Supporting Information for

O^2-(6-Oxocyclohex-1-en-1-yl)methyl diazen-1-ium-1,2-diolates: a new class of nitric oxide donors activatable by GSH/GSTπ with both anti-proliferative and anti-metastatic activities against melanoma

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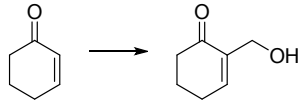
Contents

1. General Information

^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance 300 MHz spectrometer at 303 K, using TMS as an internal standard. MS spectra were recorded on a Mariner mass spectrometer (ESI) and high resolution mass spectrometry (HRMS) spectra on an Agilent Technologies LC/MSD TOF instrument. Analytical and preparative TLC was performed on silica gel (200−300 mesh) GF/UV 254 plates, and the chromatograms were visualized under UV light at 254 and 365 nm. Flash chromatography was carried out on ISCO (Combiflash, *Rf* 200). HPLC was performed on a Shimadzu Series (LC-20AT) using a Phenomenex Luna 5 μm C_{18} column (250 × 10.00 mm). All solvents were reagent grade and, when necessary, were purified and dried by standard methods. Solutions after reactions and extractions were concentrated using a rotary evaporator operating at a reduced pressure of ~20 Torr. Individual compounds with a purity of > 97% were used for biological experiments.

2. Experimental procedure and characterization of compounds

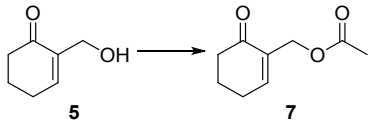
2-(Hydroxymethyl)-2-cyclohexen-1-one (5) [1]



4 **5**

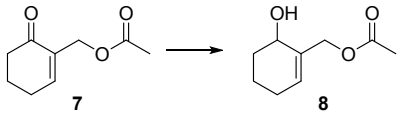
The title compound **5** was prepared via a Baylis-Hillman reaction starting from commercially available 2-cyclohexen-1-one **4**. Briefly, to a solution of **4** (48 g, 0.5 mol) in THF (100 mL), formaldehyde (42 g, 0.6 mol) and DMAP (6.3 g, 0.05 mol) were added. The obtained reaction mixture was stirred at room temperature for 2 days, and then was quenched by adding water 200 mL. Followed by extracted with ethyl acetate (100 mL × 3), the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The obtained crude product was purified by silica column chromatography to give compound **5** as a yellow oil (50.7 g, 80.5%). ^{1}H-NMR ($DMSO_{d6}$, 300 MHz): δ 6.95 (s, 1H), 4.76 (t, 1H, *J* = 5.4 Hz), 4.03 (dd, 2H, *J* = 1.8, 4.8 Hz), 2.35-2.31 (m, 4H), 1.94-1.85 (m, 2H); ESI-MS: $[M+Na]^{+}$, found 149.1. $C_7H_{10}O_2$ requires 126.1.

(6-Oxocyclohex-1-en-1-yl)methyl acetate (7) [2]



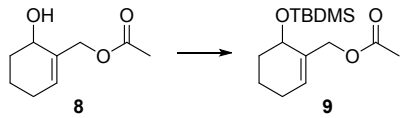
To a solution of compound **5** (12.6 g, 0.1 mol) in dichloromethane (50 mL), acetic anhydride (15.3 g, 0.15 mol) and triethylamine (15.2 g, 0.15 mol) were added. The mixture was stirred at room temperature for 2h, and was quenched by adding water 100 mL. Followed by extracted with dichloromethane (100 mL × 3), the organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude **7** was obtained as a yellow oil (13.9 g, 83%), which was used for the next reaction without further purification. H^1-NMR ($CDCl_3$, 300 MHz) δ: 6.94 (s, 1H), 4.67 (s, 2H), 2.42-2.37 (m, 4H), 2.04-1.94 (m, 5H). ESI-MS: $[M+Na]^+$, found 191.1. $C_9H_{12}O_3$ requires 168.1.

(6-Hydroxycyclohex-1-en-1-yl)methyl acetate (8) [2]



A solution of compound **7** (16.8 g, 0.1 mol) and $CeCl_3 \cdot 7H_2O$ (3.72 g, 0.01 mol) in methanol (50 mL) was stirred at -10 ℃,while $NaBH_4$ (18.5 g, 0.5 mol) was slowly added. The final solution was stirred for 2 h and then quenched by adding saturated NH_4Cl aqueous solution (100 mL). Followed by extracted with ethyl acetate (100 mL × 3), the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Compound **8** was obtained without further purified as a yellow oil (12.1 g, 71%). ^1H NMR (300 MHz, $CDCl_3$) δ 5.89 (t, J = 3.0 Hz, 1H), 4.80 (dd, J = 3.0 Hz, J = 12.0 Hz, 1H), 4.43 (d, J = 12.0 Hz, 1H), 4.14 (t, J = 6.0 Hz, 1H), 2.36 (s, 1H), 2.12-2.00 (m, 5H), 1.76-1.56 (m, 4H); ESI-MS: $[M+Na]^+$, found 193.1. $C_9H_{14}O_3$ requires 170.1.

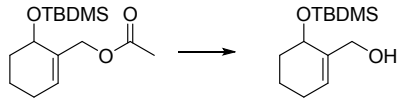
(6-((*tert*-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl acetate (9) [2]



A solution of compound **8** (17 g, 0.1 mol), TBDMSCl (22.5 g, 0.15 mol) and triethylamine (15.2 g, 0.15 mol) were dissolved in CH_2Cl_2 (70 mL), and then refluxed for 8 h. Deionized water (100 mL) was added into the mixture to quench the reaction. Followed by separated and extracted with CH_2Cl_2 (50 mL × 3), the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Compound **9** was obtained

through purified with silica column chromatography, as a light brown oil (17.6 g, 62%). ^{1}H-NMR ($CDCl_3$, 300MHz) δ 5.83 (t, *J* = 3.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H) 4.25 (s, 1H), 2.04 (s, 3H), 1.83-1.63 (m, 6H), 0.88 (s, 9H), 0.04 (s, 6H). ESI-MS: $[M+Na]^+$, found 307.2. $C_{15}H_{28}O_3Si$ requires 284.2.

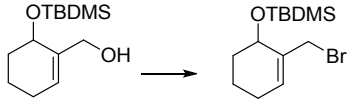
(6-((*tert*-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methanol (10) [2]



9 **10**

To a stirred solution of compound **9** (28.4 g, 0.1 mol) in methanol (100 mL), potassium carbonate (18 g, 0.13 mol) was added. The mixture was stirred at 0 ℃ for 3h, followed by extracted with ethyl acetate (100 mL × 3), the organic layers were dried over Na_2SO_4, filtered, and concentrated to produce compound **10** as a yellow oil (20 g, 83%) without further purified.^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (t, *J* = 3.0 Hz, 1H), 4.36 (d, *J* = 6.0 Hz, 1H), 4.15-4.11 (m, 1H), 4.02 (t, *J* = 10.5 Hz, 1H), 2.19-1.65 (m, 7H), 0.9 (s, 9H), 0.13 (s, 6H); ESI-MS: $[M+Na]^+$, found 265.2. $C_{13}H_{26}O_2Si$ requires 242.2.

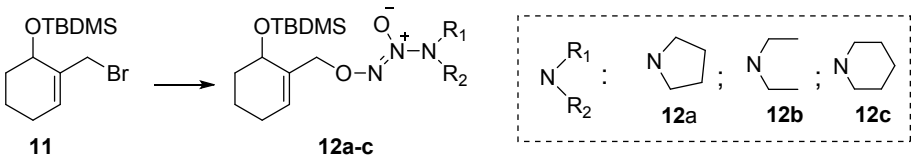
((2-(Bromomethyl)cyclohex-2-en-1-yl)oxy)(tert-butyl)dimethylsilane (11).



10 **11**

To a stirred solution of compound **10** (500 mg, 2.07 mmol) and triphenylphosphine (649 mg, 2.47 mmol) in 5 ml dichloromethane was added carbon tetrabromide (817 mg, 2.47 mmol) dissolved in 3 ml dichloromethane slowly at 0 °C. The solution was stirred for 8 h, followed by extracted with 10 ml CH_2Cl_2. The combined organic layers were washed with saturated with saturated NaCl, dried over Na_2SO_4, filtered, and concentrated to a yellowish oil, which was purified by flash column chromatograph afford **11** as a colorless oil (460 mg, 1.51 mmol) in 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (t, *J* = 3.0 Hz, 1H), 4.44 (s, 1H), 4.27 (d, *J* = 9.0 Hz, 1H), 3.87 (d, *J* = 9.0 Hz, 1H), 2.11-1.93 (m, 2H), 1.86-1.58 (m, 4H), 0.91 (s, 9H), 0.14 (d, *J* = 11.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 127.28, 126.55, 71.14, 36.67, 32.48, 29.70, 25.89, 25.82, 25.24; ESI-MS: $[M+H]^+$, found 305.3. $C_{13}H_{25}BrOSi$ requires 304.1.

Synthesis of compound 12a-c



Compounds **12a-c** were synthesized using a similar method. A typical procedure can be described as follows using **12a** as the example. To a solution of compound **11** (305mg, 1mmol) in anhydrous N, N-dimethylformamide (2 ml), diazeniumdiolate (202 mg, 1.3 mmol) was added, the resulting mixture was stirred at 0℃ for 6 h under N_2 protected. After the reaction mixture was warmed to room temperature, ethyl acetate (10 ml) was added, followed by washed with deionized water several times, the organic layers were dried over Na_2SO_4, filtered, and concentrated. The obtained crude product was purified by silica column chromatography to yield compound **12a** as a yellow oil (70mg, 19.7 %), **12b** (14 %), **12c** (16.2%).

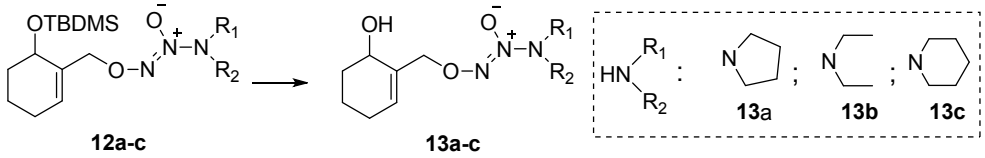
Compound **12a** was obtained in 19.7% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (s, 1H), 4.80 (d, J = 9.0 Hz, 1H), 4.44 (d, J = 9.0 Hz, 1H), 4.31 (s, 1H), 3.50 (t, J = 6.0 Hz, 4H), 1.95-1.91 (m, 5H), 1.76-1.53 (m, 5H), 0.88 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.59, 130.53, 74.19, 64.78, 50.63, 31.82, 29.21, 25.38, 24.86, 22.23, 17.85. ESI-MS: $[M+Na]^+$, found 378.3. $C_{17}H_{33}N_3O_3Si$ requires 355.2.

Compound **12b** was obtained in 14% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90 (s, 1H), 4.89 (d, J = 12.0 Hz, 1H), 4.53 (d, J = 12.0 Hz, 1H), 4.27 (s, 1H), 3.08-3.02 (m, 4H), 2.07-1.66 (m, 6H), 1.07 (t, J = 6.0 Hz, 6H), 0.89 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.36, 130.88, 74.68, 64.67, 48.44, 31.82, 25.45, 25.36, 24.85, 17.86, 11.09. ESI-MS: $[M+Na]^+$, found 380.2. $C_{17}H_{35}N_3O_3Si$ requires 357.2.

Compound **12c** was obtained in 16.2% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (t, J = 3.0 Hz, 1H), 4.85 (d, J = 12.0 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.30 (s, 1H), 3.30 (t, J = 6.0 Hz, 4H), 1.79-1.66 (m, 6H), 1.56-1.46 (m, 6H), 0.88 (s, 9H), 0.072 (d, J = 3.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.90, 131.15, 74.97,

65.39, 52.89, 32.63, 25.96, 25.86, 25.65, 24.78, 23.39, 18.28. ESI-MS: $[M+Na]^+$, found 392.3. $C_{18}H_{35}N_3O_3Si$ requires 369.2.

Synthesis of compound 13a-c



12a-c 13a-c

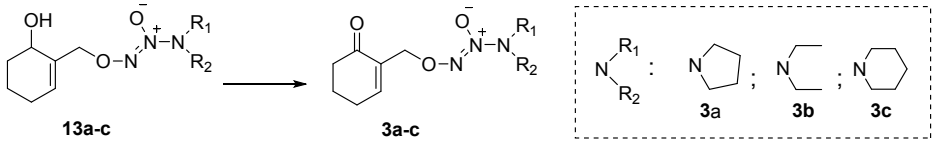
The solution of compound **12a** (357 mg, 1 mmol) in THF (3 ml) was added tetrabutylammonium fluoride (TBAF, 1 ml, 1M dissolved in THF). The solution was stirred at rt for 12 h, followed by purified with flash chromatography to yield compound **13a** (170 mg, 70.5%). Synthesis of **13b-c** were in the similar way with yield (65.8%, 58.5%).

Compound **13a** was obtained in 70.5% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (d, *J* = 3.0 Hz, 1H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.25 (s, 1H), 3.52 (t, *J* = 6.0 Hz, 4H), 2.37 (s, 1H), 2.15-2.02 (m, 2H), 1.96-1.91 (m, 4H), 1.83-1.61 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.69, 132.22, 75.94, 65.13, 50.96, 31.29, 25.41, 22.81, 17.80. ESI-MS: $[M+H]^+$, found 242.3. $C_{11}H_{19}N_3O_3$ requires 241.1.

Compound **13b** was obtained in 65.8% yield as a yellow oil; ^{1}H NMR (300 MHz, CDCl3) δ 6.06 (s, 1H), 4.93 (s, 1H), 4.13 (s, 2H), 3.08 (q, *J* = 6.0 Hz, 4H), 2.13-2.05 (m, 4H), 1.87-1.81 (m, 4H), 1.32 (t, *J* = 12.0 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.43, 131.84, 77.59, 64.98, 48.82, 28.45, 24.97, 17.65, 11.63. ESI-MS: $[M+H]^+$, found 244.3. $C_{11}H_{21}N_3O_3$ requires 243.2.

Compound **13c** was obtained in 58.8% yield as a yellow oil; ^{1}H NMR (300 MHz, CDCl3) δ 6.02 (s, 1H), 4.83 (s, 1H), 4.11-4.04 (m, 2H), 3.31 (t, *J* = 6.0 Hz, 4H), 2.26 (s, 1H), 2.16-1.96 (m, 3H), 1.75-1.69 (m, 6H), 1.54-1.44 (m, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 134.22, 131.72, 77.09, 64.96, 52.75, 28.26, 25.00, 24.80, 23.40, 17.58. ESI-MS: $[M+Na]^+$, found 278.1. $C_{12}H_{21}N_3O_3$ requires 255.2.

Synthesis of compound 3a-c.



A solution of compound **13a** (243 mg, 1 mmol) and 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) (295 mg, 1.3 mmol) were dissolved in toluene (5 ml). The solution was refluxed at 110 ℃ for 12 h. The mixture was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatograph of the residue afford the target compound **3a** (152 mg, 59.3%). Compounds **3b** and **3c** were synthesized using a similar method with 61.4% and 59.2 % yield.

Compound **3a** was obtained in 59.3% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05 (s, 1H), 4.84 (s, 2H), 3.51 (d, J = 6.0 Hz, 4H), 2.48-2.41 (m, 4H), 2.06-1.91 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.00, 148.56, 134.40, 69.56, 50.97, 38.07, 25.78, 22.79, 22.63. ESI-MS: $[M+Na]^+$, found 262.1. $C_{11}H_{17}N_3O_3$ requires 239.1. HRMS m/z calcd for $C_{11}H_{17}N_3O_3Na$ $[M + Na]^+$: 262.1168, found 262.1162, ppm error 4.2.

Compound **3b** was obtained in 61.4% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (s, 1H), 4.93 (s, 2H), 3.09 (q, J = 3.0 Hz, 12.0 Hz, 4H), 2.47-2.42 (m, 4H), 2.01-1.99 (m, 2H), 1.10-1.06 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.90, 148.75, 134.30, 69.94, 52.71, 38.04, 24.73, 23.39, 22.61. ESI-MS: $[M+Na]^+$, found 264.1. $C_{11}H_{19}N_3O_3$ requires 241.1. HRMS m/z calcd for $C_{11}H_{19}N_3O_3Na$ $[M + Na]^+$: 264.1324, found 264.1328, ppm error 1.5.

Compound **3c** was obtained in 59.2% yield as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (t, J = 6.0 Hz, 1H), 4.89 (s, 2H), 3.33 (t, J = 6.0 Hz, 4H), 2.48-2.39 (m, 4H), 2.06-1.98 (m, 2H), 1.78-1.70 (m, 4H), 1.53-1.47 (m, 2H). ^{13}C NMR (75 MHz, CDCl3) δ 197.01, 155.81, 148.27, 69.45, 52.22, 37.55, 25.29, 24.24, 22.89, 22.11. ESI-MS: $[M+Na]^+$, found 276.1. $C_{12}H_{19}N_3O_3$ requires 253.1. HRMS m/z calcd for $C_{12}H_{19}N_3O_3Na$ $[M + Na]^+$: 276.1324, found 276.1325, ppm error 0.4.

3. MTT Assays

Murine melanoma B16 cells, human colon HT-29 cells, human melanoma A375 cells, normal epithelial CRL-2007 cells, and metastatic melanoma B16-BL6 cells were purchased from American Tissue Culture Collection (ATCC, Rockville, MD, USA). Murine gliosarcoma 9L-2 cell line was from department of neurological surgery tissue bank at University of California, San Francisco.

Cells were planked in a 96 well plate with a concentration of 10^4 cells/well and cultured in 37 °C 5% CO_2 for 24 h. Then cells were respectively treated with **3a**, **3b**, **3c**, JS-K, or COMC-6 (10 nM, 50 nM, 200 nM, 1000 nM, 5000 nM) containing EMEM. Each concentration was repeated 5 times in parallel. After incubation for 68 h, 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2-H-tetrazolium bromide (MTT, 20 μL, 5 mg/mL) was added into each well, and the cells were incubated for additional 4h. Then the medium was carefully removed. Dimethyl sulfoxide (150 μL/well) was added and oscillated gently to make crystal dissolved. The absorbance at 570 nm was measured using a microplate reader. The cell viability was expressed as a percentage of OD570.

4. NO releasing and compound decomposition behaviors.

A PBS solution (0.1 M, pH 7.4) containing 1 mM GSH, 5 μg/mL GST and 100 μM **3c** were incubated at 37 °C. The concentrations of NO released from **3c** in each sample at the indicated time were determined by using a NO-sensitive probe fluorophore 4-amino-5-(methylamino)-2',7'-difluorofluorescein (DAF-FM).[3] A saturated NO solution (at 20 °C, NO ≈ 1.8 mM) was prepared by using previously reported method.[4] It was observed that the amount of NO was rapidly increased and reached up to 85.4-89.8 μM during 40-60 minutes. (Fig. S1A) In addition, at the same concentrations and incubation conditions, the reaction was monitored over 50 mins using an ultraviolet spectrophotometer with the wavelength ranging from 235 to 400 nm. As shown in Fig S1B, the maximal absorbance of **3c** at 241 nm decreased over time, indicating the decomposition of diazeniumdiolate moiety. These data supported that **3c** acts as a GSH/GSTπ promoted NO donor.

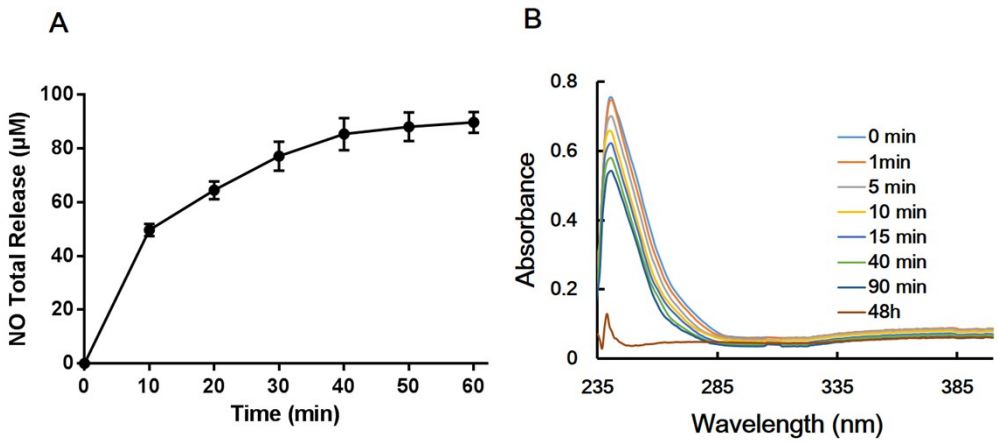


Figure S1. (A) Levels of NO produced by compound **3c**. (B) Decomposition behaviors of **3c** in the presence of GSH and GSTπ.

The NO released from **3c** and JS-K in B16 and CRL-2007 cells were measured using an NO-sensitive reagent fluorophore DAF-FM DA.[5] When cells grown in a 96-well plate reached 80% confluence, they were washed with PBS. After being loaded with 5 μM DAF-FM DA at 37 °C for 20 min, the cells were rinsed three times with PBS and incubated with test compounds for 8 h. NO production was measured with the flow cytometer with excitation and emission wavelengths of 495 and 515 nm, respectively.

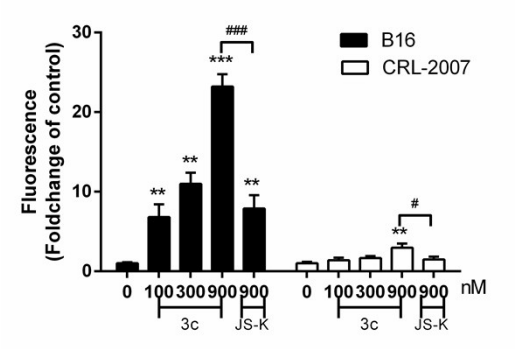


Figure S2. B16 and CRL-2007 cells were treated with the indicated concentrations of 3c and JS-K for 8h, stained with DAF-FM DA, and analyzed by fluorescence-activated cell sorting (FACS). Data shown here were representative of three different

experiments. Data are presented as means ± SD (n=3). *P<0.05, **P<0.01, ***P<0.001 vs. Control group, # P<0.05, ### P<0.001.

5. Effects of compounds on B16-BL6 cells viability

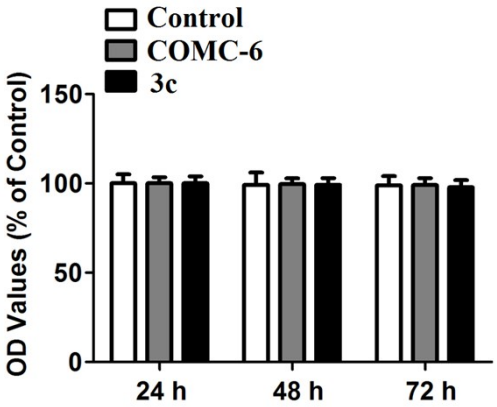


Figure S3. Incubation with COMC-6 (5 nM) or **3c** (5 nM) for 24, 48 or 72 h did not affect B16-BL6 cells viability. Data were calculated as the mean ± SD of each group of cells from three individual experiments. The results of MTT assay mentioned-above were described as % of Control.

6. Cells migration, invasion and lateral migration

Cells migration. B16-BL6 cells were treated with COMC-6 (5 nM) or **3c** (5 nM) for 72 h. Cells that migrated through the chambers were stained with crystal violet. Representative images were captured, and the cells were counted from three independent experiments.

Invasion assay. B16-BL6 cells were seeded on matrigel-coated chambers. COMC-6 (5 nM) or **3c** (5 nM) was treated on the lower surface for 72 h. Cells that migrated through the matrigel-coated chambers were stained with crystal violet. Representative images were captured and the cells were counted from three independent experiments

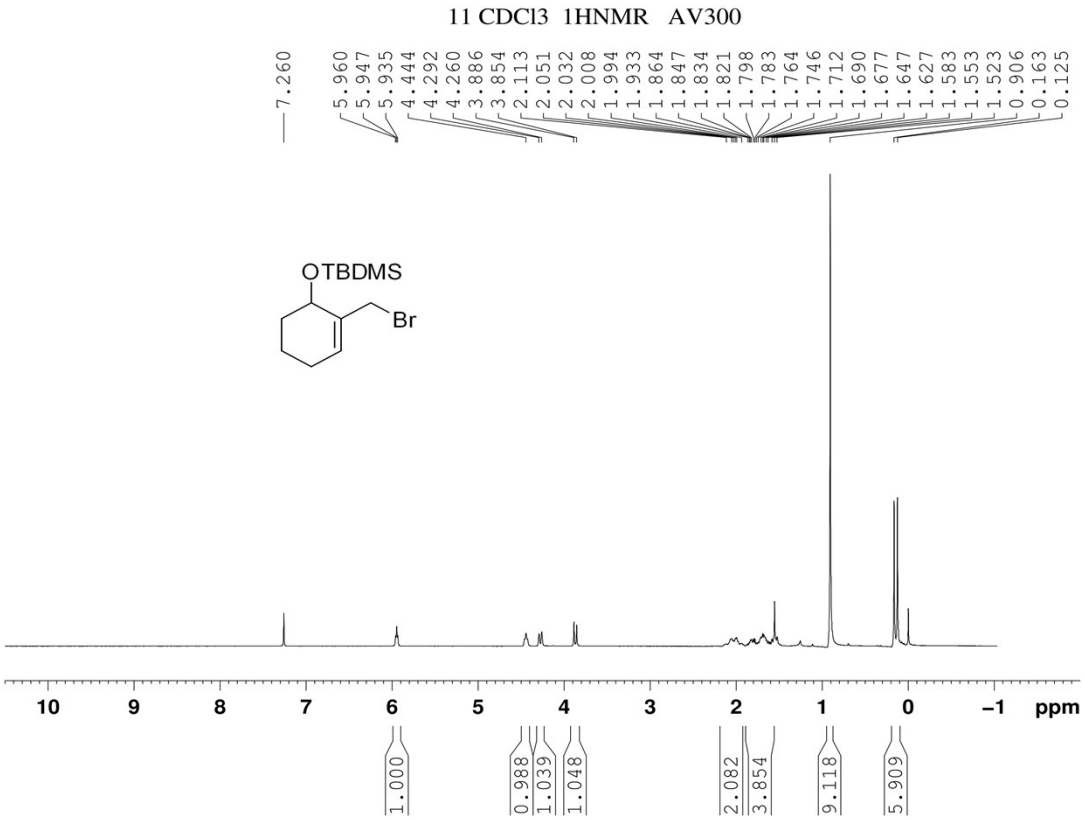
Lateral migration assay. B16-BL6 cells were seeded on 48-well plates. After 24 or 48 h incubation with COMC-6 (5 nM) or **3c** (5 nM), representative images of wound were captured, and the healed rate is presented. Experiment was confirmed for three independent times.

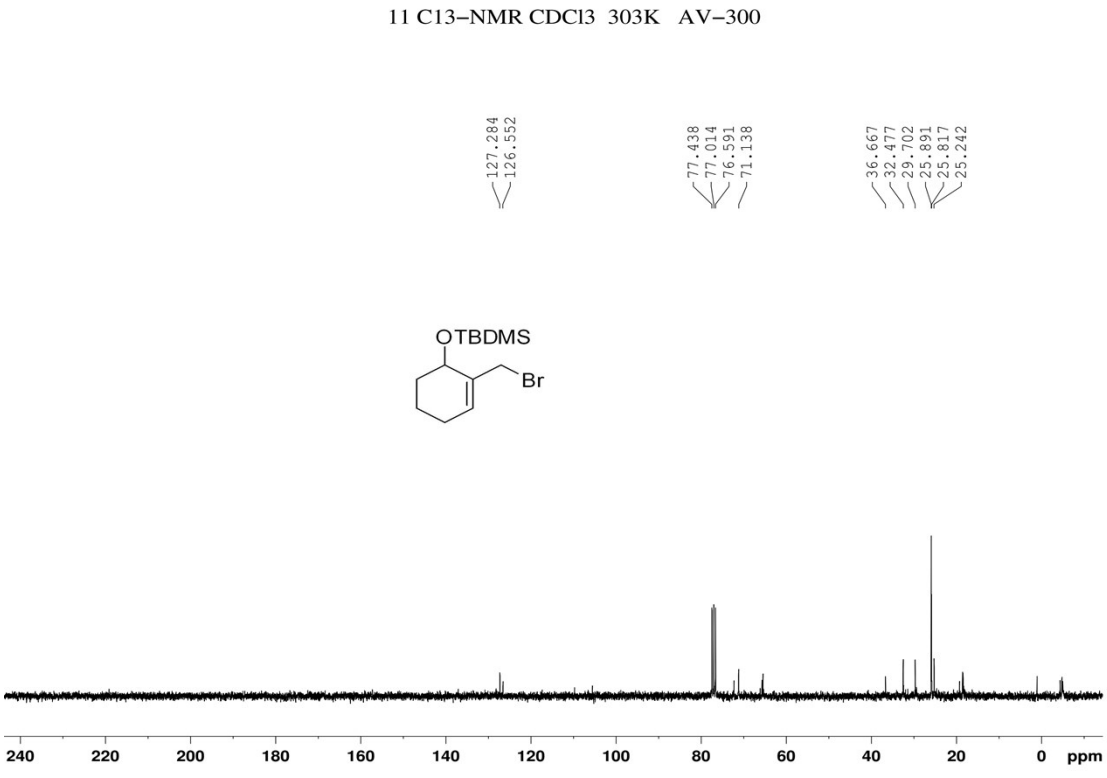
7. Adhesion assay

Fluorescence-based analysis was used to evaluate effects of **3c** and COMC-6 on the hetero-adhesion. HUVECs grown to confluence in 24-well tissue culture plates were pretreated with IL-1β (1 ng/ml) for 4 h. Rhodamine 123-labeled B16 cells were co-cultured with the HUVECs monolayers in each well, followed by treatment with **3c** or COMC-6 for 1 h. After incubation, non-adhered B16 cells were removed by washing three times (drop-to-drop) with 1 mL PBS. We randomly selected 20 visual fields for each well and took pictures under a fluorescence microscope. Expression of ICAM-1 and VCAM-1 in HUVECs was measured by flow cytometry.

8. The scanning copy of NMR and HPLC spectra for compounds

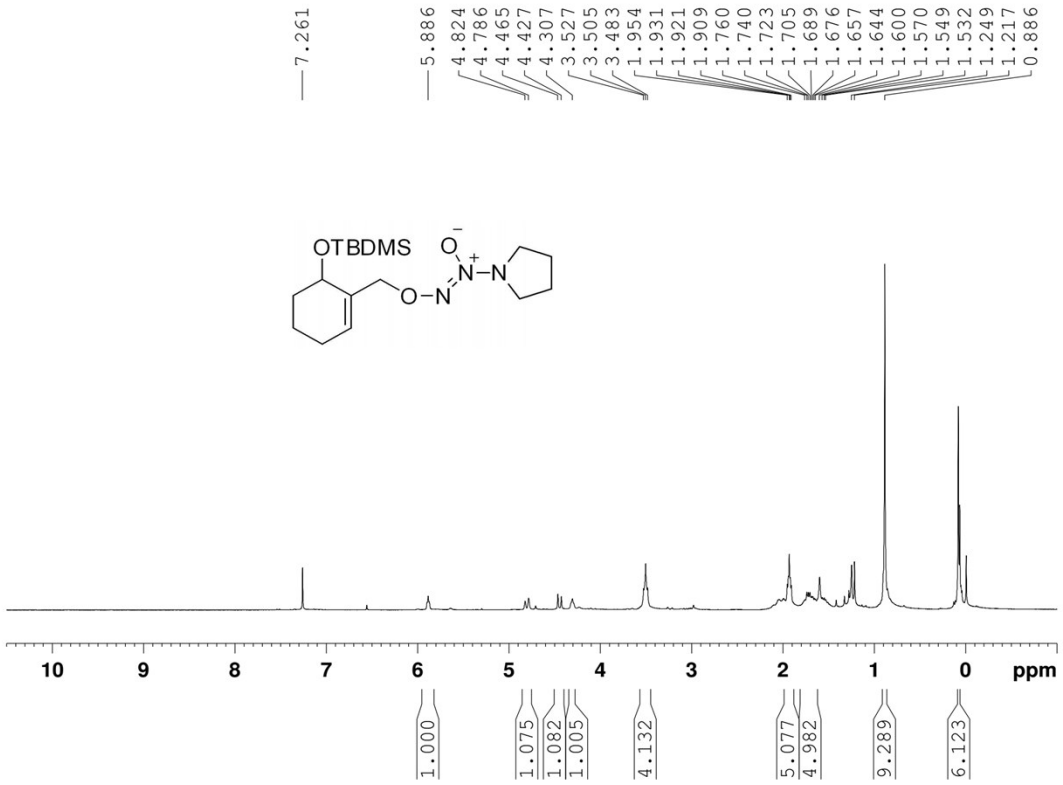
Compound **11**



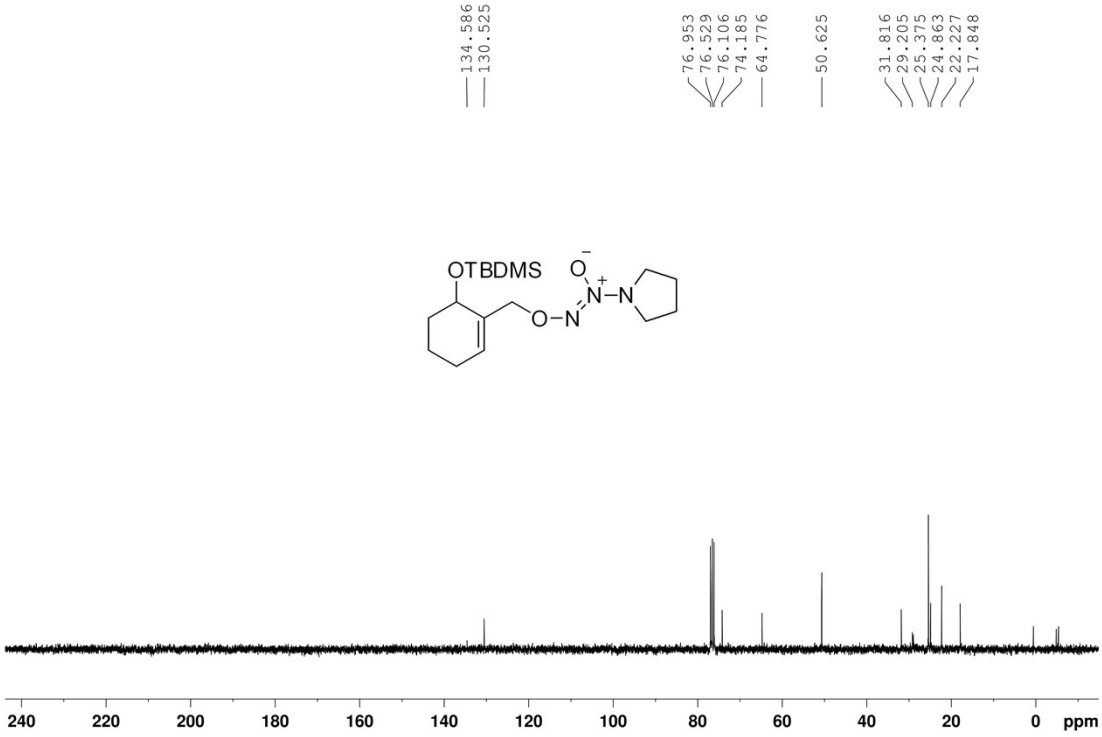


Compound 12a

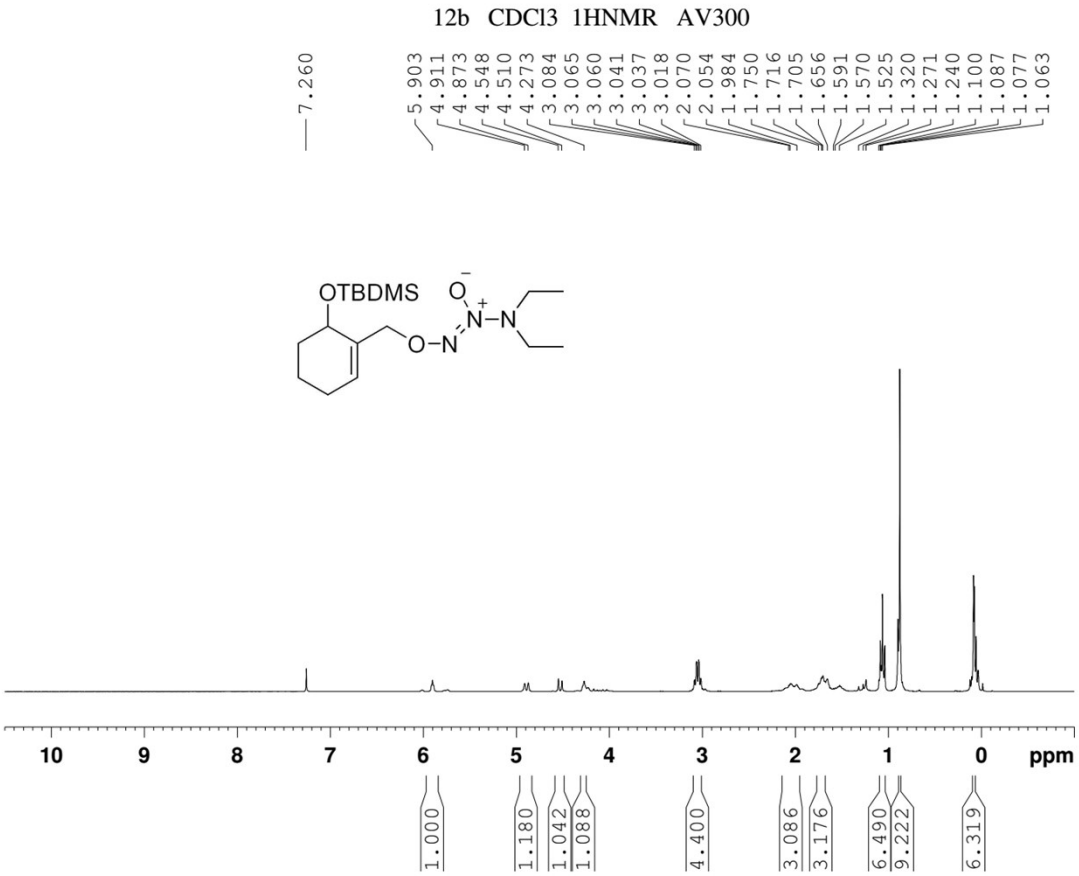
12a CDCl3 1HNMR AV300

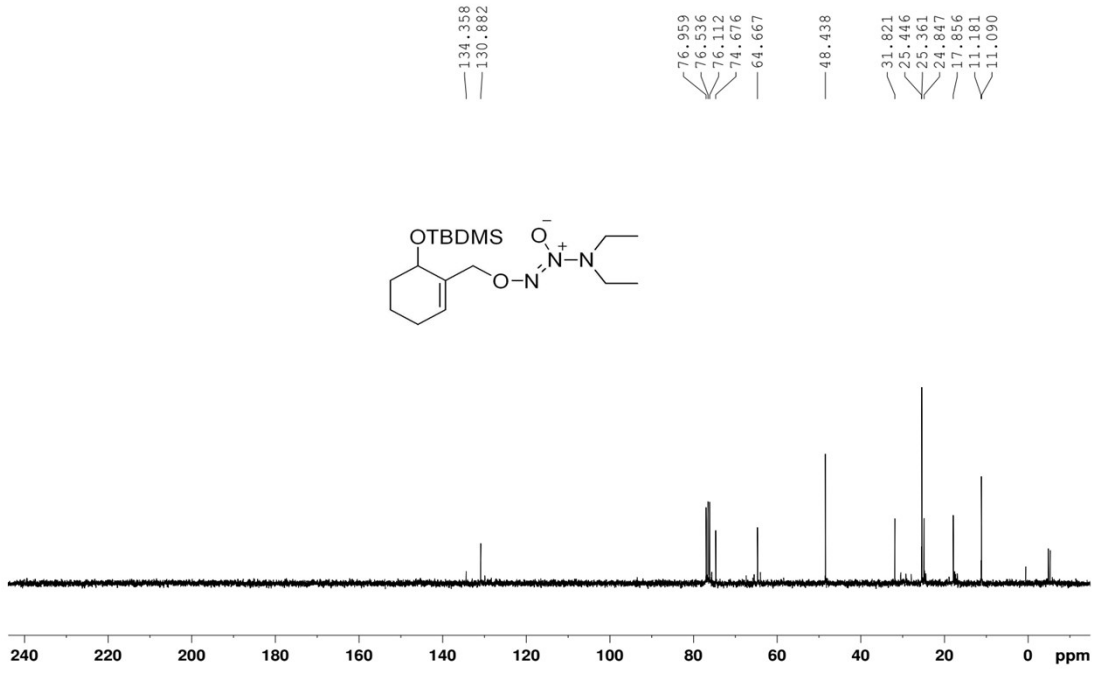


12a C13−NMR CDCl3 303K AV−300

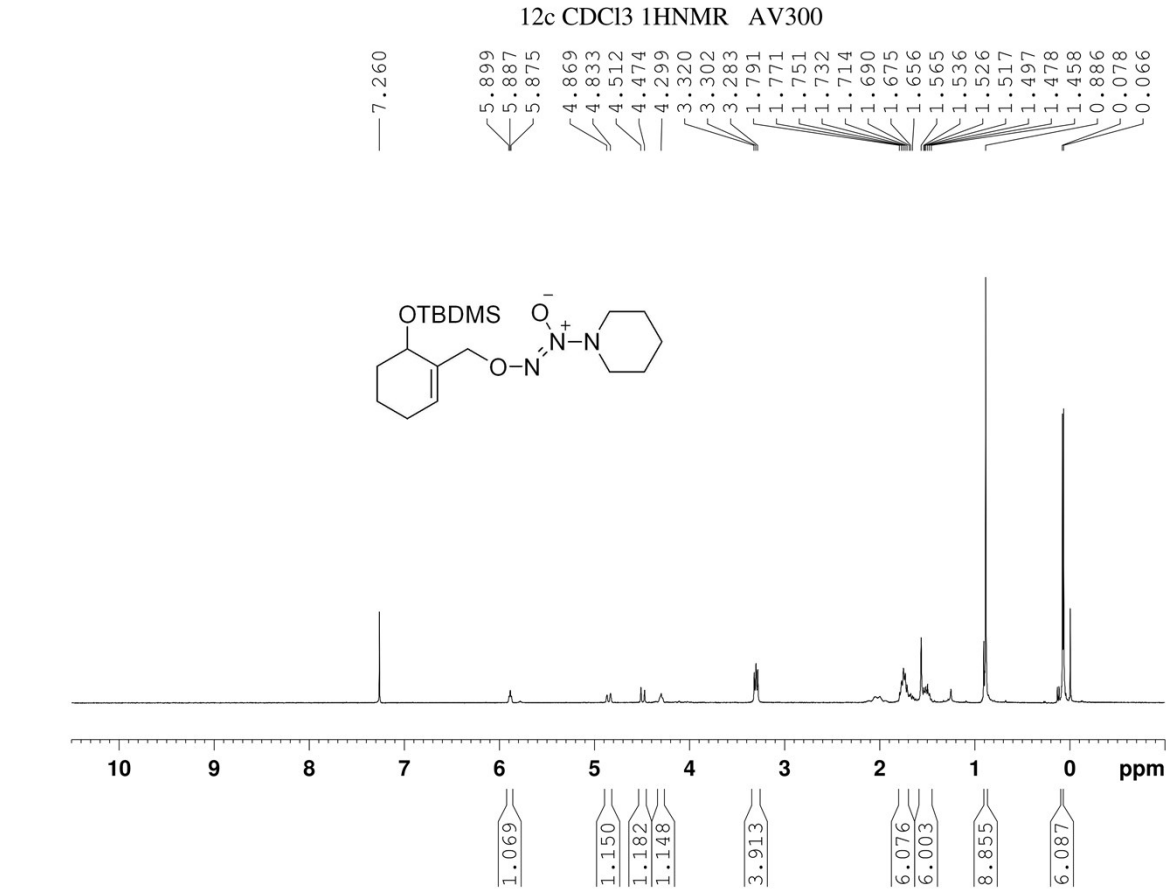


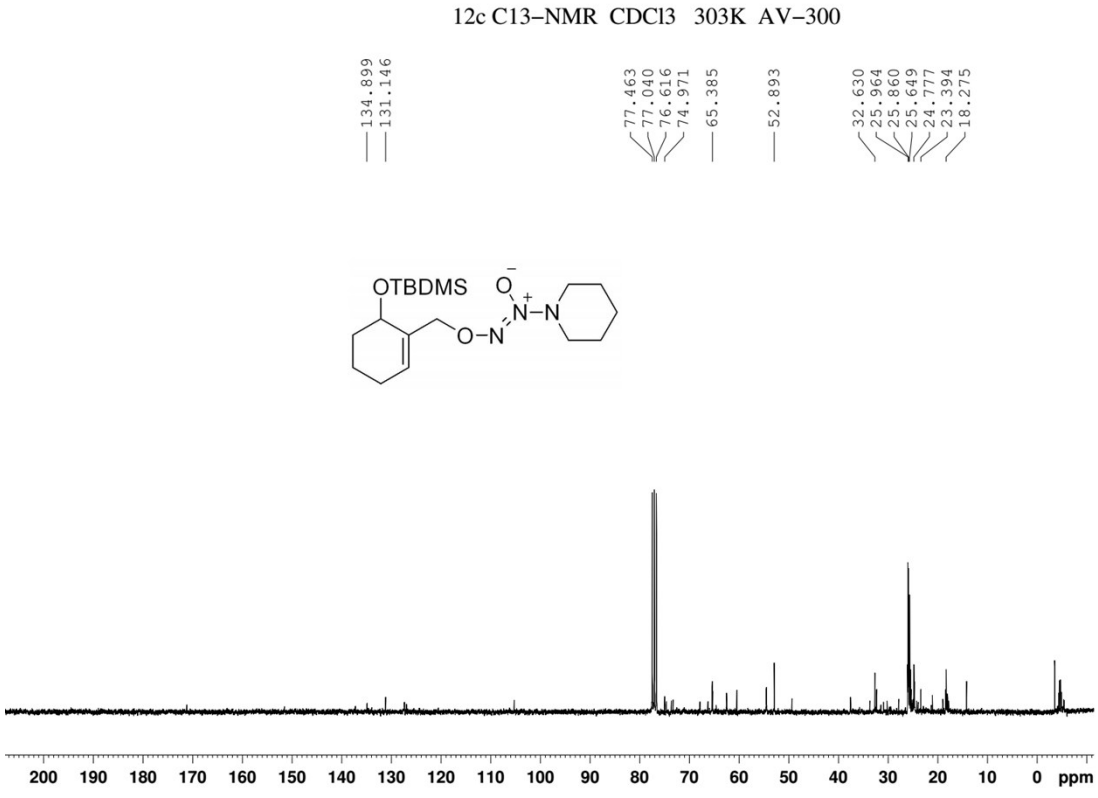
Compound 12b





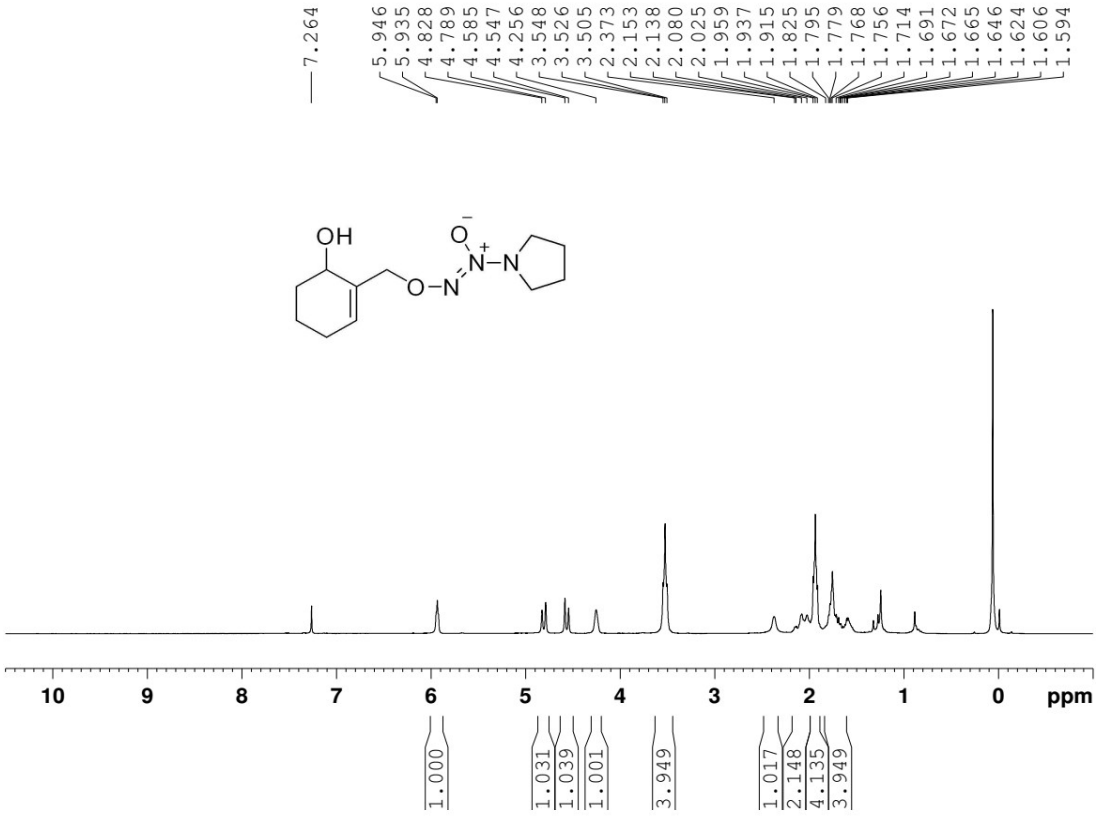
Compound 12c



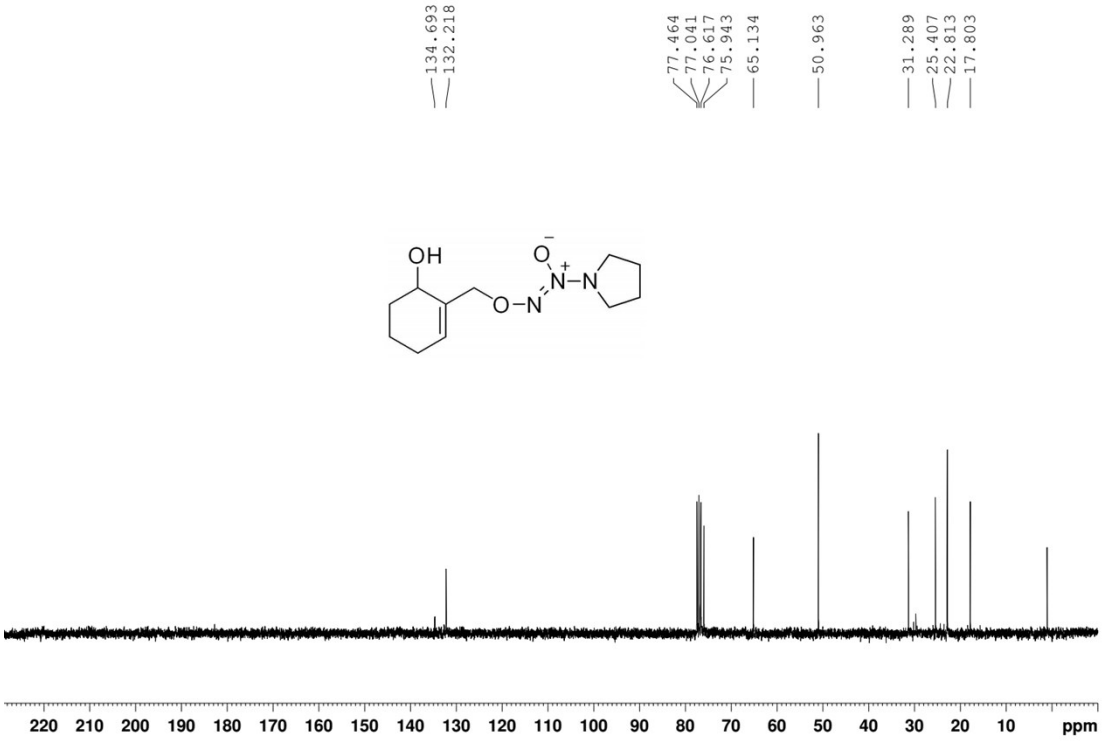


Compound 13a

13a CDCl3 1HNMR AV300

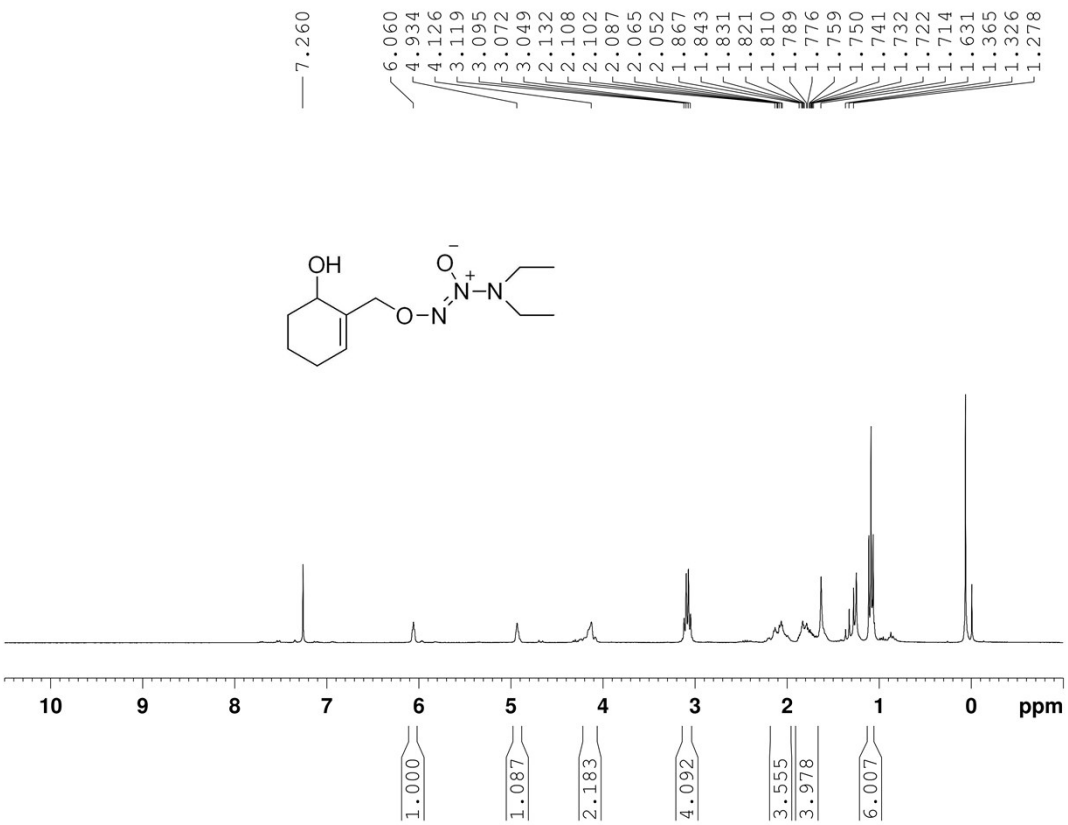


13a C13–NMR CDCl3 303K AV–300

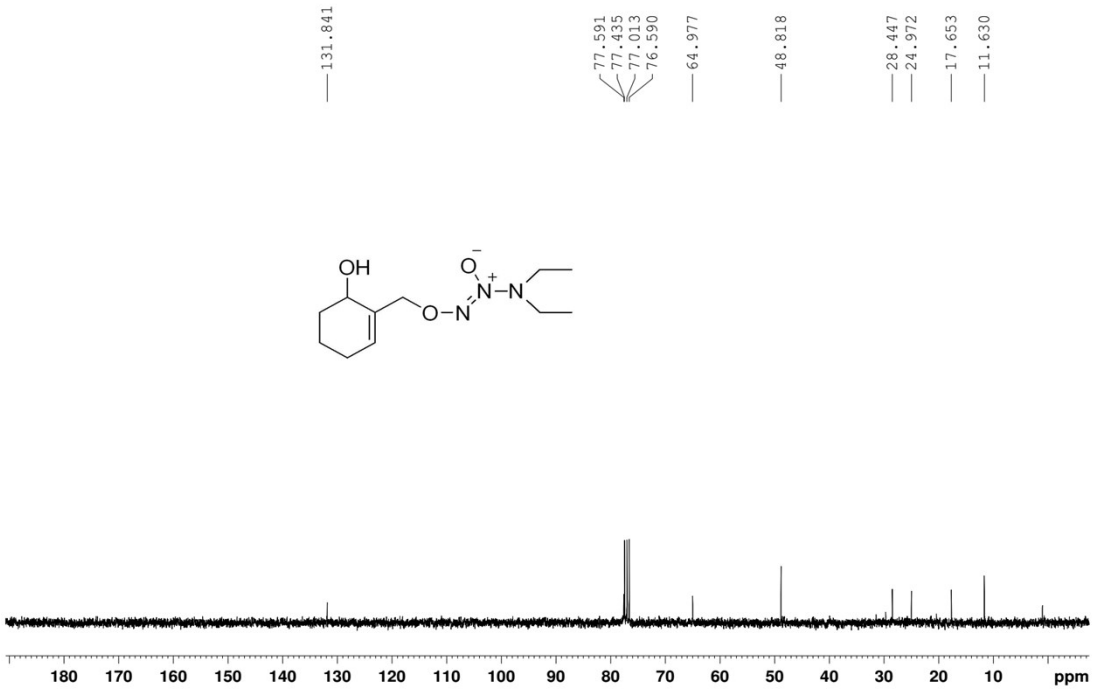


Compound 13b

13b CDCl3 1HNMR AV300

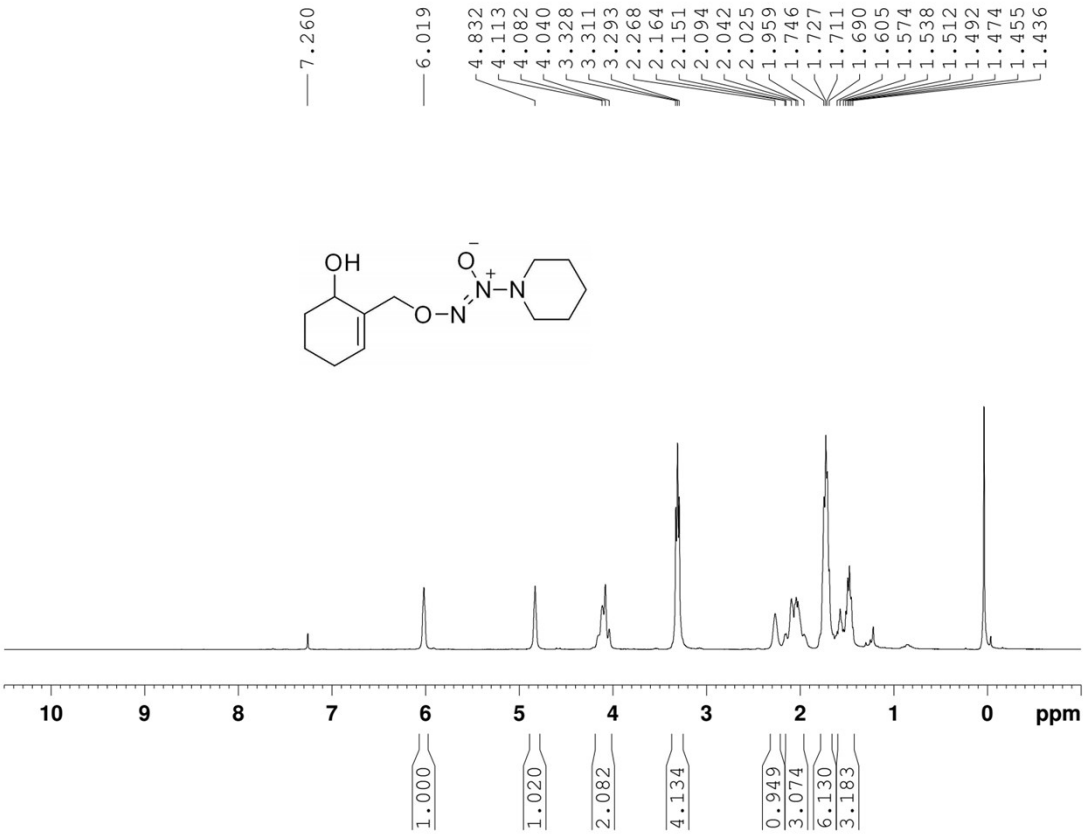


13b C13–NMR CDCL3 303K AV–300

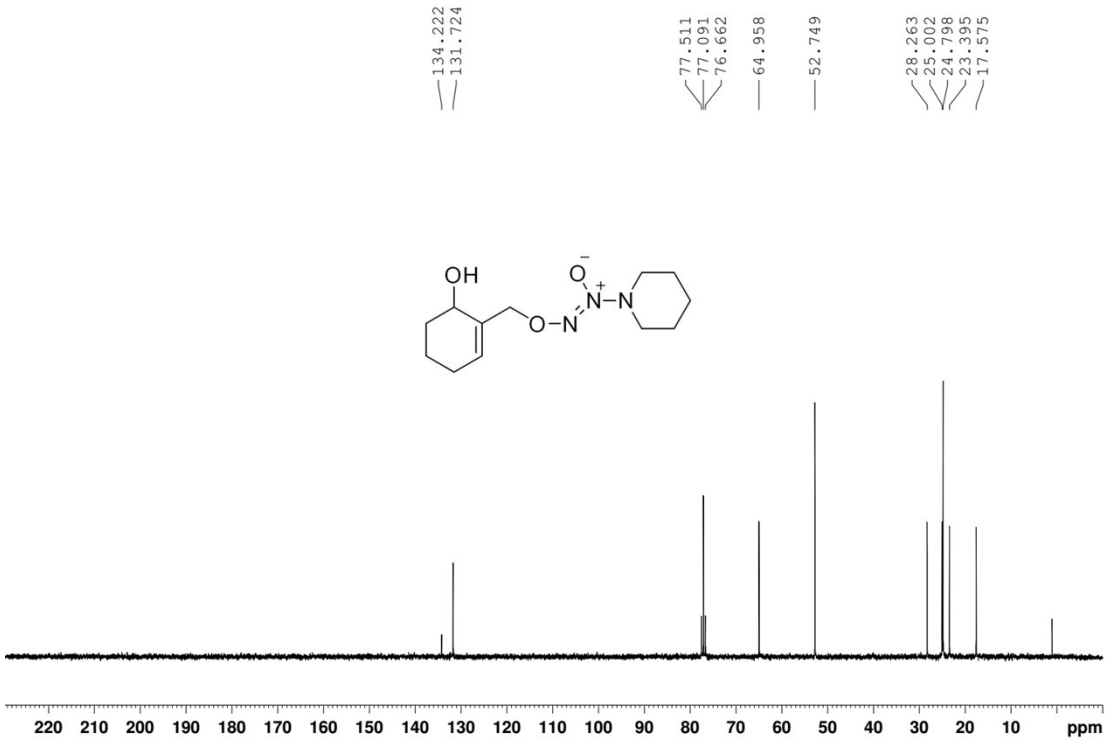


Compound 13c

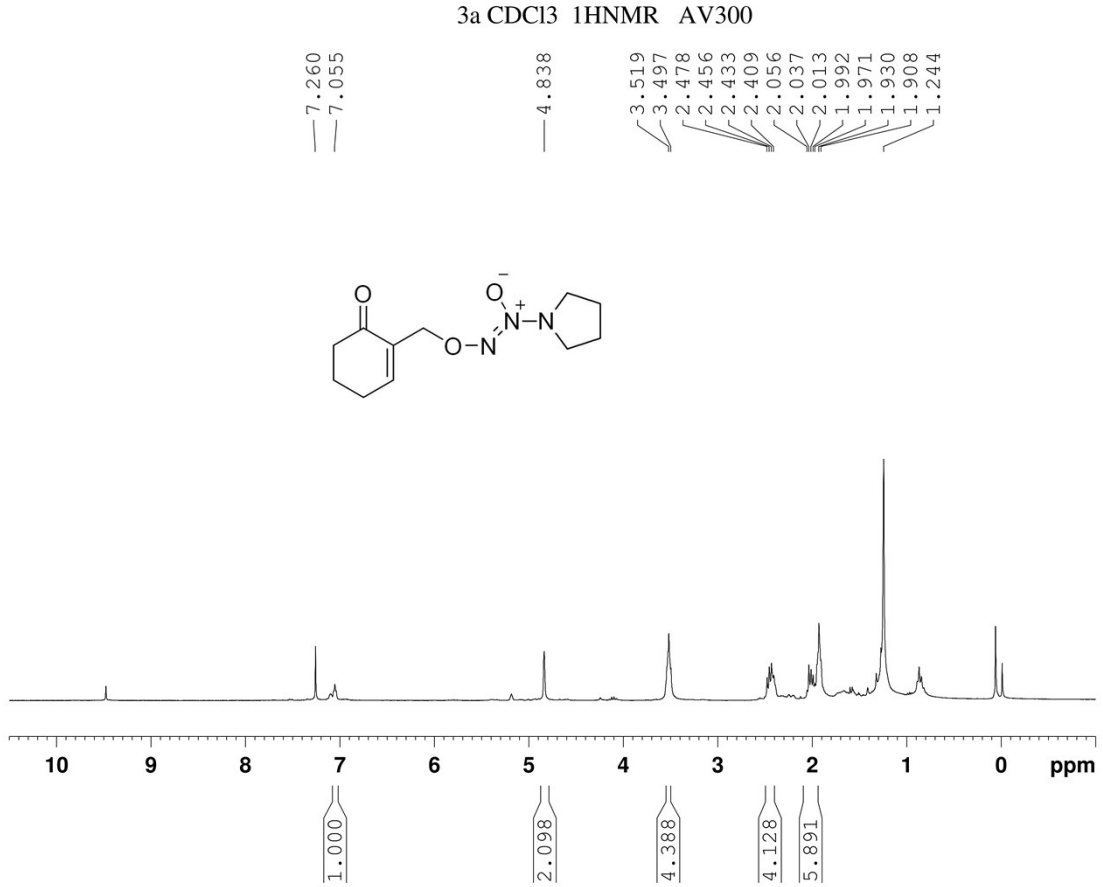
13c CDCl3 1HNMR AV300

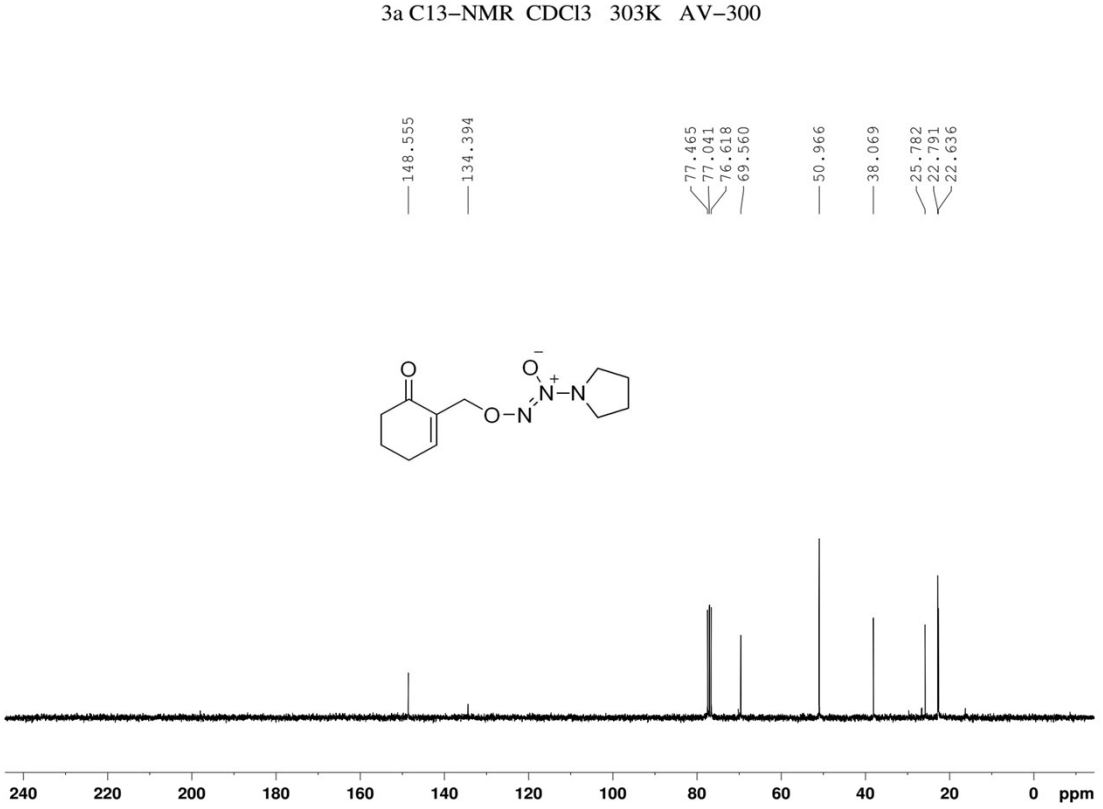


13c C13–NMR CDCl3 303K AV–300



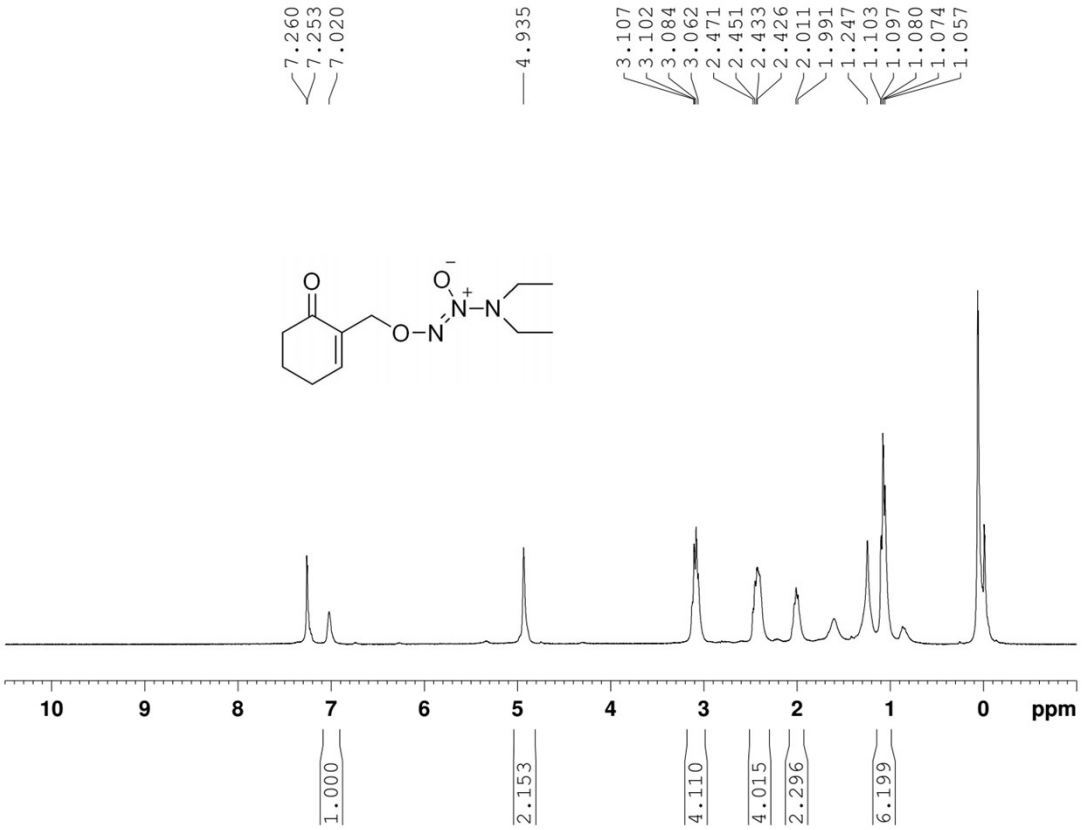
Compound 3a



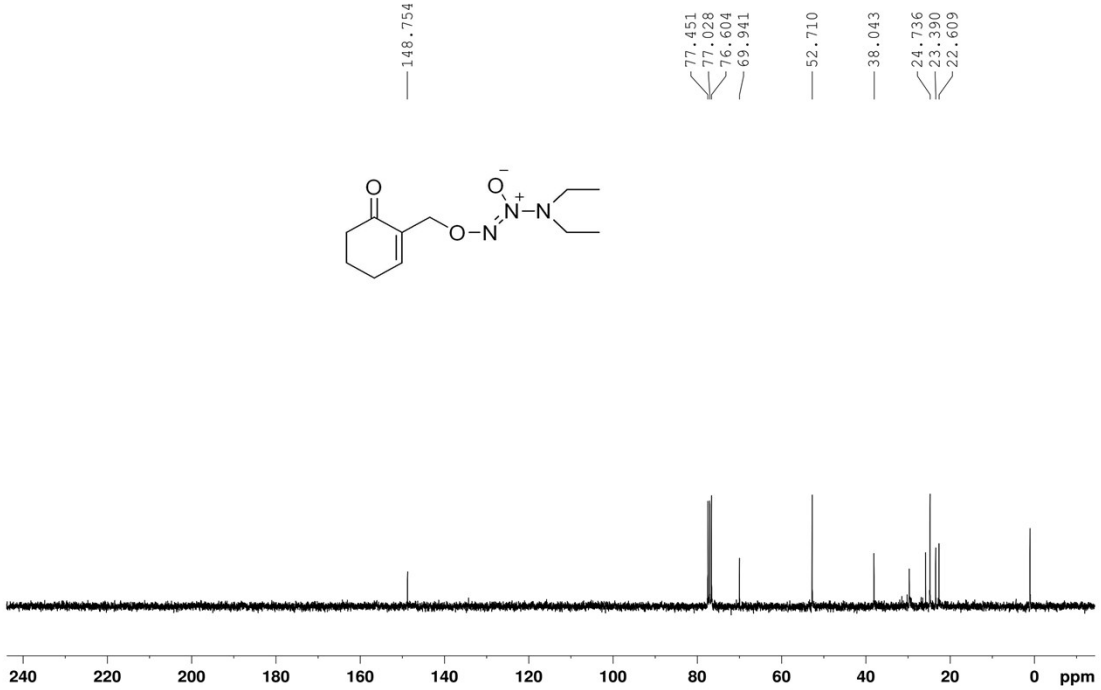


Compound 3b

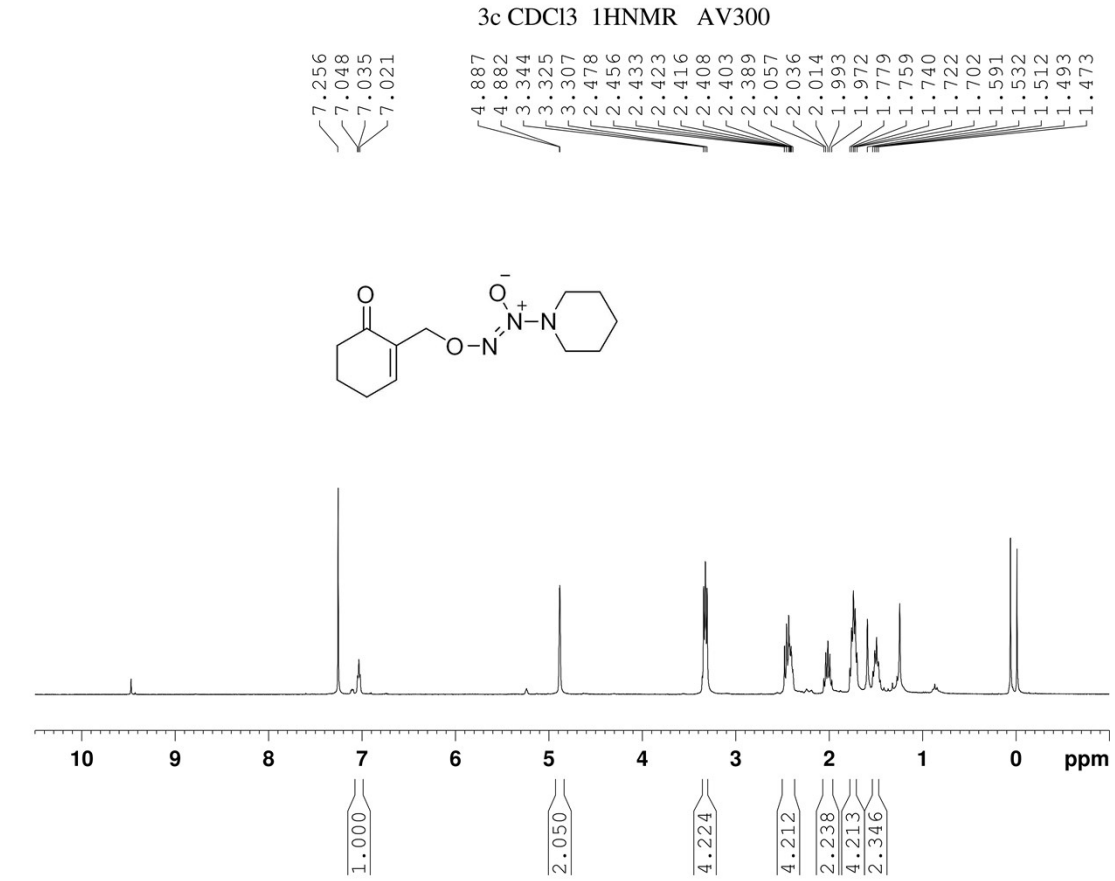
3b CDCl3 1HNMR AV300

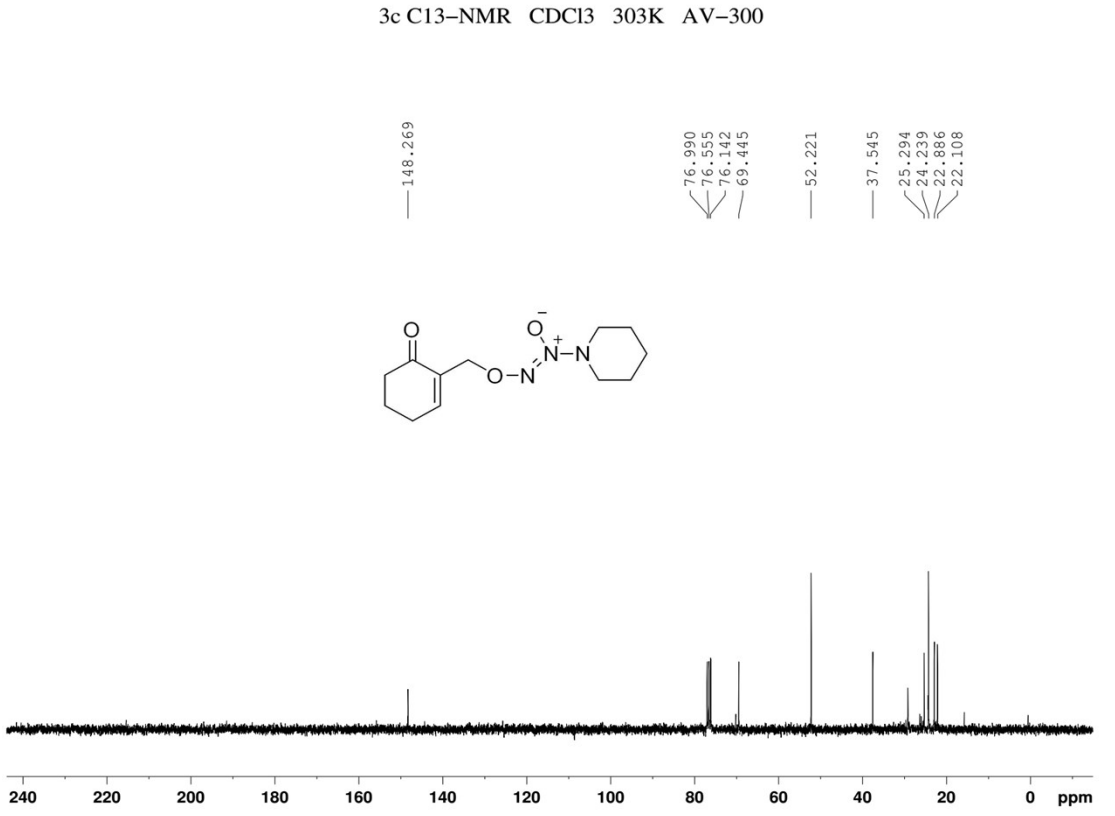


3b C13–NMR CDCl3 303K AV–300



Compound 3c





HPLC assessment of compound purities

All tested compounds (**3a-c**) with a purity of >97% were used for subsequent biological assays. We provided the spectra of HPLC assays as below.

Column: Venusil MP C18（250 mm × 4.6 mm × 5 μm）;

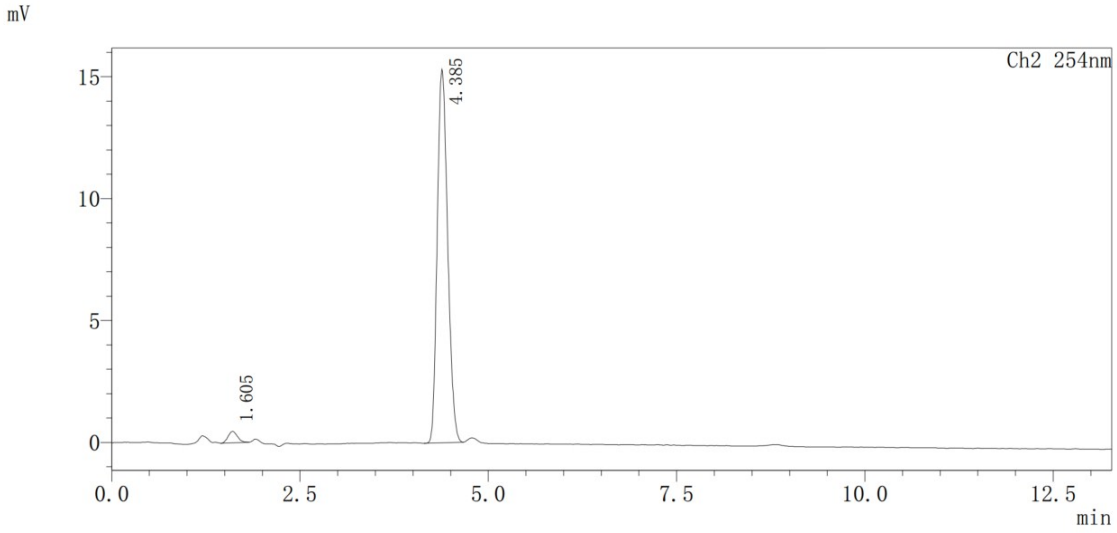
Mobile phase: Acetonitrile -Water (78:22 to 60:40, v/v);

Wavelength: 254 nm;

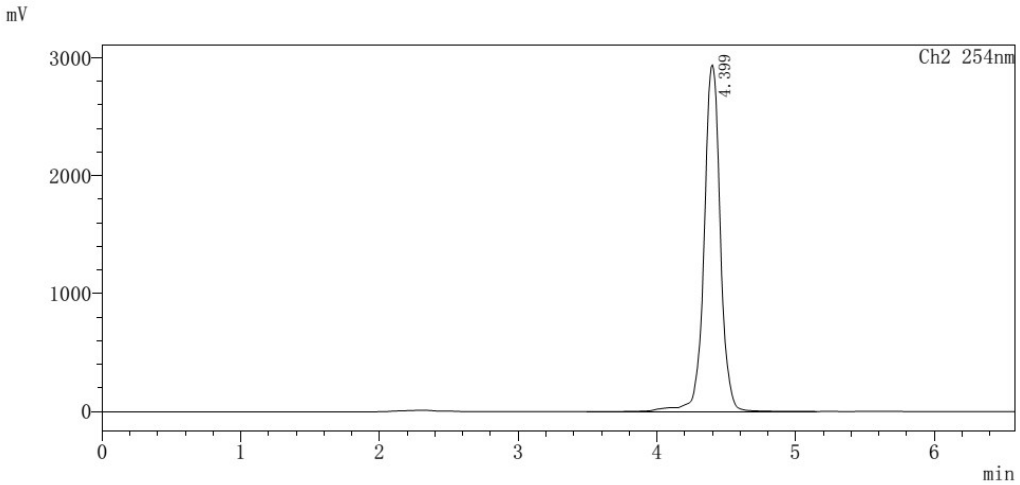
Rate: 1 mL/min;

Temperature: 25 °C;

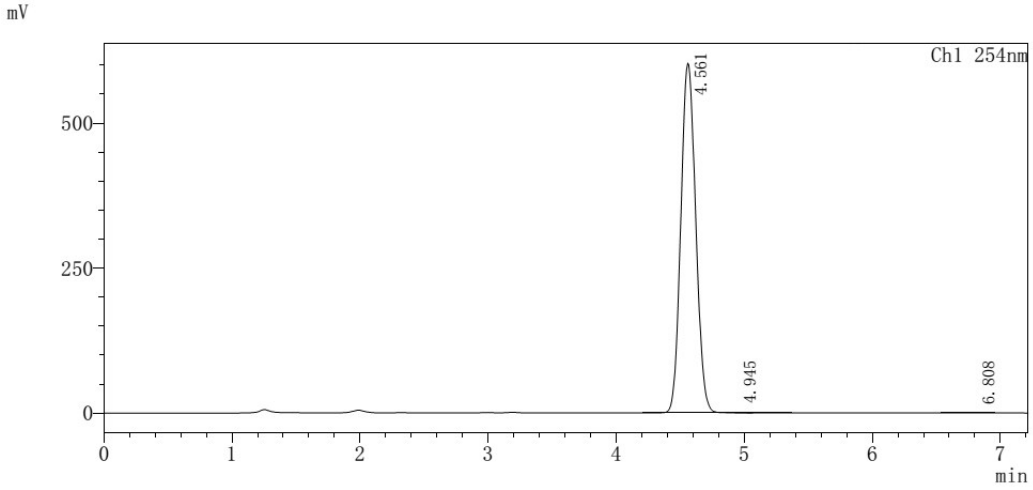
3a, 97.4%



3b, 100%



3c, purity of 99.9%



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(2) Yeh, M. C.; Liang, C.; Huang, T.; Hsu, H.; Tsau, Y. *J. Org. Chem.* **2013**, 78, 5521.

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(5) Kojima, H.; Urano, Y.; Kikuchi, K.; Higuchi, T.; Hirata, Y.; Nagano, T. *Angew. Chem., Int. Ed.* 1999, 38, 3209.