Supporting Information

Umpolung of Halide Reactivity: Efficient (Diacetoxyiodo)benzene Mediated Electrophilic α-Halogenation of 1,3-Dicarbonyl Compounds

Ramulu Akula, Marc Galligan and Hasim Ibrahim*

Centre for Synthesis and Chemical Biology, School of Chemistry and Chemical Biology,

University College Dublin, Belfield, Dublin 4, Ireland.

hasim.ibrahim@ucd.ie

I. General remarks

NMR spectra were recorded on Varian Inova 300 MHz, Varian 400 MHz FT spectrometers at room temperature with $CDCl_3$ as the internal standard. The reference values used for $CDCl_3$ were 7.26 and 77.00 ppm for ^1H and ^{13}C NMR spectra, respectively. High resolution mass spectra were measured on a Waters/Micromass GCT and Waters 2996 Photodiode Array Detector instruments. Infrared spectra were recorded on a Varian 3100 FT-IR spectrometer at room temperature. Elemental analysis was performed by UCD's School of Chemistry and Chemical Biology micro analytical service. Melting points were recorded in open capillaries on a digital Barnsted Electro Thermal 9300 melting point apparatus and are uncorrected.

II. Materials

All reagents were obtained from commercial suppliers and used without further purification. HPLC grade acetonitrile was purchased from Sigma-Aldrich and used as received. β-Keto esters (Table 2, entries 1,[1] 3,[1] 4,[1] 5,[2] 8[3]), 2-methyl-1-phenylbutane-1,3-dione,[4] β-keto amides (Table 2, entries 12, 13),[5] diethyl 3-oxobutan-2-ylphosphonate[6] and (diacetoxyiodo)benzene (DIB)[7] were prepared according to literature procedures. Thin layer chromatography was performed on Merck Aluminium sheets (silica gel 60 F_{254}). Detection was by UV or by colouration with ceric ammonium molybdate (CAM) or vanillin. Flash column chromatography was performed using Merck silica gel 60 (230-400 mesh).

III. General procedure for the (diacetoxyiodo)benzene mediated electrophilic halogenation of 1,3-dicarbonyl compounds

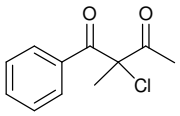
TiX_4 (0.3 mmol) was added *via* a syringe ($TiCl_4$) or as a solid in one portion ($TiBr_4$) to a stirred solution of the substrate (1 mmol) in acetonitrile (2 mL) which resulted in an

immediate colour change to brick red. DIB (1.2 mmol) was added in one portion to the above solution. The reaction mixture became homogenous as the reaction progressed and a colour change to pale yellow was observed. At that time TLC analysis showed the disappearence of the starting material. The reaction mixture was then diluted with diethyl ether (15 mL) and washed with water (20 mL). The aqueous layer was extracted with diethyl ether (10 mL), the combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, pentane-diethyl ether).

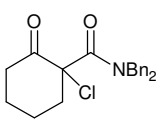
IV. Dichlorination of benzyl 3-oxobutanoate

$TiCl_4$ (0.55 mmol) was added *via* a syringe to a stirred solution of the substrate (1 mmol) in acetonitrile (2 mL) which resulted in an immediate colour change to brick red. DIB (2.2 mmol) was added in one portion to the above solution. The reaction mixture became homogenous as the reaction progressed and a colour change to pale yellow was observed. At that time TLC analysis showed the disappearence of the starting material.Work-up was as GP III.

V. Spectroscopic data of the new halogenated compounds

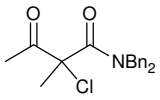


2-Chloro-2-methyl-1-phenylbutane-1,3-dione: Isolated as a colorless oil in 97% yield; Anal. cal. for $C_{11}H_{11}ClO_2$ (210.6568): C 62.72, H 5.26; found: C 62.65, H 5.37; IR (neat, cm^{-1}): 3000, 1709, 1700, 1595, 1447, 1251, 693; ^1H NMR (300 MHz, $CDCl_3$): δ 8.01 – 7.80 (2 H, m, Ph), 7.65 – 7.51 (1 H, m, Ph), 7.49 – 7.36 (2 H, m, Ph), 2.39 (3 H, s, COMe), 1.95 (3 H, s, CMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.3, 191.9, 133.6, 133.2, 129.8, 128.5, 75.0, 25.7, 25.2; CI-HRMS $C_{11}H_{12}ClO_2$ $[M+H]^+$ calculated: 211.0526, found: 211.0527.

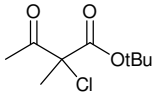


***N,N'*-Dibenzyl-1-chloro-2-oxocyclohexanecarboxamide:** Isolated as a white solid in 94% yield; mp: 68-70 °C; IR (KBr, cm^{-1}): 3030, 1730, 1651, 1496, 1418, 1235, 701; ^1H NMR (300 MHz, $CDCl_3$): δ 7.37 – 7.14 (6 H, m), 7.21 – 7.12 (4 H, m), 4.68 (1 H, d, J = 14.9, NCH_2), 4.60 (1 H, d, J = 16.2, NCH_2), 4.41 (1 H, d, J = 14.9, NCH_2), 4.34 (1 H, d, J = 16.2, NCH_2), 3.07 – 2.95 (1 H, m, $ClCH_2$), 2.84 – 2.71 (1 H, m, $ClCH_2$), 2.49 – 2.34 (1 H, m, $COCH_2$), 2.27 – 2.14 (1 H, m, $COCH_2$), 2.12 – 1.79 (4 H, m, CH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3, 166.4, 136.3, 135.5, 128.6, 128.5,

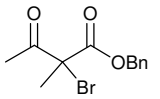
127.9, 127.6, 127.4, 127.3, 74.1, 50.8, 48.5, 43.2, 40.0, 28.7, 22.9; ESI-HRMS $C_{21}H_{23}ClNO_2$ $[M+H]^+$ calculated: 356.1417, found: 356.1412.



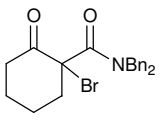
2-Chloro-2-methyl-3-oxo-*N,N*-diphenylmethylbutanamide: Isolated as a crystalline solid in 98% yield; mp: 94-98 °C; ; IR (KBr, cm^{-1}): 2941, 1714, 1642, 1496, 1420, 1220, 700. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.24 (6 H, m, Ph), 7.22 – 7.07 (4 H, m, Ph), 4.69 (1 H, d, *J* = 14.8, NCH_2), 4.54 (1 H, d, *J* = 15.7, NCH_2), 4.32 (1 H, d, *J* = 14.8, NCH_2), 4.28 (1 H, d, *J* = 15.7, NCH_2), 2.39 (3 H, s, COMe), 1.97 (3 H, s, CMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.8, 167.7, 136.2, 135.1, 128.8, 128.6, 128.1, 127.9, 127.6, 127.5, 71.5, 50.7, 48.0, 26.6, 25.2; ESI-HRMS $C_{19}H_{21}ClNO_2$ $[M+H]^+$ calculated: 330.1261, found: 330.1275.



***tert*-Butyl 2-chloro-2-methyl-3-oxobutanoate:** Isolated as a colorless oil in 87% yield; Anal. cal. for $C_9H_{15}ClO_3$ (206.6666): C 52.30, H 7.32; found: C 52.63, H 7.32; IR (neat, cm^{-1}): 2983, 2940, 1732, 1258, 775; ^1H NMR (400 MHz, $CDCl_3$): δ 2.35 (3 H, s, COMe), 1.78 (3 H, s, CMe), 1.49 (9 H, s, ^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.8, 166.9, 84.1, 71.6, 27.6, 25.3, 24.1; ESI-LRMS $C_9H_{15}ClNaO_3$ $[M+Na]^+$ calculated: 229.3, found: 229.1

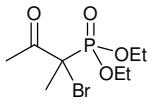


Benzyl 2-bromo-2-methyl-3-oxobutanoate: Isolated as a colorless oil in 92% yield; Anal. cal. for $C_{12}H_{13}BrO_3$ (284.0048): C 52.55, H 4.60; found: C 52.30, H 4.59; IR (neat, cm^{-1}): 3066, 3034, 2936, 1725, 1719, 1456, 1444, 1201, 596; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.28 (5 H, m, Ph), 5.27 (1 H, d, *J* = 12.2, OCH_2), 5.22 (1 H, d, *J* = 12.2, OCH_2), 2.37 (3 H, s, COMe), 1.99 (3 H, s, CMe). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 168.0, 134.5, 128.7, 128.7, 128.2, 68.5, 62.5, 25.7, 25.2; CI-HRMS $C_{12}H_{14}BrO_3$ $[M+H]^+$ calculated: 285.0126, found: 285.0126.



***N,N'*-Dibenzyl-1-bromo-2-oxocyclohexanecarboxamide:** Isolated as a colorless oil in 97% yield; IR (neat, cm^{-1}): 3063, 3029, 2944, 2869, 1717, 1650, 1496, 1452, 1228, 701; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.23 (6 H, m, Ph), 7.22 – 7.14 (4 H, m, Ph), 4.63 (1 H, d, *J* = 14.8, NCH_2), 4.56 (1 H, d, *J* = 16.1, NCH_2), 4.53 (1 H, d, *J* = 14.8, NCH_2), 4.38 (1 H, d, *J* = 16.1, NCH_2), 3.24 – 3.03 (1 H, m, $BrCCH_2$), 2.96 – 2.71 (1 H, m, $BrCCH_2$), 2.50 – 2.38 (1 H, m, $COCH_2$), 2.38 – 2.27 (1 H, m, $COCH_2$), 2.14 – 1.73 (4 H, m, CH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 166.4,

136.3, 135.3, 128.5, 128.4, 127.9, 127.5, 127.4, 127.3, 68.1, 51.2, 48.5, 44.2, 40.0, 28.7, 23.8; ESI-HRMS $C_{21}H_{23}BrNO_2$ $[M+H]^+$ calculated: 400.0912, found: 400.0925.



Diethyl 2-bromo-3-oxobutan-2-ylphosphonate: Isolated as a colorless oil in 97% yield; IR (neat, cm^{-1}): 2986, 2934, 1716, 1444, 1258, 1199, 578; ^1H NMR (400 MHz, $CDCl_3$): δ 4.33 – 3.95 (4 H, m, OCH_2), 2.52 (3 H, s, COMe), 1.92 (1 H, d, J = 14.5, CMe), 1.30 (3 H, t, J = 13.4, CH_2Me), 1.28 (3 H, t, J = 13.0, CH_2Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2 (J = 2.3), 64.7 (d, J = 7.2), 64.4 (d, J = 7.2), 58.5 (d, J = 143.4), 27.1, 23.7 (d, J = 1.9), 16.3 (d, J = 6.0) 16.2 (d, J = 6.3); ^{31}P NMR (121 MHz, $CDCl_3$): δ 16.97; CI-HRMS $C_8H_{17}0_4PBr$ $[M+H]^+$ calculated: 287.0048, found: 287.0037.

References

1) W.E. Wyman, R. Davis, J. W. Patterson Jr. and J. R. Pfister, *Synth. Commun*., 1988, 1379.
2) L. Hintermann and A. Togni, *Helv. Chim. Acta*, 2000, **83**, 2425-2435.
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4) D. F. Taber, D. M. Gleave, R. J. Herr, K. Moody and M. J. Hennessy, *J. Org. Chem.*, 2002, **60**, 2283-2285.
5) R. Hilgenkamp and C. K. Zercher, *Tetrahedron*, 2001, **57**, 8793-8800.
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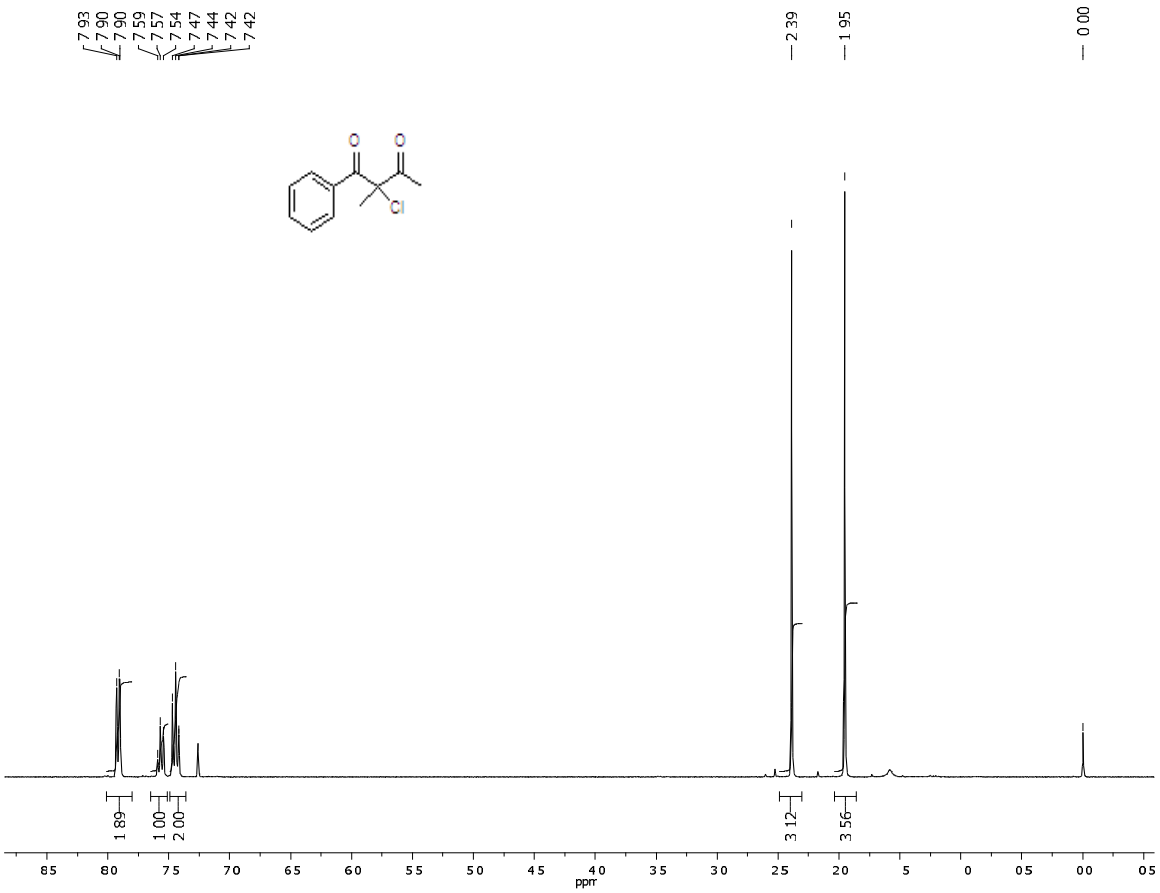
7) J. G. Sharefkin and H. Saltzman, *Org. Synth., Coll. Vol. **V***, 1973, 660-662.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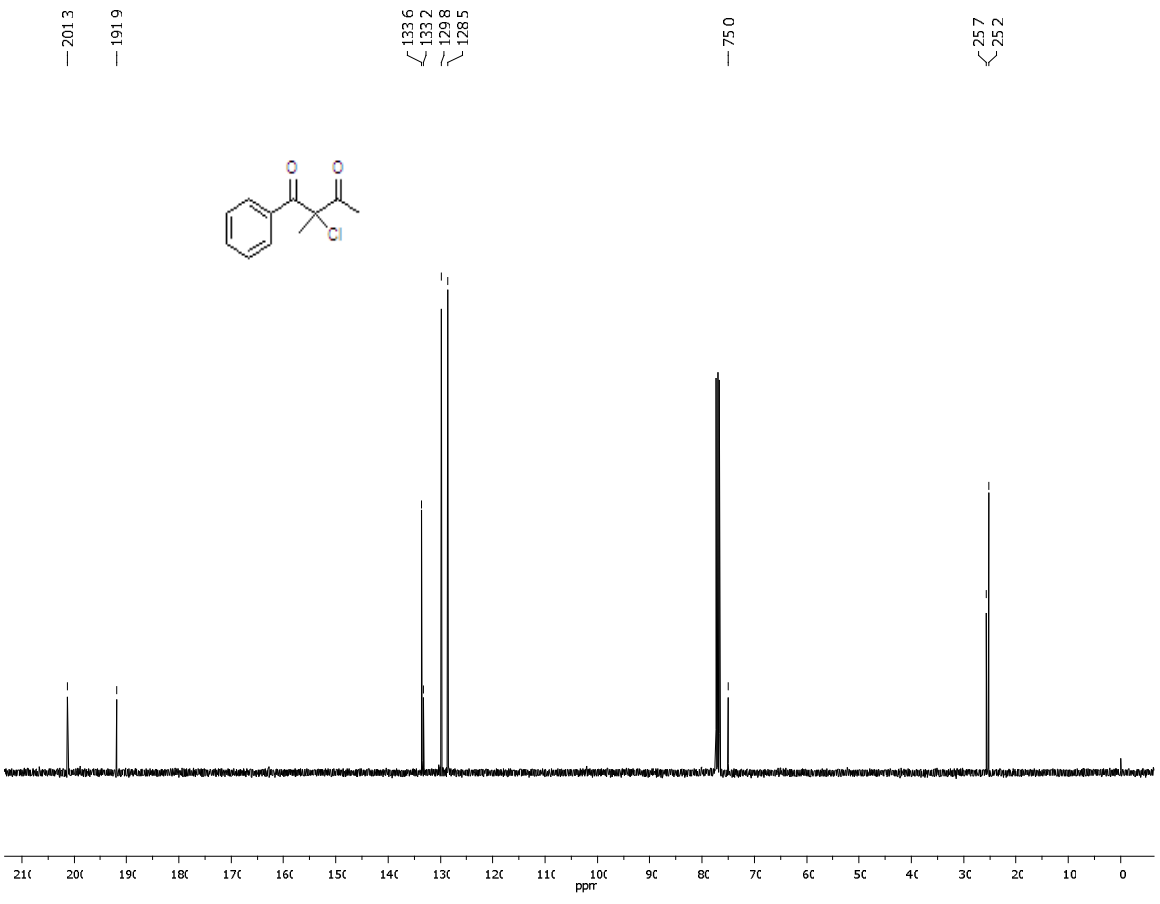
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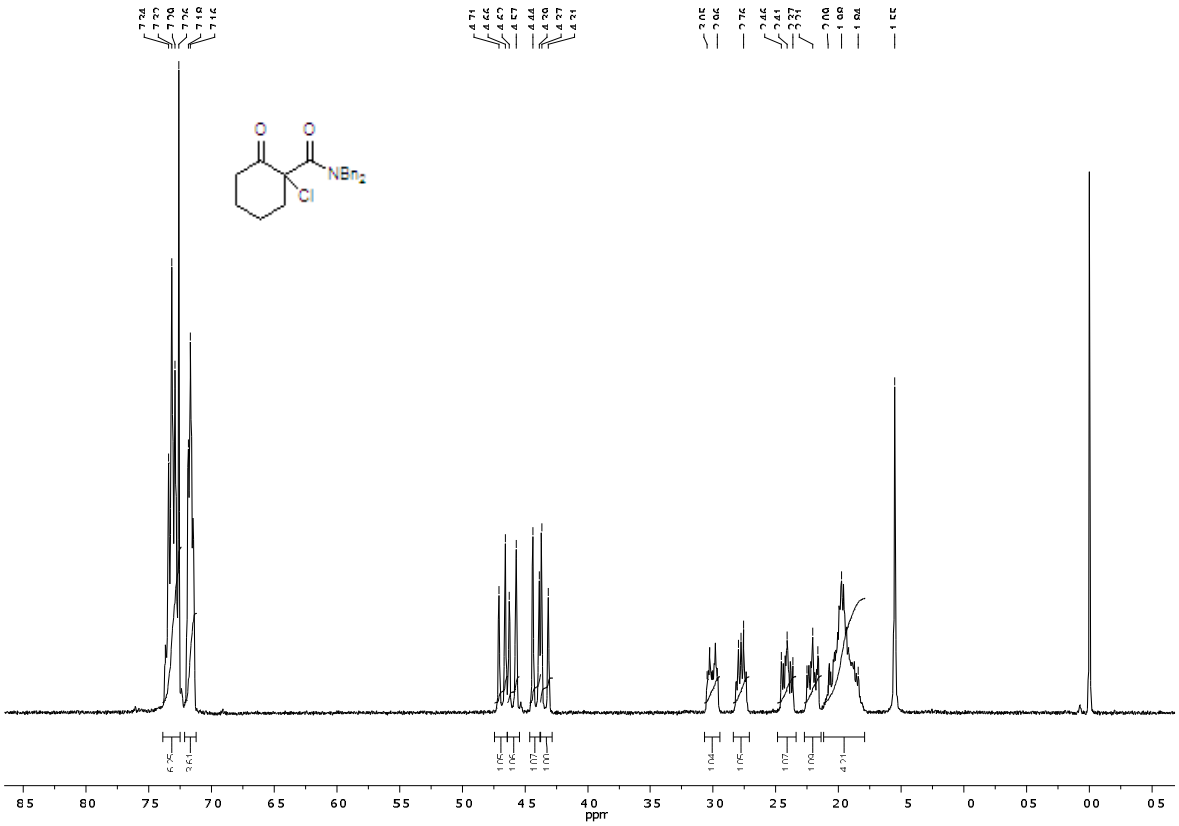
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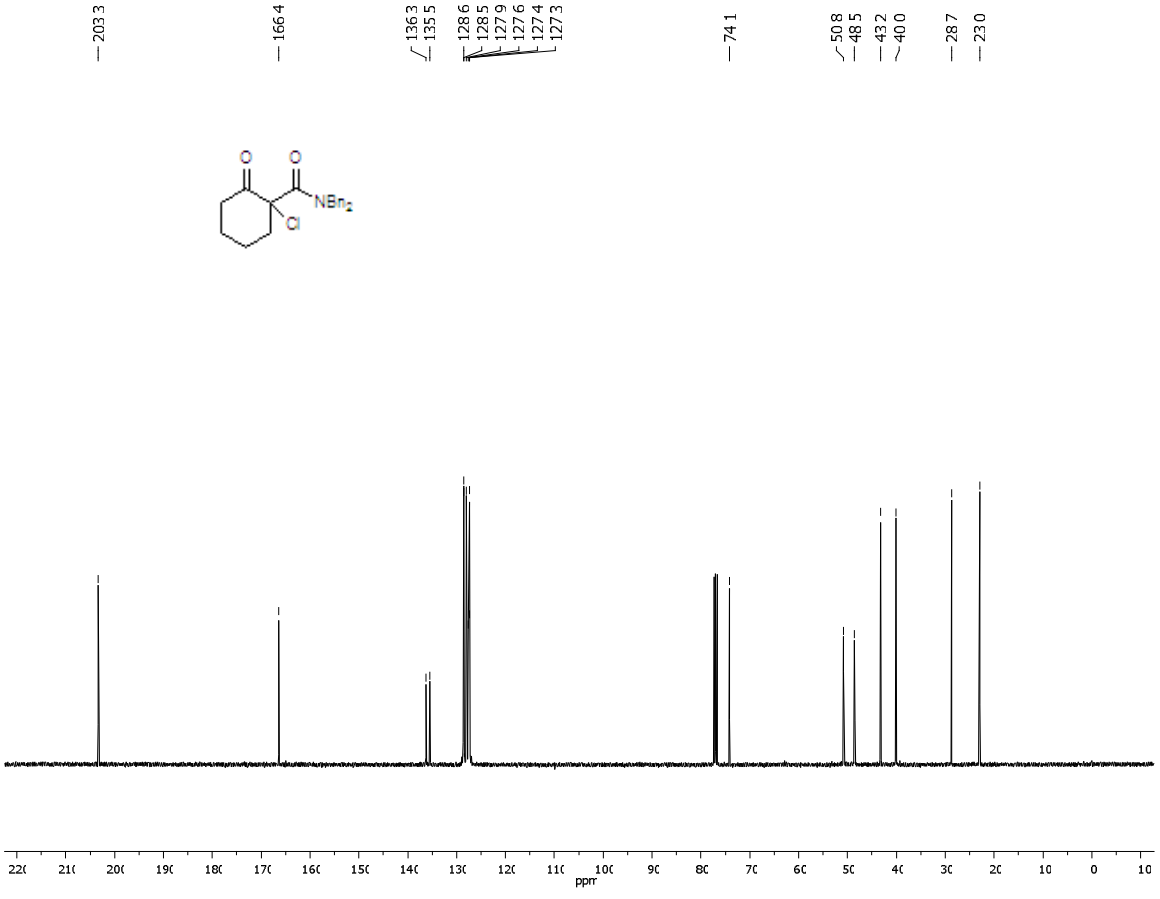
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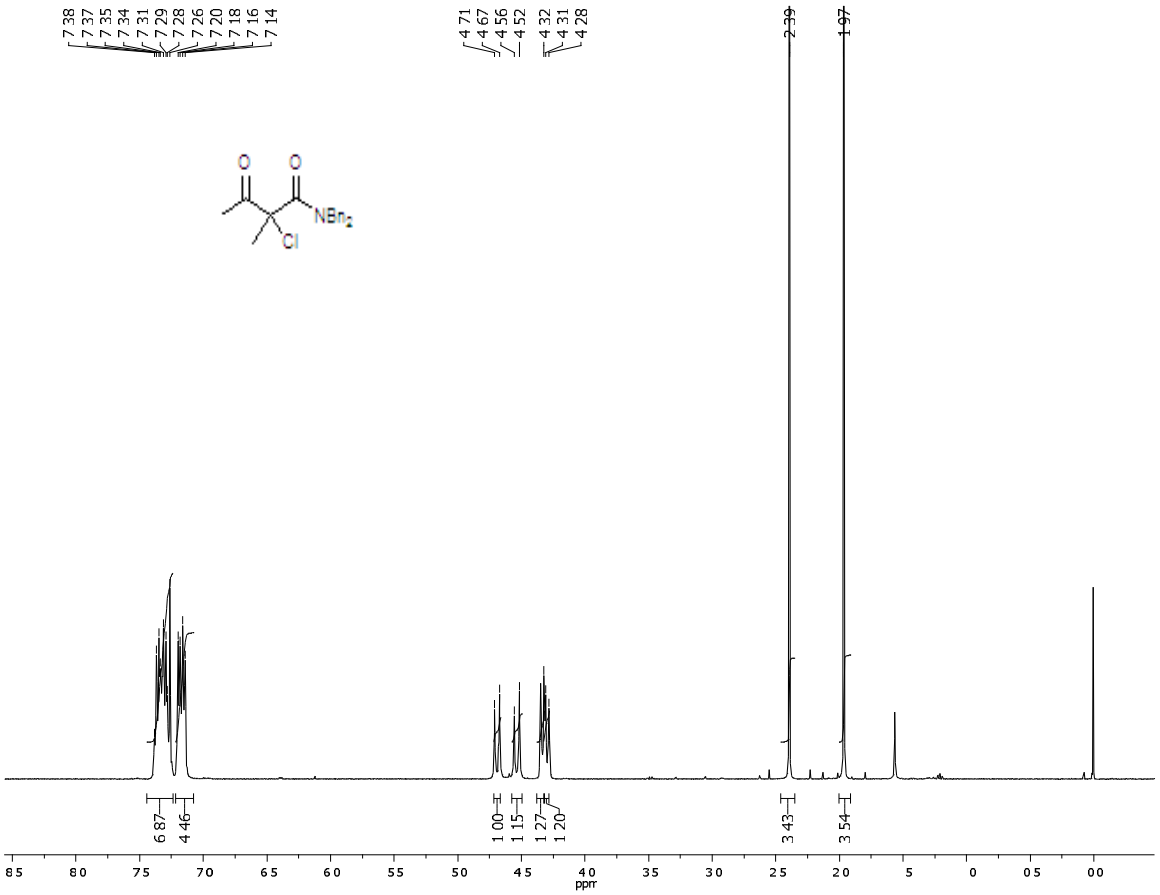

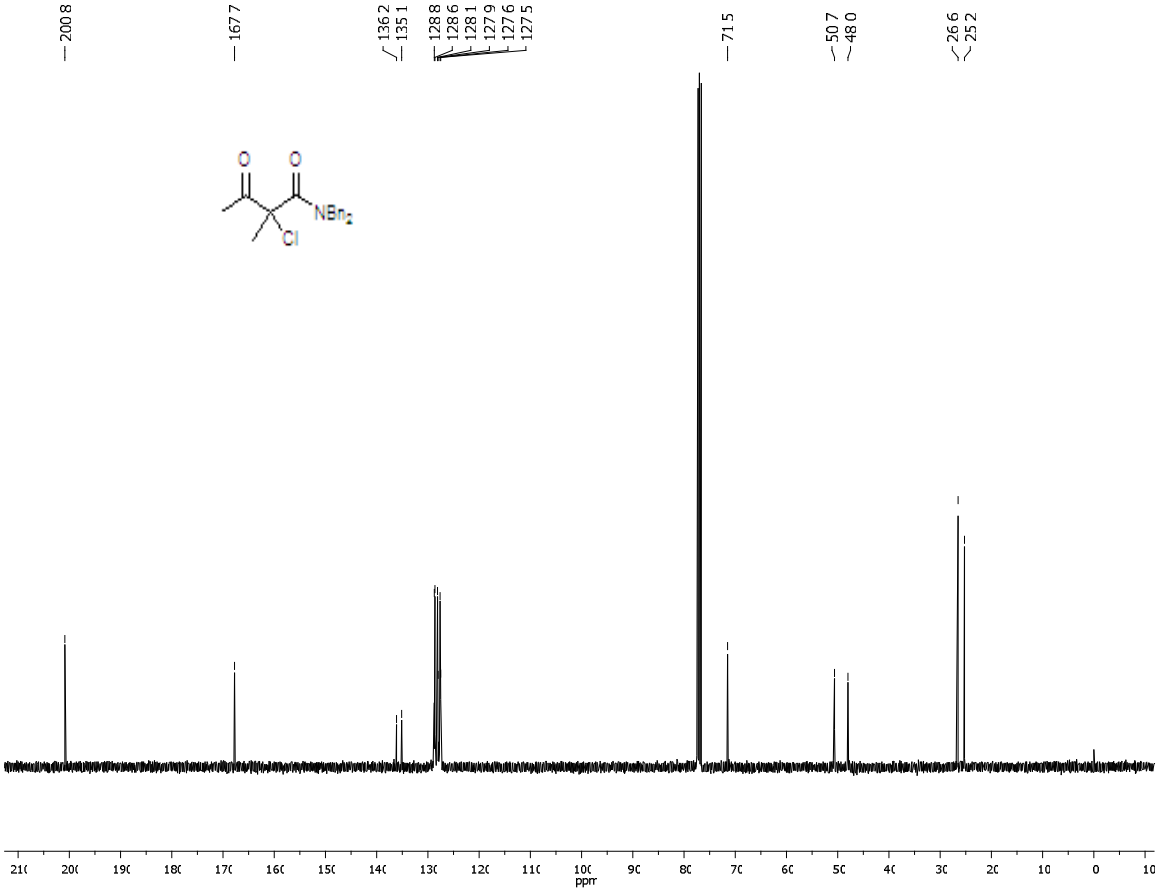

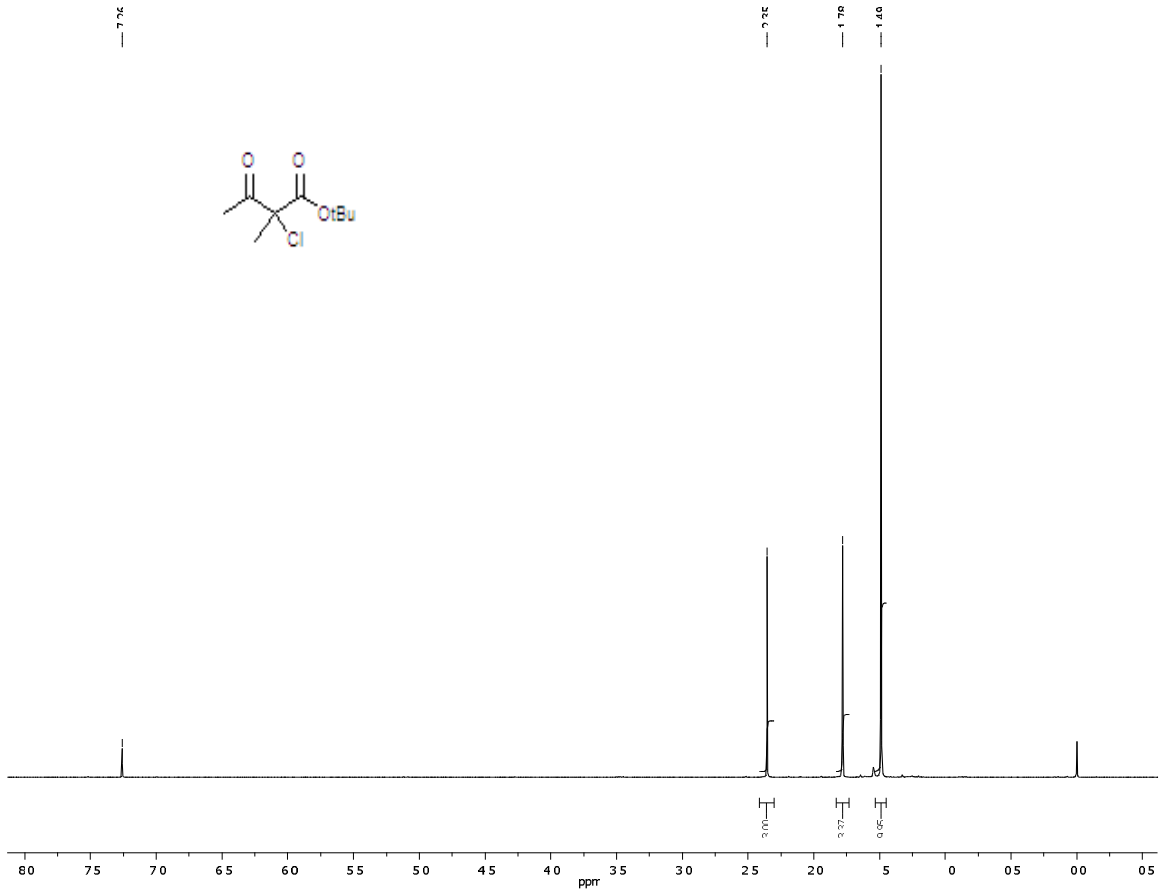
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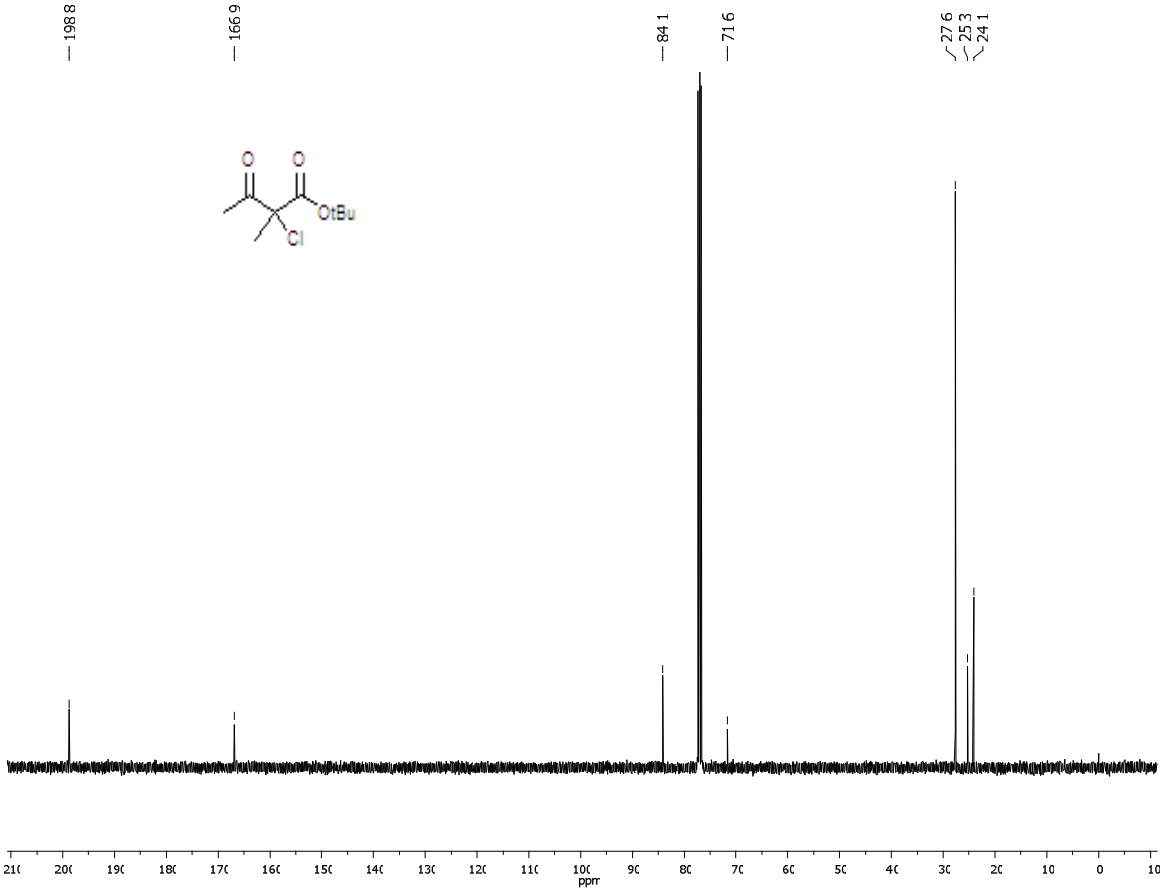
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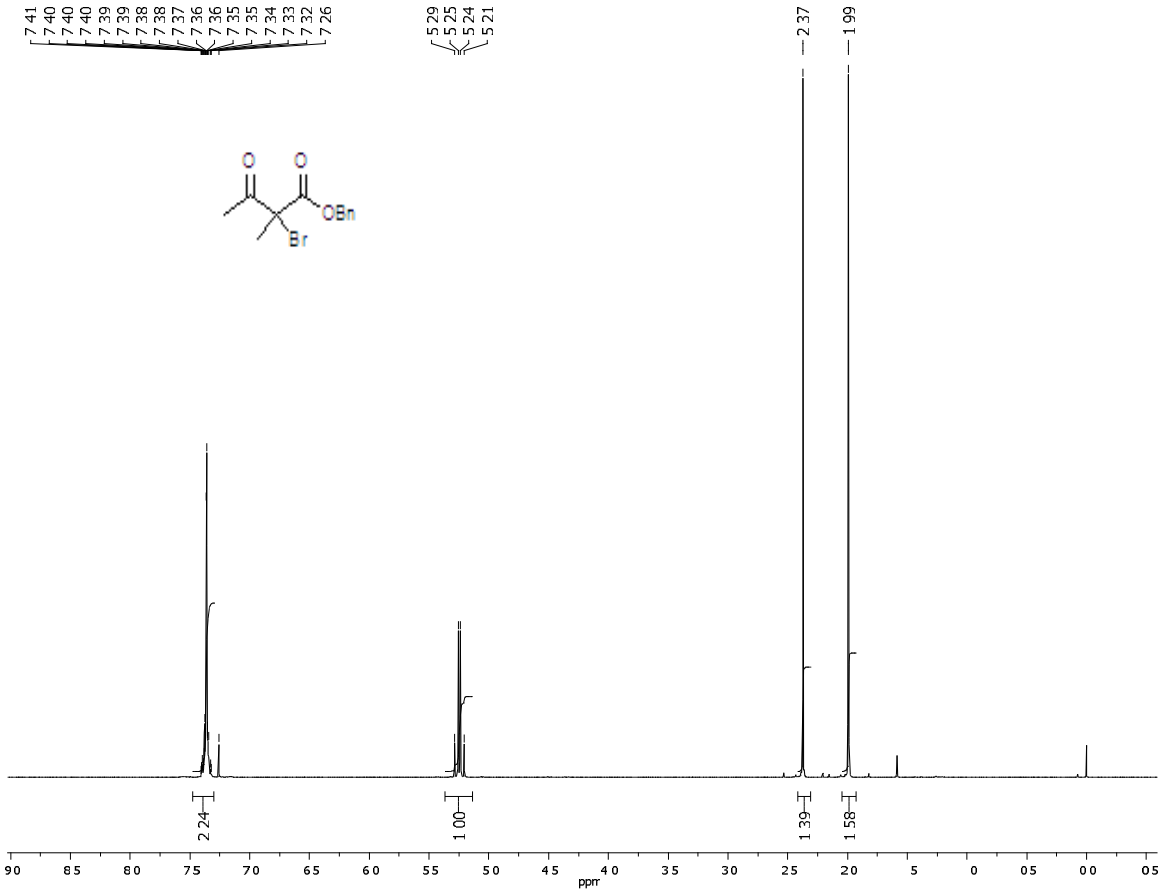
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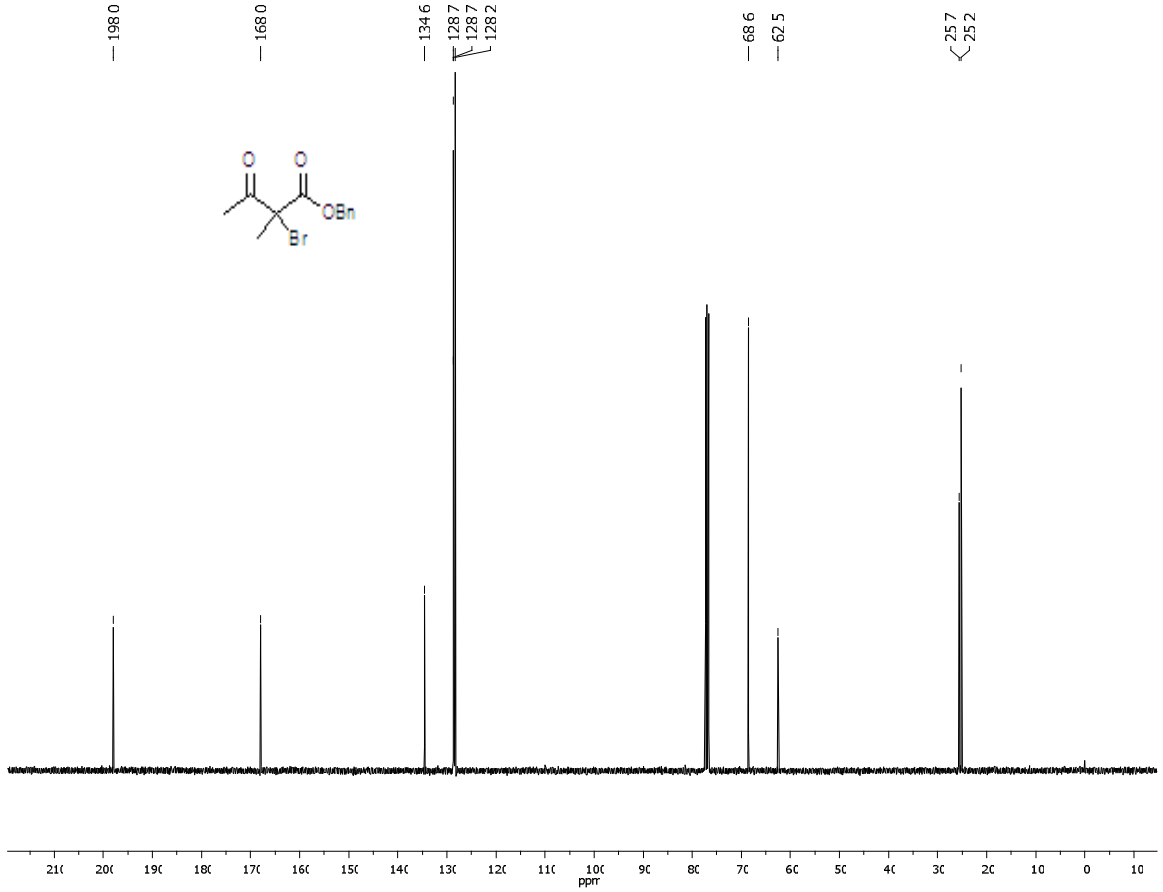
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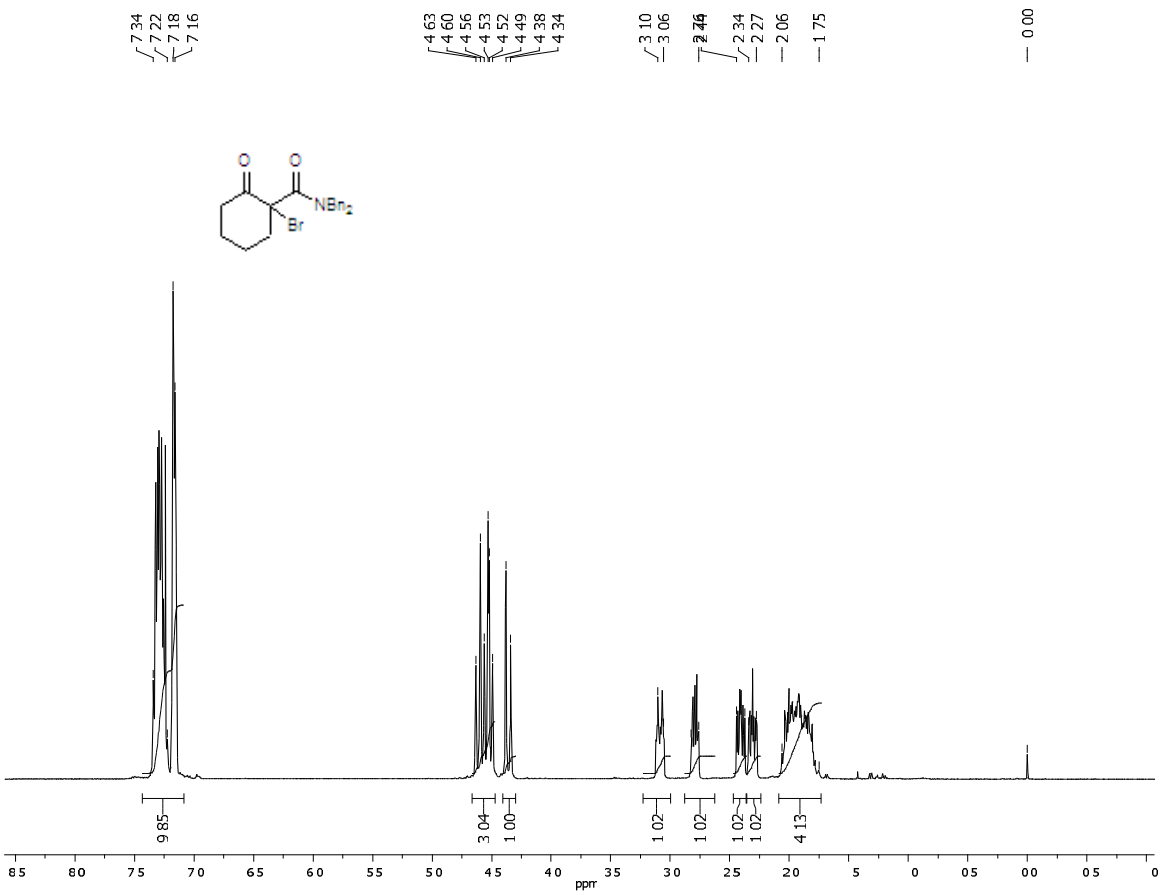
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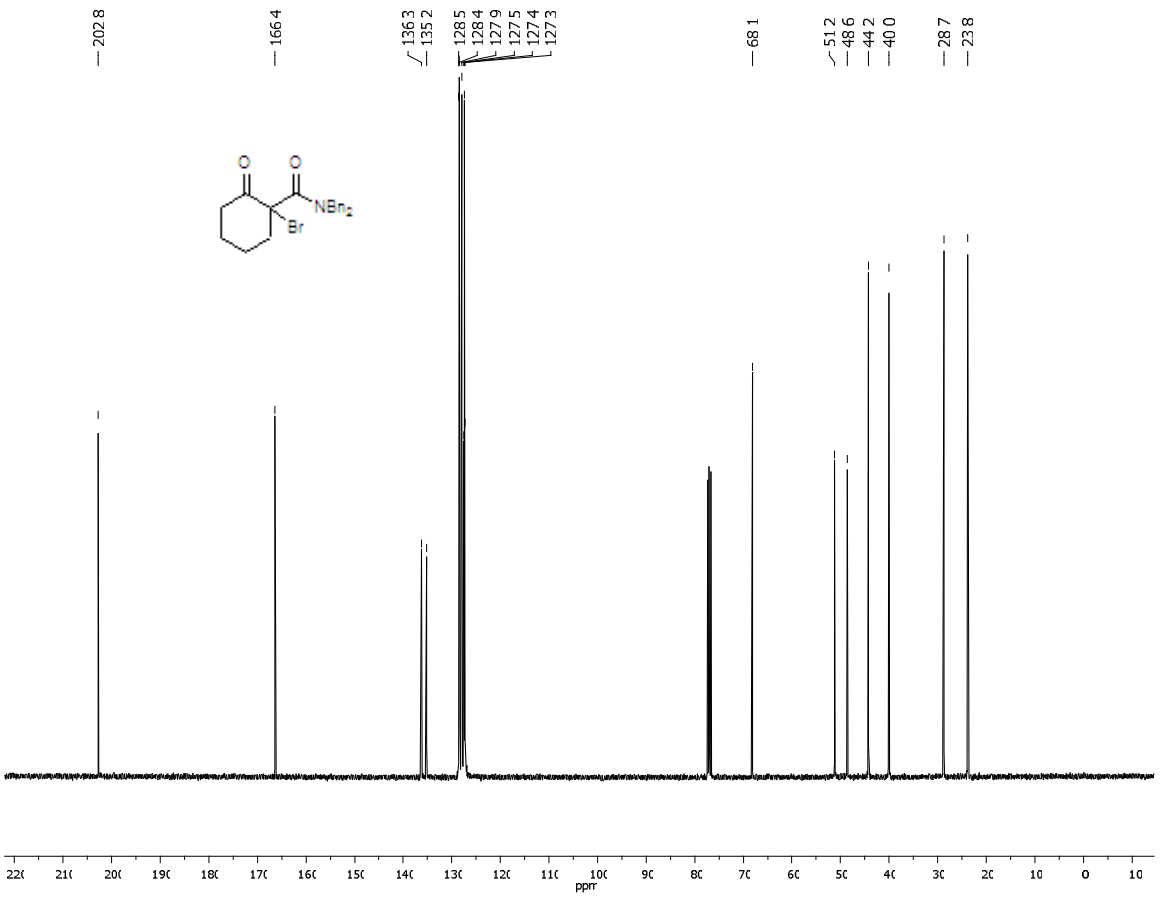
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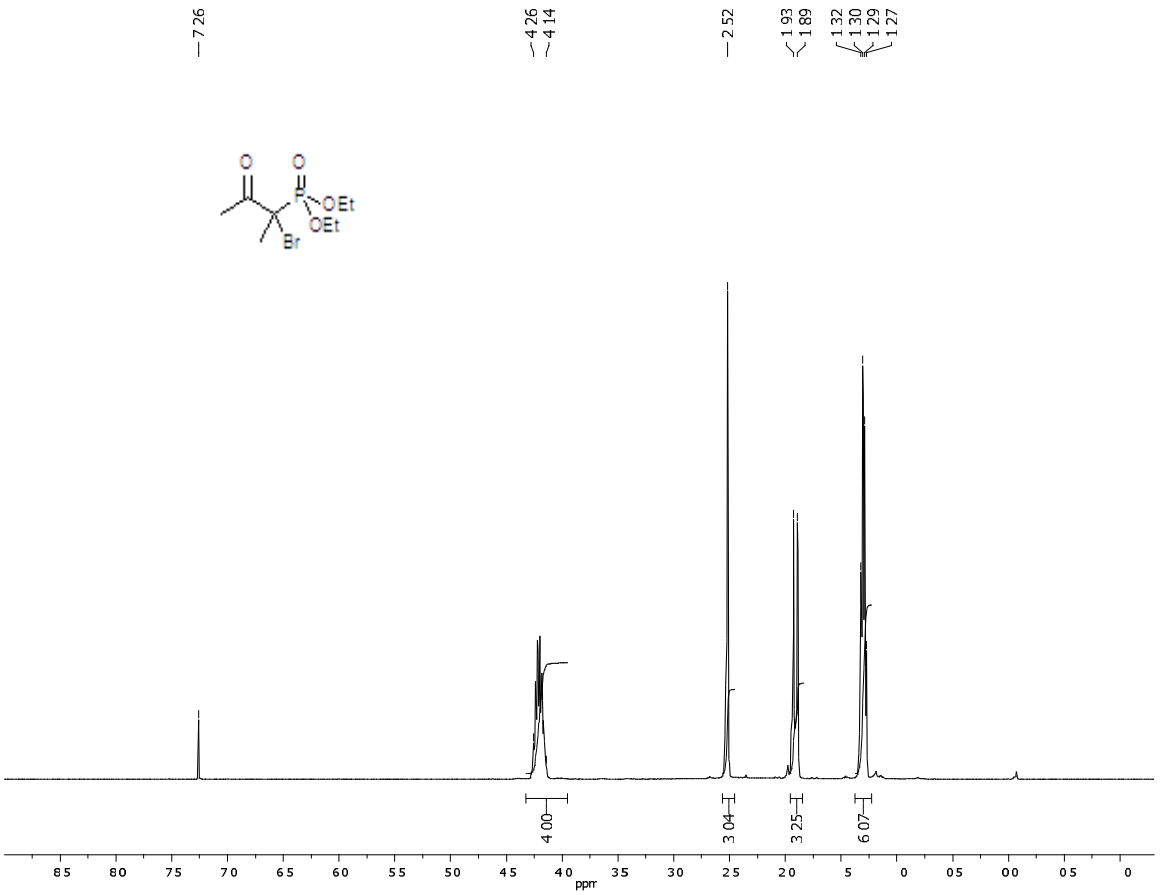
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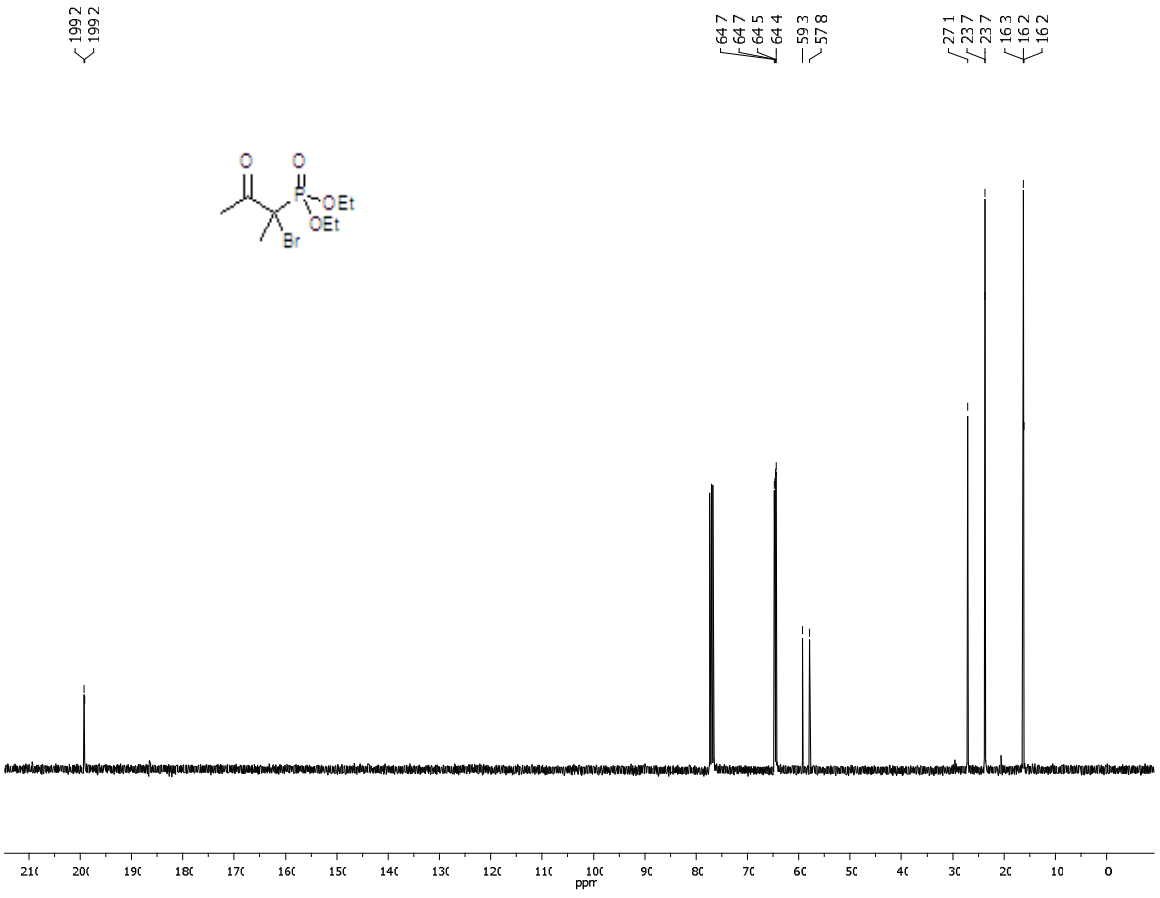
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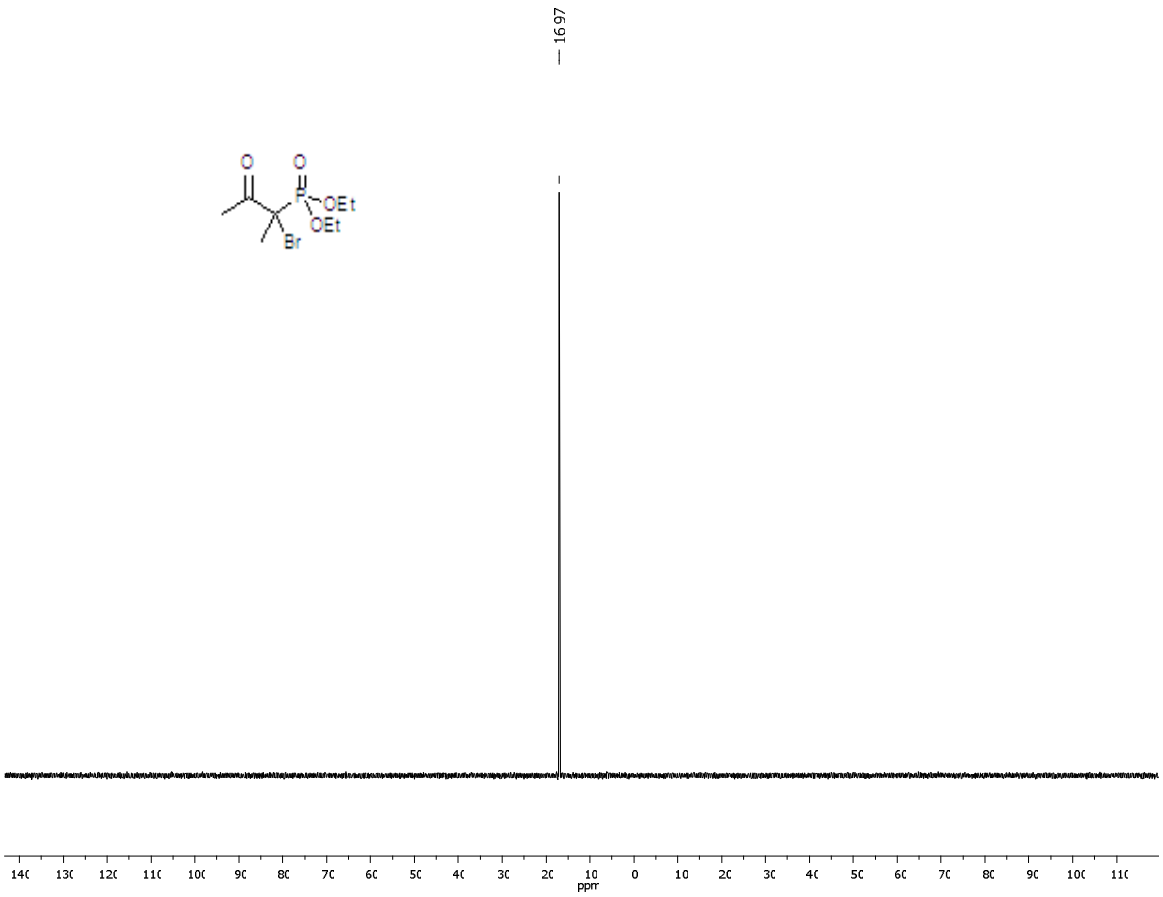
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