Supplementary Information

Dual Catalytic Synthesis of Antiviral Compounds Based on Metallocarbene-Azide Cascade Chemistry

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Table of Contents

Compound Stability Studies:

A. Differential Scanning Calorimetry (DSC).

An example of a DSC experiment for compound **1a**[1] is shown (Figure S1). These data show the temperature at which the crystals of **1a** began to melt (endotherm, positive peak, 75.5 °C) and began to decompose (exotherm, negative peak, 127 °C to 168 °C). The heat released after the decomposition is about 1730 J/g material.

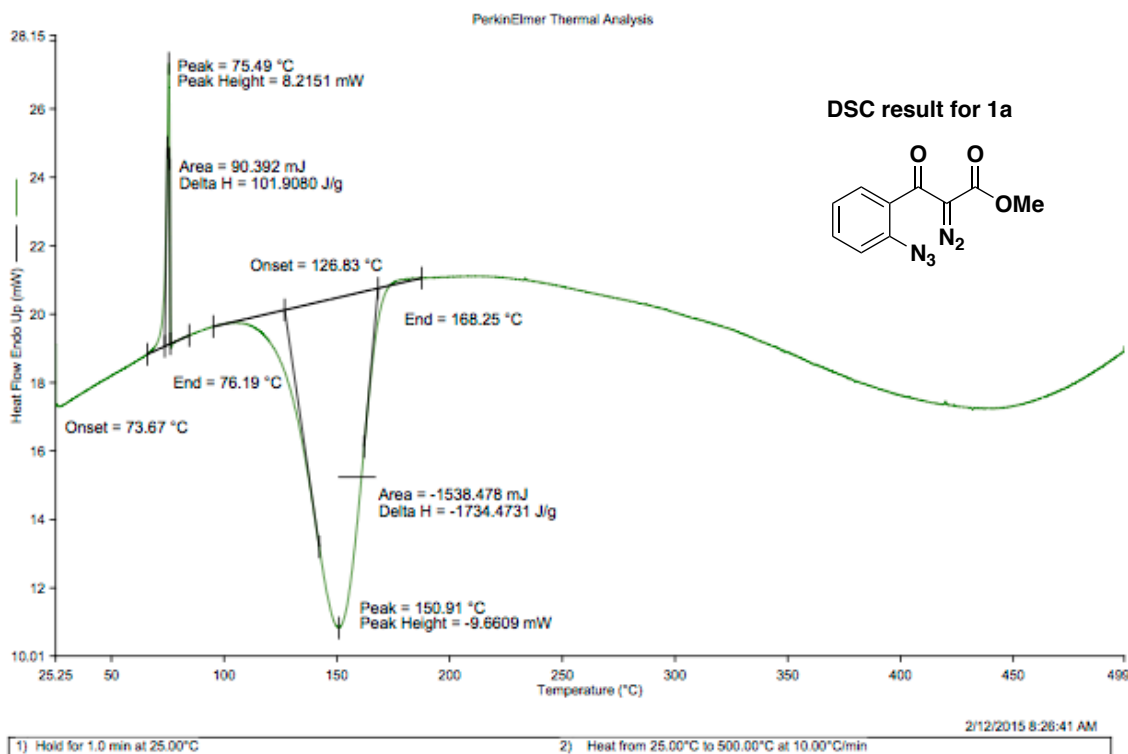[1]Bott, T. M.; Atienza, B. J.; West, F. G. *RSC Adv*. **2014**, *4*, 31955-31959.

Figure S1: Differential Scanning Calorimetry (DSC) data for 1a.

B. Thermogravimetric analysis (TGA)

The decomposition pattern was further monitored using a TGA experiment. An example of a TGA experiment for compound **1a** is shown in Figure S2. We found that dicarbonyl stabilized diazo crystals of **1a** generally exhibited one sharp inflection point, starting at temperatures around 130 °C, in agreement with the DSC experiment. No substantial mass change was noticed during the solid to liquid phase transition, indicative of no decomposition of material during melting phase transition.
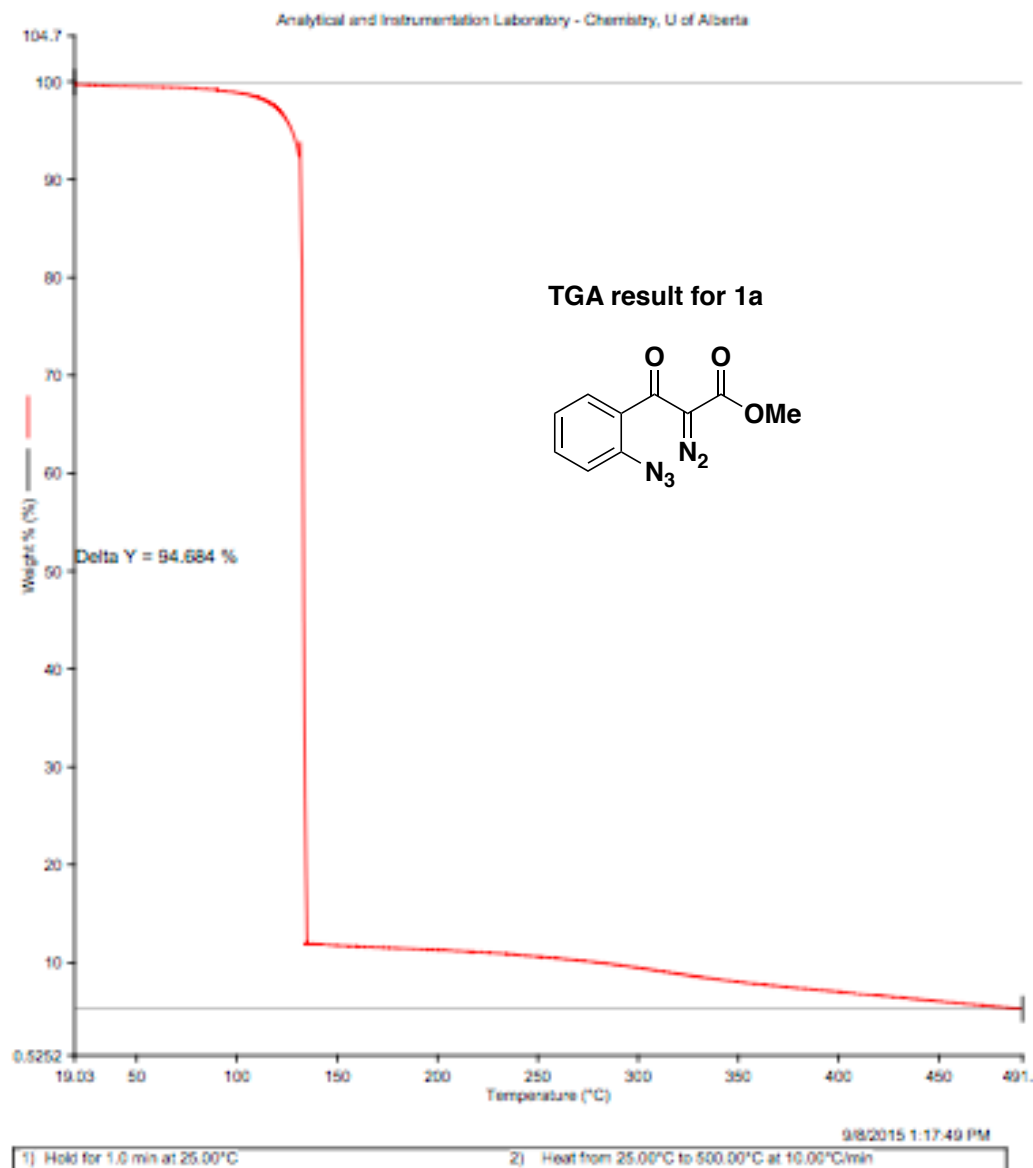
Figure S2: Thermogravimetric analysis (TGA) data for 1a.

Both of these experiments shed some light on the thermal stability of **1a**. These experiments provide clear and compelling evidence that the metal catalyzed transformation, associated with the starting material **1a**, at ambient temperature (22 °C to 40 °C), described in the manuscript, is not merely heat driven as the starting material **1a** is stable at this temperature range. Moreover, using the DSC data, we anticipated that there would be significantly less risk of detonation, due to thermal runaway, associated with compound **1a**, or analogous diazoazides, provided the material is stored at freezer temperature (< 0 °C) when not in use.

Long-term storage (> 1 week) is generally not advisable for compound **1a**, especially for a large-scale preparation, but we noticed that compound **1a** and the other analogues survived with little or no decomposition during storage at freezer temperature (–20 °C) for >3 months (monitored weekly using ^{1}H NMR).

These experiments (DSC and TGA) alone should not, however, be taken as an indication that the material is completely safe for handling. Other parameters, for example potential shock sensitivity, are equally important. Attempts to carry out a hammer test for compound **1a** (ca. 0.5 mg) to evaluate its shock sensitivity were inconclusive. A small spark was observed, but in the absence of a reliable benchmark, we are unable to draw any conclusions regarding the shock sensitivity of **1a**. Similar to other common potentially explosive materials used in organic synthesis laboratories, such as peroxides, we caution potential users to treat the starting material **1a** and analogues with due care and respect. In our hands, we did not observe any unanticipated detonation of these diazo azide starting materials and we performed most of our large-scale reactions involving these substrates in a well-ventilated fume hood equipped with a blast shield. We also recommend wearing a Kevlar® apron and safety gloves and using earplugs as added safety precautions, especially for large-scale reactions.

Mechanistic Considerations:

A. Copper Oxidation State in the Catalytic Cycle
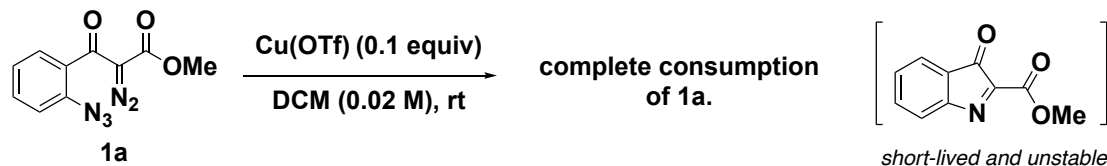
Conversion Studies (% Recovery):

Copper (II) oxidation state:
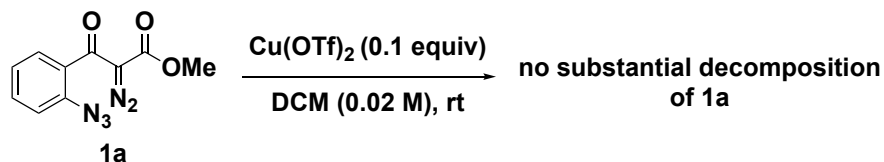
A solution of diazo-azide **1a** (50 mg, 0.20 mmol) in DCM (5 mL) was added to a solution of Cu(OTf)$_2$ (7.3 mg, 0.020 mmol) in DCM (5 mL) at room temperature *via* syringe pump over 1 h. Once the addition was complete, the reaction was monitored by TLC for consumption of the diazo-azide starting material. After 24 h, the solution was extracted

with water (10 mL, 3×) to remove the copper salt, and the DCM solution was dried with MgSO₄, filtered and concentrated under reduced pressure. The crude oil was purified using silica gel flash column chromatography eluting with 20% EtOAc/Hexanes. This procedure resulted in the recovery of diazo-azide **1a**, in 81-93% (three repeats). Using identical conditions but allowing the mixture to stir for 5 d instead of 24 h resulted to the recovery of 73-84% (three repeats) starting material **1a**. Analysis of the TLC and NMR spectra of the crude mixture revealed the presence of starting material, and a faint spot on the baseline using 20% EtOAc/Hexanes as the eluent (TLC).
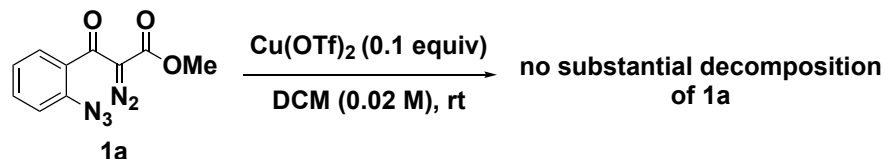
Copper (I) oxidation state:

A solution of diazo-azide **1a** (50 mg, 0.20 mmol) in DCM (5 mL) was added to a solution of Cu(OTf)(PhMe) (10 mg, 0.020 mmol) in DCM (5 mL) at room temperature *via* syringe pump over 1 h. Once the addition was complete, the reaction was monitored by TLC for consumption of the diazo-azide starting material. After 24 h, the solution was extracted with water (10 mL, 3×) to remove the copper salt, the DCM solution was dried with MgSO₄, filtered and concentrated under reduced pressure. The crude oil was purified using silica gel flash column chromatography eluting with 20% EtOAc/Hexanes. This procedure resulted to the recovery of trace amount of **1a** (< 5%). Analysis of the TLC chromatogram of the crude mixture revealed the presence of multiple colored spots. The crude NMR spectra revealed an intractable mixture of multiple compounds.
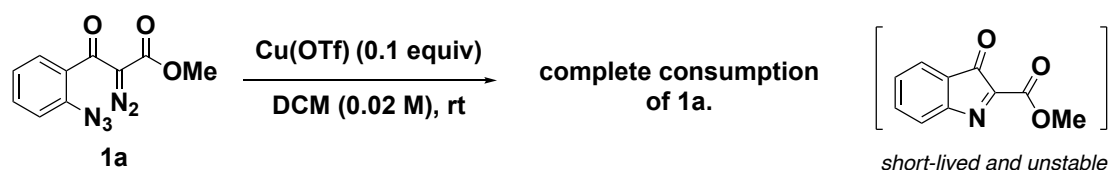
Conversion Studies (*in-situ* IR analysis and ¹H-NMR spectroscopy)
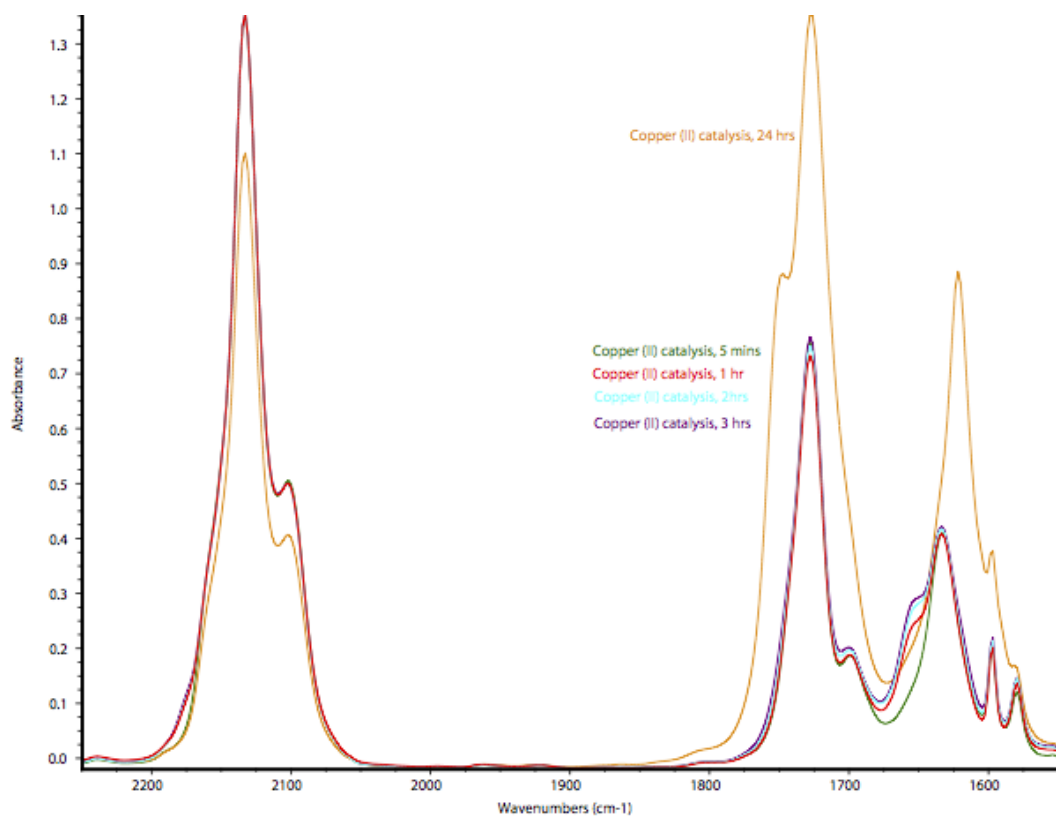
Copper (II) oxidation state:

A solution of diazo-azide **1a** (50 mg, 0.20 mmol) in DCM (5 mL) was added to a solution of Cu(OTf)₂ (7.6 mg, 0.02 mmol) in DCM (5 mL) at room temperature *via* syringe pump over 1 h. Once the addition was complete, the reaction was monitored by TLC for consumption of the diazo-azide starting material. An aliquot of the stirred solution (0.5 mL), was taken after *ca*. 5 min, 1 h, 2 h, 3 h, and 24 h of stirring, each aliquot was diluted with DCM (1 mL). The diluted solution was analyzed using IR spectroscopy and plotted as overlaid spectra (Figure S3a).

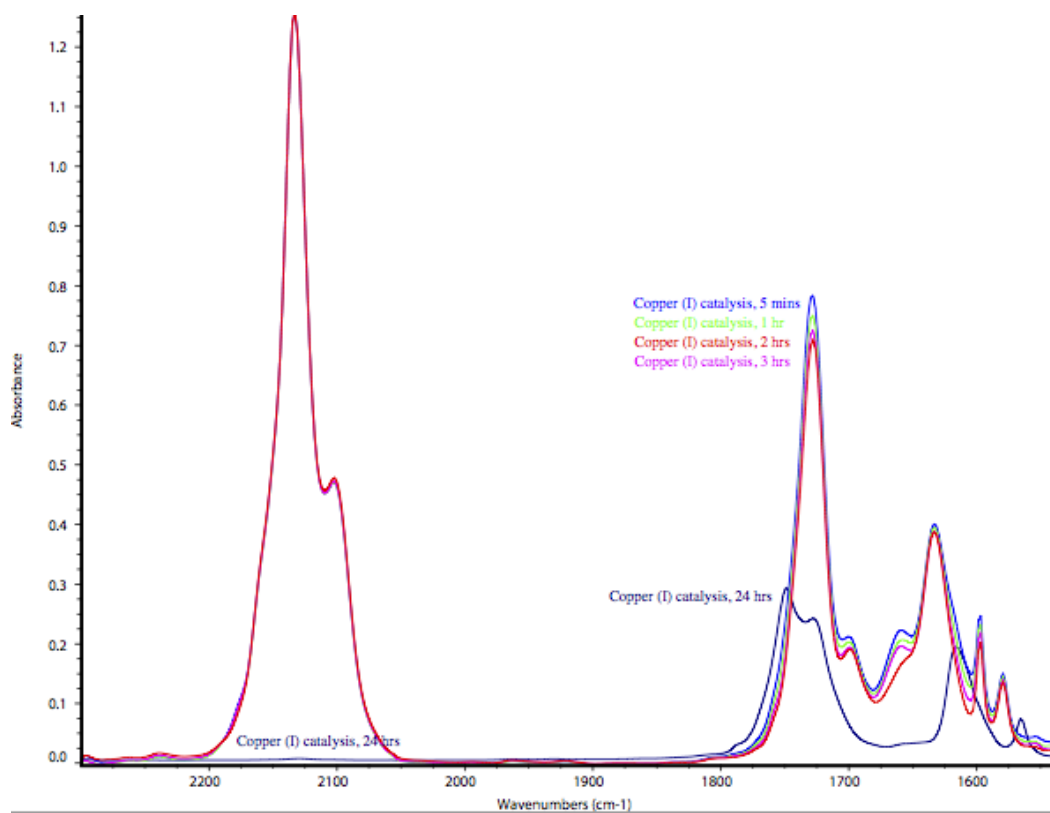**Copper (I) oxidation state:**

Using IR spectroscopy

A solution of diazo-azide **1a** (50 mg, 0.20 mmol) in DCM (5 mL) was added to a solution of Cu(OTf)(PhMe) (10 mg, 0.020 mmol) in DCM (5 mL) at room temperature *via* syringe pump over 1 h. Once the addition was complete, the reaction was monitored by TLC for consumption of the diazo-azide starting material. An aliquot of the stirred solution (0.5 mL), was taken after *ca*. 5 min, 1 h, 2 h, 3 h and 24 h of stirring, each aliquot was diluted with DCM (1 mL). The diluted solution was analyzed using IR spectroscopy and plotted as overlaid spectra (Figure S3b).

Figure S3: In-situ IR spectroscopic analysis of the decomposition of compound 1a.

Discussion of *in-situ* IR analysis:

The complete absence of a broad peak at 2137 cm⁻¹ indicated complete decomposition of the diazoketone and the azide functional groups. An increase in the absorbance and broadening of signal around 1730 cm⁻¹ was noticed on diazo-azide starting material upon exposure with copper (II) triflate over 24 h, indicative of carbonyl interaction (dative bond) with copper (II), which did not progress to substantial diazo-ketone decomposition (notice the continued substantial absorbance at 2137 cm⁻¹). However, a notable *decrease* in the absorbance of the signal around 2137 cm⁻¹ was noticed on diazo-azide starting material upon exposure with copper (I) triflate over 24 h, indicative of complete decomposition of diazoketone and azide over a 24 h period. This time period is within the observed optimized reaction time (16-36 h, depending on the substitution of indole substrate) for azide-metallocarbene coupling, followed by Friedel-Crafts alkylation with indole. This pair of experiments, together with the recovery analysis, and ¹H NMR spectroscopy (*vide infra*) provided a clear distinction between the catalytic behaviors of the two copper oxidation states.

Using ¹H-NMR spectroscopy
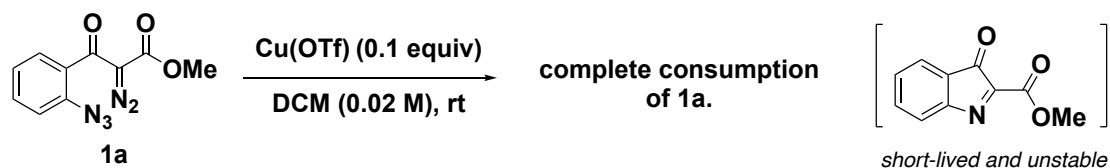
In a 2.0 mL vial, a solution of diazo-azide **1a** (10 mg, 0.040 mmol) in deuterated DCM (0.5 mL) at room temperature was added to Cu(OTf)(PhMe) (*ca.* 2.0 mg, 0.0039 mmol) as a solid. The solution was quickly transferred in an NMR tube, capped with septum, and purged with argon. NMR spectra (400 MHz) were acquired once per hour over a 10 h period. The array of spectra was plotted. After 8-10 h, the starting material **1a** was completely consumed. These data, corroborated with the IR results, provide compelling evidence that copper (I) is the kinetically competent oxidation state during the conversion of diazoazide into *C*-acylimine.

Bren Atienza, BA_MI(CAT+Sub), +25C
399.951 MHz H1 1D in cd2cl2 (ref. to CD2Cl2 @ 5.32 ppm), temp -0.1 C -> actual temp = -2.3 C, sw400 probe
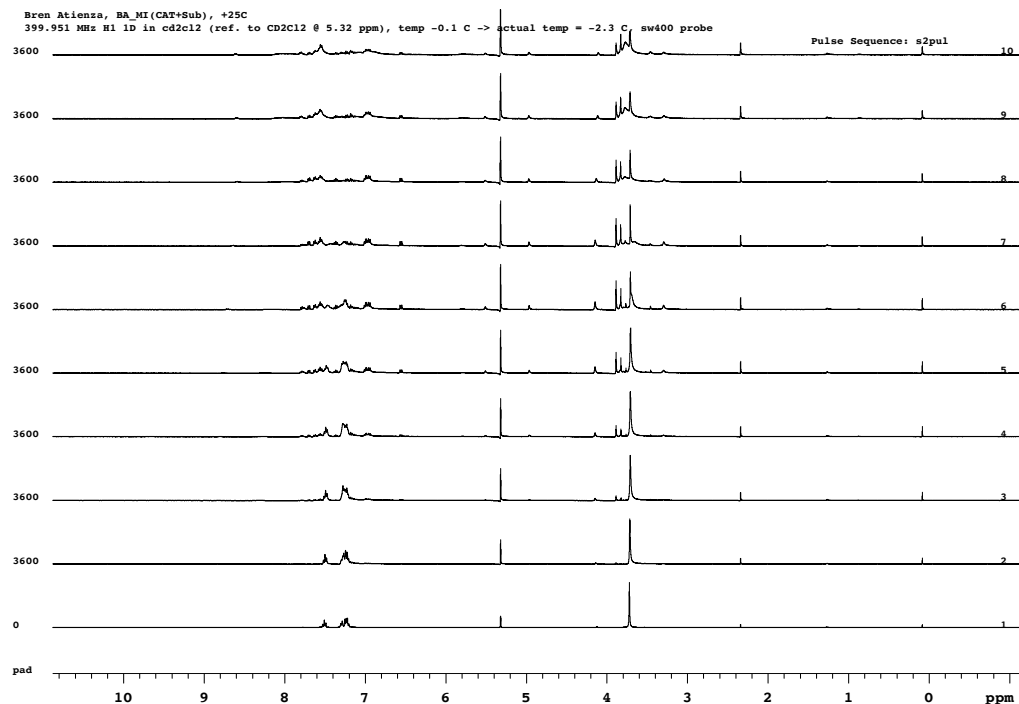Pulse Sequence: s2pul

Figure S4: Decomposition analysis of 1a, in the presence of Cu (I) catalyst, using NMR.

After extensive analysis of the copper oxidation state necessary for the decomposition of the starting material **1a**, we posited that copper (I) was the kinetically competent oxidation state. This, however, was not expected since our initially loaded catalyst was copper (II) triflate. A logical next step was to examine whether the indole could function as a competent reductant.

Formation of Active Copper (I) Catalyst from Copper (II) Precatalyst

Using UV spectroscopy, formation of a new σ-copper indole complex.
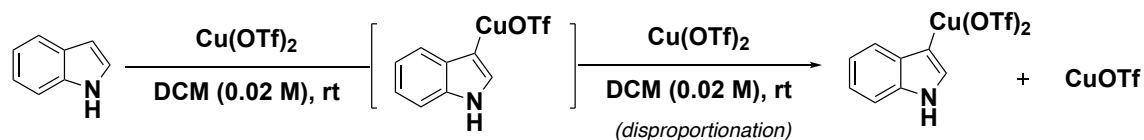
Solution A: A solution of indole (55 mg, 0.47 mmol) was added to Cu(OTf)$_2$ (7.3 mg, 0.020 mmol) in DCM (5 mL) at room temperature. Once the addition was complete, noticeable formation of light green solution occurred after 1 h. An aliquot of this solution (1 mL) was diluted with 5 mL of DCM and was subjected to UV spectroscopy. **Solution B**: An aliquot (1 mL) of a solution of indole dissolved in DCM (0.02 M, 10 mL) at room temperature was also subjected to UV spectroscopy. **Solution C:** An aliquot (1 mL) of a solution of Cu(OTf)$_2$ dissolved in DCM (0.02 M, 10 mL) at room temperature was also subjected to UV spectroscopy. Further dilution was necessary until the peaks (> 300 nm) can be seen. After analysis of the three spectra, formation a broad new peak at 395 nm was seen from **Solution A**, indicating the formation of a new colored complex (Figure S5). This new peak at 395 nm does not persist and generally has low relative concentration. Hence, a concentrated reaction mixture was needed to observe the absorption at 395 nm. Notably, similar copper-indole species was detected by Toste et. al. upon mixing of Cu(II) chiral phosphate and indole.[2]
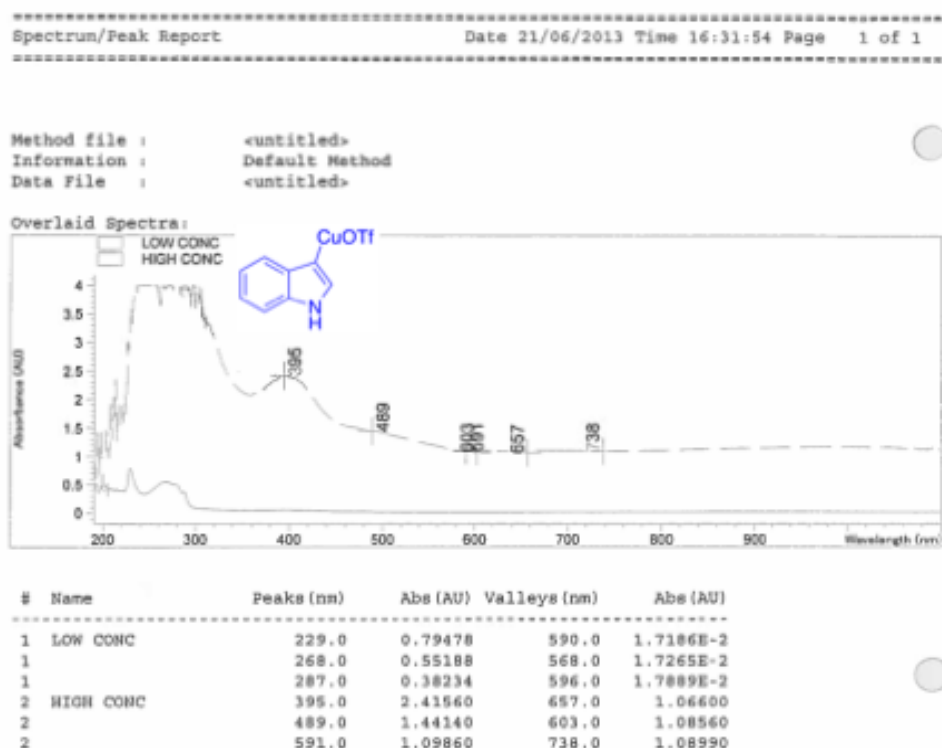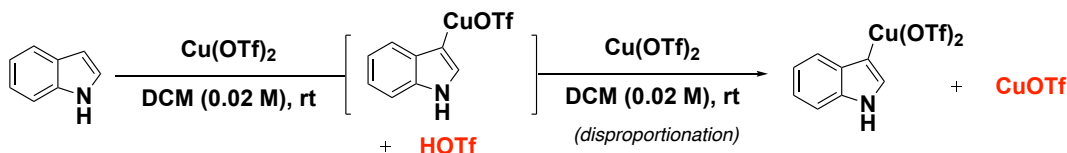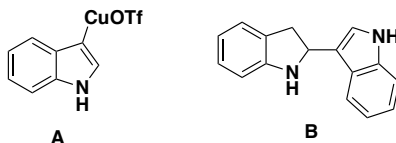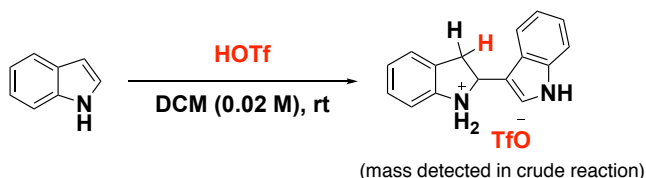

Figure S5: UV-VIS spectra of solution A.

[2]Rauniyar, V.; Wang, Z. J.; Burks, H. E.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 8486-8489.

Using ESI-MS, detection of the mass fragments corresponding to the dimer and the copper-indole complex.

Primary reaction:

Possible pathway to dimer:

(mass detected in crude reaction)

A solution of indole (55 mg, 0.47 mmol) in DCM (5 mL) was added to Cu(OTf)$_2$ (7.3 mg, 0.020 mmol) in DCM (5 mL) at room temperature. Once the addition was done, noticeable formation of light green solution occurred after one hour. An aliquot of this solution (1 mL) was diluted with acetonitrile and directly subjected to ESI-MS analysis. After analysis of the ESI-MS (Figure 6), the following fragments were detected and partially ascribed to the formation: **A** HRMS calc'd for C$_9$H$_6$CuF$_3$NO$_3$S [M]$^+$ 327.9316, found 327.9645 (fleeting), for **B** HRMS calc'd for C$_{16}$H$_{14}$N$_2$O [M+H]$^+$ 235.1230, found 235.1230, and protonated and sodiated **2a**. *N.B.*: Compound **B** was likewise detected in the crude reaction mixture to make **2a**.
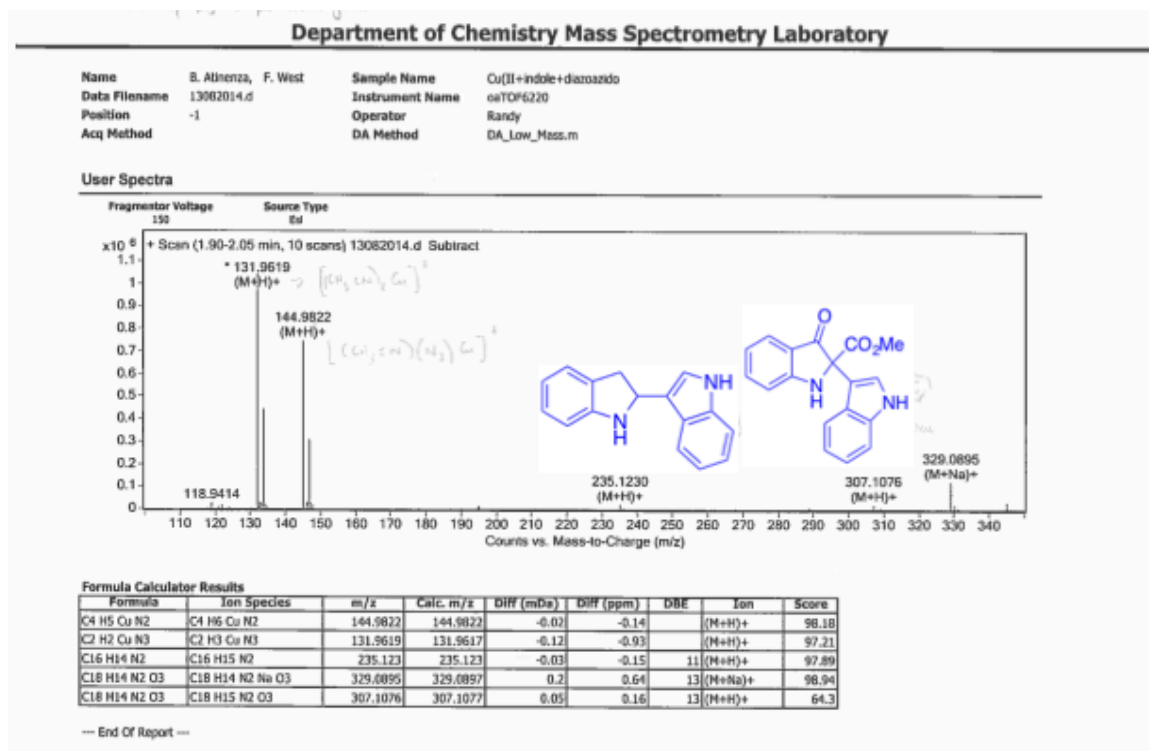
Figure S6: Electrospray mass spectra of the crude reaction mixture to make 2a.

Discussion. Given an apparent reaction between the indole and copper (II) triflate to afford an initially colored complex, the absorption detected through UV-VIS spectroscopy, and literature precedent,[2] we posit the reduction of copper (II) triflate through the initially formed metallated indole, followed by disproportionation reaction. This disproportionation reaction could theoretically generate copper (I) triflate, and copper (III) triflate indole complex. The latter could, conceivably, reductively eliminate to copper (I) triflate and indole triflate. Based on these experiments, the kinetically competent copper (I) triflate is proposed to result from a redox process involving copper (II) precatalyst and indole. However, this proposal on its own cannot explain the substantial difference in isolated yield of **2a** between Cu(OTf)$_2$ and CuOTf. An additional component in the reaction, presumably derived from the activation reaction of Cu(OTf)$_2$ and indole, was necessary for efficient Friedel Crafts alkylation with indole. We took a cue from the reduction reaction scheme and the result of ESI-MS analysis of the crude reaction. We propose a Brønsted acid catalyst, either TfOH or its salt with indole dimer **B**,

acts to catalyze Friedel-Crafts addition of indole to the intermediate *C*-acylimine formed from metallocarbene-azide coupling.

**Evidence for Brønsted Acid Catalysis of Friedel-Crafts Alkylation**

*NOTE: Since the putative C-acylimine occuring in the Cu(I)-catalyzed coupling step is transient and cannot be isolated, we used isolable C-acylimine **6** as a model to help understand the second catalytic cycle.*

Stirring *C*-acylimine 6 with Indole in the Presence of Cu(OTf)(PhMe):
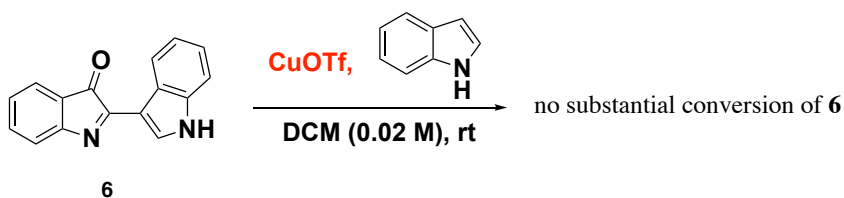
A solution of *C*-acylimine **6** (50 mg, 0.20 mmol) and indole (50 mg, 0.43 mmol) in DCM (5 mL) was added to Cu(OTf)(PhMe) (9.7 mg, *ca* 0.020 mmol) in DCM (5 mL) at room temperature. Once the addition was complete, the solution was allowed to stir overnight. After stirring for 16 h, the solution was extracted with water (5 mL, 2x), and the organic layer was dried with MgSO₄, filtered and concentrated under reduced pressure. Analysis of crude reaction mixture indicated that substantial quantities of **6** were present. Upon purification via a short pad of silica (20% EtOAc/Hexanes), *ca*. 91% of **6** was recovered. This model reaction showed that, although copper (I) triflate can convert **1a** to the *C*-acylimine (see the previous experiments), copper (I) could not efficiently catalyze the Friedel-Crafts alkylation reaction with indole.
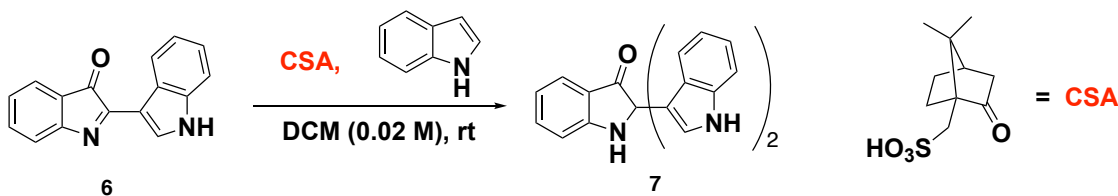
Stirring *C*-acylimine 6 with Indole in the Presence of TfOH:
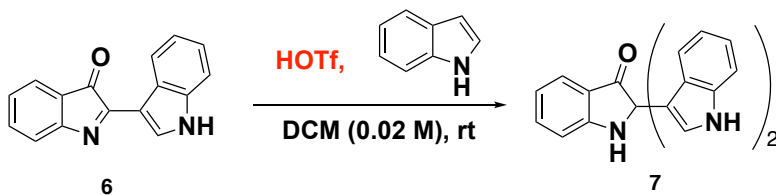
A solution of *C*-acylimine **6** (50 mg, 0.20 mmol) and indole (50 mg, 0.43 mmol) in DCM (5 mL) was mixed with excess TfOH (ca. 50 μL, ca. 0.57 mmol) in DCM (5 mL) at room

temperature. Once the mixing was complete, within 5 minutes a change in color was noticed, from deep purple to light orange. The solution was diluted with water (5 mL) and extracted with DCM (5 mL, 3x). The organic layer was dried using MgSO₄, and concentrated under reduced pressure. Analysis of the crude mixture indicated that **6** was completely consumed, and adduct **7** can be detected using crude NMR. The purification of **7**, however, was hampered by the presence of several side products.

Stirring *C*-acylimine 6 with Indole in the Presence of CSA:

A solution of *C*-acylimine **6** (50 mg, 0.20 mmol) and indole (50 mg, 0.43 mmol) in DCM (5 mL) was mixed with camphorsulfonic acid (CSA; 4.0 mg, *ca*. 0.020 mmol) in DCM (5 mL) at room temperature. Once the addition was complete, the solution gradually (overnight) changed color from deep purple to a yellow suspension. Analysis of the TLC indicated that **6** was completely consumed. The suspension was filtered. The filtered solid was dissolved in deuterated DMSO and was analyzed using NMR spectroscopy. Analysis of the spectra revealed that the 2:1 adduct, **7**, (indole:indol-3-one), along with water and DMSO, were the only detectable components present in the solution.

These results indicate that Brønsted acid, produced during the reduction of copper (II) triflate by indole, could activate the *C*-acylimine towards Friedel-Crafts alkylation reaction.

Using a (+)-Camphorsulfonic Acid as a Chiral Co-catalyst:
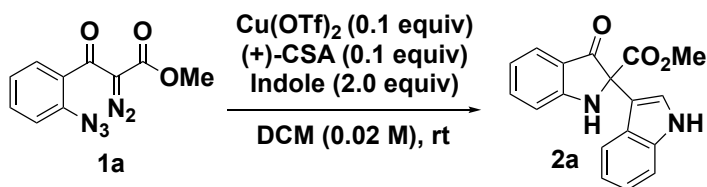
A solution of diazo-azide **1a** (50 mg, 0.20 mmol) in DCM (5 mL) was added to a solution of indole (46 mg, 0.39 mmol), $Cu(OTf)_2$ (7.3 mg, 0.020 mmol), and (+)-CSA (4.0 mg, $ca.$ 0.02 mmol) in DCM (5 mL) at room temperature via syringe pump over 1 h. The reaction mixture turned light green over 2 h, then slowly turned dark brown over 24 h. Once the addition was complete, the reaction was monitored by TLC for consumption of **1a**. Upon consumption of **1a**, the reaction mixture was poured in an Erlenmeyer flask, thoroughly dissolved in ethyl acetate (ca. 10 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash chromatography. (*N.B.*: the crude mixture after concentration was noticeably insoluble in DCM. In this case, necessarily, ethyl acetate was used as a solvent to load the sample onto silica gel (silica gel, 7:3 hexanes:EtOAc). All pure fractions of **2a** were concentrated together to afford yellow oil. Upon standing for at least 24 h, this oil slowly formed a yellow solid. Analysis of the yellow oil using chiral HPLC revealed that the product was formed in a 68:32 enantiomeric ratio. HPLC condition: Chiralpak AD-H, 80:20, Hexanes:i-PrOH, rt, retention time = 33.77 min (major), 37.71 min (minor).

X-ray Crystallographic Data

Compound: Methyl 2-diazo-3-(2-azido-3-methylphenyl)-3-oxopropanoate (**1b**)

Formula: $C_{11}H_9N_5O_3$

Procedure: Following the steps to make **1b** (see the manuscript), and purification using EtOAc:Hexanes (1:9)→EtOAc:Hexanes (2:8)→EtOAc:Hexanes (3:7). The yellow oil, after reduced pressure evaporation of solvent was left undisturbed at room temperature until yellow crystals suitable for X-ray crystallography were obtained.

Crystallographic Experimental Details:

A. Crystal Data

formula	$C_{11}H_9N_5O_3$
formula weight	259.23
crystal dimensions (mm)	$0.26 \times 0.18 \times 0.06$
crystal system	triclinic
space group	$P\bar{1}$ (No. 2)
unit cell parameters^a	
a (Å)	7.3874 (3)
b (Å)	8.0591 (4)
c (Å)	10.8556 (5)
α (deg)	96.711 (2)
β (deg)	104.962 (2)
γ (deg)	105.019 (2)
V (Å^3)	591.25 (5)
Z	2
ρ_{calcd} (g cm^{-3})	1.456
μ (mm^{-1})	0.938

B. Data Collection and Refinement Conditions

diffractometer	Bruker D8/APEX II CCD
radiation (λ [Å])	Cu Kα (1.54178) (microfocus source)
temperature (°C)	–100
scan type	ω and ϕ scans (1.0°) (5 s exposures)
data collection 2θ limit (deg)	148.11
total data collected	4241 ($-9 \leq h \leq 9, -10 \leq k \leq 10, -12 \leq l \leq 10$)
independent reflections	2302 (R_{int} = 0.0177)
number of observed reflections (*NO*)	2041 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods/dual space (*SHELXD*)
refinement method	full-matrix least-squares on F^2 (*SHELXL–2014*)

absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	1.0000–0.7941
data/restraints/parameters	2302 / 0 / 173
goodness-of-fit $(S)^e$ [all data]	1.056
final R indices^f	
$\quad R_1$ [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0328
$\quad wR_2$ [all data]	0.0919
largest difference peak and hole	0.205 and –0.202 e Å^{-3}

ORTEP Structure for compound 1b.

Perspective view of methyl 2-diazo-3-(2-azido-3-methylphenyl)-3-oxopropanoate. Non-hydrogen atoms are represented by Gaussian ellipsoids at 30% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.
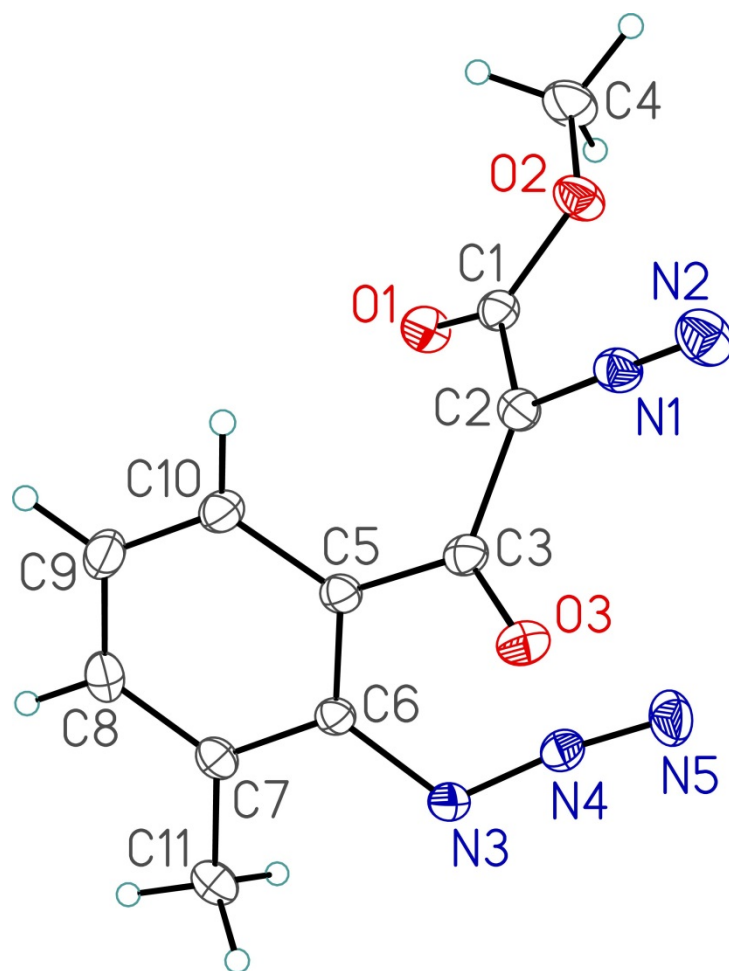
Compound: Methyl 3-oxo-1,3-dihydro-1'H,2H-2,3'-biindole-2-carboxylate (**2a**)

Formula: $C_{18}H_{14}N_2O_3$

Procedure: Following the steps to make **2a** (see the manuscript), and purification using flash column chromatography on silica gel [eluent, EtOAc:Hexanes (3:7)]. The yellow oil, after reduced pressure evaporation of solvent, was added with minimum amount of MeOH:EtOAc (1:1), and was left undisturbed at room temperature until yellow crystals suitable for X-ray crystallography were obtained.

Crystallographic Experimental Details:

A. Crystal Data

formula	$C_{18}H_{14}N_2O_3$
formula weight	306.31
crystal dimensions (mm)	$0.26 \times 0.26 \times 0.11$
crystal system	monoclinic
space group	$P2_1/c$ (No. 14)
unit cell parameters	
a (Å)	11.9170 (4)
b (Å)	7.9729 (3)
c (Å)	15.3812 (5)
β (deg)	92.5421 (4)
V (Å^3)	1459.98 (9)
Z	4
ρ_{calcd} (g cm^{-3})	1.394
μ (mm^{-1})	0.097

B. Data Collection and Refinement Conditions

diffractometer	Bruker PLATFORM/APEX II CCD
radiation (λ [Å])	graphite-monochromated Mo Kα (0.71073)
temperature (°C)	–100
scan type	ω scans (0.3°) (15 s exposures)
data collection 2θ limit (deg)	54.96
total data collected	12628 ($-15 \leq h \leq 15$, $-10 \leq k \leq 10$, $-19 \leq l \leq 19$)
independent reflections	3347 ($R_{int} = 0.0219$)
number of observed reflections (*NO*)	2932 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods/dual space (*SHELXD*)
refinement method	full-matrix least-squares on F^2 (*SHELXL–2013*)
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	1.0000–0.9333
data/restraints/parameters	3347 / 0 / 216

goodness-of-fit $(S)^e$ [all data]   1.042

final R indices^f

    R_1 [$F_o^2 \geq 2\sigma(F_o^2)$]   0.0355

    wR_2 [all data]   0.0965

largest difference peak and hole   0.301 and –0.203 e Å^{-3}

ORTEP Structure for compound 2a.

Perspective view of methyl 3-oxo-1,3-dihydro-1'H,2H-2,3'-biindole-2-carboxylate. Non-hydrogen atoms are represented by Gaussian ellipsoids at 30% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.
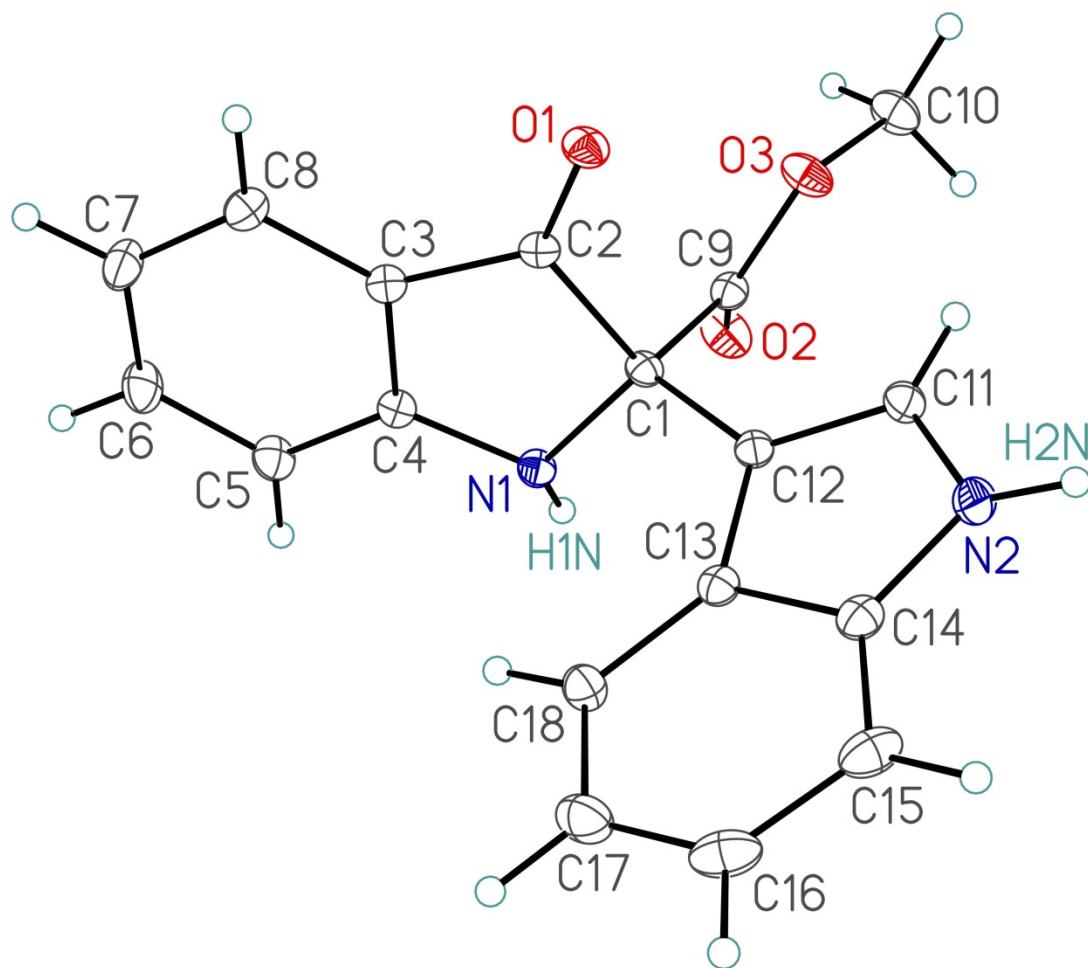
Compound: Methyl 6-chloro-3-oxo-1,3-dihydro-1'*H*,2*H*-2,3'-biindole-2 carboxylate (**2o**)

Formula: $C_{18}H_{13}ClN_2O_3$

Procedure: Following the steps to make **2o** (see the manuscript), and purification using flash column chromatography on silica gel [eluent, EtOAc:Hexanes (3:7)]. The yellow oil, after reduced pressure evaporation of solvent, was left undisturbed at room temperature until yellow crystals suitable for X-ray crystallography were obtained.

Crystallographic Experimental Details:

A. Crystal Data

formula	$C_{18}H_{13}ClN_2O_3$
formula weight	340.75
crystal dimensions (mm)	$0.28 \times 0.12 \times 0.06$
crystal system	monoclinic
space group	$P2_1/c$ (No. 14)
unit cell parameters^a	
a (Å)	12.1387 (2)
b (Å)	8.0853 (2)
c (Å)	15.9792 (3)
β (deg)	98.1986 (6)
V (Å^3)	1552.25 (5)
Z	4
ρ_{calcd} (g cm^{-3})	1.458
μ (mm^{-1})	2.351

B. Data Collection and Refinement Conditions

|	
diffractometer	Bruker D8/APEX II CCD
radiation (λ [Å])	Cu Kα (1.54178) (microfocus source)
temperature (°C)	–100
scan type	ω and ϕ scans (1.0°) (5 s exposures)
data collection 2θ limit (deg)	148.09
total data collected	10664 ($-15 \leq h \leq 15, -10 \leq k \leq 9, -19 \leq l \leq 19$)
independent reflections	3143 (R_{int} = 0.0134)
number of observed reflections (*NO*)	3010 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods/dual space (*SHELXD*)
refinement method	full-matrix least-squares on F^2 (*SHELXL–2014*)
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.9006–0.6955
data/restraints/parameters	3143 / 0 / 225
goodness-of-fit (*S*)^e [all data]	1.061

final R indices$f$

R_1 $[F_o{}^2 \geq 2\sigma(F_o{}^2)]$	0.0303
wR_2 [all data]	0.0822

largest difference peak and hole   0.283 and -0.266 e Å^{-3}

ORTEP Structure for compound 2o.

Perspective view of methyl 6-chloro-3-oxo-1,3-dihydro-1'H,2H-2,3'-biindole-2 carboxylate. Non-hydrogen atoms are represented by Gaussian ellipsoids at 30% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.
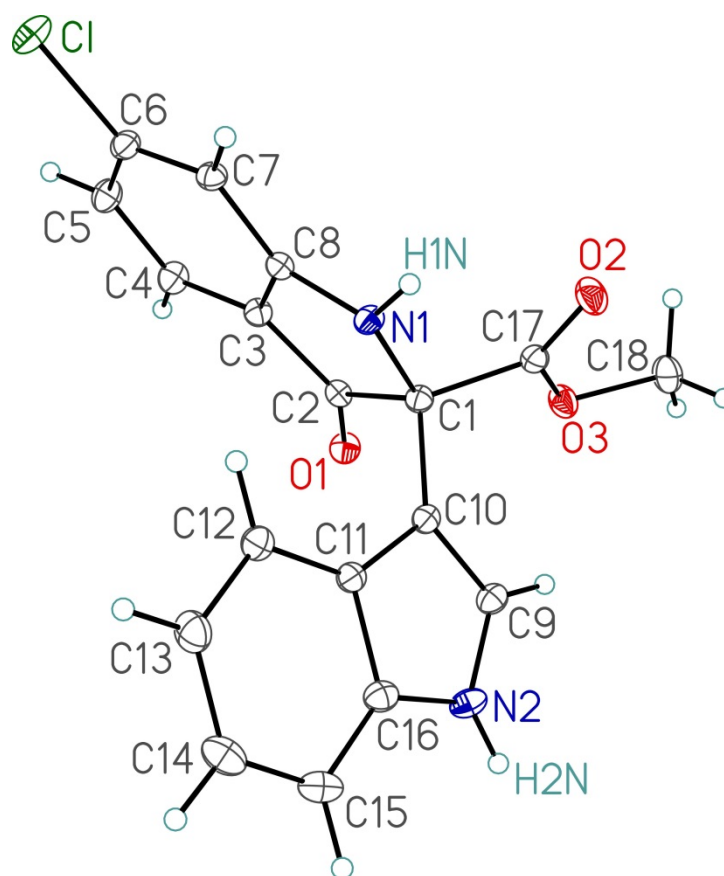
Compound: (-)-Menthyl (2*R*)-1'-benzyl-3-oxo-1,3-dihydro-1'*H*,2*H*-2,3'-biindole-2-carboxylate (**2za**)

Formula: $C_{34}H_{36}N_2O_3$

Procedure: Following the steps to make **2z** (1.0 mmol scale, see the manuscript), and purification using flash column chromatography on silica gel [eluent, EtOAc:Hexanes (1:9)→EtOAc:Hexanes (2:8)→EtOAc:Hexanes (3:7)]. Fractions containing the major diastereomer (**2za**) slowly formed needles. These needles were filtered and dried under vacuum, and were suitable enough for X-ray crystallography.

Crystallographic Experimental Details:

A. Crystal Data

formula	$C_{34}H_{36}N_2O_3$
formula weight	520.65
crystal dimensions (mm)	$0.75 \times 0.14 \times 0.12$
crystal system	monoclinic
space group	$P2_1$ (No. 4)
unit cell parameters	
a (Å)	11.0321 (5)
b (Å)	11.4646 (5)
c (Å)	11.5824 (5)
β (deg)	95.6775 (6)
V (Å^3)	1457.74 (11)
Z	2
ρ_{calcd} (g cm^{-3})	1.186
μ (mm^{-1})	0.075

B. Data Collection and Refinement Conditions

diffractometer	Bruker D8/APEX II CCD
radiation (λ [Å])	graphite-monochromated Mo Kα (0.71073)
temperature (°C)	–100
scan type	ω scans (0.3°) (20 s exposures)
data collection 2θ limit (deg)	56.62
total data collected	13193 ($-14 \le h \le 14$, $-15 \le k \le 15$, $-14 \le l \le 14$)
independent reflections	6914 ($R_{int} = 0.0192$)
number of observed reflections (*NO*)	6090 [$F_o^2 \ge 2\sigma(F_o^2)$]
structure solution method	direct methods/dual space (*SHELXD*)
refinement method	full-matrix least-squares on F^2 (*SHELXL–2013*)
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	1.0000–0.9186

data/restraints/parameters	6914 / 0 / 356
Flack absolute structure parameter[e]	-0.1(3)
goodness-of-fit $(S)^f$ [all data]	1.033
final R indices[g]	
R_1 [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0385
wR_2 [all data]	0.0952
largest difference peak and hole	0.203 and –0.207 e Å^{-3}

ORTEP structure for compound 2za.

Perspective view of (-)-Menthyl (2R)-1'-benzyl-3-oxo-1,3-dihydro-1'H,2H-2,3'-biindole-2-carboxylate. Non-hydrogen atoms are represented by Gaussian ellipsoids at 30% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters. Assignment of absolute structure for this compound is based on the known stereochemistry of the (-)-menthyl group.
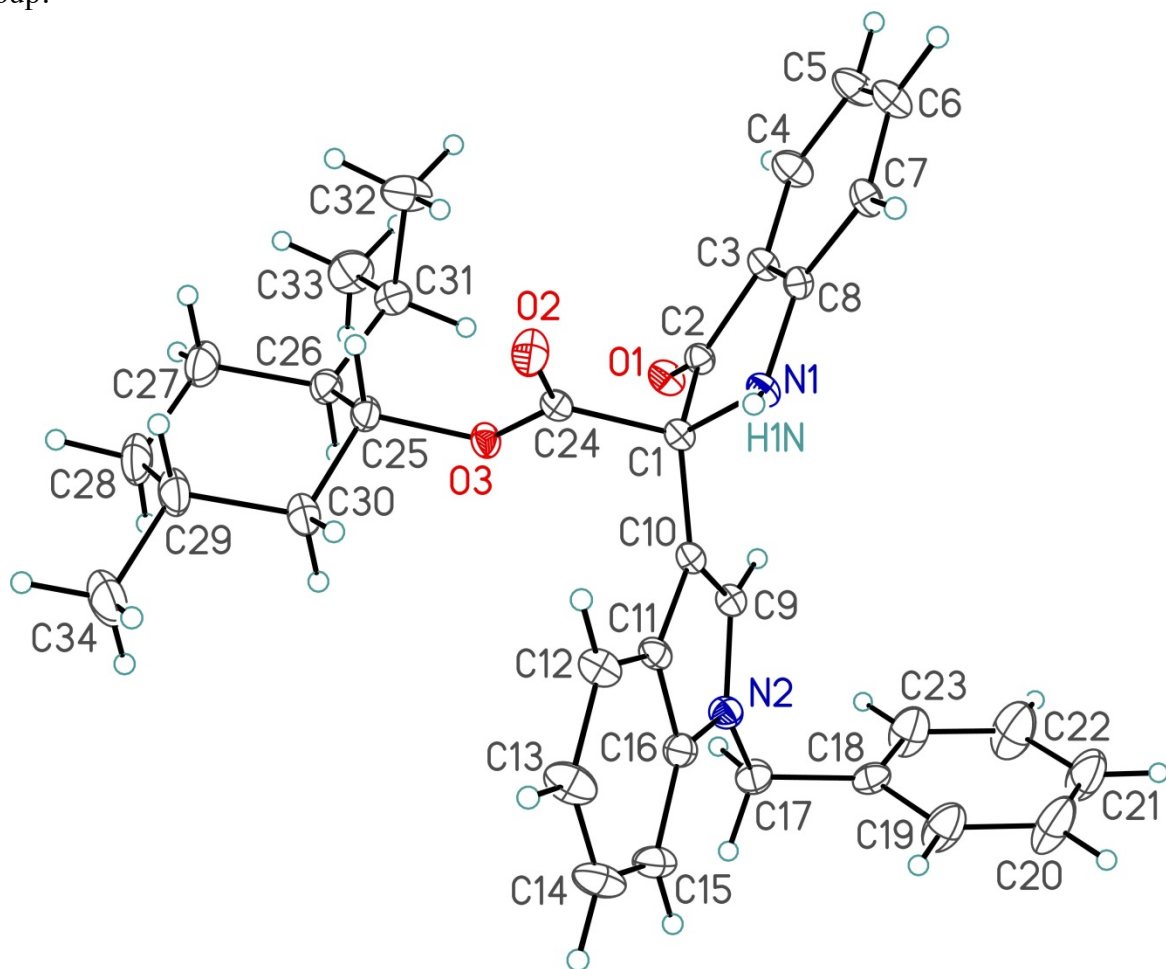
NMR spectra of the starting materials and products:

N.B.: The presence of significant signals for residual water in the ^{1}H NMR spectra of **2a**, **2e**, **2l**, **2o**, **2t** and **2v** may raise questions about proof of purity. It should be noted that the presence of one or more heavy halogen atoms and/or an unprotected indole nitrogen atom render these compounds only sparingly soluble in common deuterated NMR solvents (CDCl$_3$, CD$_2$Cl$_2$, C$_6$D$_6$, C$_3$D$_6$O, CD$_3$OD, and C$_2$D$_6$SO). Consequently, minor amounts of water contaminant in these solvents may appear to have anomalously enhanced signals relative to the those of the compounds of interest. The ^{1}H NMR spectra of these compounds are not representative of the bulk material, and cannot be used as the sole judge or proof of purity. Also, regardless of these trace impurities, we deemed the spectra suitable for characterization purposes.

However, we would to like to point out the following observations from the data presented earlier as reasonable proof of purity, apart from the ^{1}H NMR spectra presented in the next section:

(1) Reasonable accuracy of experimental elemental analysis (C, H, and N) compared to the theoretical value (0.05–0.34 %) in those cases where combustion analysis was performed.
(2) Sharp (1-3 °C) and high (> 100 °C) melting points.
(3) Substantially higher melting points compared to the reported literature value (**2a** and **2b**).[3]
(4) High degree of crystallinity, and with X-ray crystal structures and measurements for **2a**, **2o**, and **2za**.
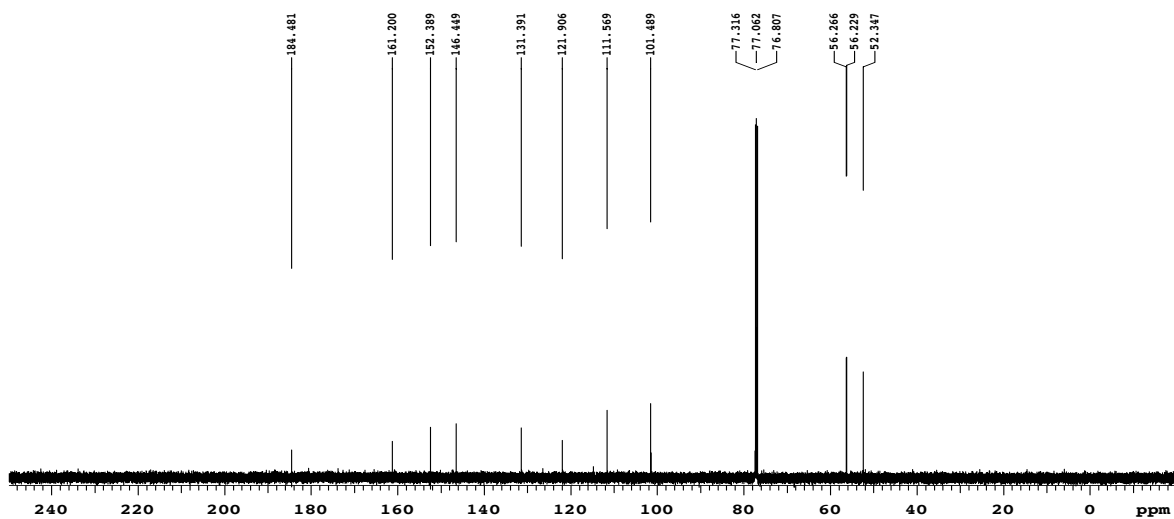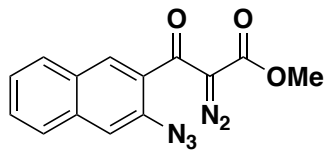
1c
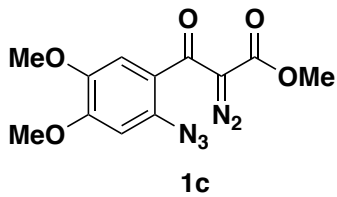
DIMETHOXYAZIDODIAZOKETONE

7.260
6.873
6.624

3.941
3.941
3.858
3.785

10 9 8 7 6 5 4 3 2 1 0 ppm

0.97 0.98

3.05
3.01
3.00
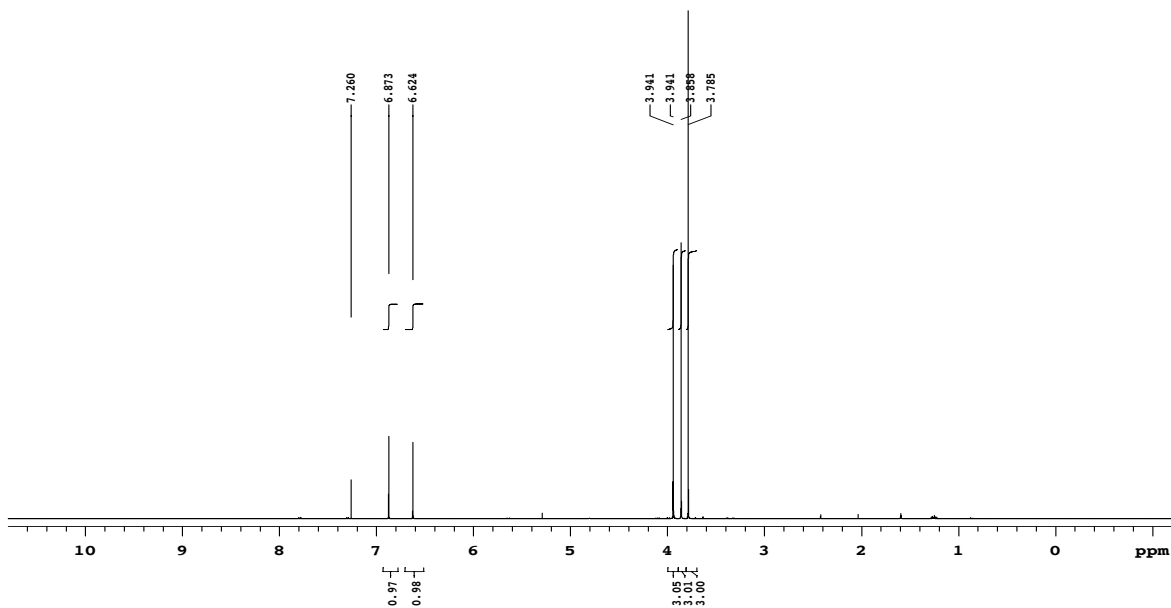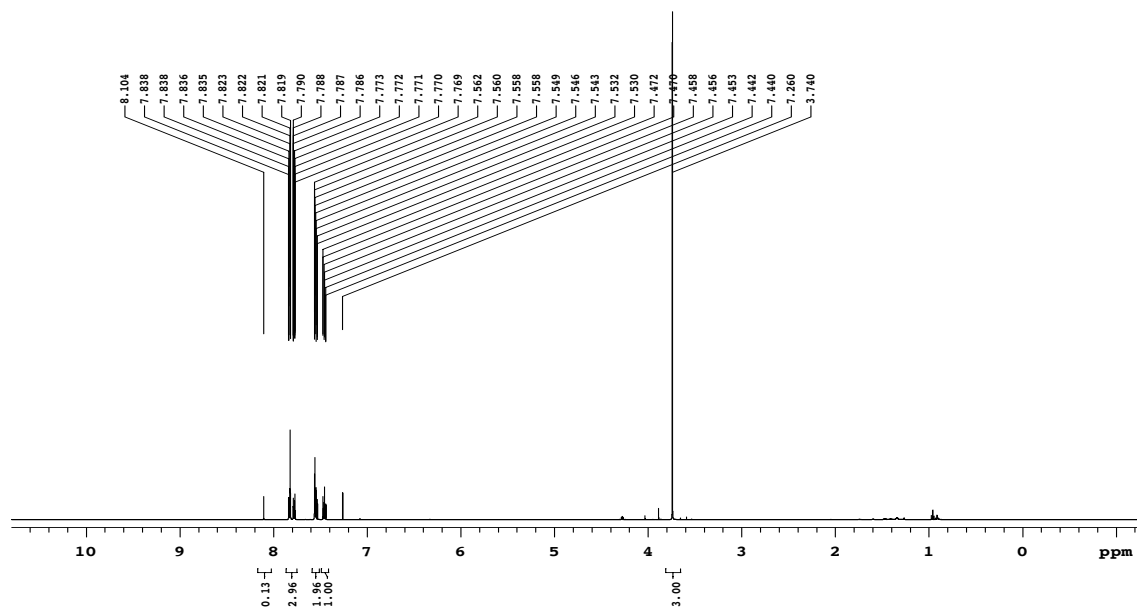
Pulse Sequence: s2pul

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Dimethoxydiazoazide

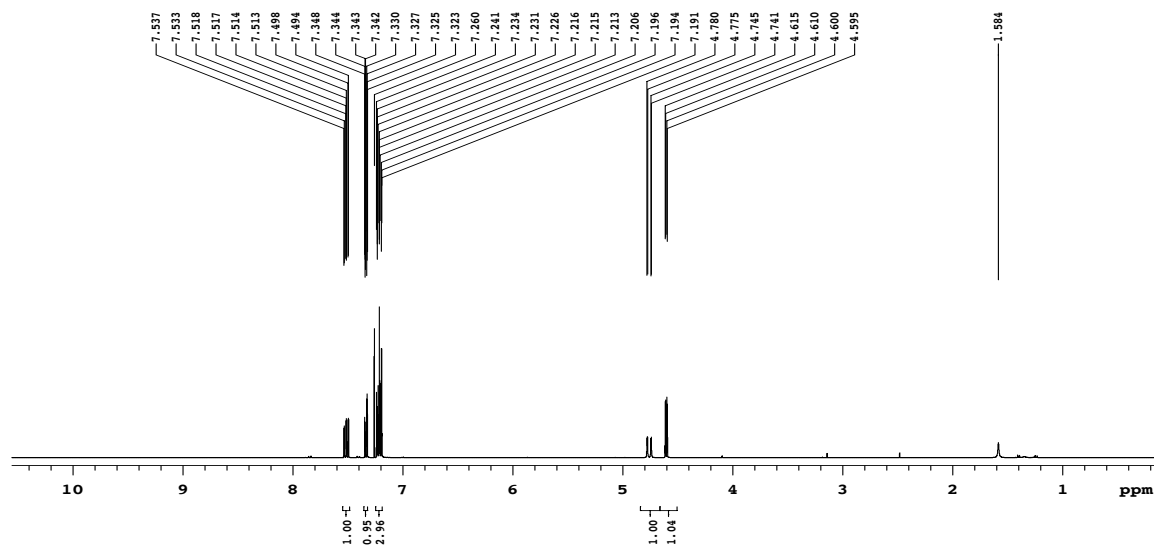184.481

161.200
152.389
146.449

131.391
121.906
111.569
101.489

77.316
77.062
76.807

56.266
56.229
52.347

240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

S-26

1f

8.104
7.838
7.838
7.836
7.835
7.823
7.822
7.821
7.819
7.790
7.788
7.787
7.786
7.773
7.772
7.771
7.770
7.769
7.562
7.560
7.558
7.558
7.549
7.546
7.543
7.532
7.530
7.472
7.470
7.458
7.456
7.453
7.442
7.440
7.260
3.740

10 9 8 7 6 5 4 3 2 1 0 ppm

0.13
2.96
1.96
1.00

3.00

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

185.603
160.941
135.218
134.674
130.310
130.279
129.492
128.911
128.694
128.348
126.665
126.148
115.614
77.310
77.055
76.799
52.327

240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

1h
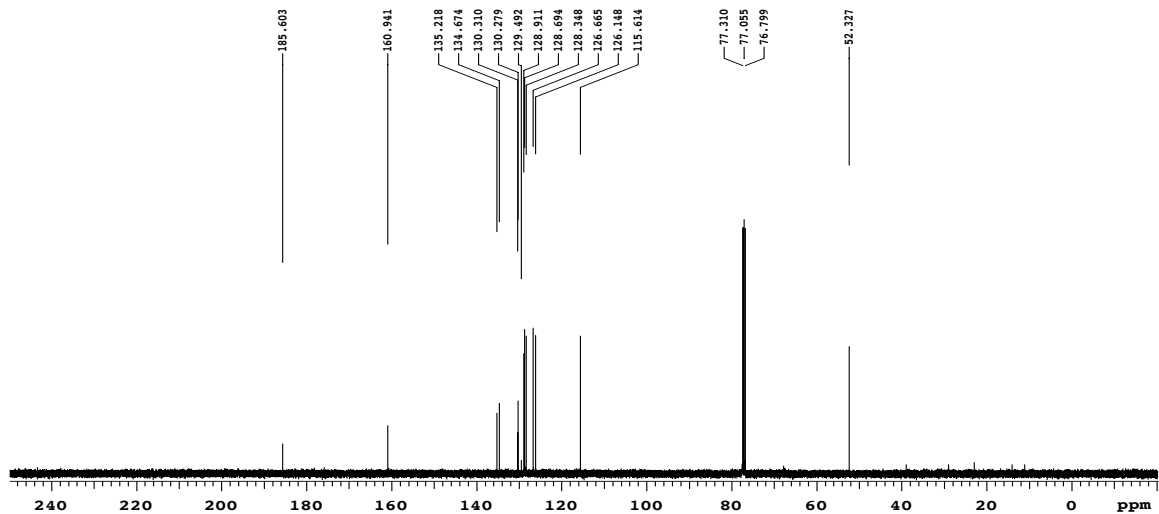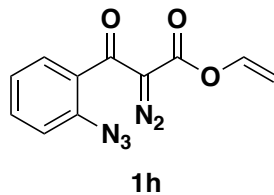
Diazo-azide with vinyl side chain (ester)

7.537
7.533
7.518
7.517
7.514
7.513
7.498
7.494
7.348
7.344
7.343
7.342
7.330
7.327
7.325
7.323
7.260
7.241
7.234
7.231
7.226
7.216
7.215
7.213
7.206
7.196
7.194
7.191
4.780
4.775
4.745
4.741
4.615
4.610
4.600
4.595
1.584

1.00
0.95
2.96

1.00
1.04

Pulse Sequence: s2pul

Diazo-azide with allyl sidechain (ester)

185.252
157.716
140.129
137.893
132.156
130.163
128.577
124.832
118.267
98.490
77.374
77.056
76.739

Pulse Sequence: s2pul

S-28

1i

10 9 8 7 6 5 4 3 2 1 0 ppm

0.991.97   1.07   3.30 1.02.8100
0.97   0.04   1.02   1.14 1.1904

185.881 | 160.278 | 137.630 131.718 130.828 128.345 124.692 118.072 | 77.429 77.112 76.793 75.958 | 46.884 40.939 34.033 31.337 26.358 23.397 21.908 20.656 16.264

240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

S-29

1j

7.351
7.347
7.346
7.342
7.334
7.330
7.193
7.176

3.780

10   9   8   7   6   5   4   3   2   1   0   ppm

1.93 1.02   3.00
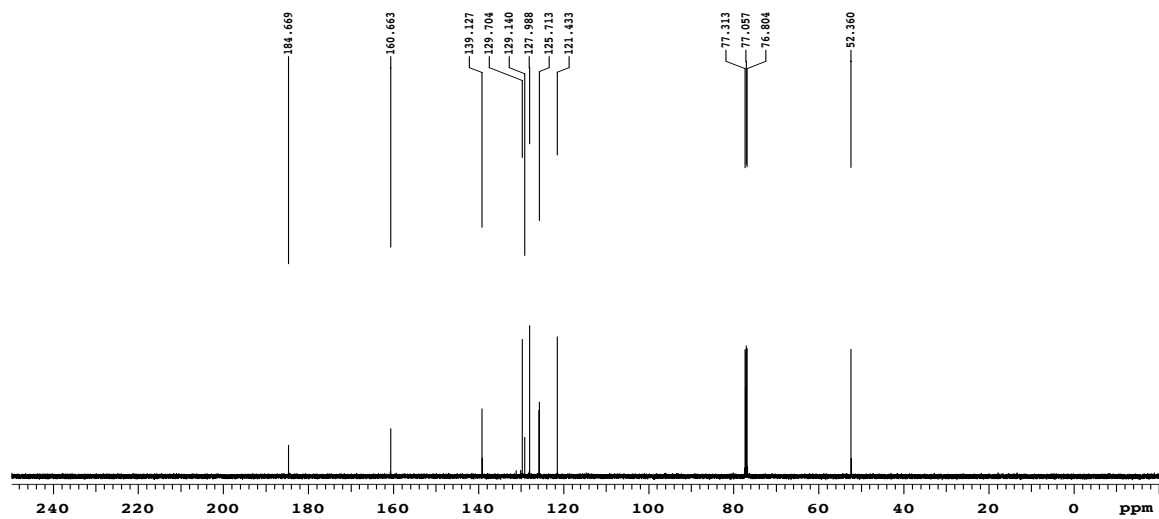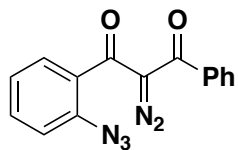
Pulse Sequence: s2pul   Department of Chemistry, University of Alberta

184.669

160.663

139.127
129.704
129.140
127.988
125.713
121.433

77.313
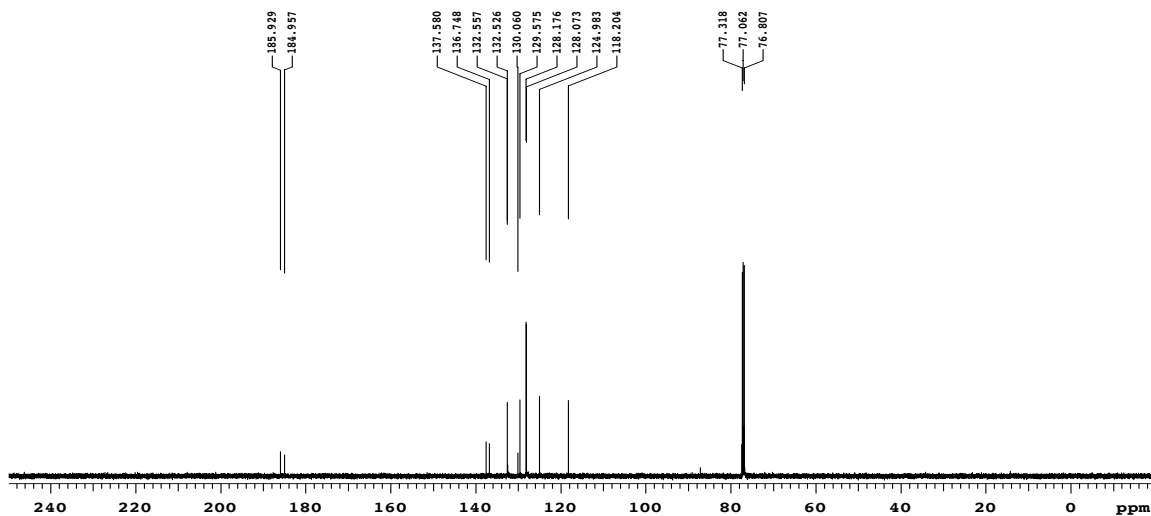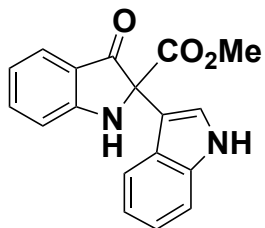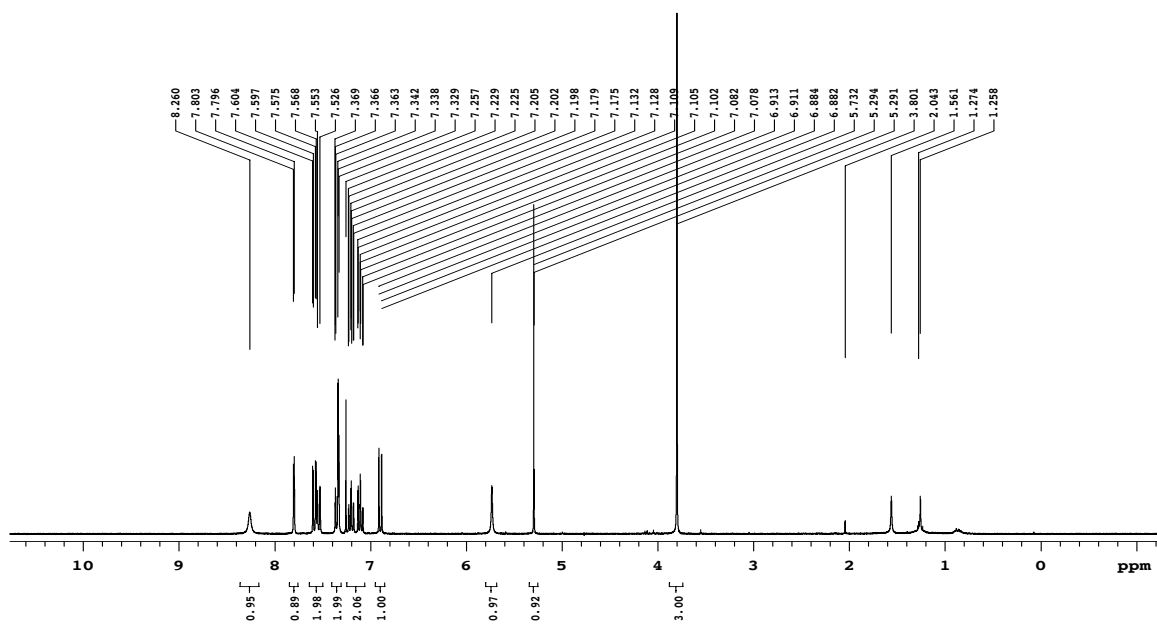77.057
76.804

52.360

240   220   200   180   160   140   120   100   80   60   40   20   0   ppm

S-30

1k

Phenyldiazoketoneazide

7.551
7.549
7.537
7.532
7.528
7.437
7.434
7.431
7.420
7.416
7.411
7.400
7.397
7.394
7.389
7.385
7.369
7.366
7.365
7.350
7.346
7.317
7.313
7.297
7.283
7.279
7.260
7.155
7.153
7.136
7.134
7.118
7.115
6.934
6.933
6.914
6.913
5.292

1.583

1.98
2.99
1.99
1.01
0.97

0.06

Department of Chemistry, University of Alberta

185.929
184.957

137.580
136.748
132.557
132.526
130.060
129.575
128.176
128.073
124.983
118.204

77.318
77.062
76.807

2a

¹H NMR peaks: 8.260, 7.803, 7.796, 7.604, 7.597, 7.575, 7.568, 7.553, 7.526, 7.369, 7.366, 7.363, 7.342, 7.338, 7.329, 7.257, 7.229, 7.225, 7.205, 7.202, 7.198, 7.179, 7.175, 7.132, 7.128, 7.109, 7.105, 7.102, 7.082, 7.078, 6.913, 6.911, 6.884, 6.882, 5.732, 5.294, 5.291, 3.801, 2.043, 1.561, 1.274, 1.258

Integrations: 0.95, 0.89, 1.98, 1.99, 2.06, 1.00, 0.97, 0.92, 3.00

BA HO

Pulse Sequence: s2pul

¹³C NMR peaks: 194.712, 169.001, 161.041, 137.925, 136.537, 125.454, 125.436, 123.521, 122.710, 120.413, 120.405, 119.892, 119.481, 113.604, 111.673, 111.619, 77.288, 77.0__, 76.778, 72.395, 53.780

2b

N-methylindole trap

7.708
7.692
7.587
7.570
7.531
7.528
7.516
7.514
7.500
7.498
7.313
7.297
7.275
7.260
7.254
7.239
7.238
7.223
7.122
7.106
7.092
6.992
6.975
6.940
6.925
6.911
5.762
3.804
3.738

0.97
0.98
1.00
3.08
1.01
0.99
1.00

0.99

2.99
3.00

N-methyl indole trap

194.824
169.058
161.002
137.905
137.366
128.024
125.977
125.395
122.238
120.314
119.955
119.822
119.498
113.585
109.812
109.758
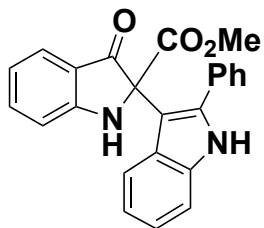77.315
77.063
76.806
72.368
53.760
32.905

2c

N-benzylindole trap on parent diazoazide
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

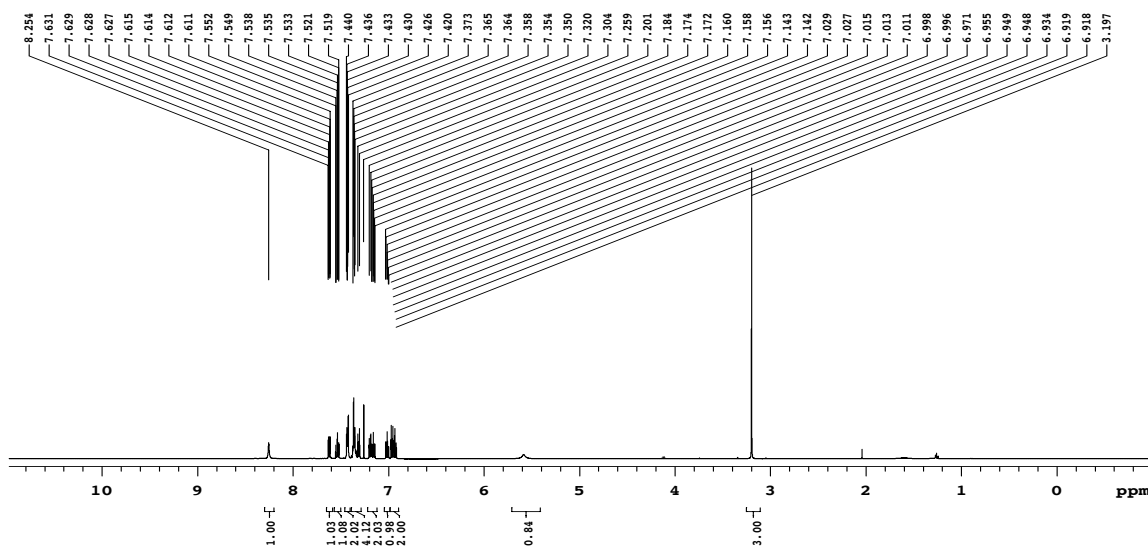7.701 7.698 7.697 7.685 7.684 7.681 7.620 7.618 7.616 7.604 7.602 7.600 7.545 7.543 7.531 7.528 7.526 7.514 7.512 7.382 7.298 7.294 7.285 7.281 7.278 7.269 7.266 7.260 7.254 7.250 7.244 7.239 7.237 7.184 7.182 7.169 7.167 7.165 7.153 7.151 7.128 7.125 7.121 7.114 7.112 7.100 7.098 7.096 7.084 7.081 7.016 7.001 7.000 6.946 6.932 6.918 6.916 5.283 3.803

0.98 0.99 1.02 0.98 5.03 1.07 1.02 3.02 1.03   2.09   3.00

Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

N-benzylindole trap on parent diazoazide
125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

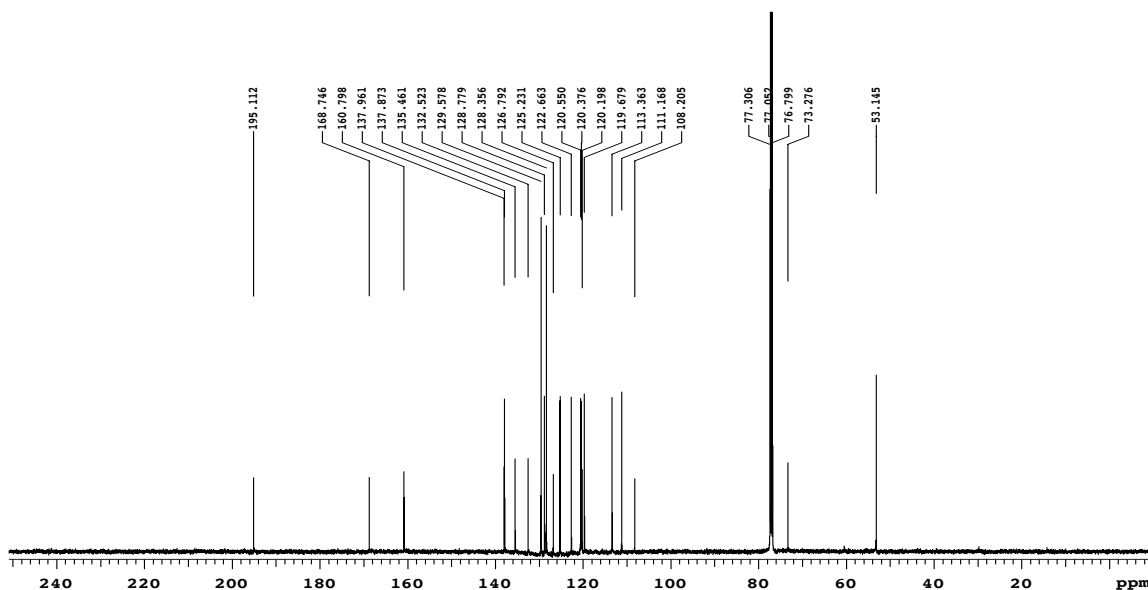194.736 169.057 161.039 137.909 137.026 136.954 128.837 127.764 127.609 126.916 126.307 125.492 122.439 120.410 120.214 119.956 119.801 113.642 110.523 110.357 77.316 77.060 76.807 72.447 53.816 50.439

Pulse Sequence: s2pul

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S-34

2d

2-Phindole trap

8.254
7.631 7.629 7.628 7.627 7.615 7.614 7.612 7.611 7.552 7.549 7.538 7.535 7.533 7.521 7.519 7.440 7.436 7.433 7.430 7.426 7.420 7.373 7.365 7.364 7.358 7.354 7.350 7.320 7.304 7.259 7.201 7.184 7.174 7.172 7.160 7.158 7.156 7.143 7.142 7.029 7.027 7.015 7.013 7.011 6.998 6.996 6.971 6.955 6.949 6.948 6.934 6.919 6.918 3.197

```
10    9    8    7    6    5    4    3    2    1    0   ppm
```

1.00 1.03 1.08 2.02 4.12 2.03 0.98 2.00 0.84 3.00

Phenyl indole trap

195.112   168.746 160.798 137.961 137.873 135.461 132.523 129.578 128.779 128.356 126.792 125.231 122.663 120.550 120.376 120.198 119.679 113.363 111.168 108.205   77.306 77.052 76.799 73.276   53.145

```
240   220   200   180   160   140   120   100   80    60    40    20   ppm
```

2e

1H NMR peaks: 7.603, 7.555, 7.540, 7.527, 7.525, 7.511, 7.497, 7.494, 7.456, 7.440, 7.279, 7.264, 7.104, 7.099, 7.076, 7.060, 7.051, 7.045, 7.034, 6.823, 6.808, 6.793, 3.605, 3.499, 2.500, 2.496, 2.493

Integrations: 0.97, 2.00, 1.01, 0.96, 0.92, 2.00, 1.00, 3.01

Bromoindole (H4) (in DMSO and water)

13C NMR peaks: 195.536, 169.546, 161.823, 138.226, 138.208, 126.054, 124.699, 124.585, 123.656, 122.953, 118.546, 117.665, 113.664, 112.585, 111.699, 111.050, 72.012, 53.129, 40.003, 39.923, 39.835, 39.757, 39.667, 39.591, 39.500, 39.166, 38.998

2f

Methoxyindole trap

8.181 7.727 7.726 7.711 7.711 7.567 7.565 7.551 7.536 7.534 7.362 7.356 7.283 7.267 7.249 7.046 7.041 7.038 7.022 6.971 6.970 6.956 6.942 6.940 6.886 6.882 6.868 6.864 5.320 3.834 3.792 2.068

10 9 8 7 6 5 4 3 2 1 0 ppm

0.95 1.00 1.02 1.00 1.12 1.06 1.95 0.98 1.00 0.73 3.01 3.00

Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

Methoxyindole trap

194.852 168.994 161.044 154.498 137.961 131.703 125.850 125.414 124.262 120.452 120.015 113.591 112.786 112.352 111.306 101.581 77.316 77.052 76.809 72.414 55.815 53.776

240 220 200 180 160 140 120 100 80 60 40 20 ppm

Pulse Sequence: s2pul

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2h

Benzofuran trap

1.03
2.02
1.01
0.99
1.00
0.97
1.93

0.98

3.01

Benzofuran trap

191.301

166.603
161.188
155.027
150.971
138.269
127.735
125.728
124.925
123.172
121.630
120.869
119.320
113.696
111.350
105.661

77.318
77.063
76.809
71.900

54.236

2i

Pyrrole trap

7.594
7.575
7.539
7.536
7.518
7.501
7.498
7.257
7.061
7.040
6.925
6.906
6.887
6.833
6.826
6.822
6.816
6.292
6.283
6.279
6.273
6.151
6.144
6.137
6.129
5.605
3.804

1.255

10   9   8   7   6   5   4   3   2   1   0   ppm

0.85

0.97
0.99

0.93
0.96
0.89

0.91
0.92

0.92

2.99

193.182

167.605
161.614

138.002
125.774
124.790
120.676
119.197
118.826
113.549
108.204
106.262

77.314
77.059
76.805
71.831

53.896

240 220 200 180 160 140 120 100 80   60   40   20   0 ppm

2j

Furan trap
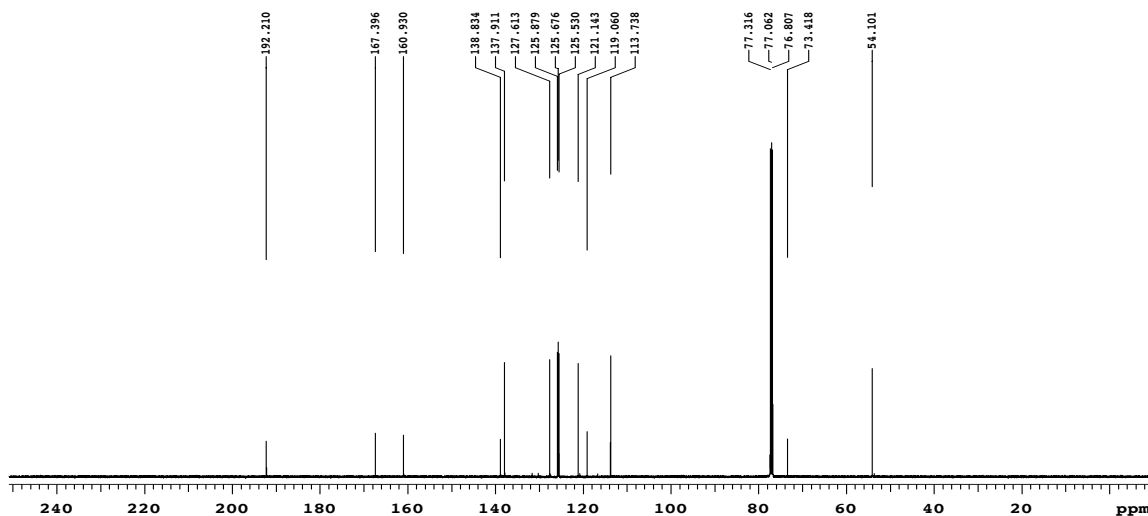499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

7.668
7.667
7.666
7.653
7.651
7.650
7.540
7.526
7.523
7.521
7.509
7.507
7.410
7.409
7.406
7.405
7.259
7.012
6.996
6.948
6.947
6.933
6.919
6.917
6.527
6.526
6.521
6.519
6.388
6.384
6.381
6.377
5.591
3.830

0.99
1.04
0.96
1.02
1.05
0.95
0.98
0.94
3.00

Pulse Sequence: PRESAT
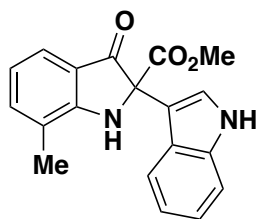
Department of Chemistry, University of Alberta

Furan trap
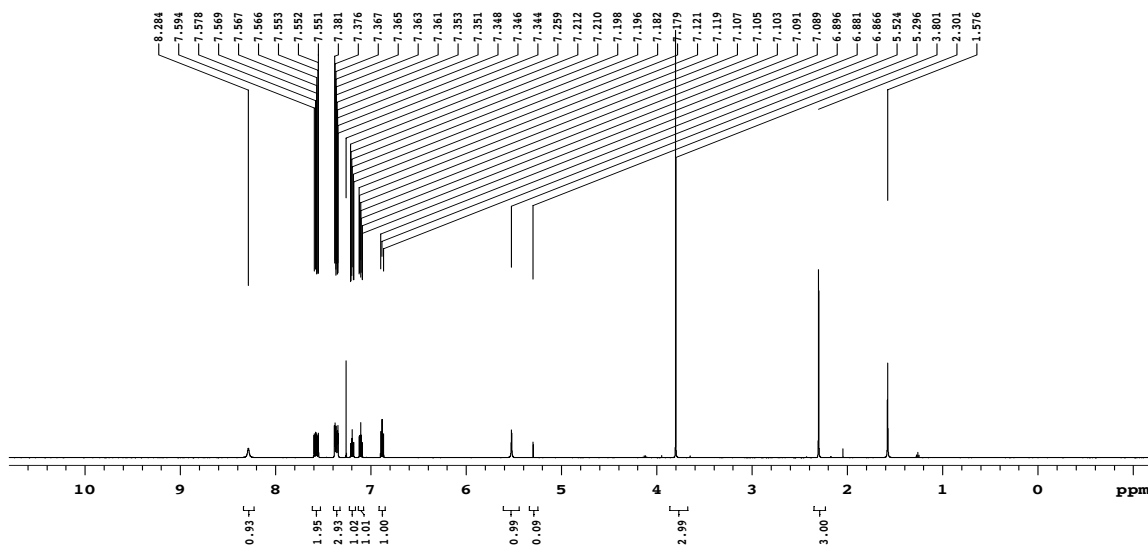125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

191.779
166.897
161.138
148.463
143.281
138.133
125.686
120.772
119.360
113.643
110.745
108.782
77.314
76.805
71.695
54.100

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

2k

Thiophene trap
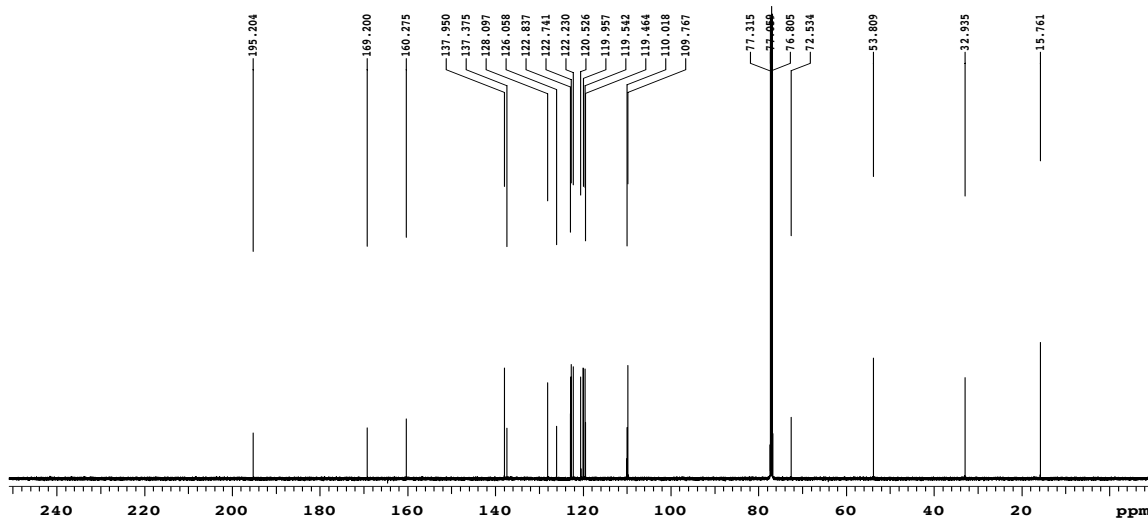499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

7.663
7.661
7.660
7.659
7.647
7.646
7.645
7.643
7.590
7.587
7.576
7.573
7.571
7.559
7.557
7.527
7.525
7.520
7.517
7.297
7.281
7.278
7.270
7.268
7.116
7.100
7.076
7.069
7.066
7.059
6.998
6.996
6.982
6.968
6.966
3.883

0.96
0.99
0.98
0.94
0.96
0.98
0.98

0.91

3.00

Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

Thiophene trap
125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

192.210
167.396
160.930
138.834
137.911
127.613
125.879
125.530
125.676
121.143
119.060
113.738
77.316
77.062
76.807
73.418
54.101

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

S-41

2l

BA MeO 1H

8.284
7.594
7.578
7.569
7.567
7.566
7.553
7.552
7.551
7.381
7.376
7.367
7.365
7.363
7.361
7.353
7.351
7.348
7.346
7.344
7.259
7.212
7.210
7.198
7.196
7.182
7.179
7.121
7.119
7.107
7.105
7.103
7.091
7.089
6.896
6.881
6.866
5.524
5.296
3.801
2.301
1.576

0.93 1.95 2.93 1.02 1.01 1.00   0.99 0.09   2.99   3.00

BA MeO 13C

208.100
195.178
169.167
160.340
137.988
136.574
125.543
123.678
122.841
122.784
122.674
120.581
120.396
119.551
119.501
111.791
111.671
77.323
77.020
76.814
72.613
53.815
15.785
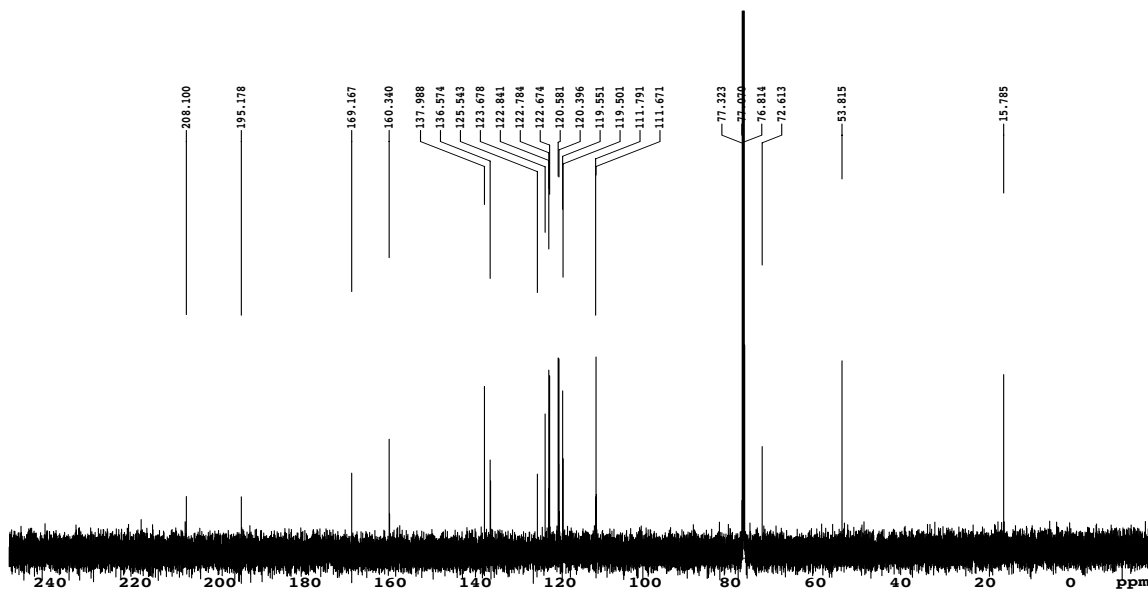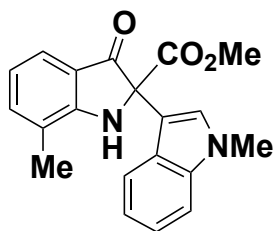
2m

N-methylindole trap on methyldiazoazide
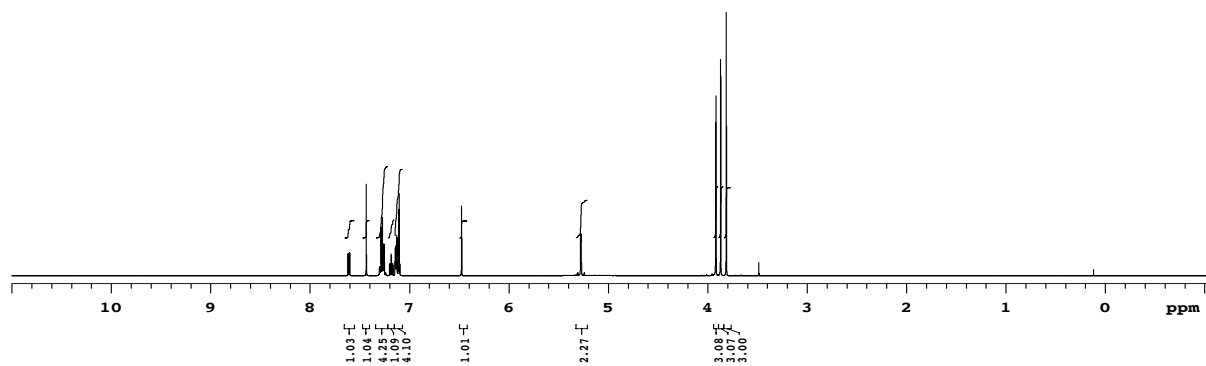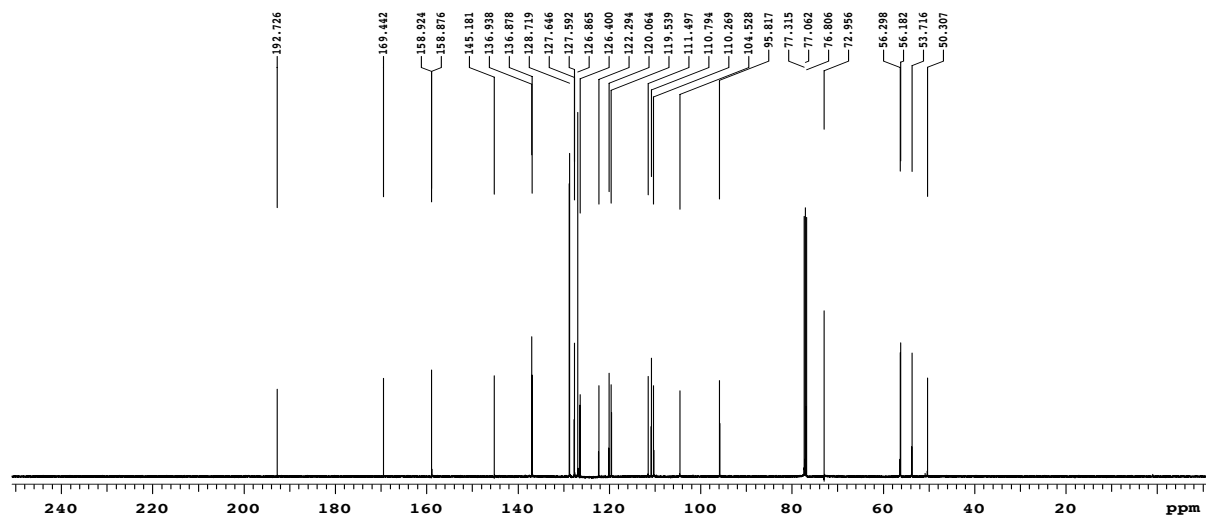499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

7.566 7.549 7.533 7.337 7.322 7.295 7.278 7.260 7.236 7.217 7.203 7.103 7.087 7.073 6.869 6.855 6.840 5.520   3.783 3.729   2.274

1.96 4.28 1.02 1.00   0.94   2.96 3.08   3.00

Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

N-methylindole trap on methyldiazoazide
125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

195.204   169.200   160.275   137.950 137.375 128.097 126.058 122.837 122.741 122.230 120.526 119.957 119.542 119.464 110.018 109.767   77.315 77.049 76.805 72.554   53.809   32.935   15.761

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

S-43

2n

N-benzylindoletrap on dimethoxydiazoazide
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

1.03 1.04 4.25 1.09 4.10   1.01   2.27   3.08 3.07 3.00
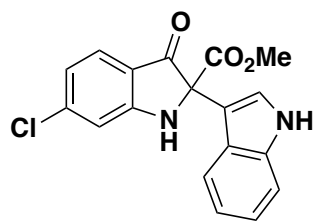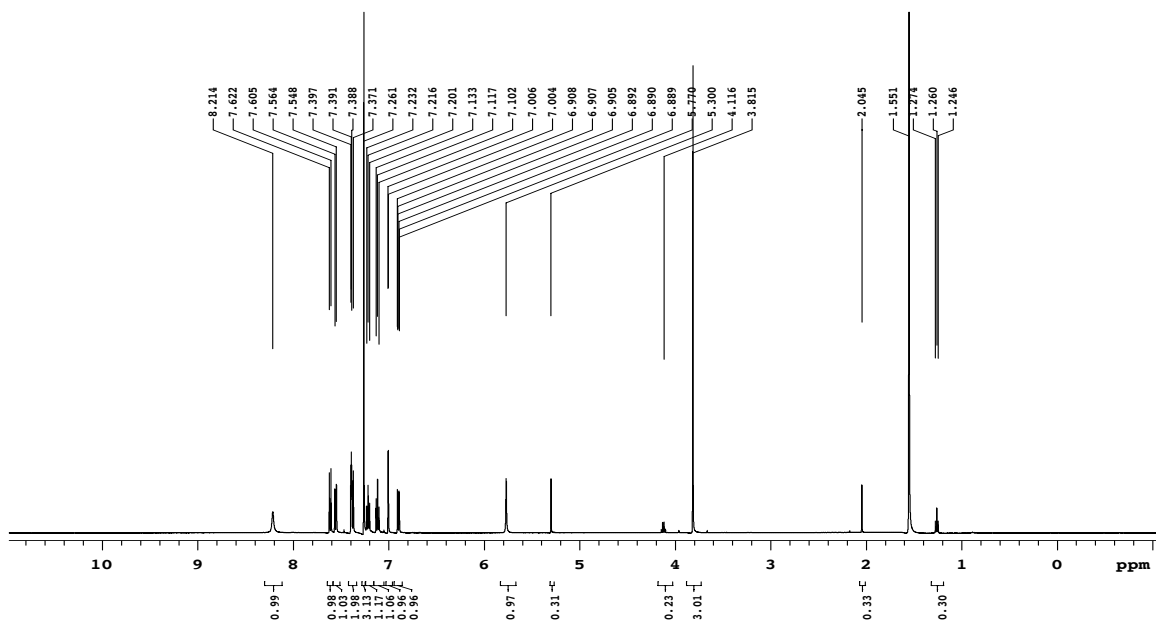
Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

N-benzylindole trap on dimethoxydiazoazide
125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

192.726 169.442 158.924 158.876 145.181 136.938 136.878 128.719 127.646 127.592 126.865 126.400 122.294 120.064 119.539 111.497 110.794 110.269 104.528 95.817 77.315 77.062 76.806 72.956 56.298 56.182 53.716 50.307

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

S-44

2o

C10

8.214 7.622 7.605 7.564 7.548 7.397 7.391 7.388 7.371 7.261 7.232 7.216 7.201 7.133 7.117 7.102 7.006 7.004 6.908 6.907 6.905 6.892 6.890 6.889 5.770 5.300 4.116 3.815 2.045 1.551 1.274 1.260 1.246

| 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | ppm |

0.99 0.98 1.03 1.98 3.13 1.17 1.06 0.96 0.96 0.97 0.31 0.23 3.01 0.33 0.30

Department of Chemistry, University of Alberta

C10

193.185 168.601 161.168 145.151 144.502 136.542 126.462 125.323 123.554 122.875 121.226 120.571 119.450 118.282 113.362 111.686 111.321 77.315 77.061 76.808 72.812 53.901

| 240 | 220 | 200 | 180 | 160 | 140 | 120 | 100 | 80 | 60 | 40 | 20 | ppm |

Department of Chemistry, University of Alberta

S-45

2p

N-methylindole trap on chlorodiazoazide
399.984 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 25.9 C -> actual temp = 27.0 C, onenmr probe

0.96
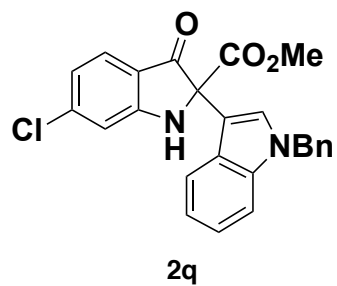1.00
1.00
2.42
1.04
0.96
1.01

1.01

3.02
3.12

Department of Chemistry, University of Alberta

N-methylindole trap on chlorodiazoazide
100.587 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 25.9 C -> actual temp = 27.0 C, onenmr probe
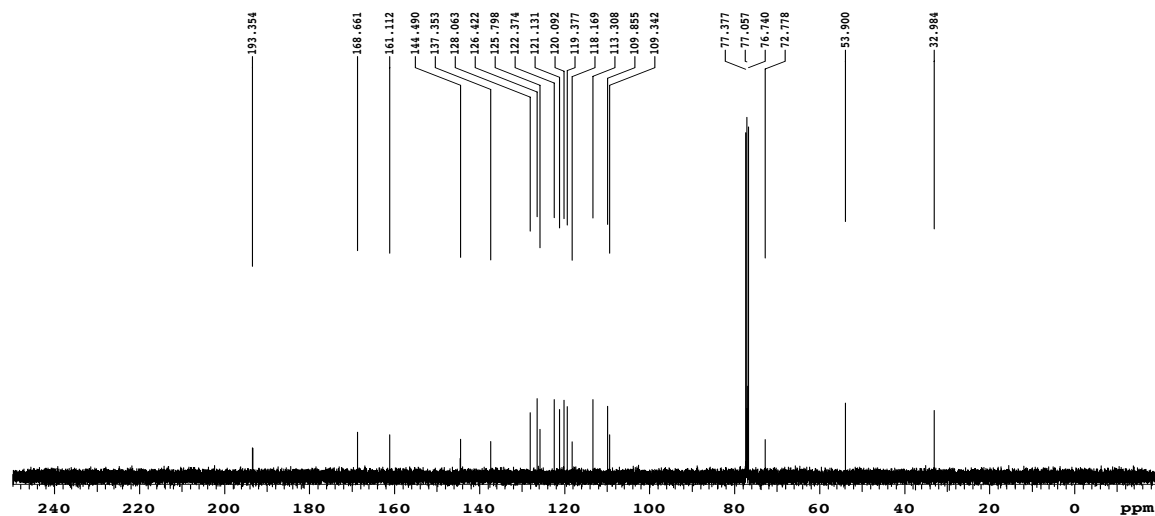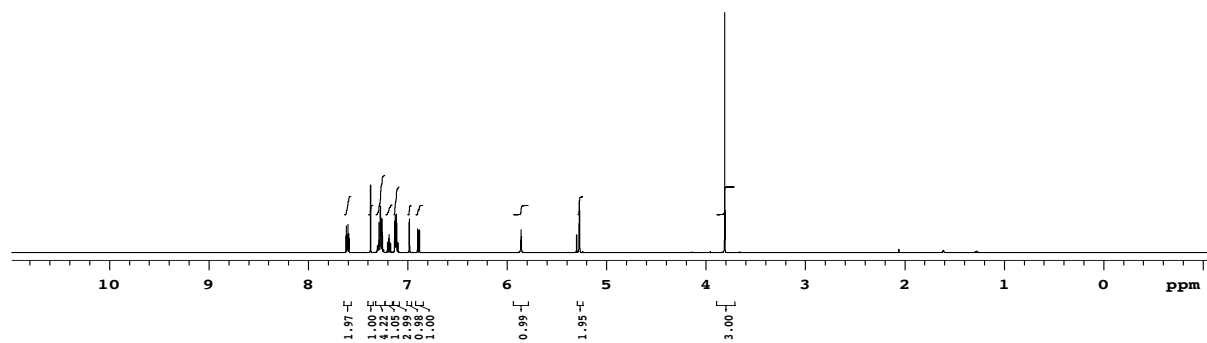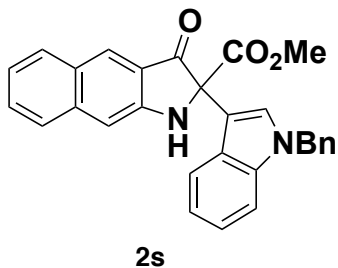
193.354
168.661
161.112
144.490
137.353
128.063
126.422
125.798
122.374
121.131
120.092
119.377
118.169
113.308
109.855
109.342
77.377
77.057
76.740
72.778
53.900
32.984

Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

2q

N-Benzylindole trap on chlorodiazoazide
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

1.97
1.00
4.22
4.05
2.99
2.98
0.00
1.00

0.99

1.95

3.00

N-benzylindole trap on chlorodiazoazide
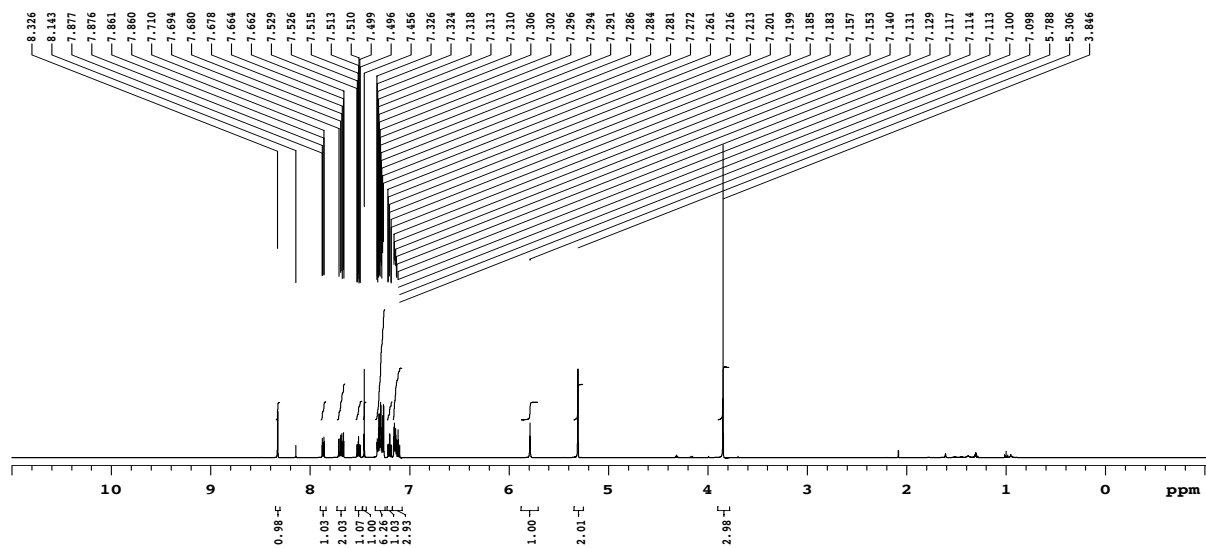125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

193.245
168.634
161.126
144.421
136.987
136.845
128.817
127.773
127.585
126.880
126.437
126.101
122.515
121.079
120.282
119.707
118.174
113.279
110.392
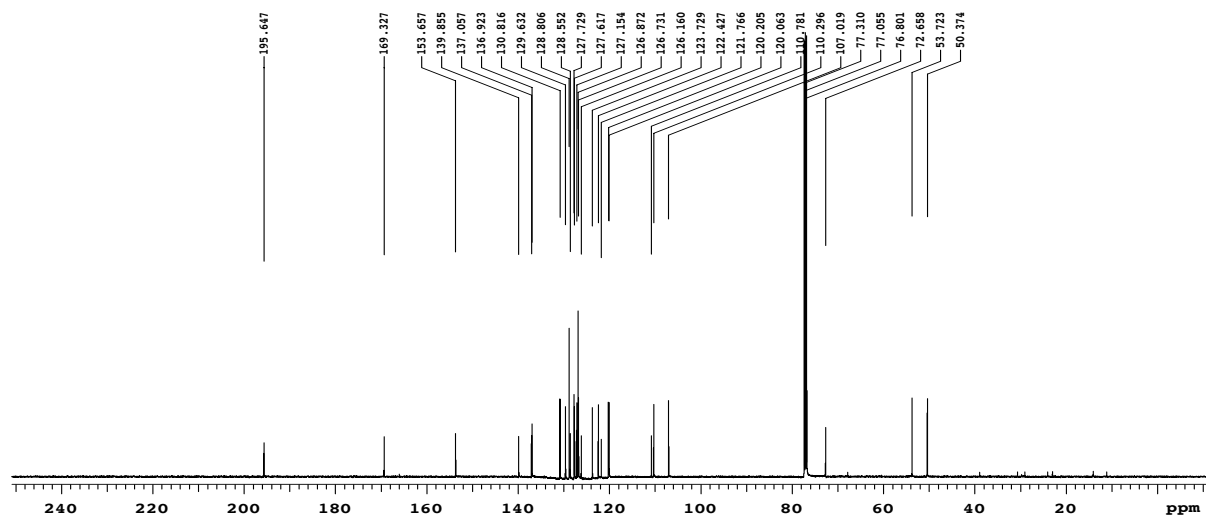110.034
77.316
77.061
76.807
72.809
53.844
50.386

2s

N-benzylindoletrap on naphtalene diazoazide
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
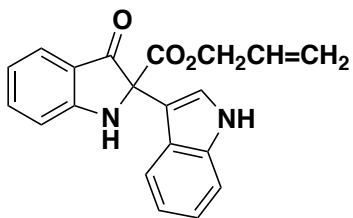
Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

N-benzylindole trap on Napthalenediazoazide
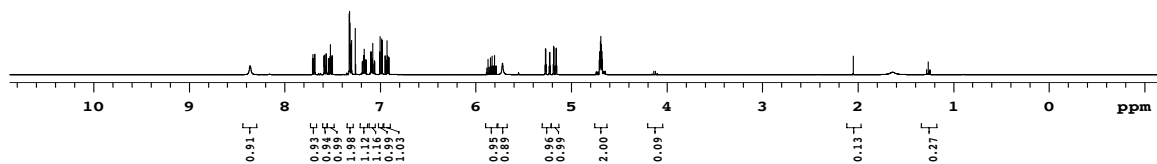125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

Pulse Sequence: s2pul
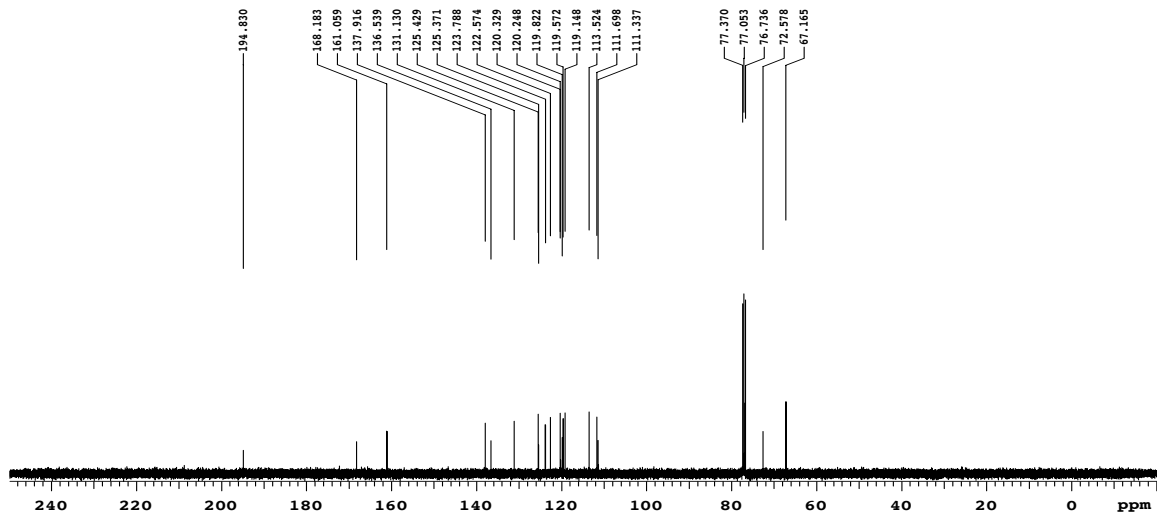
Department of Chemistry, University of Alberta

O

$CO_2CH_2CH=CH_2$

NH

N
H

NH

2t

Indole trap on allyldiazoazide

10   9   8   7   6   5   4   3   2   1   0   ppm

0.91

0.93
0.94
0.99
1.98
1.18
1.16
0.99
1.03

0.95
0.89

0.96
0.99

2.00

0.09

0.13

0.27

Pulse Sequence: s2pul   Department of Chemistry, University of Alberta

Indole trap on allyldiazoazide

194.830

168.183
161.059
137.916
136.539
131.130
125.429
125.371
123.788
122.574
120.329
120.248
119.822
119.572
119.148
113.524
111.698
111.337

77.370
77.053
76.736
72.578
67.165

240   220   200   180   160   140   120   100   80   60   40   20   0   ppm
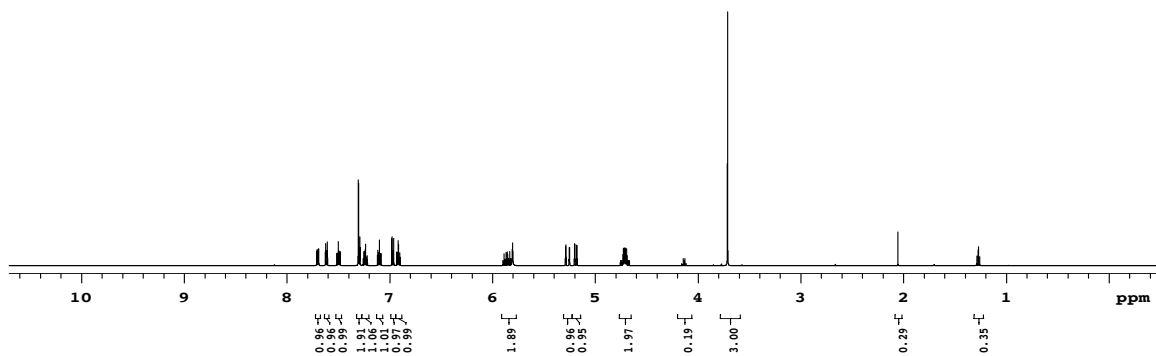
Pulse Sequence: s2pul   Department of Chemistry, University of Alberta

2u

N-methyl indole trap on allyldiazoazide

N-methylindole trap on allyl diazoazide

S-50

2v

Pulse Sequence: PRESAT

7.7   7.5   7.3   7.1   ppm

1.04   1.08   1.09   1.08   1.04   1.00
1.03   1.04   3.03   1.02   0.99

10   9   8   7   6   5   4   3   2   1   0   ppm

1.03   1.03 1.03 1.02   0.98   0.99
1.04 0.809 1.0804   1.00
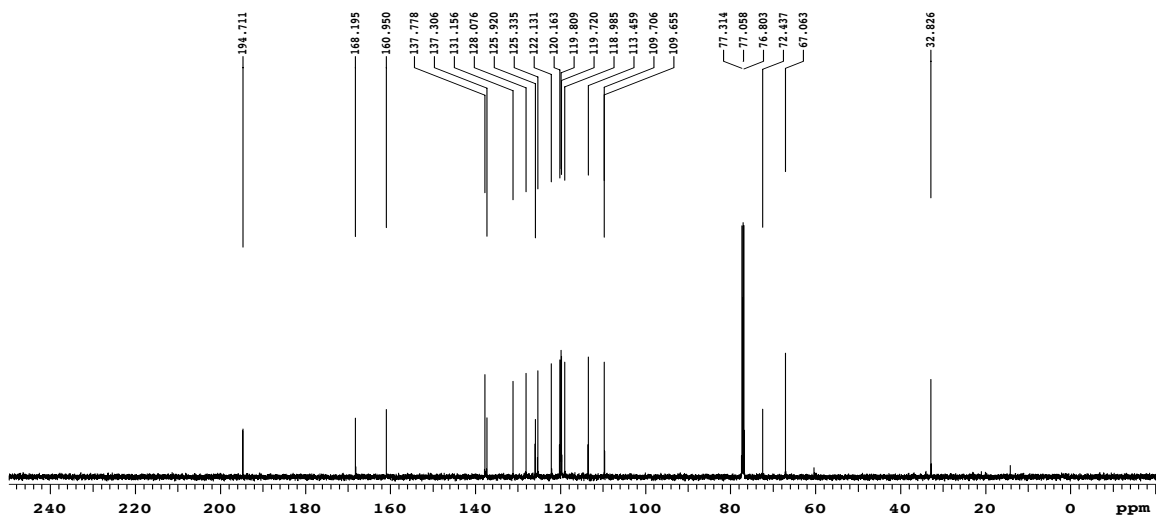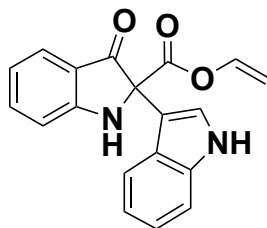
BA INDOLE TRAP(VINYL DIAZOAZIDE)

Pulse Sequence: s2pul

194.007

165.818
160.905

141.361
138.001
136.535
125.542
125.320
123.750
122.772
120.503
120.479
119.748
119.597
119.496
113.496
111.653
111.052
99.997

77.288
76.778
72.102

240   220   200   180   160   140   120   100   80   60   40   20   ppm

S-51

2w

BA Ac1

8.165, 8.162, 8.158, 8.149, 8.144, 8.141, 7.670, 7.667, 7.648, 7.645, 7.530, 7.527, 7.512, 7.509, 7.506, 7.492, 7.488, 7.457, 7.454, 7.450, 7.440, 7.435, 7.431, 7.420, 7.416, 7.413, 7.400, 7.379, 7.377, 7.319, 7.314, 7.310, 7.296, 7.280, 7.275, 7.260, 7.234, 7.231, 7.216, 7.213, 7.210, 7.198, 7.193, 7.076, 7.074, 7.059, 7.056, 7.054, 7.038, 7.036, 7.020, 6.999, 6.932, 6.912, 6.895, 6.265, 3.766

1.94, 0.99, 1.06, 2.11, 2.99, 2.04, 1.03, 1.05, 0.93, 3.00
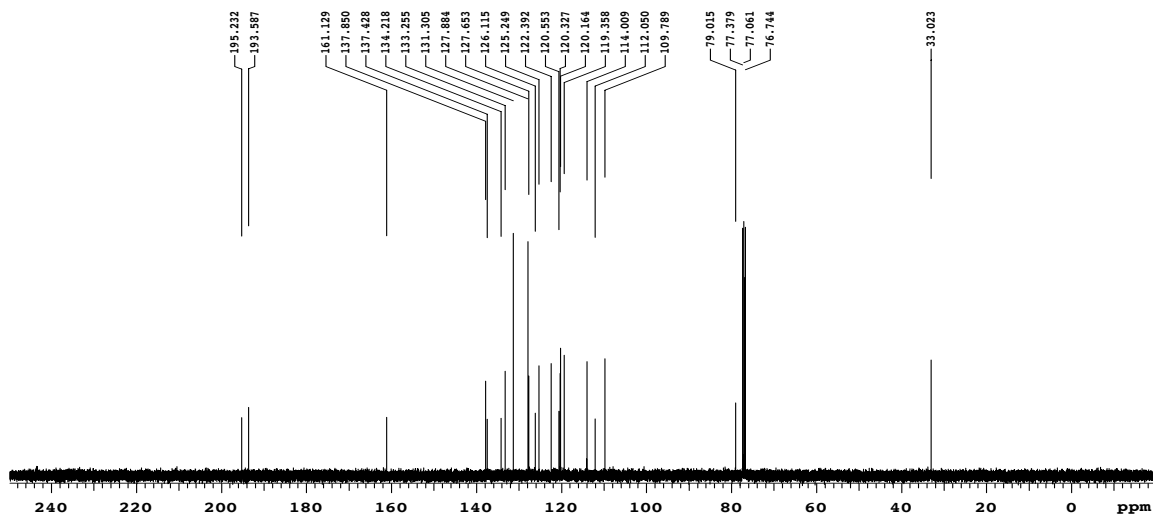
Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

BA Ac1

195.232, 193.587, 161.129, 137.850, 137.428, 134.218, 133.255, 131.305, 127.884, 127.653, 126.115, 125.249, 122.392, 120.553, 120.327, 120.164, 119.358, 114.009, 112.050, 109.789, 79.015, 77.379, 77.061, 76.744, 33.023
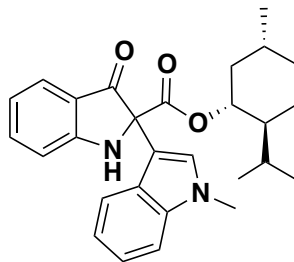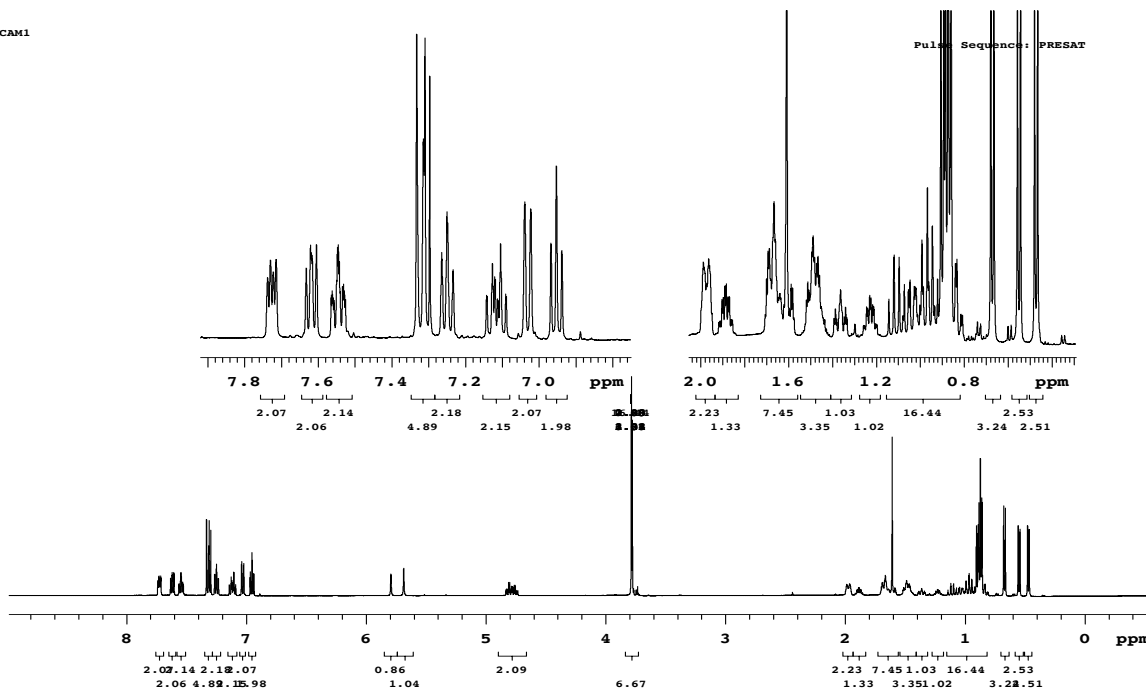
Pulse Sequence: s2pul

Department of Chemistry, University of Alberta

2xa:2xb, 1.1:1

BA CAM0

Pulse Sequence: PRESAT

7.7   7.5   7.3   7.1   ppm   2.0   1.6   1.2   0.8   ppm

1.99 2.06 2.08 2.09 1.95   2.17 7.95 2.27 16.14   2.68
   2.06 1.96 2.15 1.95   1.27 3.47 1.14   3.07 2.61

11   10   9   8   7   6   5   4   3   2   1   0   ppm

1.89   0.84   1.92   1.27 3.41.14   3.07.61
1.290.6020.0995   0.94   2.177.952.2716.14 2.68

BA CAM0

Pulse Sequence: s2pul

194.843
194.644
168.048
167.971
161.183
160.997
137.711
137.609
136.521
136.479
125.635
125.434
125.320
123.658
123.351
122.552
122.522
120.244
120.206
120.146
120.116
120.056
120.042
119.910
119.607
113.664
113.488
111.825
111.781
111.499
111.459
77.451
77.355
77.294
77.040
76.786
72.820
72.733
46.746
46.651
40.284
40.228
34.084
34.062
31.446
25.741
25.487
23.139
23.045
21.934
20.738
20.403
15.916
15.720

240   220   200   180   160   140   120   100   80   60   40   20   ppm

S-53

2ya:2yb; 1.3:1
(after column chromatography)

BA CAM1
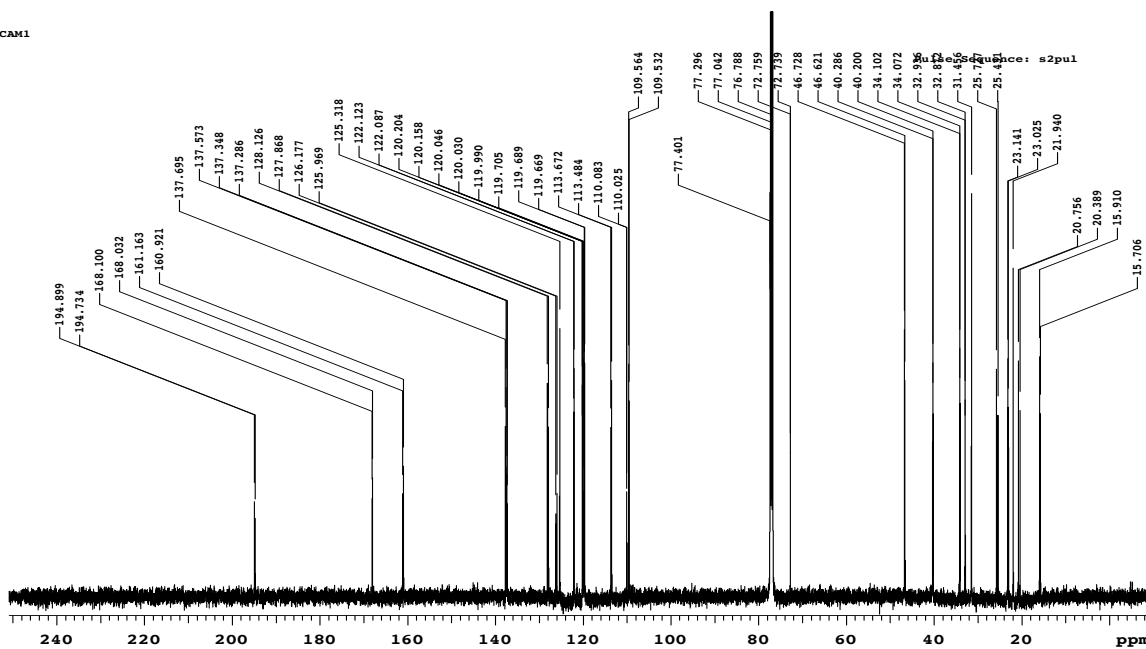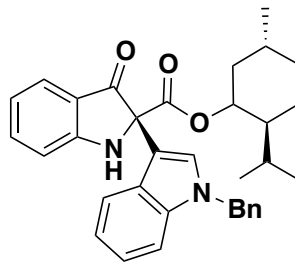
Pulse Sequence: PRESAT

BA CAM1

Pulse Sequence: s2pul

2za

Benzylindole trap on mentholdiazoazide(single diastereomer, with X-ray)

7.714
7.698
7.655
7.639
7.559
7.545
7.531
7.416
7.326
7.313
7.286
7.273
7.256
7.187
7.173
7.150
7.101
7.087
7.073
7.048
7.031
6.961
6.947
6.933
5.679
5.345
5.308
5.276
4.784
4.762
4.748
1.927
1.903
1.860
1.846
1.832
1.818
1.804
1.675
1.651
1.574
1.483
1.466
1.445
1.421
1.053
1.027
1.007
0.981
0.929
0.905
0.883
0.864
0.851
0.838
0.824
0.798
0.642
0.628

2.51
2.55
2.54
13.33
7.76
2.72
2.63
2.67

2.48

5.25

2.59

2.64
2.62
5.26
3.11
5.20

2.84
21.03

7.70
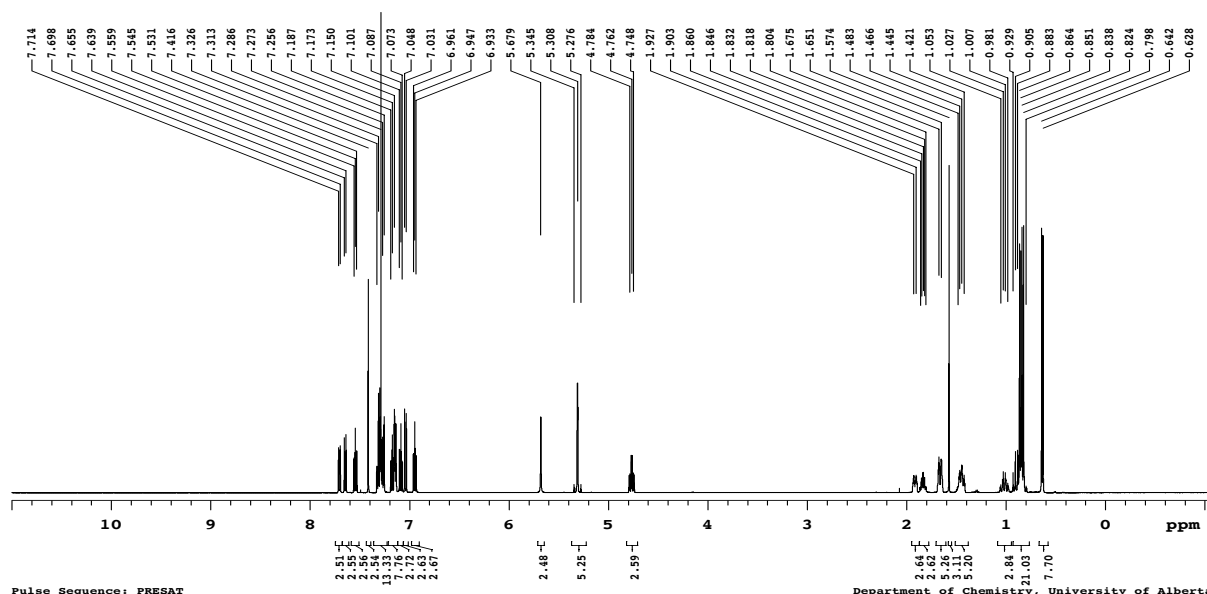
Pulse Sequence: PRESAT

Department of Chemistry, University of Alberta

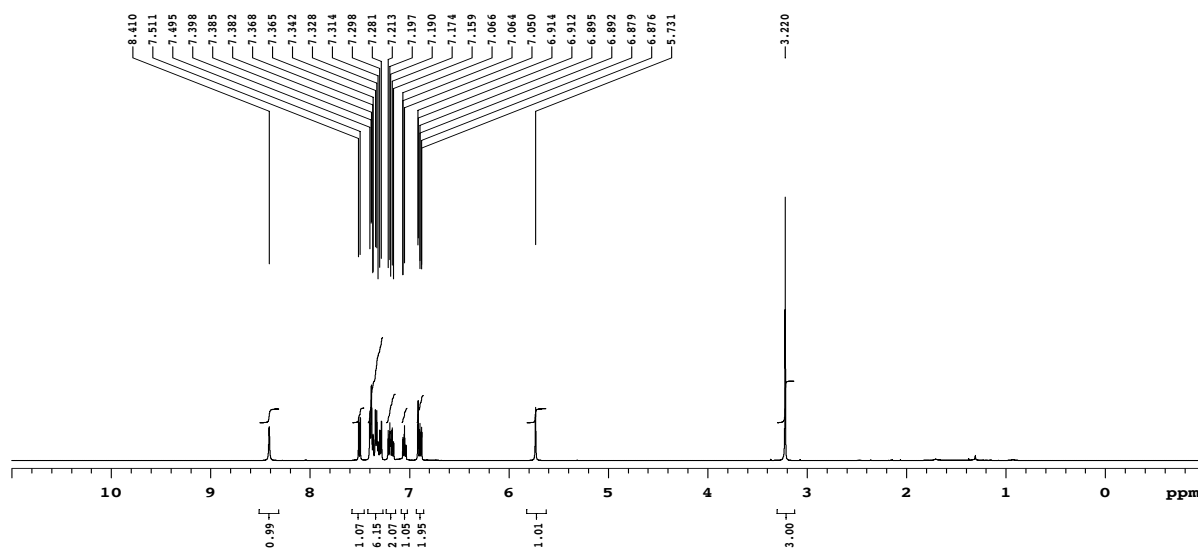Benzylindole trap on mentholdiazoazide (single diastereomer, with X-ray)

194.769
167.925
160.979
137.559
137.084
136.954
128.823
127.754
127.650
126.985
126.274
125.382
122.261
120.292
120.222
120.140
119.960
113.508
110.670
110.093
77.369
77.315
77.060
76.806
72.850
50.319
46.824
40.210
34.134
31.452
25.778
23.182
21.986
20.752
15.946
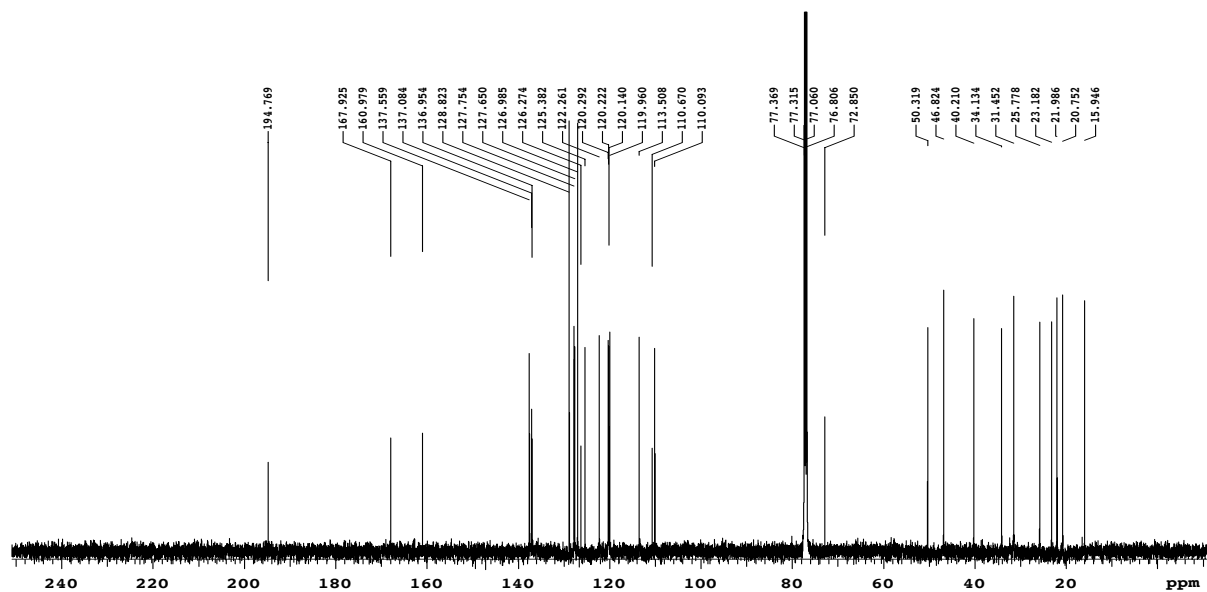
Pulse Sequence: s2pul

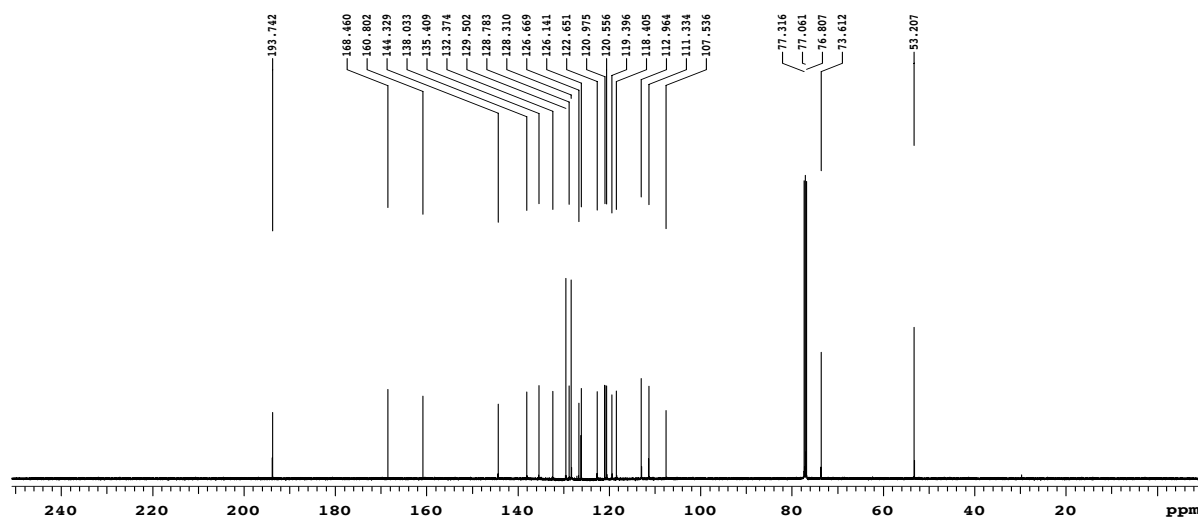Department of Chemistry, University of Alberta

5a

2-phenylindole trap on chlorodiazoazide
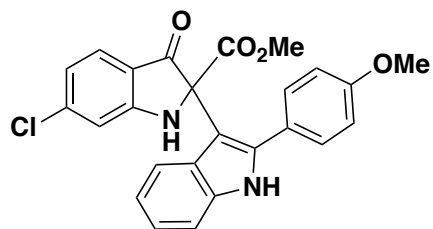499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
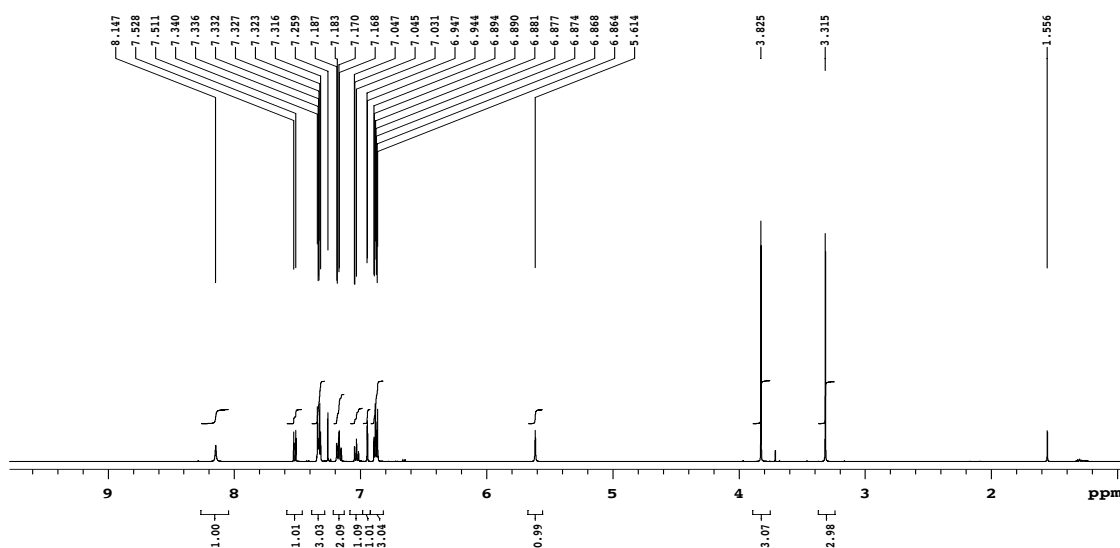
8.410
7.511
7.495
7.398
7.385
7.382
7.368
7.365
7.342
7.328
7.314
7.298
7.281
7.213
7.197
7.190
7.174
7.159
7.066
7.064
7.050
6.914
6.912
6.895
6.892
6.879
6.876
5.731
—3.220

0.99
1.07
6.15
2.07
1.05
1.95
1.01
3.00

2-phenylindole trap on chlorodiazide
125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

193.742
168.460
160.802
144.329
138.033
135.409
132.374
129.502
128.783
128.310
128.669
126.141
122.651
120.975
120.556
119.396
118.405
112.964
111.334
107.536
77.316
77.061
76.807
73.612
53.207

5b

ClO2Me

8.147 7.528 7.511 7.340 7.336 7.332 7.327 7.323 7.316 7.259 7.187 7.183 7.170 7.168 7.047 7.045 7.031 6.947 6.944 6.894 6.890 6.881 6.877 6.874 6.868 6.864 5.614   3.825   3.315   1.556

9   8   7   6   5   4   3   2   ppm

1.00   1.01 3.03 2.09 1.09 1.01 3.04   0.99   3.07   2.98

ClO2OMe

193.667   168.565 160.805 160.120 144.325 137.928 135.332 130.924 126.771 126.238 124.646 122.630 121.082 120.622 119.390 118.651 113.803 113.089 111.143 107.560   77.321 77.066 76.812 73.639   55.419 53.448

240   220   200   180   160   140   120   100   80   60   40   20   0   ppm

5c

C1O2F

| 0.87 | | 0.89 1.92 0.99 1.59 1.02 2.97 0.94 0.98 | 1.02 | 3.01 |
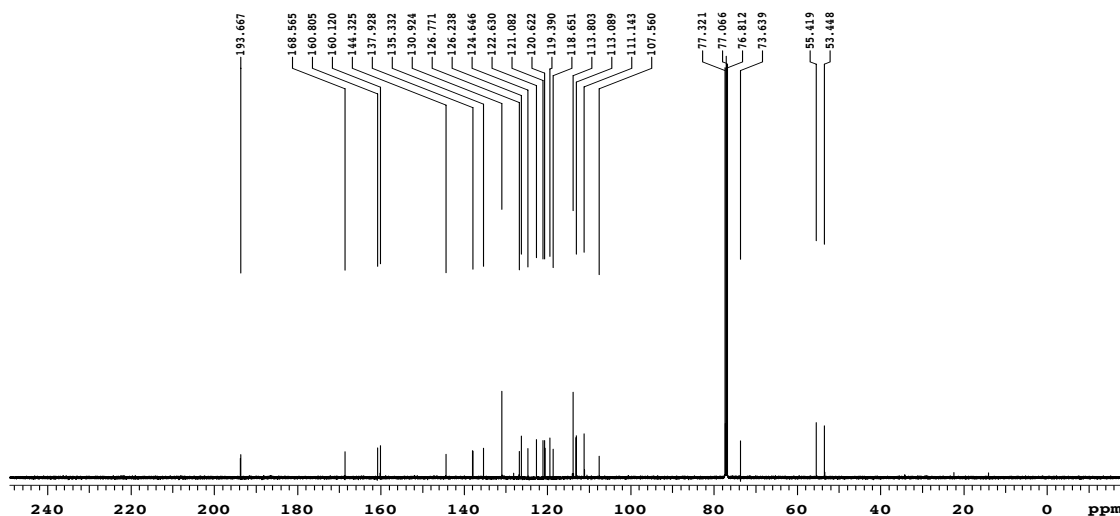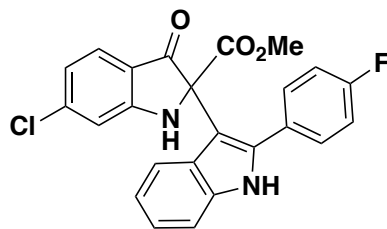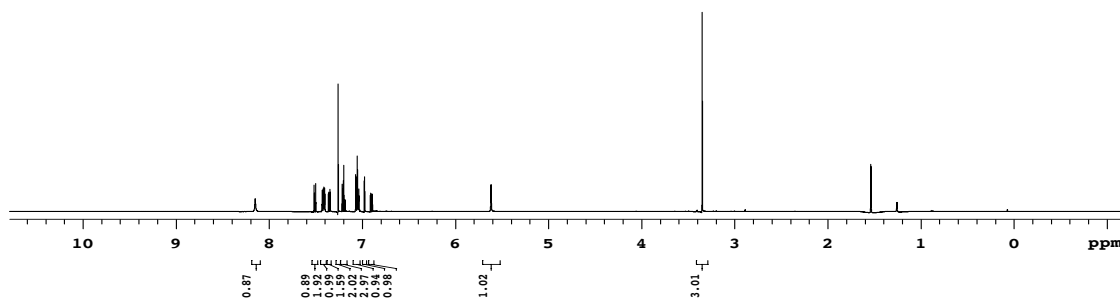
Bren+Jordan, BA_ClO2F_clean
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)
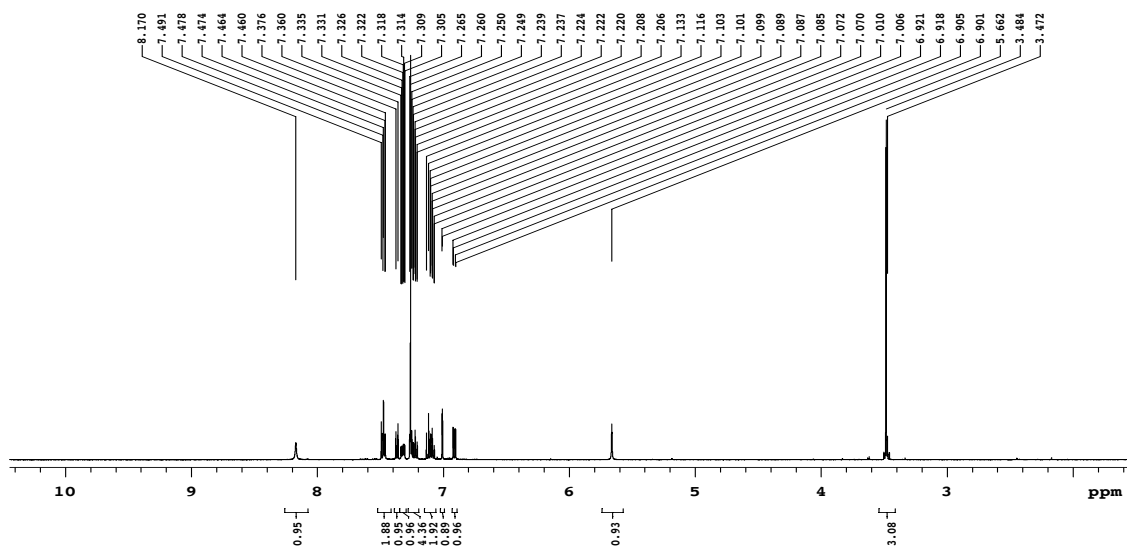temp 27.7 C -> actual temp = 27.0 C, colddual probe

193.437 168.475 164.080 162.095 160.663 144.487 136.805 135.389 131.593 131.527 128.463 128.490 126.730 126.228 122.987 121.275 120.856 119.415 118.652 115.557 115.384 113.110 111.233 108.233 77.317 77.062 76.808 73.445 53.462

5d

C1O2FC1

0.95

1.88 0.95 0.96 4.36 1.92 0.89 0.96

0.93

3.08

10   9   8   7   6   5   4   3   ppm

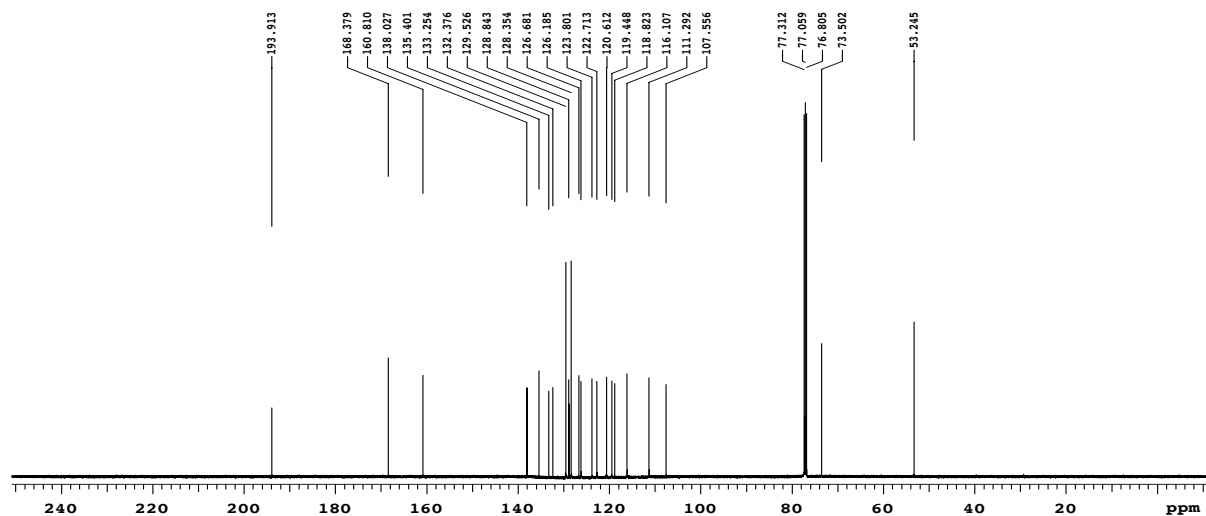240   220   200   180   160   140   120   100   80   60   40   20   0   ppm

5e

2-phenylindole trap on bromo diazo azide
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

8.316
7.426
7.410
7.391
7.388
7.385
7.382
7.375
7.372
7.367
7.356
7.353
7.350
7.340
7.328
7.324
7.312
7.297
7.280
7.260
7.187
7.177
7.174
7.171
7.163
7.161
7.147
7.144
7.098
7.095
7.046
7.044
7.038
7.035
7.030
7.022
7.019
7.016
7.014
5.665
3.208

10   9   8   7   6   5   4   3   2   1   0   ppm

0.97   7.30 2.08 1.00 2.03   1.00   3.00
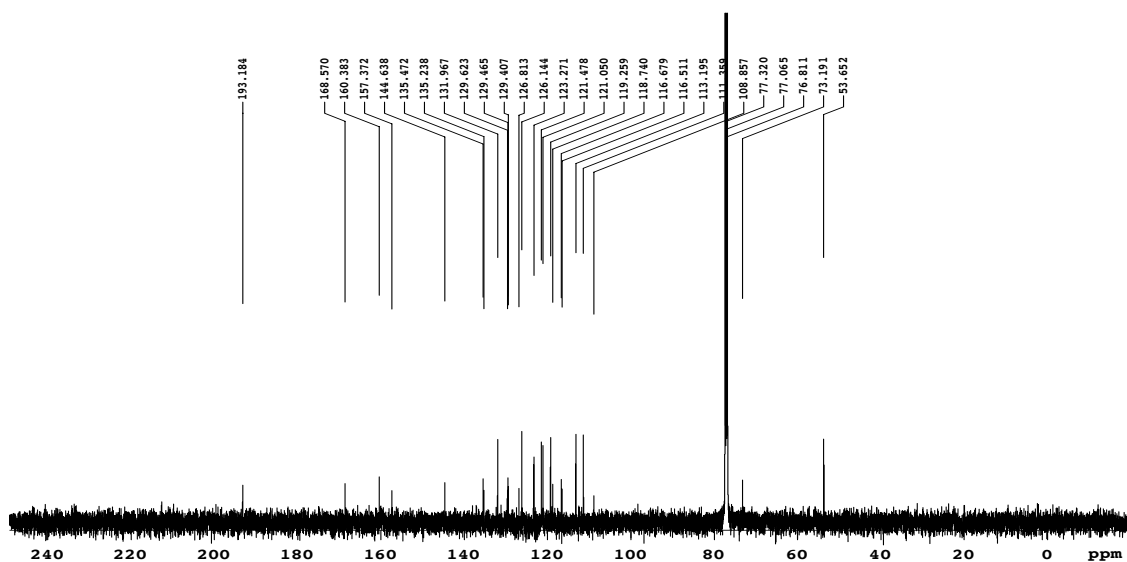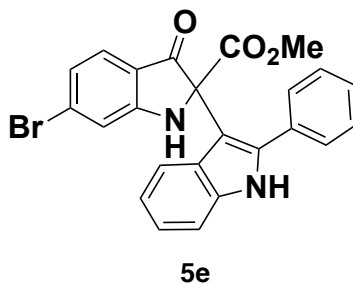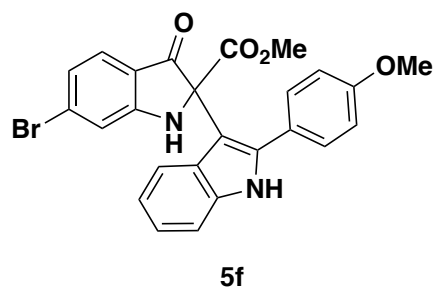
Pulse Sequence: PRESAT

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2-phenylindole trap on bromodiazoazide
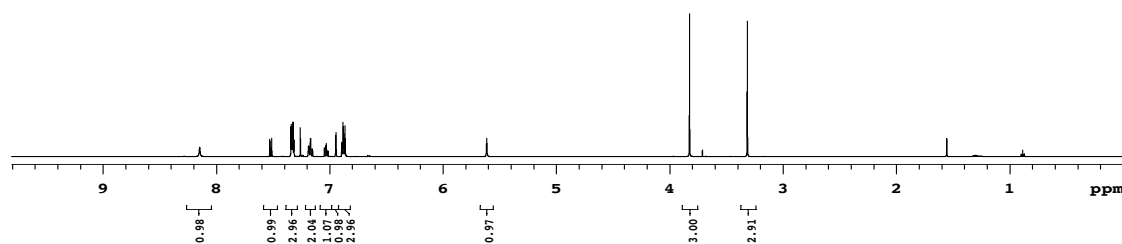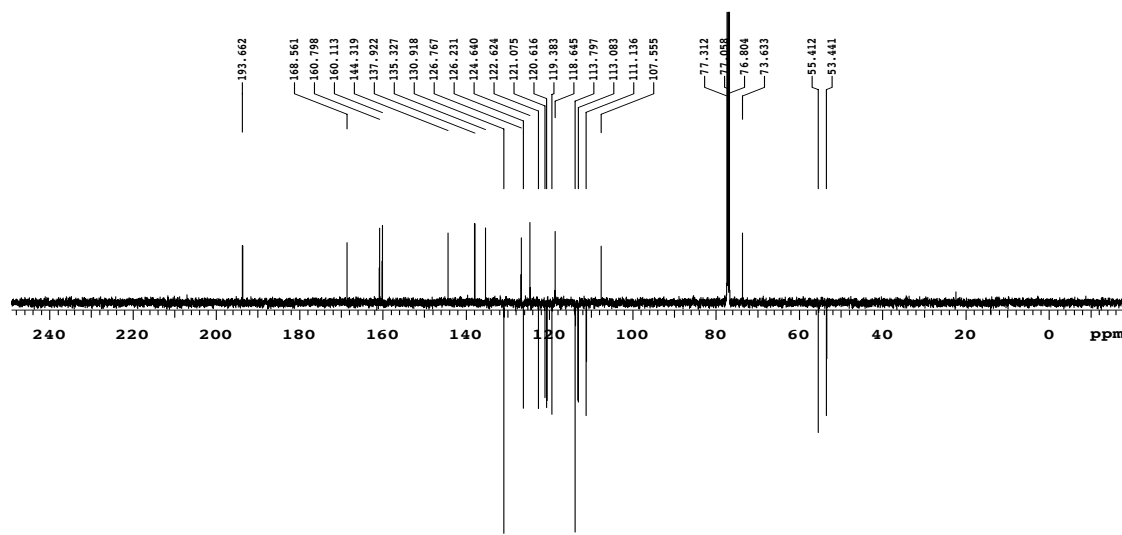125.691 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe

193.913
168.379
160.810
138.027
135.401
133.254
132.376
129.526
128.843
128.354
126.681
126.185
123.801
122.713
120.612
119.448
118.823
116.107
111.292
107.556
77.312
77.059
76.805
73.502
53.245

240   220   200   180   160   140   120   100   80   60   40   20   ppm

Pulse Sequence: s2pul

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S-60

5f

BrO2Me
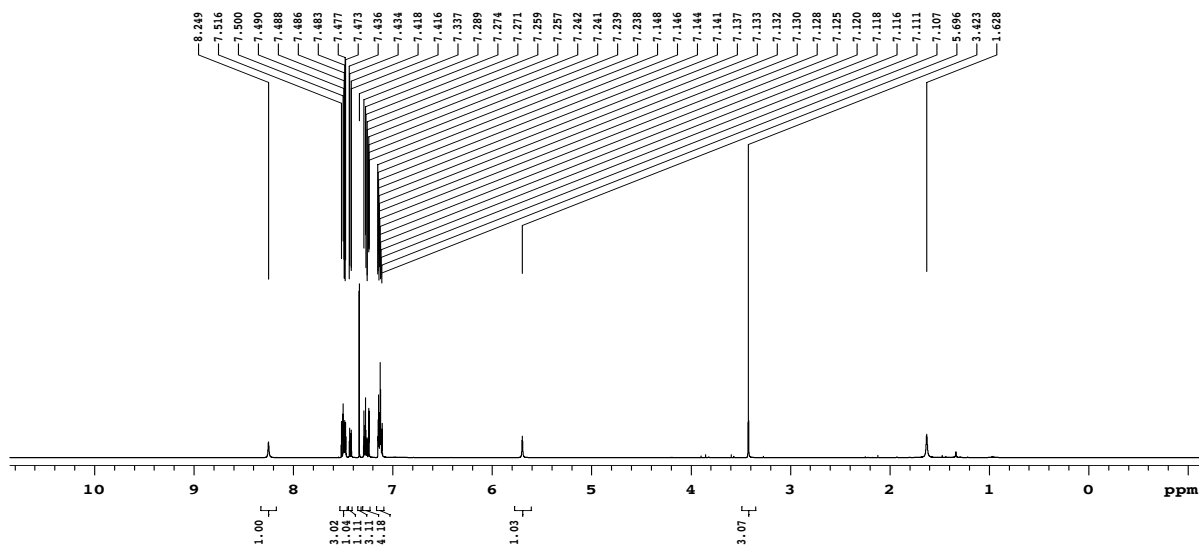
0.98

0.99 2.96 2.04 1.07 0.98 2.96

0.97

3.00 2.91

193.662

168.561
160.798
160.113
144.319
137.922
135.327
130.918
126.767
126.231
124.640
122.624
121.075
120.616
119.383
118.645
113.797
113.083
111.136
107.555

77.312
77.058
76.804
73.633

55.412
53.441

5g

BA Br02F

8.249
7.516
7.500
7.490
7.488
7.486
7.483
7.477
7.473
7.436
7.434
7.418
7.416
7.337
7.289
7.274
7.271
7.259
7.257
7.242
7.241
7.239
7.238
7.148
7.146
7.144
7.141
7.137
7.133
7.132
7.130
7.128
7.125
7.120
7.118
7.116
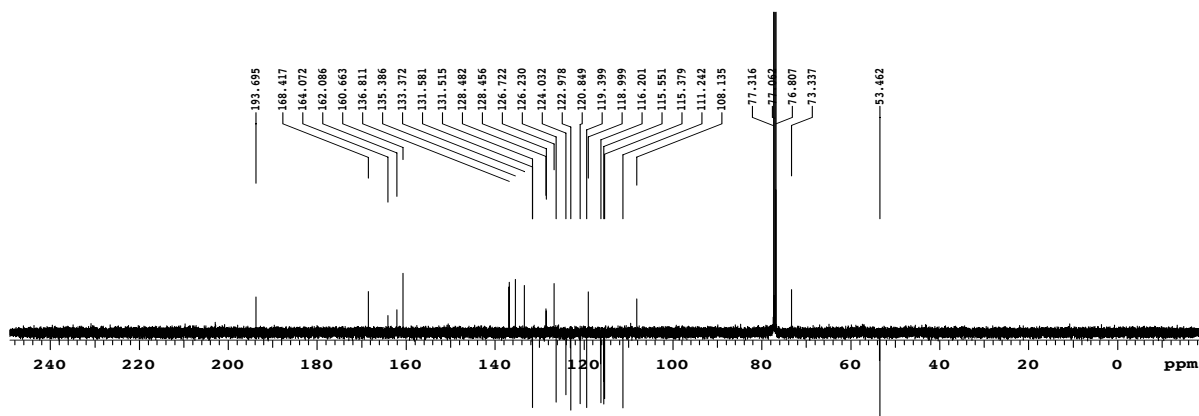7.111
7.107
5.696
3.423
1.628

1.00
3.02
1.04
1.11
3.11
4.18
1.03
3.07

Pulse Sequence: PRESAT
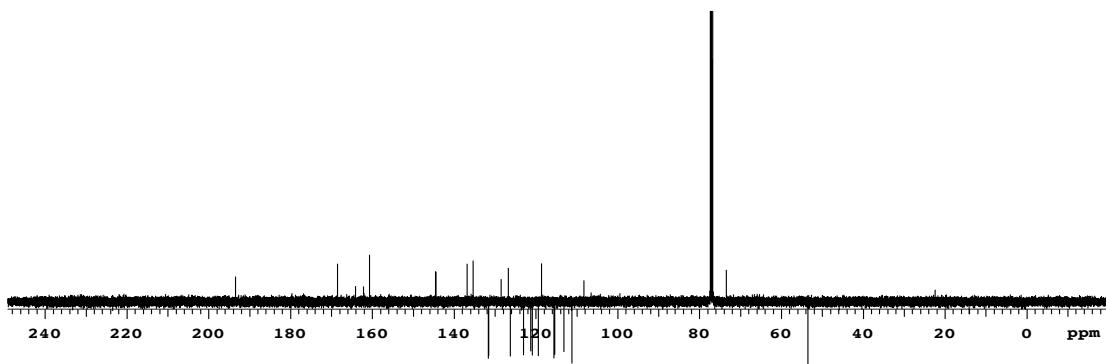
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Br02F

193.695
168.417
164.072
162.086
160.663
136.811
135.386
133.372
131.581
131.515
128.482
128.456
126.722
126.230
124.032
122.978
120.849
119.399
118.999
116.201
115.551
115.379
111.242
108.135
77.316
77.062
76.807
73.337
53.462

Pulse Sequence: APT_ad

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5h

BrO2FCl