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# Supporting Information



69451 Weinheim, Germany

# Palladium-Catalyzed g-Arylation of a,b-Unsaturated Ketones: Application to a One-Pot Synthesis of Tricyclic Indolines

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**Reagents**

Toluene and THF were purchased from J.T. Baker in CYCLE-TAINER solvent-deliver kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina and copper(II) oxide. Anhydrous dioxane was purchased from Aldrich and used as received. $Pd_2(dba)_3$, dppe, and dippf were purchased from Strem Chemicals. (R)-SEGPHOS and (R)-DTBM-SEGPHOS were received as gifts from Takasago. $Pd(OAc)_2$ was obtained as a gift from BASF. $Cs_2CO_3$ was obtained as a gift from Chemetall and the bulk of the material was stored in a nitrogen-filled glovebox. Periodically, a scintillation vial containing ~10g of $Cs_2CO_3$ was removed from the glovebox and stored in a desicator over anhydrous $CaSO_4$. $K_2CO_3$ was purchased from Aldrich and the bulk of the material was stored in a nitrogen-filled glovebox. Periodically, a scintillation vial containing ~10g of $K_2CO_3$ was removed from the glovebox and stored in a desicator over anhydrous $CaSO_4$. $K_3PO_4$ was purchased from Riedel-de Haën and stored outside the glovebox. 4-methylanisole was purchased from Aldrich, 3,4-dimethylanisole was purchased from Acros, and 4-*n*-propylanisole was purchased from Pfaltz and Bauer and all were used as received. All other commercially available reagents were used as received except for α,β-unsaturated ketone (**4**) which was distilled prior to use. All ketones were stored under argon in a refrigerator at 5 °C.

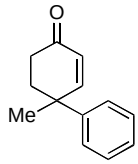
**Analytical Methods**

All $^1H$ and $^{13}C$ NMR spectra were recorded on a Varian Inova 500 MHz NMR. Chemical shifts are reported in ppm from tetramethylsilane with solvent as the internal standard ($^1H$ $CDCl_3$: δ 7.27; $^{13}C$ $CDCl_3$: δ 77.16). Gas chromatographic analysis was performed on an Agilent 6890 system equipped with an FID detector and a Hewlett-Packard 10 m x 0.2 mm HP-1 capillary column using dodecane as an internal standard. IR spectra were recorded on a Perkin-Elmer 2000 FT-IR system using KBr plates coated with a thin film of the analyte. Elemental analyses were performed by Atlantic Microlabs Inc.; Norcross, GA. Melting points (uncorrected) were obtained using a Mel-Temp capillary melting point apparatus. Enantiomeric excess was measured with a Hewlett-Packard 1100 HPLC system using a Chiralcel OJ column (25 cm x 0.46 cm). Optical rotations were measured with a JASCO P-1010 Polarimeter. Single crystal X-ray analysis was performed at UCSD with a Bruker Kappa APEXII X-ray diffractometer using a copper source.

**General Procedure A for the Arylation of a,b and b,g-Unsaturated Ketones at the g-Position:**
A culture tube (18 x 150mm, VWR) equipped with a Teflon-coated magnetic stir bar was charged with $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), and $Cs_2CO_3$ (489 mg, 1.50 mmol). The tube was then sealed with an inverted 14/20 rubber septum and electrical tape. A needle was next inserted and the tube was evacuated and backfilled with argon; this process was repeated three times. The aryl bromide (1.0 mmol) was then added by syringe, followed by a solution of the ketone (1.4 mmol) in toluene (4 mL). The reaction mixture was stirred at 100 °C in an oil bath for 8 h. Following this, the reaction vial was allowed to cool to room temperature and was diluted with ethyl acetate (~ 4 mL). This mixture was then filtered through a pad of celite (eluted with ethyl acetate) and concentrated under reduced pressure. The crude reaction material was purified by flash chromatography on silica gel using a Biotage SP-4 system (25+S cartridge).

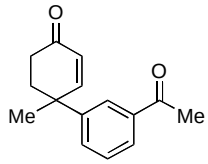
**General Procedure B for the One-Pot Synthesis of Ketoindolines:**
A culture tube (18 x 150mm, VWR) equipped with a Teflon-coated magnetic stir bar was charged with $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), and $Cs_2CO_3$ (816 mg, 2.50 mmol). The tube was then sealed with an inverted 14/20 rubber septum and electrical tape. A needle was next inserted and the tube was evacuated and backfilled with argon; this process was repeated three times. The *o*-bromoaniline (1.0 mmol) was then added by syringe if a liquid, or if it was if a solid, added with the other solids prior to sealing the tube. This was followed by addition by syringe of a solution of the ketone (1.4 mmol) in toluene (4 mL). The reaction mixture was stirred at 100 °C in an oil bath for 8 h. Following this, the reaction vial was allowed to cool to room temperature and was diluted with ethyl acetate (~ 4 mL). This mixture was then filtered through a pad of celite (rinsed with ethyl acetate) and concentrated under reduced pressure. The crude reaction material was purified by flash chromatography on silica gel using a Biotage SP-4 system (25+S cartridge).

**General Procedure C for the Asymmetric Synthesis of Ketoindolines:**
A culture tube (18 x 150mm, VWR) equipped with a Teflon-coated magnetic stir bar was charged with $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), (R)-DTBM-SEGPHOS (47 mg, 0.040 mmol), and $K_3PO_4$ (531 mg, 2.50 mmol). The tube was then sealed with an inverted 14/20 rubber septum and electrical tape. A needle was next inserted and the tube was evacuated and backfilled with argon; this procedure was repeated three times. The *o*-bromoaniline (1.0 mmol) was then added by syringe if a liquid, or if it was if a solid, added with the other solids prior to sealing the tube. This was followed by addition by syringe of a solution of the ketone (1.4 mmol) in toluene (4 mL). The reaction mixture was stirred at 100 °C in an oil bath for 8 h. Following this, the reaction vial was allowed to cool to room temperature and was diluted with ethyl acetate (~ 4 mL). This mixture was then filtered through a pad of celite (rinsed with ethyl acetate) and concentrated under reduced pressure. The crude reaction material was purified by flash chromatography on silica gel using a Biotage SP-4 system (25+S cartridge).

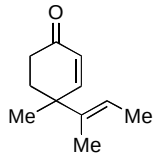



**4-methyl-4-phenylcyclohex-2-enone (Table 2, entry 1)**: General procedure A was followed using 4-methylcyclohex-3-enone[1] (154 mg, 1.40 mmol), bromobenzene (157 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0-15% gradient of ethyl acetate in hexanes to provide the title compound in a 87% yield (161 mg) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.34 (4H, m), 7.28-7.25 (1H, m), 6.94 (1H, d, *J*=10.0Hz), 6.13 (1H, d, *J*=10.0Hz), 2.44-2.38 (1H, m), 2.32-2.24 (2H, m), 2.18-2.12 (1H, m), 1.57 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 199.53, 157.19, 145.28, 128.66, 128.58, 126.81, 126.20, 40.62, 38.13, 34.66, 27.64. IR (KBr plates): 3085, 3058, 3024, 2964, 2869, 1683, 1600, 1222, 1110 $cm^{-1}$.

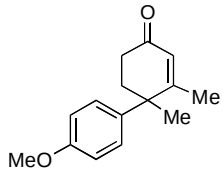
**4-methyl-4-phenylcyclohex-2-enone (Table 2, entry 2)**: General procedure A was followed using 4-methylcyclohex-2-enone[2] (154 mg, 1.40 mmol), bromobenzene (157 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0-15% gradient of ethyl acetate in hexanes to provide the title compound in a 68% yield (126 mg) as a colorless oil. The $^1$H NMR and GC spectra matched the data for the above compound.



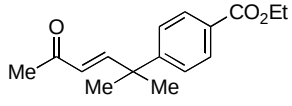

**4-(3-ethanoylphenyl)-4-methylcyclohex-2-enone (Table 2, entry 3):** General procedure A was followed using 4-methylcyclohex-3-enone (154 mg, 1.40 mmol), 3'-bromoacetophenone (199 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0%-35% gradient of ethyl acetate in hexanes to provide the title compound in a 80% yield (182 mg) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.91 (1H, s), 7.90 (1H, d, *J*=7.5Hz), 7.51 (1H, d, *J*=8.0Hz), 7.41 (1H, t, *J*=7.5Hz), 6.91 (1H, d, *J*=10.5Hz), 6.09 (1H, d, *J*=11.0Hz), 2.55 (3H, s), 2.39-2.34 (1H, m), 2.26-2.10 (3H, m), 1.54 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 198.86, 197.91, 156.22, 146.11, 137.34, 130.91, 128.84, 127.06, 125.52, 40.55, 37.88, 34.45, 27.51, 26.67. IR (KBr plates): 3027, 2964, 2869, 1684, 1598, 1582, 1426, 1358, 1273, 1232, 1113, 808 $cm^{-1}$.




**(*E*)-4-(but-2-en-2-yl)-4-methylcyclohex-2-enone (Table 2, entry 5)**: General procedure A was followed using 4-methylcyclohex-3-enone (154 mg, 1.40 mmol), (*E)*-2-bromo-2-butene (135 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and 3:1 dioxane/THF (4 mL) at 110 °C. The product was purified by column chromatography employing a 0-20% gradient of ethyl acetate in hexanes to provide the title compound in a 66% yield (109 mg) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.00 (1H, d, *J*=10.5Hz) 5.88 (1H, dd, *J*=11, 3Hz) 5.36 (1H, q, *J*=7.5Hz) 2.43 (2H, m) 2.22 (1H, m) 1.91 (1H, m) 1.72 (3H, s) 1.62 (3H, d, *J*=7.5Hz) 1.28 (3H, s). $^{13}$C NMR (500 MHz, $CDCl_3$) δ: 199.82, 160.82, 138.98, 126.26, 122.65, 40.64, 34.72, 34.56, 25.25, 23.35, 15.55. IR (KBr plates): 3023, 2968, 2866, 1684, 1456, 1380, 1233, 1112, 804 $cm^{-1}$.

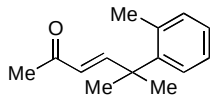



**4-(4-methoxyphenyl)-3,4-dimethylcyclohex-2-enone (Table 2, entry 4)**: General procedure A was followed using 3,4-dimethylcyclohex-3-enone[3] (174 mg, 1.40 mmol), 4-bromoanisole (187 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0-30% gradient of ethyl acetate in hexanes to provide the title compound in a 61% yield (141 mg) as a white solid, m.p. = 67-70 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.19 (2H, m), 6.88 (2H, m), 6.07 (1H, d, *J*=1.5 Hz), 3.80 (3H, s), 2.35 (1H, m), 2.23 (1H, m), 2.09 (2H, m), 1.83 (3H, d, *J*=1.0 Hz), 1.57 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 199.50, 166.78, 158.30, 136.17, 128.71, 127.61, 113.91, 55.31, 43.37, 39.90, 34.48, 25.36, 21.23. IR (KBr plates): 2951, 1670, 1653, 1506, 1030 $cm^{-1}$.




**(*E*)-ethyl 4-(2-methyl-5-oxohex-3-en-2-yl)benzoate (Table 2, entry 6):** General procedure A was followed using (*E*)-5-methylhex-3-en-2-one (157 mg, 1.40 mmol), ethyl 4-bromobenzoate (229 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppe (16 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and toluene (4 mL) at 110 °C. The product was purified by column chromatography employing a 0-25% gradient of ethyl acetate in

hexanes to provide the title compound in a 52% yield (134 mg) as a colorless oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ: 7.98 (2H, d, *J*=6.5Hz), 7.34 (2H, d, *J*=6.5Hz), 6.89 (1H, d, *J*=16.5Hz), 6.06 (1H, d, *J*=16.0Hz), 4.34 (2H, q, *J*=7.0 Hz), 2.25 (3H, s), 1.47 (6H, s), 1.36 (3H, t, *J*=7.0 Hz). $^{13}$C NMR (125 MHz $CDCl_3$) δ: 198.90, 166.34, 155.18, 151.57, 129.76, 128.79, 127.81, 126.17, 60.93, 41.33, 27.76, 27.32, 14.37. IR (KBr plates): 3044, 2975, 2935, 1718, 1678, 1608, 1366, 1286, 1188, 1113, 1021, 857, 775, 708 cm$^{-1}$. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.75; H, 7.70.




**(*E*)-5-methyl-5-*o*-tolylhex-3-en-2-one (Table 2, entry 7)**: General procedure A was followed using (*E*)-5-methylhex-3-en-2-one (157 mg, 1.40 mmol), 2-bromotoluene (171 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), dppb (17 mg, 0.040 mmol), $Cs_2CO_3$ (489 mg, 1.50 mmol), and dioxane (4 mL) at 110 °C. The product was purified by column chromatography employing a 0-20% gradient of ethyl acetate in hexanes to provide the title compound in a 70% yield (142 mg) as a colorless oil. $^{1}$H NMR (500 MHz) δ: 7.39 (1H, dd, *J*=6.5, 2.0Hz), 7.22-7.15 (3H, m), 7.07 (1H, d, *J*=16.5Hz), 6.04 (1H, d, *J*=16.5Hz), 2.32 (3H, s), 2.26 (3H, s), 1.54 (6H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 199.08, 157.54, 144.14, 136.61, 132.51, 127.91, 126.94, 126.08, 125.89, 41.72, 28.44, 27.09, 22.40. IR (KBr plates): 3059, 2969, 2932, 2874, 1717, 1697, 1675, 1619, 1456, 1360, 1255, 984 cm$^{-1}$.

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
INOVA-500 "bullwinkle"

Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417206 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

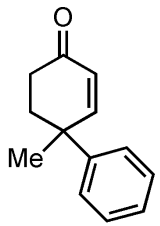
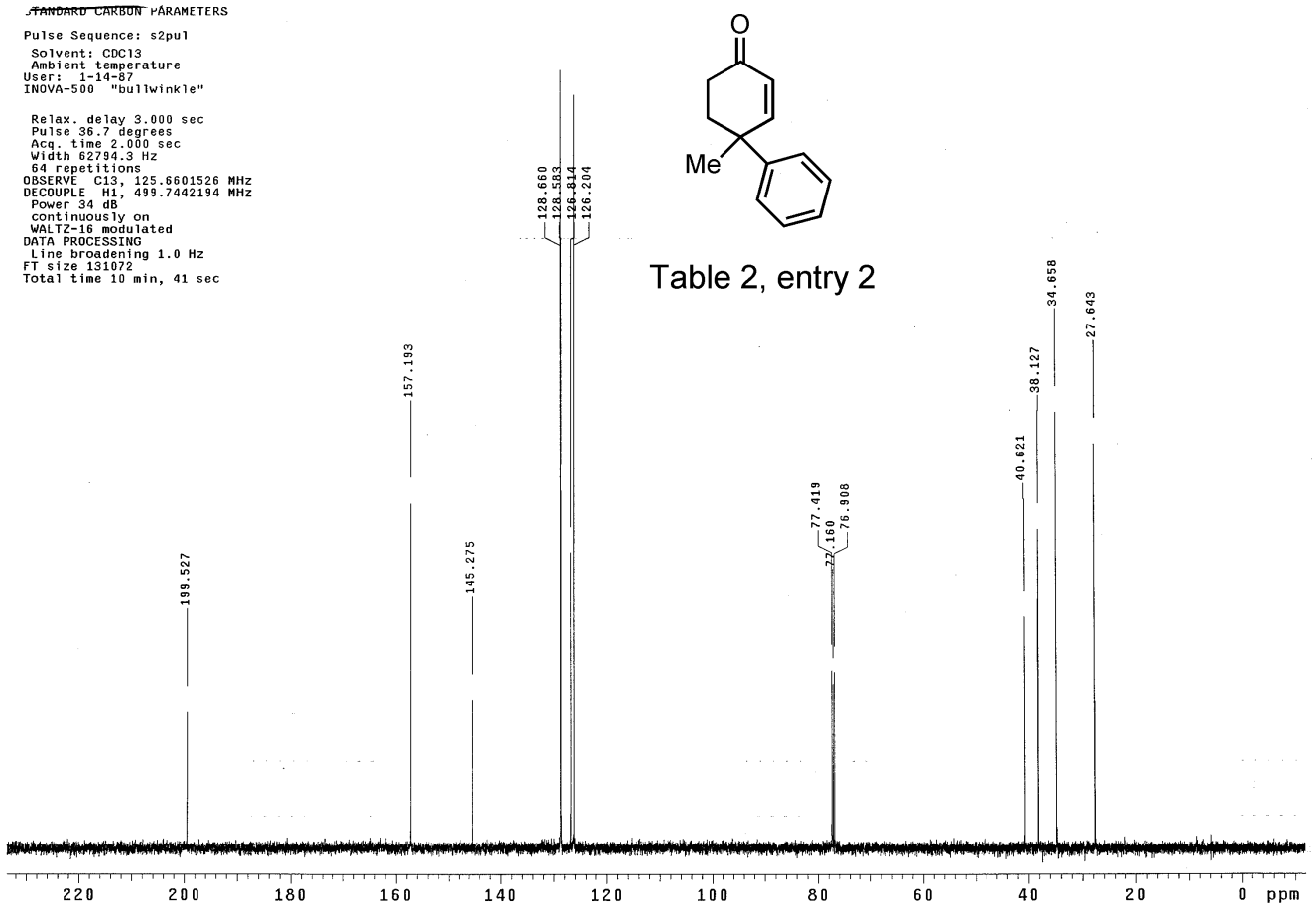



Table 2, entry 2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Ambient temperature
User: 1-14-87
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Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
64 repetitions
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DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
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160
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100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

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Ambient temperature
File: AMH-VI-68
INOVA-500 "zippy"

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Relax. delay 2.000 sec
Pulse 89.0 degrees
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8 repetitions
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DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

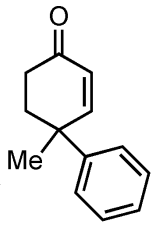


Table 2, entry 1

STANDARD PROTON PARAMETERS

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DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

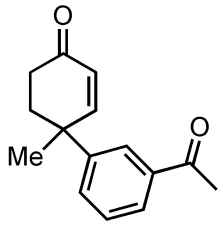
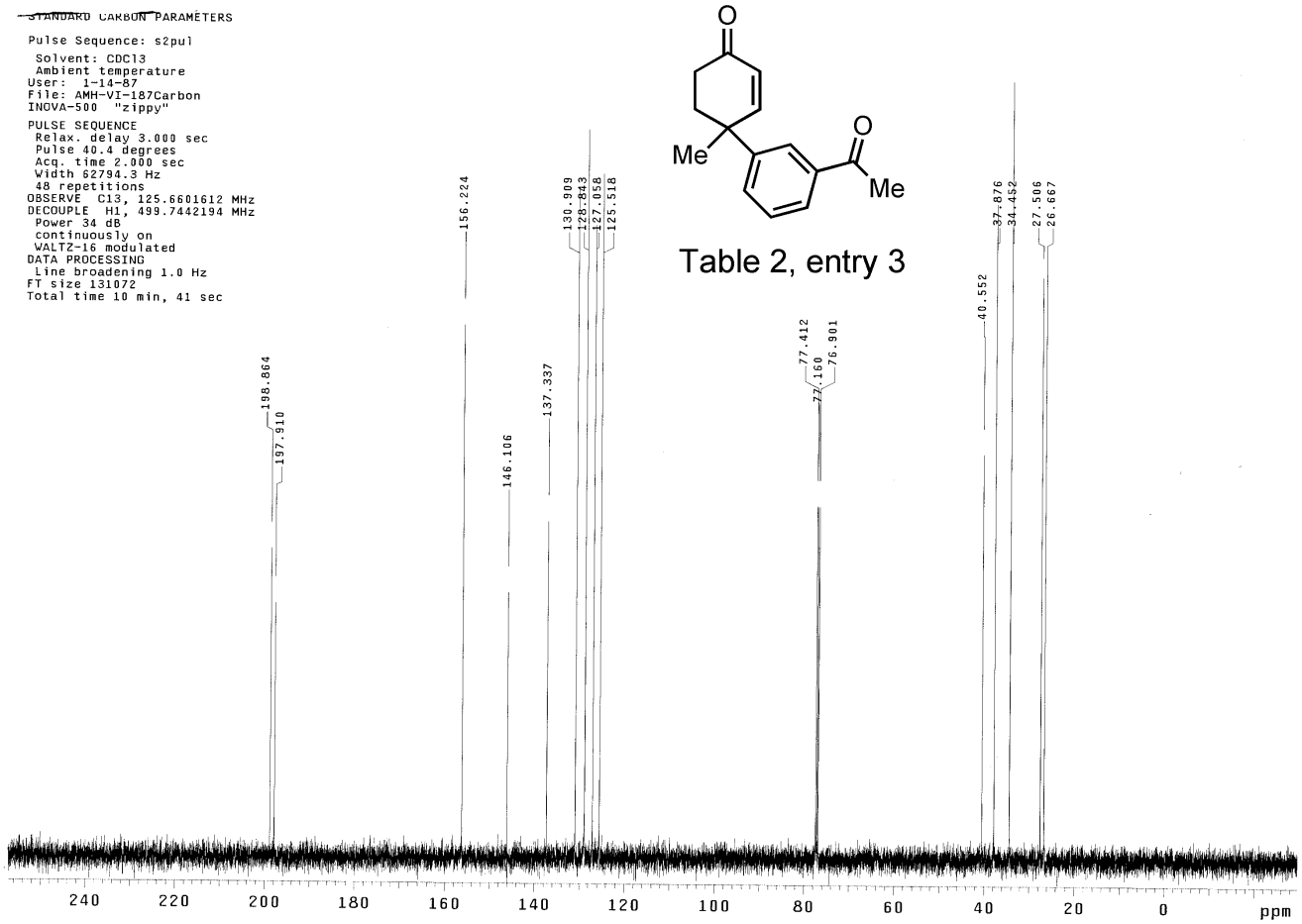



Table 2, entry 3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Ambient temperature
User: 1-14-87
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Pulse 40.4 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
48 repetitions
OBSERVE C13, 125.6601612 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec
O
Me
O
Me
Table 2, entry 3
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197.910
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40.552
37.876
34.452
27.506
26.667
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-VI-67
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
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DATA PROCESSING
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Total time 0 min, 40 sec

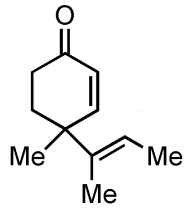
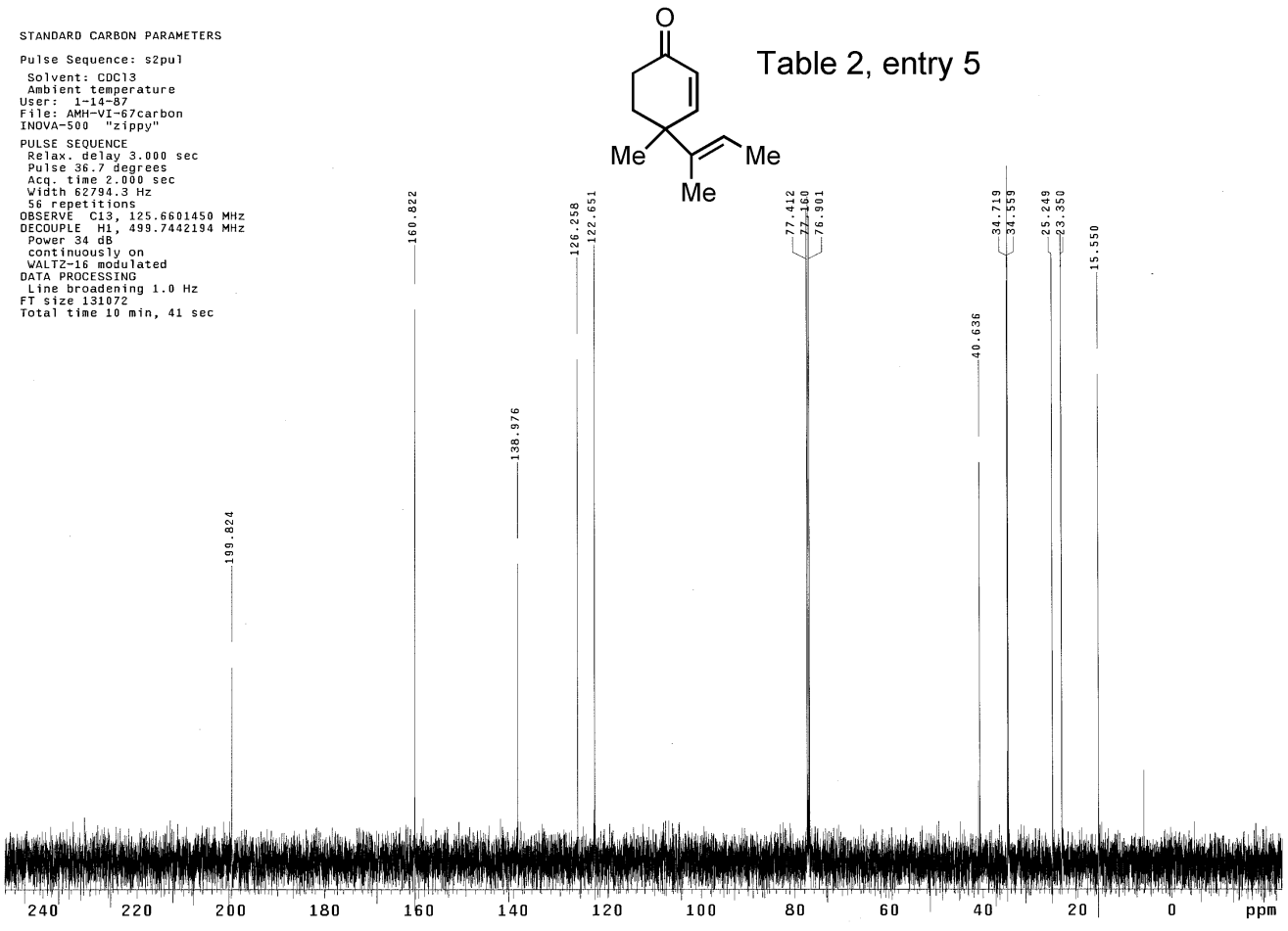



Table 2, entry 5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Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-67carbon
INOVA-500 "zippy"
PULSE SEQUENCE
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Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
56 repetitions
OBSERVE C13, 125.6601450 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec
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Me
Me
Me
Table 2, entry 5
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77.412
77.160
76.901
40.636
34.719
34.559
25.249
23.350
15.550
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-V-236
INOVA-500 "zippy"

PULSE SEQUENCE
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Pulse 89.0 degrees
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8 repetitions
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DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

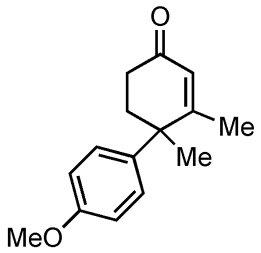
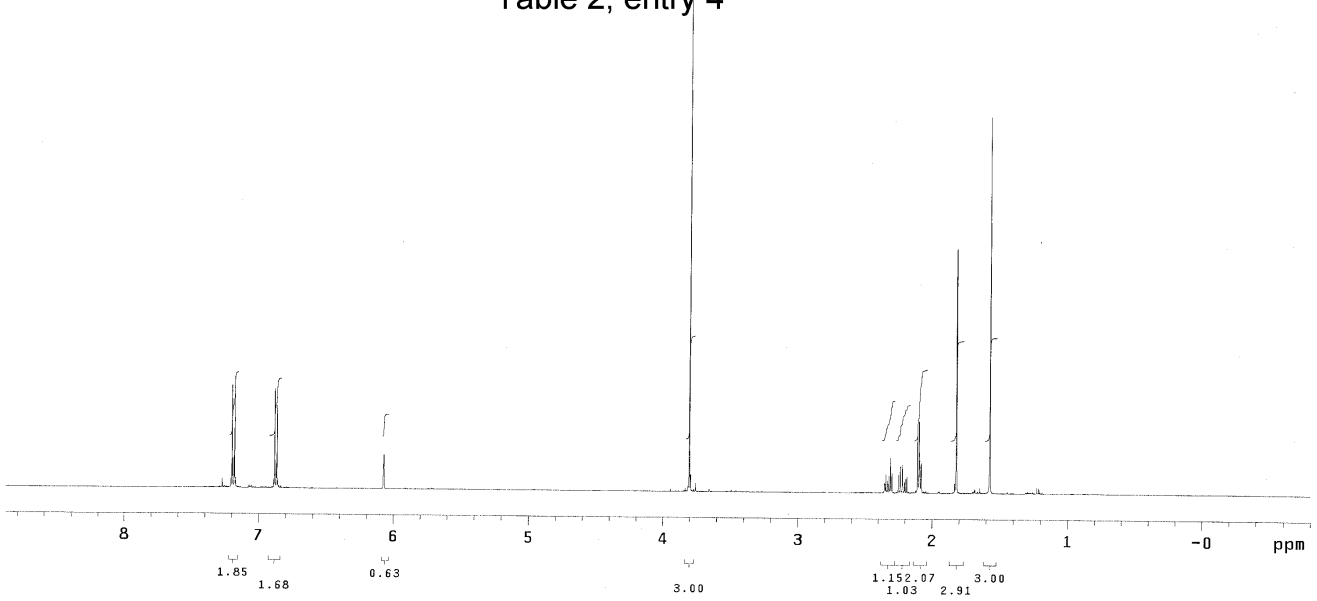
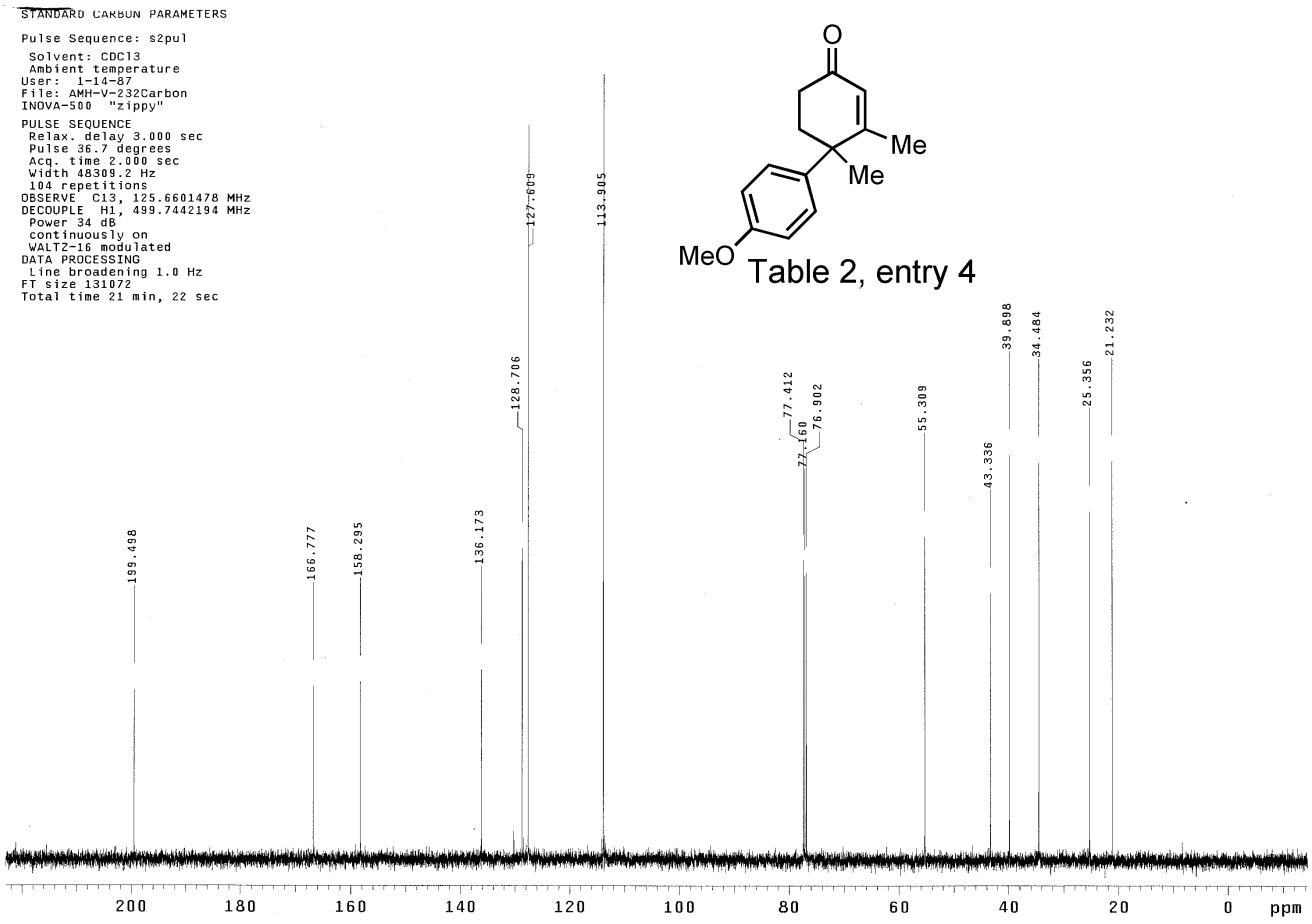



Table 2, entry 4




STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-V-232Carbon
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 48309.2 Hz
104 repetitions
OBSERVE C13, 125.6601478 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 21 min, 22 sec
O
Me
Me
MeO
Table 2, entry 4
199.498
166.777
158.295
136.173
128.706
127.609
113.905
77.412
77.160
76.902
55.309
43.336
39.898
34.484
25.356
21.232
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-VI-190b
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 94.4 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417184 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

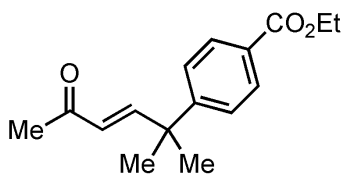
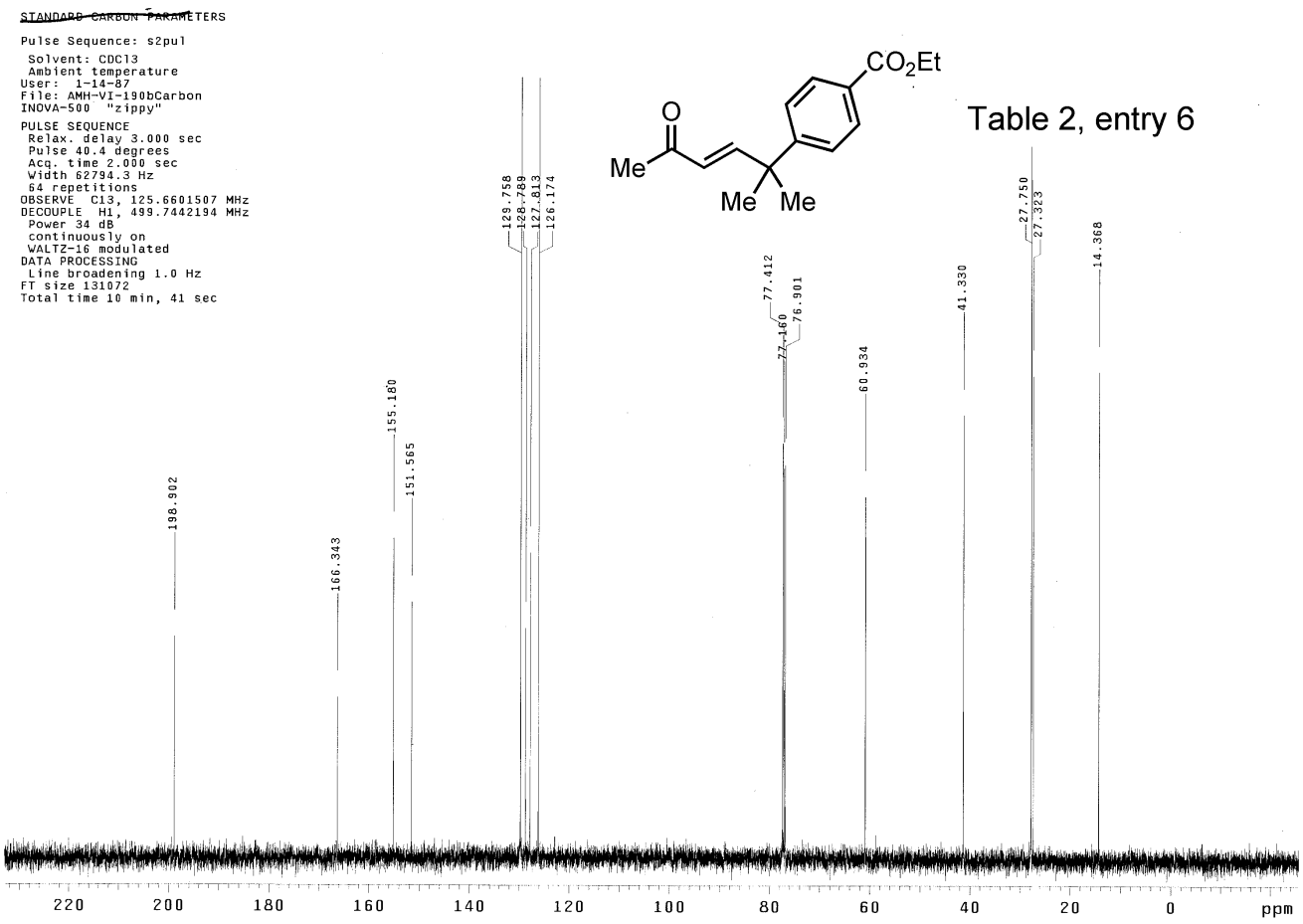



Table 2, entry 6


STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-190bCarbon
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 40.4 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
64 repetitions
OBSERVE C13, 125.6601507 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec
CO2Et
O
Me
Me Me
Table 2, entry 6
198.902
166.343
155.180
151.565
129.758
128.789
127.813
126.174
77.412
77.160
76.901
60.934
41.330
27.750
27.323
14.368
220
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: AMH-VI-27
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
8 repetitions
OBSERVE H1, 300.0986361 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 32 sec

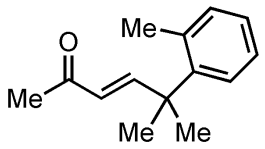



Table 2, entry 7

~~STANDARD CARBON PARAMETERS~~

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
INOVA-500 "bullwinkle"

Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
72 repetitions
OBSERVE C13, 125.6601545 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

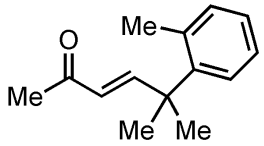
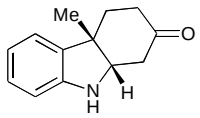
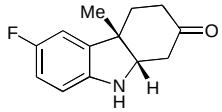


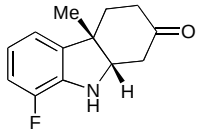

Table 2, entry 7




**4a-methyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 1)**: General procedure B was followed using 4-methylcyclohex-3-enone (154 mg, 1.4 mmol), 2-bromoaniline (172 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $Cs_2CO_3$ (815 mg, 2.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 10-35% gradient of ethyl acetate in hexanes to provide the title compound in a 83% yield (166 mg) as an off-white solid, m.p. = 97-101 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.05 (2H, m), 6.77 (1H, td, *J*=7.5, 1.0Hz), 6.58 (1H, d, *J*=8.0Hz), 4.00 (1H, m), 3.88 (1H, bs), 2.71 (1H, dd, *J*=16.0, 3.0 Hz), 2.56 (1H, dd, *J*=16.5, 3.5Hz), 2.23 (1H, dt, *J*=18.0, 4.5Hz), 2.13-2.06 (1H, m), 2.00-1.95 (2H, m), 1.48 (3H, s). $^{13}$C NMR (500 MHz, $CDCl_3$) δ: 212.02, 149.98, 135.64, 127.93, 122.84, 118.83, 109.03, 63.92, 43.51, 42.22, 36.04, 35.15, 27.91. IR (KBr plates): 3339, 2950, 1701, 1608, 1486, 741 cm$^{-1}$. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.28; H, 7.78.

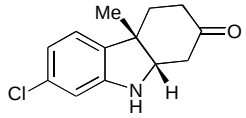



**6-fluoro-4a-methyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 2)**: General procedure B was followed using 4-methylcyclohex-3-enone (154 mg, 1.40 mmol), 2-bromo-4-fluoroaniline (190 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $K_2CO_3$ (346 mg, 2.50 mmol), and toluene (4 mL) at 110 °C. The product was purified by column chromatography employing a 15-50% gradient of ethyl acetate in hexanes to provide the title compound in a 63% yield (138 mg) as a beige solid, m.p. = 118-120 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ: 6.78-6.72 (2H, m), 6.47 (1H, m), 4.02 (1H, s), 3.82 (1H, bs), 2.67 (1H, dd, *J*=16.0, 3.0Hz), 2.54 (1H, dd, *J*=16.5, 3.8Hz), 2.24 (1H, dt, *J*=17.5, 4.0Hz), 2.12-2.05 (1H, m), 1.94 (2H, m), 1.45, (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.66, 157.20 (d, *J*=234Hz), 145.92, 137.50 (d, *J*=7.6Hz), 114.17 (d, *J*=22.9Hz), 110.27 (d, *J*=23.9Hz), 109.55 (d, *J*=8.6Hz), 64.70, 44.02, 42.28, 36.02, 35.08, 27.75. IR (KBr plates): 3325, 2968, 2956, 1705, 1491, 808 cm$^{-1}$.

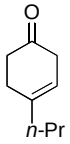



**8-fluoro-4a-methyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 3):** General procedure B was followed using 4-methylcyclohex-3-enone (154 mg, 1.40 mmol), 2-bromo-6-fluoroaniline (190 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $K_2CO_3$ (346 mg, 2.50 mmol), and toluene (4 mL) at 110

°C. The product was purified by column chromatography employing a 5-30% gradient of ethyl acetate in hexanes to provide the title compound in a 60% yield (131 mg) as a white solid, m.p. = 81-83 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ: 6.86-6.80 (2H, m), 6.68 (1H, m), 4.09 (1H, bs), 4.04 (1H, q, *J*=3.5 Hz), 2.68 (1H, dd, *J*=16.5, 3.5 Hz), 2.59 (1H, dd, *J*=16.5, 3.5 Hz), 2.23 (1H, dt, *J*=18.0, 4.0 Hz), 2.10-1.90 (3H, m), 1.46, (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.43, 148.42 (d, *J*=240 Hz), 139.43 (d, *J*=4 Hz), 137.00 (d, *J*=13 Hz), 119.55 (d, *J*=6 Hz), 118.40 (d, *J*=3 Hz), 114.52 (d, *J*=17 Hz), 64.82, 44.42 (d, *J*=2 Hz), 42.14, 36.05, 35.05, 27.87. IR (KBr plates): 3379, 2956, 1715, 1628, 1487, 1473 $cm^{-1}$. Anal. Calcd for $C_{13}H_{14}FNO$: C, 71.21; H, 6.44. Found: C, 71.40; H, 6.48.

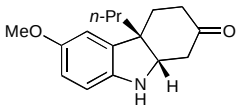



**7-chloro-4a-methyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 4)**: General procedure B was followed using 4-methylcyclohex-3-enone (154 mg, 1.4 mmol), 2-bromo-4-chloroaniline (207 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $K_2CO_3$ (346 mg, 2.50 mmol), and toluene (4 mL) at 110 °C. The product was purified by column chromatography employing a 15-50% gradient of ethyl acetate in hexanes to provide the title compound in a 63% yield (148 mg) as an off-white solid, m.p. = 144-147 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ: 6.99 (2H, m), 6.47 (1H, d, *J*=7.5Hz), 4.02 (1H, m), 3.92 (1H, bs), 2.68 (1H, dd, *J*=16.3, 3.3Hz), 2.55 (1H, dd, *J*=16.0, 3.5Hz), 2.24 (1H, dt, *J*=17.8, 3.8Hz), 2.10-2.05 (1H, m), 1.95 (2H, m) 1.45 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.59, 148.57, 147.07, 137.66, 127.85, 123.25, 109.92, 64.43, 43.88, 42.19, 35.99, 35.08, 27.89. IR (KBr plates): 3315, 2962, 1706, 1653, 1480, 1237, 807$cm^{-1}$.

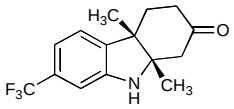



**4-propylcyclohex-3-enone**: To a flame dried 2L 3-neck round bottom flask with mechanical stirrer was added THF (160 mL), EtOH (33 mL), 4-*n*-propylanisole (20.6 g, 137 mmol) and purged with Ar. A Dry-ice condenser was attached and the flask and condenser were cooled to -78 °C with a dry ice-actone mixture. Liquid ammonia (500 mL) was then condensed in the flask by passing a stream of gaseous ammonia through the apparatus for 45 min. At this time, small pieces of Li wire (4.2 g) were added potionwise over 5 min. The resulting deep blue solution was vigorously stirred for 40 min at -78 °C followed by addition of EtOH (20 mL) and solid ammonium chloride (5.0 g). Once the blue color faded, the reaction was warmed to rt with a water bath and the ammonia was allowed to boil off. The residue was dissolved in $Et_2O/H_2O$ and the organic layer was washed with water (3x). The etheral solution was then dried with $MgSO_4$ and then concentrated with the aid of a rotary evaporator to give 1-methoxy-4-

propylcyclohexa-1,4-diene as a colorless oil. This material was dissolved in a 3:1 MeOH/$H_2O$ solution (350 mL) in a 1L round bottom flask. Oxalic acid (650 mg, 7.22 mmol) was added and the reaction was stirred at rt for 2 h. The solution was then diluted with water and extracted with dichloromethane (4x). The organic layer was washed with water (2x), dried over $MgSO_4$, and concentrated by rotary evaporator. The crude product was purified by flash chromatography on silica gel, eluting with 87:13 hexanes/ethyl acetate to provide the title compound in 73% yield (13.8 g) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) δ: 5.44 (1H, s), 2.86 (2H, s), 2.48 (2H, t, *J*=6.5Hz), 2.39 (2H, t, *J*=7.0Hz), 2.04 (2H, t, *J*=7.5Hz), 1.45 (2H, m), 0.91 (3H, t, *J*=7.5Hz). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.44, 138.83, 117.86, 39.77, 39.31, 38.86, 28.61, 20.84, 13.90. IR (KBr plates): 2959, 2734, 1718, 1457, 1337, 1191, 970, 894 cm$^{-1}$.

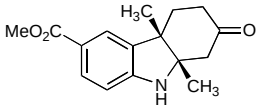



**6-methoxy-4a-propyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 5)** : General procedure B was followed using 4-propylcyclohex-3-enone (193 mg, 1.4 mmol), 2-bromo-4-methoxyaniline[4] (202 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $Cs_2CO_3$ (815 mg, 2.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 15-40% gradient of ethyl acetate in hexanes to provide the title compound in a 71% yield (190 mg) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ: 6.61 (2H, m), 6.48 (1H, d, *J*=7.5Hz), 4.13 (1H, m), 3.77 (3H, s), 3.62 (1H, bs), 2.63 (1H, dd, *J*=16.0, 3.5Hz), 2.52 (1H, dd, *J*=16.3, 3.8Hz), 2.23 (1H, m), 2.11-1.99 (2H, m), 1.90 (1H, s), 1.76 (1H, m), 1.66 (1H, m) 1.41 (1H, m), 1.25 (1H, m), 0.92 (3H, t, *J*=7.3Hz). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 212.32, 153.50, 144.38, 135.67, 112.63, 110.31, 109.60, 61.11, 55.89, 48.11, 43.30, 43.08, 36.00, 33.57, 17.62, 14.66. IR (KBr plates): 3364, 2956, 1715, 1653, 1494, 1214, 1034 cm$^{-1}$.

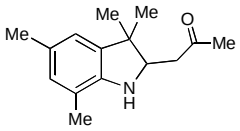



**4a,9a-dimethyl-7-(trifluoromethyl)-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 3, entry 6):** General procedure B was followed using 3,4-dimethylcyclohex-3-enone (174 mg, 1.40 mmol), 2-bromo-5-(trifluoromethyl)aniline (240 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $K_2CO_3$ (346 mg, 2.50 mmol), and toluene (4 mL) at 110 °C. The product was purified by column chromatography employing a 8-35% gradient of ethyl acetate in hexanes to provide the title compound in a 48% yield (135 mg) as yellow oil which crystallized upon standing, m.p. = 108-112 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.12 (1H, d, *J*=7.5Hz), 7.01 (1H, d, *J*=7.5Hz), 6.74 (1H, s), 3.82 (1H, bs), 2.65 (1H, d, *J*=16.0Hz), 2.48 (1H, d, *J*=16.0Hz), 2.26-2.12 (2H, m) 1.96 (2H, m), 1.40 (3H, s), 1.28 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$)

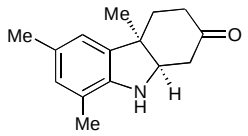
δ: 211.29, 149.03, 139.40, 130.39 (q, *J*=32Hz), 126.62 (q, *J*=271Hz), 123.25, 121.21, 116.02, 115.99, 105.61, 67.14, 49.15, 45.73, 36.71, 36.14, 24.72, 22.58. IR (KBr plates): 3395, 1716, 1653, 1457, 1320, 1161, 1118 $cm^{-1}$. Anal. Calcd for $C_{15}H_{16}F_3NO$: C, 63.60; H, 5.69. Found: C, 63.63; H, 5.72.



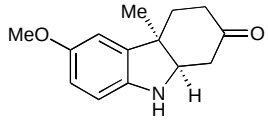

**methyl 4a,9a-dimethyl-2-oxo-2,3,4,4a,9,9a-hexahydro-1*H*-carbazole-6-carboxylate (Table 3, entry 7)**: General procedure B was followed using 3,4-dimethylcyclohex-3-enone (174 mg, 1.40 mmol), methyl 4-amino-3-bromobenzoate (230 mg, 1.00 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), dippf (16.7 mg, 0.040 mmol), $K_2CO_3$ (346 mg, 2.50 mmol), and toluene (4 mL) at 110 °C. The product was purified by column chromatography employing a 15-50% gradient of ethyl acetate in hexanes to provide the title compound in a 68% yield (185 mg) as yellow oily solid. $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.74 (1H, dd, *J*=8.5, 1.8Hz), 7.69 (1H, d, *J*=1.5Hz), 6.43 (1H, d, *J*=8.5Hz), 4.40 (1H, s) 3.82, (3H, s), 2.64 (1H, d, *J*=16.0Hz), 2.43 (1H, d, *J*=16.0Hz), 2.17 (1H, dt, *J*=17.5, 3.8Hz), 2.10 (1H, m), 1.93 (2H, m), 1.37 (3H, s), 1.22 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.43, 167.29, 153.03, 135.08, 131.30, 124.97, 120.05, 107.73, 67.07, 51.63, 49.13, 45.82, 36.71, 36.04, 24.81, 22.81. IR (KBr plates): 3343, 2951, 1708, 1610, 1435, 1291, 1220, 1110 $cm^{-1}$.




**1-(3,3,5,7-tetramethylindolin-2-yl)propan-2-one (Table 3, entry 8)**: General procedure B was followed using 5-methylhex-4-en-2-one[5] (157 mg, 1.40 mmol), 2-bromo-4,6-dimethylaniline (200 mg, 1.00 mmol), $Pd_2(dba)_3$ (9 mg, 0.010 mmol), dippf (17 mg, 0.040 mmol), $Cs_2CO_3$ (815 mg, 2.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0-25% gradient of ethyl acetate in hexanes to provide the title compound in a 70% yield (162 mg) as yellow oil which solidified upon standing, m.p. = 78-84 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ: 6.72 (2H, s), 4.27 (1H, bs), 3.74 (1H, dd, *J*=8.0, 5.0Hz), 2.75 (2H, m), 2.27 (3H, s), 2.26 (3H, s) 2.13 (3H, s), 1.30 (3H, s), 1.05 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 208.68, 145.34, 137.88, 129.03, 128.42, 120.07, 118.92, 64.66, 43.95, 43.19, 30.56, 25.98, 23.30, 20.90, 16.63. IR (KBr plates): 2958, 1717, 1559, 1457, 1167 $cm^{-1}$. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15. Found: C, 78.00; H, 9.04.




**(4a*R*,9a*R*)-4a,6,8-trimethyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 4, entry 1)**: General procedure C was followed using 4-methylcyclohex-3-enone (154 mg, 1.4 mmol), 2-bromo-4,6-dimethylaniline (200 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), (R)-DTBM-SEGPHOS (47 mg, 0.040 mmol), $K_3PO_4$ (531 mg, 2.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 0-30% gradient of ethyl acetate in hexanes to provide the title compound in a 51% yield (117 mg) as a pale yellow oil which solidified upon standing, m.p. = 145 °C (dec). $^1$H NMR (500 MHz, $CDCl_3$) δ: 6.76 (1H, s), 6.75 (1H, s), 3.99 (1H, t, *J*=3.5Hz), 3.67 (1H, bs), 2.71 (1H, dd, *J*=16.0, 3.5Hz), 2.59 (1H, dd, *J*=16.0, 3.5Hz), 2.78 (3H, s), 2.23 (1H, dt, *J*=17.5, 4.0Hz), 2.14-2.07 (1H, m), 2.08 (3H, s), 2.00-1.90 (2H, m), 1.47 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 212.24, 146.21, 135.40, 129.60, 128.52, 120.91, 118.55, 64.24, 43.91, 42.44, 36.24, 35.28, 27.98, 20.87, 16.70. IR (KBr plates): 3447, 1700, 1653, 1559, 1457 cm$^{-1}$. $\alpha_D$ (589nm $CHCl_3$) = +22.5 (c = 0.069 g/mL in chloroform). A crystal suitable for X-ray diffraction was grown by vapor diffusion of hexane into an ethyl acetate solution of **5** at room temperature.




**(4a*R*,9a*R*)-6-methoxy-4a-methyl-4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (Table 4, entry 2)**: General procedure C was followed using 4-methylcyclohex-3-enone (154 mg, 1.40 mmol), 2-bromo-4-methoxyaniline[4] (202 mg, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), (R)-DTBM-SEGPHOS (47 mg, 0.040 mmol), $K_3PO_4$ (531 mg, 2.50 mmol), and toluene (4 mL) at 100 °C. The product was purified by column chromatography employing a 15-40% gradient of ethyl acetate in hexanes to provide the title compound in a 37% yield (86 mg) as yellow solid, m.p. = 104 °C (dec). $^1$H NMR (500 MHz, $CDCl_3$) δ: 6.67 (1H, d, *J*=2.5Hz), 6.63 (1H, dd, *J*=8.0, 2.5Hz), 6.51 (1H, d, *J*=8.5Hz), 3.98 (1H, t, *J*=3.5Hz), 3.76 (3H, s), 3.71 (1H, bs), 2.67 (1H, dd, *J*=16.3, 3.3Hz), 2.54 (1H, dd, *J*=16.0, 3.5Hz), 2.22 (1H, dt, *J*=17.6, 4.3Hz), 2.14-2.07 (1H, m), 2.00-1.93 (2H, m), 1.45 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 211.95, 153.81, 143.80, 137.54, 112.84, 109.94, 109.89, 64.69, 56.01, 44.13, 42.47, 36.19, 35.20, 27.82. IR (KBr plates): 2952, 1717, 1700, 1653, 1559, 1221, 1031 cm$^{-1}$. $\alpha_D$ (589nm $CHCl_3$) = +34.6 (c = 0.0059 g/mL in chloroform). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.54; H, 7.48.

References


1. E. J. Corey; D. S. Watt, *J. Am. Chem. Soc*. **1973**, *95*, 2303.
2. M. E. Hoke; M. Brescia; S. Bogaczyk; P. DeShong; B. W. King; M. T. Crimmins, *J. Org. Chem.* **2002**, *67*, 327.
3. J. B. Lambert; D. E. Marko, *J. Am. Chem. Soc*. **1985**, *107*, 7978.
4. H. Ishibashi; T. Kobayashi; N. Machida; O. Tamura, *Tetrahedron* **2000**, *56*, 1469.
5. S. Allenmark; K. Kalén, *Tetrahedron Lett*. **1975**, *16*, 3175.

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-V-242
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417188 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

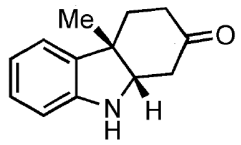



Table 3, entry 1

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-13carbon
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
32 repetitions
OBSERVE C13, 125.6601680 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

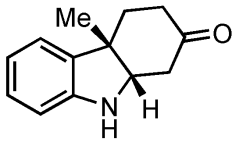
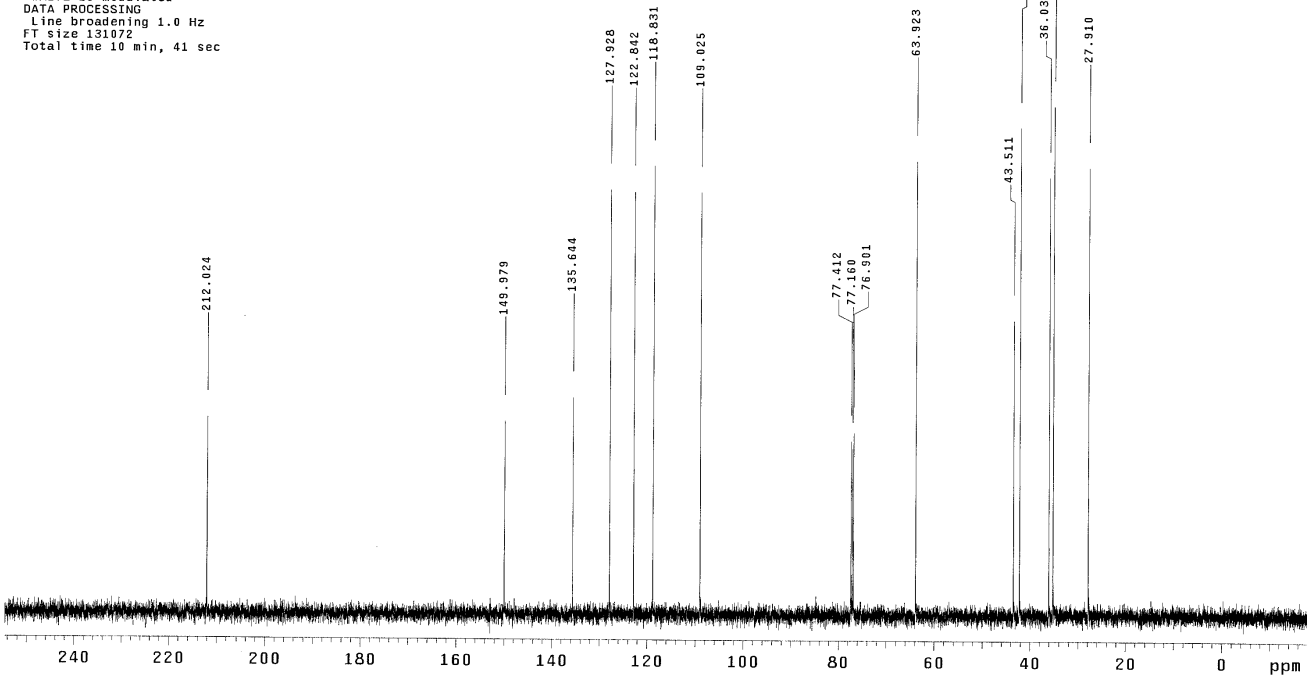



Table 3, entry 1



STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-V-287
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417191 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

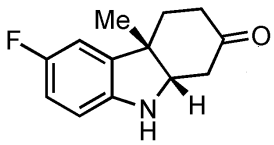



Table 3, entry 2

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
INOVA-500 "bullwinkle"

Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
128 repetitions
OBSERVE C13, 125.6601526 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

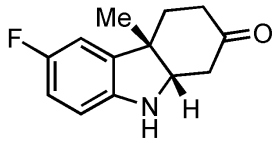



Table 3, entry 2

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
INOVA-500 "bullwinkle"

Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417192 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

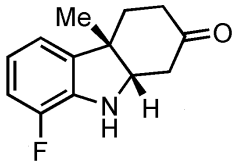



Table 3, entry 3

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-96carbon
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
72 repetitions
OBSERVE C13, 125.6601555 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

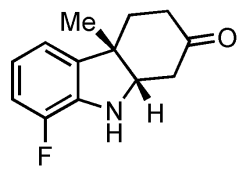
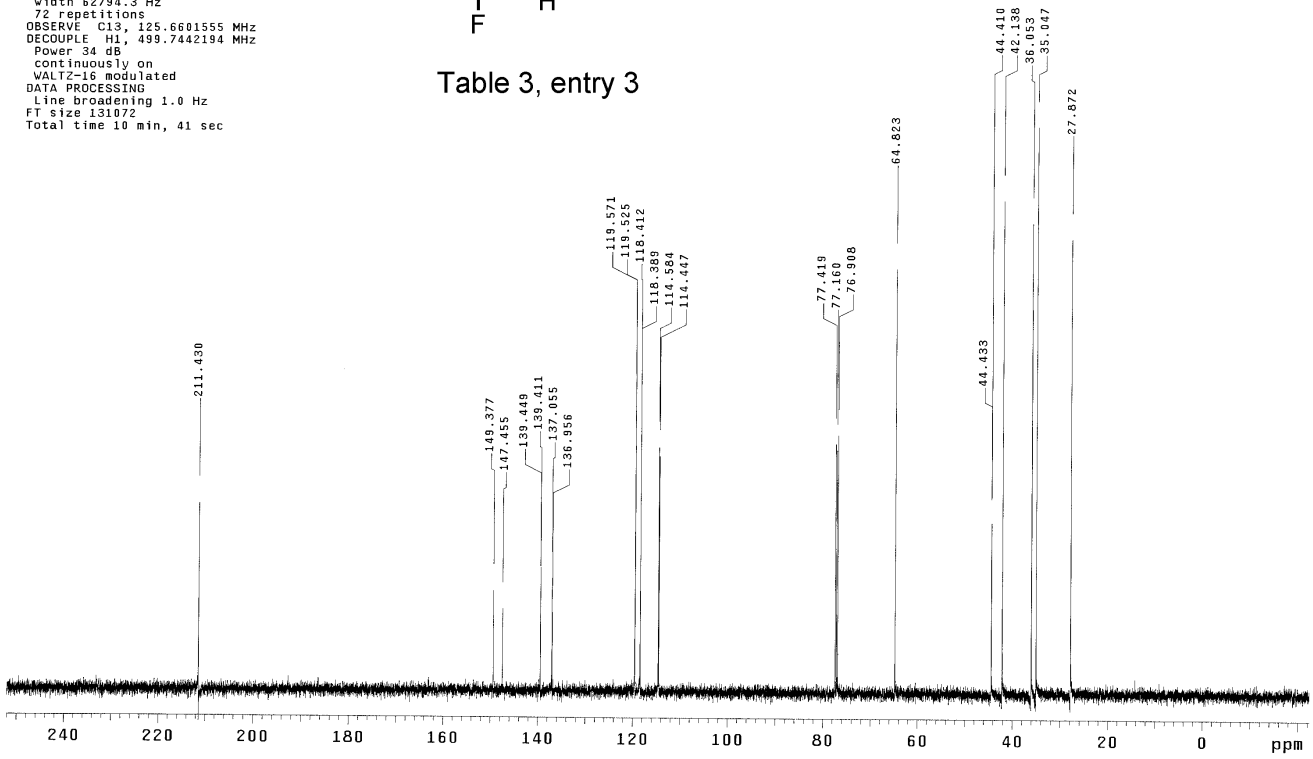



Table 3, entry 3



STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-VI-9
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417182 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

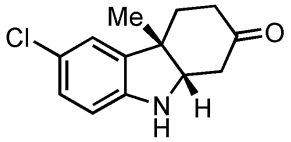
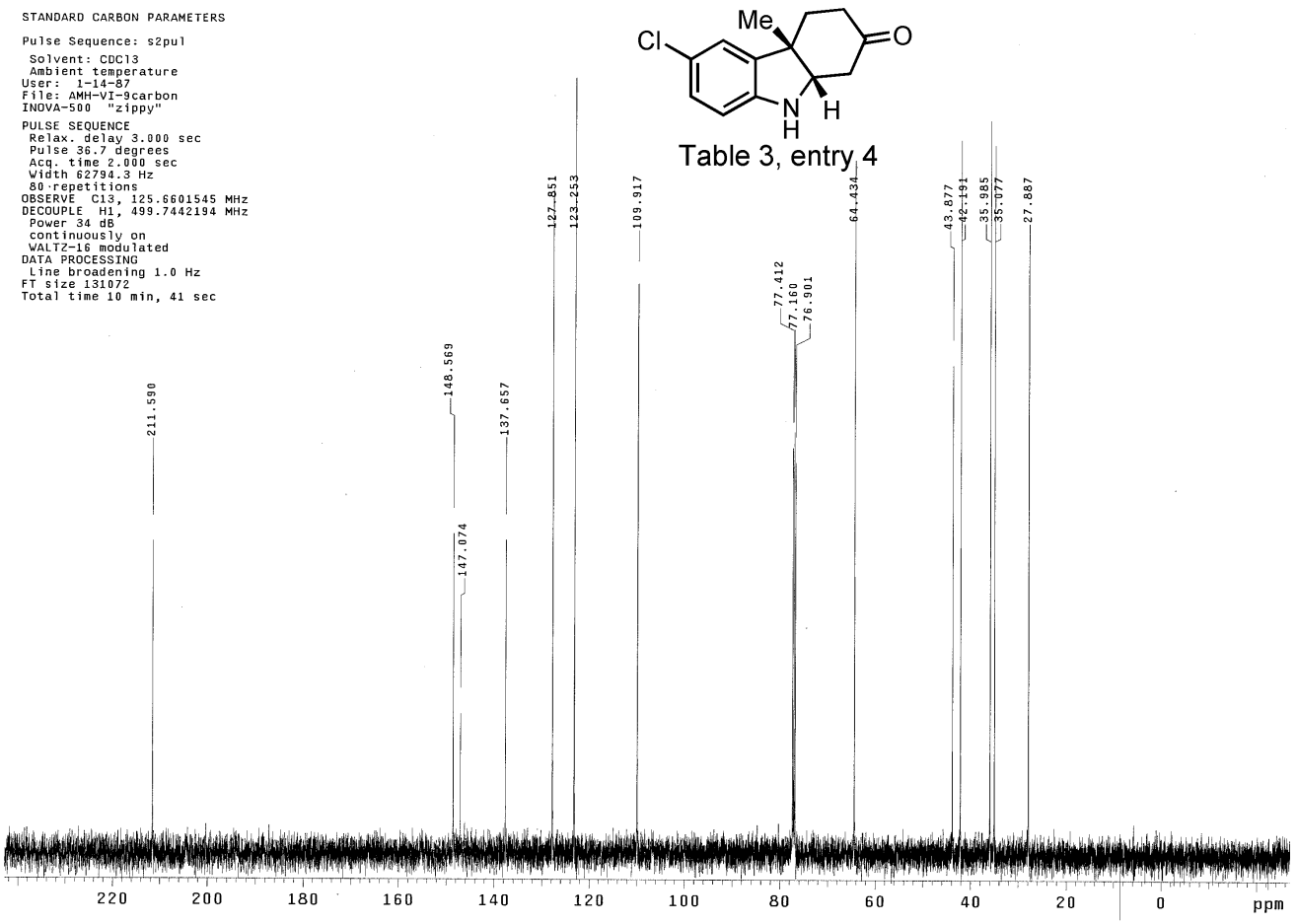



Table 3, entry 4


STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-9carbon
INOVA-500 "z1ppy"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
80 repetitions
OBSERVE C13, 125.6601545 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec
Me
Cl
O
N H
H
Table 3, entry 4
211.590
148.569
147.074
137.657
127.851
123.253
109.917
77.412
77.160
76.901
64.434
43.877
42.191
35.985
35.077
27.887
220
200
180
160
140
120
100
80
60
40
20
0
ppm

~~STANDARD PROTON~~ PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
INOVA-500 "bullwinkle"

Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417199 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

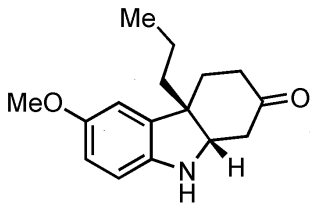



Table 3, entry 5

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-22carbon
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
64 repetitions
OBSERVE C13, 125.6601555 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

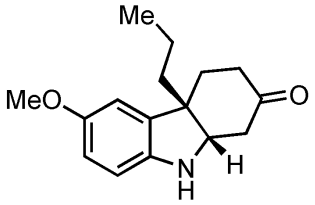
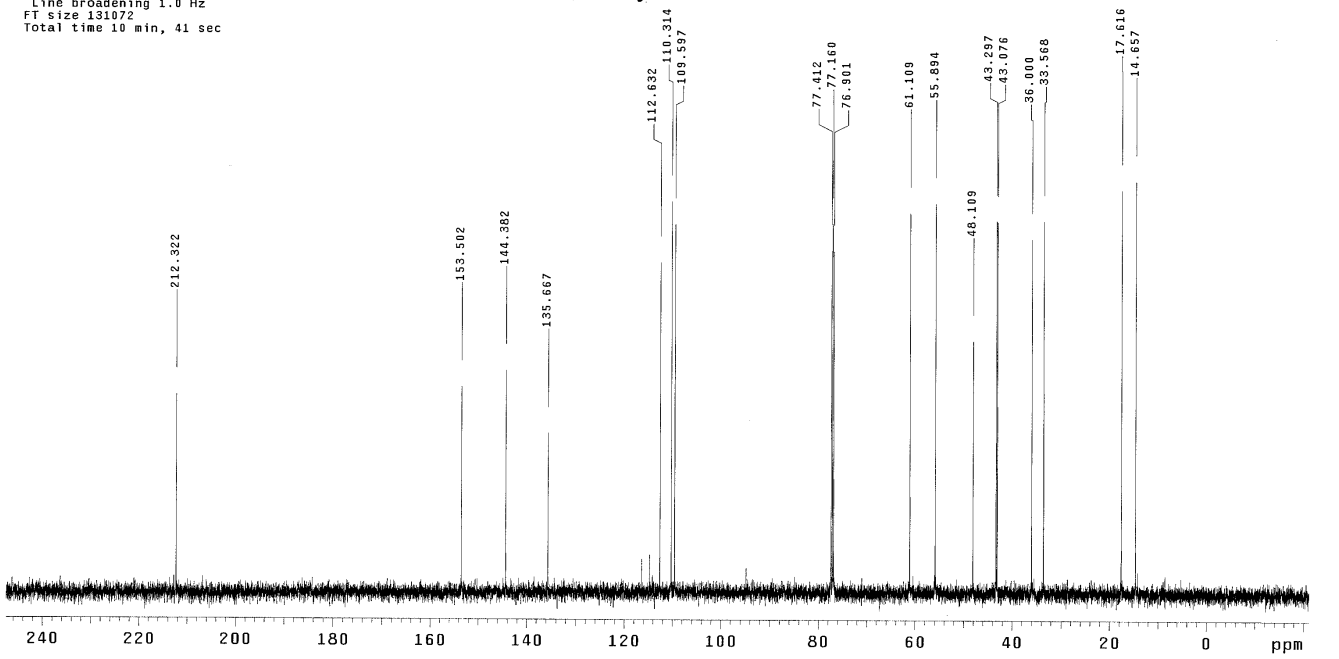



Table 3, entry 5



STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Temp. 20.0 C / 293.1 K
File: AMH-VI-2
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417190 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

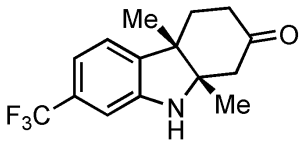



Table 3, entry 6

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-2carbon
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
112 repetitions
OBSERVE C13, 125.6601498 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

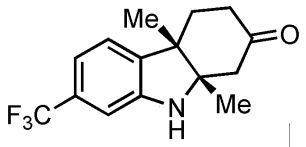
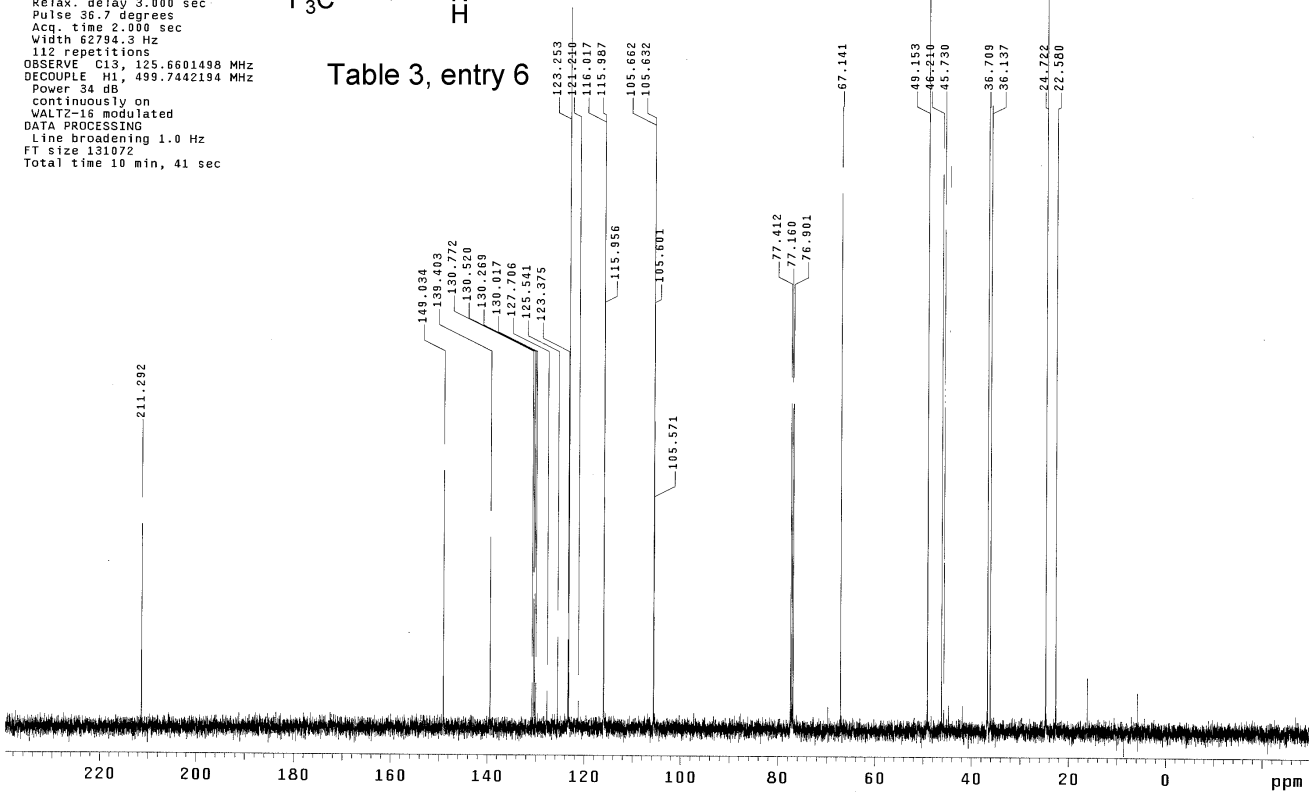



Table 3, entry 6



new experiment

Pulse Sequence: presat
Solvent: CDCl3
Ambient temperature
INOVA-500 "bullwinkle"

Relax. delay 20.000 sec
Pulse 94.4 degrees
Acq. time 3.000 sec
Width 4404.3 Hz
Single scan
OBSERVE H1, 499.7417206 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 52 sec

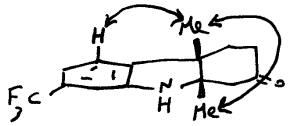



Table 3, entry 6

STANDARD PROTON PARAMETERS
Solvent: CDCl3
Ambient temperature
INOVA-500 "rocky"

PULSE SEQUENCE
Pulse 91.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 500.2312741 MHz
DATA PROCESSING
FT size 131072
Total time 1 minute

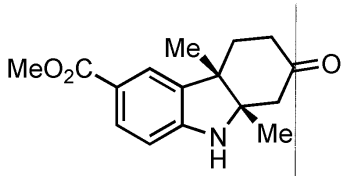
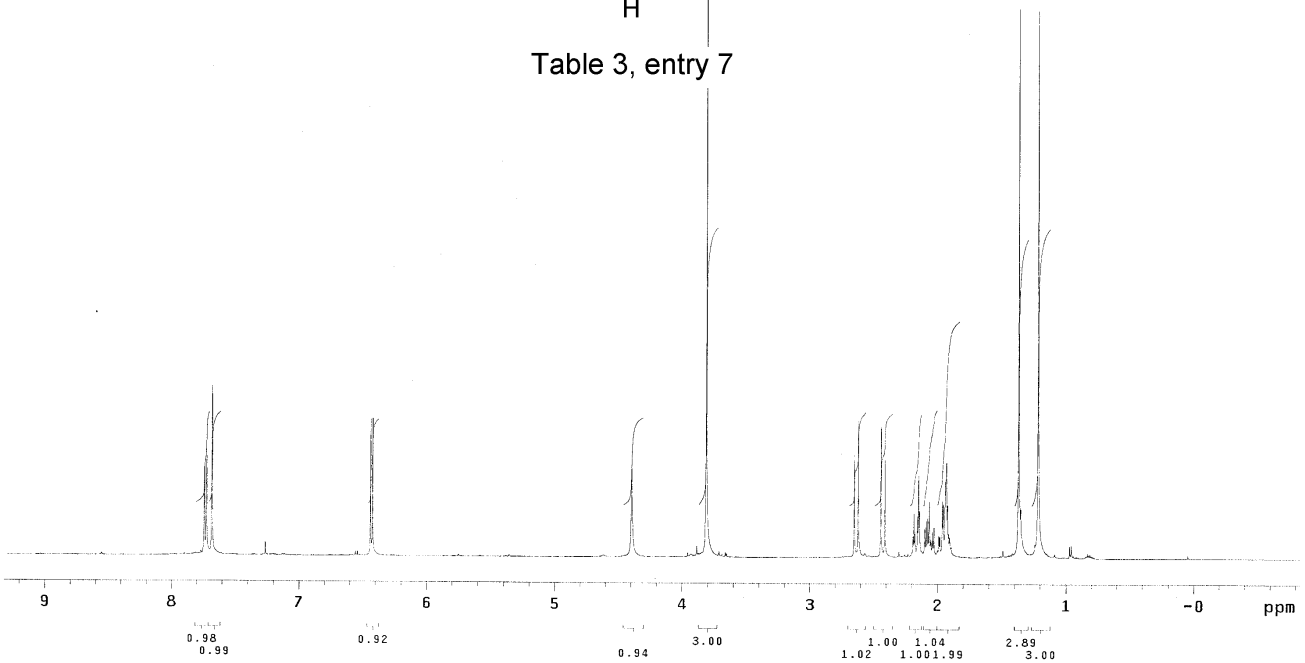
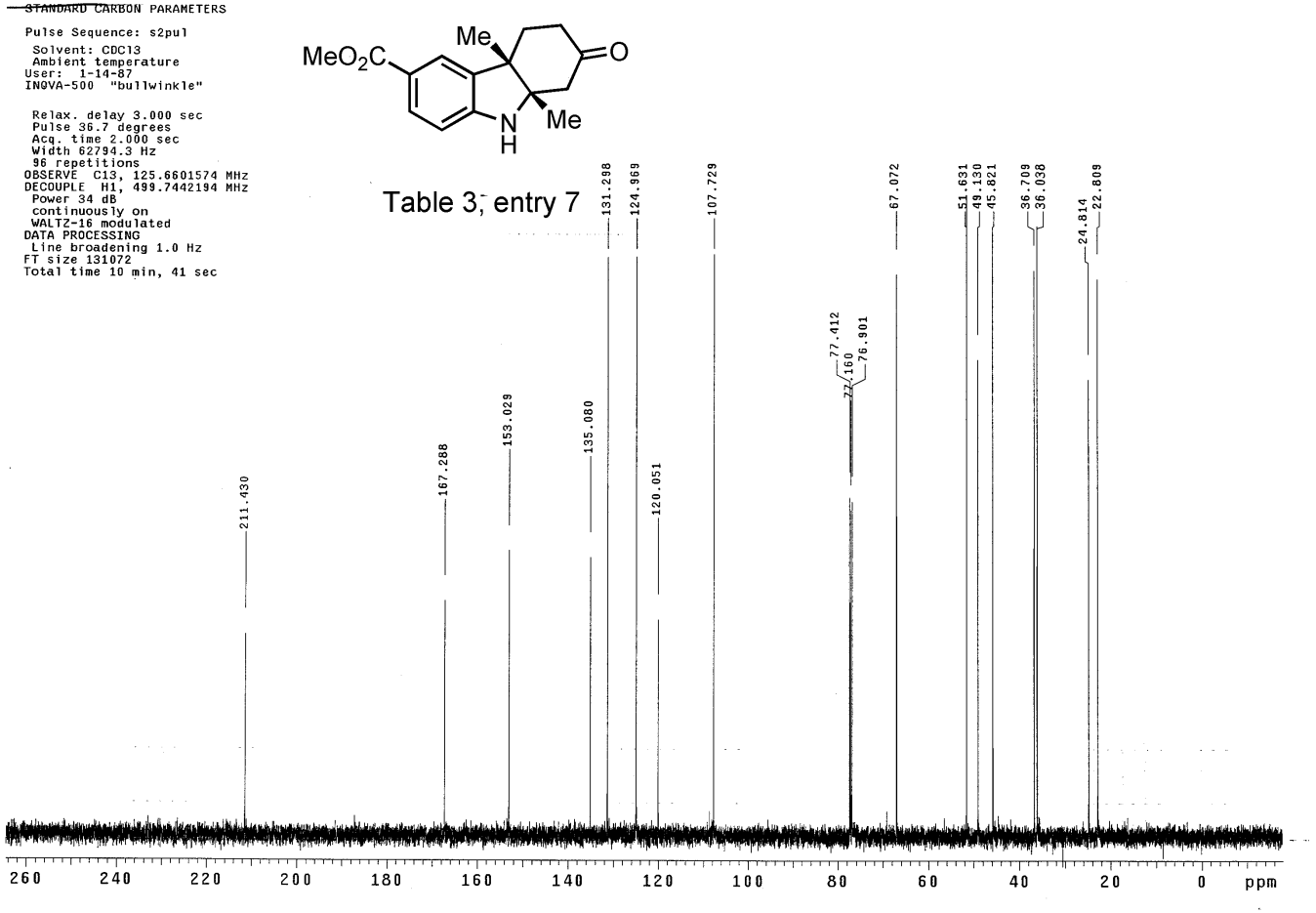



Table 3, entry 7




STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
INOVA-500 "bullwinkle"
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
96 repetitions
OBSERVE C13, 125.6601574 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec
MeO2C
Me
O
N
H
Me
Table 3, entry 7
211.430
167.288
153.029
135.080
131.298
124.969
120.051
107.729
77.412
77.160
76.901
67.072
51.631
49.130
45.821
36.709
36.038
24.814
22.809
260
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Temp. 22.0 C / 295.1 K
INOVA-500 "bullwinkle"

Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417179 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

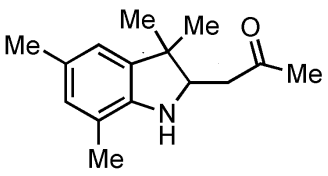
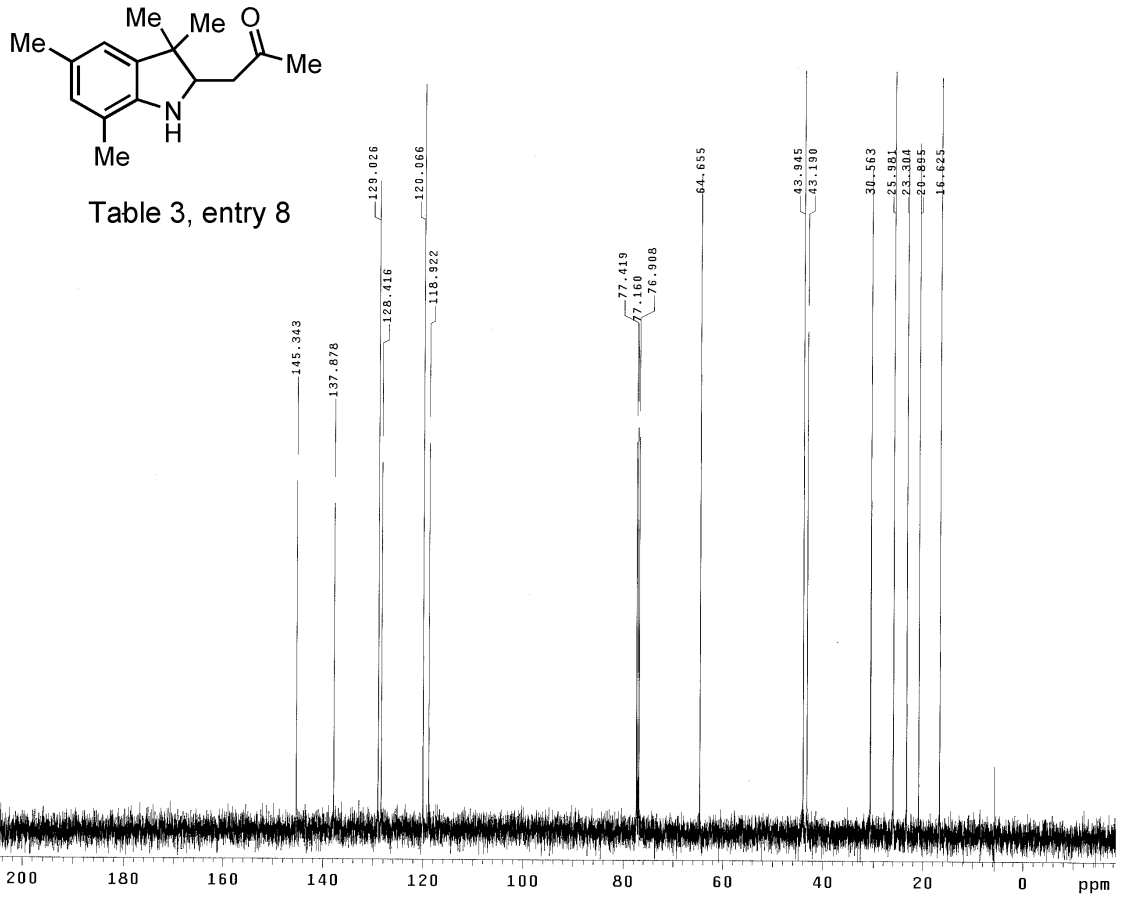



Table 3, entry 8


Me
Me
Me
O
Me
N
H
Me
Table 3, entry 8
208.677
145.343
137.878
129.026
128.416
120.066
118.922
77.419
77.160
76.908
64.655
43.945
43.190
30.563
25.981
23.304
20.895
16.625
220
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-VI-70
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417174 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

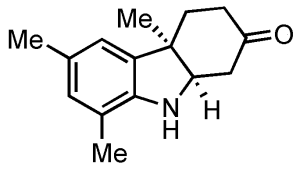



Table 4, entry 1

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-VI-95carbon
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 36.7 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
32 repetitions
OBSERVE C13, 125.6601584 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

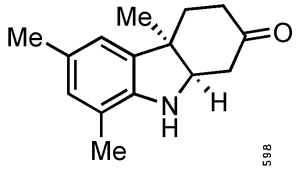



Table 4, entry 1

Data File C:\CHEM32\2\DATA\ALAN\AMH-VI-70.D
Sample Name: AMH-VI-70

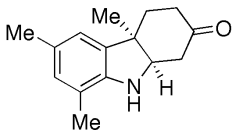
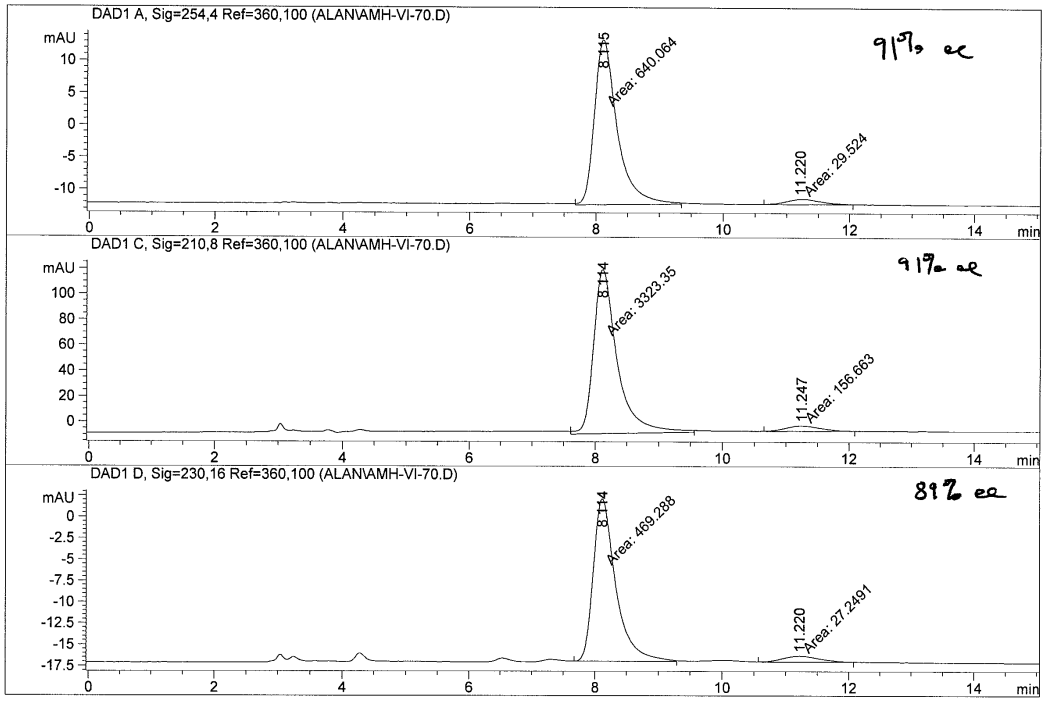



Table 4, entry 1

```
==========================================================================
Acq. Operator    : Alan
Acq. Instrument  : Instrument 2                    Location : Vial 21
Injection Date   : 6/9/2007 10:50:13 AM
                                                   Inj Volume : 2 µl
Acq. Method      : C:\CHEM32\1\METHODS\BB964-1.M
Last changed     : 6/7/2007 6:39:34 PM by BB
Analysis Method  : C:\CHEM32\2\DATA\AM\139-OC.D\DA.M (AM9010-1.M)
Last changed     : 9/25/2007 1:49:11 PM by ANA
                   (modified after loading)
Method Info      : 90% n-Hexane
                   10% i-propanol
                   1 mll/min
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: AMH-VI-100b
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 94.4 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
8 repetitions
OBSERVE H1, 499.7417188 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 40 sec

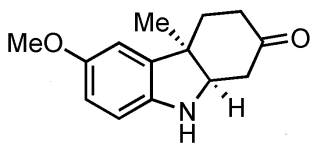
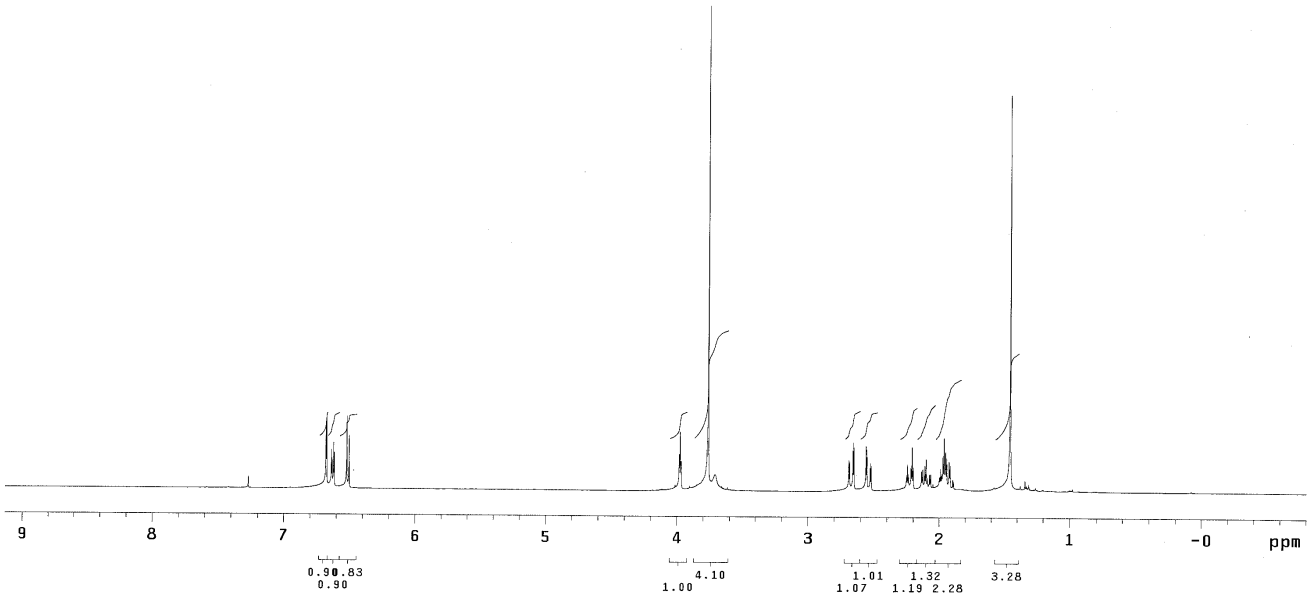



Table 4, entry 2



STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
User: 1-14-87
File: AMH-100bCarbon
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 40.4 degrees
Acq. time 2.000 sec
Width 62794.3 Hz
80 repetitions
OBSERVE C13, 125.6601469 MHz
DECOUPLE H1, 499.7442194 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 41 sec

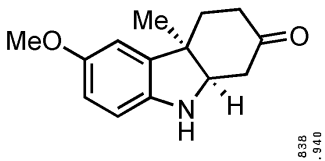



Table 4, entry 2

Data File C:\CHEM32\2\DATA\ALAN\AMH-VI-87.D
Sample Name: AMH-VI-87

```
==========================================================================
Acq. Operator   : ALAN
Acq. Instrument : Instrument 2                    Location : Vial 42
Injection Date  : 6/13/2007 7:08:53 PM
                                                  Inj Volume : 1 µl
Acq. Method     : C:\CHEM32\1\METHODS\AMH.M
Last changed    : 6/13/2007 5:05:30 PM by ALAN
Analysis Method : C:\CHEM32\2\DATA\AM\139-OC.D\DA.M (AM9010-1.M)
Last changed    : 9/25/2007 1:42:54 PM by ANA
                  (modified after loading)
Method Info     : 90% n-Hexane
                  10% i-propanol
                  1 mll/min
```

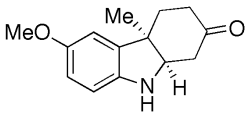
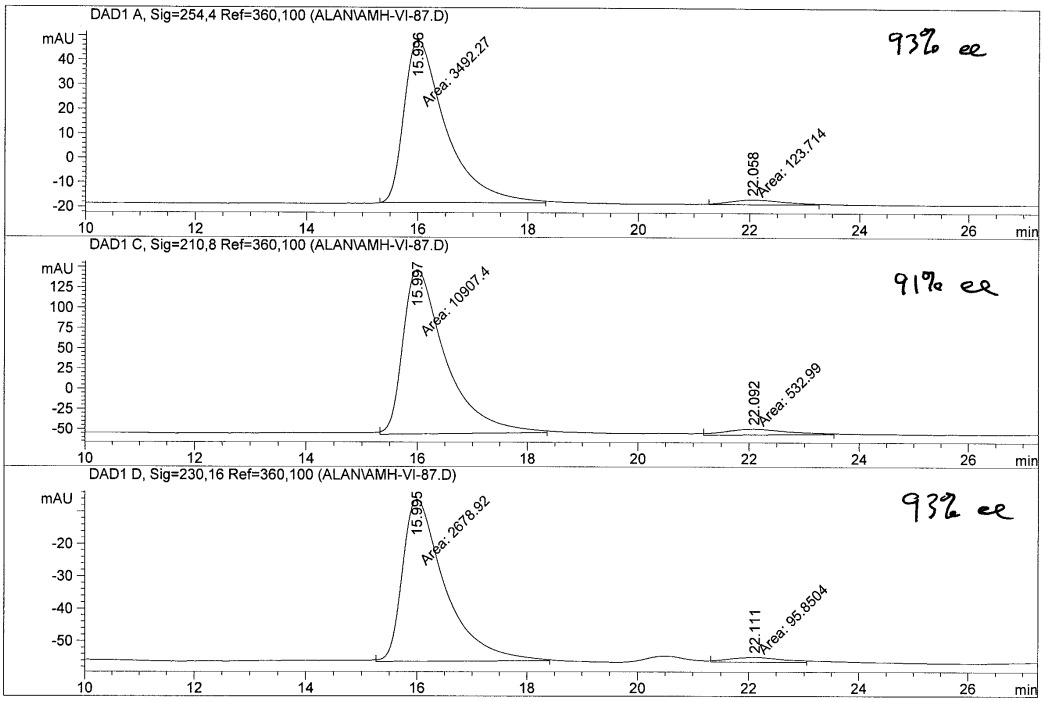



Table 4, entry 2

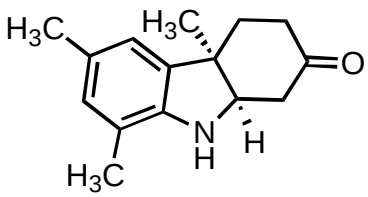



```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

X-ray crystal structure of **5**.

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.




X-ray Crystal Structure of **5** (thermal ellipsoids at 30% probability)