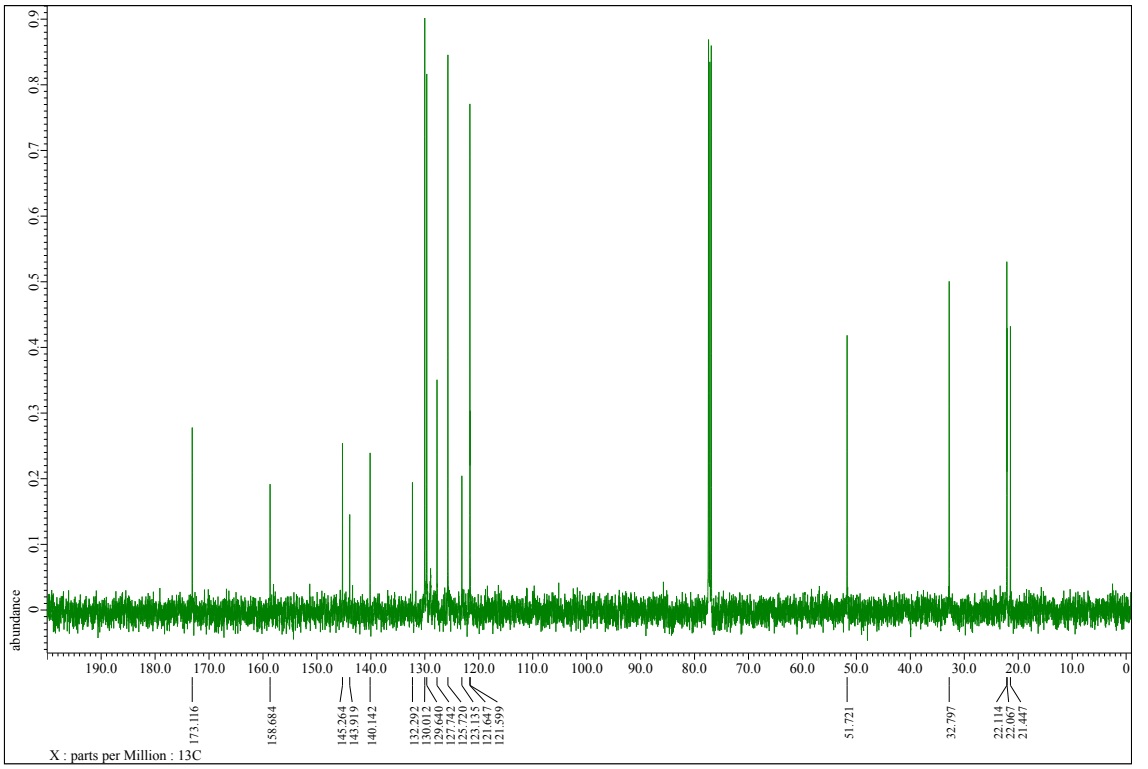
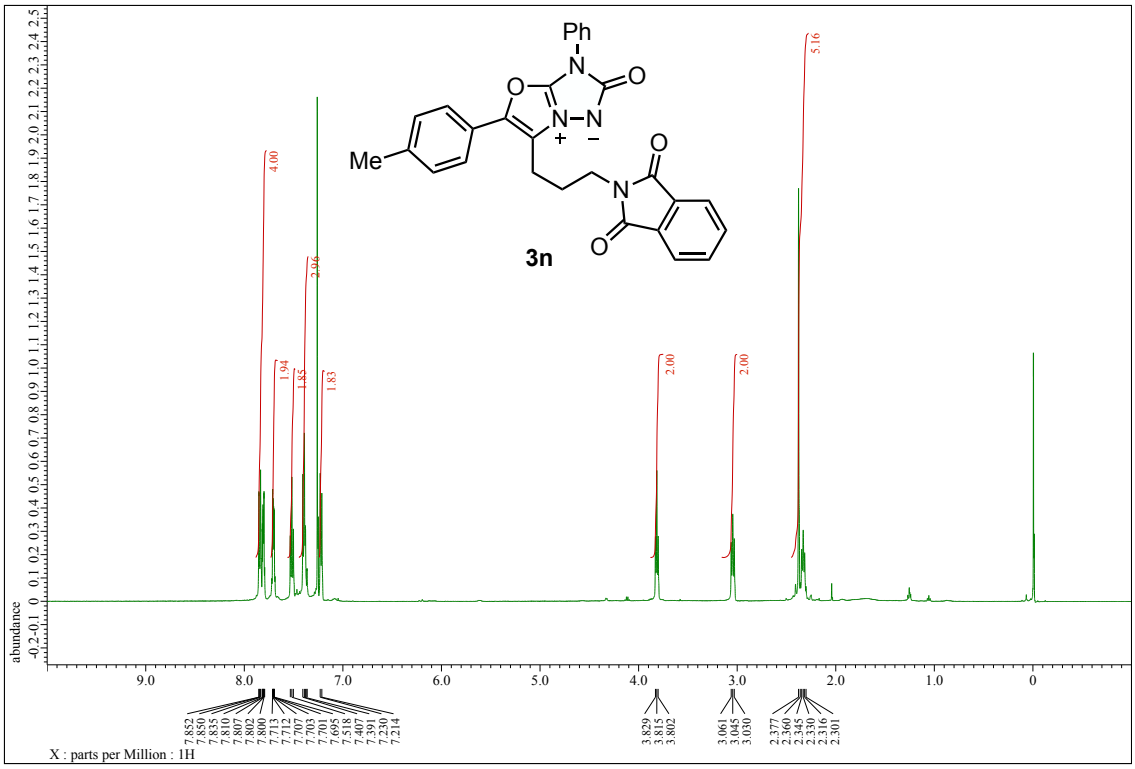
21.656
X : parts per Million : 13C

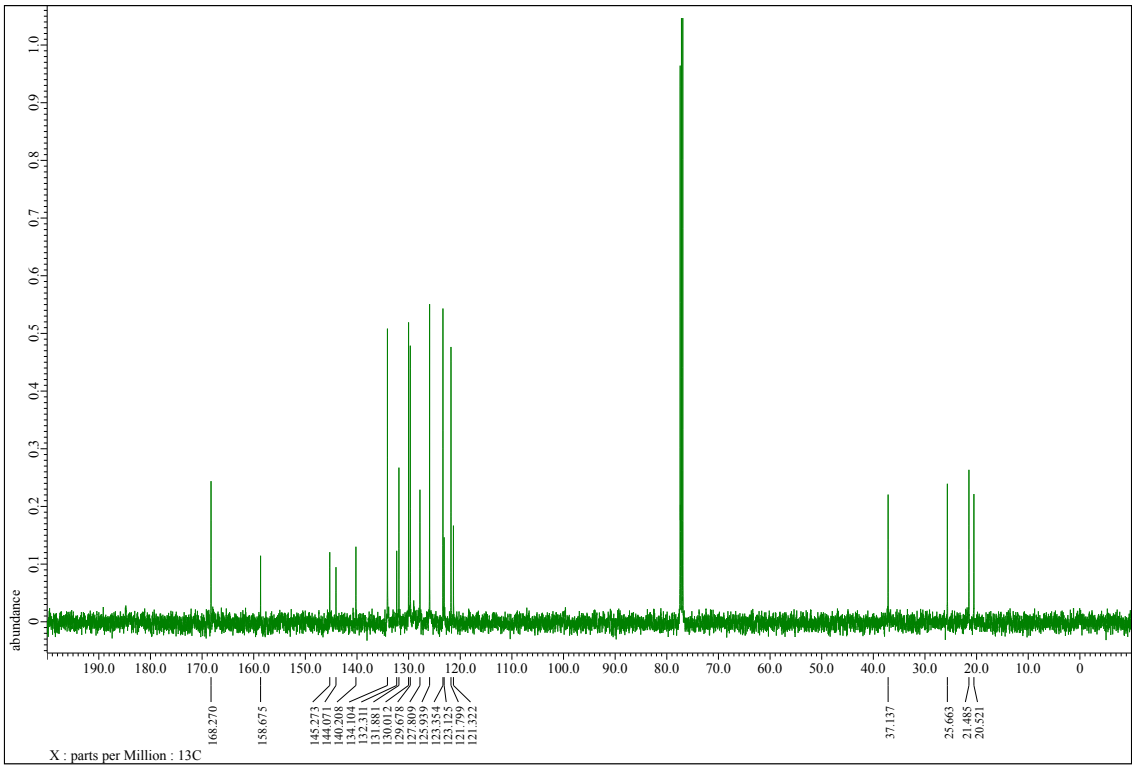

Ph
N
O
O
N–N
+ –
Me
Cl
3l
abundance
X : parts per Million : Proton

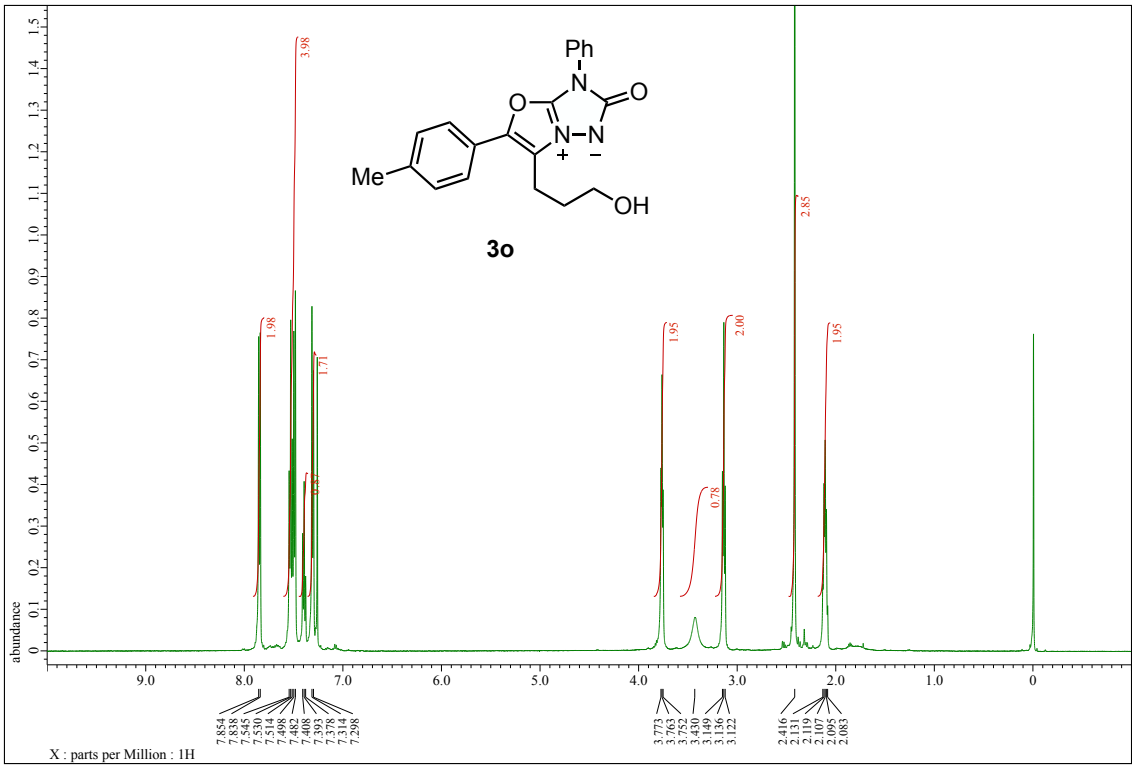

(thousandths)
X : parts per Million : Carbon13

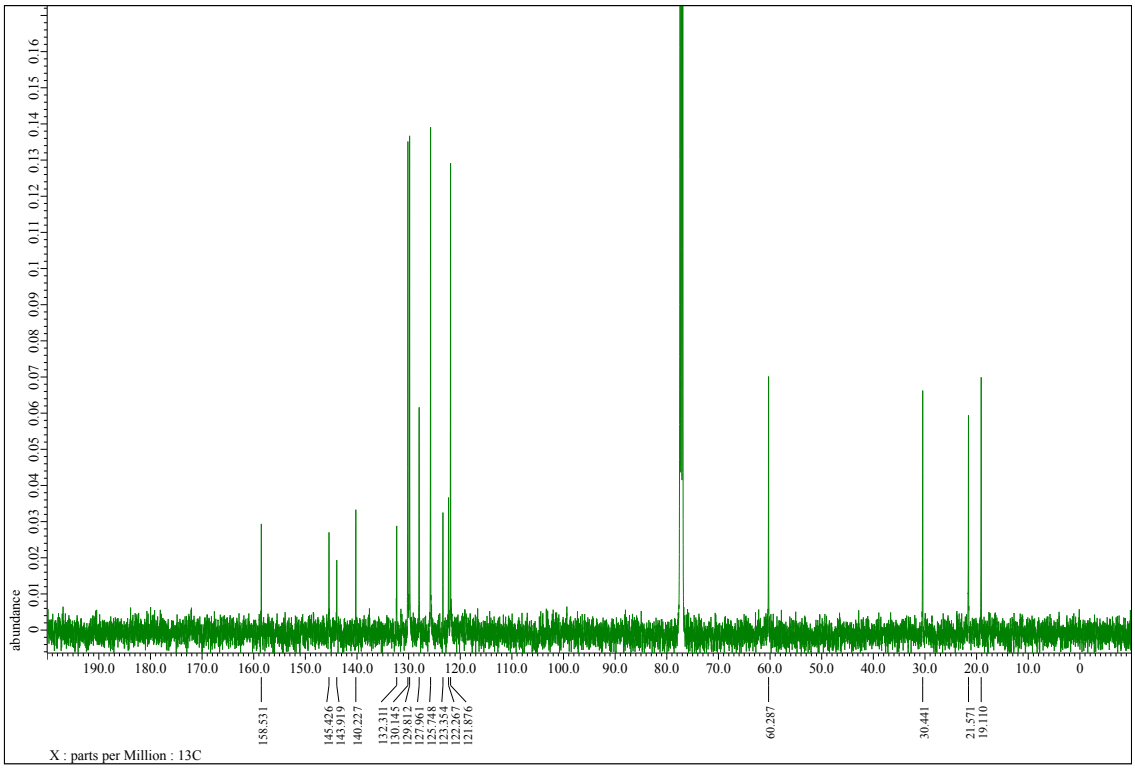

Ph
N
O
O
N–N
+ –
Me
CO2Me
3m
4.22
3.32
2.89
2.06
2.00
1.92
1.97
1.87
0.85
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C


Ph
N
O
O
N–N
+ –
Me
O
N
O
3n
4.00
2.06
1.94
1.85
1.83
2.00
2.00
5.16
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C


Ph
N
O
O
N–N
+
–
Me
OH
3o
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C