Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Oxidative Azidations of Phenols and Ketones using Iodine Azide after Release from an Ion Exchange Resin

Teresa Kösel, Gerald Dräger and Andreas Kirschning*

Abstract. The oxidative oligoazidation of phenols and ketones using iodine azide (IN_3) provided by its release from an ion exchange resin is reported. Preliminary mechanistic studies indicate a previously unknown reactivity of iodine azide toward phenols and ketones.

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1. Materials and methods

General information

^{1}H NMR spectra were recorded at 400 MHz with a BRUKER Avance-400 and BRUKER Ascend-400 or at 600 MHz with a BRUKER Ascend-600 spectrometer at 323K. ^{13}C NMR spectra were recorded at 100 MHz with a BRUKER Avance-400 and BRUKER Ascend-400 or at 150 MHz with a BRUKER Ascend-600 instrument. Multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, sex = sextet, m = multiplet, br = broad. Substitutions of carbons are described using the following abbreviations: p = primary, s = secondary, t = tertiary, q = quaternary. Chemical shift values of ^{1}H and ^{13}C NMR spectra are commonly reported in ppm relative to residual solvent signal as internal standard. The multiplicities refer to the resonances in the off-resonance decoupled spectra and were elucidated using phase-sensitive HSQC experiments.

Mass spectra were obtained with a lockspray dual ion source in combination with a WATERS Alliance 2695 LC system, or with a type Q-TOF premier (MICROMASS) spectrometer (ESI mode) in combination with a WATERS Acquity UPLC system equipped with a WATERS Acquity UPLC BEH C18 1.7 µm (SN 01473711315545) column (solvent A: water + 0.1 % {v/v} formic acid, solvent B: MeCN or MeOH {given in experimental part} + 0.1 % {v/v} formic acid; flow rate = 0.4 mL/min; gradient {t [min]/solvent B [%]}: {0/5} {2.5/95} {6.5/95} {6.6/5} {8/5}; retention times {r_t} given in the experimental part). Ion mass signals (*m/z*) are reported as values in atomic mass units.

High-resolution mass spectrometry (HRMS) was measured with a Micromass LCT with lockspray source. The injection proceeded in loop-mode with a HPLC system by WATERS (Alliance 2695). Alternatively, mass spectra were recorded with an Acquity-UPLC system by WATERS in combination with a Q-Tof Premier mass spectrometer by WATERS in lockspray mode. The ionization happened by electrospray ionization (ESI) or by chemical ionization at atmospheric pressure (APCI). The calculated and found mass are reported.

GC/MS analyses were carried out with an HP 6890 chromatograph with KAS 4, coupled to an HP 5973 quadrupole mass selective detector. Samples were analyzed on an OPTIMA 5 column (poly(5%-phenyl-95%-methylsiloxane), 30 m x 0.32 mm i.d. x film thickness 0.25 µm). Carrier gas, He; injector temp., 60 °C to 300 °C at 12 °C/min, splitless; temp. program: 50 °C (isothermal 1 min) to 300 °C, at 20 °C/min and held isothermal for 6 min at 300 °C; ion source: EI, ionization energy, 70 eV; electron mass spectra were acquired over the mass range of 40 – 500 amu.

Semi-preparative HPLC was performed using an Alliance 2695 HPLC-system by WATERS with a WATERS 996 diode array detector (λ = 200-350 nm) and a NUCLEODUR 100-5 C18 CN-RP column (5 *µ*m, 250 mm, Ø 8 mm) by MACHERY NAGEL. Mass detection was conducted with a WATERS Quattro micro API mass spectrometer in negative ionization mode.

Analytical thin-layer chromatography was performed using precoated silica gel plates (MACHERY NAGEL, DÜREN) and the spots were visualized with UV light at 254 nm or alternatively by staining with permanganate or 4-methoxybenzaldehyde solutions.[S1]

Commercially available reagents, chromatography type or dry solvents were used as received or purified by standard techniques according to the literature.[S1]

Flash column chromatography was performed using mesh silica by MACHERY NAGEL (grain size 40-63 *µ*m), with the indicated solvent system according to the standard techniques. Alternatively, a BÜCHI purification system was applied containing two pump modules (C-605), a UV-Vis detector (C-630), a fraction collector (C-660) and the control unit C-620. The separation was performed with a Cartridge PP 12/150 column and a FC60 (60 x 20 mL) rack. The system was controlled with Sepacore® control software. Infrared spectra (ν_{max}, FTIR) were recorded in reciprocal centimeters (cm^{-1}) as thin films or compressed solids on a SHIMADZU FT-IR Affinity-1S spectrometer.

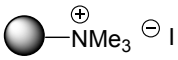
Melting points were determined on an SRS OptiMelt apparatus and are not corrected.

Specific Optical rotation values $[\alpha]^{T}_{D}$ were measured in a quartz cuvette on a polarimeter 341 by PERKINELMER at a wavelength of 589 nm (D) and given temperature *T*.

2. Chemical syntheses

2.1 Preparations of polymer-supported reagents

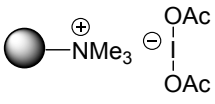
2.1.1 Synthesis of polymer S1



S1

Polymer-bound hydroxide (Amberlyst® A26-resin from abcr; 4.2 mmol/g hydroxide) was flushed successively with 1M NaOH (4 mL/g polymer), sat. LiI-solution (5 mL/g polymer), distilled water (4 mL/g polymer), isopropyl alcohol (4 mL/g polymer) and CH_2Cl_2 (4 mL/g polymer). Drying *in vacuo* afforded a light pink resin S**1**. It was prepared that way on a 50 g scale.

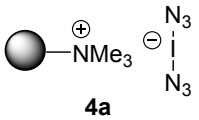
2.1.2 Synthesis of polymer S2



S2

A suspension of polymer-bound iodide **S1** (4.2 mmol iodide per gram resin, 1.0 equiv.) and $PhI(OAc)_2$ (1.8 equiv.) was shaken in dry CH_2Cl_2 (3 mL/mmol iodide) at 665 rpm for 6 h at room temperature under an argon atmosphere. During this time, the reaction mixture was protected from light. The light yellow resin **S2** was filtered, washed with CH_2Cl_2 (30 mL/g resin) and dried *in vacuo*. Practically, the effective loading was found to be up to 2.1 mmol reagent per g resin. It can be stored several months under an argon atmosphere at –15 °C in the dark without loss of activity.

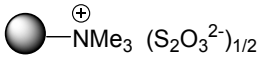
2.1.3 Synthesis of polymer 4a



4a

A suspension of polymer-bound iodide **S2** (4.2 mmol iodide per gram resin, 1.0 equiv.) and trimethylsilyl azide (2.6 equiv.) was shaken in dry CH_2Cl_2 (4 mL/mmol iodide) at 665 rpm for 6 h at room temperature under an argon atmosphere. During this time, the reaction mixture was protected from light. The orange-colored resin **4a** was filtered, washed with CH_2Cl_2 (30 mL/g resin) and dried *in vacuo*. Practically, the effective loading was found to be up to 2.1 mmol reagent per g resin. It can be stored several months under an argon atmosphere at –15 °C in the dark without loss of activity.

2.1.4 Preparation of polymer-bound thiosulfate S3



S3

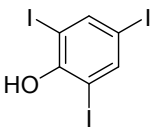
Polymer-bound hydroxide (Amberlyst® A26-resin from abcr; 4.2 mmol/g hydroxide) was flushed successively with 1M NaOH (4 mL/g polymer), a sat. $Na_2S_2O_3$-solution (5 mL/g polymer), methanol (4 mL/g polymer), acetone (4 mL/g polymer) and Et_2O (4 mL/g polymer). Drying *in vacuo* afforded the light pink resin **S3.** It was prepared on a 50 g scale.

2.2 Azidation of phenols

General procedure

A mixture of the phenol (0.5 mmol, 1.00 equiv.) and polymer-bound iodine azide (**4a**, 1.19 g, 2.50 mmol, 5.00 equiv.) was stirred in absolute MeCN (4.16 mL, 3.5 mL/g polymer) at ambient temperature under an argon atmosphere. After the full consumption of the starting material was monitored by TLC the reaction was terminated by filtration and the resin was washed with EtOAc and the combined filtrates were concentrated under reduced pressure.

2,4,6-Triiodophenol (6)



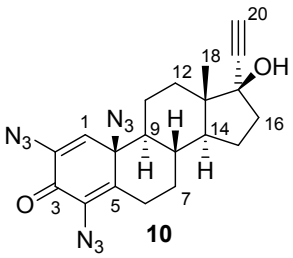
6

The title compound was prepared according to the general procedure using phenol (**5**) as starting material (150 mg, 1.59 mmol, 1.0 equiv). After 18 h, the triiodophenol **6** was obtained as a brown solid (675.1 mg, 143 *µ*mol; 90% yield).

R_f = 0.69 (toluene/EtOAc = 9:1); **m.p.** = 148 °C, [Lit.: m.p. = 152-159 °C]; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.93 (s, 2 H, H_{Ar}), 5.78 (s, 1 H, O*H*); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 153.9 (q, *C*-OH), 146.5 (t, *C*-H), 83.5 (q, *C*-I), 83.4 (q, *C*-I); **HRMS** (ESI^-) *m/z* Calculated for $C_6H_2I_3O^-$ $[M-H]^-$ 470.7240; Found 470.7240.

The analytical data are consistent with those reported in the literature.[S2]

(8*S*,9*S*,13*S*,14*S*,17*R*)-2,4,10-Triazido-17-ethynyl-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (10)

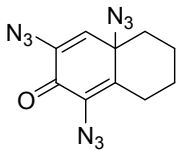


10

A mixture of ethinylestradiol (**7**, 200 mg, 0.675 mmol, 1.0 equiv) and polymer **4a** (5 equiv with respect to substrate) was stirred at 300 rpm under light protection in absolute MeCN (3.5 mL/g resin) at room temperature under an argon atmosphere. After 60 h the reaction was terminated by filtration and the resin was washed with CH_2Cl_2 (3 x 20 mL/g resin). The filtrate was washed with 10 mL of 5% sodium thiosulfate and dried over magnesium sulfate. The solvent was removed under reduced pressure. Purification by flash column chromatography (Büchi, solvent A: toluene, solvent B: ethyl acetate; tube volume: 10.0 mL; flow rate: 10.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/5; 30/25; t_R = 6.0 min) afforded azide **10** (268.8 mg, 0.641 mmol, 95%) as a brown oil.

R_f = 0.26 (toluene/EtOAc = 9:1); **$[\alpha]_D^{29.4}$** = - 7.3° (*c* 0.12, CH_2Cl_2); **IR** ν_{max} [cm^{-1}] 2110, 2093 *v*(N_3), 1661 *v*(C=O), 1603, 1333, 1315, 1292, 1263, 1213, 1057, 735, 656; **^{1}H-NMR** ($CDCl_3$, 600 MHz): *δ* [ppm] 6.57 (s, 1H, *H*-1), 3.10 – 3.07 (m, 1H, *H*-6), 2.53 (s, 1H, *H*-20), 2.31 – 2.26 (m, 1H, *H*-16), 2.23 – 2.18 (m, 12H, *H*-6), 2.02 – 1.97 (m, 1H, *H*-16), 1.94 – 1.90 (m, 1H, *H*-7), 1.82 – 1.77 (m, 2H, *H*-8/(11/15)), 1.75 – 1.63 (m, 4H, *H*-7/12/2x(11/15)), 1.46 – 1.41 (m, 1H, *H*-14), 1.39 – 1.34 (m, 1H, *H*-(11/15)), 1.20 – 1.16 (m, 1H, *H*-9), 1.05 – 0.98 (m, 1H, *H*-7), 0.91 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 150 MHz): *δ* [ppm] 176.1 (q, *C*-3), 145.4 (q, *C*-5), 135.1 (q, *C*-2), 129.7 (q, *C*-4), 128.7 (t, *C*-1), 87.1 (q, *C*-19), 79.6 (q, *C*-17), 74.4 (t, *C*-20), 66.2 (q, *C*-10), 53.9 (t, *C*-9), 48.9 (t, *C*-14), 46.9 (q, *C*-13), 38.9 (s, *C*-16), 32.1 (s, *C*-12), 31.8 (s, *C*-7), 26.5 (s, *C*-6), 23.3 (s, *C*--(11/15)), 23.2 (s, *C*--(11/15)), 12.7 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* Calculated for $C_{20}H_{20}N_9O_2^-$ $[M-H]^-$ 418.1740; Found 418.1744.

1,3,4a-Triazido-5,6,7,8-tetrahydronaphthalen-2(4a*H*)-one (11)

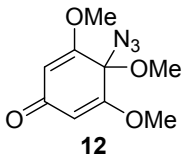


11

The title compound was prepared according to the general procedure using 5,6,7,8-tetrahydronaphthalen-2-ol as starting material. After 3 h, the azide **11** was obtained as a yellow foam (120.4 mg, 444 *µ*mol; 89% yield).

IR ν_{max} [cm^{-1}] 2941, 2862, 2091 ν(N_3), 1659 ν(C=O), 1605, 1435, 1339, 1325, 1310, 1202, 1167, 1136, 1078, 1051, 964, 939, 926, 895, 876, 781, 671, 650, 556, 528; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ [ppm] 6.26 (s, 1H, C*H*), 3.04 (d, *J* = 13.8 Hz, 1H, N_3C=CCH_2), 2.08 – 2.16 (m, 1H, N_3C=CCH_2), 2.04 – 2.00 (m, 1H, N_3-CCH_2), 2.00 – 1.96 (m, 1H, N_3C=CCH_2CH_2), 1.79 – 1.72 (m, 1H, N_3-CCH_2CH_2), 1.79 – 1.72 (m, 1H, N_3-CCH_2CH_2), 1.68 – 1.65 (m, 1H, N_3-CCH_2CH_2), 1.41 – 1.33 (m, 1H, N_3-CCH_2), 1.28 – 1.23 (m, 1H, N_3C=CCH_2CH_2); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ [ppm] 176.7 (q, *C*=O), 143.9 (q, C=*C*CH_2), 134.7 (q, N_3*C*=CH), 130.0 (t, *C*H), 129.8 (q, N_3*C*=CCH_2), 63.2 (q, N_3-*C*CH_2), 38.7 (s, N_3-C*C*H_2), 26.6 (s, N_3-C=C*C*H_2), 26.3 (s, N_3-C=CCH_2*C*H_2), 20.7 (s, N_3-CCH_2*C*H_2).
MS methods (ESI, EI, APCI, GC) were performed to collect mass data, but without success.

4-Azido-3,4,5-trimethoxycyclohexa-2,5-dien-1-one (12)

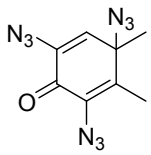


12

The title compound was prepared according to the general procedure using 3,4,5-trimethoxyphenol as starting material. After 2.5 h, the azide **12** was obtained as a yellow foam (107.8 mg, 479 *µ*mol; 96% yield).

IR ν_{max} [cm^{-1}] 2116 ν(N_3), 1663 ν(C=O), 1630, 1605, 1458, 1360, 1335, 1246, 1211, 1148, 1105, 1049, 1007, 912, 856, 727, 646, 627, 604, 554, 469; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ [ppm] 5.51 (s, 2H, 2xC*H*), 3.77 (s, 6H, 3xC=COCH_3), 3.18 (s, 3H, N_3-COCH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ [ppm] 185.5 (q, *C*=O), 165.3 (q, 2xC=*C*OCH_3), 103.2 (t, 2x*C*H), 85.2 (q, N_3-*C*OCH_3), 56.5 (p, 2xC=CO*C*H_3), 53.0 (p, N_3-C*C*H_3); **ESI-MS** (ESI$^+$) *m/z* calculated for $C_9H_{11}N_3O_4Na^+$ $[M+Na]^+$ 248.0647; found 248.0644.

2,4,6-Triazido-3,4-dimethylcyclohexa-2,5-dien-1-one (13)

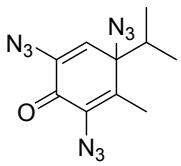


13

The title compound was prepared according to the general procedure using 3,4-dimethylphenol as starting material. After 2 h, the azide **13** was obtained as a yellow foam (107.2 mg, 437 *µ*mol; 87% yield).

IR ν_{max} [cm^{-1}] 2114 ν(N_3), 1600-1700 ν(C=O), 1489, 1451, 1327, 1258, 1045, 928, 527, 467, 407; **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ [ppm] 6.31 (s, 1H, C*H*), 2.02 (s, 3H, HCH_3), 1.41 (s, 3H, N_3-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ [ppm] 176.2 (q, *C*=O), 141.8 (q, C=*C*CH_3), 134.2 (q, N_3-*C*=CH), 131.6 (q, N_3-*C*=CCH_3), 130.5 (t, *C*H), 63.2 (q, N_3-*C*CH_3), 25.0 (p, N_3-C*C*H_3), 14.3 (p, C=C*C*H_3).
Various MS methods (ESI, EI, APCI, GC) were performed to collect mass data, but without success.

2,4,6-Triazido-4-isopropyl-3-methylcyclohexa-2,5-dien-1-one (14)



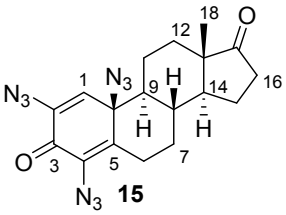
14

The title compound was prepared according to the general procedure using 3-methyl-4-isopropylphenol as starting material. After 2 h, the reaction was terminated. Purification by flash column chromatography (Büchi, solvent A: petroleum ether, solvent B: ethyl acetate; tube volume: 10.0 mL; flow rate: 20.0 ml/min; 30sec/fraction; gradient: (*t* [min]/solvent B [%]): 0/0;

18/0; 30/20; t_R = 5.0 – 6.0 min) afforded azide **14** as a yellow oil (102.6 mg, 375 *µ*mol; 75% yield).

IR ν_{max} [cm^{-1}] 2968, 2112 *v*(N_3), 1662 *v*(C=O), 1645, 1602 *v*(C=O), 1464, 1389, 1368, 1327, 1209, 1032, 941, 885, 739, 671, 532, 411; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.32 (s, 1H, C=C*H*), 2.08 (p, *J* = 6.9 Hz, 1H, *H*C(CH_3)$_2$), 1.98 (s, 3H, C=C-CH_3), 1.09 (d, 3H, *J* = 6.8 Hz, HC(CH_3)$_2$), 0.65 (d, 3H, *J* = 6.9 Hz, HC(CH_3)$_2$); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 176.3 (q, *C*=O), 142.1 (q, C=*C*CH_3), 136.5 (q, N_3-*C*=CH), 132.9 (q, N_3-*C*=CCH_3), 126.0 (t, C=*C*H), 70.5 (q, N_3-*C*-CH(CH_3)$_2$), 35.4 (t, H*C*(CH_3)$_2$), 17.3 (p, HC(*C*H_3)$_2$), 16.8 (p, HC(*C*H_3)$_2$), 14.0 (p, C=C-*C*H_3).
Various MS methods (ESI, EI, APCI, GC) were performed to collect mass data, but without success.

(8*S*,9*S*,10*R*,13*S*,14*S*)-2,4,10-Triazido-13-methyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione (15)

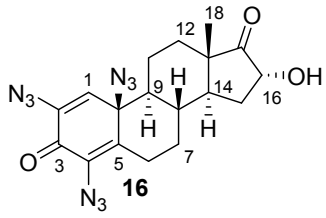


15

The title compound was prepared according to the general procedure using estrone (**21**) as starting material. After 2 h, the reaction was terminated. Purification by flash column chromatography (Büchi, solvent A: toluene, solvent B: ethyl acetate; tube volume: 10.0 mL; flow rate: 10.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/5; 30/25; t_R = 5.0 – 14.0 min) afforded azide **15** as a white solid (172.4 mg, 454 *µ*mol; 91% yield).

mp = > 150 °C (decomposition); **$[\alpha]_D^{20.0}$** = + 88.3° (*c* 1.0, $CHCl_3$); **IR** ν_{max} [cm^{-1}] 2943, 2116, 2095 *v*(N_3), 1736, 1663 *v*(C=O), 1603 *v*(C=O), 1454, 1339, 1317, 1231, 1063, 1034, 1005, 905, 727, 648, 559; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.53 (s, 1H, *H*-1), 3.13 – 3.10 (m, 1H, *H*-6), 2.45 (dd, *J* = 19.4, 8.7 Hz, 1H, *H*-16), 2.22 (td, *J* = 13.7, 4.8 Hz, 1H, *H*-6), 2.14 – 2.00 (m, 2H, *H*-(7/12)/16), 1.96 – 1.89 (m, 2H, *H*-8/15), 1.85 – 1.79 (m, 2H, *H*-11/(7/12)), 1.77 – 1.72 (m, 1H, *H*-11), 1.62 – 1.51 (m, 1H, *H*-15), 1.25 – 1.13 (m, 3H, *H*-9/14/(7/12)), 1.10 – 1.00 (m, 1H, *H*-(7/12)), 0.90 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 219.7 (q, *C*-17), 175.9 (q, *C*-3l), 144.7 (q, *C*-5), 135.1 (q, *C*-2), 129.8 (q, *C*-4), 128.2 (t, *C*-1), 66.0 (q, *C*-10), 53.9 (t, *C*-9), 49.7 (t, *C*-14), 47.6 (q, *C*-13), 35.6 (s, *C*-16), 35.1 (t, *C*-8), 30.9 (s, *C*-(7/12)), 30.8 (s, *C*-(7/12), 26.3 (s, *C*-6), 22.6 (s, *C*-11), 21.9 (s, *C*-15), 13.7 (p, *C*-18).
The structure was unequivocally proven by X-ray crystal analysis (see chapter 3). Various MS methods (ESI, EI, APCI, GC) were performed to collect mass data, but without success.

(8*S*,9*S*,10*R*,13*S*,14*S*,16*R*)-2,4,10-Triazido-16-hydroxy-13-methyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione (16)



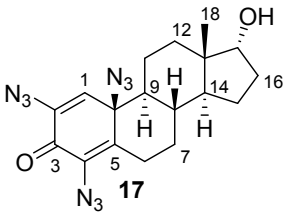
16

The title compound was prepared according to the general procedure using 16*α*-hydroxyestrone (19.2 *µ*mol) as starting material. After 2 h, the azide **16** was obtained as a yellow foam (3.9 mg, 9.5 *µ*mol; 50% yield).

$[\alpha]_D^{24.2}$ = + 22.3° (*c* 0.39, $CDCl_3$); **IR** ν_{max} [cm^{-1}] 2114 *v*(N_3), 1748, 1603 *v*(C=O), 1339, 1315, 1009, 910, 731, 648, 552, 409; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.52 (s, 1H, *H*-1), 4.38 (d, *J* = 8.1 Hz, 1H, *H*-16), 3.16 – 3.12 (m, 1H, *H*-6), 2.22 (td, *J* = 13.8, 5.1 Hz, 1H, *H*-6), 1.99 – 1.86 (m, 5H, *H*-7/8/12/15), 1.82 – 1.76 (m, 2H, *H*-11), 1.49 – 1.42 (m, 1H, *H*-14), 1.38 – 1.31 (m, 1H, *H*-7/12/15), 1.21 – 1.15 (m, 1H, *H*-9), 1.07 – 1.04 (m, 1H, *H*-7//12/15), 1.02 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 218.2 (q, *C*-17), 176.0 (q, *C*-3), 144.2 (q, *C*-5), 135.4 (q, *C*-2), 130.1

(q, *C*-4), 127.8 (t, *C*-1), 71.2 (t, *C*-16), 66.0 (q, *C*-10), 53.8 (t, *C*-9), 47.6 (q, *C*-13), 46.8 (t, *C*-14), 35.1 (t, *C*-8), 30.8 (s, *C*-7/12/15), 30.7 (s, *C*-7/12/15), 30.6 (s, *C*-7/12/15), 26.2 (s, *C*-6), 22.2 (s, *C*-11), 14.1 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* calculated for $C_{18}H_{18}N_9O_3^-$ $[M-H]^-$ 408.1533; found 408.1530.

(8*S*,9*S*,13*S*,14*S*,17*R*)-2,4,10-Triazido-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one (17)

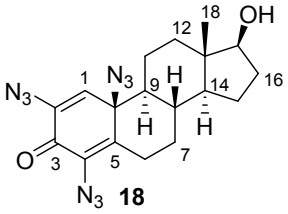


17

The title compound was prepared according to the general procedure using 17α-estradiol (0.3 mmol) as starting material. After 2 h, the azide **17** was obtained as a yellow foam (90.0 mg, 228 *µ*mol; 76% yield).

$[\alpha]_D^{26.2}$ = + 7.5° (*c* 1.6, MeOH); **IR** ν_{max} [cm^{-1}] 2938, 2116 *v*(N_3), 1663 *v*(C=O), 1603, 1339, 1317, 1211, 934, 885, 419, 403; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.57 (s, 1H, *H*-1), 3.75 (d, *J* = 5.7 Hz, 1H, *H*-17), 3.09 – 3.06 (m, 1H, *H*-6), 2.24 – 2.13 (m, 2H, *H*-6/16), 1.96 – 1.93 (m, 1H, *H*-16), 1.86 – 1.82 (m, 1H, *H*-11), 1.79 – 1.70 (m, 3H, *H*-8/11/15), 1.56 – 1.42 (m, 3H, *H*-7/12), 1.39 – 1.32 (m, 1H, *H*-14), 1.27 – 1.22 (m, 1H, *H*-15), 1.18 – 1.12 (m, 1H, *H*-9), 1.09 – 0.99 (m, 1H, *H*-7), 0.71 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 176.1 (q, *C*-3), 145.5 (q, *C*-5), 134.9 (q, *C*-2), 129.6 (q, *C*-4), 128.7 (t, *C*-1), 79.6 (t, *C*-17), 66.3 (q, *C*-10), 54.0 (t, *C*-9), 47.3 (t, *C*-14), 45.4 (q, *C*-13), 35.8 (t, *C*-8), 32.6 (s, *C*-(7/16)), 32.5 (s, *C*-(7/16)), 30.8 (s, *C*-12), 26.7 (s, *C*-6), 24.9 (s, *C*-15), 22.9 (s, *C*-11), 16.9 (p, *C*-18); **ESI-MS** (ESI^+) *m/z* calculated for $C_{18}H_{21}N_9O_2Na^+$ $[M+Na]^+$ 418.1716; found 418.1728.

(8*S*,9*S*,13*S*,14*S*,17*S*)-2,4,10-Triazido-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one (18)

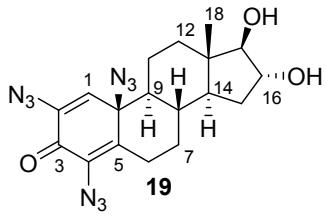


18

The title compound was prepared according to the general procedure using 17β-estradiol as starting material. After 3 h, the azide **18** was obtained as a yellow foam (135.5 mg, 343 *µ*mol; 69% yield).

$[\alpha]_D^{26.8}$ = + 33.0° (*c* 0.8, MeOH); **IR** ν_{max} [cm^{-1}] 2943, 2112, 2093 *v*(N_3), 1661 *v*(C=O), 1601, 1333, 1314, 1263, 1213, 1055, 939, 895, 864, 735, 704, 656, 559, 656; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.55 (s, 1H, *H*-1), 3.59 (t, *J* = 8.4 Hz, 1H, *H*-17), 3.07 – 3.04 (m, 1H, *H*-6), 2.22 – 2.14 (m, 1H, *H*-6), 2.08 – 2.03 (m, 1H, *H*-16), 1.91 – 1.73 (m, 4H, *H*-7/8/11/12), 1.66 – 1.64 (m, 1H, *H*-11), 1.58 – 1.56 (m, 1H, *H*-15), 1.48 – 1.40 (m, 1H, *H*-16), 1.34 – 1.26 (m, 1H, *H*-15), 1.10 – 1.03 (m, 2H, *H*-9/12), 0.95 – 0.87 (m, 2H, *H*-7/14), 0.78 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 176.0 (q, *C*-3), 145.5 (q, *C*-5), 134.9 (q, *C*-2), 129.5 (q, *C*-4), 128.7 (t, *C*-1), 81.3 (t, *C*-17), 66.2 (q, *C*-10), 54.2 (t, *C*-9), 49.5 (t, *C*-14), 43.1 (q, *C*-13), 36.0 (s, *C*-12), 35.6 (t, *C*-8), 31.7 (s, *C*-7), 30.4 (s, *C*-16), 26.5 (s, *C*-6), 23.5 (s, *C*-15), 23.0 (s, *C*-11), 11.0 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* calculated for $C_{18}H_{20}N_9O_2^-$ $[M-H]^-$ 394.1740; found 394.1741.

(8*S*,9*S*,13*S*,14*S*,16*R*,17*R*)-2,4,10-triazido-16,17-dihydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (19)

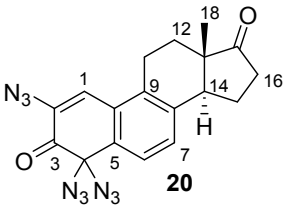


19

The title compound was prepared according to the general procedure using estriol (0.24 mmol) as starting material. After 3.5 h, the azide **19** was obtained as a yellow foam (31.8 mg, 77.3 *µ*mol; 32% yield).

[*α*]$_D^{24.2}$ = + 22.2° (*c* 0.5, MeOH); **IR** ν_{max} [cm^{-1}] 3337, 2936, 2122 *v*(N_3), 1653 *v*(C=O), 1339, 1213, 1061, 941, 883, 419; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.54 (s, 1H, *H*-1), 4.16 – 4.12 (m, 1H, *H*-16), 3.48 – 3.47 (m, 1H, *H*-17), 3.11 – 3.06 (m, 1H, *H*-6), 2.23 – 2.15 (m, 1H, *H*-6), 1.87 – 1.76 (m, 5H, *H*-7/8/11/12/15), 1.69 – 1.64 (m, 1H, *H*-11), 1.57 – 1.51 (m, 1H, *H*-15), 1.33 – 1.30 (m, 1H, *H*-14), 1.18 – 1.13 (m, 2H, *H*-9/12), 1.03 – 0.93 (m, 1H, *H*-7), 0.82 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 176.1 (q, *C*-3), 145.1 (q, *C*-5), 135.2 (q, *C*-2), 129.8 (q, *C*-4), 128.4 (t, *C*-1), 89.5 (t, *C*-17), 78.5 (t, *C*-16), 66.2 (q, *C*-10), 54.1 (t, *C*-9), 47.4 (t, *C*-14), 43.8 (q, *C*-13), 35.9 (s, *C*-12), 35.1 (t, *C*-8), 34.1 (s, *C*-15), 31.6 (s, *C*-7), 26.5 (s, *C*-6), 22.7 (s, *C*-11), 12.2 (p, *C*-18); **ESI-MS** (ESI$^-$) *m/z* calculated for $C_{18}H_{20}N_9O_3^-$ [M-H]$^-$ 410.1689; found 410.1687.

(13*S*,14*S*)-2,4,4-triazido-13-methyl-11,12,13,14,15,16-hexahydro-3*H*-cyclopenta[*a*]phen-anthrene-3,17(4*H*)-dione (20)



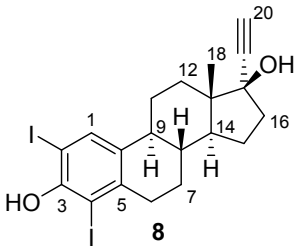
20

The title compound was prepared according to the general procedure using equilenin (93.9 *µ*mol) as starting material. After 3 h, the azide **20** was obtained as a yellow foam (11.4 mg, 29.3 *µ*mol; 31% yield).

[*α*]$_D^{25.8}$ = + 20.8° (*c* 0.4, EtOH); **IR** ν_{max} [cm^{-1}] 2922, 2104 *v*(N_3), 1738, 1699 *v*(C=O), 1460, 1406, 1346, 1069, 909, 731, 648, 552; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 8.47 (s, 1H, *H*-1), 7.57 (d, *J* = 19.4, 7.4 Hz, 1H, *H*-6), 7.30 (d, *J* = 7.4 Hz, 1H, *H*-7), 3.12 – 3.08 (m, 1H, *H*-11), 3.03 – 2.98 (m, 1H, *H*-14), 2.74 – 2.67 (m, 2H, *H*-11/16), 2.53 – 2.36 (m, 2H, *H*-15/16), 2.15 – 2.09 (m, 1H, *H*-12), 2.02 – 1.96 (m, 1H, *H*-15), 1.90 – 1.86 (m, 1H, *H*-12), 0.74 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 218.4 (q, *C*-17), 186.96 (q, *C*-3), 150.3 (t, *C*-1), 141.5 (q, *C*-Ar), 135.4 (q, *C*-Ar), 135.3 (q, *C*-Ar), 132.7 (q, *C*-Ar), 128.3 (q, *C*-Ar), 128.2 (t, *C*-7), 126.1 (t, *C*-6), 96.1 (q, *C*-4), 46.8 (t, *C*-14), 46.7 (s, *C*-13), 36.4 (s, *C*-16), 28.7 (s, *C*-12), 23.9 (s, *C*-11), 21.5 (s, *C*-16), 13.8 (p, *C*-18).
Various MS methods (ESI, EI, APCI, GC) were performed to collect mass data, but without success.

2.3 Mechanistic studies

(8*R*,9*S*,13*S*,14*S*,17*R*)-17-Ethynyl-2,4-diiodo-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*α*]phenanthrene-3,17-diol (8)

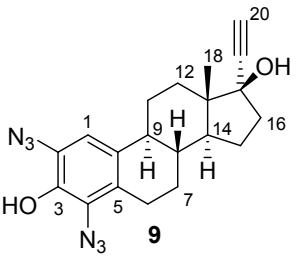


8

A mixture of ethinylestradiol (**7**, 300 mg, 1.01 mmol, 1.0 equiv) and polymer-bound iodine azide **4a** (1.92 g, 4.04 mmol, 4.0 equiv.) was stirred at 805 rpm in dry and degassed MeCN (6.7 mL) at 83 °C under an argon atmosphere. After 4 h the reaction was terminated by filtration and the resin was washed with CH_2Cl_2 (3 x 20 mL/g resin). The filtrate was washed with 10 mL of 5% sodium thiosulfate and dried over magnesium sulfate. The solvent was removed under reduced pressure. Purification by preparative HPLC (solvent A: water + 0.1% (v/v) formic acid, solvent B: MeCN + 0.1% (v/v) formic acid; flow rate: 15.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/5; 80/100; 100/100; t_R = 57.0 min) afforded diiodide **8** (221.3 mg, 404 *μ*mol, 20%) as a brown oil.

R_f = 0.38 (toluene/EtOAc = 9:1); $[\alpha]_D^{28.5}$ = – 1.5 ° (*c* 0.2, CH_2Cl_2); **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 7.63 (s, 1H, *H*-1), 2.83 – 2.77 (m, 1H, *H*-6), 2.67 – 2.62 (m, 1H, *H*-6), 2.61 (s, 1H, *H*-20), 2.38 – 2.33 (m, 1H, *H*-16), 2.33 – 2.28 (m, 1H, *H*-11), 2.25 – 2.20 (m, 1H, *H*-9), 2.07 – 1.99 (m, 1H, *H*-16), 1.97 – 1.93 (m, 1H, *H*-7), 1.91 – 1.86 (m, 1H, *H*-12), 1.82 – 1.77 (m, 1H, *H*-15), 1.75 – 1.71 (m, 1H, *H*-12), 1.68 – 1.63 (m, 1H, *H*-14), 1.52 – 1.37 (m, 3H, *H*-8/11/15), 1.37 – 1.31 (m, 1H, *H*-7), 0.87 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 151.4 (q, *C*-3), 140.9 (q, *C*-10), 136.6 (q, *C*-5), 136.0 (t, *C*-1), 92.2 (q, *C*-4), 87.4 (q, *C*-2), 79.9 (q, *C*-19), 78.4 (q, *C*-17), 74.4 (t, *C*-20), 49.3 (t, *C*-14), 47.1 (q, *C*-13), 43.6 (t, *C*-9), 39.1 (s, *C*-16), 38.5 (t, *C*-8), 37.3 (s, *C*-6), 32.7 (s, *C*-12), 28.1 (s, *C*-7), 26.8 (s, *C*-11), 22.9 (s, *C*-15), 12.7 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* calculated for $C_{20}H_{21}I_2O_2^-$ $[M-H]^-$ 546.9631; found 546.9630.

(8*R*,9*S*,13*S*,14*S*,17*R*)-2,4-Diazido-17-ethynyl-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*α*]phenanthrene-3,17-diol (9)

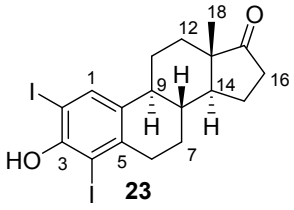


9

A mixture of ethinylestradiol (**7**, 300 mg, 1.01 mmol, 1.0 equiv) and polymer-bound iodine azide **4a** (1.92 g, 4.04 mmol, 4.0 equiv.) was stirred at 805 rpm in dry and degassed MeCN (6.7 mL) at 83 °C under an argon atmosphere. After 4 h the reaction was terminated by filtration and the resin was washed with CH_2Cl_2 (3 x 20 mL/g resin). The filtrate was washed with 10 mL of 5% sodium thiosulfate and dried over magnesium sulfate. The solvent was removed under reduced pressure. Purification by preparative HPLC (solvent A: water + 0.1% (v/v) formic acid, solvent B: MeCN + 0.1% (v/v) formic acid; flow rate: 15.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/5; 80/100; 100/100; t_R = 62.0 min) afforded steroid **9** (137.5 mg, 0.364 mmol, 17%) as a brown oil.

R_f = 0.34 (toluene/EtOAc = 9:1); $[\alpha]_D^{29.5}$ = – 1.5 ° (*c* 0.13, CH_2Cl_2); ν_{max} (film)/cm^{-1} 2924, 2108 (N_3), 1490, 1325, 1261, 1051, 1020, 735, 702, 659; **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 6.82 (s, 1H, *H*-1), 2.82 (dd, *J* = 17.9, 5.5 Hz, 1H, *H*-6), 2.60 (s, 1H, *H*-20), 2.58 – 2.51 (m, 1H, *H*-6), 2.38 – 2.28 (m, 2H, *H*-11/16), 2.21 – 2.15 (m, 1H, *H*-9), 2.07 – 1.99 (m, 1H, *H*-16), 1.94 – 1.91 (m, 1H, *H*-7), 1.91 – 1.87 (m, 1H, *H*-12), 1.81 – 1.73 (m, 1H, *H*-15), 1.73 – 1.68 (m, 1H, *H*-12), 1.68 – 1.64 (m, 1H, *H*-14), 1.52 – 1.40 (m, 3H, *H*-8/11/16), 1.35 – 1.30 (m, 1H, *H*-7), 0.88 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 139.6 (q, *C*-3), 133.9 (q, *C*-10), 127.4 (q, *C*-5), 125.1 (q, *C*-4), 123.9 (q, *C*-2), 111.5 (t, *C*-1), 87.5 (q, *C*-19), 79.9 (q, *C*-17), 74.3 (t, *C*-20), 49.5 (t, *C*-14), 47.1 (q, *C*-13), 43.7 (t, *C*-9), 39.1 (s, *C*-16), 38.7 (t, *C*-8), 32.7 (s, *C*-12), 26.8 (s, *C*-7), 26.7 (s, *C*-11), 25.4 (s, *C*-6), 22.9 (s, *C*-15), 12.8 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* Calculated for $C_{20}H_{21}N_6O_2^-$ $[M-H]^-$ 377.1726; Found 377.1723.

(8*R*,9*S*,13*S*,14*S*)-3-hydroxy-2,4-diiodo-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]-phenanthren-17-one (23)



23

Estrone (200 mg, 0.74 mmol, 1.00 equiv.) was dissolved in TFA (10.0 mL), NIS (350 mg, 1.55 mmol, 2.10 equiv.) was added and the reaction mixture was stirred at ambient temperature under an argon atmosphere. After 4 h, the mixture was poured onto 100 mL H_2O and extracted with CH_2Cl_2 (3x). The combined organic layers were washed with a saturated solution of sodium thiosulfate and water and dried over $MgSO_4$. Purification by flash column chromatography (Büchi, solvent A: petroleum ether, solvent B: ethyl acetate; tube volume: 10.0 mL; flow rate: 20.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/10; 30/15; t_R = 3.5 – 11.0 min) afforded diiodide **23** as a white solid (216.4 mg, 414 *µ*mol; 56% yield).

mp = 220 °C; **$[\alpha]_D^{22.7}$** = + 101.5° (*c* 0.4, CH_2Cl_2); **^{1}H-NMR** ($CDCl_3$, 400 MHz): *δ* [ppm] 7.62 (s, 1H, *H*-1), 5.78 (s, 1H, O*H*), 2.89 – 2.83 (m, 1H, *H*-6), 2.72 – 2.63 (m, 1H, *H*-6), 2.55 – 2.48 (m, 1H, *H*-16), 2.38 – 2.34 (m, 1H, *H*-11), 2.30 – 2.21 (m, 1H, *H*-9), 2.20 – 2.13 (m, 1H, *H*-16), 2.11 – 2.05 (m, 2H, *H*-7/15), 1.98 – 1.94 (m, 1H, *H*-12), 1.66 – 1.60 (m, 1H, *H*-15), 1.52 – 1.47 (m, 4H, *H*-8/11/12/14), 1.43 – 1.36 (m, 1H, *H*-7), 0.90 (s, 3H, *H*-18); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 220.6 (q, C-17), 151.6 (q, *C*-3), 140.8 (q, *C*-5), 136.1 ((t/q), *C*-(1/10)), 136.0 ((t/q), *C*-(1/10)), 92.1 (q, *C*-4), 78.5 (q, *C*-2), 50.3 (t, *C*-14), 47.9 (q, *C*-13), 44.0 (t, *C*-9), 37.5 (t, *C*-8), 37.2 (s, *C*-6), 35.9 (s, *C*-16), 31.5 (s, *C*-12), 27.4 (s, *C*-7), 26.4 (s, *C*-11), 21.7 (s, *C*-15), 13.9 (p, *C*-18); **ESI-MS** (ESI^-) *m/z* calculated for $C_{18}H_{19}I_2O_2^-$ [M-H]$^-$ 520.9475; found 520.9473.

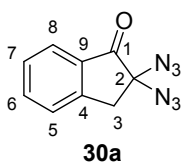
The analytical data are consistent with those reported in the literature.[S3]

2.4 Azidation of ketones

General procedure

A mixture of the ketone (0.5 mmol, 1.00 equiv.) and polymer-bound iodine azide **4a** (952 mg, 2.10 mmol, 4.00 equiv.) was stirred in absolute MeCN (3.33 mL) at 83 °C under an argon atmosphere. After the full consumption of the starting material was monitored by TLC the reaction was terminated by filtration and the resin was washed with EtOAc. Polymer-bound thiosulfate **2** was added to the combined organic phases and the reaction mixture was stirred for 10 min until the solution was nearly colorless. This was filtered through a pad of cotton and concentrated under reduced pressure.

2,2-Diazido-3,4-dihydroinden-1-one (30a)



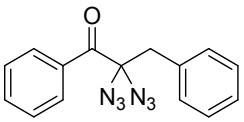
30a

The title compound was prepared according to the general procedure with 1-indanone (200 mg, 1.51 mmol, 1.0 equiv) as starting material. After 15 h, the azide **30a** was obtained as a green oil (227.2 mg, 106 *µ*mol; 70% yield).

***R*$_f$** = 0.33 (PE/EtOAc = 9:1); **IR** ν_{max} [cm^{-1}] 2099 $\nu(N_3)$; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.86 – 7.84 (m, 1 H, *H*-8), 7.73 – 7.68 (m, 1 H, *H*-6), 7.49 – 7.42 (m, 2 H, *H*-5/7), 3.30 (s, 2 H, *H*-3); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 194.9 (s, *C*-1), 149.3 (s, *C*-9), 137.2 (d, *C*-6), 132.1 (s, *C*-4), 128.9 (d, *C*-7), 126.7 (d, *C*-5), 126.0 (d, *C*-8), 80.4 (s, *C*-2), 39.6 (t, *C*-3).

The analytical data are consistent with those reported in the literature.[S4]

2,2-Diazido-1,3-diphenylpropan-1-one (30b)



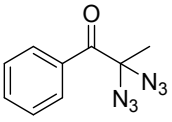
30b

The title compound was prepared according to the general procedure with 1,3-diphenylpropan-1-one as starting material. After 23 h, the product was purified using flash column chromatography (Büchi, solvent A: petroleum ether, solvent B: EtOAc; tube volume: 10.0 mL; flow rate: 20.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/0; 30/10; t_R = 7.5 min). The azide **30b** was obtained as a yellow liquid (122.8 mg, 420 *µ*mol; 84% yield).

^{1}H-NMR ($CDCl_3$, 400 MHz): *δ* [ppm] 8.04 – 8.01 (m, 2H, ArC*H*), 7.63 – 7.59 (m, 1H, ArC*H*), 7.50 – 7.45 (m, 2H, ArC*H*), 7.31 – 7.28 (m, 3H, ArC*H*), 7.21 – 7.18 (m, 2H, ArC*H*), 3.41 (s, 2H, CH_2); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 193.1 (q, *C*=O), 133.9 (t, Ar*C*), 133.7 (q, Ar*C*), 132.5 (q, Ar*C*), 130.8 (t, 2xAr*C*), 130.3 (t, 2xAr*C*), 128.7 (t, 2xAr*C*), 128.6 (t, 2xAr*C*), 128.1 (t, Ar*C*), 85.8 (q, *C*$(N_3)_2$), 43.2 (s, *C*H_2);

The analytical data are consistent with those reported in the literature.[S4]

2,2-Diazido-1-phenylpropan-1-one (30c)



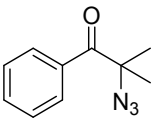
30c

The title compound was prepared according to the general with propiophenone as starting material. After 3 d, the product was purified using flash column chromatography (Büchi, solvent A: petroleum ether, solvent B: EtOAc; tube volume: 10.0 mL; flow rate: 20.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/0; 30/10; t_R = 9.0 min). The azide **30c** was obtained as a yellow liquid (103.1 mg, 477 *µ*mol; 95% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): *δ* [ppm] 8.13 – 8.11 (m, 2H, ArC*H*), 7.63 – 7.59 (m, 1H, ArC*H*), 7.50 – 7.46 (m, 2H, ArC*H*), 1.86 (s, 3H, CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): *δ* [ppm] 192.1 (q, *C*=O), 134.0 (q, Ar*C*), 132.8 (t, 2xAr*C*), 130.4 (t, 2xAr*C*), 128.7 (t, Ar*C*), 83.4 (q, *C*N_3), 22.6 (p, CH_3);

The analytical data are consistent with those reported in the literature.[S4]

2-Azido-2-methyl-1-phenylpropan-1-one (30d)



30d

The title compound was prepared according to the general procedure except that 8 formal equiv. of polymer **3** and 6.66 mL absolute MeCN were used. 2-Methyl-1-phenylpropan-1-one served as starting material. After 3 d, the product was purified using flash column chromatography (Büchi, solvent A: petroleum ether, solvent B: EtOAc; tube volume: 10.0 mL; flow rate: 20.0 ml/min; gradient: (*t* [min]/solvent B [%]): 0/0; 30/5; t_R = 10.5 min). The azide **30d** was obtained as a yellow liquid (54.2 mg, 287 *µ*mol; 57% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): *δ* [ppm] 8.11 – 8.09 (m, 2H, ArC*H*), 7.57 – 7.55 (m, 1H, ArC*H*), 7.47 – 7.44 (m, 2H, ArC*H*), 1.62 (s, 6H, 2xCH_3); **^{13}C-NMR** ($CDCl_3$, 150 MHz): *δ* [ppm] 199.6 (q, *C*=O), 134.7 (q, Ar*C*), 133.0 (t, Ar*C*), 129.9 (t, 2xAr*C*), 128.5 (t, 2xAr*C*), 67.7 (q, *C*N_3), 25.1 (p, 2xCH_3);

The analytical data are consistent with those reported in the literature.[S4]

3. X-ray crystal structure analysis of 15

Determination of the relative configuration of compound **15** was confirmed by X-ray structure analysis using a BRUKER SMART X2S benchtop crystallographic system. The data are deposited at the Cambridge Crystallographic Data Center (CCDC 2049506).

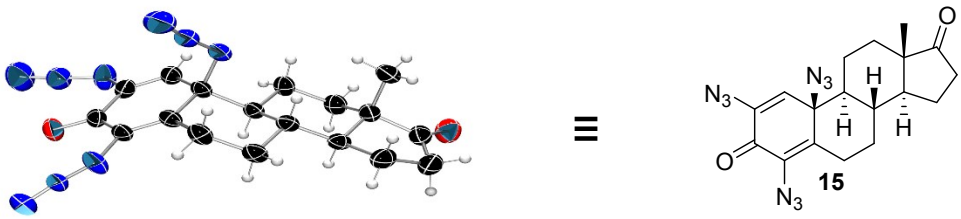


Table S1: Sample and crystal data for **15**.

Identification code	TK287b	
Chemical formula	$C_{18}H_{19}N_9O_2$	
Formula weight	393.42 g/mol	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal size	0.130 x 0.470 x 0.510 mm	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.7974(12) Å	α = 90°
	b = 13.920(2) Å	β = 91.655(6)°
	c = 9.9497(18) Å	γ = 90°
Volume	941.0(3) $Å^3$	
Z	2	
Density (calculated)	1.388 g/cm^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	412	

Table S2: Data collection and structure refinement for **15**.

Theta range for data collection	2.52 to 27.80°
Index ranges	-8<=h<=8, -18<=k<=18, -13<=l<=12
Reflections collected	21262
Independent reflections	4350 [R(int) = 0.0843]
Coverage of independent reflections	98.1%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9870 and 0.9520
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)

Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	4350 / 1 / 263	
Goodness-of-fit on F^2	0.866	
Final R indices	3248 data; I>2σ(I)	R1 = 0.0486, wR2 =
	all data	R1 = 0.0730, wR2 =
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1000P)^2]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	1.0(10)	
Largest diff. peak and hole	0.238 and -0.179 eÅ^{-3}	
R.M.S. deviation from mean	0.040 eÅ^{-3}	

4. References

[S1] J. Leonard, B. Lygo, G. Procter, *Praxis der organischen Chemie*. *Ein Handbuch*, VCH, Weinheim, New York, Basel, Cambridge, Tokyo, **1996**.

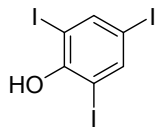
[S2] Y. Satkar, L. F. Yera-Ledesma, N. Mali, D. Patil, P. Navarro-Santos, L. A. Segura-Quezada, P. I. Ramírez-Morales, and C. R. Solorio-Alvarado, *J. Org. Chem.* **2019**, *84*, 4149–4d164.

[S3] I. Bacsa, B. E. Herman, R. Jójárt, K. S. Herman, J. Wölfling, G. Schneider, M. Varga, C. Tömböly, T. L. Rižner, M. Szécsi, E. Mernyák, *J. Enzyme Inhib. Med. Chem*. **2018**, *33*, 1271-1282.

[S4] D. A. Kamble, P. U. Karabal, P. V. Chouthaiwale, A. Sudalai, *Tetraheron Lett*. **2012**, *53*, 4195 – 4198.

Attachments: ^{1}H-, ^{13}C-NMR and IR spectra

2,4,6-Triiodophenol (6)



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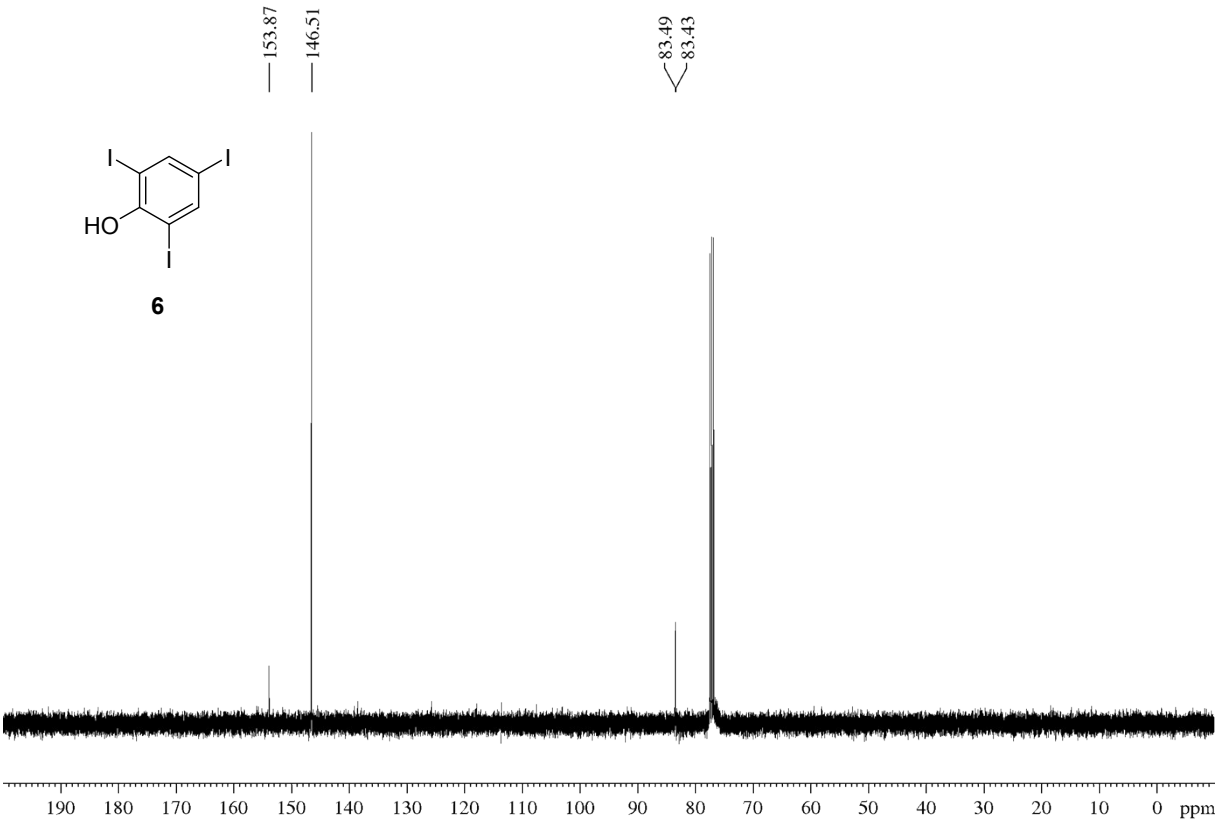
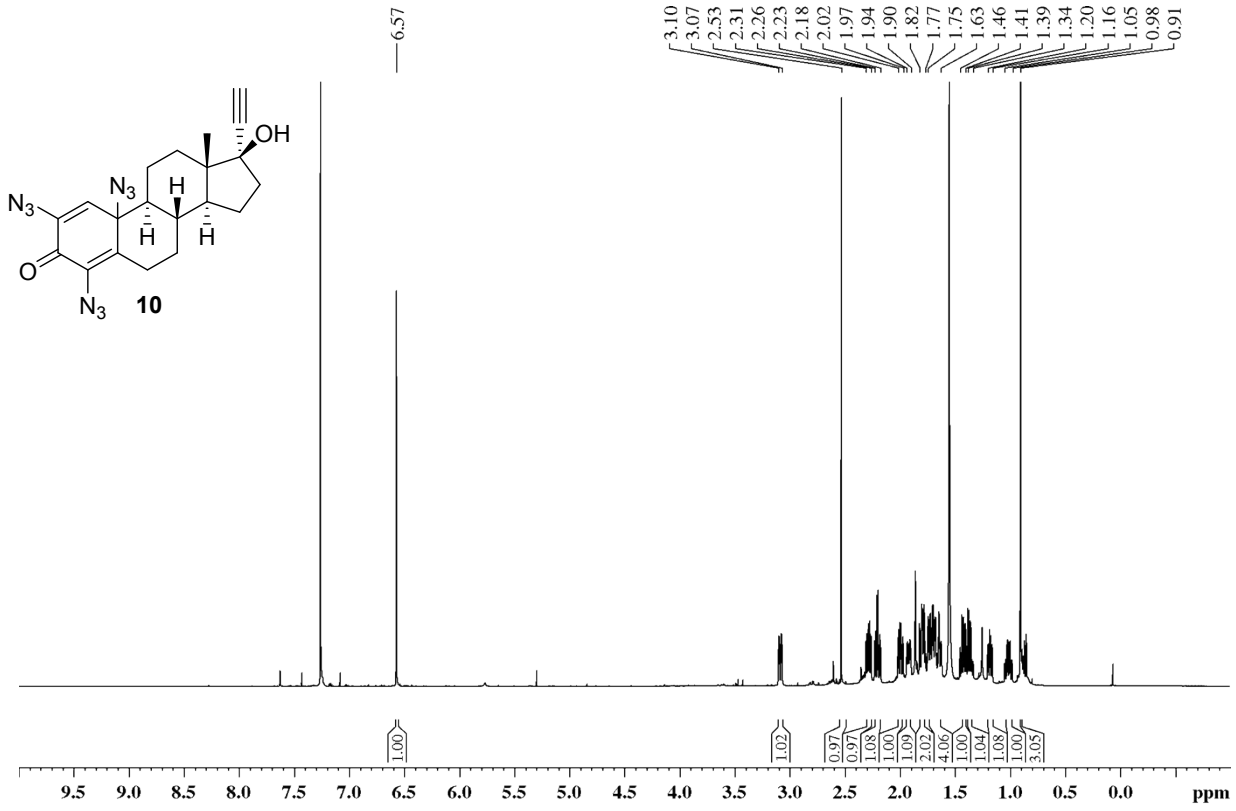
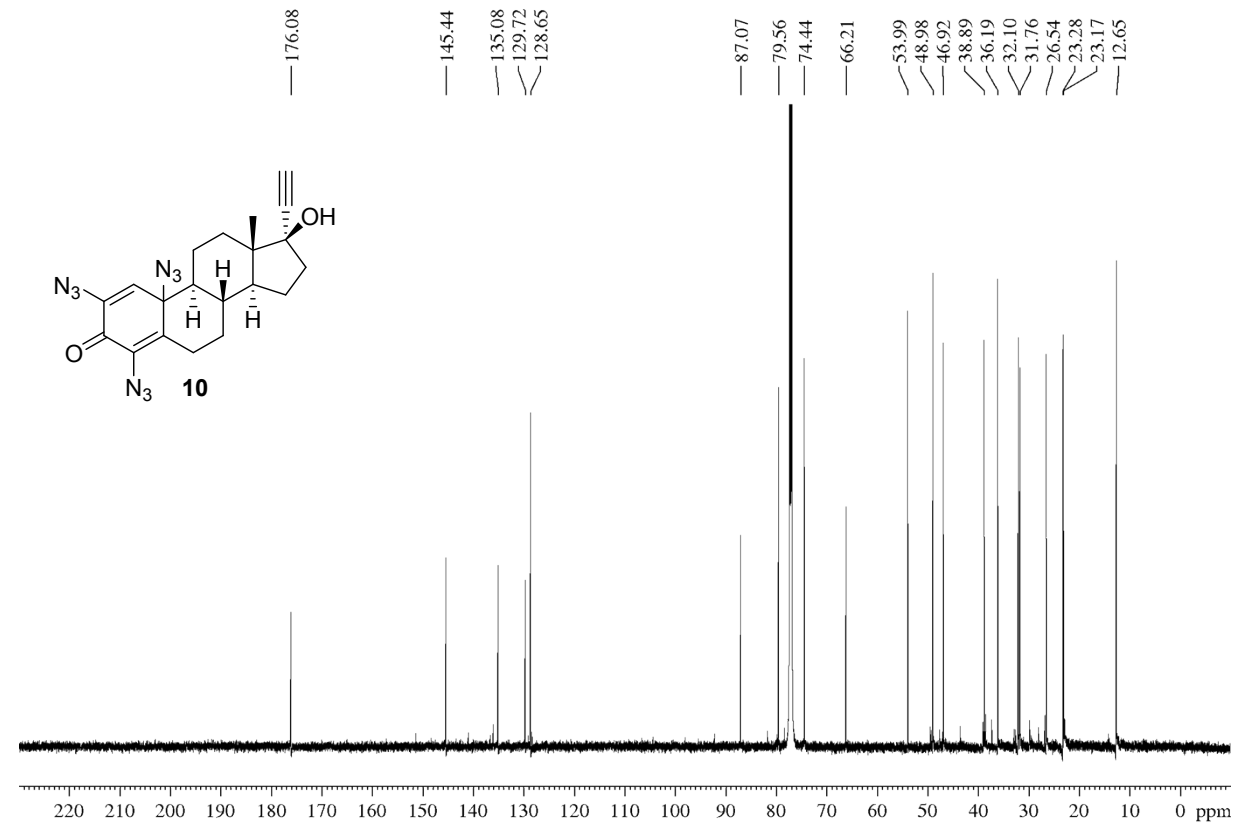
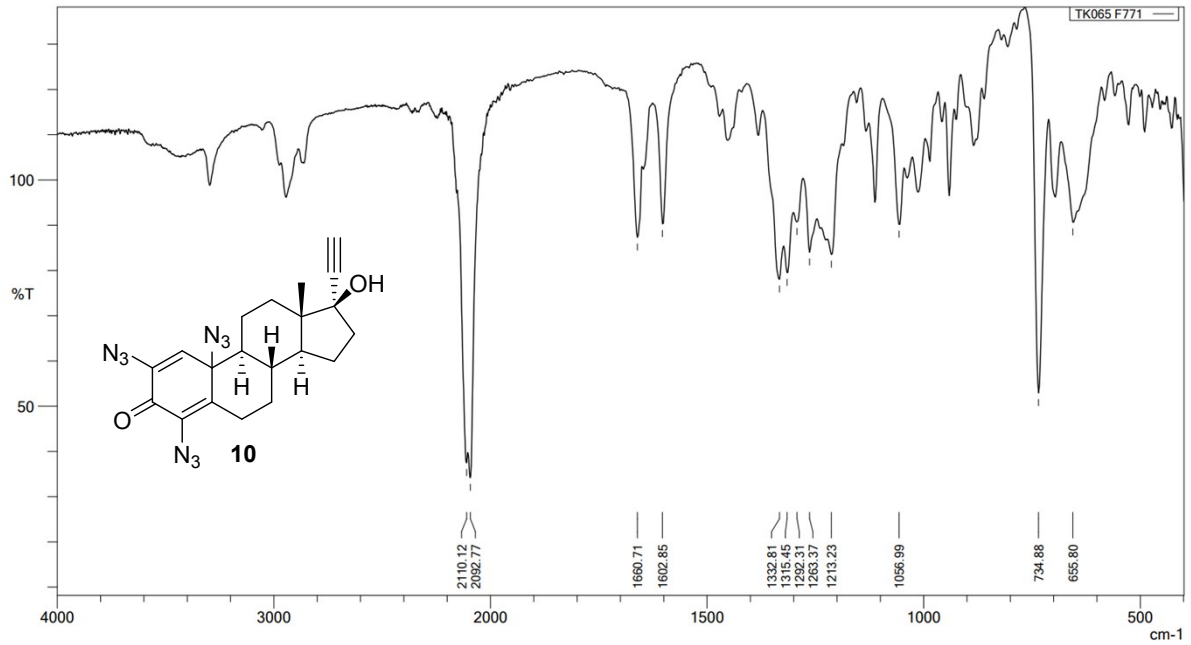


6

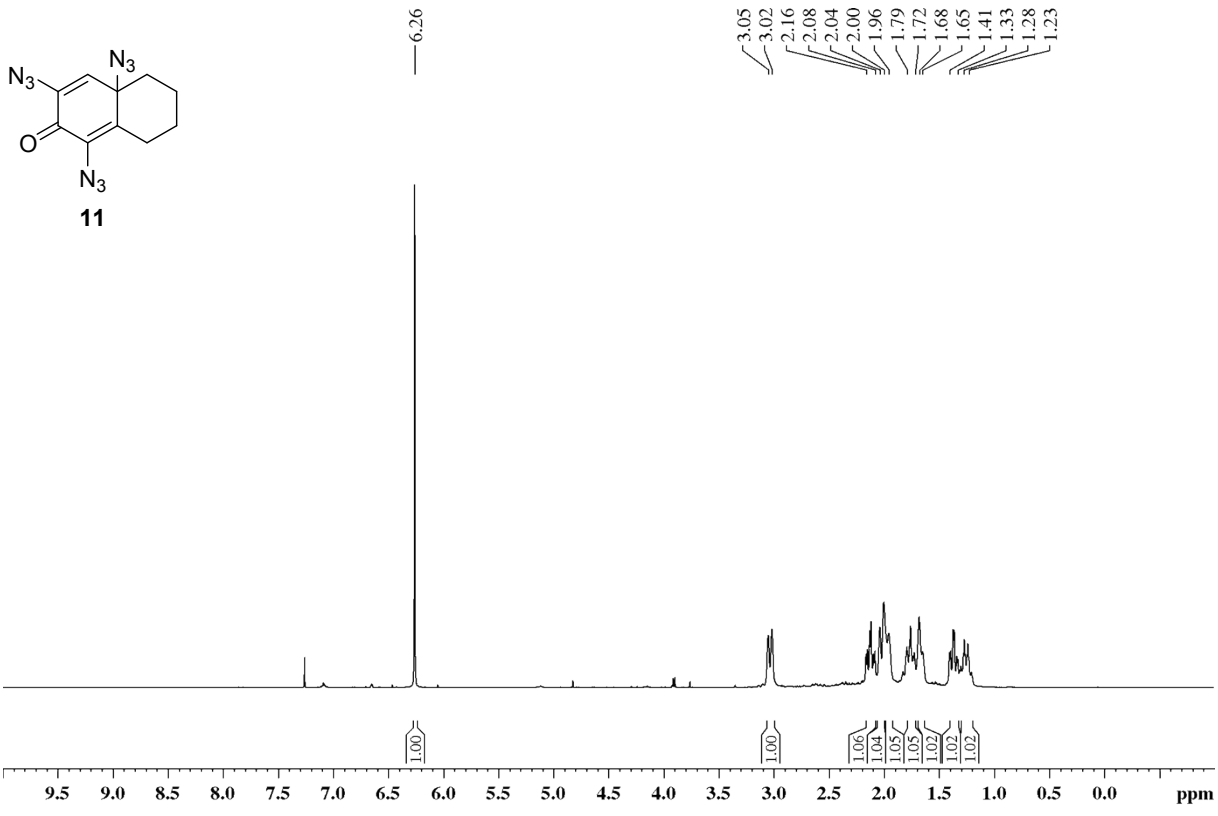
(8*S*,9*S*,13*S*,14*S*,17*R*)-2,4,10-Triazido-17-ethynyl-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (10)

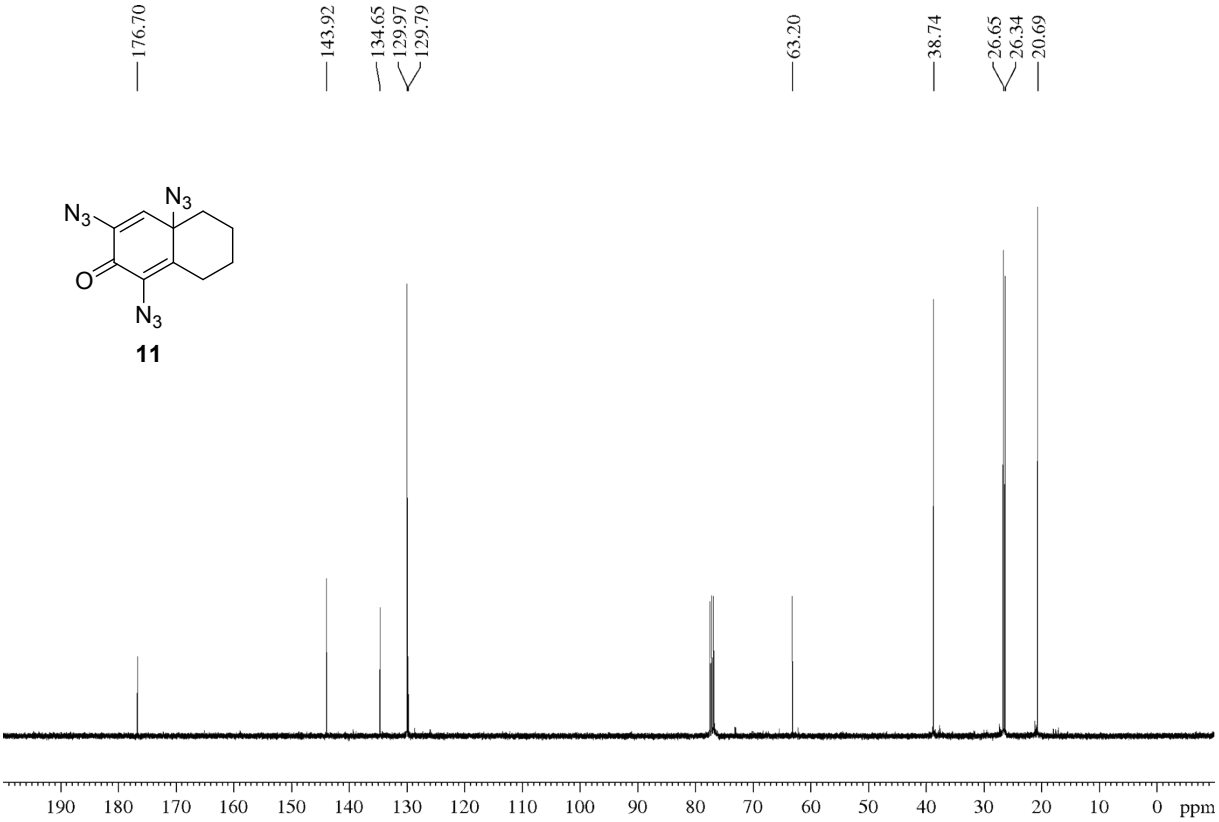


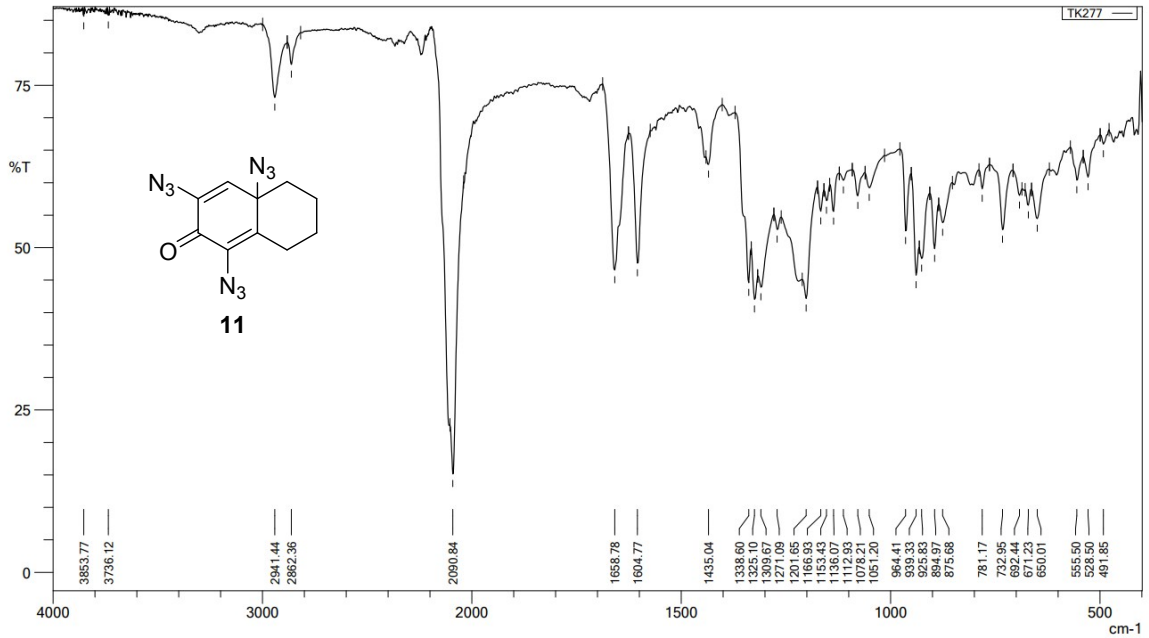




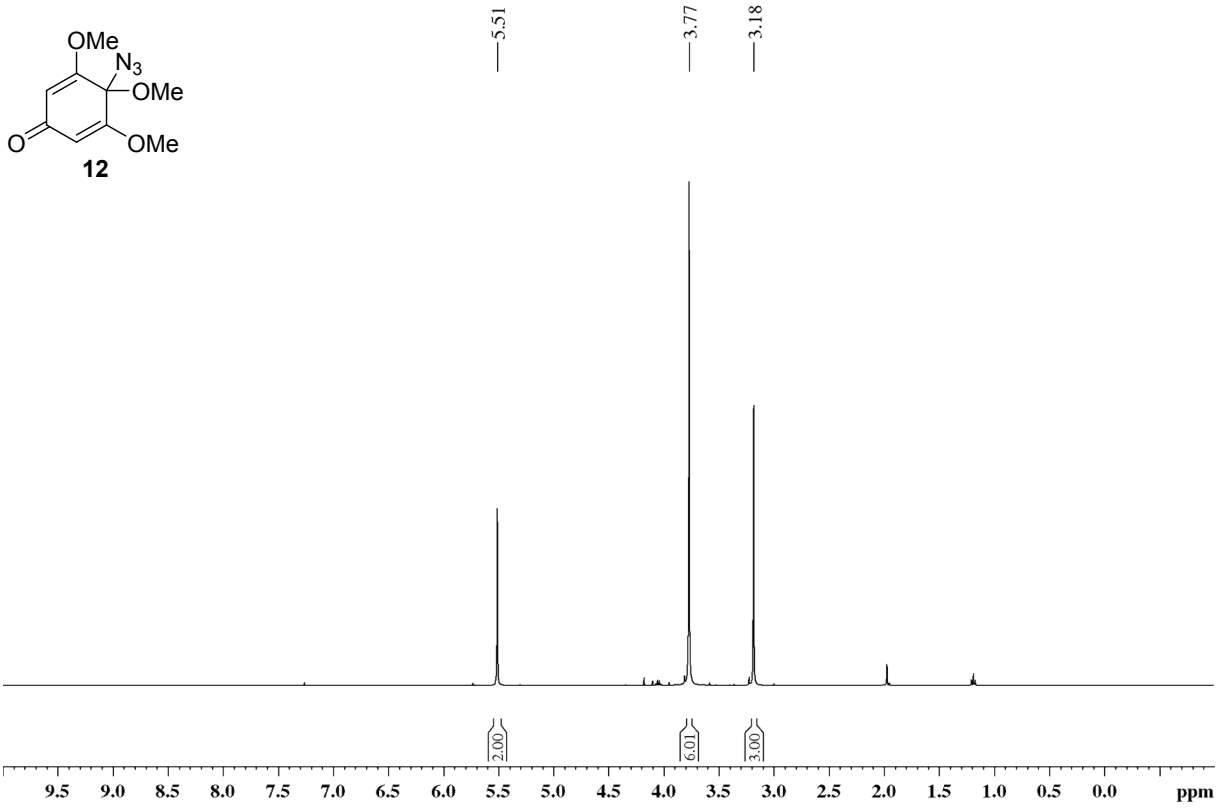
1,3,4a-Triazido-5,6,7,8-tetrahydronaphthalen-2(4a*H*)-one (11)

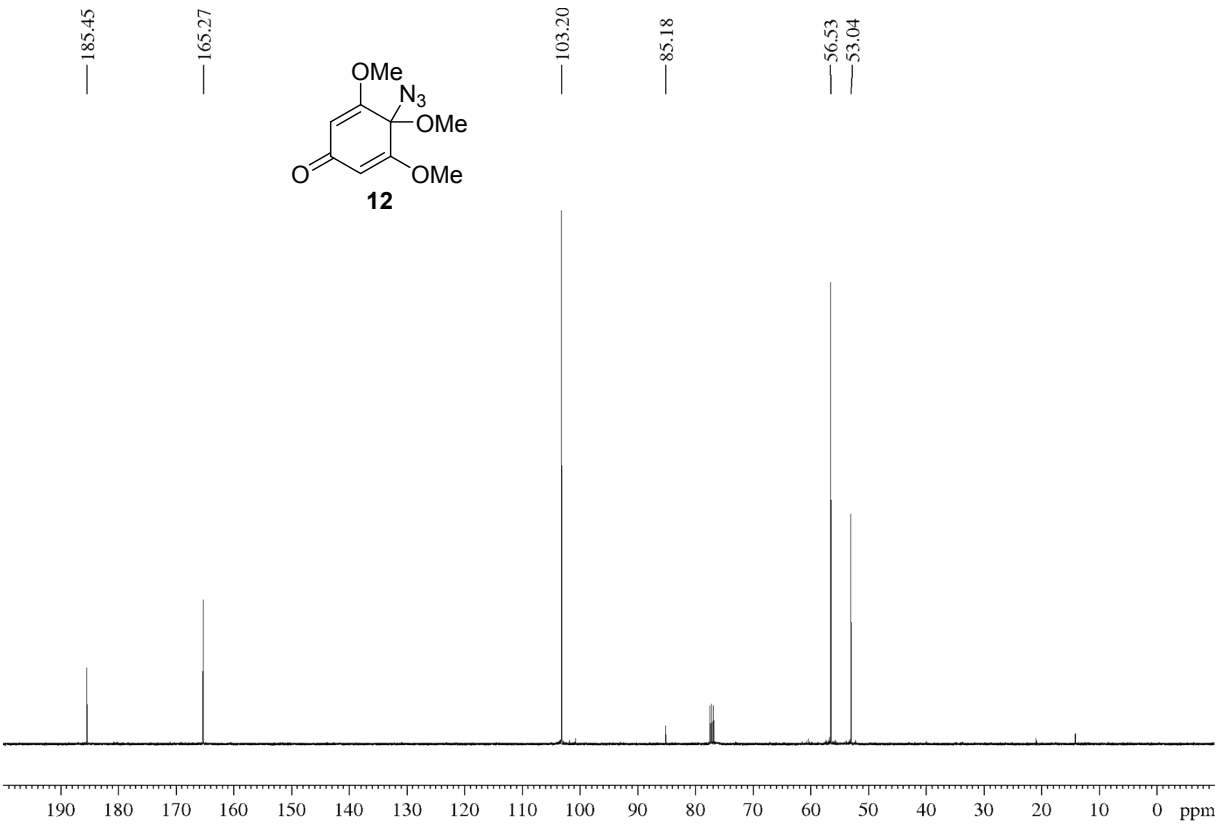


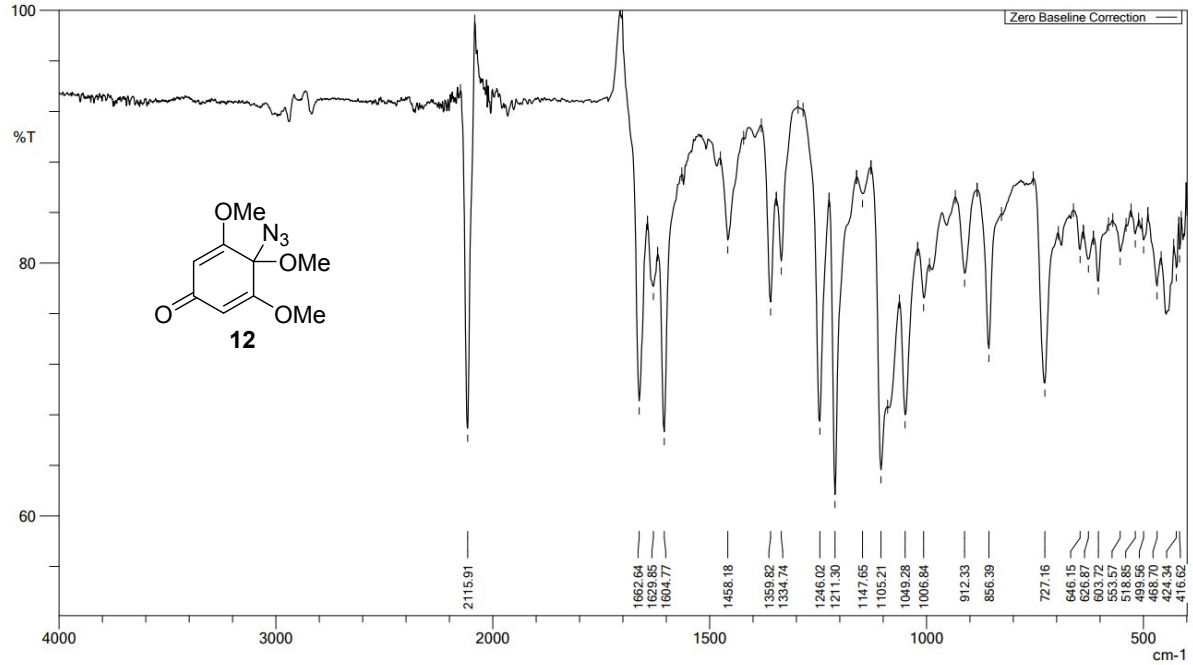

176.70
143.92
134.65
129.97
129.79
63.20
38.74
26.65
26.34
20.69
N3
N3
O
N3
11
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


TK277
%T
75
50
25
0
N3
N3
O
N3
11
3853.77
3736.12
2941.44
2862.36
2090.84
1658.78
1604.77
1435.04
1338.60
1325.10
1309.67
1271.09
1201.65
1166.93
1153.43
1136.07
1112.93
1078.21
1051.20
964.41
939.33
925.83
894.97
875.68
781.17
732.95
692.44
671.23
650.01
555.50
528.50
491.85
4000 3000 2000 1500 1000 500
cm-1

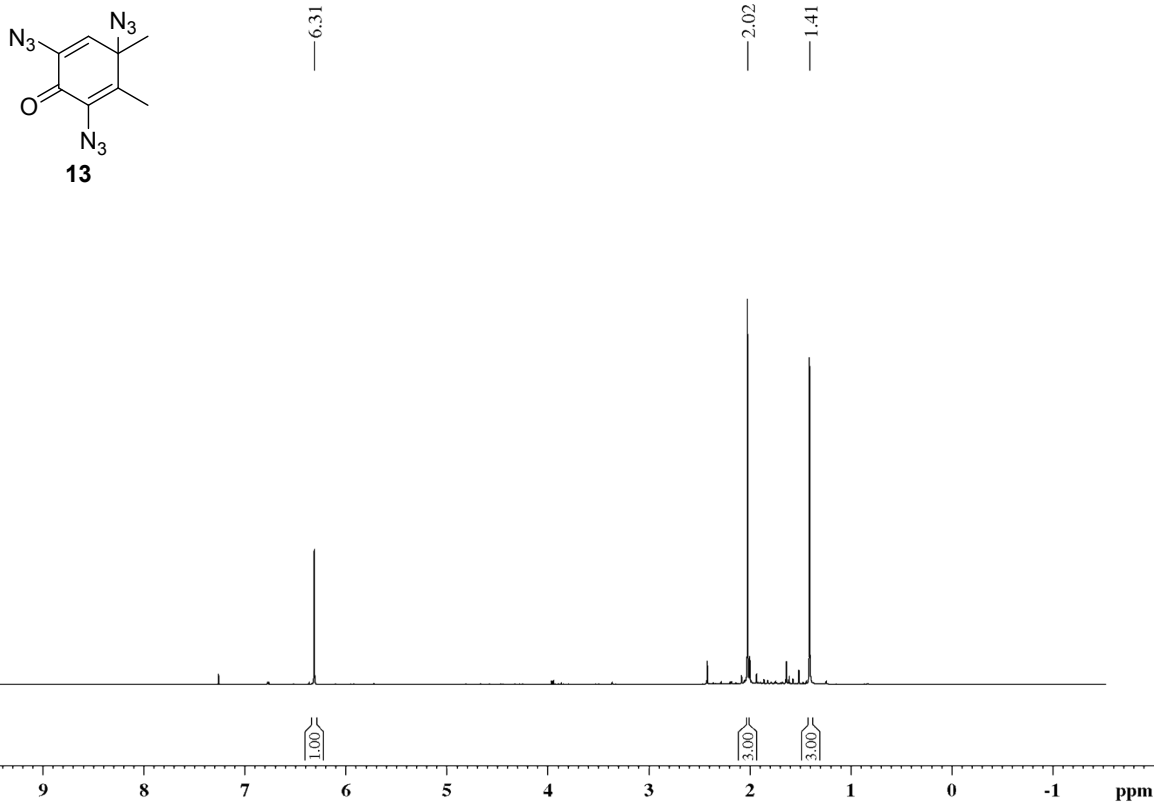
4-Azido-3,4,5-trimethoxycyclohexa-2,5-dien-1-one (12)

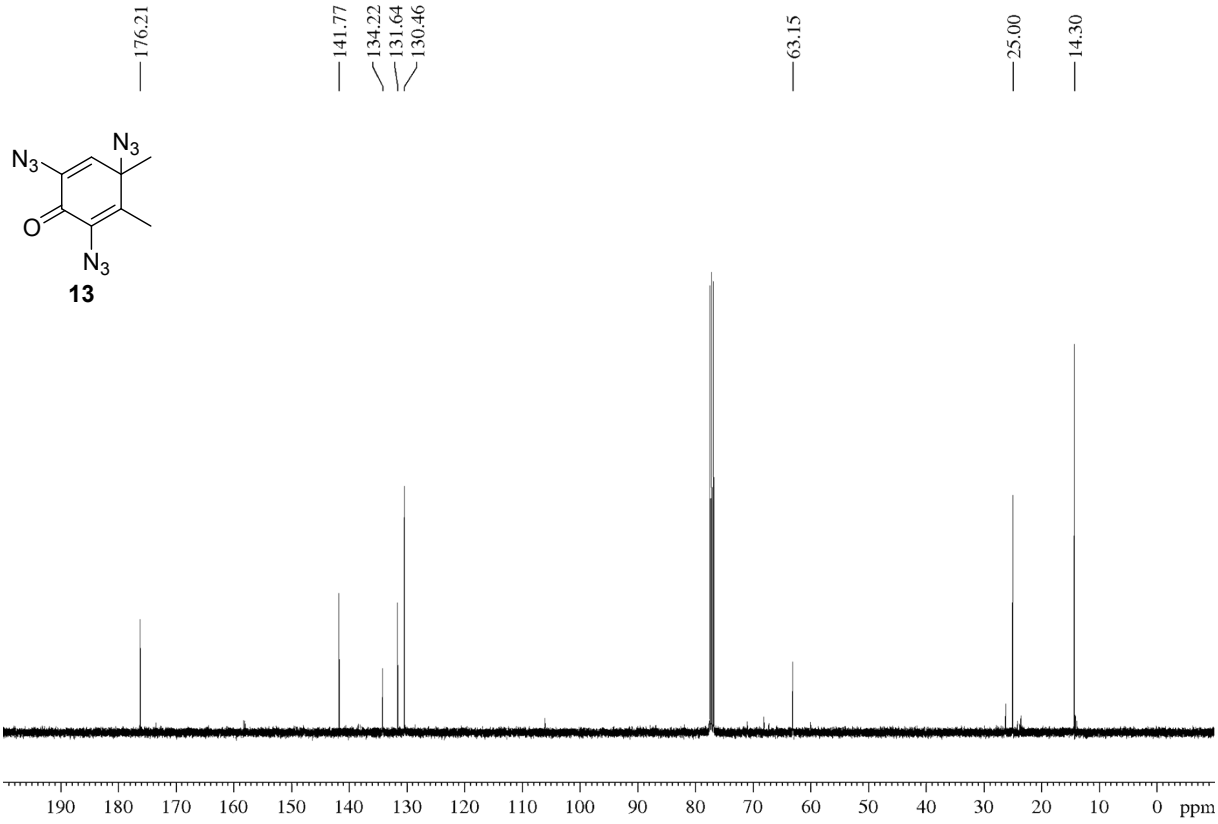


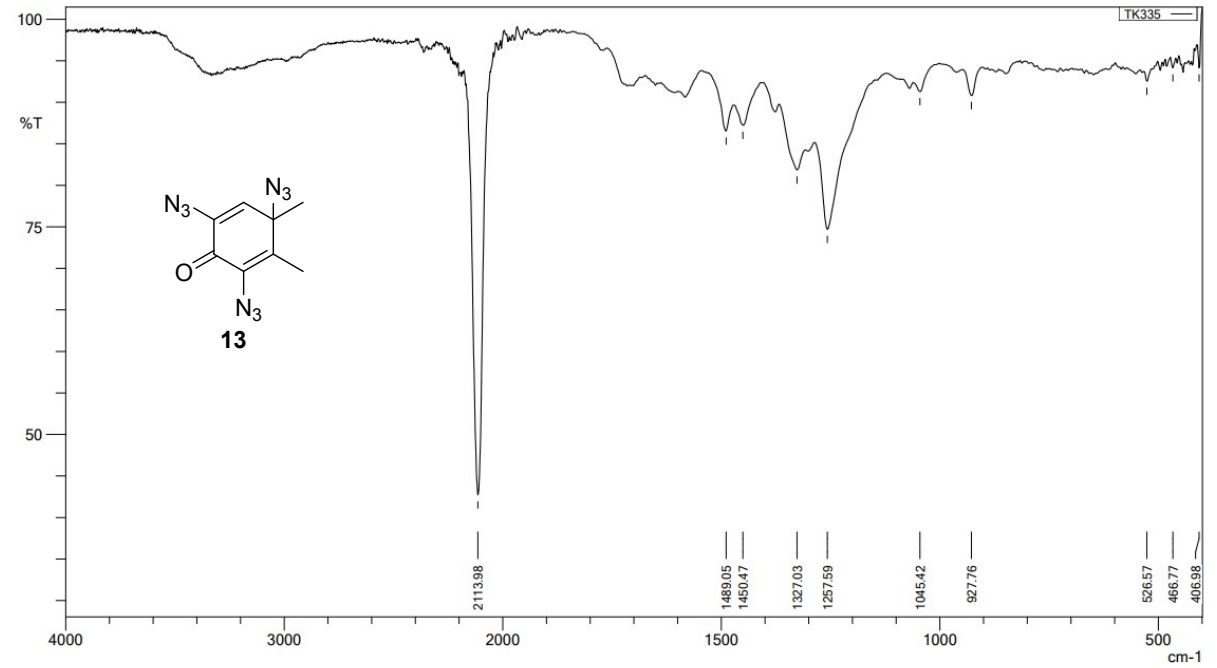




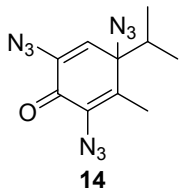
2,4,6-Triazido-3,4-dimethylcyclohexa-2,5-dien-1-one (13)



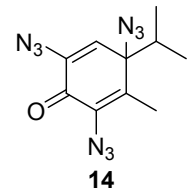

176.21
141.77
134.22
131.64
130.46
63.15
25.00
14.30
N3
N3
O
N3
13
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


TK335
100
%T
75
50
N3
N3
O
N3
13
2113.98
1489.05
1450.47
1327.03
1257.59
1045.42
927.76
526.57
466.77
406.98
4000 3000 2000 1500 1000 500
cm-1

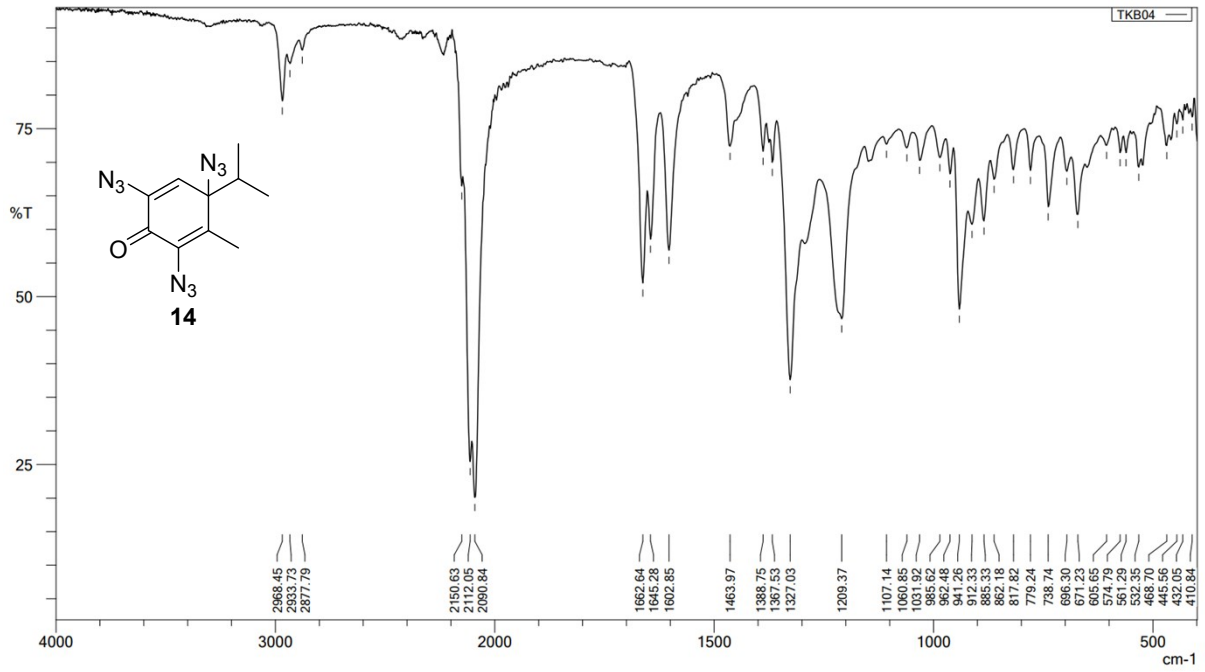
2,4,6-Triazido-4-isopropyl-3-methylcyclohexa-2,5-dien-1-one (14)



14

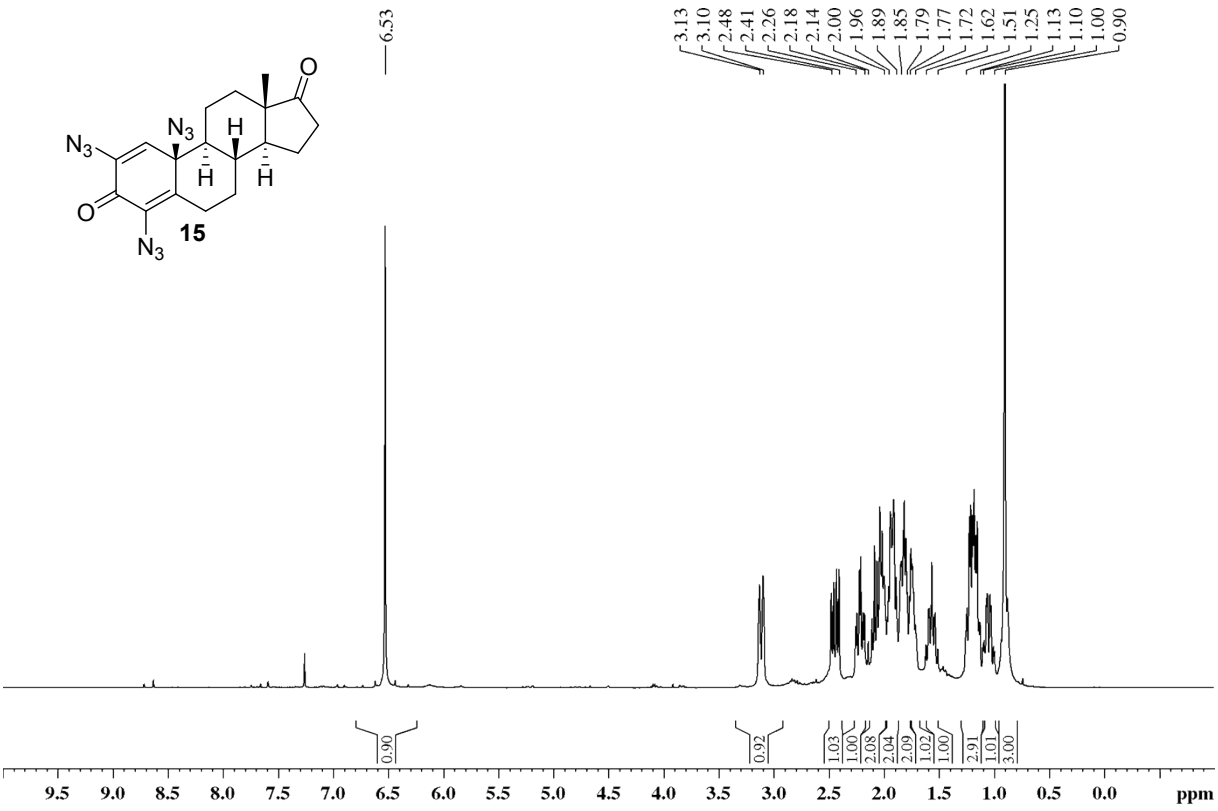


14

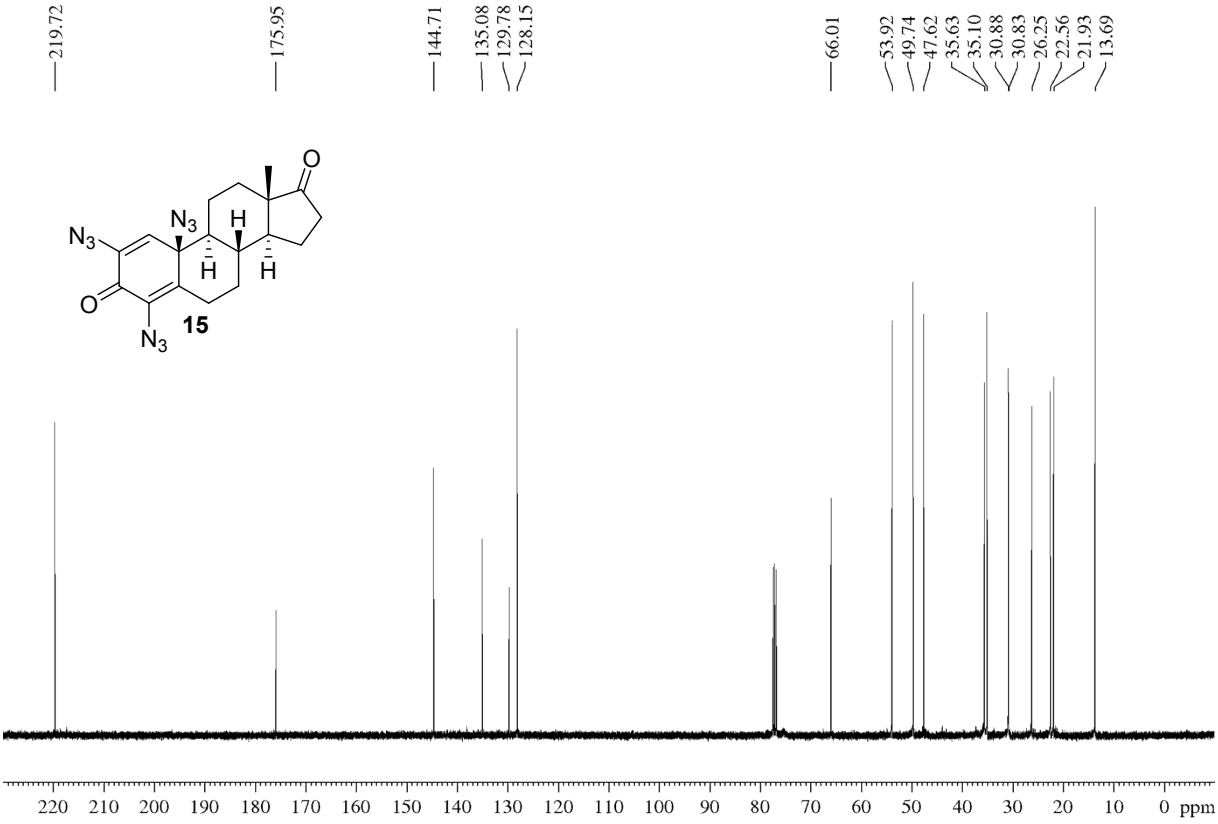


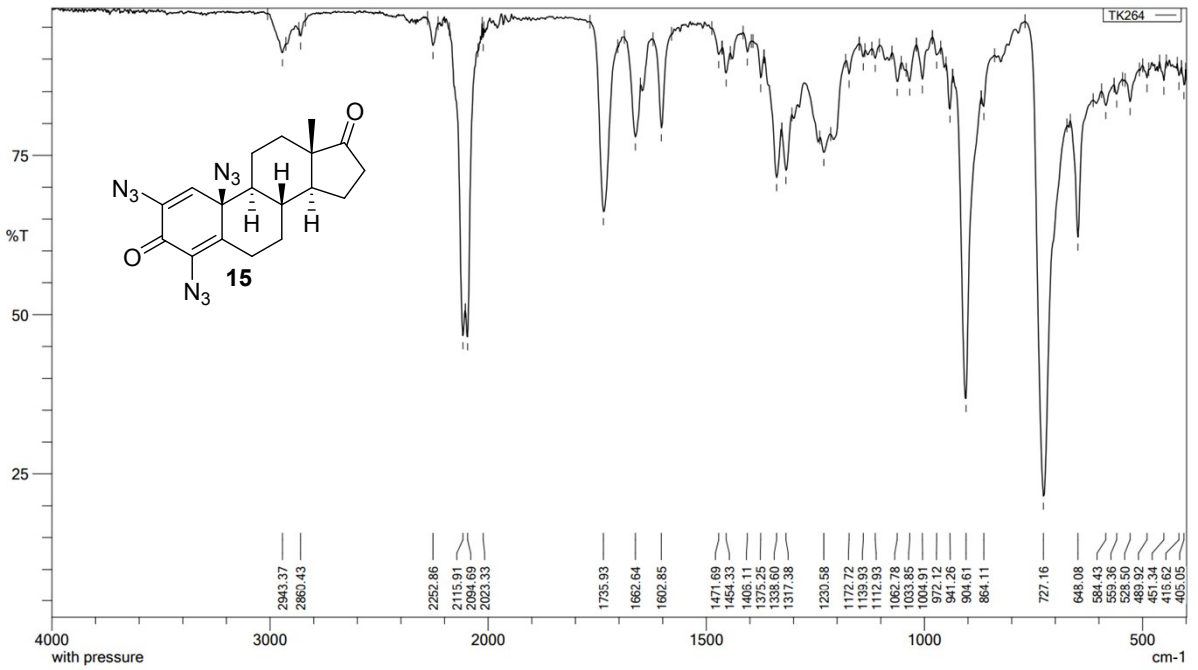
14

(8*S*,9*S*,10*R*,13*S*,14*S*)-2,4,10-Triazido-13-methyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione (15)

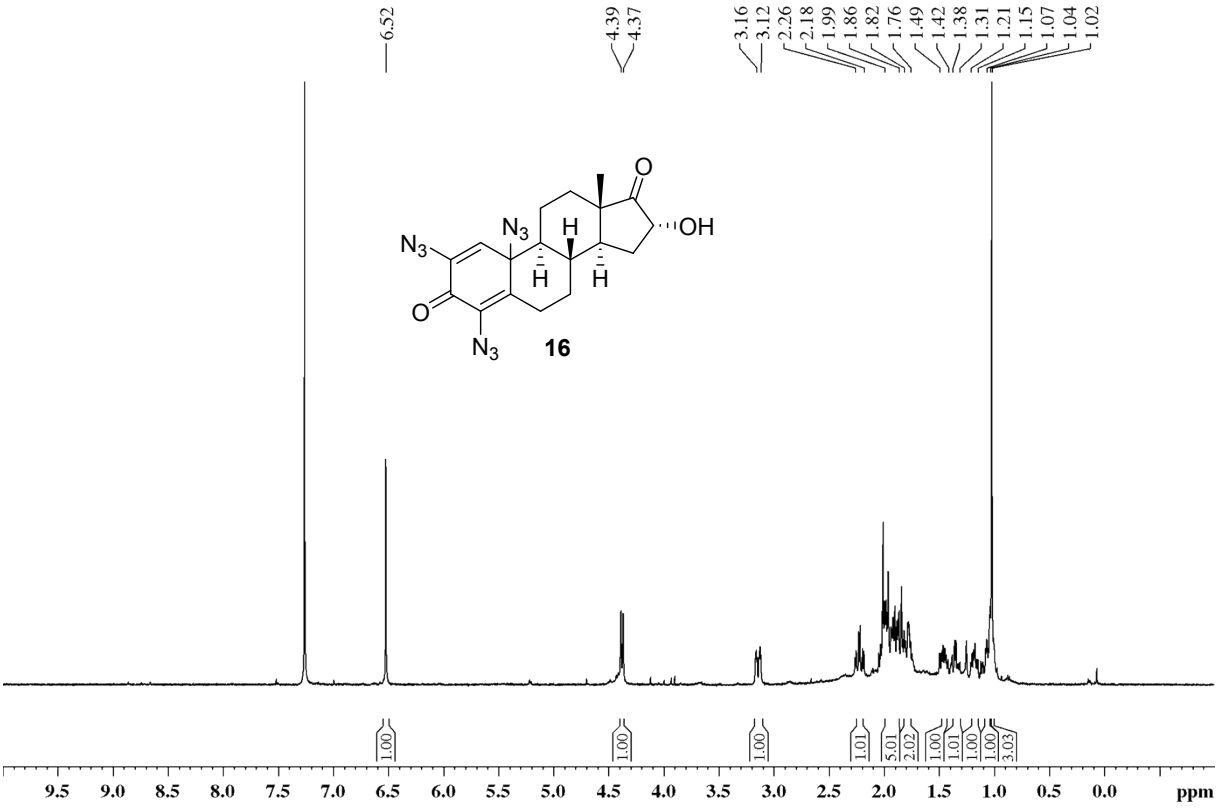


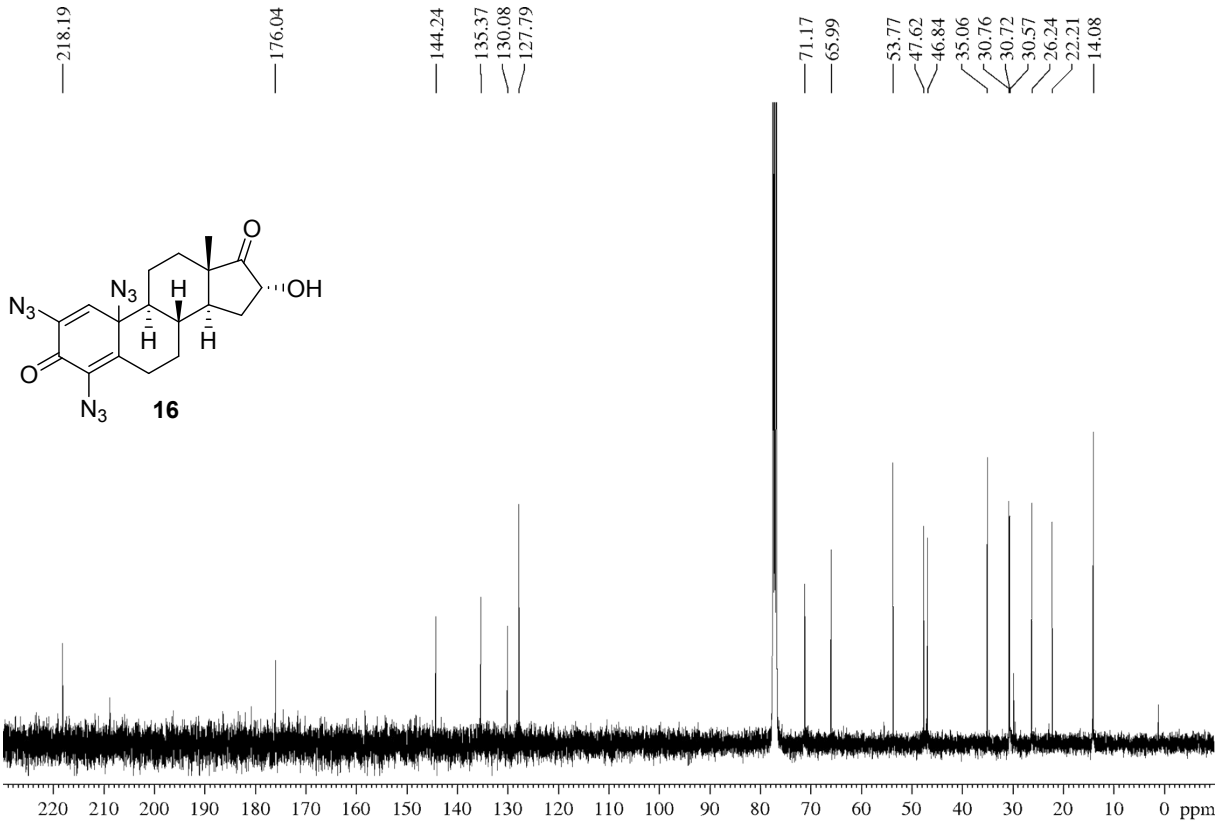
15

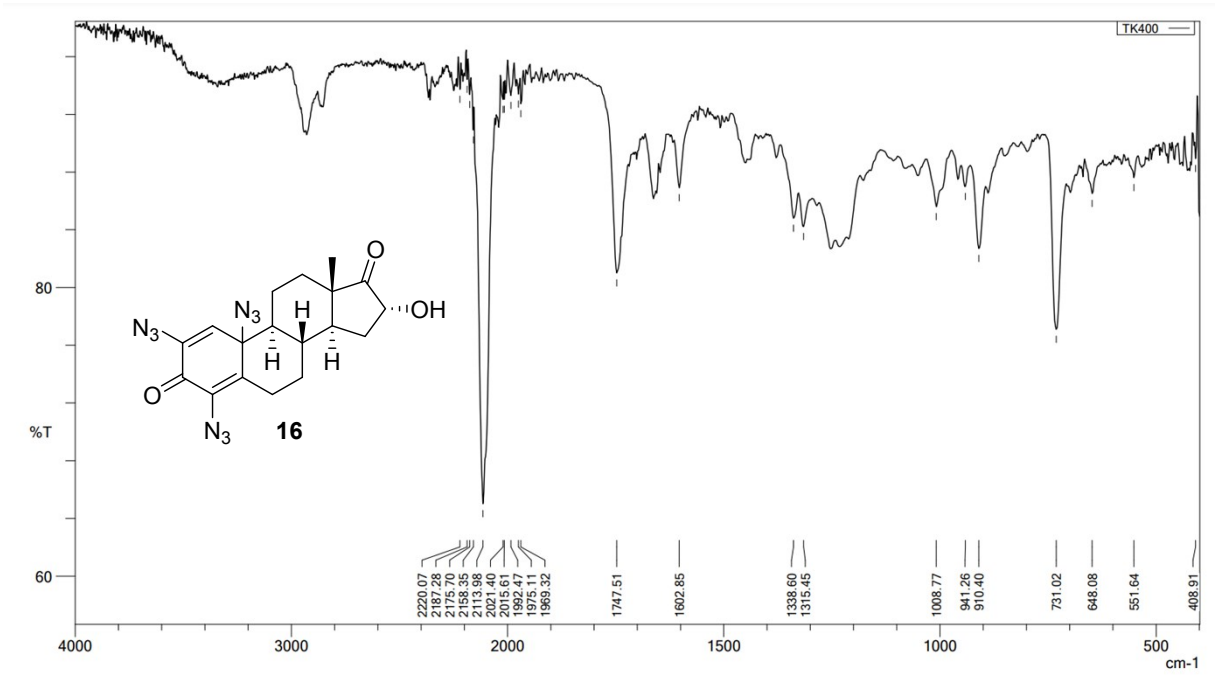

219.72
175.95
144.71
135.08
129.78
128.15
66.01
53.92
49.74
47.62
35.63
35.10
30.88
30.83
26.25
22.56
21.93
13.69
N3
N3
H
H
H
O
O
N3
15
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


TK264
%T
75
50
25
N3
N3
H
H
H
O
O
N3
15
2943.37
2860.43
2252.86
2115.91
2094.69
2023.33
1735.93
1662.64
1602.85
1471.69
1454.33
1406.11
1375.25
1338.60
1317.38
1230.58
1172.72
1139.93
1112.93
1062.78
1033.85
1004.91
972.12
941.26
904.61
864.11
727.16
648.08
584.43
559.36
528.50
489.92
451.34
416.62
405.05
4000
with pressure
3000
2000
1500
1000
500
cm-1

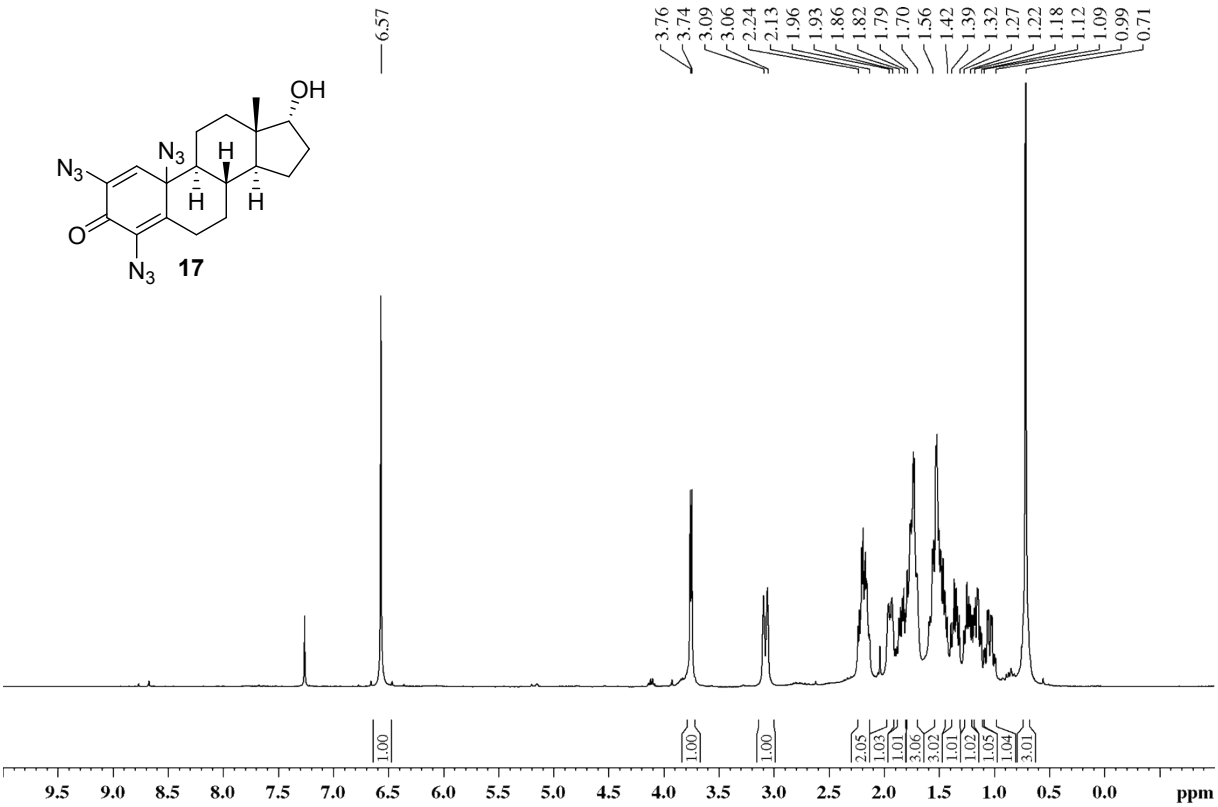
(8*S*,9*S*,10*R*,13*S*,14*S*,16*R*)-2,4,10-Triazido-16-hydroxy-13-methyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione (16)

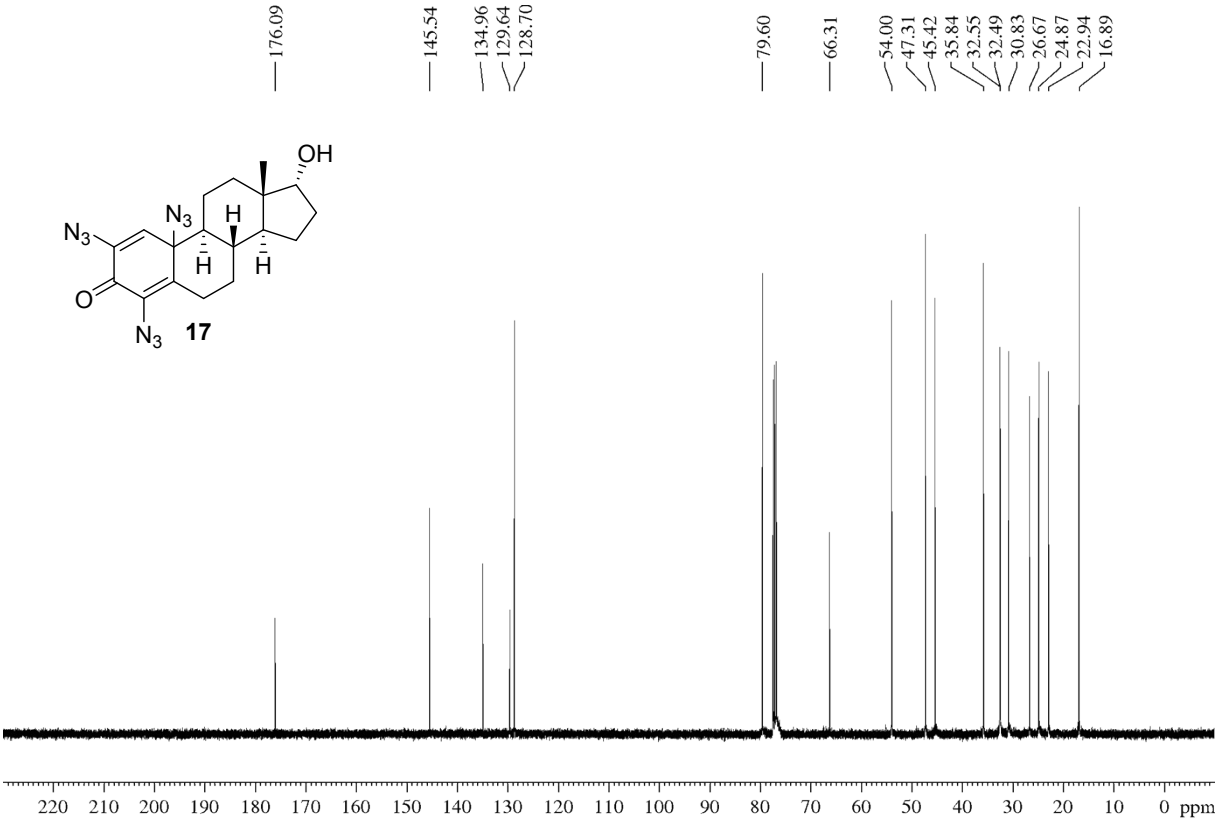


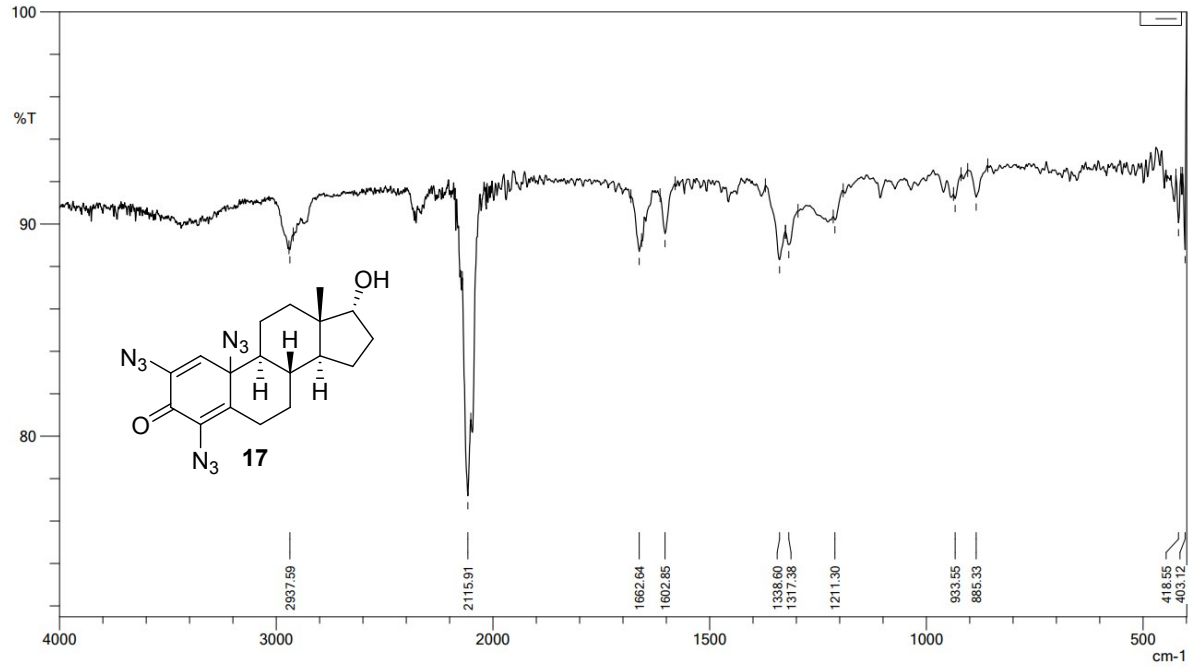




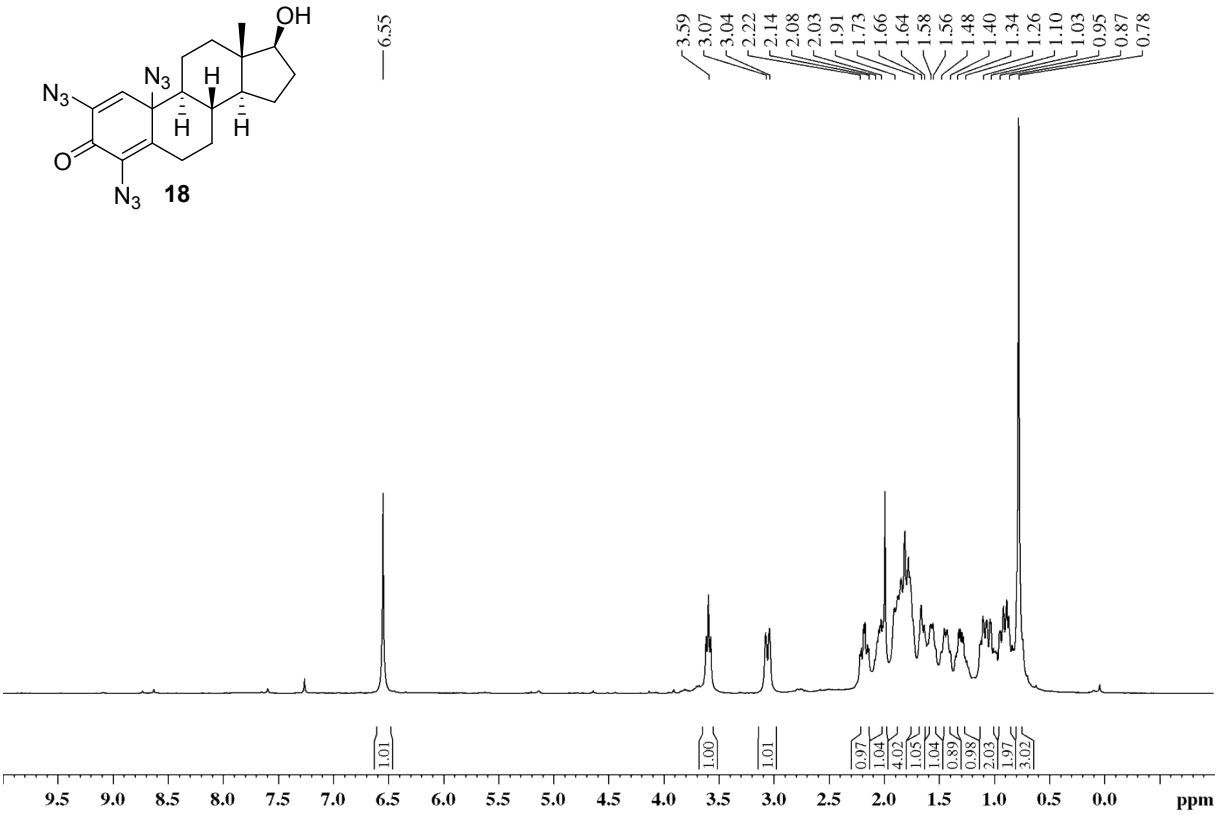
(8*S*,9*S*,13*S*,14*S*,17*R*)-2,4,10-Triazido-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one (17)

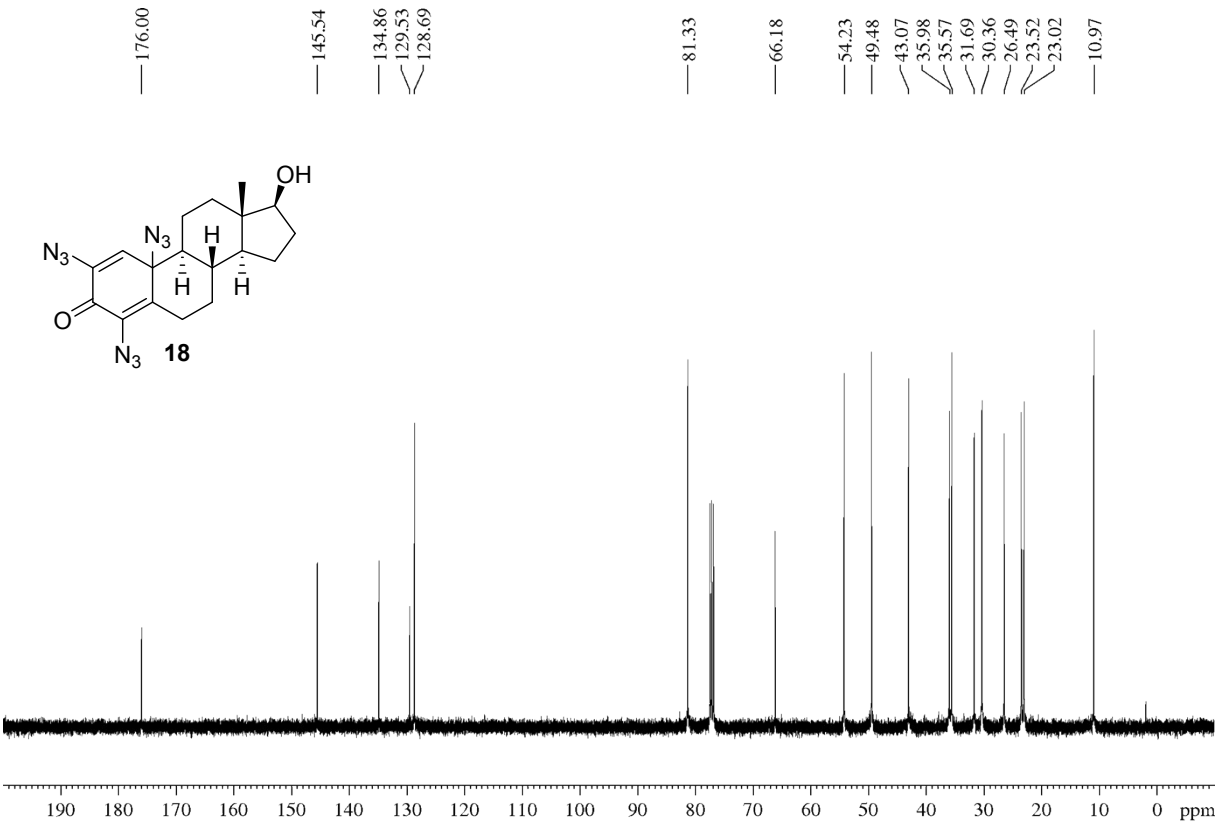


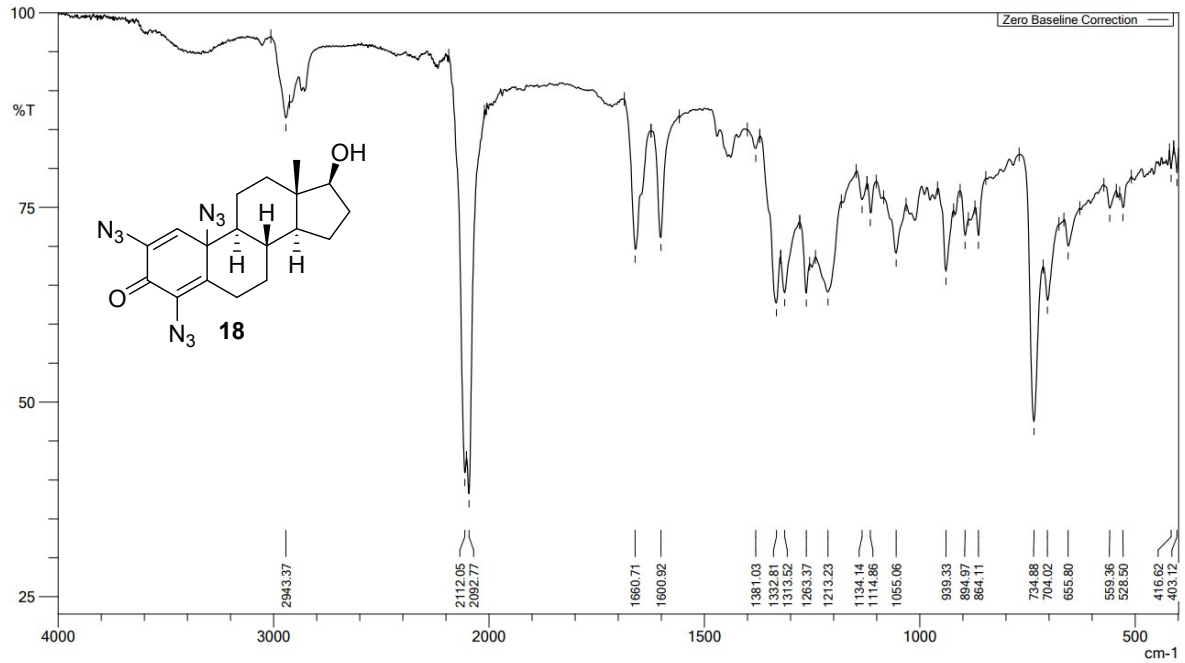

176.09
145.54
134.96
129.64
128.70
79.60
66.31
54.00
47.31
45.42
35.84
32.55
32.49
30.83
26.67
24.87
22.94
16.89
OH
N3
N3
H
H
H
O
N3
17
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


100
%T
90
80
OH
N3
N3
H
H
H
O
N3
17
2937.59
2115.91
1662.64
1602.85
1338.60
1317.38
1211.30
933.55
885.33
418.55
403.12
4000
3000
2000
1500
1000
500
cm-1

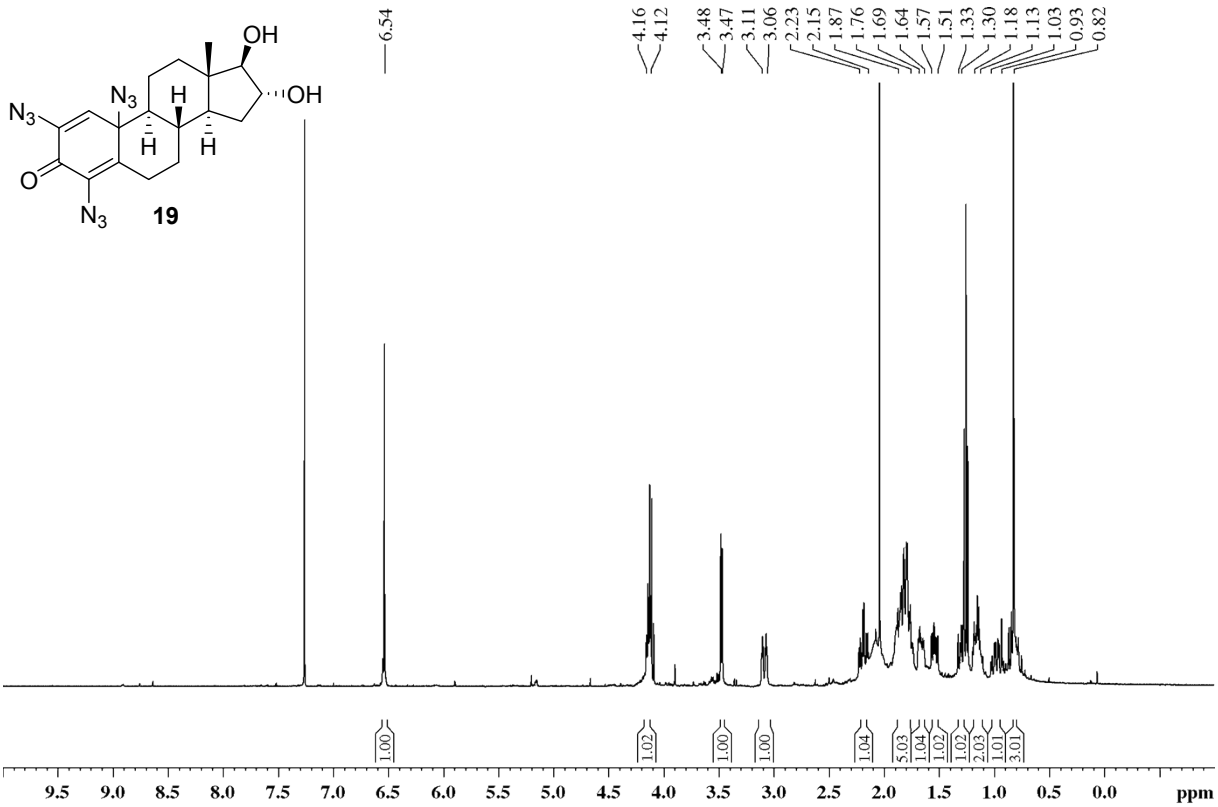
(8*S*,9*S*,13*S*,14*S*,17*S*)-2,4,10-Triazido-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one (18)

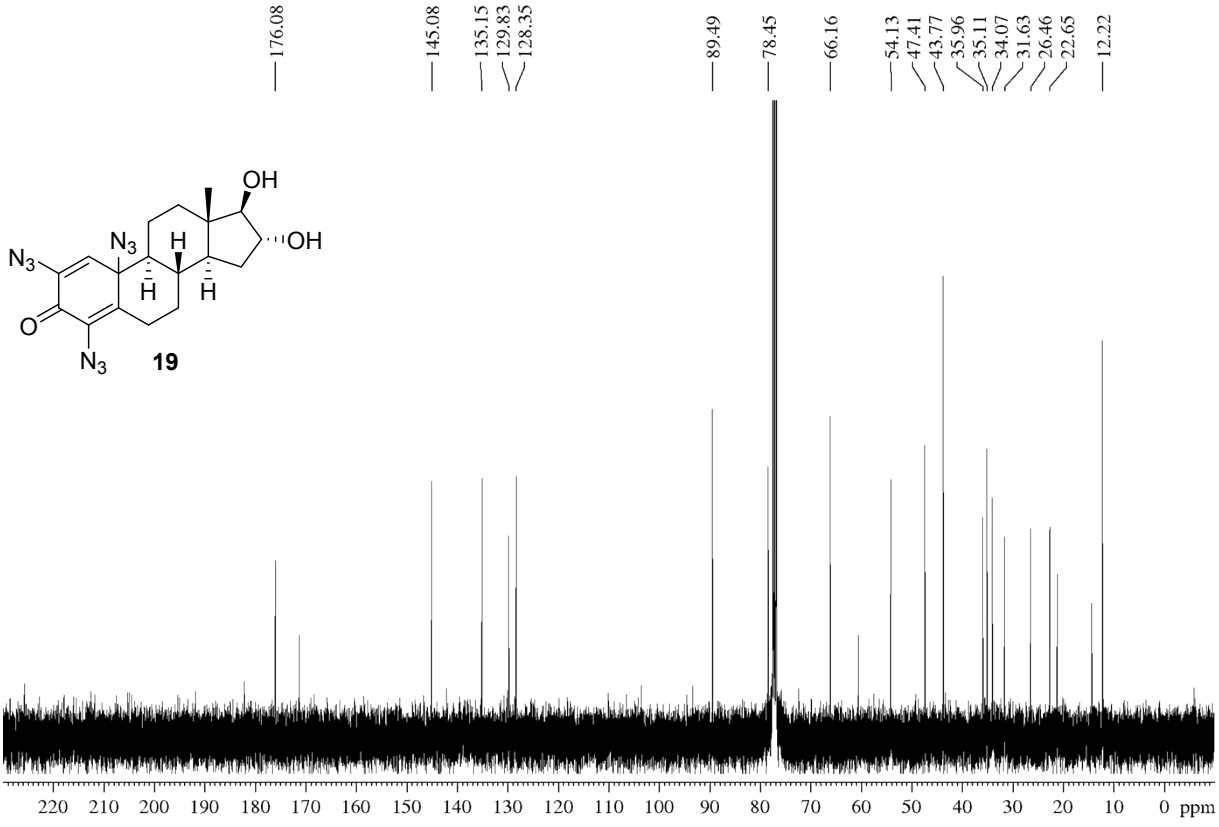


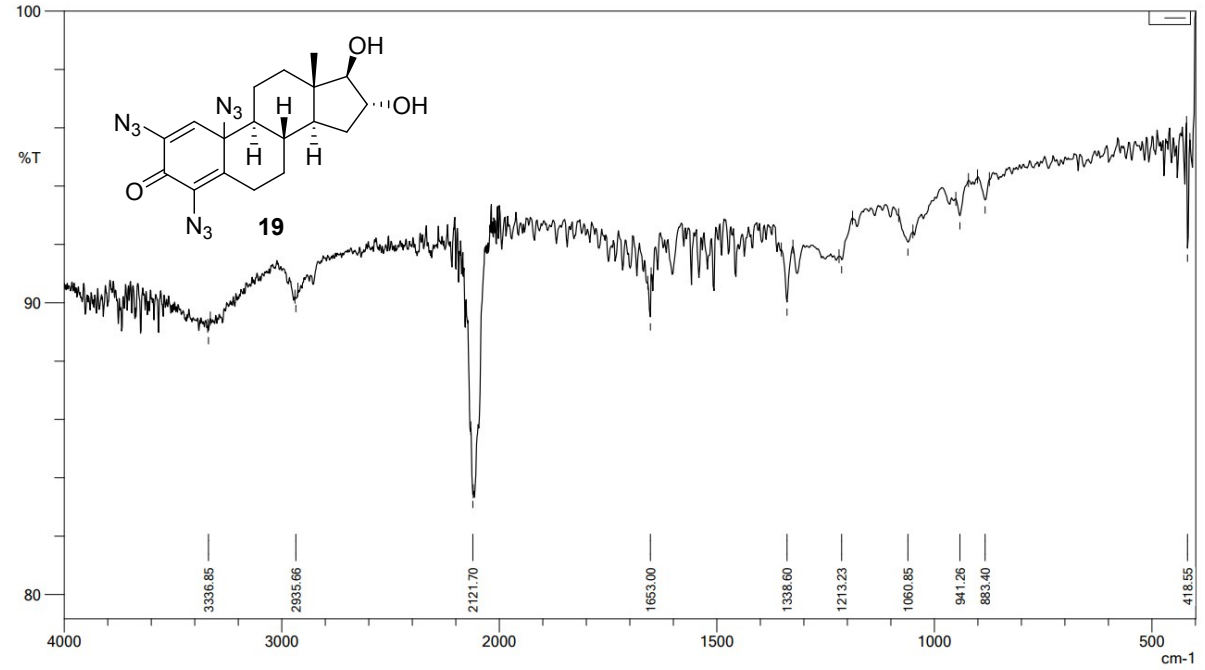




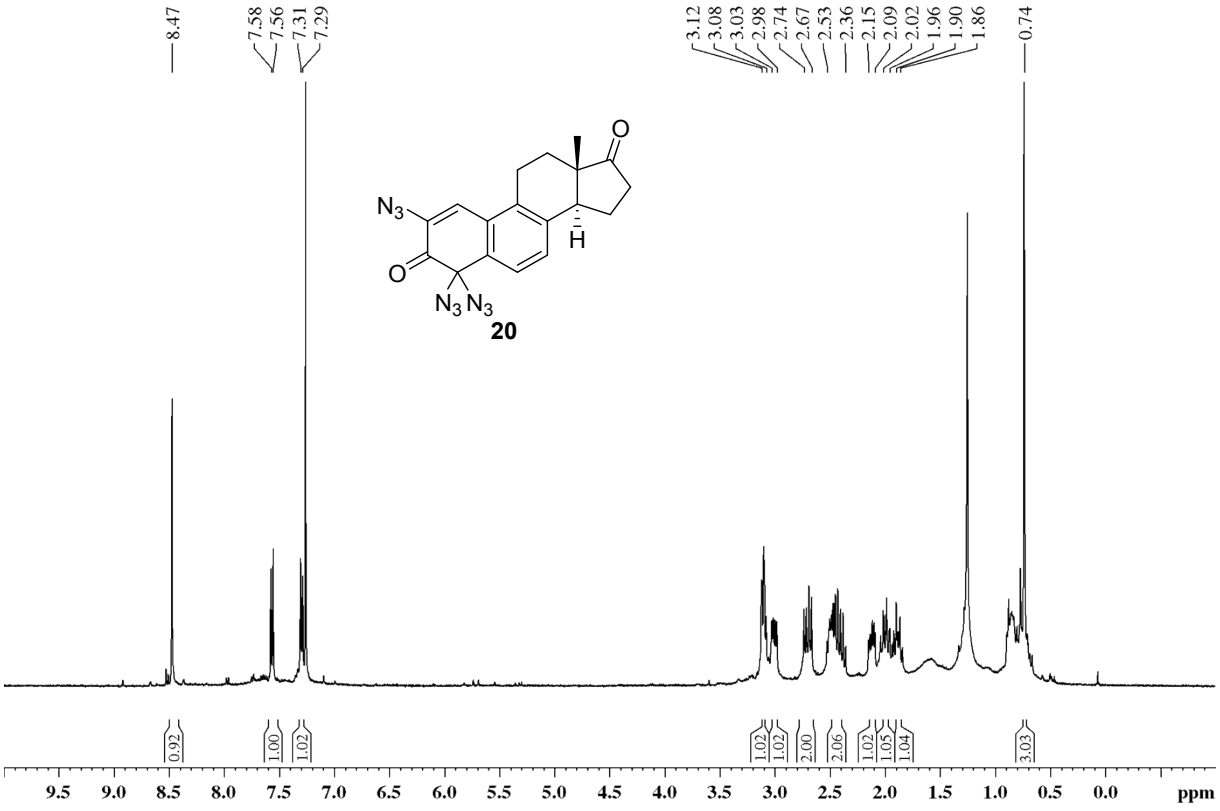
(8*S*,9*S*,13*S*,14*S*,16*R*,17*R*)-2,4,10-triazido-16,17-dihydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (19)

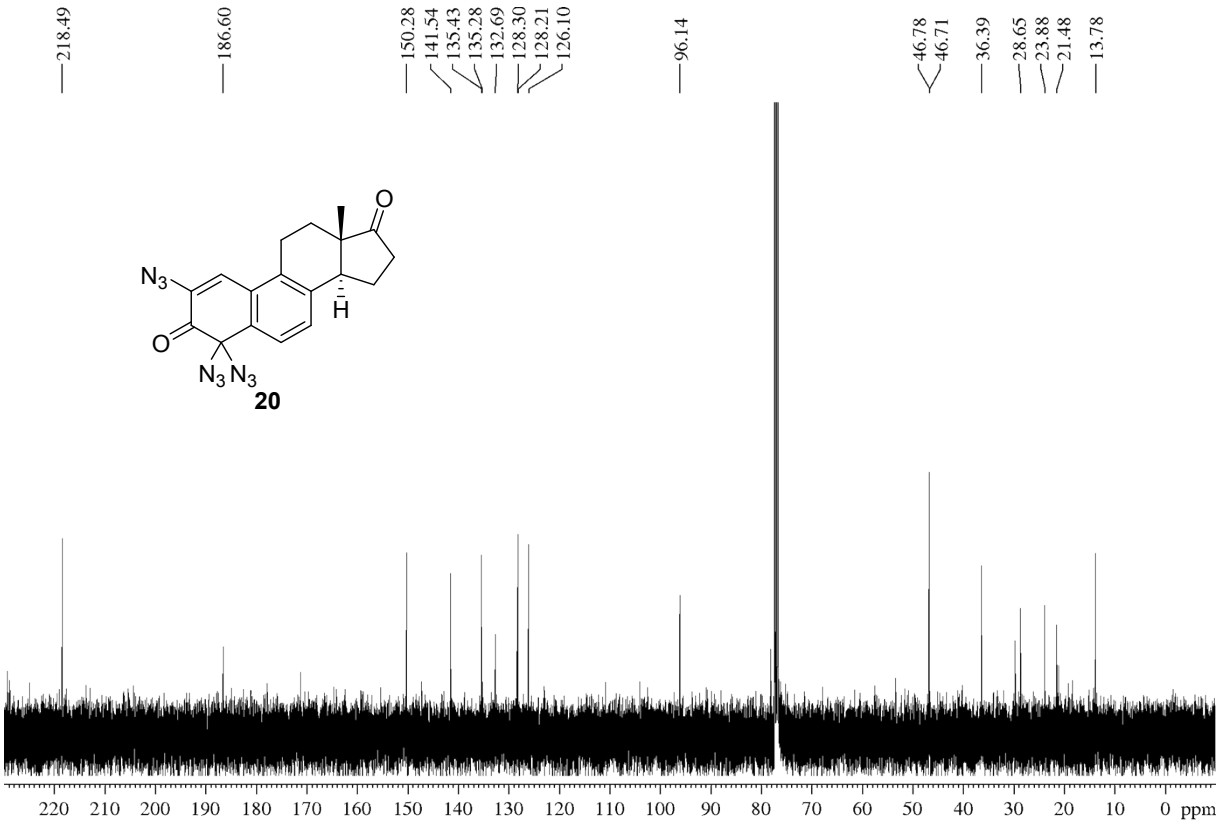


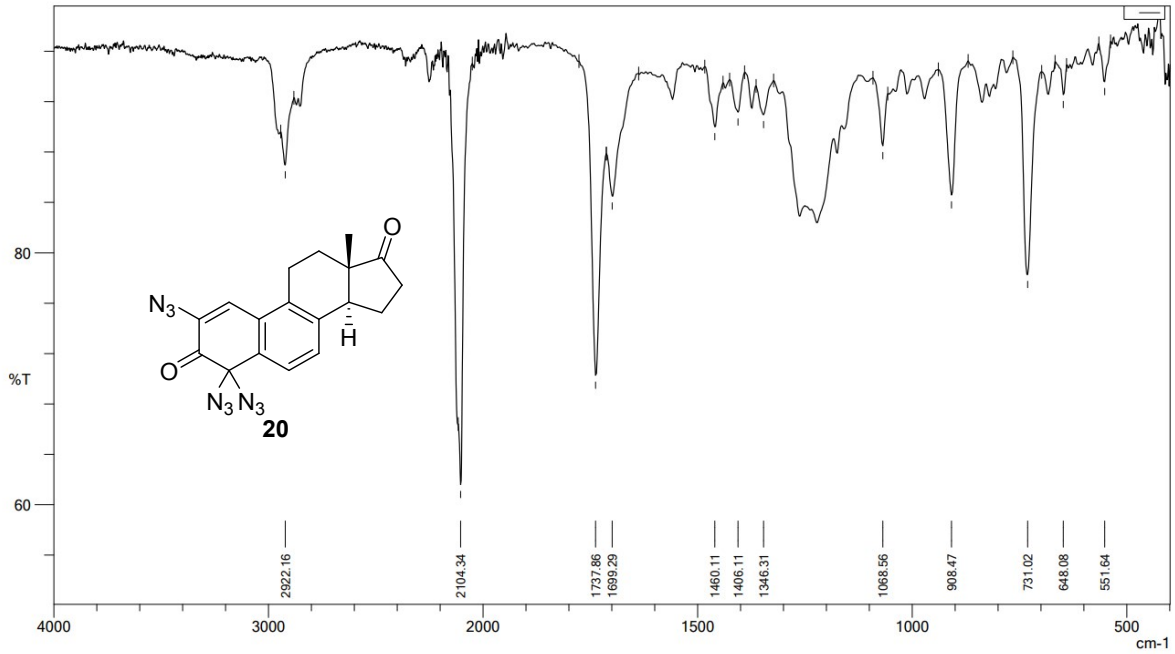

176.08
145.08
135.15
129.83
128.35
89.49
78.45
66.16
54.13
47.41
43.77
35.96
35.11
34.07
31.63
26.46
22.65
12.22
OH
N3
N3
H
OH
N3
H
H
O
N3
19
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


100
%T
90
80
OH
N3
N3
H
OH
N3
H
H
O
N3
19
3336.85
2935.66
2121.70
1653.00
1338.60
1213.23
1060.85
941.26
883.40
418.55
4000
3000
2000
1500
1000
500
cm-1

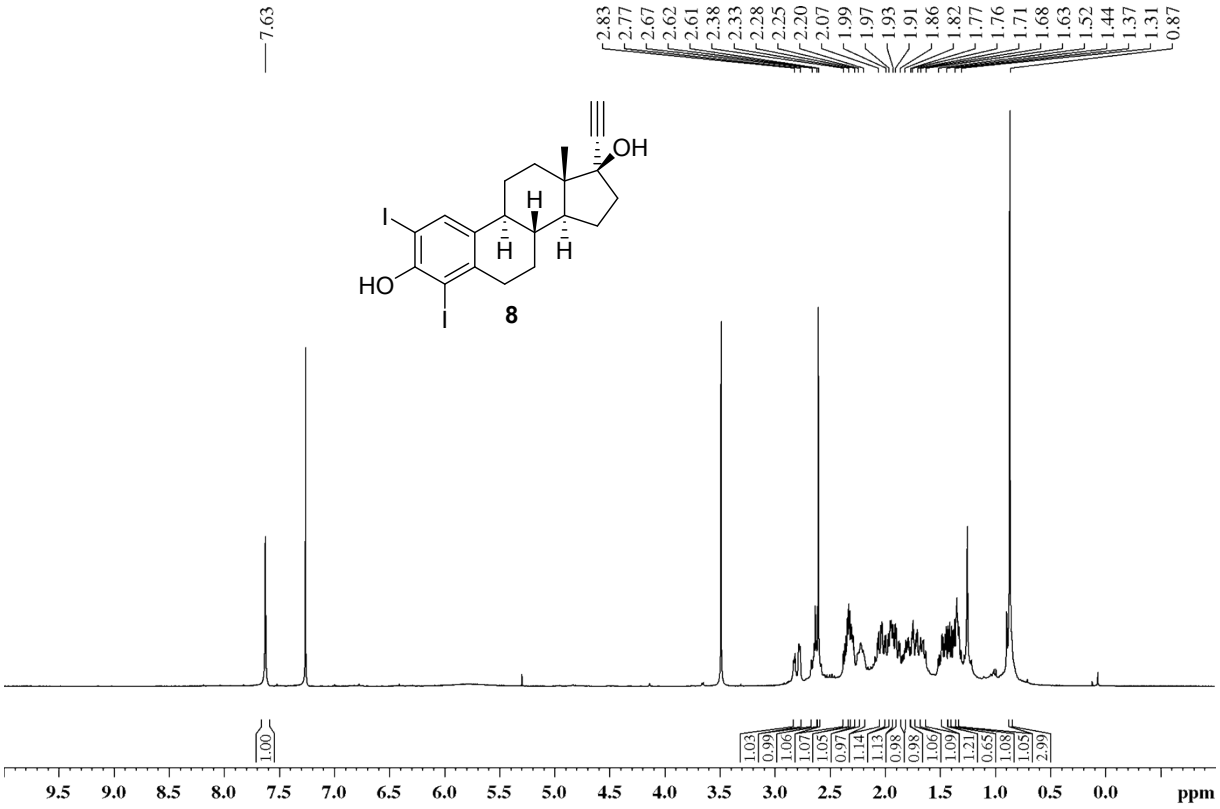
(13*S*,14*S*)-2,4,4-triazido-13-methyl-11,12,13,14,15,16-hexahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(4*H*)-dione (20)

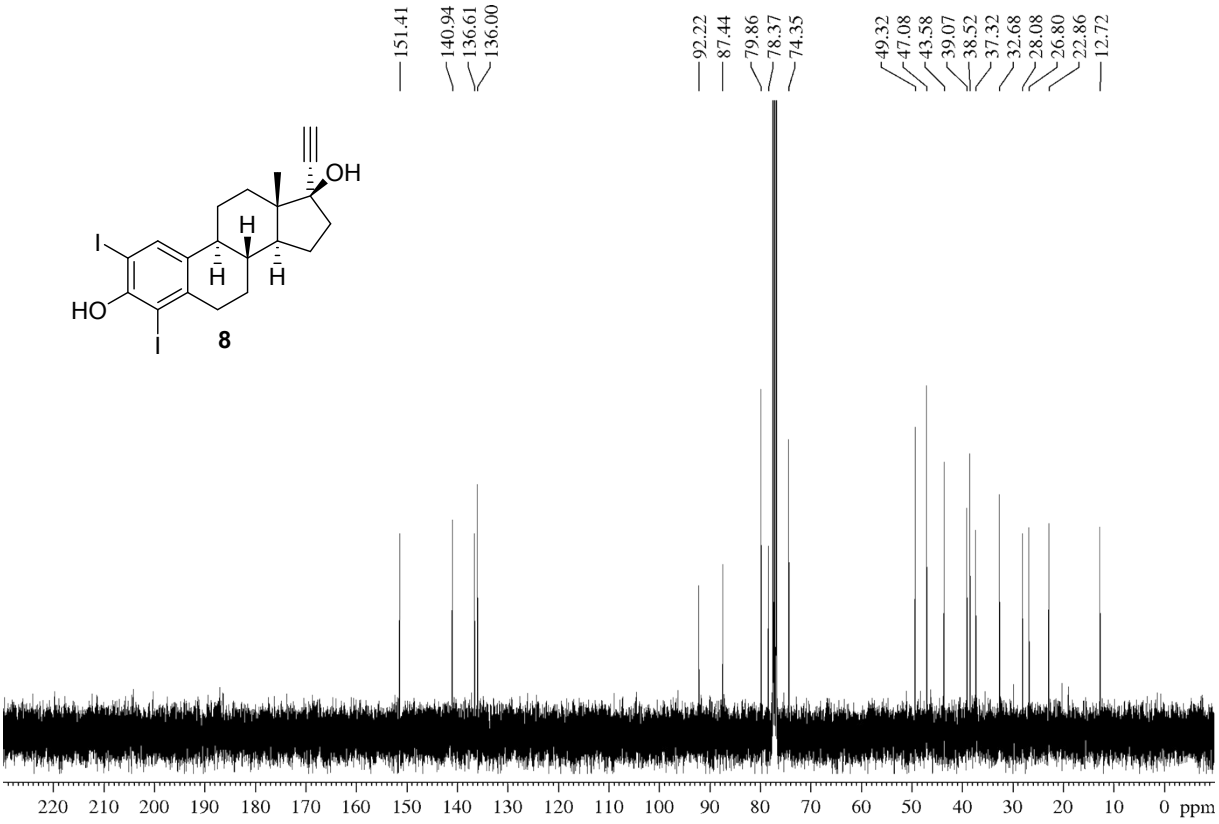




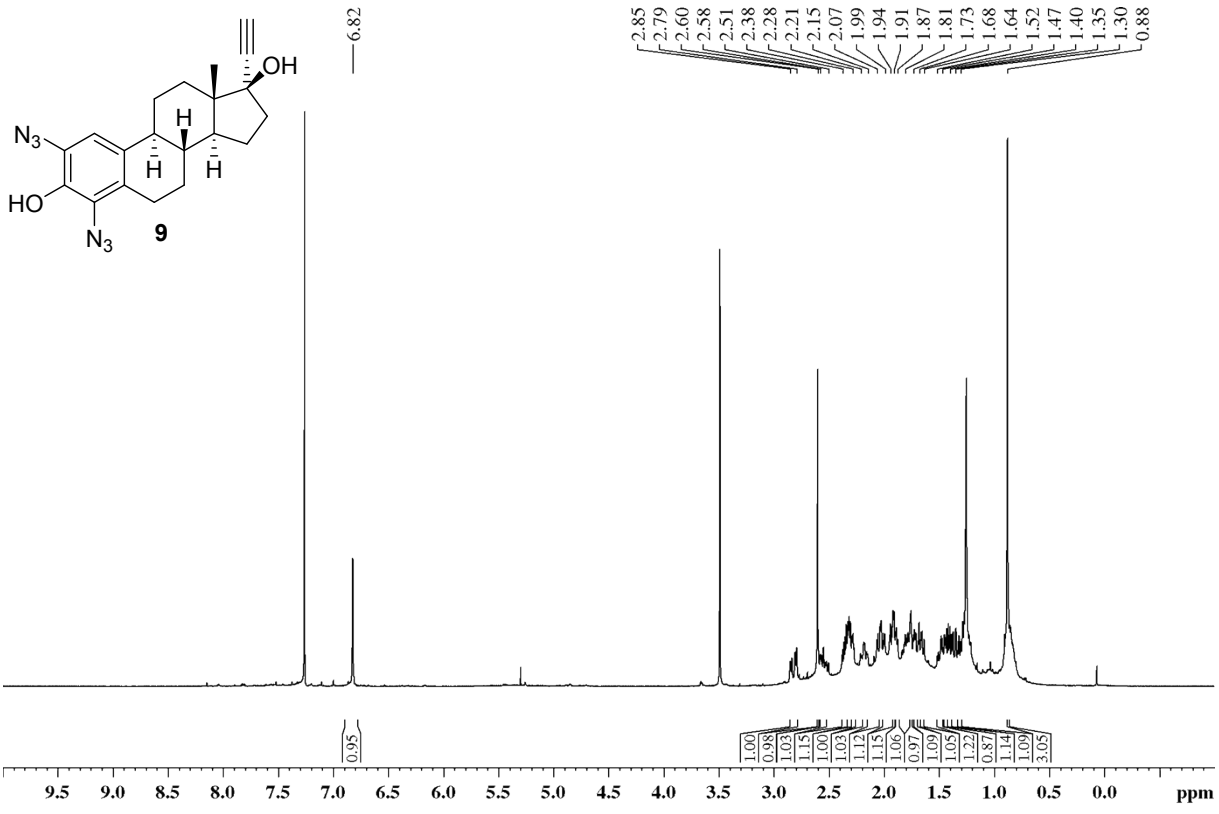


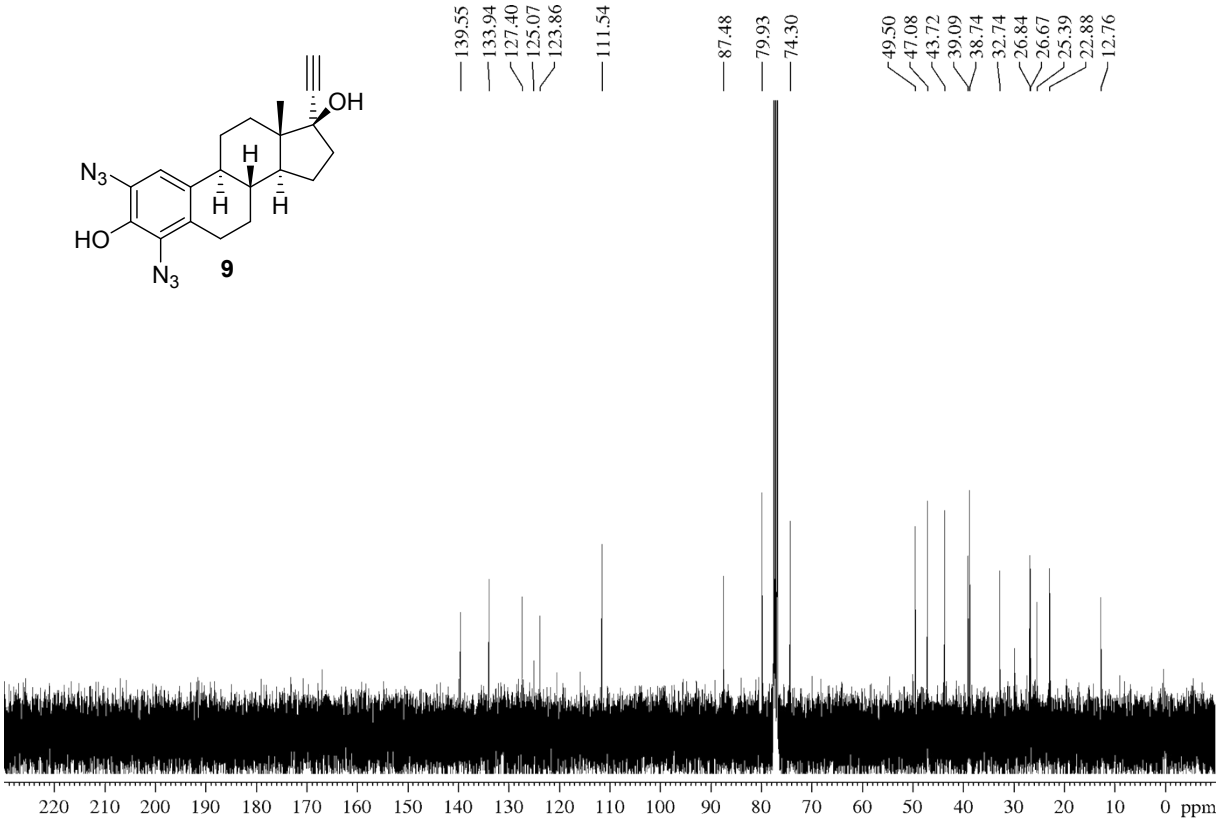
(8*R*,9*S*,13*S*,14*S*,17*R*)-17-Ethynyl-2,4-diiodo-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*α*]phenanthrene-3,17-diol (8)

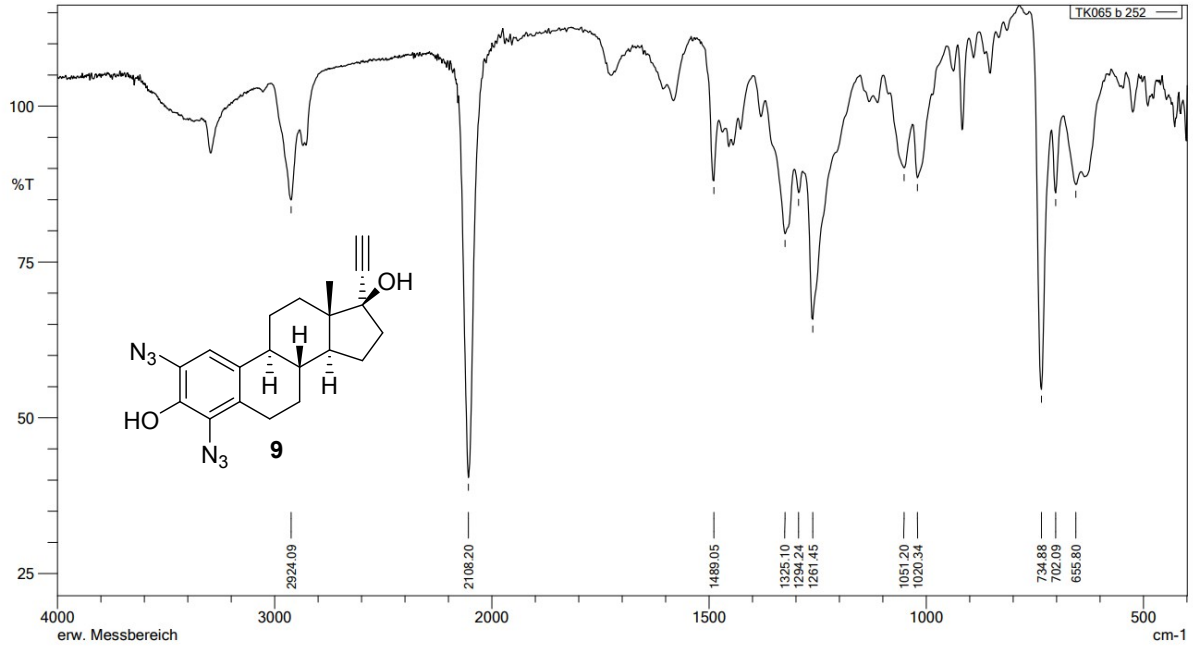




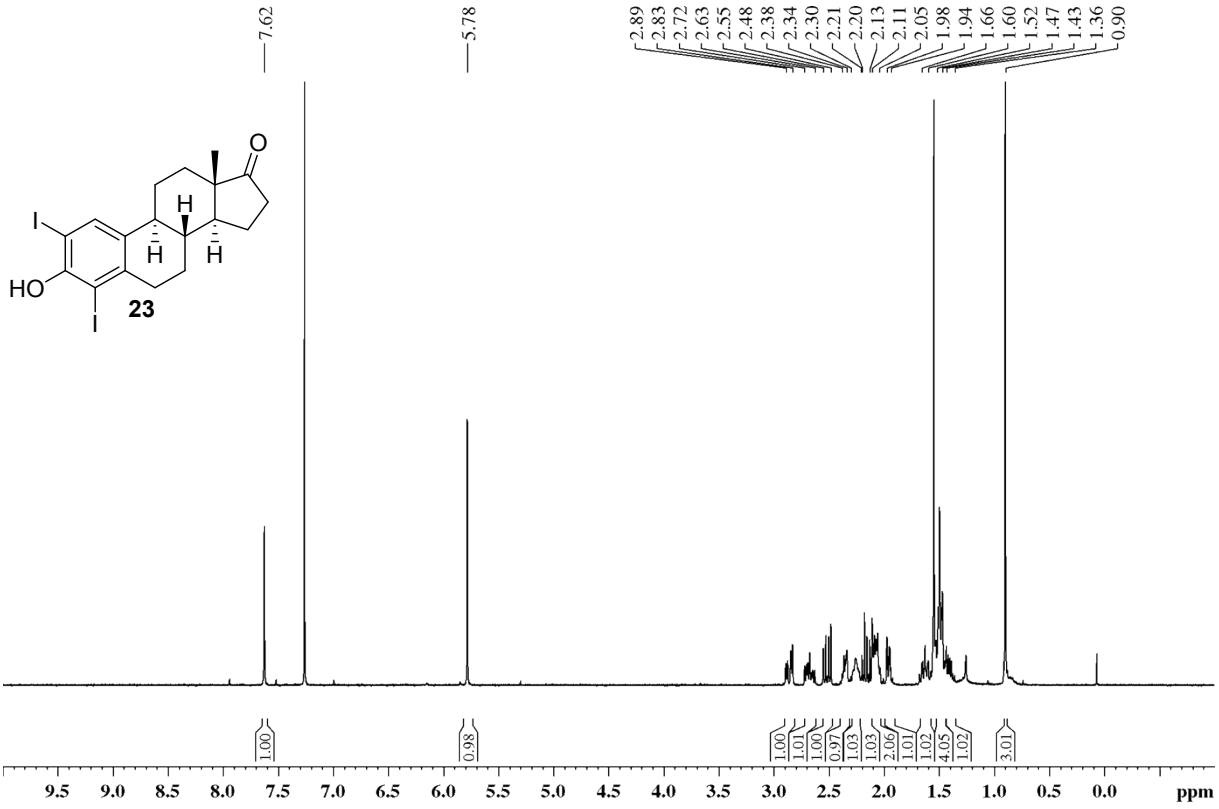
(8*R*,9*S*,13*S*,14*S*,17*R*)-2,4-Diazido-17-ethynyl-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*α*]phenanthrene-3,17-diol (9)

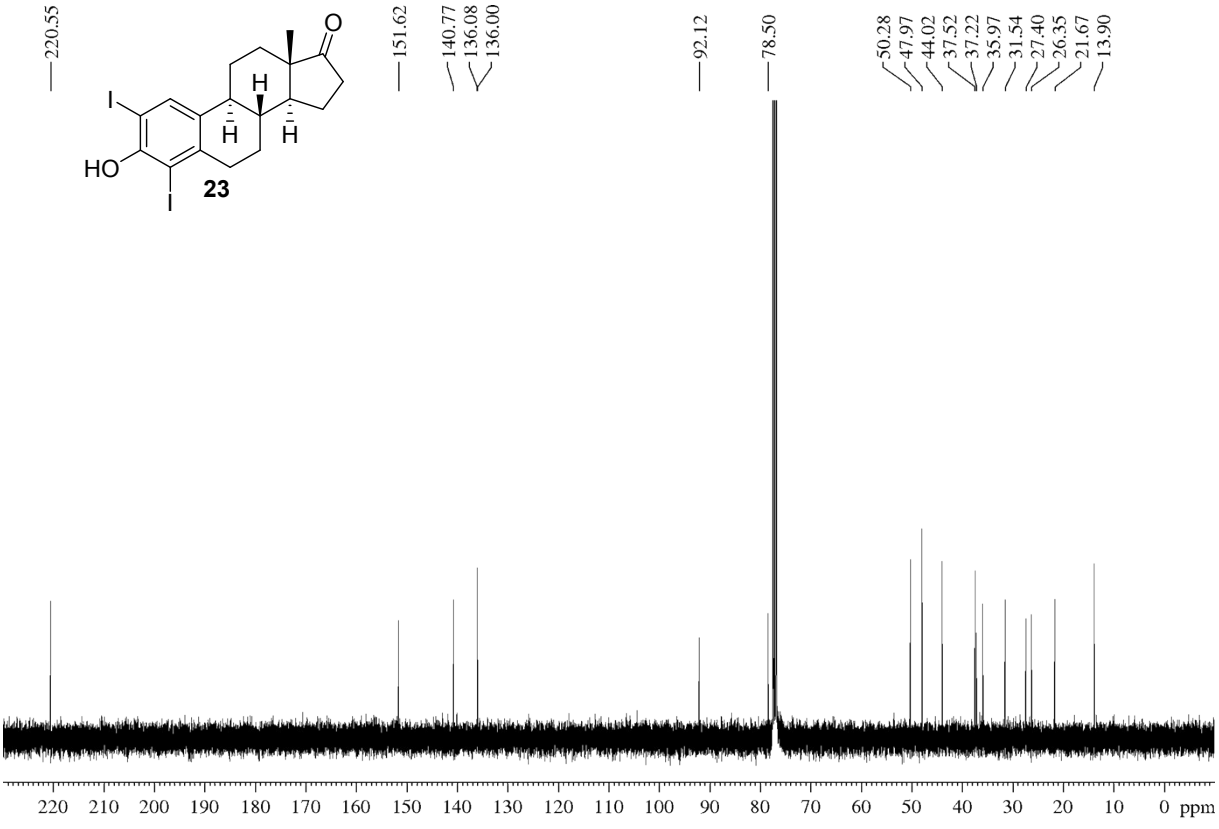



139.55
133.94
127.40
125.07
123.86
111.54
87.48
79.93
74.30
49.50
47.08
43.72
39.09
38.74
32.74
26.84
26.67
25.39
22.88
12.76
OH
H
H
H
N3
HO
N3
9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

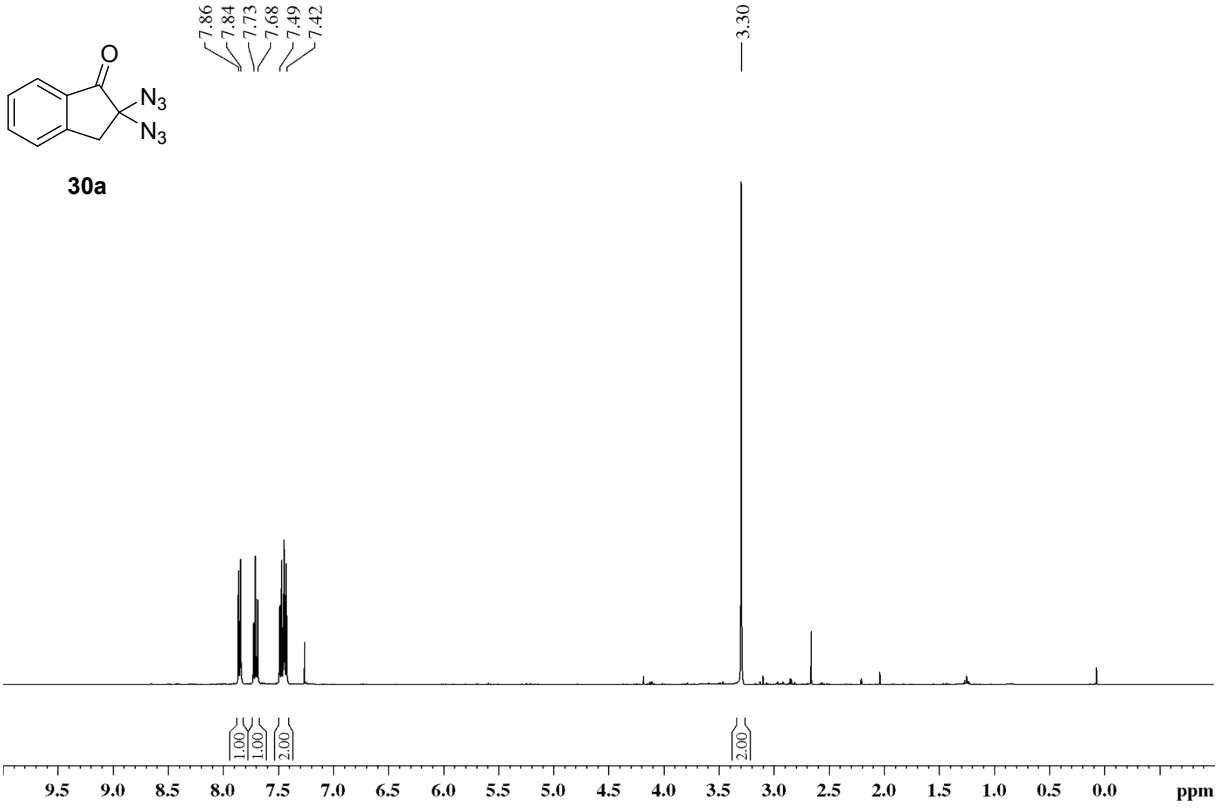

TK065 b 252
100
%T
75
50
25
OH
H
H
H
N3
HO
N3
9
2924.09
2108.20
1489.05
1325.10
1294.24
1261.45
1051.20
1020.34
734.88
702.09
655.80
4000
3000
2000
1500
1000
500
erw. Messbereich
cm-1

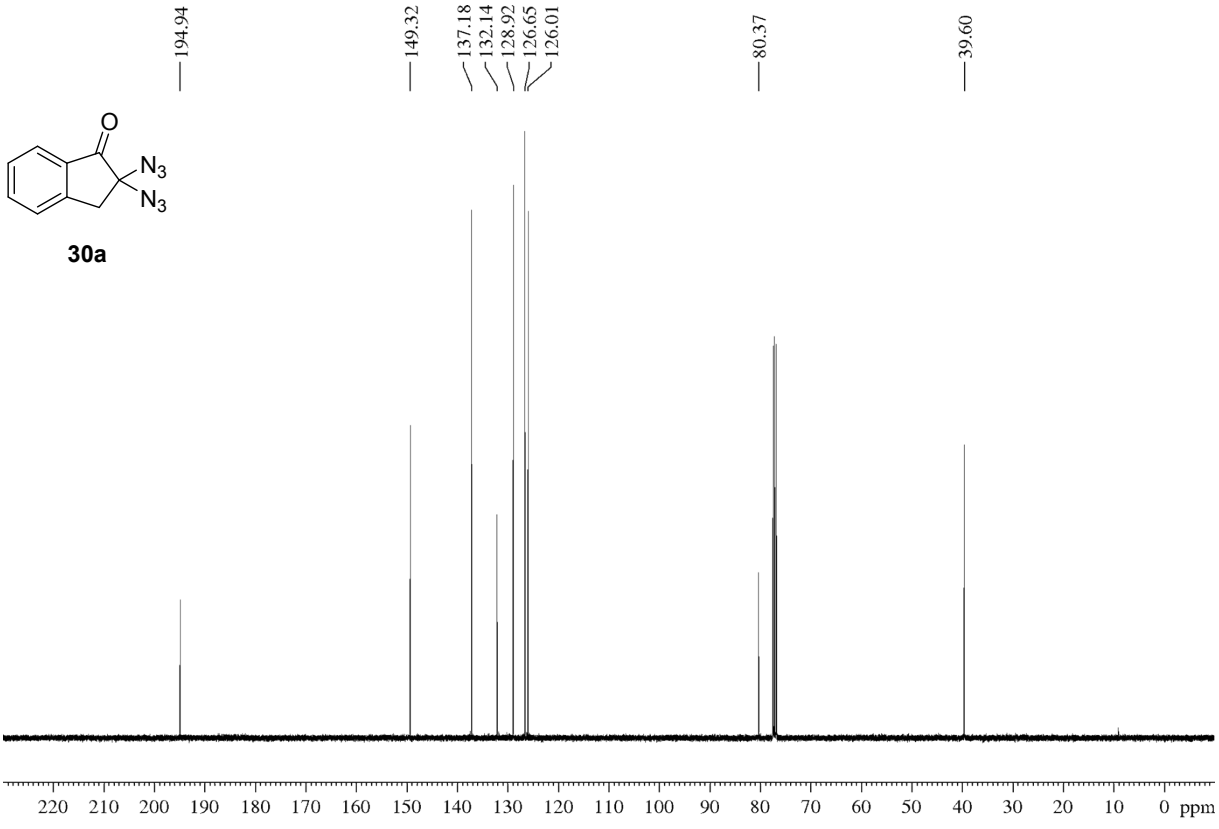
(8*R*,9*S*,13*S*,14*S*)-3-hydroxy-2,4-diiodo-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (23)



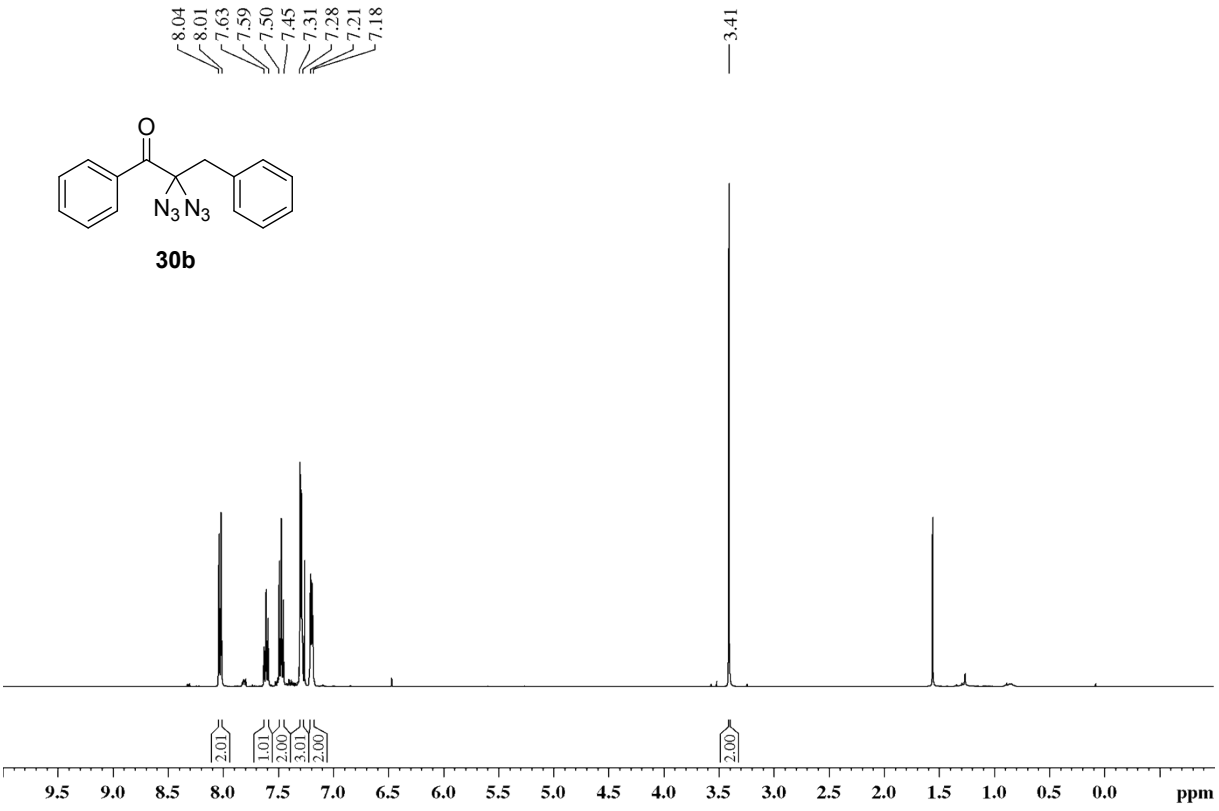


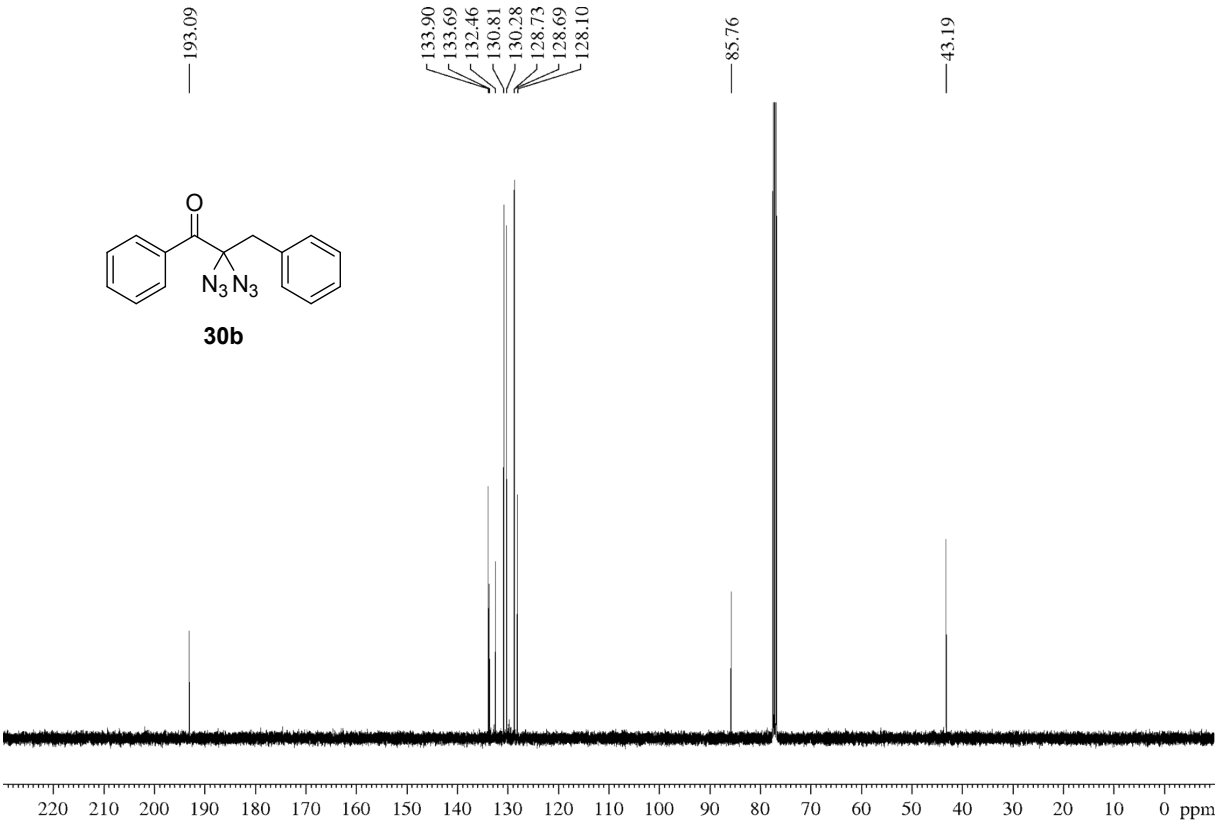
2,2-Diazido-3,4-dihydroinden-1-one (30a)



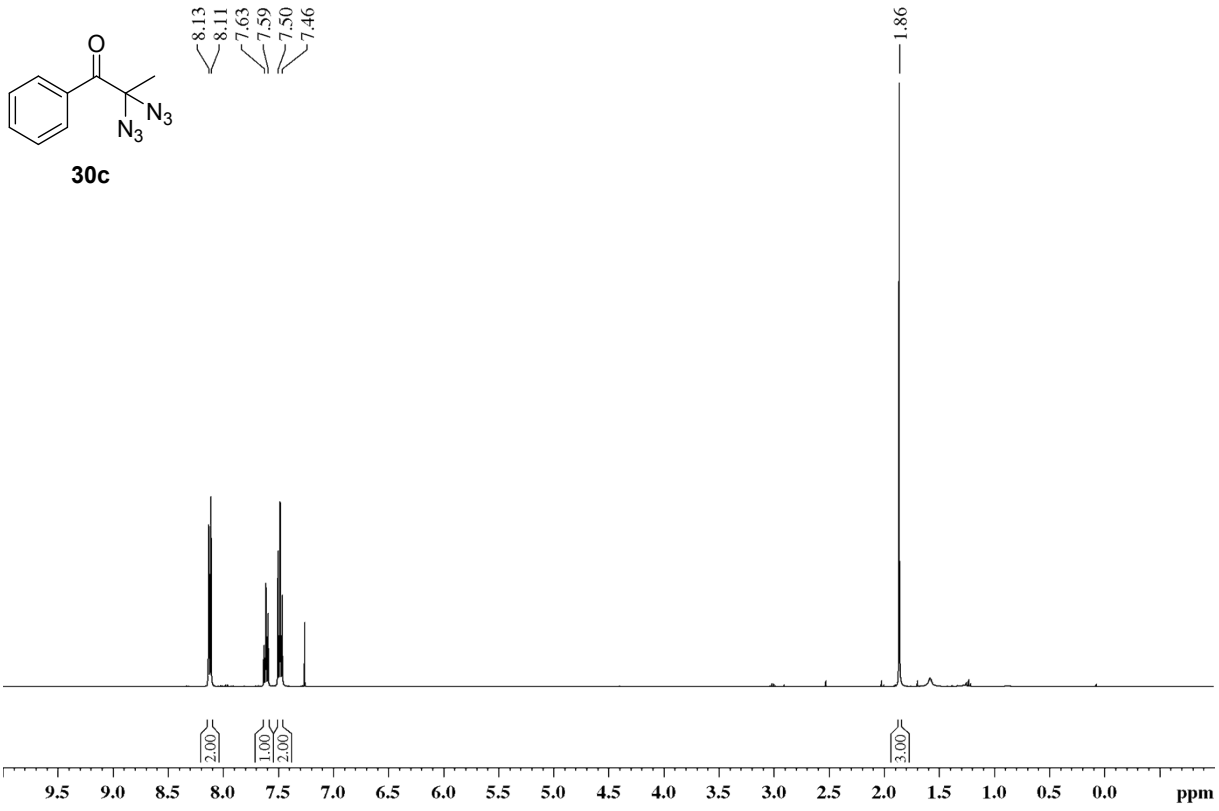


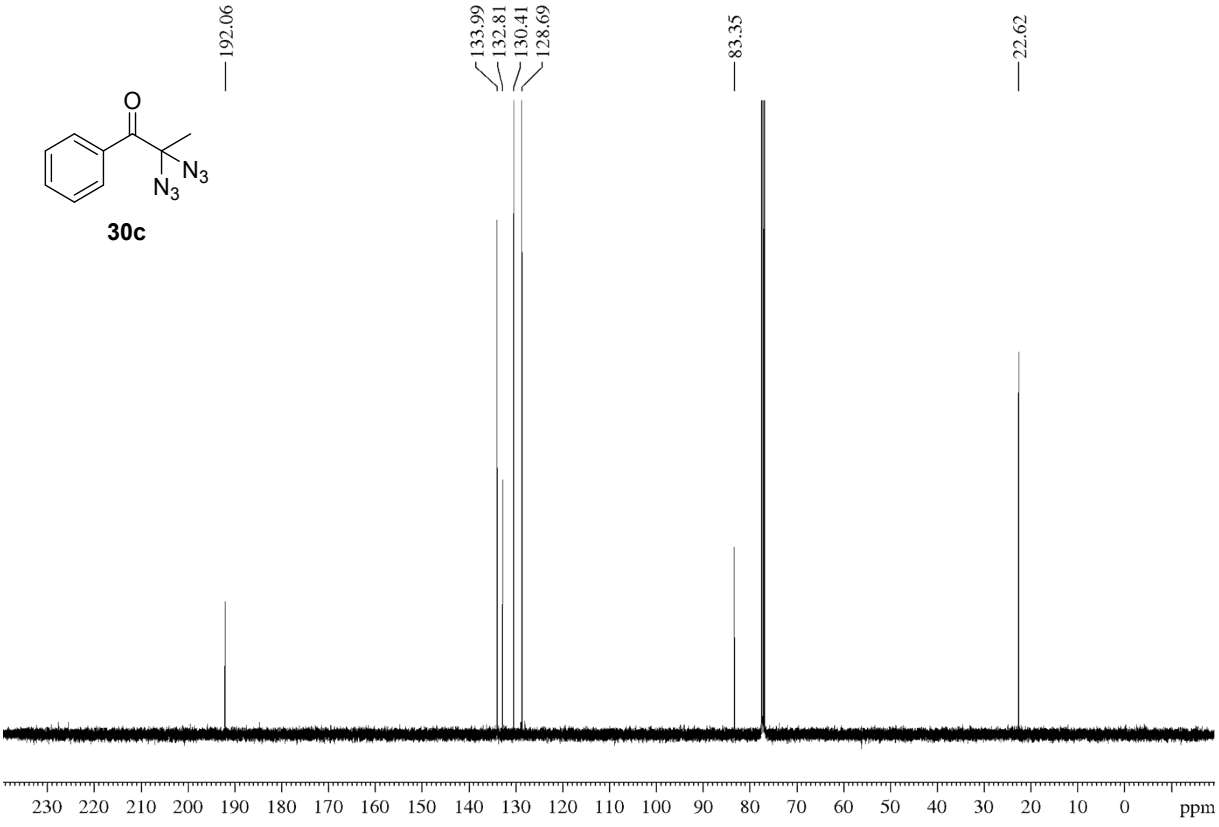
2,2-Diazido-1,3-diphenylpropan-1-one (30b)





2,2-Diazido-1-phenylpropan-1-one (30c)





2-Azido-2-methyl-1-phenylpropan-1-one (30d)