Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Copper-catalyzed Oxidative Condensation of α-Oxocarboxylic Acids with Formamides: Synthesis of α-Ketoamides

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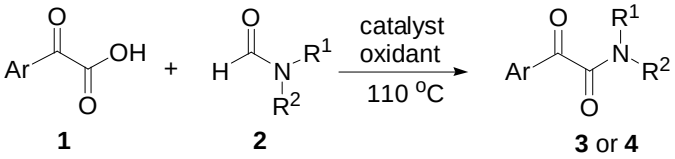
General Information

All Reactions were carried out under an atmosphere of nitrogen with the strict exclusion of moisture. The dry DMF were distilled from CaH_2 under nitrogen and stored over molecular sieves under nitrogen. Column chromatography was carried out on silica gel. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance III-400 in solvents as indicate. Chemical shift are reported in ppm from $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a Bruker Tensor 27 spectrometer and only major peaks are reported in cm^{-1}. HRMS were obtained on a Q-TOF micro spectrometer. Melting points were determined on a microscopic apparatus and were uncorrected.

Starting Materials

N,*N*-Diethylformamide, *N*-formylpiperidine, and *N*-formylmorpholine were purchased from Sigma-Aldrich and TCI. Phenylglyoxylic acid **1a** was purchased from Sigma-Aldrich. Other α-oxocarboxylic acids were prepared from the corresponding methyl ketones according to the reported procedure.[1]

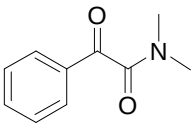
General Procedure for the Coupling of Formamides with α-Oxocarboxylic acids



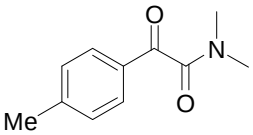
1 **2** **3** or **4**

A 10 mL oven-dried Schlenk-tube was charged with $Cu(OAc)_2$ (1.8 mg, 5 mol %). The tube was evacuated and backfilled with nitrogen (three times). α-Oxocarboxylic acids (**1**, 0.2 mmol, 1.0 equiv) and Di-*tert*-butyl peroxide (DTBP, 0.4 mmol, 2.0 equiv) in substituted formamides (2 mL) were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred for 3 h at 110 ^{o}C. Upon completion of the reaction (monitored by TLC), the mixture was diluted with EtOAc, filtered through a pad of Celite, and the filtrate was washed with water, dried over Na_2SO_4. After the solvent was removed, the residue was purified with chromatography column on silica gel (gradient eluent of EtOAc/petroleum ether: 1/10 to 1/5) to give the corresponding products **3** or **4** in yields listed in Table 2 and Table 3.

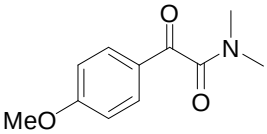
Characterization of Products 3



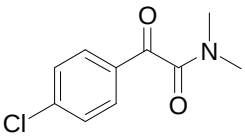
***N*,*N*-Dimethyl-2-oxo-2-phenyl-acetamide** (**3a**):[2a,2d] A pale yellow oil, R_f 0.3 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94-7.92 (d, *J* = 7.6 Hz, 2H), 7.65-7.61 (t, *J* = 7.2 Hz, 1H), 7.52-7.48 (t, *J* = 7.6 Hz, 2H), 3.11 (s, 3H), 2.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.7, 167.0, 134.7, 133.0, 129.6, 129.0, 37.0, 33.9 ppm.



***N*,*N*-Dimethyl-2-oxo-2-*p*-tolyl-acetamide** (**3b**):[2f] A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 46-48 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83-7.81 (d, *J* = 7.2 Hz, 2H), 7.30-7.28 (d, *J* = 7.6 Hz, 2H), 3.10 (s, 3H), 2.94 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 167.2, 145.9, 130.6, 129.7, 37.0, 33.9, 21.9 ppm; IR (KBr): υ_{max} 1651, 1406, 1254, 1144 cm^{-1}.

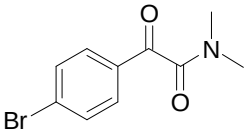


2-(4-Methoxy-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3c**):[2b] A pale yellow solid, R_f 0.1 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91-7.89 (d, *J* = 8.4 Hz, 2H), 6.97-6.95 (d, *J* = 8.4 Hz, 2H), 3.87 (s, 3H), 3.09 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.5, 167.3, 164.8, 132.1, 126.1, 114.3, 55.6, 37.1, 33.9 ppm.

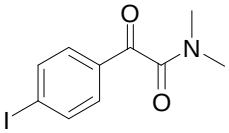


2-(4-Chloro-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3d**):[2f] A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 113-115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90-7.88 (d, *J* = 7.6 Hz, 2H), 7.49-7.47 (d, *J* = 8.0 Hz, 2H), 3.11 (s, 3H), 2.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.3, 166.4, 141.3, 131.4, 131.0, 129.4, 37.0, 34.1

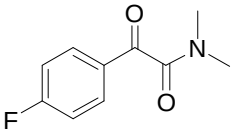
ppm; IR (KBr): υ_{max} 1641, 1406, 1246, 1147 cm^{-1}.



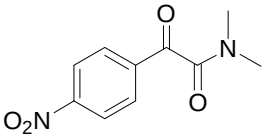
2-(4-Bromo-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3e**): A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 68-70 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82-7.80 (d, *J* = 8.0 Hz, 2H), 7.66-7.64 (d, *J* = 7.6 Hz, 2H), 3.11 (s, 3H), 2.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.5, 166.4, 132.4, 131.8, 131.0, 130.2, 37.0, 34.1 ppm; IR (KBr): υ_{max} 1641, 1400, 1246, 1145 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}BrNNaO_2$ $[M+Na]^+$ 277.9787, found 277.9794.



2-(4-Iodo-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3f**): A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 96-98 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.87 (d, *J* = 7.6 Hz, 2H), 7.65-7.63 (d, *J* = 7.6 Hz, 2H), 3.10 (s, 3H), 2.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.8, 166.4, 138.3, 132.4, 130.8, 103.3, 37.0, 34.1 ppm; IR (KBr): υ_{max} 1637, 1396, 1247, 1144 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}INNaO_2$ $[M+Na]^+$ 325.9648, found 325.9658.

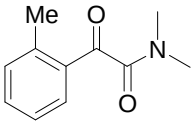


2-(4-Fluoro-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3g**):[2f] A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 63-65 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00-7.97 (t, *J* = 6.0 Hz, 2H), 7.20-7.16 (t, *J* = 8.0 Hz, 2H), 3.12 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.0, 166.7 (d, $J_{C,F}$ = 256.0 Hz), 166.6, 132.5 (d, $J_{C,F}$ = 9.8 Hz), 129.6, 116.3 (d, $J_{C,F}$ = 22.1 Hz), 37.1, 34.1 ppm; IR (KBr): υ_{max} 1648, 1409, 1239, 1147 cm^{-1}.

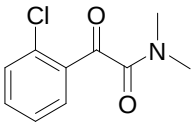


***N*,*N*-Dimethyl-2-(4-nitro-phenyl)-2-oxo-acetamide (3h):**[2f] A pale yellow solid, R_f 0.2 (EtOAc/petroleum ether = 1:2), mp: 136-138 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ =

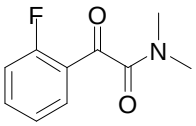
8.36-8.34 (d, *J* = 8.0 Hz, 2H), 8.16-8.14 (d, *J* = 8.4 Hz, 2H), 3.15 (s, 3H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.2, 165.6, 151.1, 137.5, 130.8, 124.1, 37.1, 34.3 ppm; IR (KBr): υ_{max} 1645, 1451, 1245, 1148 cm^{-1}.



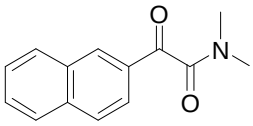
***N*,*N*-Dimethyl-2-oxo-2-o-tolyl-acetamide** (**3i**):[2f] A pale yellow solid, R_f 0.25 (EtOAc/petroleum ether = 1:5), mp: 43-45 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68-7.66 (d, *J* = 8.0 Hz, 1H), 7.48-7.44 (t, *J* = 7.6 Hz, 1H), 7.31-7.28 (t, *J* = 7.2 Hz, 2H), 3.09 (s, 3H), 2.96 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 167.7, 141.4, 133.6, 132.6, 132.5, 131.4, 126.1, 37.0, 34.0, 21.7 ppm; IR (KBr): υ_{max} 1638, 1405, 1240, 1153 cm^{-1}.



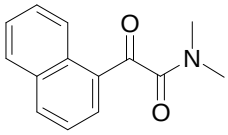
2-(2-Chloro-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3j**): A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:5), mp: 76-78 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89-7.87 (d, *J* = 7.6 Hz, 1H), 7.52-7.48 (t, *J* = 7.6 Hz, 1H), 7.44-7.38 (m, 2H), 3.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.1, 166.9, 134.3, 133.7, 133.4, 132.2, 130.7, 127.3, 37.0, 34.5 ppm; IR (KBr): υ_{max} 1644, 1412, 1275, 1151 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}ClNNaO_2$ $[M+Na]^+$ 234.0292, found 234.0304.



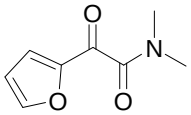
2-(2-Fluoro-phenyl)-*N*,*N*-dimethyl-2-oxo-acetamide (**3k**): A pale yellow solid, R_f 0.2 (EtOAc/petroleum ether = 1:5), mp: 53-55 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.95 (t, *J* = 7.6 Hz, 1H), 7.63-7.61 (m, 1H), 7.32-7.28 (t, *J* = 7.6 Hz, 1H), 7.18-7.13 (t, *J* = 9.6 Hz, 1H), 3.09 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.2, 167.4, 162.6 (d, $J_{C,F}$ = 256.5 Hz), 136.5 (d, $J_{C,F}$ = 9.3 Hz), 131.0, 124.8 (d, $J_{C,F}$ = 3.5 Hz), 122.2, 116.7 (d, $J_{C,F}$ = 21.6 Hz), 36.8, 34.1 ppm; IR (KBr): υ_{max} 1659, 1409, 1289, 1150 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}FNNaO_2$ $[M+Na]^+$ 218.0588, found 218.0591.



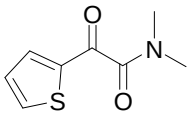
***N,N*-Dimethyl-2-naphthalen-2-yl-2-oxo-acetamide** (**3l**): A pale yellow solid, R_f 0.15 (EtOAc/petroleum ether = 1:5), mp: 112-114 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 8.04-8.02 (d, *J* = 8.8 Hz, 1H), 7.98-7.93 (m, 2H), 7.90-7.88 (d, *J* = 8.0 Hz, 1H), 7.66-7.62 (t, *J* = 7.2 Hz, 1H), 7.59-7.55 (t, *J* = 7.2 Hz, 1H), 3.18 (s, 3H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.9, 167.1, 136.3, 133.0, 132.4, 130.4, 129.9, 129.4, 129.1, 127.9, 127.1, 123.6, 37.1, 34.1 ppm; IR (KBr): υ_{max} 1641, 1458, 1274, 1145 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{13}NNaO_2$ $[M+Na]^+$ 250.0838, found 250.0850.



***N,N*-Dimethyl-2-naphthalen-1-yl-2-oxo-acetamide (3m):**[2f] A pale yellow oil, R_f 0.15 (EtOAc/petroleum ether = 1:5); ^1H NMR (400 MHz, $CDCl_3$): δ = 9.27-9.24 (d, *J* = 8.4 Hz, 1H), 8.11-8.09 (d, *J* = 8.0 Hz, 1H), 8.00-7.98 (d, *J* = 7.2 Hz, 1H), 7.92-7.90 (d, *J* = 8.0 Hz, 1H), 7.72-7.68 (t, *J* = 7.6 Hz, 1H), 7.61-7.57 (t, *J* = 7.6 Hz, 1H), 7.56-7.52 (t, *J* = 7.6 Hz, 1H), 3.15 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.2, 167.6, 135.9, 134.3, 134.0, 130.9, 129.3, 128.7, 128.3, 126.9, 125.7, 124.5, 37.2, 34.1 ppm; IR (KBr): υ_{max} 1647, 1404, 1270, 1069 cm^{-1}.

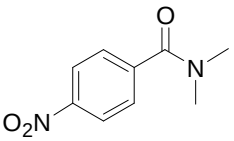


2-Furan-2-yl-*N,N*-dimethyl-2-oxo-acetamide (3n):[2f] A yellow oil, R_f 0.1 (EtOAc/petroleum ether = 1:5); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (s, 1H), 7.36 (d, *J* = 2.8 Hz, 1H), 6.60 (d, *J* = 1.6 Hz, 1H), 3.07 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.5, 165.4, 150.1, 148.7, 122.4, 112.8, 37.2, 34.5 ppm; IR (KBr): υ_{max} 1637, 1460, 1259, 1150 cm^{-1}.



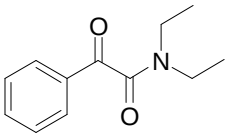
***N,N*-Dimethyl-2-oxo-2-thiophen-2-yl-acetamide (3o):** A pale yellow solid, R_f 0.15 (EtOAc/petroleum ether = 1:5), mp: 57-59 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ =

7.80-7.77 (m, 2H), 7.18-7.16 (t, *J* = 4.0 Hz, 1H), 3.08 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.5, 165.8, 140.3, 136.4, 136.1, 128.6, 37.3, 34.4 ppm; IR (KBr): υ_{max} 1648, 1407, 1246, 1142 cm^{-1}; HRMS (ESI) calcd for $C_8H_9NNaO_2S$ $[M+Na]^+$ 206.0246, found 206.0253.

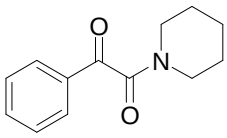


***N*,*N*-dimethyl-4-nitrobenzamide (3h'):**[3] A pale yellow solid, R_f 0.2 (EtOAc/petroleum ether = 1:5), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28-8.27 (d, *J* = 7.6 Hz, 2H), 7.59-7.57 (d, *J* = 7.6 Hz, 2H), 3.14 (s, 3H), 2.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2, 148.2, 142.5, 128.0, 123.8, 39.3, 35.3 ppm

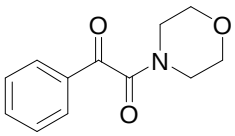
Characterization of Products 4



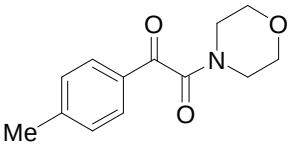
***N,N*-Diethyl-2-oxo-2-phenyl-acetamide** (**4a**):[2e] A pale yellow oil, R_f 0.3 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93-7.92 (d, *J* = 7.6 Hz, 2H), 7.64-7.61 (t, *J* = 7.2 Hz, 1H), 7.51-7.48 (t, *J* = 7.6 Hz, 2H), 3.58-3.53 (q, *J* = 7.2 Hz, 2H), 3.25-3.20 (q, *J* = 6.8 Hz, 2H), 1.29-1.26 (t, *J* = 7.2 Hz, 3H), 1.16-1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.6, 166.7, 134.5, 133.2, 129.6, 128.9, 42.0, 38.7, 14.1, 12.8 ppm.



1-Phenyl-2-piperidin-1-yl-ethane-1,2-dione (**4b**):[2c, 2d] A pale yellow solid, R_f 0.4 (EtOAc/petroleum ether = 1:5), mp: 102-104 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95-7.93 (d, *J* = 7.2 Hz, 2H), 7.65-7.61 (t, *J* = 7.6 Hz, 1H), 7.52-7.48 (t, *J* = 7.2 Hz, 2H), 3.70 (s, 2H), 3.29-3.26 (t, *J* = 5.6 Hz, 2H), 1.69-1.68 (m, 4H), 1.55-1.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.1, 165.4, 134.6, 133.2, 129.5, 128.9, 47.0, 42.1, 26.1, 25.4, 24.3 ppm; IR (KBr): υ_{max} 1645, 1446, 1216, 1137 cm^{-1}.

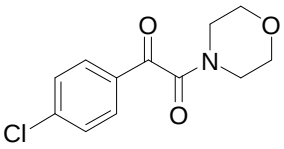


1-Morpholin-4-yl-2-phenyl-ethane-1,2-dione (**4c**):[2c, 2d] A pale yellow oil, R_f 0.2 (EtOAc/petroleum ether = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96-7.94 (d, *J* = 7.6 Hz, 2H), 7.68-7.64 (t, *J* = 7.2 Hz, 1H), 7.54-7.50 (t, *J* = 8.0 Hz, 2H), 3.79 (s, 4H), 3.66-3.64 (t, *J* = 4.8 Hz, 2H), 3.39-3.37 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.1, 165.4, 134.9, 133.0, 129.7, 129.1, 66.7, 46.2, 41.6 ppm.



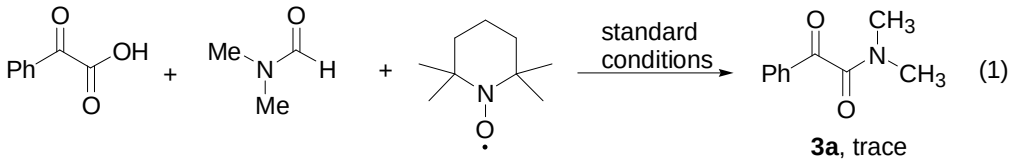
1-Morpholin-4-yl-2-*p*-tolyl-ethane-1,2-dione (**4d**):[2d] A pale yellow solid, R_f 0.15 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.83 (d, *J* = 7.6

Hz, 2H), 7.32-7.30 (d, *J* = 8.0 Hz, 2H), 3.78 (s, 4H), 3.65-3.62 (t, *J* = 4.4 Hz, 2H), 3.37-3.35 (t, *J* = 4.8 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.9, 165.6, 146.3, 130.6, 129.8, 129.7, 66.7, 66.6, 46.2, 41.5, 21.9 ppm.

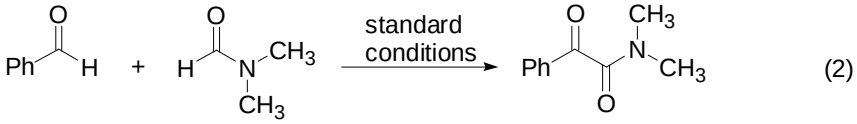


1-(4-Chloro-phenyl)-2-morpholin-4-yl-ethane-1,2-dione (**4e**):[2d] A pale yellow solid, R_f 0.2 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92-7.90 (d, *J* = 8.4 Hz, 2H), 7.51-7.49 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 4H), 3.67-3.65 (t, *J* = 4.8 Hz, 2H), 3.39-3.37 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.7, 164.9, 141.6, 131.4, 131.0, 129.5, 66.7, 66.6, 46.3, 41.7 ppm.

Investigation of the Reaction Mechanism



3a, trace



3a, < 2%

When the TEMPO was added to the reaction of DMF with phenylglyoxylic acid **2a** under the standard condition, only a trace amount of the desired product **3a** was obtained suggesting that free radical intermediate was involved in the reaction (eq 1). In addition, benzaldehyde was used instead of phenylglyoxylic acid under the standard conditions, only a trace amount of α-ketoamide **3a** was detected (eq 2). The result indicated that aldehyde was not the intermediates in this reaction.

C^{13}-Isotope Labeling Experiment

N,*N*-dimethylformamide (carbonyl-^{13}C, 99%, cat. No. CLM-503-0) were purchased from Cambridge Isotope Laboratories. The isotope reagent was used without further purification.

Cambridge Isotope Laboratories, Inc.

50 Frontage Road, Andover, MA 01810-5413 USA
800.322.1174 (N.AMERICA) 978.749.8000 (INTERNATIONAL)
www.isotope.com

CERTIFICATE OF ANALYSIS

Product Name: (Isotopic Label & Enrichment Specification)	N,N-DIMETHYLFORMAMIDE (CARBONYL-13C, 99%)
Lot Number:	I1-11572
Catalog Number:	CLM-503-0

Product Information

Chemical Purity Specification:	≥ 98%
Labeled CAS Number:	32488-43-0
Unlabeled CAS Number:	68-12-2
MW of fully enriched product:	74.09
Chemical Formula:	(CH3)2N*CHO
Storage:	Store at room temperature away from light and moisture.
Stability:	Stable if stored under recommended conditions.

Certification

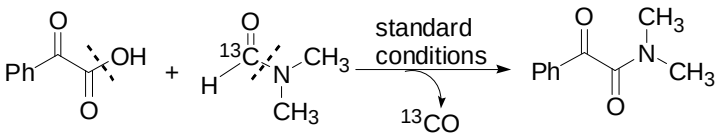
Cambridge Isotope Laboratories, Inc. guarantees that this material meets or exceeds the specifications stated. Absolute identity as well as chemical and isotopic purities are assured by the use of unambiguous synthetic routes and multiple chemical analyses whenever possible. Results are representative of QC testing at time of release from Quality Control unless otherwise stated.

Approved by: Jeffrey O Neill
Jeffrey O'Neill, Quality Assurance

Quality Control Tests and Results

13C NMR for Identification	Conforms
1H NMR for Chemical Purity	Pass
GC/MS for Chemical Purity	100%
GC/MS for Isotopic Enrichment	99.3%

The Coupling of Phenylglyoxylic Acid with ^{13}C-Labeling DMF

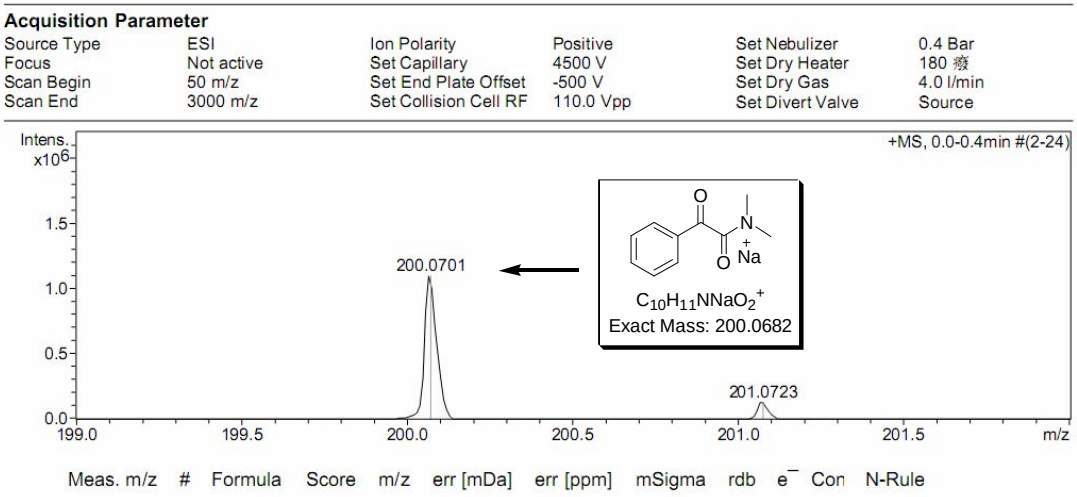


1a ^{13}C-**2a** **3a**, 72%

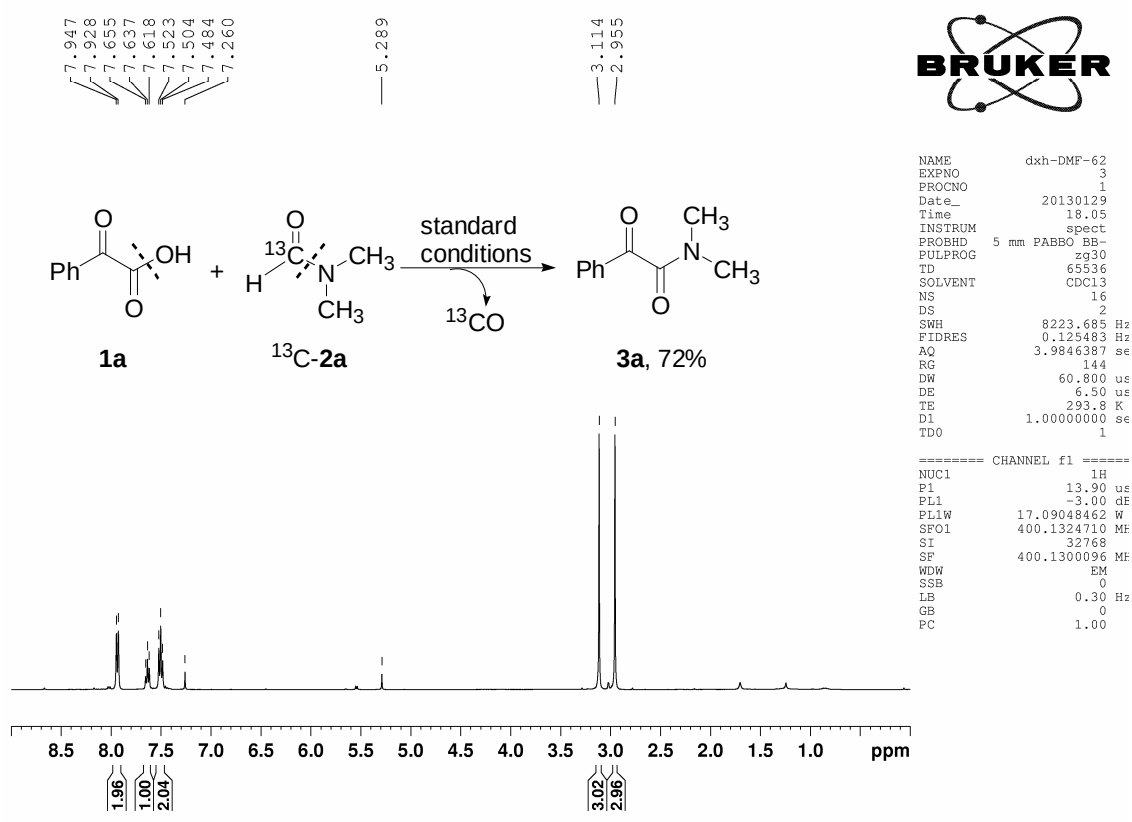
Phenylglyoxylic acid (**1**, 0.1 mmol, 1.0 equiv) and Di-*tert*-butyl peroxide (DTBP, 0.2 mmol, 2.0 equiv) in ^{13}C-labeling DMF (1 mL) were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred for 3 h at 110 ^{o}C. Upon completion of the reaction, the mixture was diluted with EtOAc, filtered through a pad of Celite, and the filtrate was washed with water, dried over Na_2SO_4. After the solvent was removed, the residue was purified with chromatography column on silica gel (gradient eluent of EtOAc/petroleum ether: 1/10 to 1/5) to give the corresponding products **3a** in 72% yield.

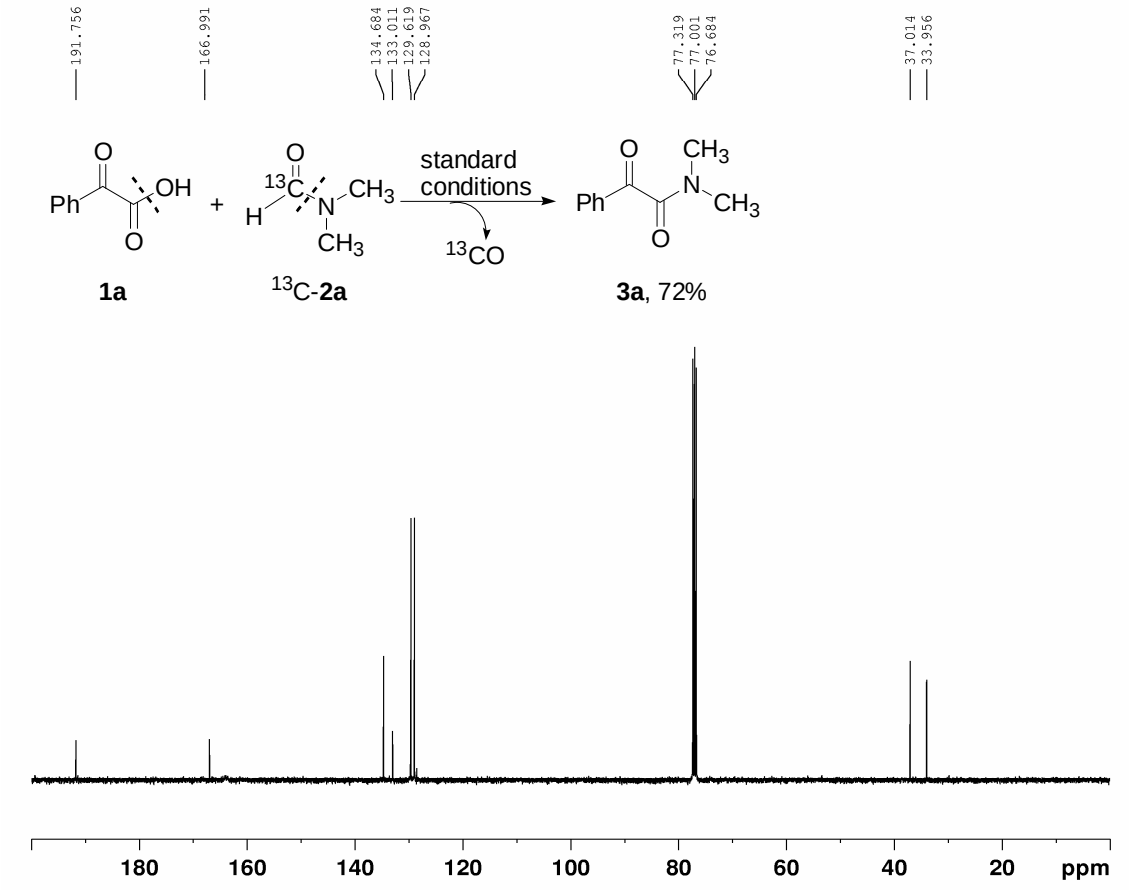
***N,N*-Dimethyl-2-oxo-2-phenyl-acetamide** (**3a**): HRMS (ESI) calcd for $C_{10}H_{11}NNaO_2$ $[M+Na]^+$ 200.0682, found 200.0701.

The HRMS Spectra of 3a



The NMR Spectra of 3a





Competing Kinetic Isotope Effect (KIE) Experiment

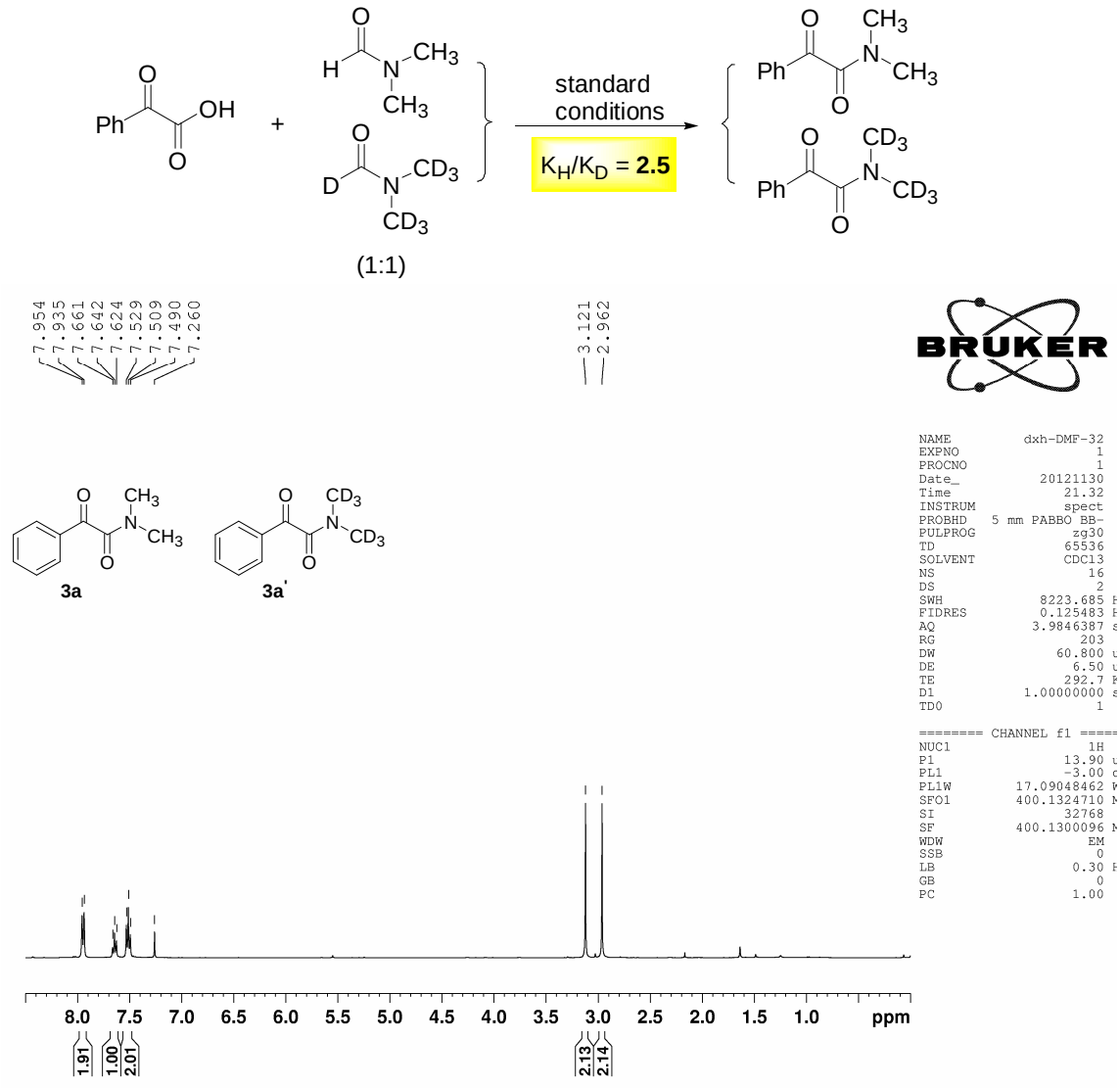


Figure. ^{1}H NMR spectra of the mixture of the product **3a** and **3a'**.

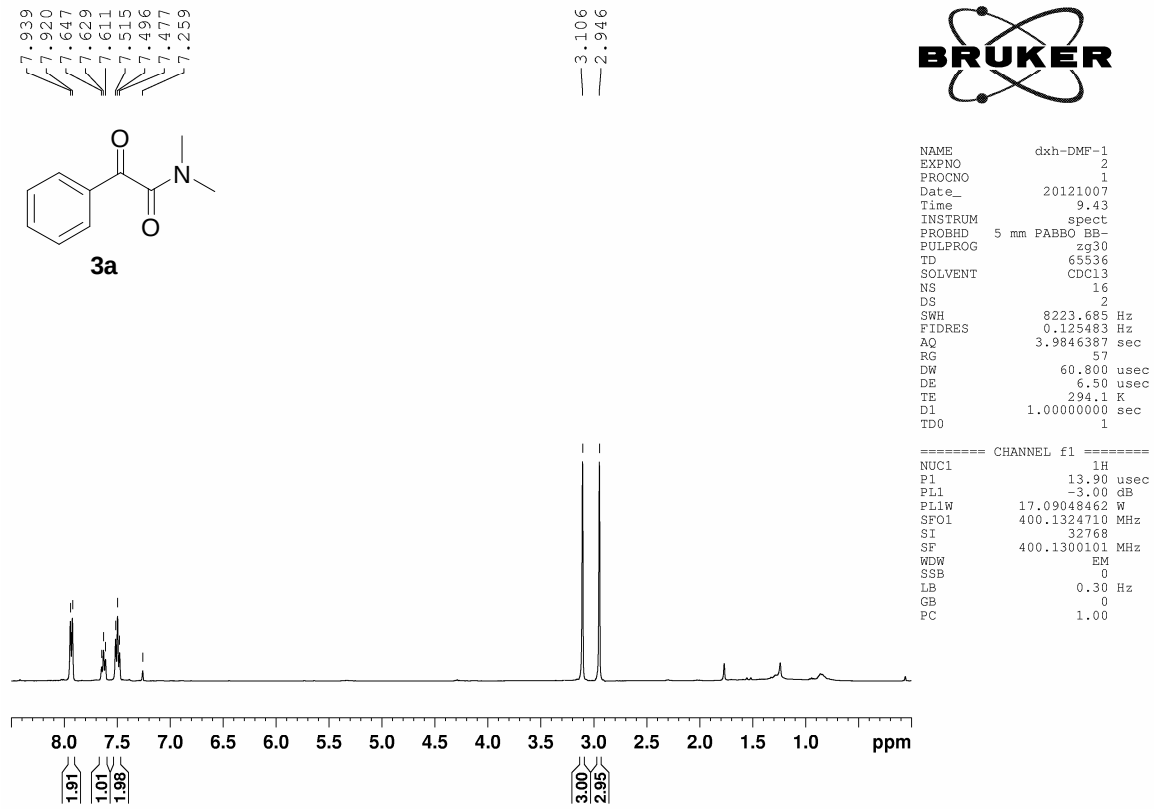
References

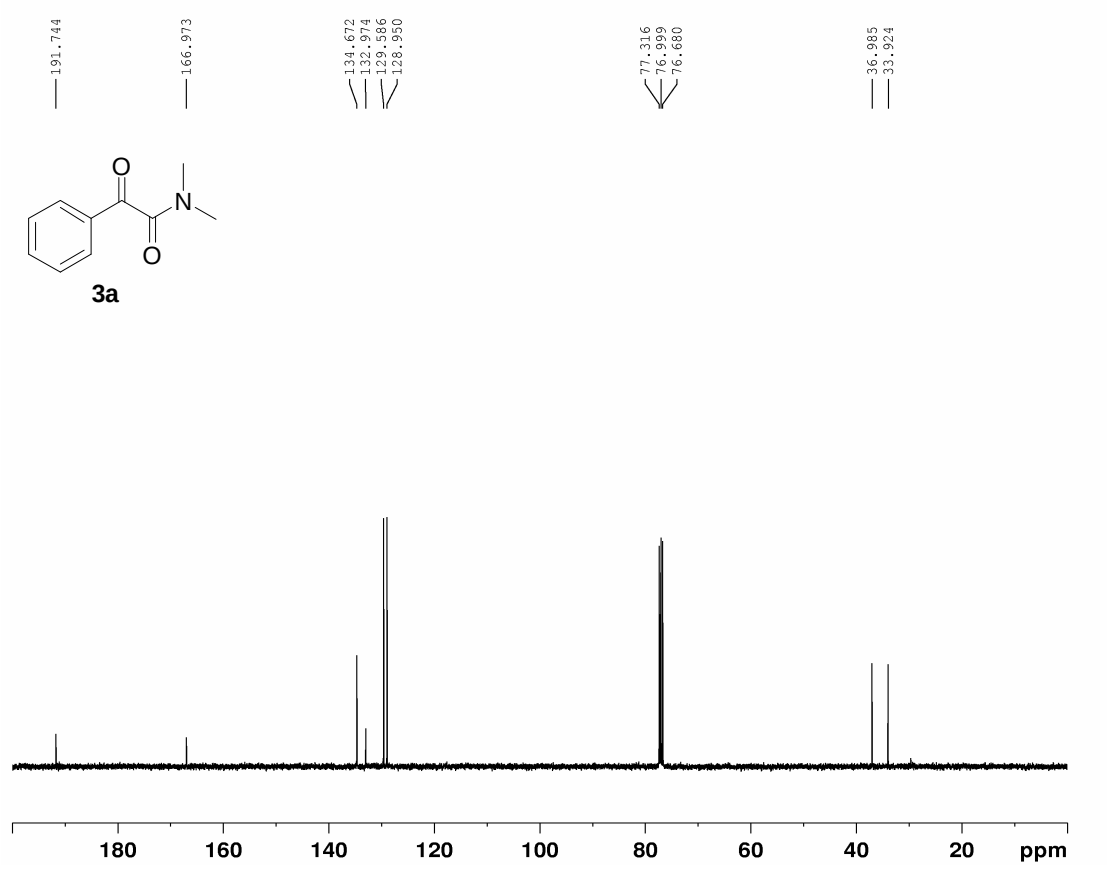
1. K. Wadhwa, C.Yang, P. R. West, K. C. Deming, S. R. Chemburkar and R. E. Reddy, *Synth. Commun.*, 2008, **38**, 4434.

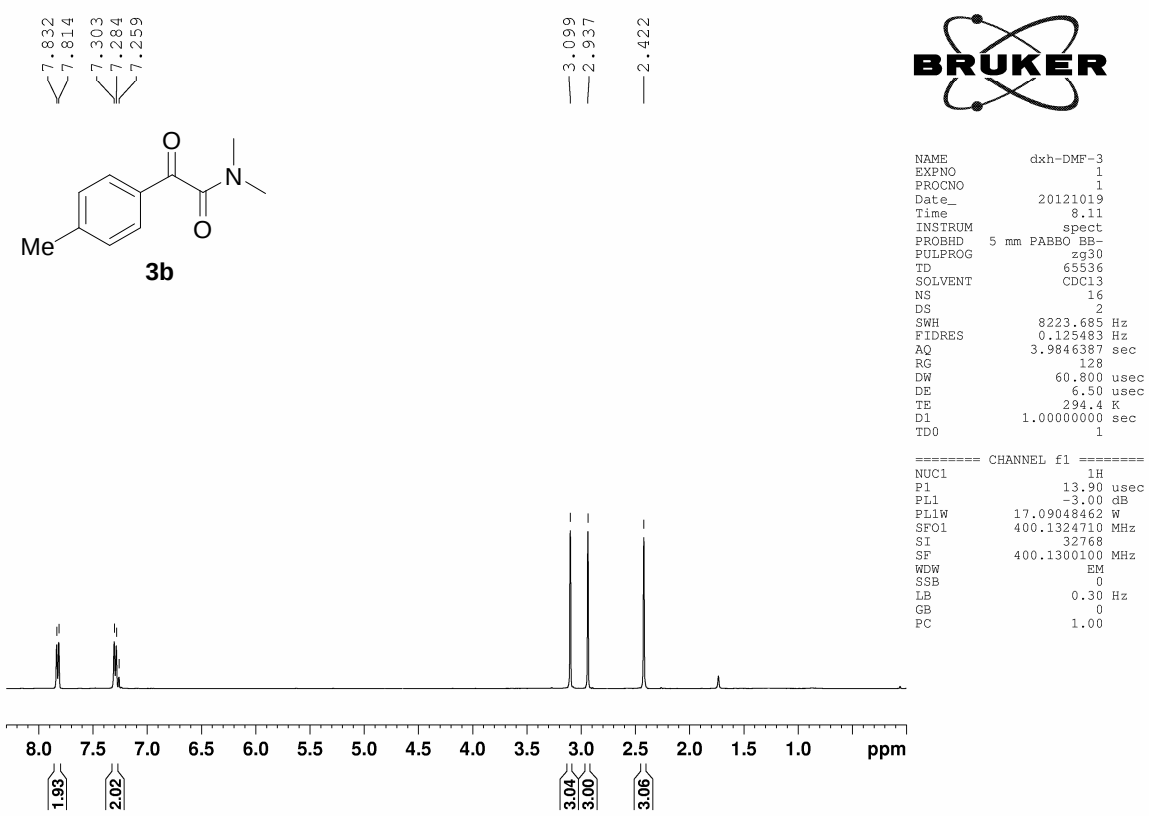
2. (a) J. Chen and R. F. Cunico, *J. Org. Chem.*, 2004, **69**, 5509; (b) D. Bonne, M. Dekhane and Zhu. J, *J. Am. Chem. Soc.*, 2005, **127**, 6926; (c) F.-T. Du and J.-X. Ji, *Chem. Sci.*, 2012, **3**, 460; (d) W. Wei, Y. Shao, H. Hu, F. Zhang, C. Zhang, Y. Xu and X. Wan, *J. Org. Chem.*, 2012, **77**, 7157; (e) X. Zhang and L. Wang, *Green. Chem.*, 2012, **14**, 2141; (f) W.-P. Mai, H.-H. Wang, Z.-C. Li, J.-W. Yuan, Y.-M. Xiao, L.-R. Yang, P. Mao and L.-B. Qu, *Chem. Commun.*, 2012, **48**, 10117.

3. Z. Liu, J. Zhang, S. Chen, E. Shi, Y. Xu and X. Wan, *Angew. Chem., Int. Ed.*, 2012, **51**, 3231.

^{1}H NMR and ^{13}C NMR Spectra of the Products



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2.422
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PROCNO 1
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FIDRES 0.125483 Hz
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RG 128
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DE 6.50 usec
TE 294.4 K
D1 1.00000000 sec
TD0 1
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PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300100 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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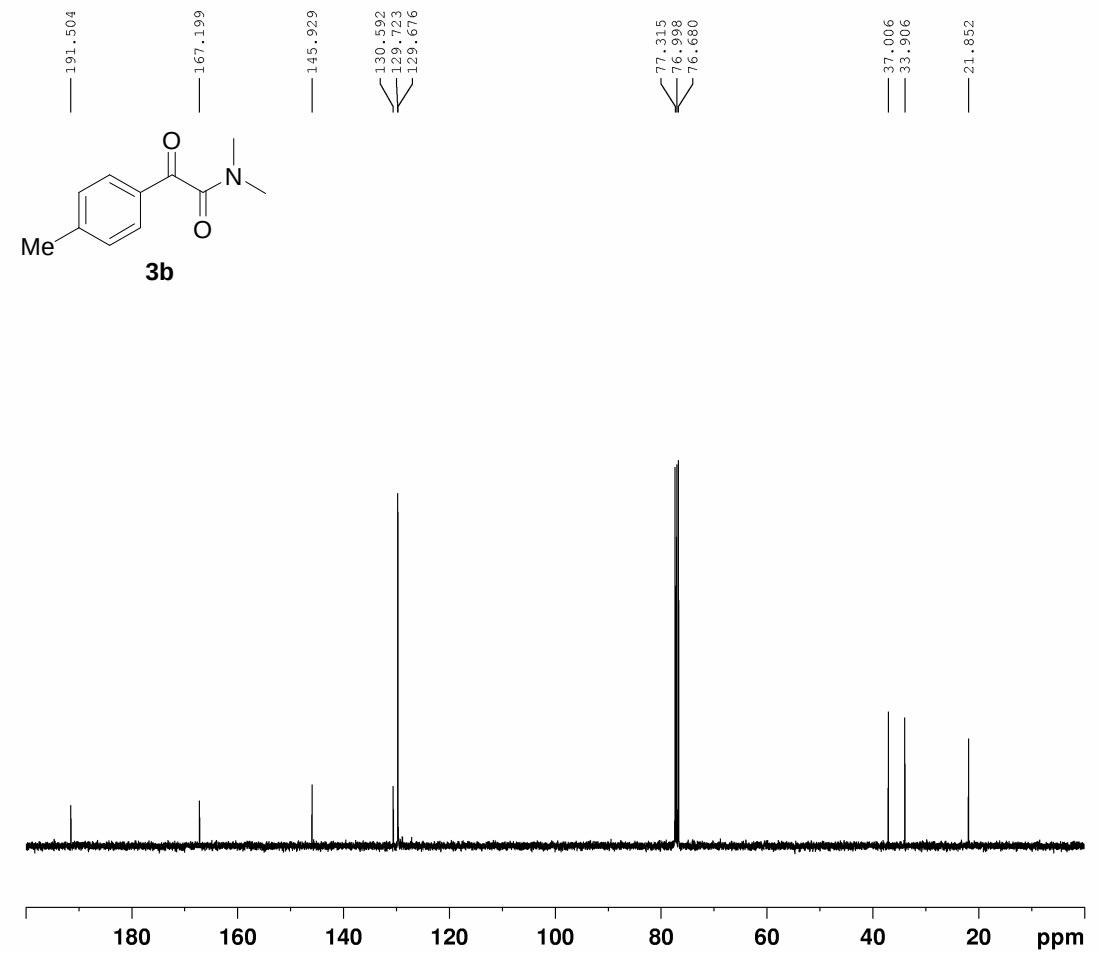
2.02
3.04
3.00
3.06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129.676
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37.006
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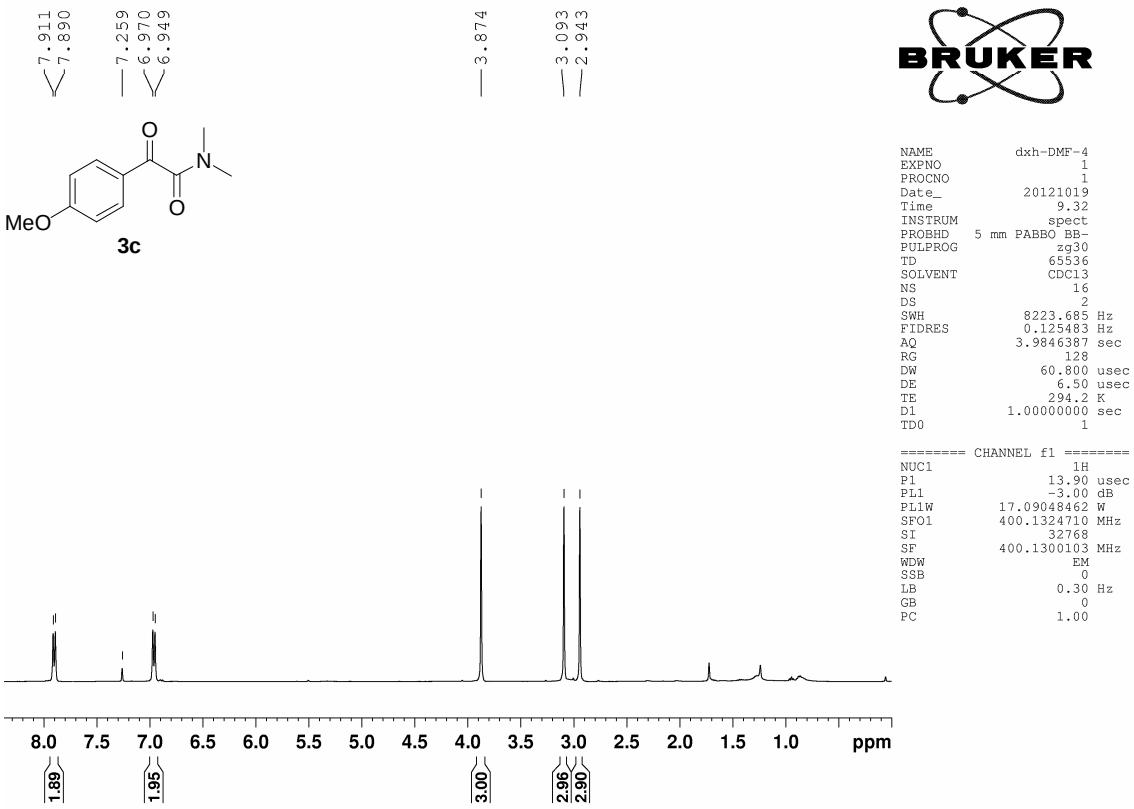
O
N
O
Me
3b
180 160 140 120 100 80 60 40 20 ppm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PROCNO 1
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Time 9.32
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DS 2
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FIDRES 0.125483 Hz
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RG 128
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DE 6.50 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
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PL1 -3.00 dB
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SFO1 400.1324710 MHz
SI 32768
SF 400.1300103 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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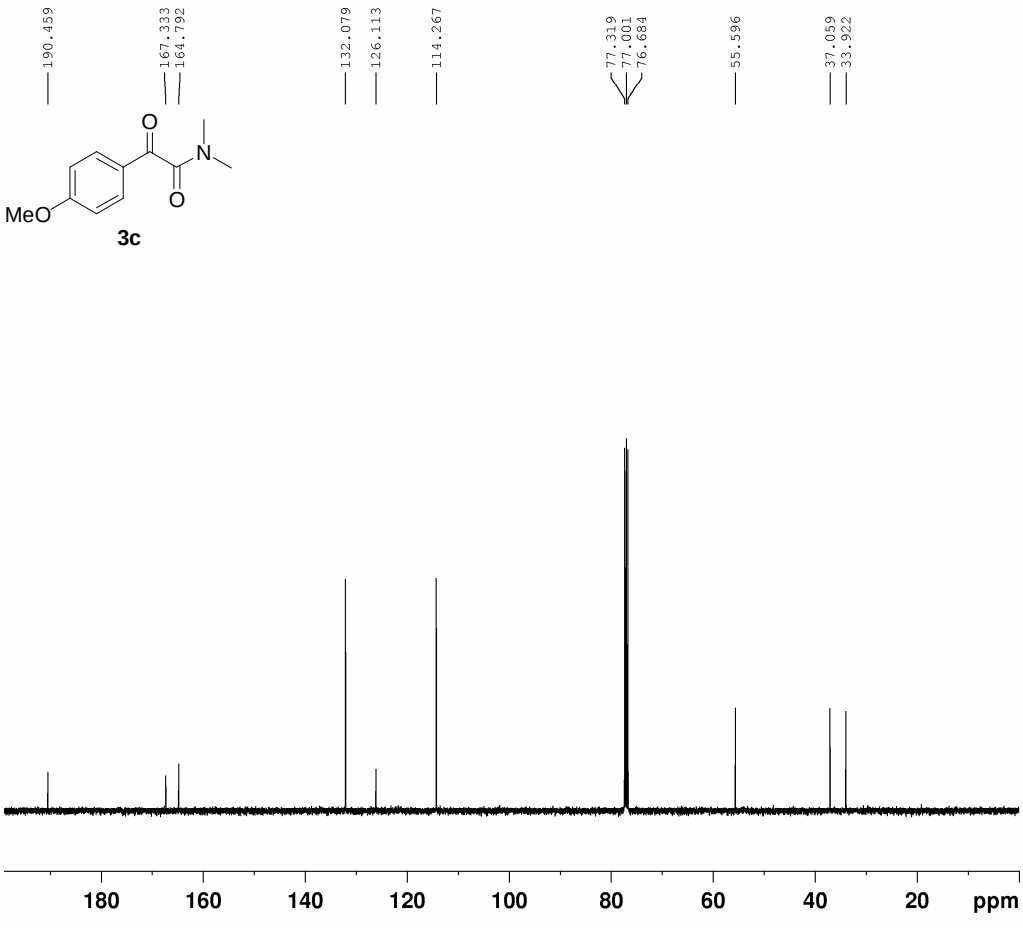
2.96
2.90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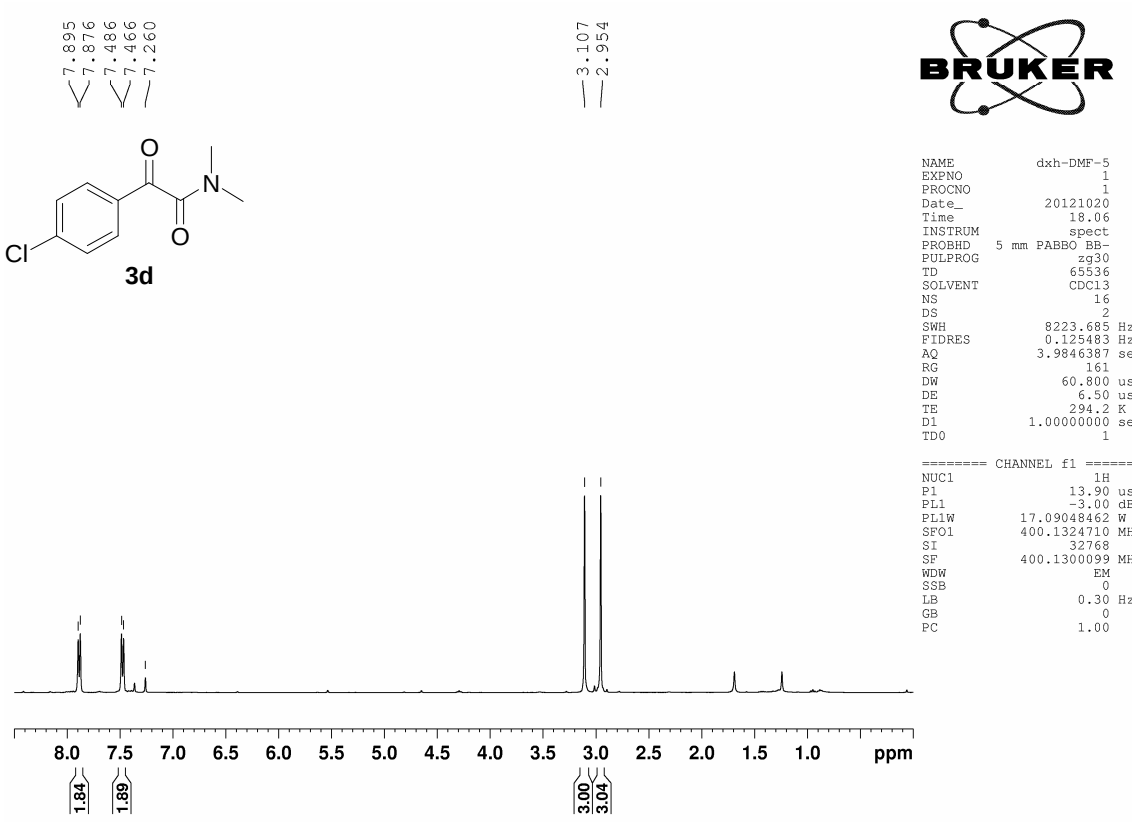
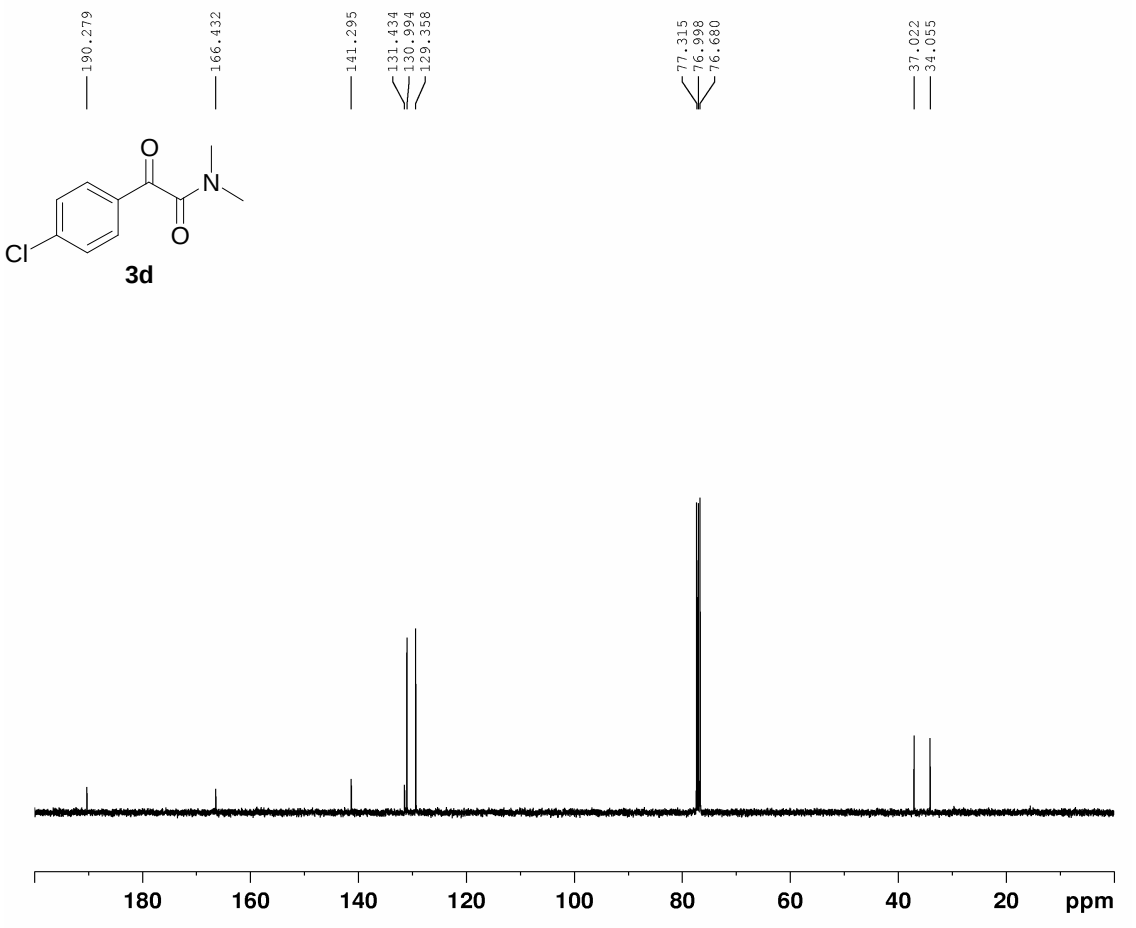
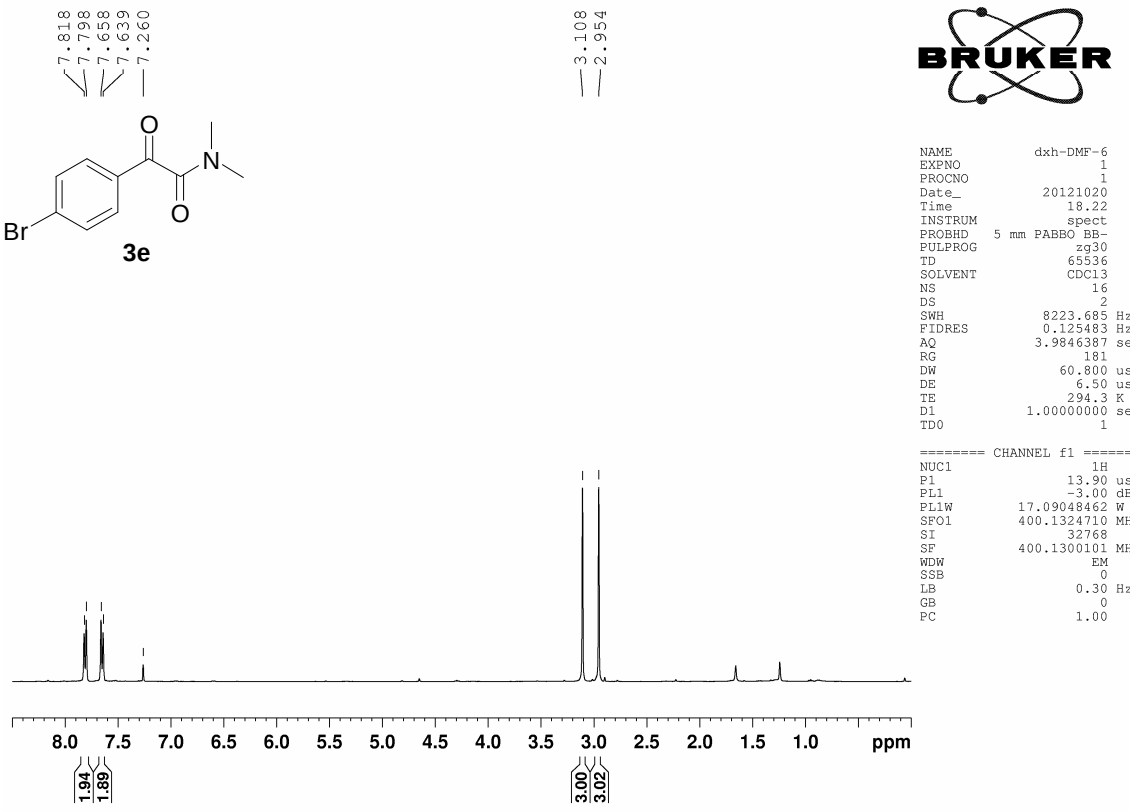
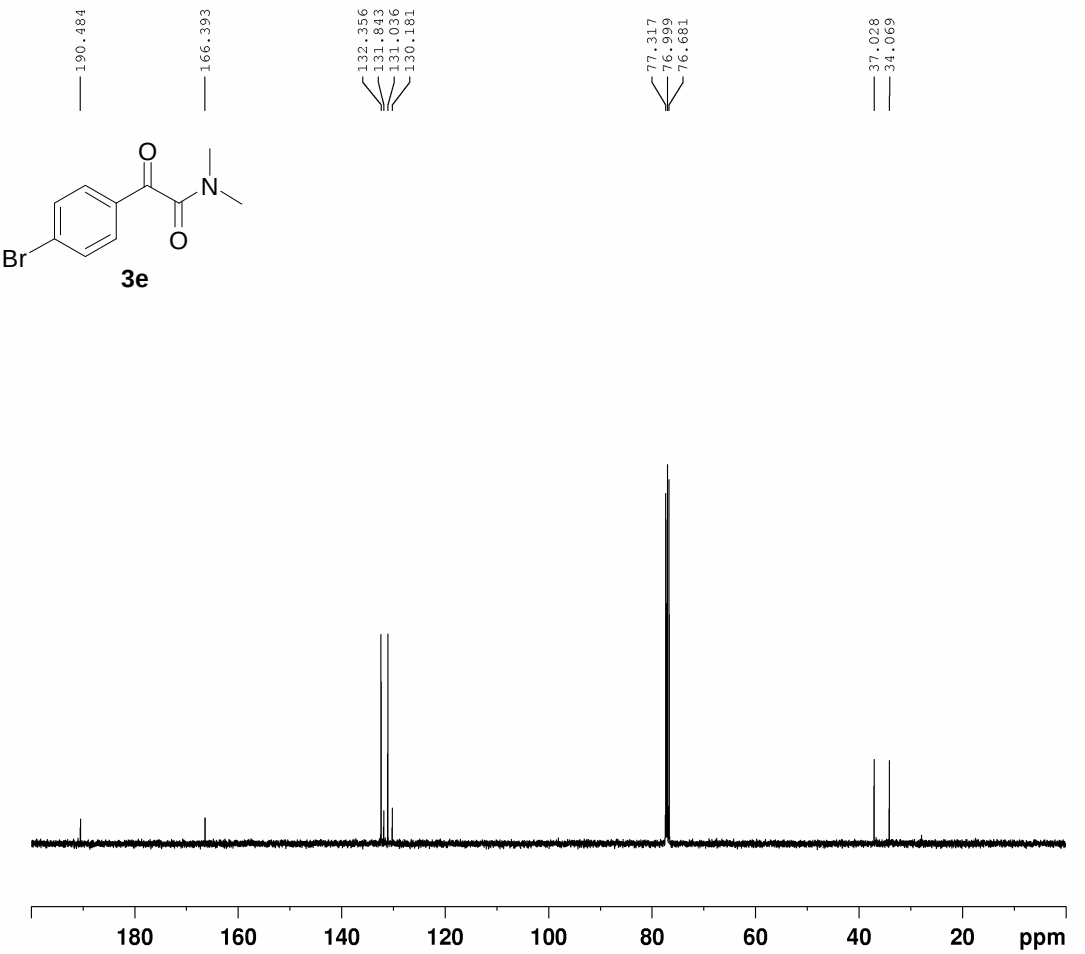
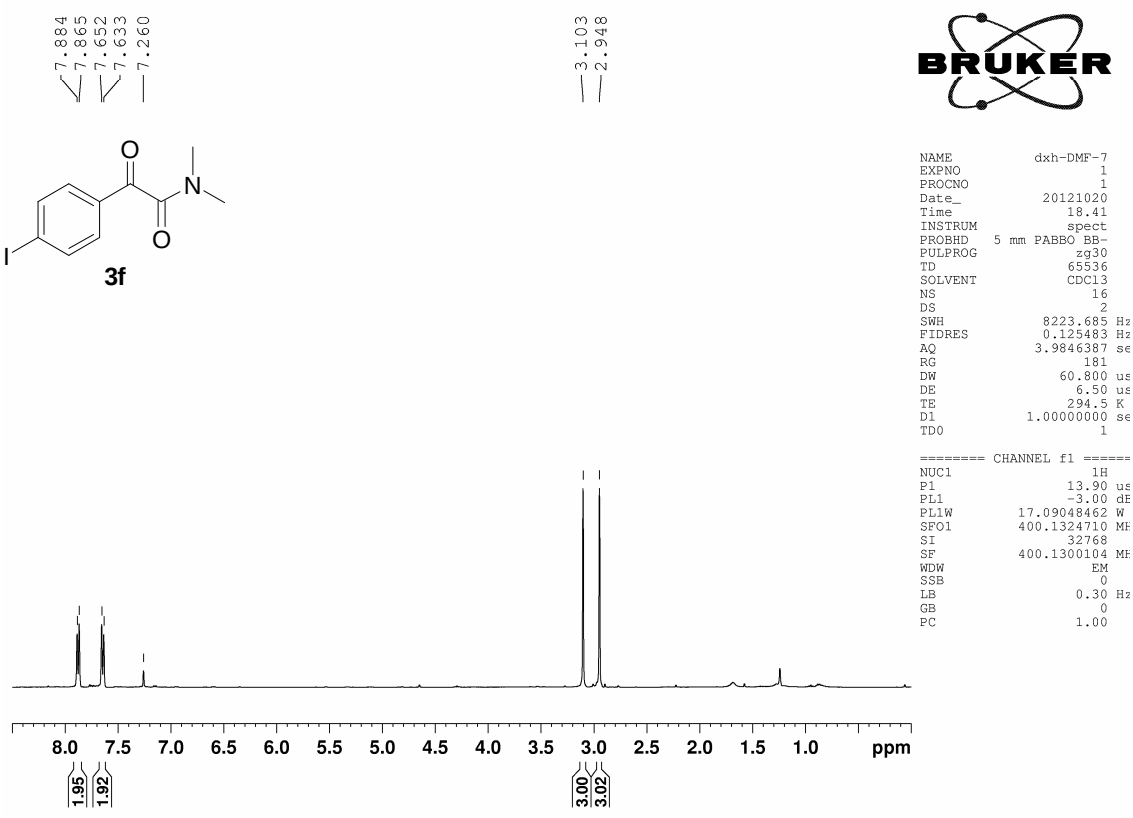
MeO
3c
180 160 140 120 100 80 60 40 20 ppm

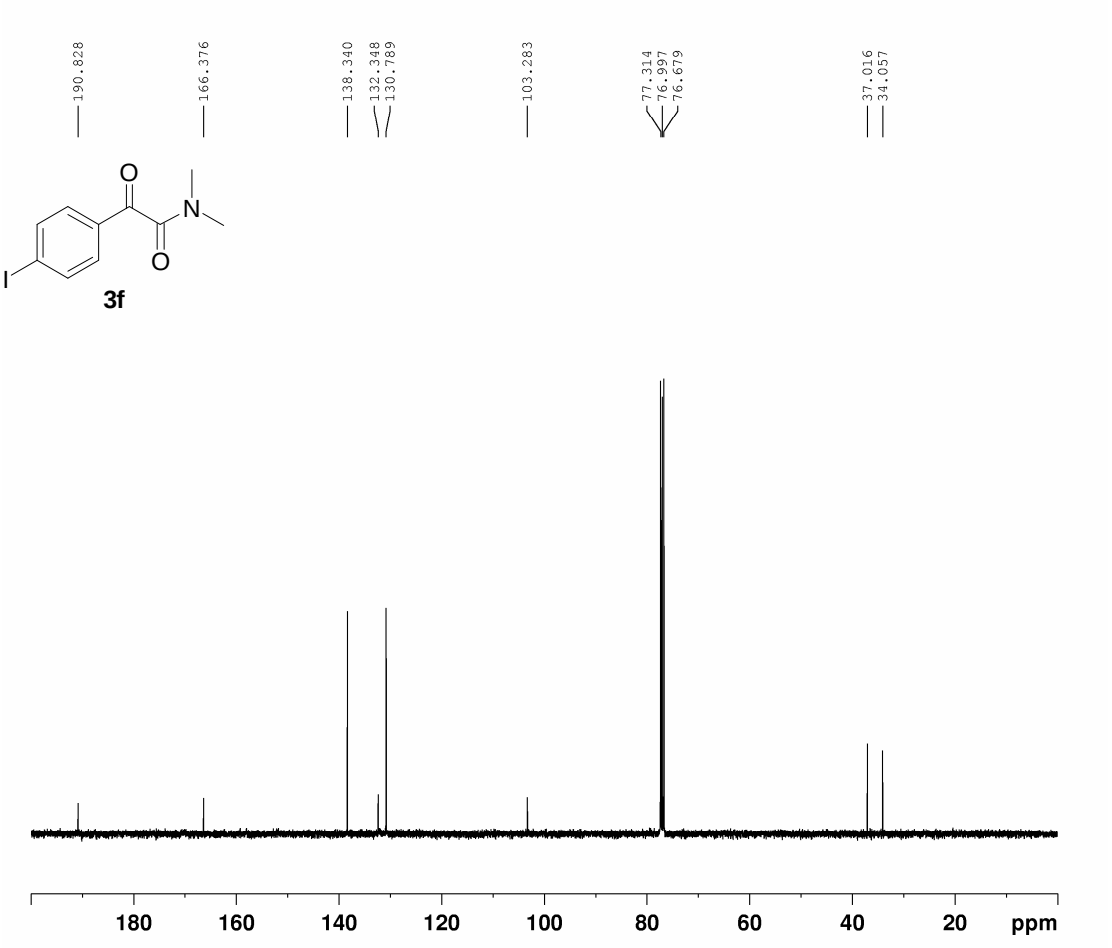


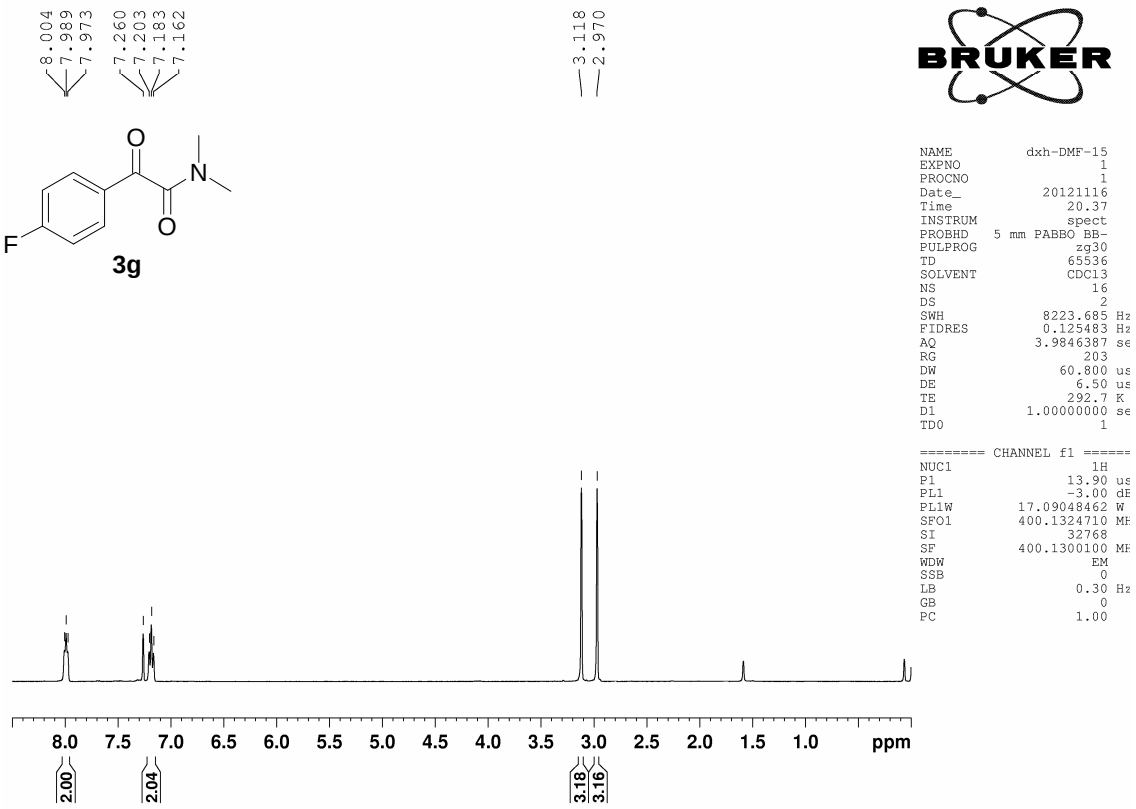


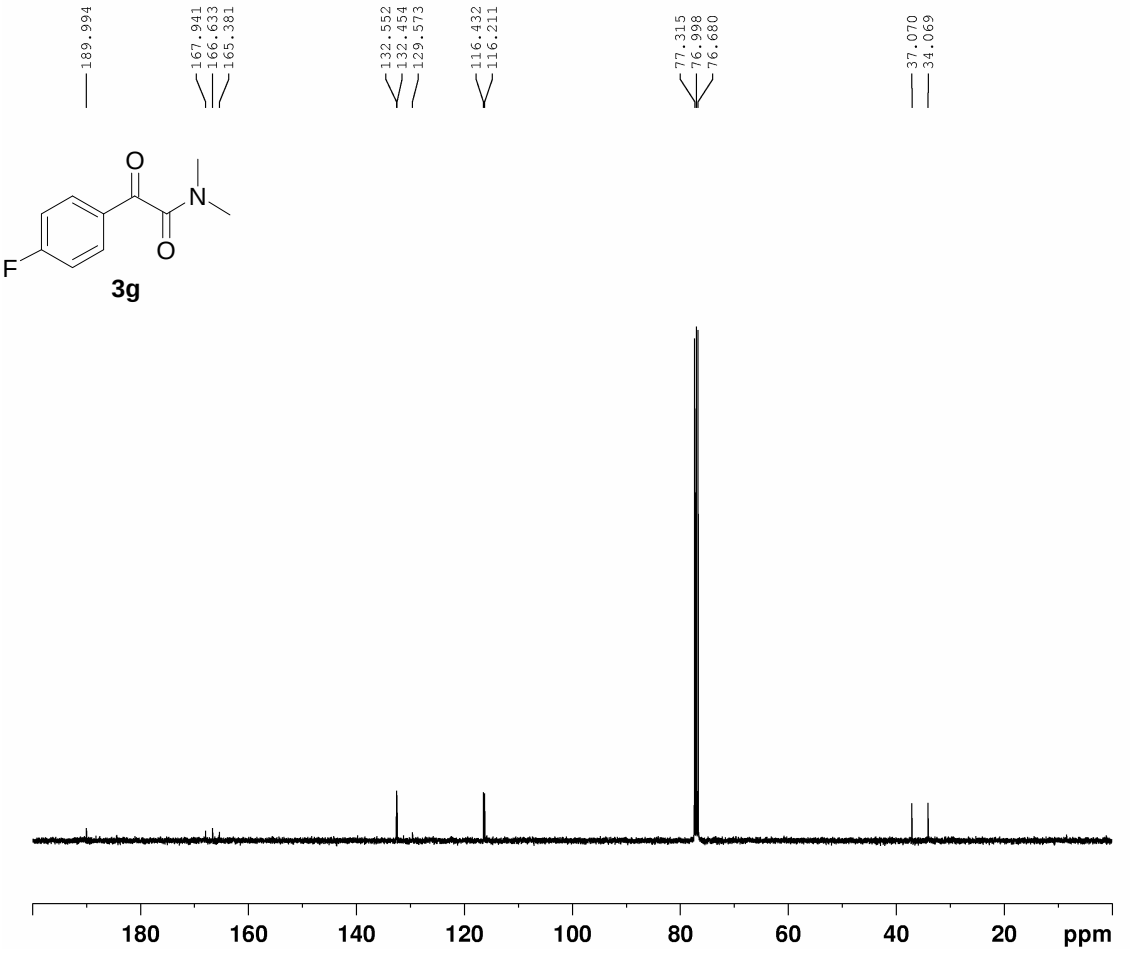


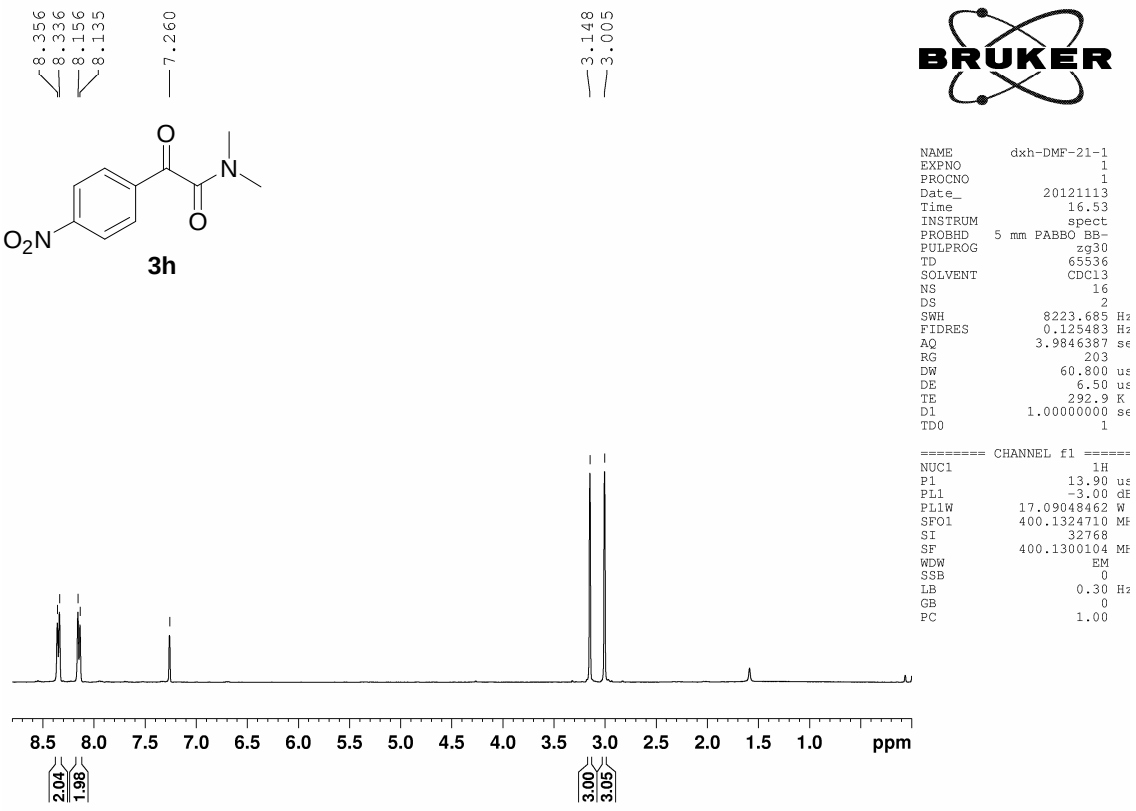








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TE 292.9 K
D1 1.00000000 se
TD0 1
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SFO1 400.1324710 MH
SI 32768
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SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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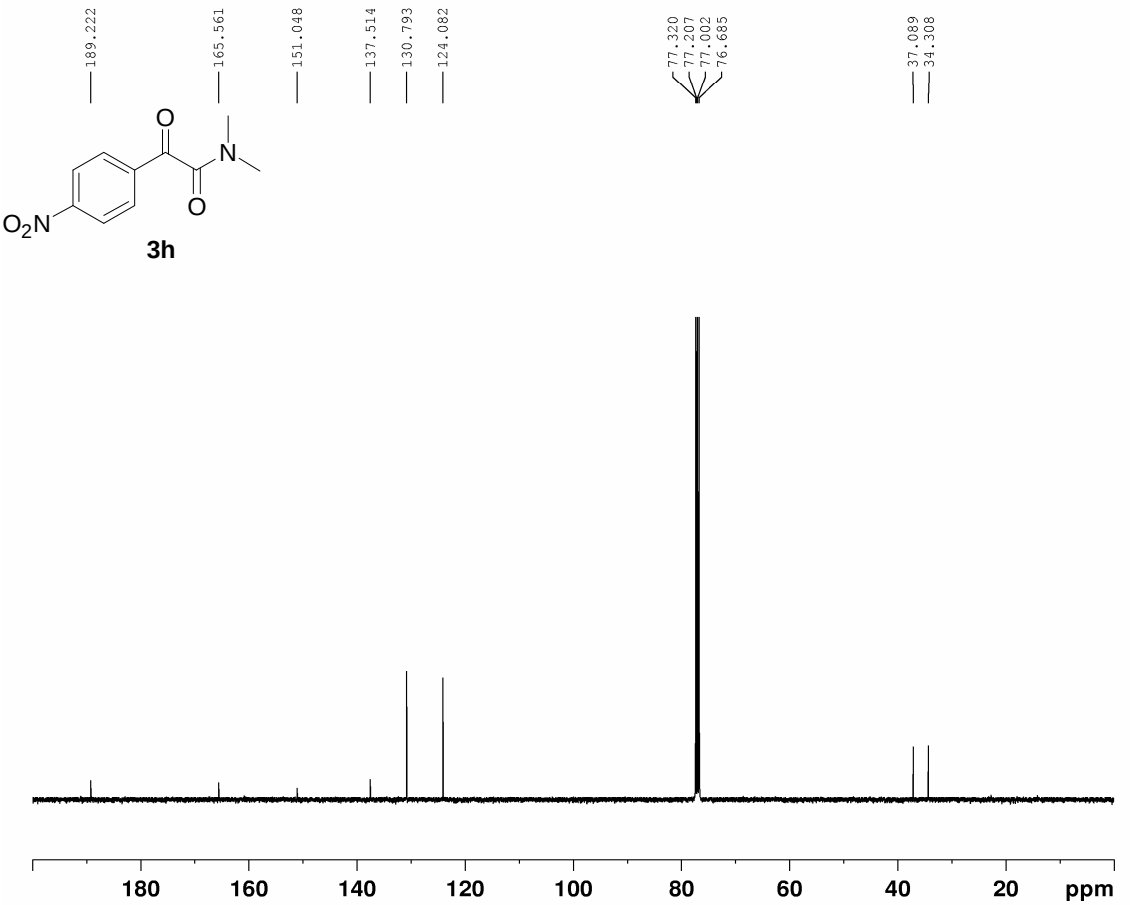
3.05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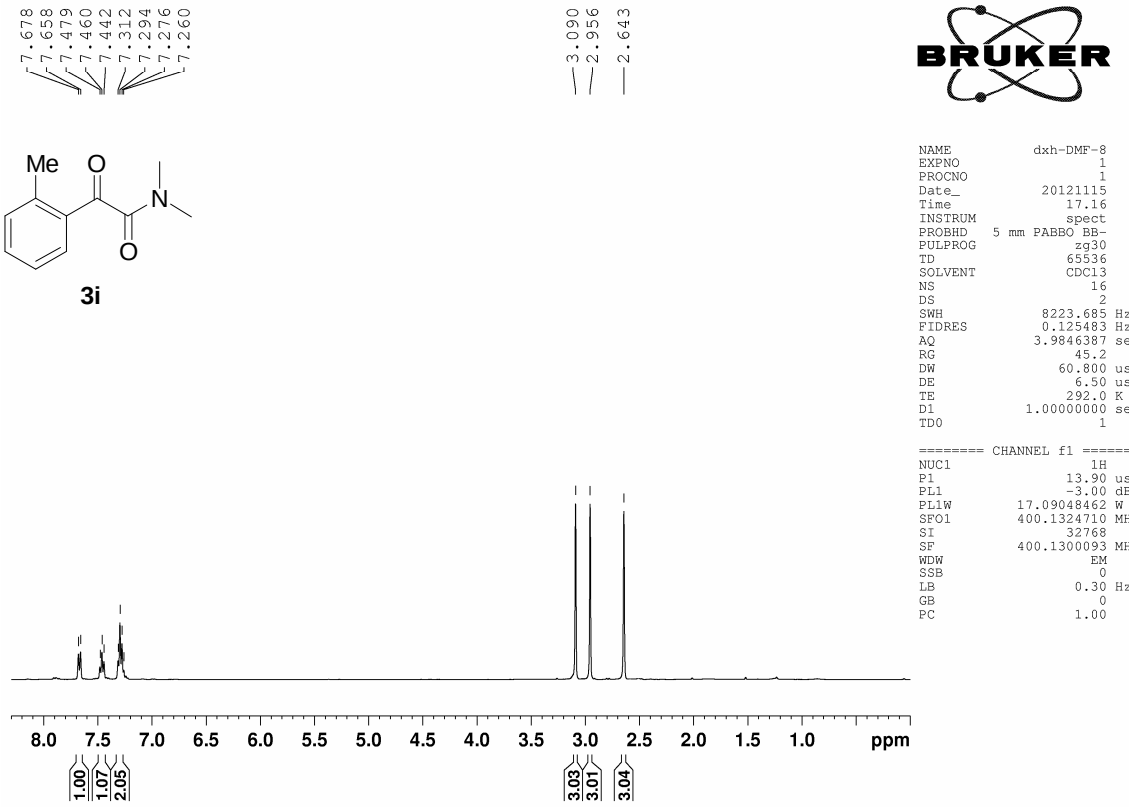

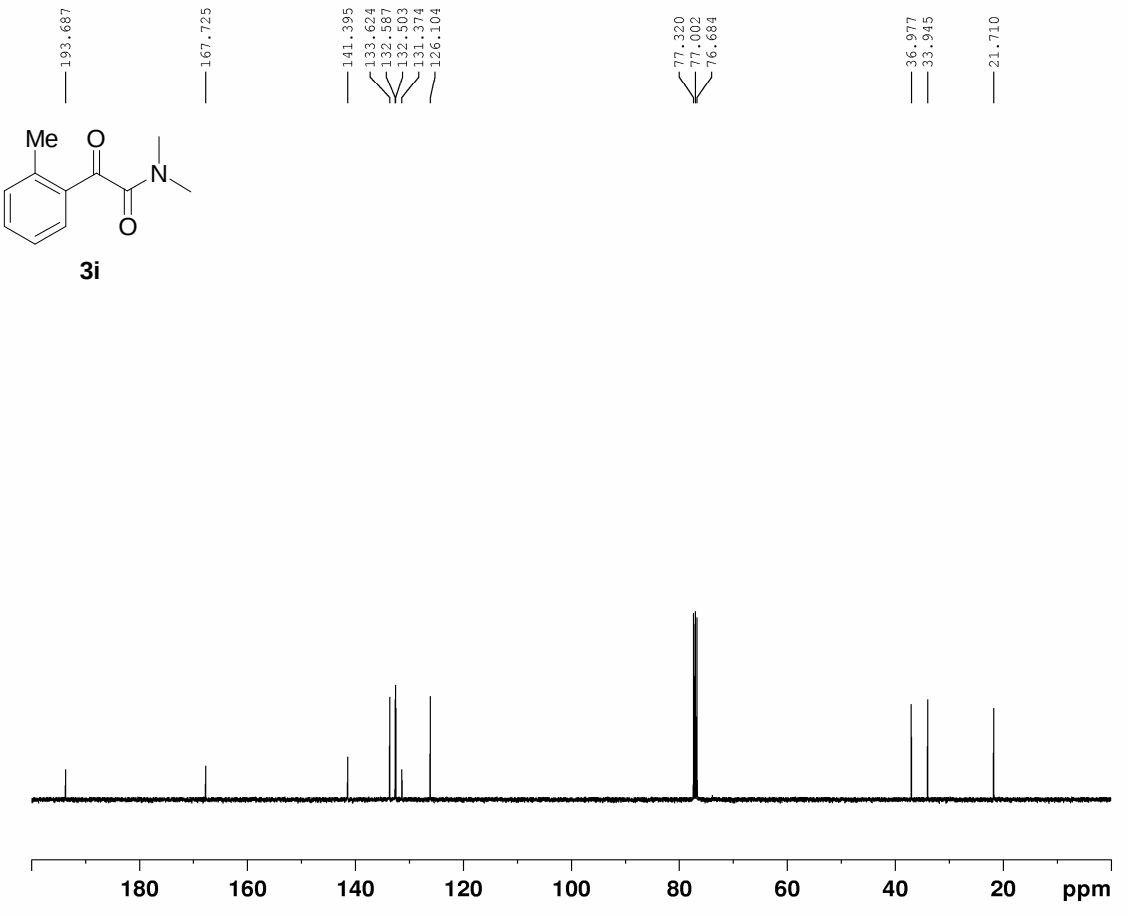

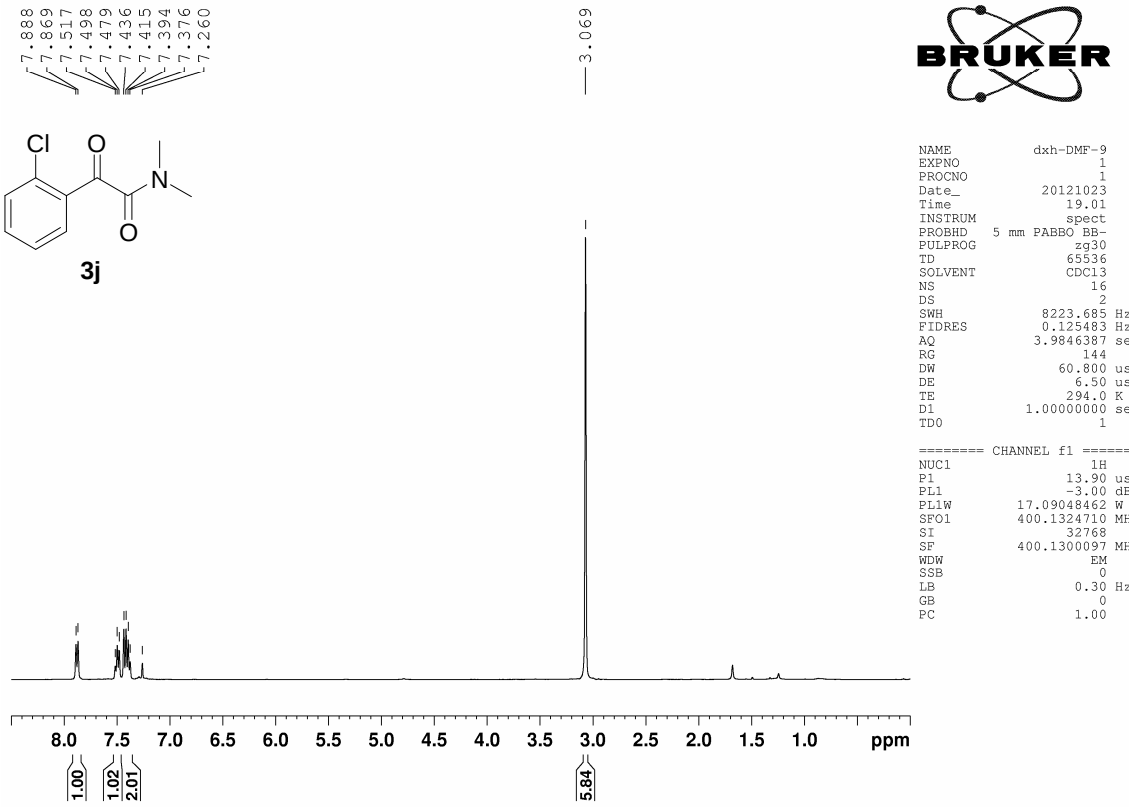
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TD0 1
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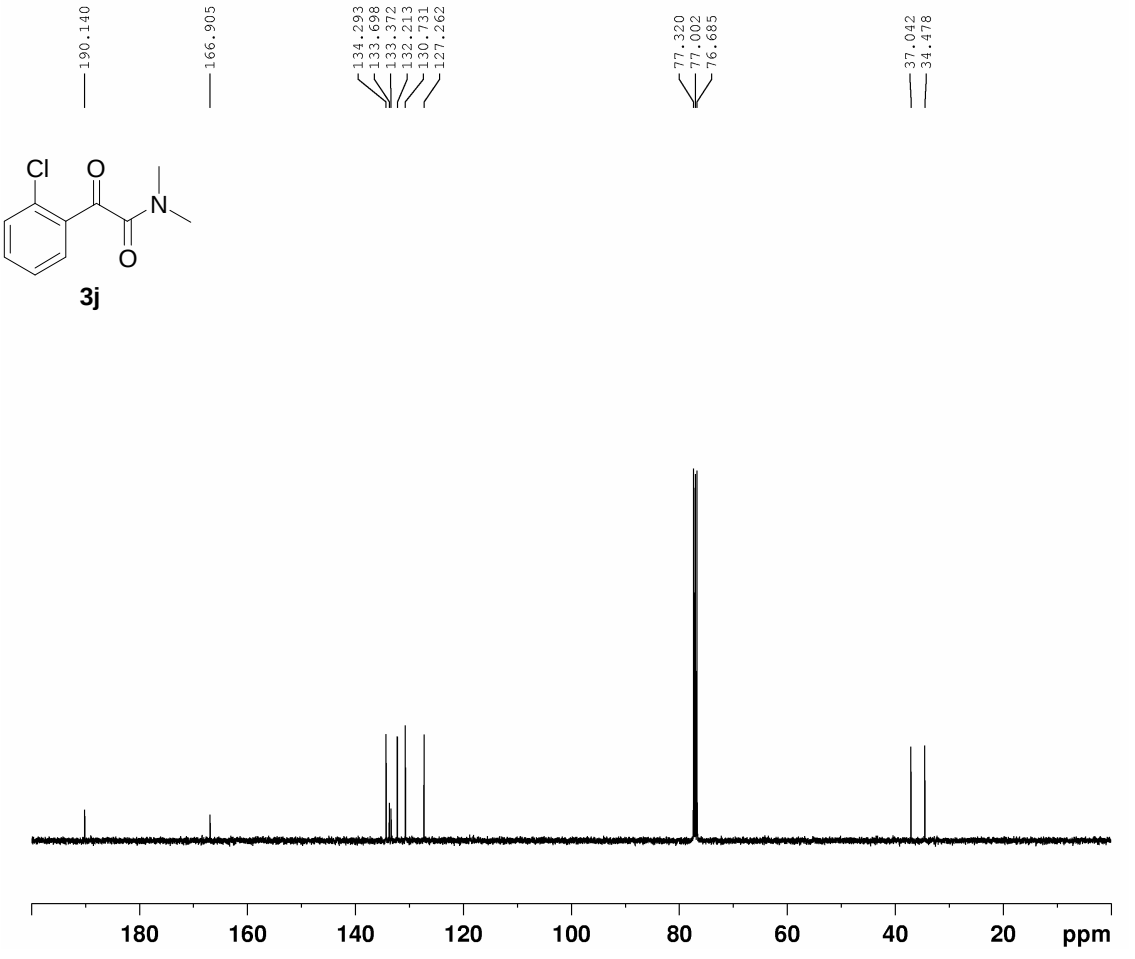
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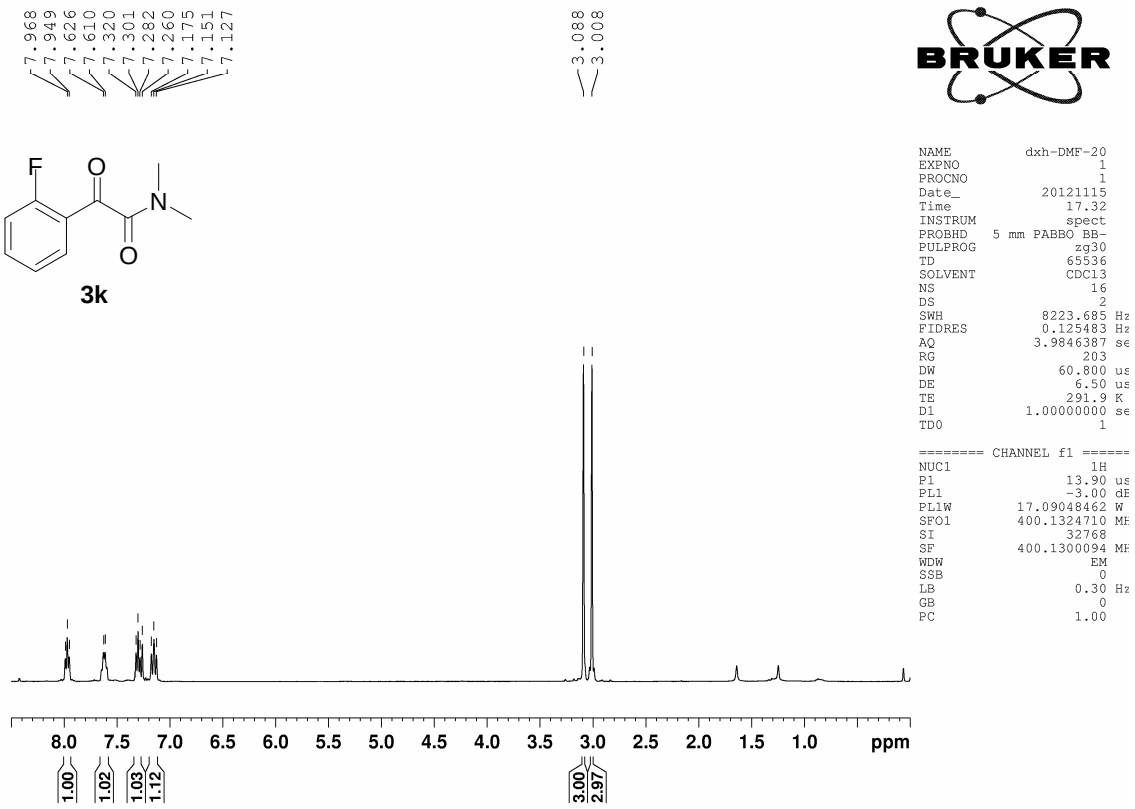
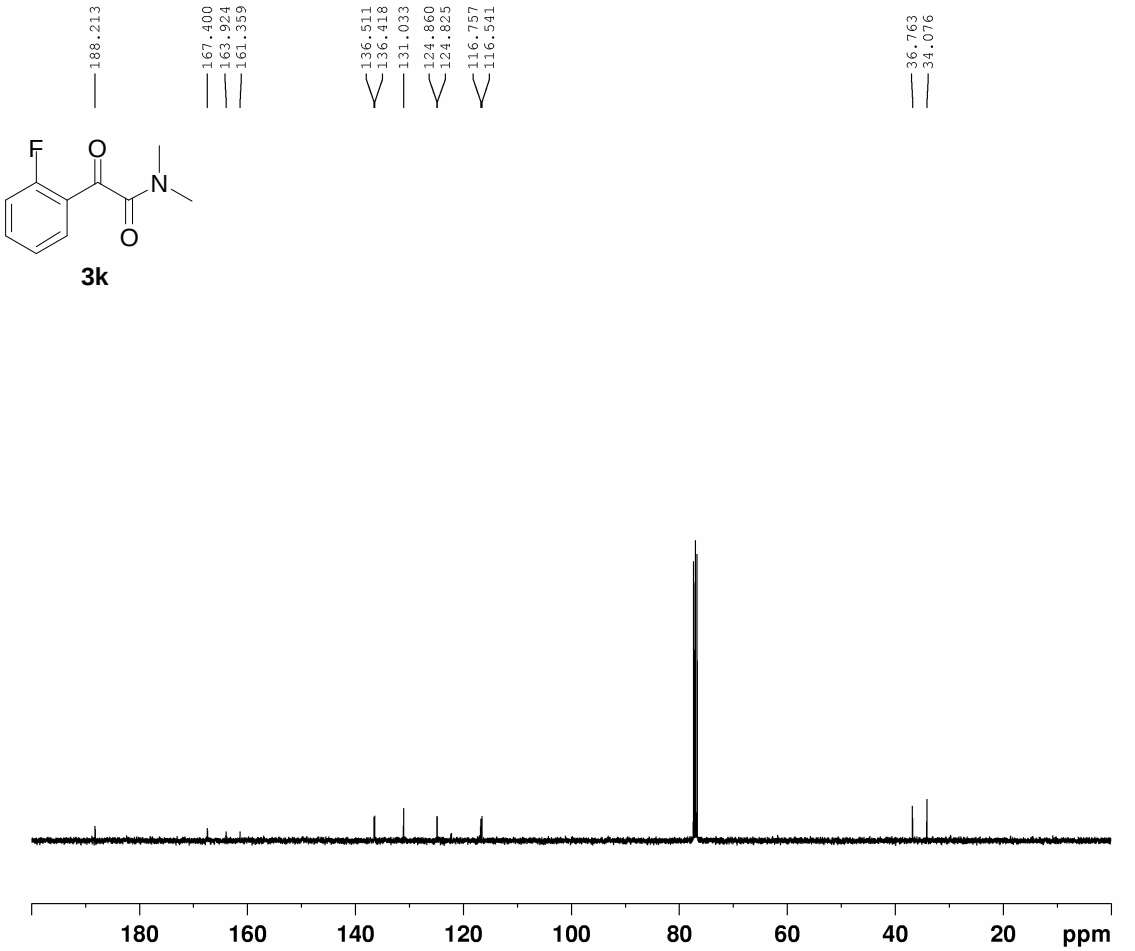
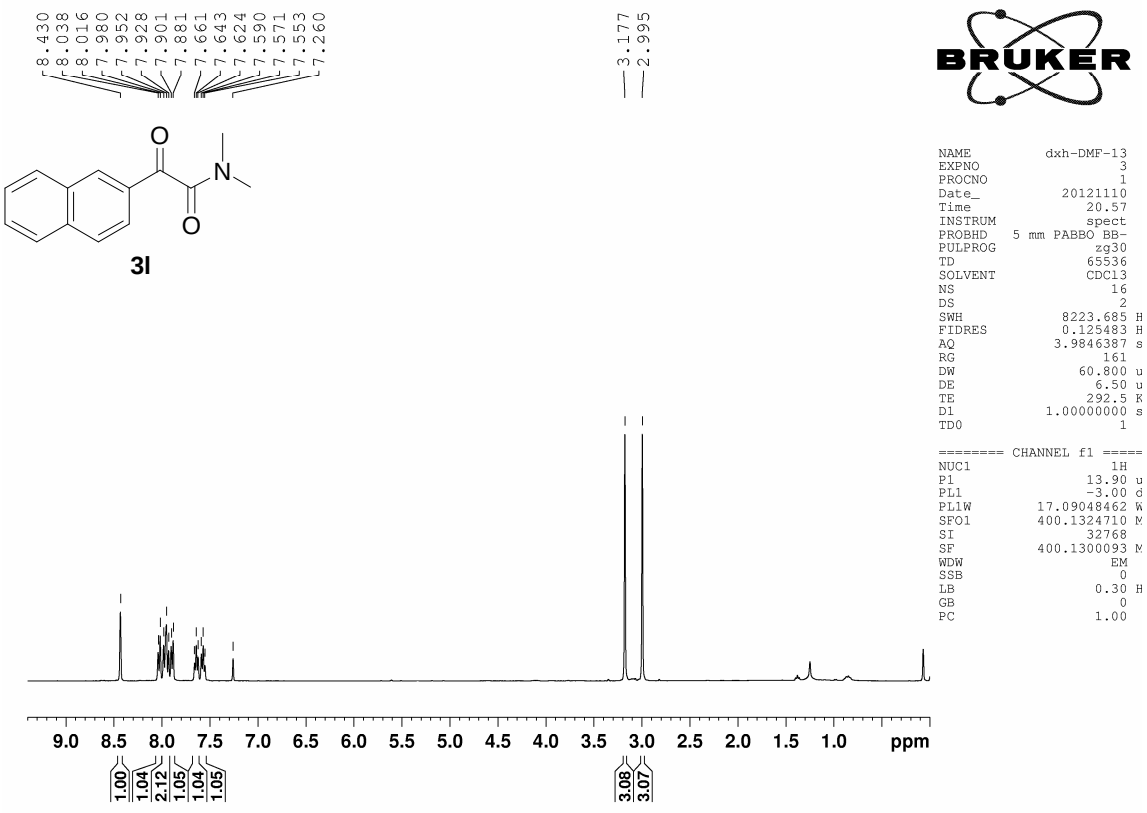
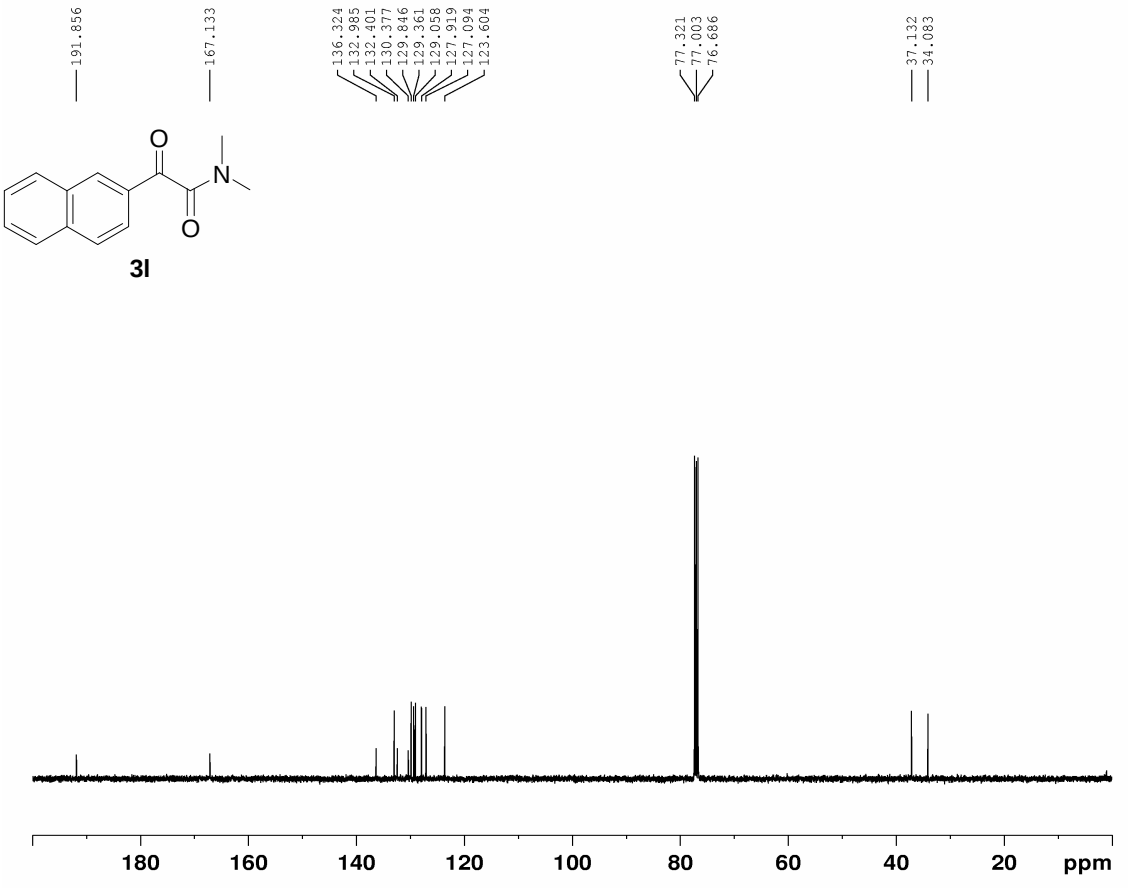
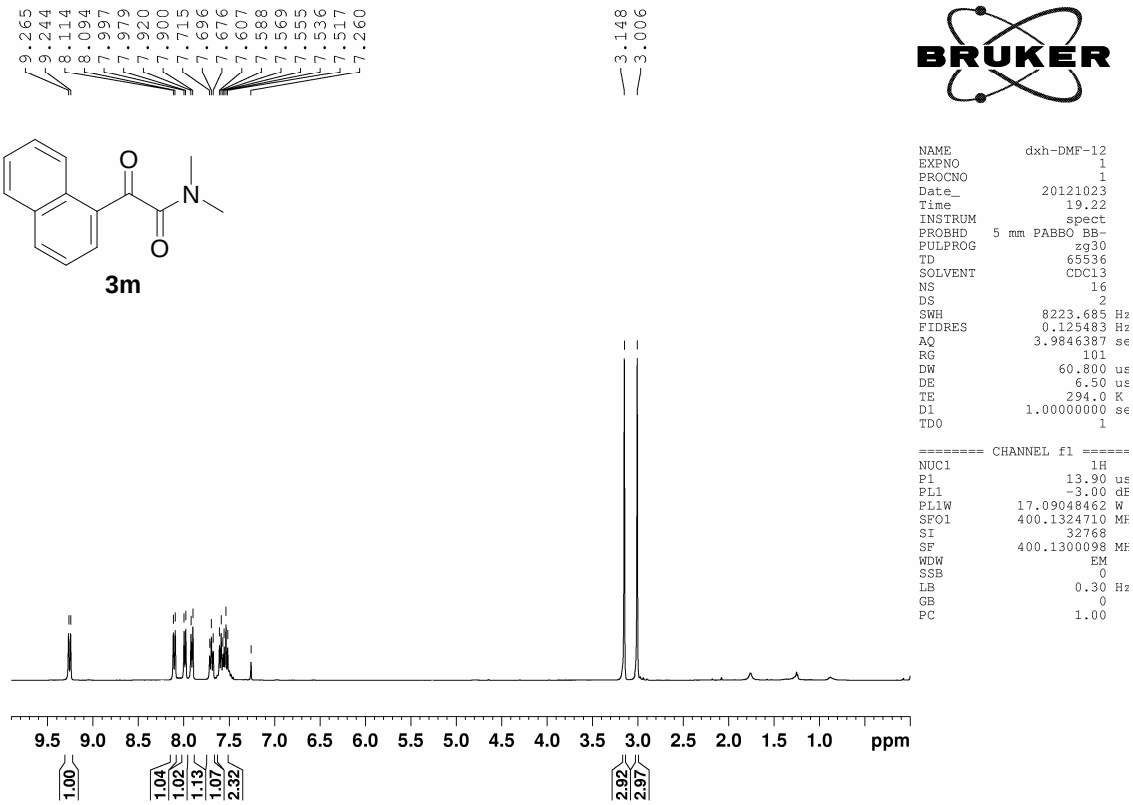
Cl
O
N
O
3j
180 160 140 120 100 80 60 40 20 ppm

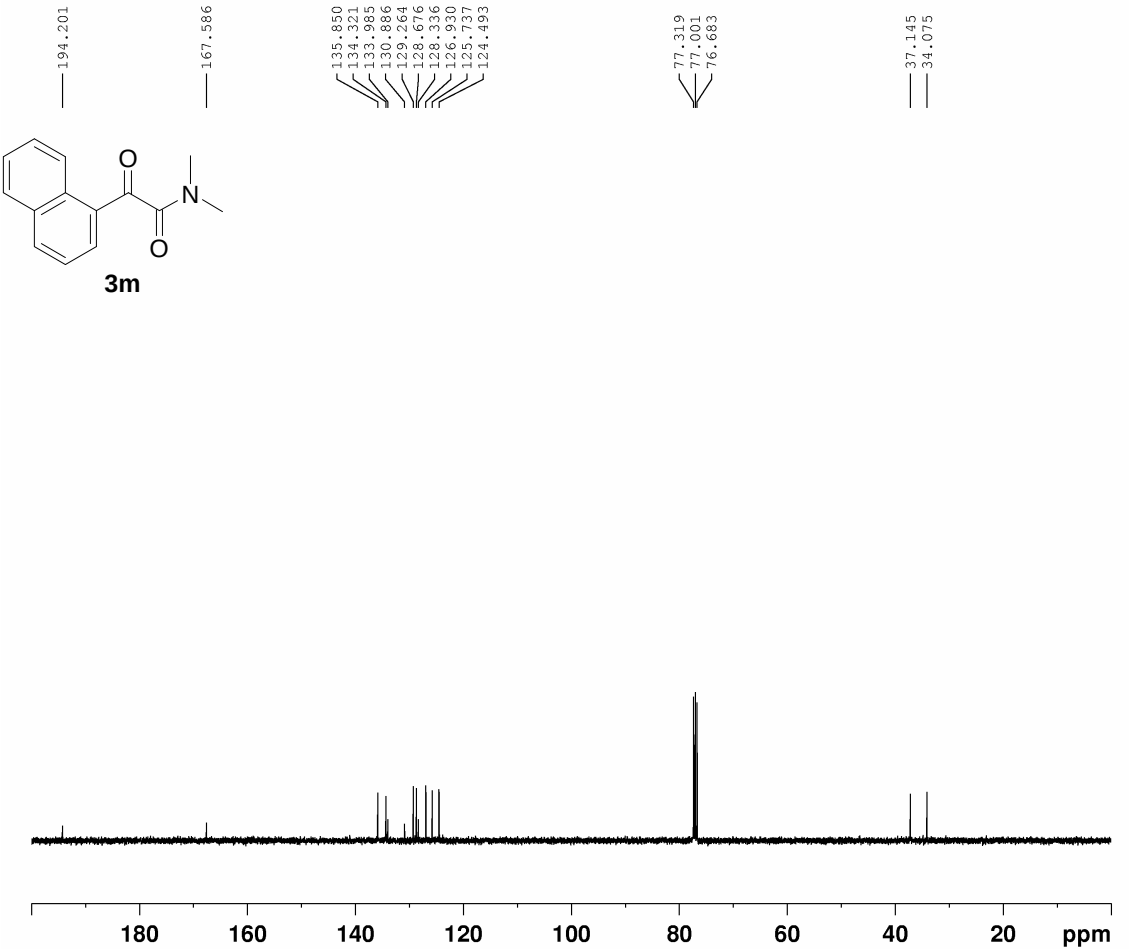

7.968
7.949
7.626
7.610
7.320
7.301
7.282
7.260
7.175
7.151
7.127
3.088
3.008
BRUKER
F
O
N
O
3k
NAME dxh-DMF-20
EXPNO 1
PROCNO 1
Date_ 20121115
Time 17.32
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 203
DW 60.800 us
DE 6.50 us
TE 291.9 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300094 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00
1.02
1.03
1.12
3.00
2.97

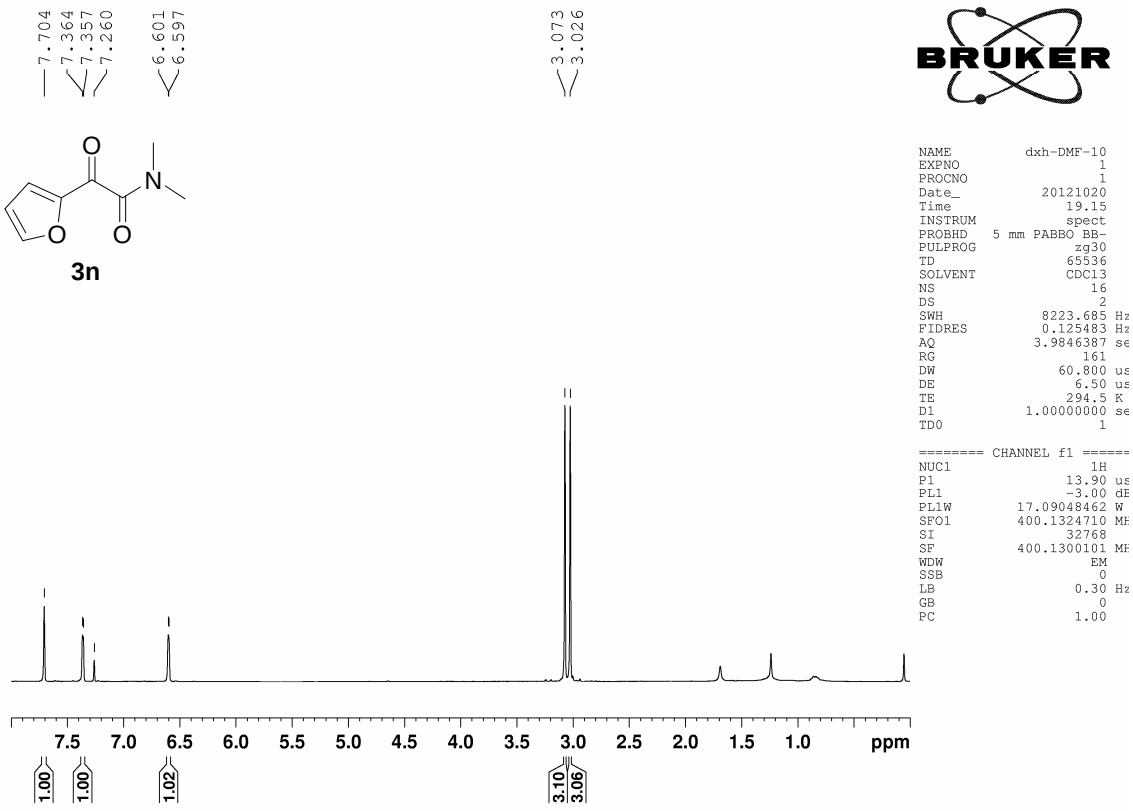

188.213
167.400
163.924
161.359
136.511
136.418
131.033
124.860
124.825
116.757
116.541
36.763
34.076
F
O
N
O
3k
180 160 140 120 100 80 60 40 20 ppm

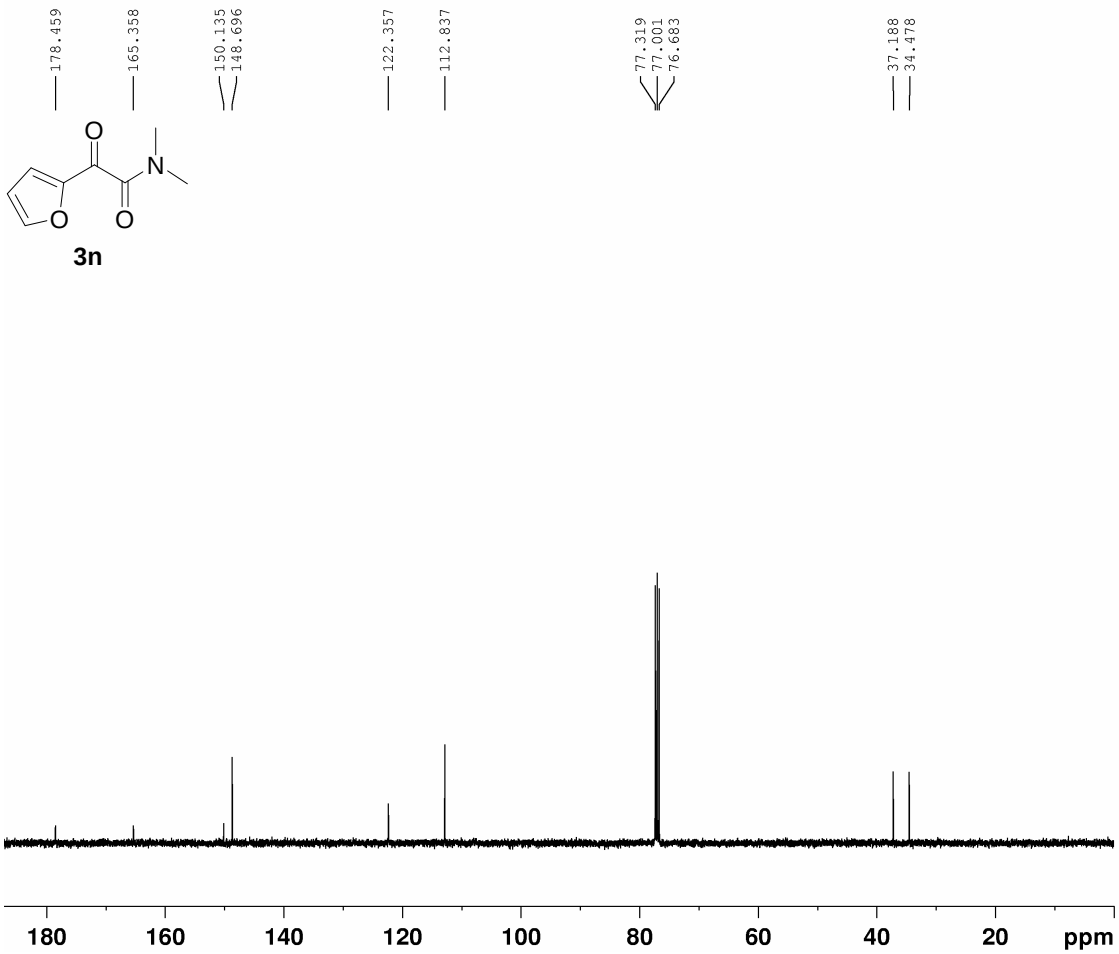

8.430
8.038
8.016
7.980
7.952
7.928
7.901
7.881
7.661
7.643
7.624
7.590
7.571
7.553
7.260
3.177
2.995
O
N
O
3l
BRUKER
NAME dxh-DMF-13
EXPNO 3
PROCNO 1
Date_ 20121110
Time 20.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 H
FIDRES 0.125483 H
AQ 3.9846387 s
RG 161
DW 60.800 u
DE 6.50 u
TE 292.5 K
D1 1.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 13.90 u
PL1 -3.00 d
PL1W 17.09048462 W
SFO1 400.1324710 M
SI 32768
SF 400.1300093 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00 1.04 2.12 1.05 1.04 1.05
3.08 3.07

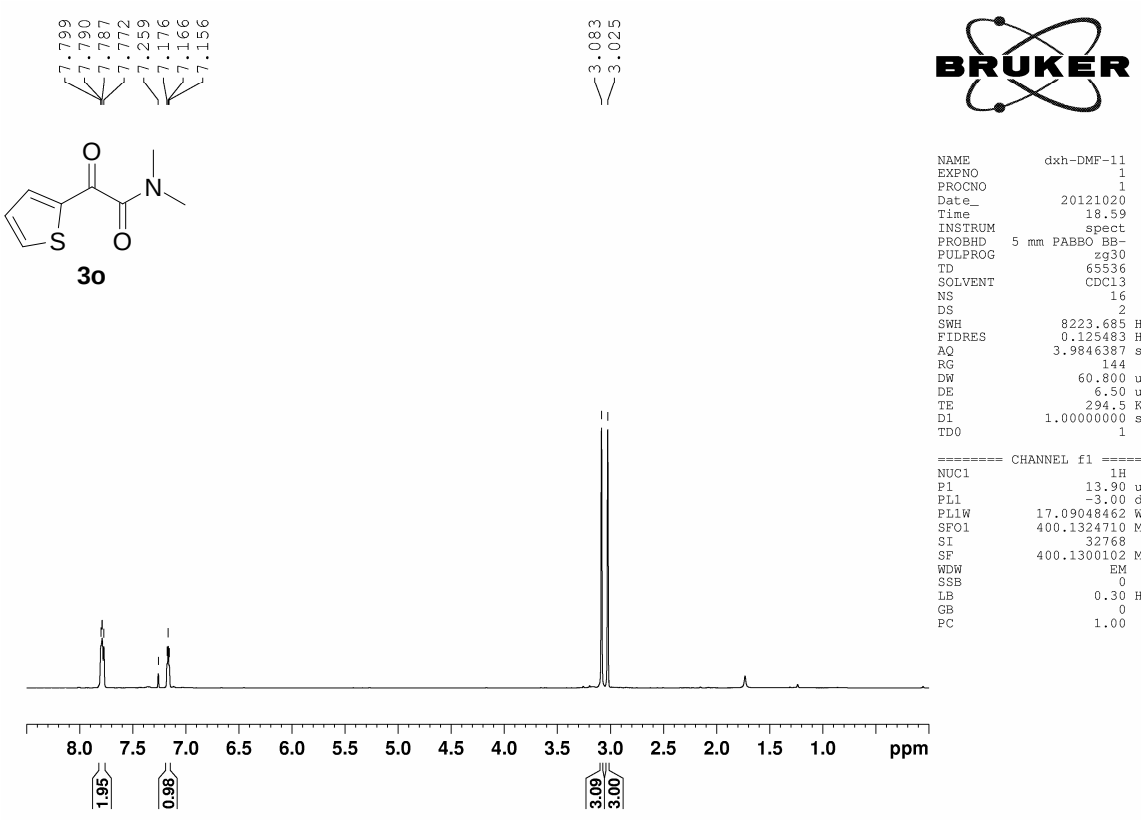

191.856
167.133
136.324
132.985
132.401
130.377
129.846
129.361
129.058
127.919
127.094
123.604
77.321
77.003
76.686
37.132
34.083
O
N
O
3l
180 160 140 120 100 80 60 40 20 ppm

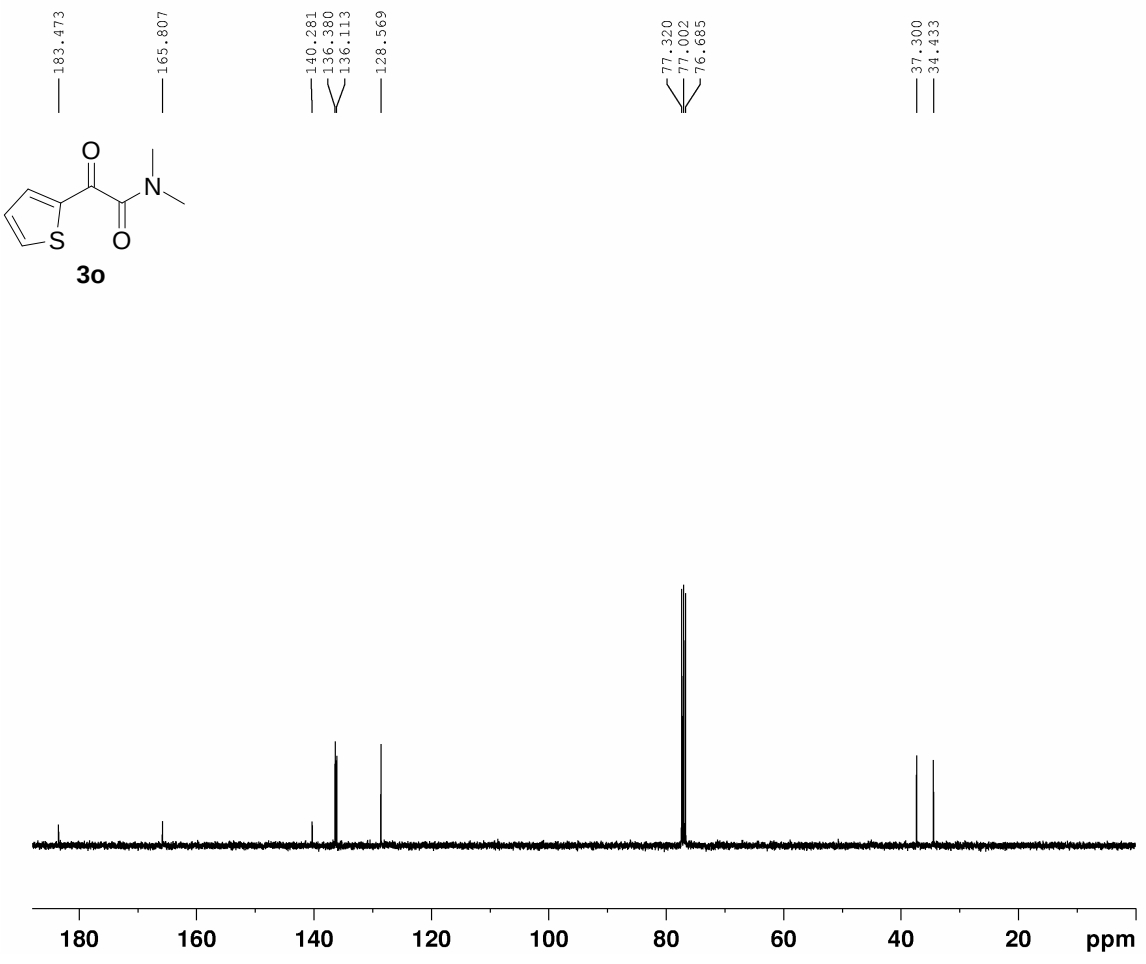

9.265
9.244
8.114
8.094
7.997
7.979
7.920
7.900
7.715
7.696
7.676
7.607
7.588
7.569
7.555
7.536
7.517
7.260
3.148
3.006
BRUKER
O
N
O
3m
NAME dxh-DMF-12
EXPNO 1
PROCNO 1
Date_ 20121023
Time 19.22
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 101
DW 60.800 us
DE 6.50 us
TE 294.0 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300098 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00
1.04
1.02
1.13
1.07
2.32
2.92
2.97

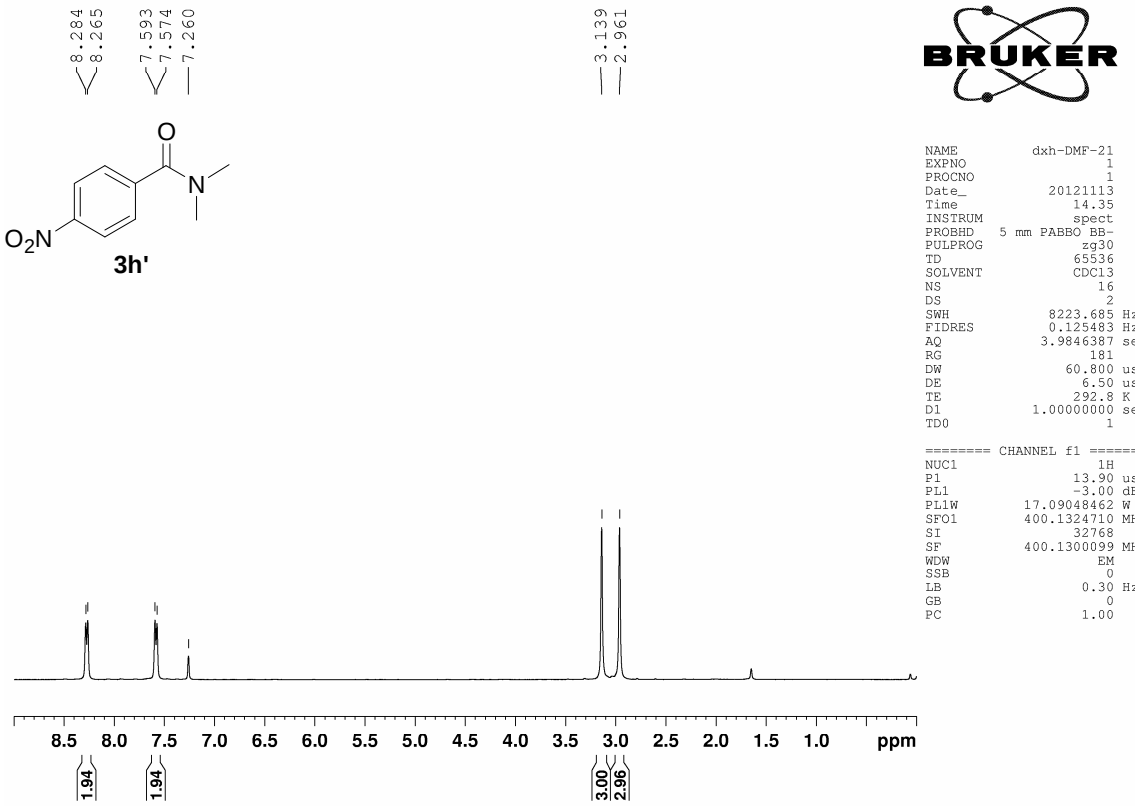

194.201
167.586
135.850
134.321
133.985
130.886
129.264
128.676
128.336
126.930
125.737
124.493
77.319
77.001
76.683
37.145
34.075
O
N
O
3m
180 160 140 120 100 80 60 40 20 ppm

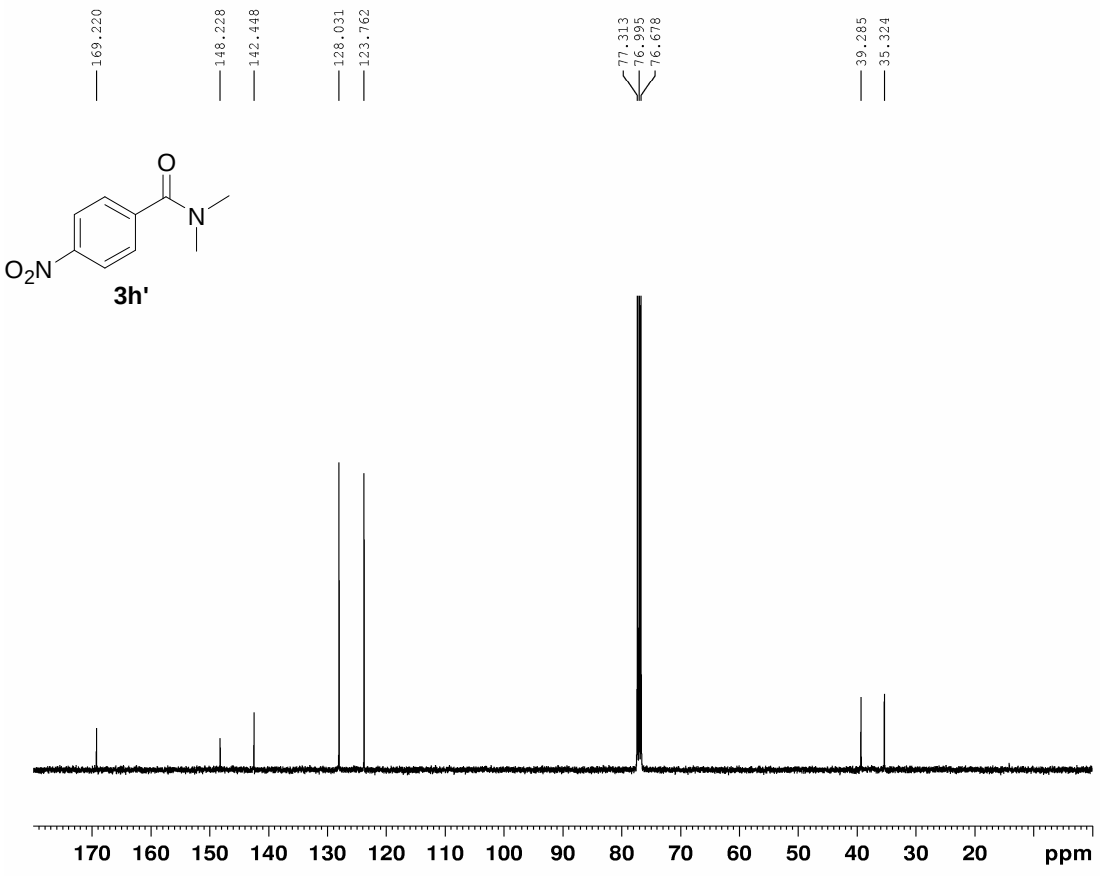

7.704
7.364
7.357
7.260
6.601
6.597
3.073
3.026
3n
NAME dxh-DMF-10
EXPNO 1
PROCNO 1
Date_ 20121020
Time 19.15
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 161
DW 60.800 us
DE 6.50 us
TE 294.5 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300101 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00
1.00
1.02
3.10
3.06

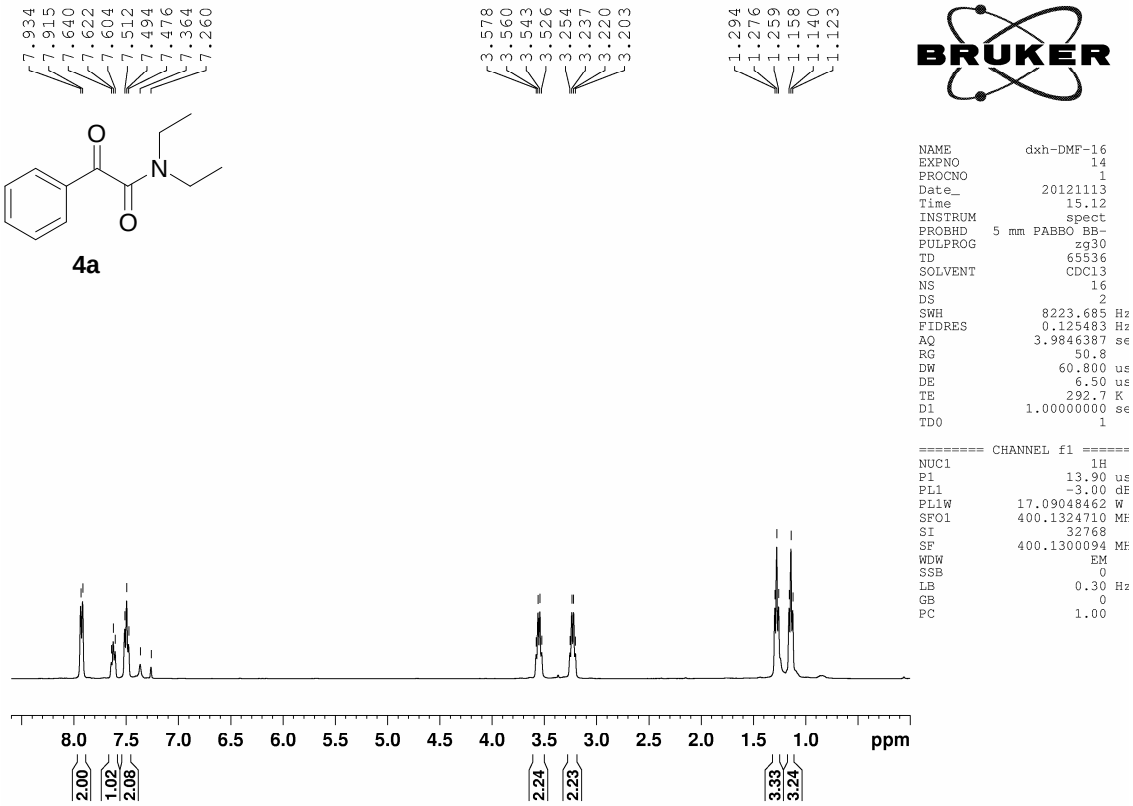

178.459
165.358
150.135
148.696
122.357
112.837
77.319
77.001
76.683
37.188
34.478
3n
180 160 140 120 100 80 60 40 20 ppm

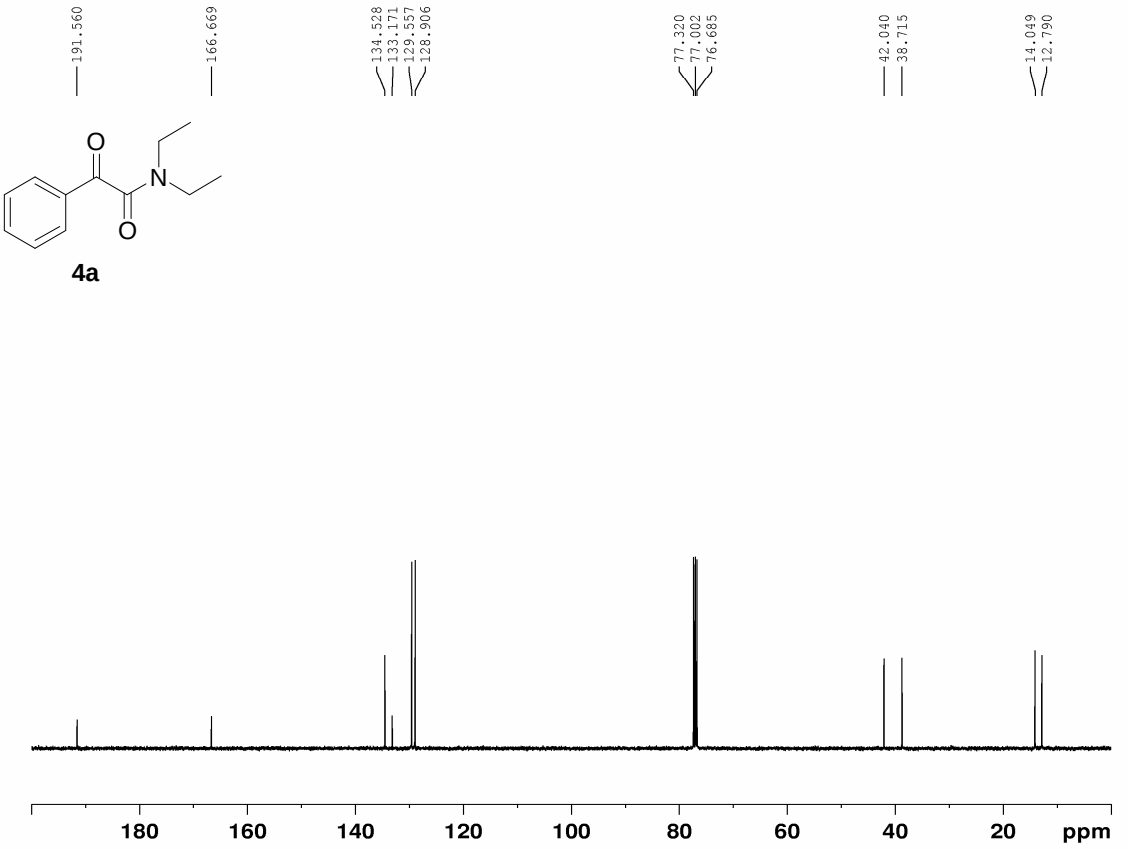


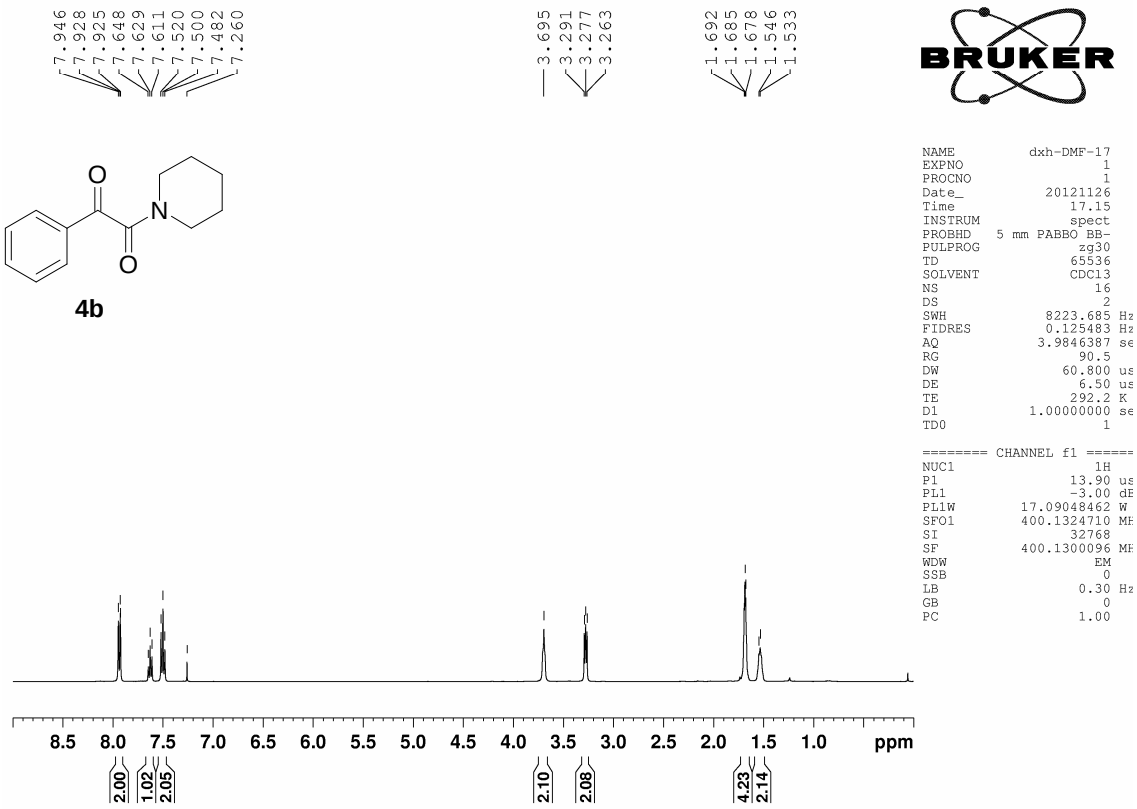


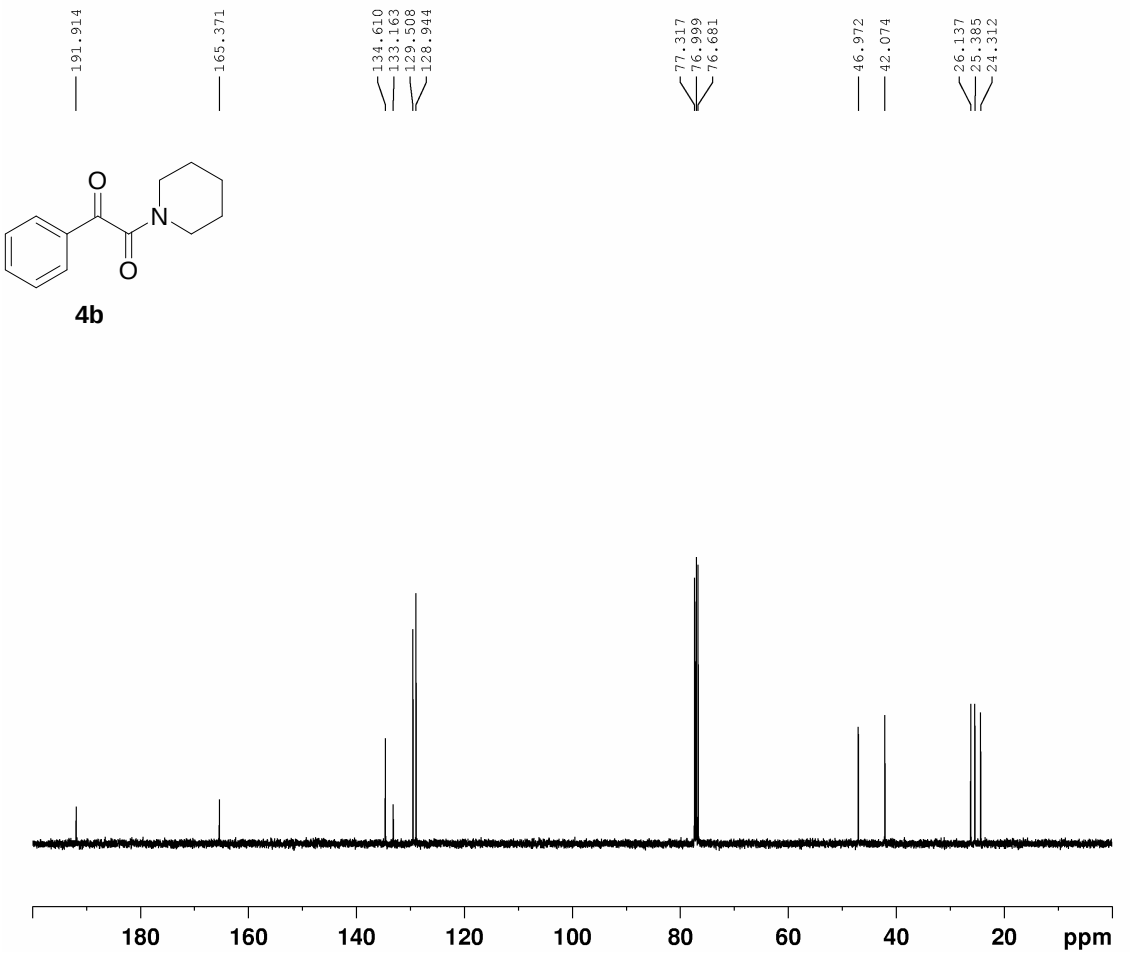

8.284
8.265
7.593
7.574
7.260
3.139
2.961
O
N
O_2N
3h'
BRUKER
NAME dxh-DMF-21
EXPNO 1
PROCNO 1
Date_ 20121113
Time 14.35
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 181
DW 60.800 usec
DE 6.50 usec
TE 292.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 usec
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300099 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.94
1.94
3.00
2.96

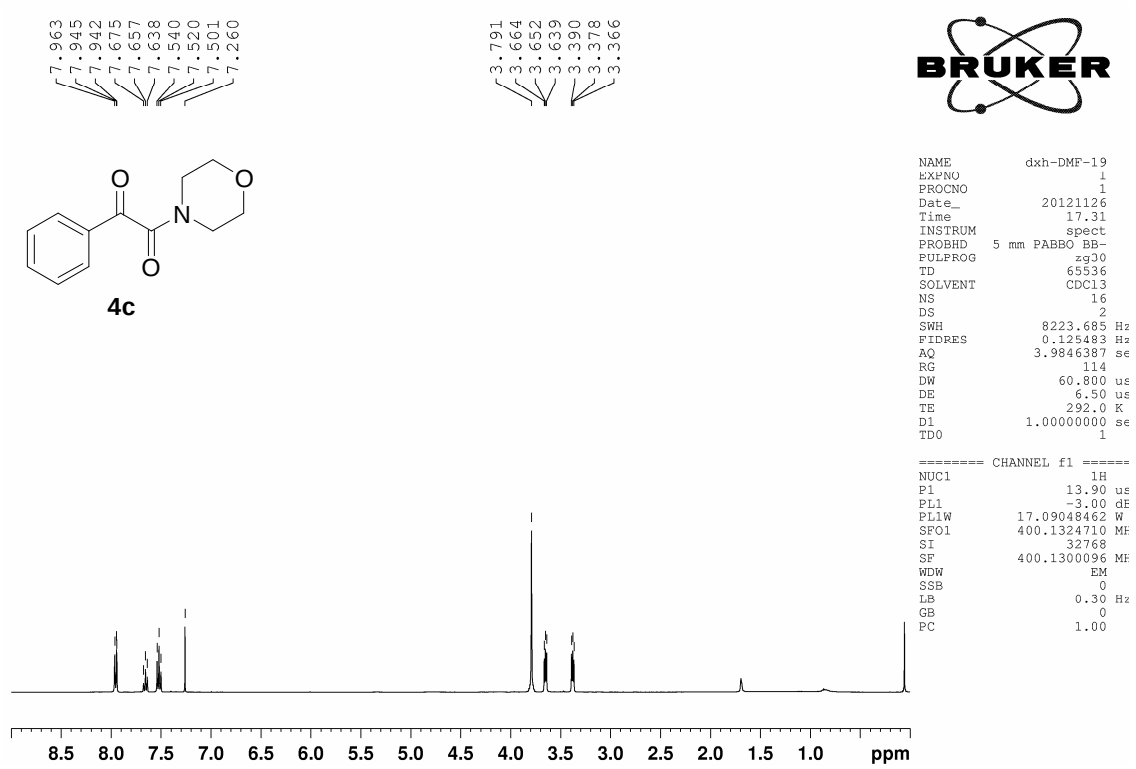

169.220
148.228
142.448
128.031
123.762
77.313
76.995
76.678
39.285
35.324
O
N
O_2N
3h'
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

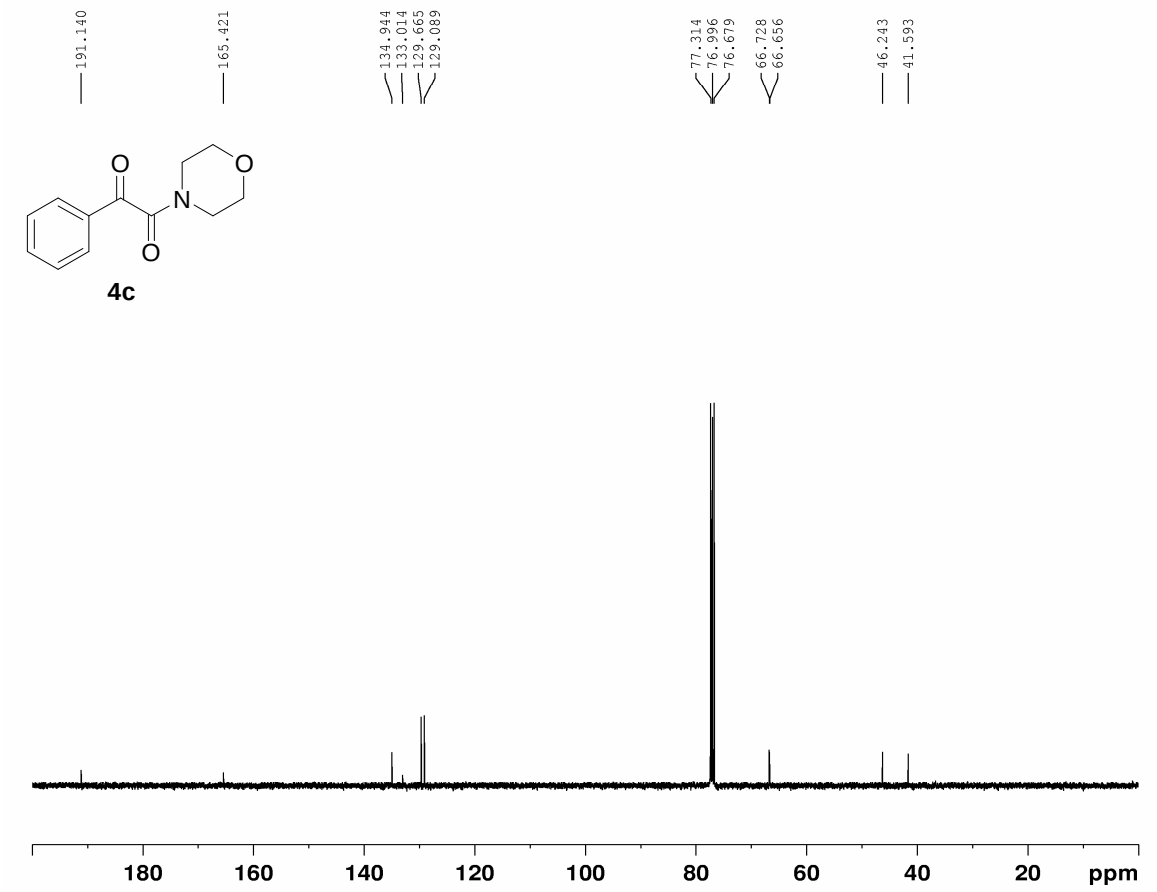

7.934
7.915
7.640
7.622
7.604
7.512
7.494
7.476
7.364
7.260
3.578
3.560
3.543
3.526
3.254
3.237
3.220
3.203
1.294
1.276
1.259
1.158
1.140
1.123
BRUKER
O
N
O
4a
NAME dxh-DMF-16
EXPNO 14
PROCNO 1
Date_ 20121113
Time 15.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 50.8
DW 60.800 us
DE 6.50 us
TE 292.7 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300094 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.00
1.02
2.08
2.24
2.23
3.33
3.24

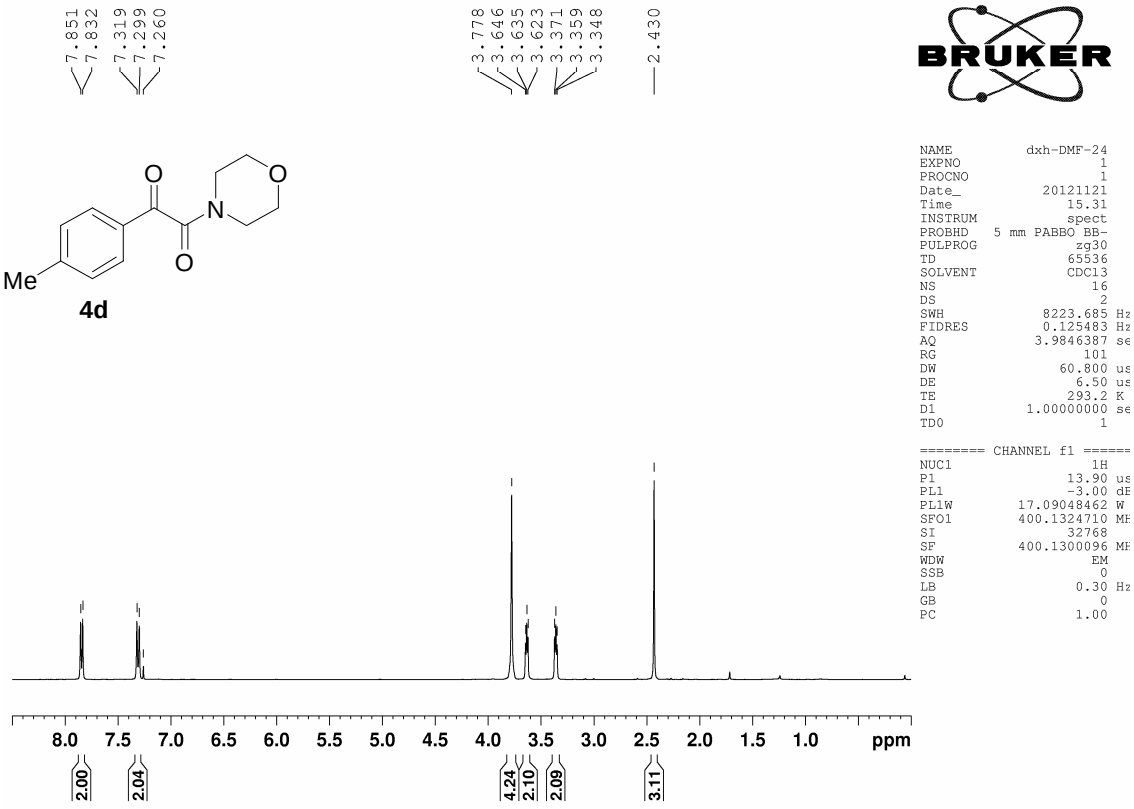

191.560
166.669
134.528
133.171
129.557
128.906
77.320
77.002
76.685
42.040
38.715
14.049
12.790
O
N
O
4a
180 160 140 120 100 80 60 40 20 ppm

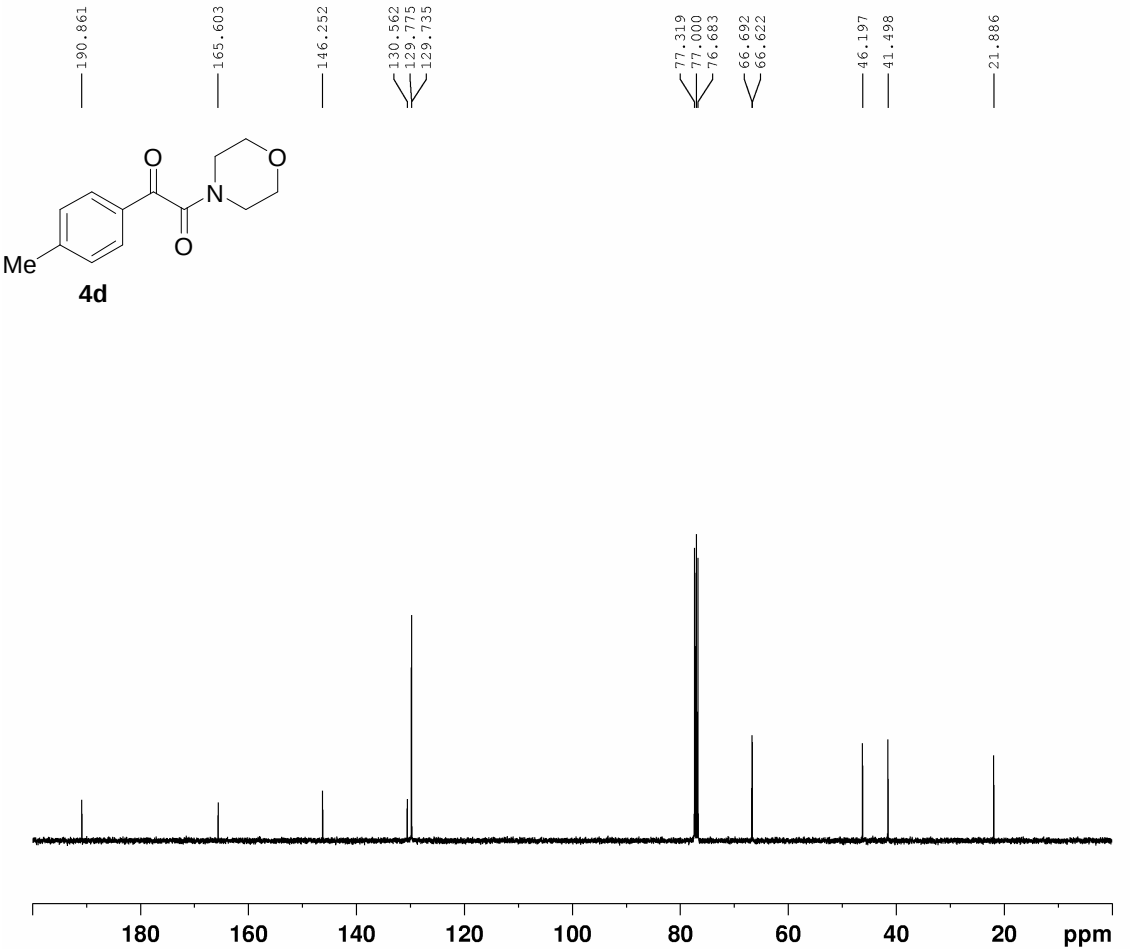

7.946
7.928
7.925
7.648
7.629
7.611
7.520
7.500
7.482
7.260
3.695
3.291
3.277
3.263
1.692
1.685
1.678
1.546
1.533
BRUKER
O
N
O
4b
NAME dxh-DMF-17
EXPNO 1
PROCNO 1
Date_ 20121126
Time 17.15
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 90.5
DW 60.800 us
DE 6.50 us
TE 292.2 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300096 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.00
1.02
2.05
2.10
2.08
4.23
2.14


191.914
165.371
134.610
133.163
129.508
128.944
77.317
76.999
76.681
46.972
42.074
26.137
25.385
24.312
O
N
O
4b
180 160 140 120 100 80 60 40 20 ppm


7.963
7.945
7.942
7.675
7.657
7.638
7.540
7.520
7.501
7.260
3.791
3.664
3.652
3.639
3.390
3.378
3.366
BRUKER
NAME dxh-DMF-19
EXPNO 1
PROCNO 1
Date_ 20121126
Time 17.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 114
DW 60.800 us
DE 6.50 us
TE 292.0 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300096 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
O
N
O
4c
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm


191.140
165.421
134.944
133.014
129.665
129.089
77.314
76.996
76.679
66.728
66.656
46.243
41.593
O
O
N
O
4c
180 160 140 120 100 80 60 40 20 ppm


7.851
7.832
7.319
7.299
7.260
3.778
3.646
3.635
3.623
3.371
3.359
3.348
2.430
BRUKER
NAME dxh-DMF-24
EXPNO 1
PROCNO 1
Date_ 20121121
Time 15.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 101
DW 60.800 us
DE 6.50 us
TE 293.2 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.90 us
PL1 -3.00 dB
PL1W 17.09048462 W
SFO1 400.1324710 MH
SI 32768
SF 400.1300096 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
O
N
O
Me
4d
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.00
2.04
4.24
2.10
2.09
3.11


190.861
165.603
146.252
130.562
129.775
129.735
77.319
77.000
76.683
66.692
66.622
46.197
41.498
21.886
O
O
N
O
Me
4d
180 160 140 120 100 80 60 40 20 ppm