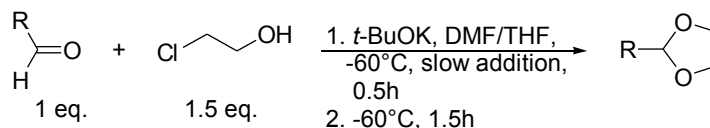


Intermolecular reactions of chlorohydrine anions – acetalisation of carbonyl compounds under basic conditions

Michał Barbasiewicz and Mieczysław Mąkosza*[‡]

General. Unless otherwise noted, all reactions were carried out under atmosphere of argon in dried glassware using standard Schlenck techniques. THF was distilled from K / benzophenone ketyl, DMF was used without purification. ¹H and ¹³C NMR spectra were recorded on Bruker 500 and Varian 200 spectrometers. Chemical shifts are reported in ppm from the solvent resonance (CDCl₃ as 7.26 ppm). Data are reported as follows: chemical shift, multiplicity, (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants and number of protons. Mass spectra were obtained on AMD 604 Intectra GmbH spectrometer in electron ionization mode or on Mariner™ in electrospray mode. IR spectra were taken on a FT-IR Perkin Elmer Spectrum 2000 using a film (for oils) or in KBr pellets (for solids). Melting points were uncorrected. Enantiomeric excesses were determined using gas chromatograph with column β-Dex 120, 30m × 0.25mm × 0.25μm film thickness, pressure 100KPa.

General procedure of synthesis of dioxolanes (Table 1 in article)



To a vigorously stirred solution of benzaldehyde (5.30 g; 50 mmol) and 2-chloroethanol (6.04g; 75 mmol) in DMF (20 mL) and THF (10 mL) at -60°C under argon, solution of *t*-BuOK (8.40g; 75 mmol) in DMF (15 mL) was added dropwise for 30 minutes. Then mixture was stirred for 90 minutes and solution of 5% NH₄Cl_{aq} (30 mL), brine (100 mL) and water were added (water was necessary to dissolve inorganic precipitates). Mixture was extracted with ethyl acetate (5×70 mL), combined organic phases were washed with brine (3×100 mL) and dried with MgSO₄. Solvent was removed in vacuo and the residue was distilled under reduced pressure. See the important notes on the next page.

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Important notes

1. The order of mixing of aldehyde, 2-chloroethanol and solvents is important. 2-Chloroethanol¹ (even freshly distilled) contains traces of acid that may catalyse formation of acetal of aldehyde with 2-chloroethanol,² which contaminate the final product. To avoid this problem 2-chloroethanol should be initially mixed with DMF to neutralize the acid and then other reagents can be added.
2. DMF solution of *t*-BuOK should be prepared immediately before use. Its prolonged storage causes substantial decomposition of the solvent (smell of dimethylamine initially, but vague yellowish precipitates, when stored overnight at RT).³ The solution should be colorless and clear with at most trace amounts of precipitate only, thus anhydrous DMF and carefully moisture protected *t*-BuOK should be used. We used commercially available DMF and *t*-BuOK (Fluka) without further purification.
3. Dropwise addition of the base solution should be directed into the layer of the stirred reaction mixture. Flowing of the solution on the wall of the cooled vessel may cause freezing of the solution.
4. **Efficient, vigorous stirring is crucial to reproduce these results**, thus proper magnetic stirrer and magnetic bar (fish) should be used. In our experiments mixing rates around 800 – 1000 rpm were used. Overconcentration of the base solution at the layer of insufficiently stirred reaction mixture cause formation of vague precipitates and results in a substantially decreased conversion of the reaction in most cases. An additive of THF to the reaction mixture decrease the viscosity of mixture and facilitate stirring, besides in some cases it improve the solubility of the substrate. Reaction performed in pure THF gave substantially decreased conversion, however.
5. After quenching the reaction with aqueous NH₄Cl, mixture should be vigorously shaken.
6. Distillation was performed on a small scale apparatus on vacuum-pump (see Figure 1, right).
7. 2-Bromoethanol gave lower conversions in reaction with benzaldehyde than 2-chloroethanol.
8. An increased excess of 2-chloroethanol to aldehyde gave no influence on conversion.

1 For 3-chloropropanol and 3-chloro-1,2-propanediol the same may apply.

2 When 2-chloroethanol was mixed directly with benzaldehyde during the weighting at RT we observed formation of some amounts of acetal of benzaldehyde with 2-chloroethanol – bis-(2-chloroethoxy)phenylmethane in this mixture: ¹H NMR (200 MHz, CDCl₃): δ 7.45–7.55 (m, 2H), 7.25–7.45 (m, 3H), 5.72 (s, 1H), 3.72–3.85 (m, 4H), 3.60–3.72 (m, 4H). ¹³C NMR (50 MHz, CDCl₃): δ 137.2, 128.7, 128.3, 126.6, 101.3, 65.3, 43.2.

3 We did not observed exothermic effect or rise of pressure in solution of base at 0.1 mol of *t*-BuOK scale, but this maybe the case when scaled-up.

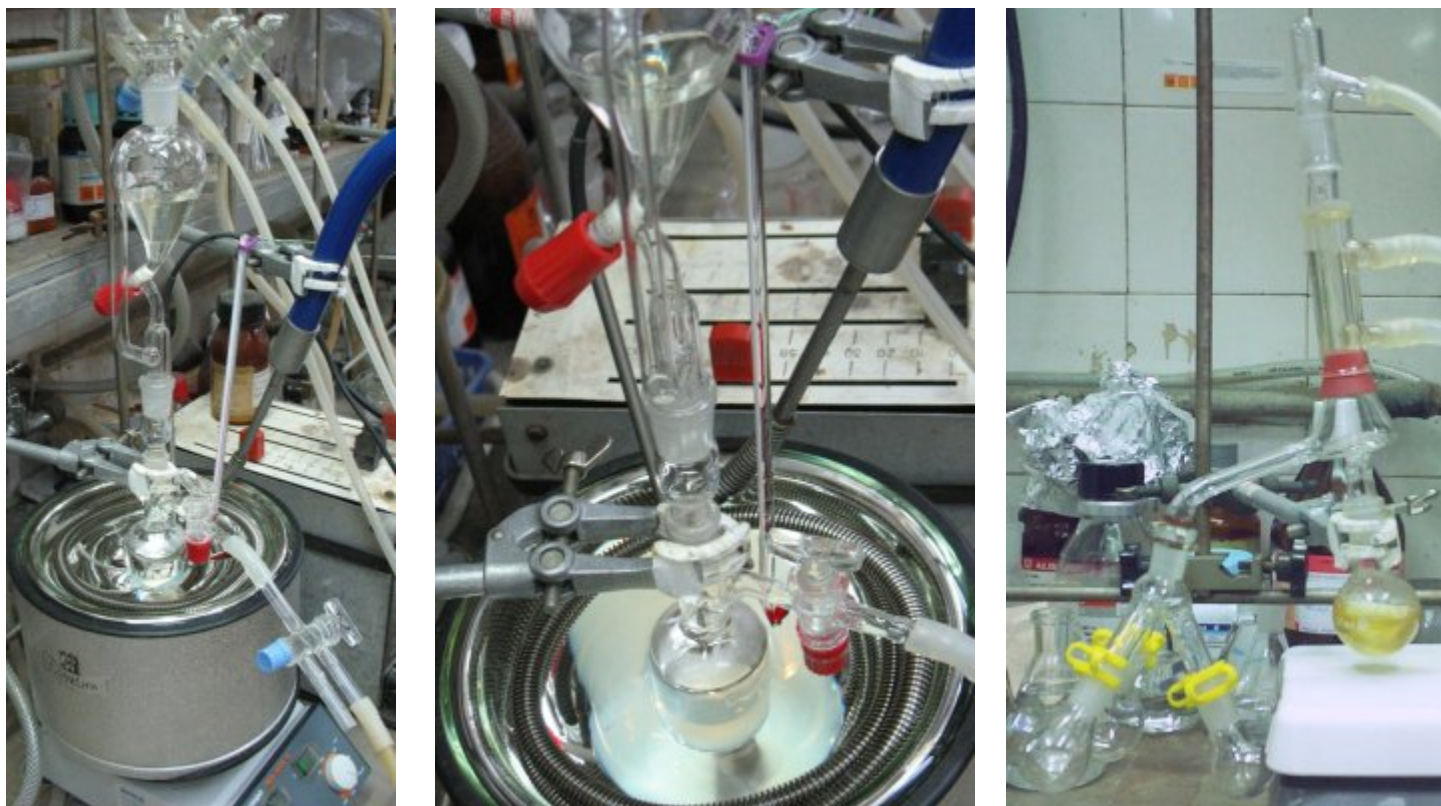
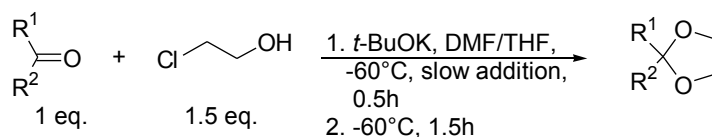


Figure 1. Reaction glassware and distillation apparatus

Procedure of synthesis of dioxolanes from ketones (Table 2 in article)

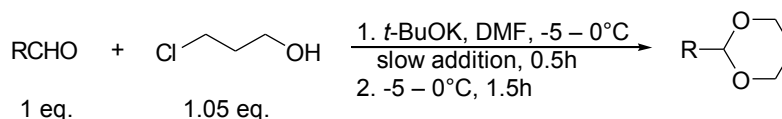


Entries 1–3 were performed according to the following procedure:

To a vigorously stirred solution of ketone (10 mmol) and 2-chloroethanol (6.04g; 75 mmol) in DMF (20 mL) and THF (10 mL) at -60°C under argon, solution of *t*-BuOK (8.40g; 75 mmol) in DMF (15 mL) was added dropwise for 30 minutes. Then mixture was stirred for 90 minutes and solution of 5% $\text{NH}_4\text{Cl}_{\text{aq}}$ (30 mL), brine (100 mL) and water were added (water was necessary to dissolve inorganic precipitates). Mixture was extracted with ethyl acetate (5×70 mL), combined organic phases were washed with brine (3×100 mL) and dried with MgSO_4 . Solvent was removed in vacuo and the residue was analyzed with GC (entries 1 and 2) or crystallized from hexanes : ethyl acetate (5 : 1, entry 3). See the important notes 1–5 on page S-2.

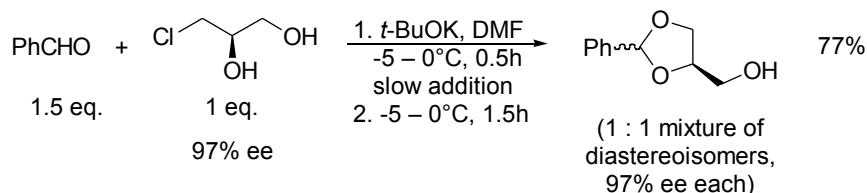
Entries 4–5 were performed according to the general procedure (page S-1).

Procedure of synthesis of dioxanes (Table 3 in article)



To a vigorously stirred solution of benzaldehyde (5.30 g; 50 mmol) and 3-chloropropanol (4.96g; 52.5 mmol) in DMF (20 mL) at $-5 - 0^\circ\text{C}$ under argon, solution of *t*-BuOK (8.40g; 75 mmol) in DMF (15 mL) was added dropwise for 30 minutes. Then mixture was stirred for 90 minutes and solution of 5% $\text{NH}_4\text{Cl}_{\text{aq}}$ (30 mL), brine (100 mL) and water were added (water was necessary to dissolve inorganic precipitates). Mixture was extracted with ethyl acetate (5×70 mL), combined organic phases were washed with brine (3×100 mL) and dried with MgSO_4 . Solvent was removed in vacuo and the residue was distilled under reduced pressure. See the important notes 1–6 on page S-2.^{4,5,6}

Reaction of benzaldehyde with 3-chloro-1,2-propanediol (Scheme 2 in article)



Enantiomerically enriched (R)-3-chloro-1,2-propanediol was obtained from reaction of epichlorohydrine with water under kinetic resolution conditions with Jacobsen cobalt-salen complex according to the procedure described in literature (isolated yield 38%, 97% ee GC).⁷

Reactions with racemic and enantiomerically enriched substrates were performed under the same conditions and gave similar result (except of the optical purity of product).

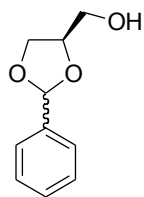
To a vigorously stirred solution of benzaldehyde (7.95 g; 75 mmol) and 3-chloro-1,2-propanediol (5.53g; 50 mmol) in DMF (15 mL) at $-5 - 0^\circ\text{C}$ under argon, solution of *t*-BuOK (11.2g; 100 mmol) in DMF (20 mL) was added dropwise for 30 minutes. Then mixture was stirred for 90 minutes and solution of 5% $\text{NH}_4\text{Cl}_{\text{aq}}$ (30 mL), brine (100 mL) and water were added (water was necessary to dissolve inorganic precipitates). Mixture was extracted with ethyl acetate (5×70 mL), combined organic phases were washed with brine (3×100 mL) and dried with MgSO_4 . Solvent was removed in vacuo and the residue was distilled under reduced pressure. Yield 77%. See the important notes 1–6 on page S-2.

4 3-Bromopropanol (1.05 eq.) in reaction with benzaldehyde (1 eq.) at -60°C , according to the general procedure, gave 94% conversion.

5 Additive of THF is not required for reactions performed at $-5 - 0^\circ\text{C}$ (no problems with stirring occurred).

6 Reaction performed at -20°C gave lower conversion.

7 (a) Furrow, M. E.; Schaus, S. E.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 6776–6777. (b) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307–1315.

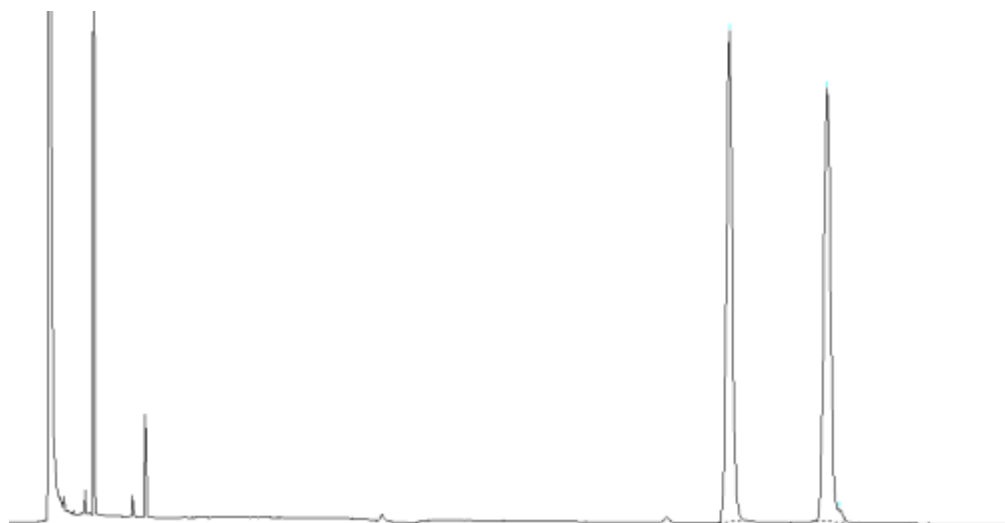


4-hydroxymethyl-2-phenyl-1,3-dioxolane (as equimolar mixture of diastereoisomers)

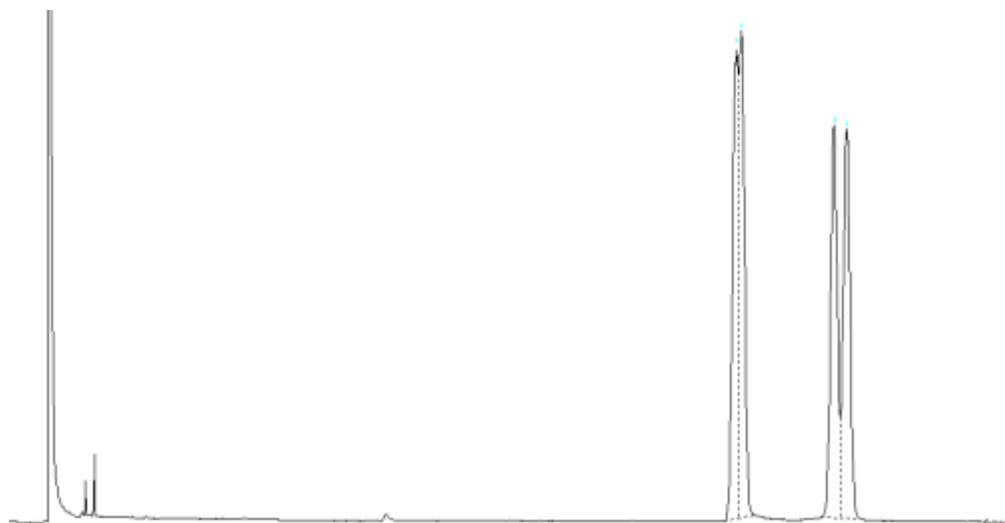
Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.28–7.55 (m, 10H), 5.93 (s, 1H), 5.81 (s, 1H), 4.26–4.39 (m, 2H), 3.92–4.23 (m, 3H), 3.56–3.86 (m, 5H), 2.38–2.67 (m, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ 137.7, 136.9, 129.4, 129.1, 128.3, 128.3, 126.5, 126.3, 104.2, 103.6, 76.9, 76.5, 66.8, 66.7, 63.1, 62.6. Optical purity was confirmed by chiral GC analysis (~ 97% ee)

This product is acid-sensitive! We observed, that the sample may isomerize during the NMR analysis in CDCl_3 (that usually contains traces of acid) or distillation at too high temperature (efficient vacuum pump is thus required). GC analysis of non-isomerized product showed only traces (< 5%) of 6-membered isomers (dioxanes).

Optical purity of this product was analysed with chiral GC analysis, after conditioning with TMS/imidazole mixture, analysis temperature 140°C (see for chromatograms below).



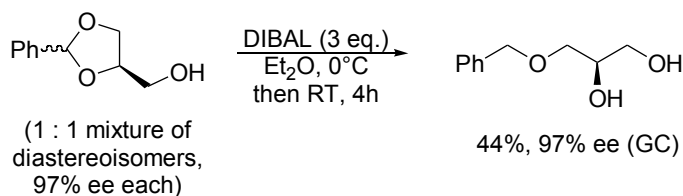
Chiral GC chromatogram of 4-hydroxymethyl-2-phenyl-1,3-dioxolane (as equimolar mixture of diastereoisomers) obtained from non-racemic substrate.



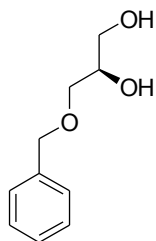
Chiral GC chromatogram of 4-hydroxymethyl-2-phenyl-1,3-dioxolane (as equimolar mixture of diastereoisomers) obtained from racemic substrate.

Reductive cleavage of 4-hydroxymethyl-2-phenyl-1,3-dioxolane

To confirm the structure and optical purity of 4-hydroxymethyl-2-phenyl-1,3-dioxolane (as equimolar mixture of diastereoisomers) reductive opening with DIBAL was performed according to the literature method.⁸



To a solution of diisobutylaluminum hydride (8 mL; 9.68 mmol; 25% wt in toluene) in Et₂O (20 mL) at 0°C under argon solution of 4-hydroxymethyl-2-phenyl-1,3-dioxolane (547 mg; 3.04 mmol, as equimolar mixture of diastereoisomers) in Et₂O (6 mL) was added. Flask was allowed to warm to rt and left for 4h, then MeOH (4 mL) and aqueous NH₄Cl (20 mL) were added and mixture was shaken vigorously. Then the mixture was extracted with ethyl acetate, washed with brine and dried MgSO₄. Chromatographic separation with hexane : ethyl acetate (3 : 1 to 1 : 1) gave *sn*-1-O-benzylglycerol (242 mg, 44%).



sn-1-O-benzylglycerol

Oil. ¹H NMR (200 MHz, CDCl₃): δ 7.28–7.42 (m, 5H), 4.54 (s, 2H), 3.83–3.94 (m, 1H), 3.47–3.79 (m, 4H), 2.45–2.60 (m, 2H). ¹³C NMR (50 MHz, CDCl₃): δ 137.6, 128.5, 127.9, 127.8, 73.6, 71.8, 70.6, 64.0. Optical purity was confirmed by chiral GC analysis (97% ee).

Optical purity of this product was analysed with chiral GC analysis, after conditioning with acetone/*p*-TsOH (cat.) mixture, analysis temperature 80°C (see for chromatograms below).



Chiral GC chromatogram of *sn*-1-O-benzylglycerol obtained from non-racemic substrate.

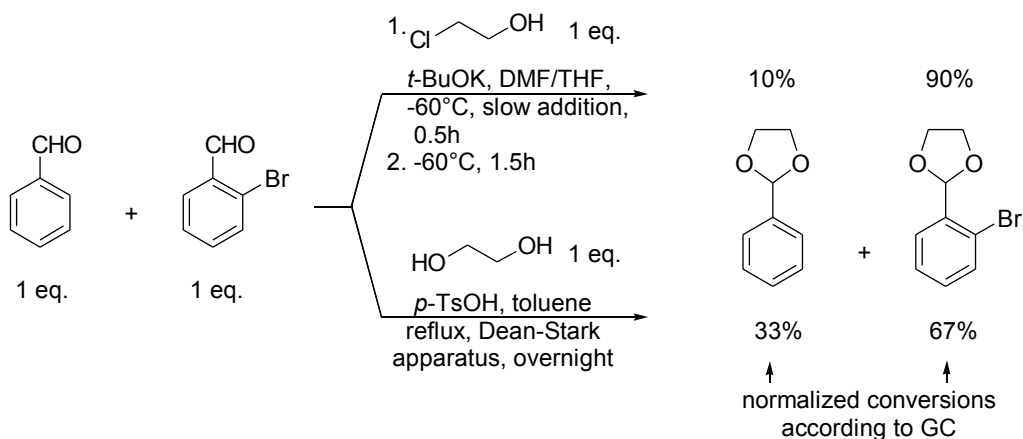
⁸ Marguet, F.; Cavalier, J.-F.; Verger, R.; Buono, G. *Eur. J. Org. Chem.* **1999**, 1671–1678.



Chiral GC chromatogram of *sn*-1-*O*-benzylglycerol obtained from racemic substrate.

Competition experiments

We compared the relative reactivity of aldehydes toward reaction with 2-chloroethanol under basic conditions and under classical acid catalysed reaction with ethylene glycol.



Reaction under basic conditions was performed according to the general procedure (page S-1) with 50 mmol of benzaldehyde, 50 mmol of *o*-Br benzaldehyde and 50 mmol of 2-chloroethanol and analysed with GC. Reaction under acid catalysed condition was performed according to typical equilibrium conditions with Dean-Stark apparatus for removal of water (25 mmol of benzaldehyde, 25 mmol of *o*-Br benzaldehyde, 25 mmol of ethylene glycol, 50 mL of toluene, 60 mg of *p*-TsOH·H₂O) and analysed with GC.⁹

We observed much greater selectivity under basic conditions that may be applied e.g. for protection of one of the two distinct carbonyl groups within the same molecule.

⁹ GC analyses of the reaction mixtures of acid catalysed reaction with ethylene glycol after equilibration at reflux and at RT gave similar results within the experimental error.

Reaction of benzaldehyde with potassium *tert*-butoxide and benzyl chloride

The optimized reaction conditions at -5 – 0°C for synthesis of dioxanes (page S-4) were applied for the reaction of benzaldehyde with simple alkylating agent – benzyl chloride (benzaldehyde 50 mmol, benzyl chloride 75 mmol, *t*-BuOK 75 mmol). We observed consumption of benzaldehyde (98% conversion according to ¹H NMR). From the reaction mixture we isolated by distillation:

Benzyl *tert*-butyl ether ¹H NMR (200 MHz, CDCl₃): δ 7.23–7.44 (m, 5H), 4.47 (s, 2H), 1.32 (s, 9H). ¹³C NMR (50 MHz, CDCl₃): δ 139.9, 128.2, 127.3, 127.0, 73.4, 64.1, 27.7.

Benzyl *tert*-butyl acetal of benzaldehyde (contaminated) ¹H NMR (200 MHz, CDCl₃): δ 7.24–7.44 (m, 5H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.28 (d, *J* = 11.6 Hz, 1H), 1.36 (s, 9H). ¹³C NMR (50 MHz, CDCl₃): δ 138.6, 128.3, 127.7, 126.8, 95.8, 75.0, 64.5, 28.8.

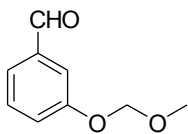
These compounds were substantially contaminated with unidentified by-products.

Reaction of benzaldehyde with 1,3-dibromo-2-propanol failed to give the expected acetal at -60°C and at 0°C.

Synthesis of substrates:

Synthesis of 3-(methoxymethyl)benzaldehyde (alkylation)

Mixture of 3-hydroxybenzaldehyde (12.2 g; 0.10 mol), MOM-chloride (8.95 g; 0.11 mol), K₂CO₃ (27.7 g; 0.20 mol), NBu₄Cl (0.39 g; 0.0014 mol) and acetonitrile 125 mL was stirred at RT for 68 h. Mixture was filtered, concentrated in vacuo then water and ethyl acetate were added. Organic phase was washed with aqueous Na₂CO₃, brine and dried with MgSO₄. Product was isolated by distillation as a colorless oil (9.0 g; yield 54%).

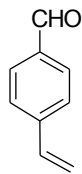


3-(methoxymethyl)benzaldehyde

Oil. IR (neat): 3375, 2958, 2828, 2731, 1703, 1586, 1484, 1455, 1392, 1321, 1281, 1255, 1208, 1155, 1079, 1013, 991, 924, 791, 738, 683, 646 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 9.97 (s, 1H), 7.47–7.56 (m, 2H), 7.39–7.46 (m, 1H), 7.25–7.33 (m, 1H), 5.23 (s, 2H), 3.48 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 192.0, 157.7, 137.8, 130.1, 123.8, 122.8, 115.9, 94.4, 56.1. MS (EI, *m/z*, relative intensity): 166 (12), 136 (2), 135 (3), 121 (1), 45 (100). Anal. calcd for C₉H₁₀O₃: C, 65.05; H, 6.07. Found C, 65.05; H, 6.09.

Synthesis of 4-vinylbenzaldehyde (Wittig reaction)

To a suspension of terephthalaldehyde (8.72 g; 65 mmol) and methyltriphenylphosphonium bromide (23.23 g; 65 mmol) in THF (100 mL) at 6°C under argon solution of *t*-BuOK (7.53 g; 67 mmol) in THF (30 mL) was added dropwise for 20 minutes. The solids were dissolved during this time. After next 1h mixture was poured into 100 mL of aqueous NH₄Cl and extracted with ethyl acetate, combined organic phases were washed with brine and dried MgSO₄. Chromatographic separation with hexane : ethyl acetate (20 : 1) gave 4-vinylbenzaldehyde as the only isolated product (1.68 g; yield 20%).

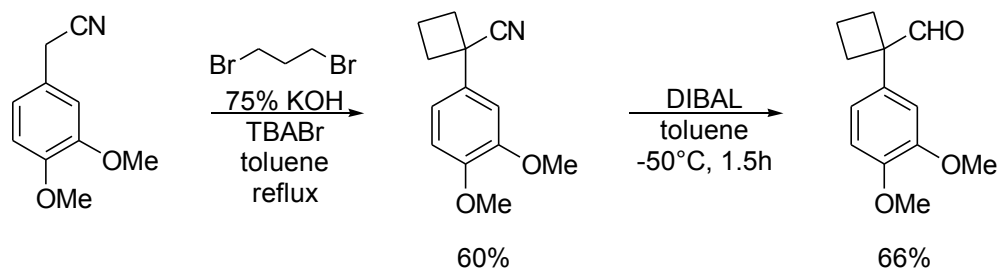


4-vinylbenzaldehyde

Oil. ^1H NMR (200 MHz, CDCl_3): δ 9.98 (s, 1H), 7.79–7.93 (m, 2H), 7.50–7.59 (m, 2H), 6.76 (dd, J = 17.6, 10.9 Hz, 1H), 5.90 (dd, J = 17.6, 0.6 Hz, 1H), 5.43 (dd, J = 10.9, 0.6 Hz, 1H). ^{13}C NMR (50 MHz, CDCl_3): δ 191.6, 143.4, 135.8, 135.6, 130.0, 126.7, 117.4.

Synthesis of 1-(3,4-dimethoxyphenyl)-1-formylcyclobutane (reduction of nitrile)

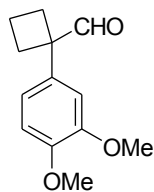
1-(3,4-Dimethoxyphenyl)-1-formylcyclobutane was obtained from 3,4-dimethoxyphenylacetonitrile in a two step synthesis, according to the following scheme:



Step 1 1-(3,4-Dimethoxyphenyl)cyclobutanecarbonitrile was prepared strictly according to the procedure described in our recent report.¹⁰

Step 2 1-(3,4-Dimethoxyphenyl)-1-formylcyclobutane was obtained by reduction with DIBAL according to the procedure described in literature for similar compound.¹¹

To a suspension of 1-(3,4-dimethoxyphenyl)cyclobutanecarbonitrile (14.12 g; 65 mmol) in toluene (100 mL) at -50°C under argon solution of diisobutylaluminum hydride (55 mL; 66.5 mmol; 25% wt in toluene) was added dropwise from syringe for 30 minutes. The solid was dissolved during this time. After next 1h at -50°C 85 mL of aqueous HCl (1 : 1) was added and mixture was stirred at RT for 2h. Separated organic phase was washed with aqueous HCl (5 : 1), saturated aqueous NaHCO_3 , brine and dried Na_2SO_4 . Chromatographic separation with hexane : ethyl acetate (6 : 1 to 4 : 1) gave 1-(3,4-dimethoxyphenyl)-1-formylcyclobutane (9.46 g; yield 66%).



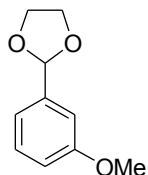
1-(3,4-dimethoxyphenyl)-1-formylcyclobutane

Oil. IR (neat): 3416, 2941, 2835, 2704, 1715, 1589, 1517, 1465, 1411, 1252, 1171, 1142, 1027, 885, 810, 762, 641 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 9.45 (s, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.67 (dd, J = 8.2, 2.1 Hz, 1H), 6.57 (d, J = 2.1 Hz, 1H), 3.83 (s, 3H), 3.83 (s, 3H), 2.58–2.74 (m, 2H), 2.24–2.42 (m, 2H), 1.78–2.06 (m, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ 199.1, 149.2, 148.0, 133.1, 118.5, 111.3, 109.4, 57.0, 55.8, 28.1, 15.5. MS (EI, m/z , relative intensity): 220 (55), 205 (4), 192 (65), 191 (72), 177 (5), 163 (100), 149 (10), 133 (13). Anal. calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$ C, 70.89; H, 7.32. Found C, 70.91; H, 7.27.

¹⁰ Barbasiewicz, M.; Marciniak, K.; Fedoryński, M. *Tetrahedron Lett.* **2006**, 47, 3871–3874.

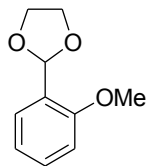
¹¹ Yamashita, M.; Ono, Y.; Tawada, H. *Tetrahedron* **2004**, 60, 2843–2849.

Characterization data of 1,3-dioxolanes (Table 1 in article)



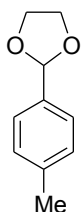
2-(3-methoxyphenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.25–7.36 (m, 1H), 7.03–7.12 (m, 2H), 6.88–6.95 (m, 1H), 5.80 (s, 1H), 3.95–4.18 (m, 4H), 3.81 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ 159.5, 139.3, 129.3, 118.6, 114.9, 111.3, 103.3, 65.1, 55.1.



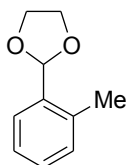
2-(2-methoxyphenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.44–7.50 (m, 1H), 7.18–7.31 (m, 1H), 6.80–6.96 (m, 2H), 6.10 (s, 1H), 3.90–4.12 (m, 4H), 3.79 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ 157.6, 130.2, 126.6, 125.7, 120.4, 110.6, 99.2, 65.2, 55.6.



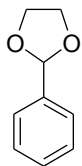
2-(4-methylphenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.34–7.43 (m, 2H), 7.16–7.25 (m, 2H), 5.80 (s, 1H), 3.96–4.20 (m, 4H), 2.37 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ 138.9, 134.9, 128.9, 126.3, 103.7, 65.2, 21.2.



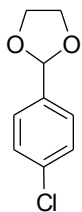
2-(2-methylphenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.53–7.64 (m, 1H), 7.17–7.35 (m, 3H), 6.00 (s, 1H), 3.99–4.23 (m, 4H), 2.46 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ 136.5, 135.3, 130.5, 128.8, 125.8, 125.6, 102.0, 65.1, 18.7.



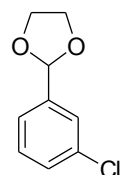
2-phenyl-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.44–7.55 (m, 2H), 7.34–7.44 (m, 3H), 5.83 (s, 1H), 3.98–4.20 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 137.8, 129.1, 128.3, 126.4, 103.7, 65.3.



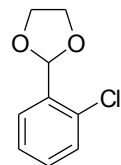
2-(4-chlorophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.39–7.49 (m, 2H), 7.30–7.39 (m, 2H), 5.78 (s, 1H), 3.97–4.17 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 136.4, 134.9, 128.5, 127.8, 102.9, 65.3.



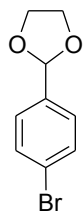
2-(3-chlorophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.47–7.52 (m, 1H), 7.25–7.40 (m, 3H), 5.79 (s, 1H), 3.97–4.17 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 140.0, 134.2, 129.6, 129.1, 126.5, 124.6, 102.7, 65.2.



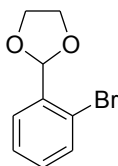
2-(2-chlorophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.57–7.67 (m, 1H), 7.24–7.43 (m, 3H), 6.16 (s, 1H), 4.01–4.21 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 135.1, 133.5, 130.2, 129.7, 127.5, 126.7, 100.7, 65.4.



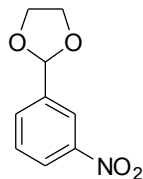
2-(4-bromophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.47–7.56 (m, 2H), 7.31–7.42 (m, 2H), 5.77 (s, 1H), 3.96–4.16 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 137.0, 131.4, 128.4, 128.1, 127.8, 123.1, 102.9, 65.2.



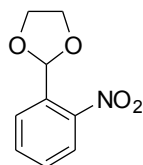
2-(2-bromophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.53–7.64 (m, 2H), 7.29–7.39 (m, 1H), 7.17–7.27 (m, 1H), 6.11 (s, 1H), 4.01–4.21 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 136.6, 132.9, 130.5, 127.8, 127.3, 122.9, 102.6, 65.4.



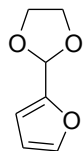
2-(3-nitrophenyl)-1,3-dioxolane (product was crystallized from crude reaction mixture after workup)

Mp: 57–58°C (ethanol, lit.¹² 57–58°C). ^1H NMR (200 MHz, CDCl_3): δ 8.27–8.31 (m, 1H), 8.16 (ddd, J = 8.2, 2.4, 1.1 Hz, 2H), 7.73–7.80 (m, 1H), 7.51 (dd, J = 7.9, 7.9 Hz, 1H), 5.83 (s, 1H), 3.97–4.15 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 148.0, 140.2, 132.5, 129.2, 123.7, 121.4, 102.0, 65.3.



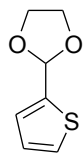
2-(2-nitrophenyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.85–7.91 (m, 1H), 7.76–7.82 (m, 1H), 7.56–7.66 (m, 1H), 7.43–7.54 (m, 1H), 6.47 (s, 1H), 3.95–4.10 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 148.7, 133.1, 132.8, 129.6, 127.5, 124.3, 99.5, 65.2.



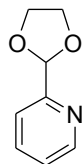
2-(2'-furyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.42 (dd, J = 1.8, 0.8 Hz, 1H), 6.42–6.47 (m, 1H), 6.35 (dd, J = 3.2, 1.8 Hz, 1H), 5.92 (s, 1H), 3.93–4.20 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 151.0, 143.1, 110.1, 108.7, 97.7, 65.1.



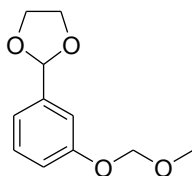
2-(2'-thienyl)-1,3-dioxolane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.33 (ddd, J = 4.9, 1.3, 0.3 Hz, 1H), 7.18 (ddd, J = 3.7, 1.3, 0.6 Hz, 1H), 7.00 (dd, J = 5.1, 3.5 Hz, 1H), 6.12 (s, 1H), 3.93–4.20 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 141.6, 126.5, 126.2, 126.1, 100.1, 65.1.



2-(2'-pyridyl)-1,3-dioxolane

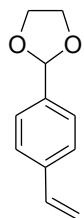
Oil. ^1H NMR (200 MHz, CDCl_3): δ 8.56–8.62 (m, 1H), 7.63–7.76 (m, 1H), 7.44–7.54 (m, 1H), 7.20–7.29 (m, 1H), 5.82 (s, 1H), 3.97–4.21 (m, 4H). ^{13}C NMR (50 MHz, CDCl_3): δ 156.8, 149.2, 136.6, 123.8, 120.5, 103.5, 65.4.



2-[3-(methoxymethyl)phenyl]-1,3-dioxolane

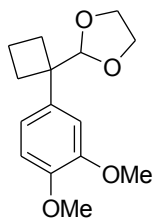
Oil. IR (neat): 2956, 2892, 1697, 1590, 1489, 1456, 1390, 1318, 1252, 1210, 1152, 1079, 1018, 994, 924, 876, 791, 696 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 7.25–7.35 (m, 1H), 6.99–7.19 (m, 3H), 5.79 (s, 1H), 5.19 (s, 2H), 3.96–4.19 (m, 4H), 3.47 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ

157.2, 139.5, 129.4, 119.9, 117.0, 114.1, 103.4, 94.4, 65.2, 56.0. HRMS (EI, m/z , relative intensity): 210 (19), 209 (12), 179 (6), 165 (5), 149 (8), 138 (3), 136 (3), 121 (2), 117 (3), 108 (4), 73 (12), 45 (100). Anal. calcd for $C_{11}H_{14}O_4$ C, 62.85; H, 6.71. Found C, 63.02; H, 6.82.



2-(4-vinylphenyl)-1,3-dioxolane

Oil. 1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.50 (m, 4H), 6.74 (dd, J = 17.6, 10.9 Hz, 1H), 5.82 (s, 1H), 5.78 (dd, J = 17.6, 0.9 Hz, 1H), 5.28 (dd, J = 10.9, 0.9 Hz, 1H), 3.97–4.19 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.4, 137.3, 136.4, 126.6, 126.1, 114.3, 103.5, 65.2.



2-[1-(3,4-dimethoxyphenyl)cyclobutyl]-1,3-dioxolane

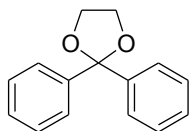
Oil. IR (neat): 2943, 2884, 1589, 1465, 1410, 1254, 1170, 1142, 1096, 1029, 966, 949, 854, 807, 763, 626 cm^{-1} . 1H NMR (200 MHz, $CDCl_3$): δ 6.72–6.90 (m, 5H), 5.07 (s, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.67–3.85 (m, 4H), 2.24–2.55 (m, 4H), 1.74–2.18 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 148.3, 147.2, 138.2, 119.3, 110.9, 110.5, 108.4, 65.4, 55.9, 55.8, 48.7, 29.1, 15.9. MS (EI, m/z , relative intensity): 264 (20), 236 (7), 233 (4), 220 (2), 191 (49), 163 (40), 73 (100). Anal. calcd for $C_{15}H_{20}O_4$ C, 68.16; H, 7.63. Found C, 68.26; H, 7.50.

Reaction with pivalaldehyde Crude reaction mixture was analysed with GC and 1H NMR. We confirmed the presence of the respective acetal in the reaction mixture [1H NMR (200 MHz, $CDCl_3$): δ 4.49 (s, 1H), 3.79–3.86 (m, 4H), 0.90 (s, 9H)], but we were unable to undoubtedly determine the conversion. After workup the residue was distilled under atmospheric pressure, but distillate was substantially contaminated with DMF and ethyl acetate (yield ~ 40%).

Reaction with 2-methylbutanal Crude reaction mixture was analysed with GC and GC/MS. The following compounds were identified:

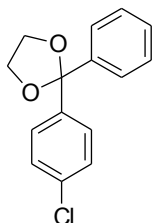
2-methylbutanal (21% GC); 2-(2-methylpropyl)-1,3-dioxolane (31% GC) MS (EI, m/z , relative intensity): 129 (2), 99 (1), 85 (1), 73 (100), 45 (15); 2,4-dimethyl-2-propyl-3-hydroxyhexanal (?) (48% GC) MS (EI, m/z , relative intensity): 172 (1), 155 (7), 137 (4), 126 (15), 115 (4), 97 (63), 86 (100), 71 (32), 69 (13), 57 (34), 55 (13), 41 (26) and some other minor by-products.

Characterization data of 1,3-dioxolanes (Table 2 in article)



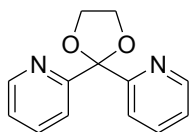
2,2-diphenyl-1,3-dioxolane

Product was not isolated from reaction mixture. Reaction mixture was analysed with GC (substrate : product = 88 : 12) and GC/MS: benzophenone MS (EI, m/z , relative intensity): 182 (42), 152 (4), 105 (100), 77 (71), 51 (31); 2,2-diphenyl-1,3-dioxolane MS (EI, m/z , relative intensity): 226 (2), 195 (3), 165 (11), 149 (100), 105 (50), 77 (33), 51 (8).



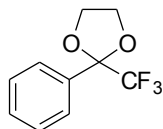
2-(4-chlorophenyl)-2-phenyl-1,3-dioxolane

Product was not isolated from reaction mixture. Reaction mixture was analysed with GC (substrate : product = 40 : 60) and GC/MS: *p*-chlorobenzophenone MS (EI, m/z , relative intensity): 218 (12), 216 (38), 181 (13), 152 (7), 141 (24), 139 (80), 111 (36), 105 (100), 77 (44), 51 (18); 2-(4-chlorophenyl)-2-phenyl-1,3-dioxolane MS (EI, m/z , relative intensity): 262 (1), 260 (2), 231 (1), 229 (3), 185 (32), 183 (100), 165 (26), 149 (75), 141 (18), 139 (60), 114 (14), 112 (39), 105 (60), 77 (65), 51 (20).



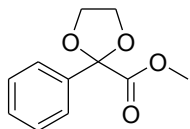
2,2-bis-(2'-pyridyl)-1,3-dioxolane (product was crystallized from crude reaction mixture after workup)

Mp: 170–171°C (hexanes : ethyl acetate 5 : 1, lit.¹³ 164–165°C). ¹H NMR (200 MHz, CDCl₃): δ 8.57 (ddd, J = 4.7, 1.7, 1.0 Hz, 2H), 7.84 (ddd, J = 7.9, 1.2, 1.0 Hz, 2H), 7.72 (ddd, J = 7.9, 7.9, 1.7 Hz, 2H), 7.18 (ddd, J = 7.5, 4.7, 1.2 Hz, 2H), 4.16 (s, 4H). ¹³C NMR (50 MHz, CDCl₃): δ 159.6, 149.4, 136.5, 123.0, 120.8, 108.2, 65.7.



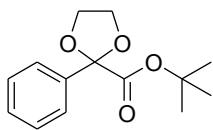
2-phenyl-2-trifluoromethyl-1,3-dioxolane

Oil. IR (neat): 2994, 2907, 1476, 1452, 1307, 1271, 1177, 1108, 1048, 957, 918, 762, 720, 697, 664 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 7.60–7.72 (m, 2H), 7.36–7.48 (m, 3H), 4.20–4.37 (m, 2H), 3.90–4.14 (m, 2H). ¹³C NMR (50 MHz, CDCl₃): δ 134.7, 129.6, 128.0, 126.8 (q, J^3_{C-F} = 11 Hz), 122.9 (q, J^1_{C-F} = 287 Hz), 104.7 (q, J^2_{C-F} = 32 Hz), 66.7. MS (EI, m/z , relative intensity): 218 (1), 199 (1), 187 (1), 158 (3), 149 (100), 105 (59), 77 (23). Anal. calcd for C₁₀H₉O₂F₃ C, 55.05; H, 4.16; F, 26.12. Found C, 54.94; H, 4.10; F, 26.38.



2-metoxycarbonyl-2-phenyl-1,3-dioxolane (distillate – mixture of methyl and *tert*-butyl esters, 86 : 14, according to GC – was separated into analytical samples of the individual compounds with column chromatography, hexanes : ethyl acetate 6 : 1)

¹H NMR (200 MHz, CDCl₃): δ 7.54–7.65 (m, 2H), 7.31–7.44 (m, 3H), 4.12–4.23 (m, 2H), 4.01–4.12 (m, 2H), 3.73 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 169.6, 137.2, 129.1, 128.1, 125.6, 105.7, 65.7, 52.8.

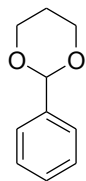


2-*tert*-butoxycarbonyl-2-phenyl-1,3-dioxolane

¹H NMR (200 MHz, CDCl₃): δ 7.50–7.67 (m, 2H), 7.30–7.42 (m, 3H), 4.11–4.24 (m, 2H), 3.98–4.11 (m, 2H), 1.41 (s, 9H). ¹³C NMR (50 MHz, CDCl₃): δ 168.1, 137.7, 128.7, 128.0, 125.7, 105.9, 82.4, 65.6, 27.7.

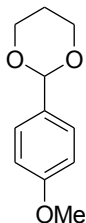
¹³ Newkome, G. R.; Sauer, J. D.; Staires, S. K. *J. Org. Chem.* **1977**, *42*, 3524–3527.

Characterization data of 1,3-dioxanes (Table 3 in article)



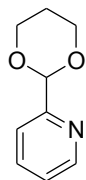
2-phenyl-1,3-dioxane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.45–7.55 (m, 2H), 7.28–7.44 (m, 3H), 5.52 (s, 1H), 4.22–4.34 (m, 2H), 3.92–4.08 (m, 2H), 2.11–2.37 (m, 1H), 1.39–1.51 (m, 1H). ^{13}C NMR (50 MHz, CDCl_3): δ 138.6, 128.7, 128.2, 125.9, 101.6, 67.3, 25.7.



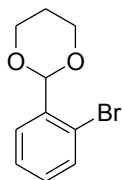
2-(4-methoxyphenyl)-1,3-dioxane

Oil. ^1H NMR (200 MHz, CDCl_3): δ 7.37–7.46 (m, 2H), 6.84–6.94 (m, 2H), 5.46 (s, 1H), 4.19–4.30 (m, 2H), 3.88–4.04 (m, 2H), 3.79 (s, 3H), 2.08–2.33 (m, 1H), 1.36–1.48 (m, 1H). ^{13}C NMR (50 MHz, CDCl_3): δ 159.8, 131.2, 127.2, 113.5, 101.4, 67.2, 55.2, 25.7.



2-(2'-pyridyl)-1,3-dioxane (after distillation analytical sample of this compound was purified with column chromatography, hexanes : ethyl acetate 3 : 1 \rightarrow 1 : 1)

Oil. ^1H NMR (200 MHz, CDCl_3): δ 8.54–8.60 (m, 1H), 7.64–7.75 (m, 1H), 7.51–7.59 (m, 1H), 7.18–7.27 (m, 1H), 5.55 (s, 1H), 4.20–4.33 (m, 2H), 3.92–4.09 (m, 2H), 2.08–2.36 (m, 1H), 1.37–1.49 (m, 1H). ^{13}C NMR (50 MHz, CDCl_3): δ 156.7, 148.9, 136.7, 123.6, 120.6, 101.5, 67.4, 25.6.



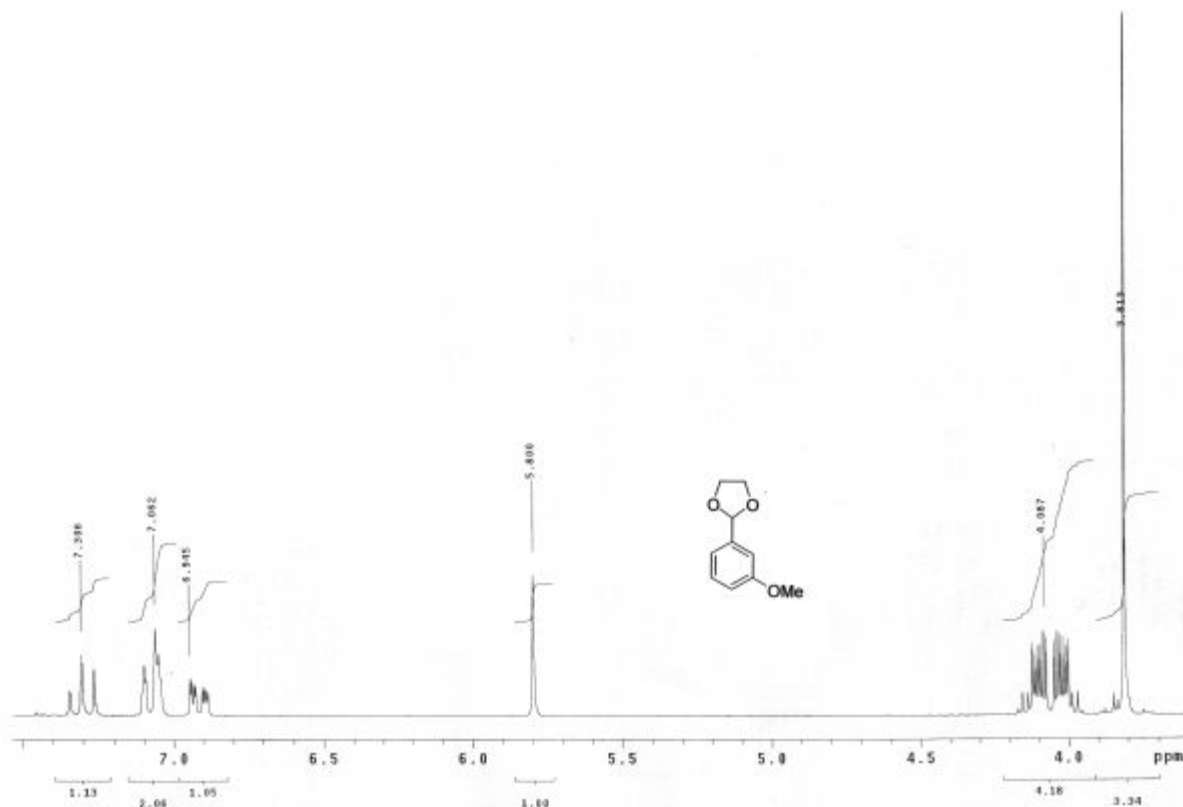
2-(2-bromophenyl)-1,3-dioxane (product solidified after distillation)

Mp. 44–47°C (Lit.¹⁴ 44–46°C). ^1H NMR (200 MHz, CDCl_3): δ 7.70 (dd, J = 7.7, 1.9 Hz, 1H), 7.53 (ddd, J = 7.9, 1.4, 0.3 Hz, 1H), 7.35 (dddd, J = 7.9, 7.7, 1.4, 0.3 Hz, 1H), 7.19 (dddd, J = 7.9, 7.7, 1.9, 0.3 Hz, 1H), 5.77 (s, 1H), 4.21–4.33 (m, 2H), 3.95–4.11 (m, 2H), 2.11–2.38 (m, 1H), 1.39–1.52 (m, 1H). ^{13}C NMR (50 MHz, CDCl_3): δ 137.4, 132.5, 130.3, 128.0, 127.5, 122.2, 100.9, 67.6, 25.7.

Spectra of the described compounds (Table 1 in article)

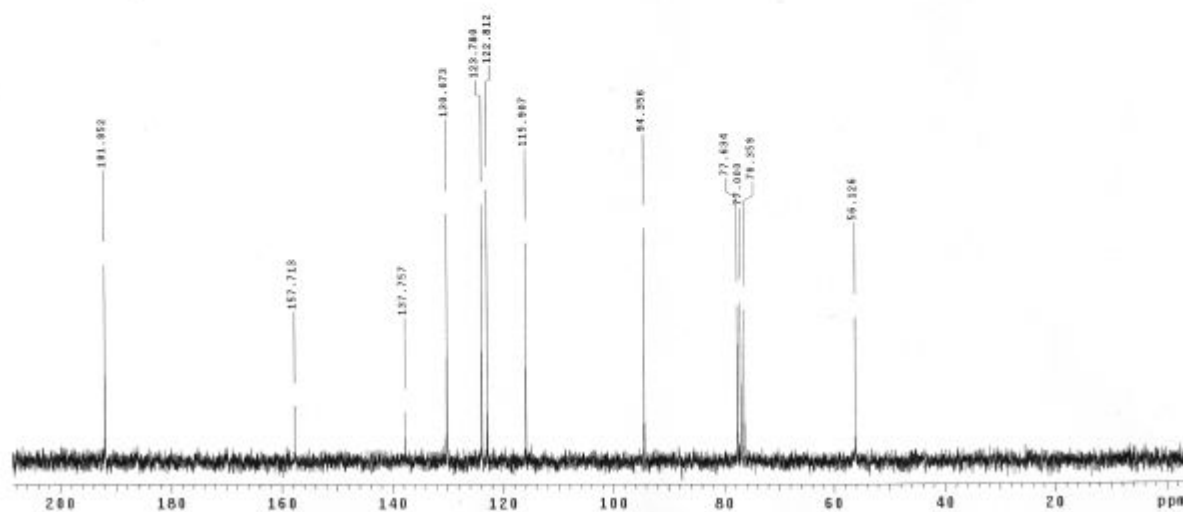
MS-1031xH

Pulse Sequence: zgpg1

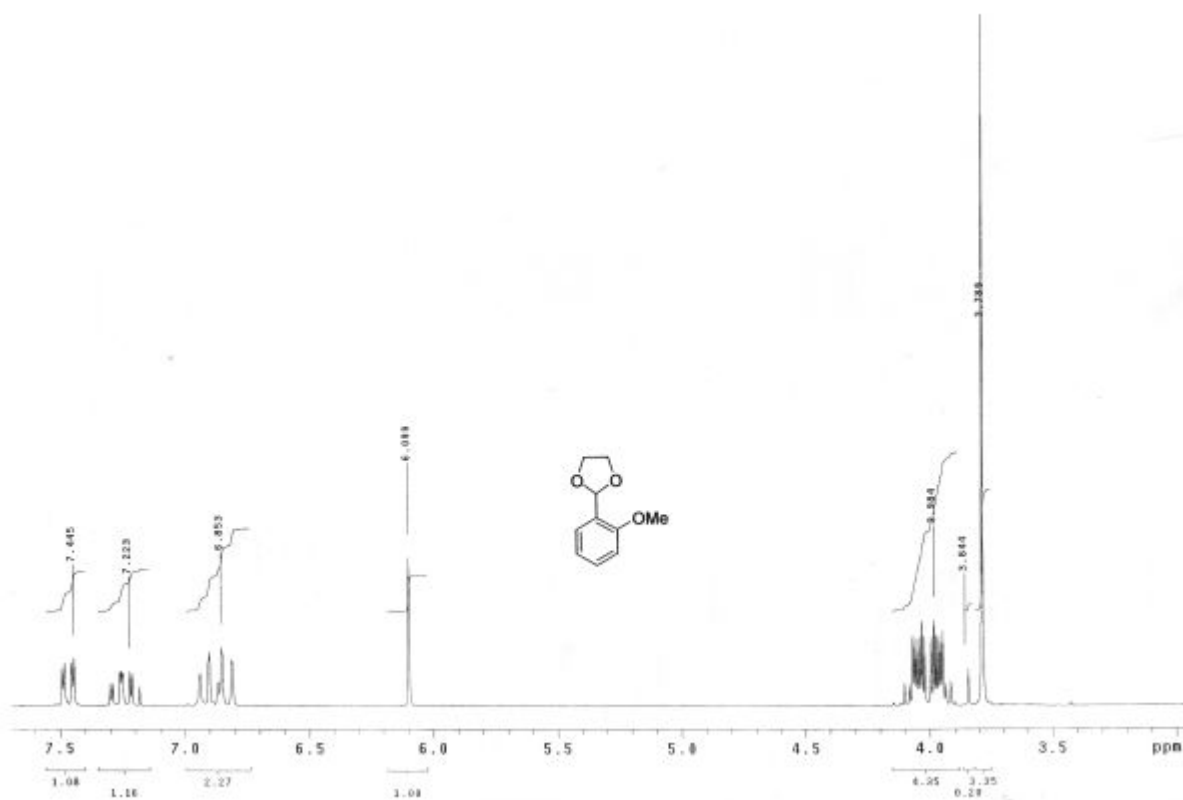


MS-1033HC

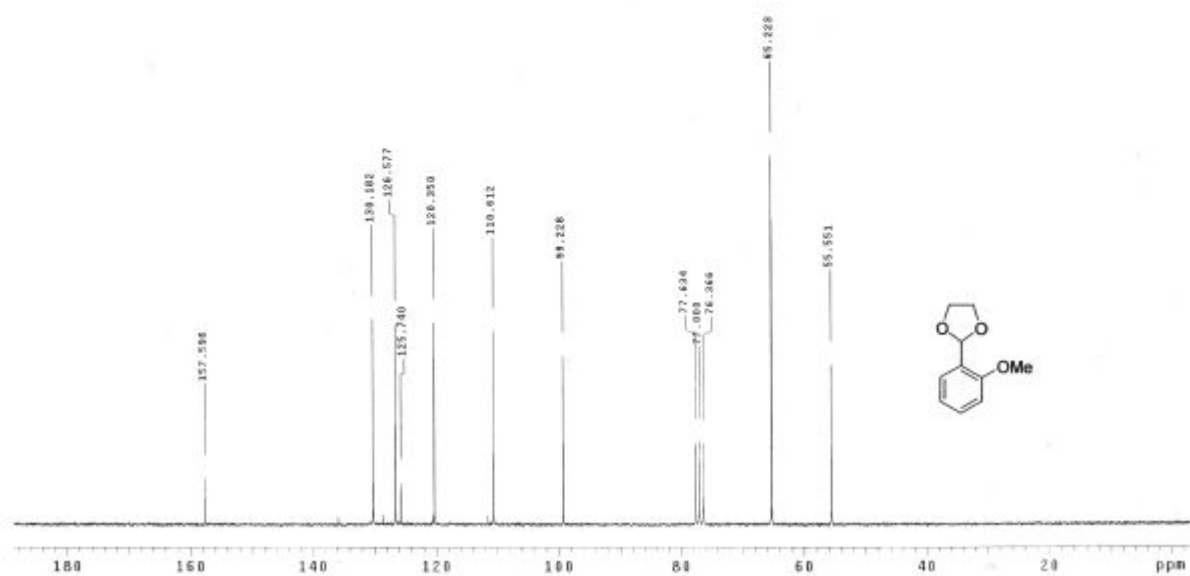
Pulse Sequence: zgpg1



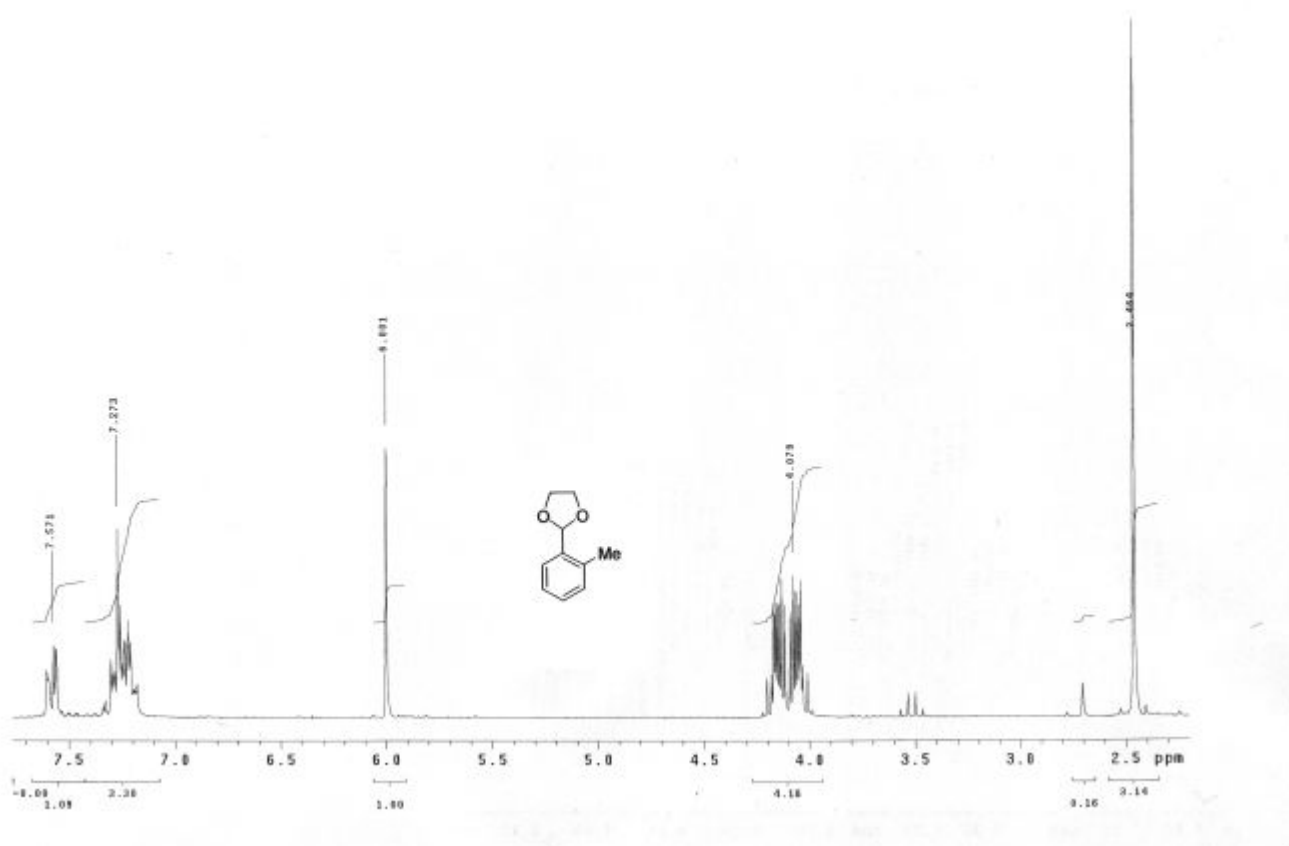
MS-1019xH
Pulse Sequence: s2pu1



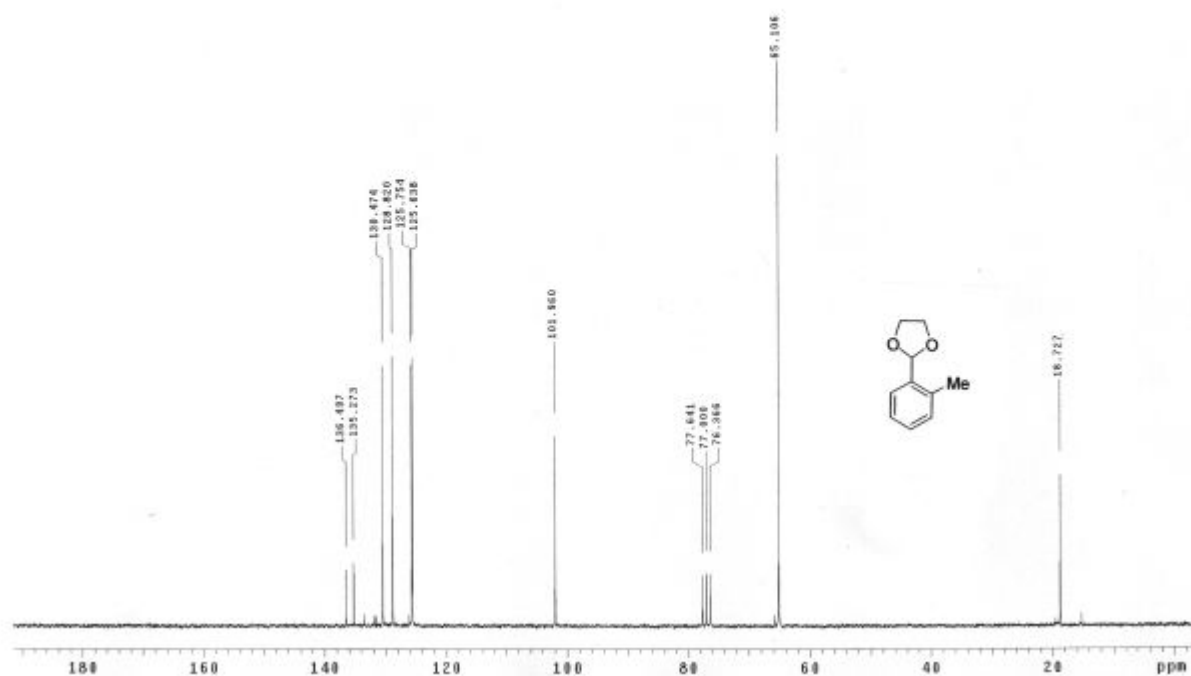
MS-1019xG
Pulse Sequence: s2pu1



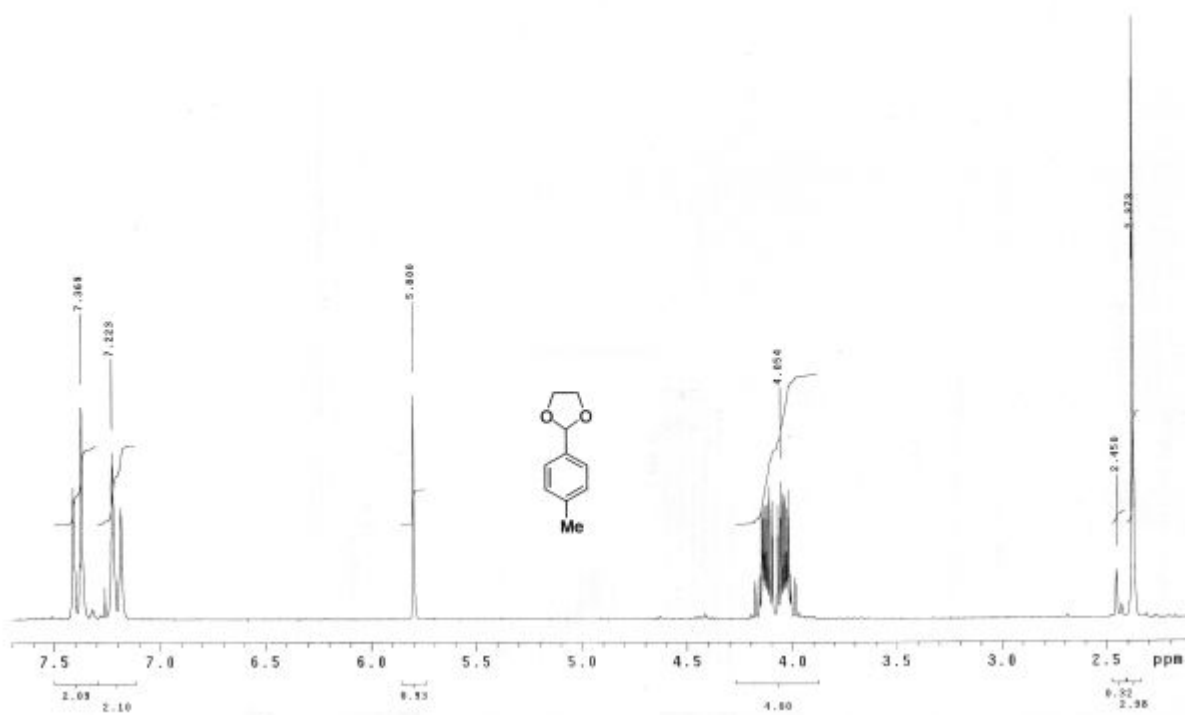
MS-1630xH
Pulse Sequence: s2pu1



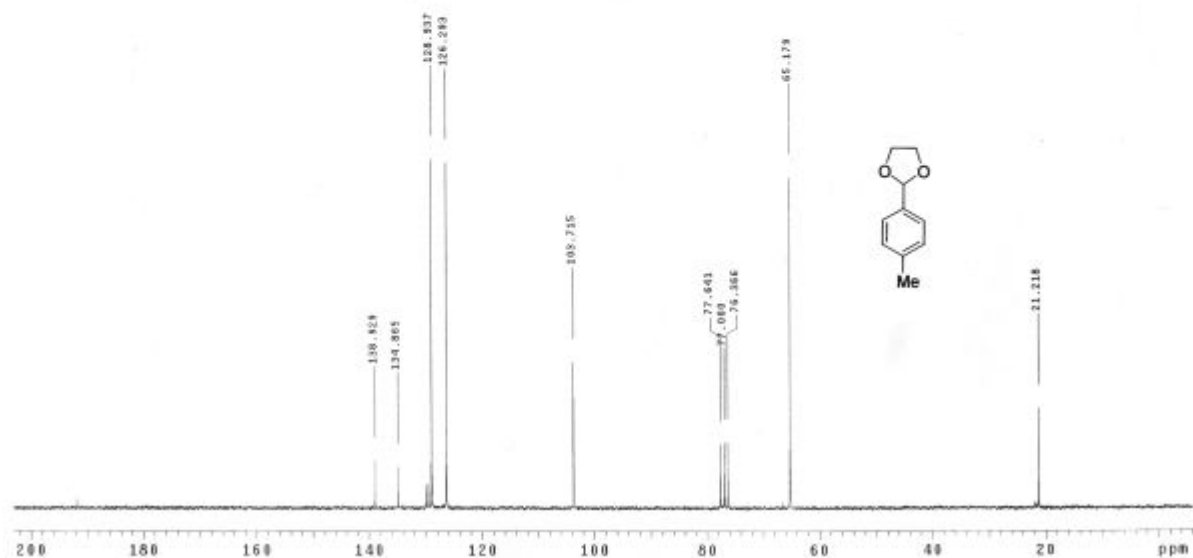
MS-1630xG
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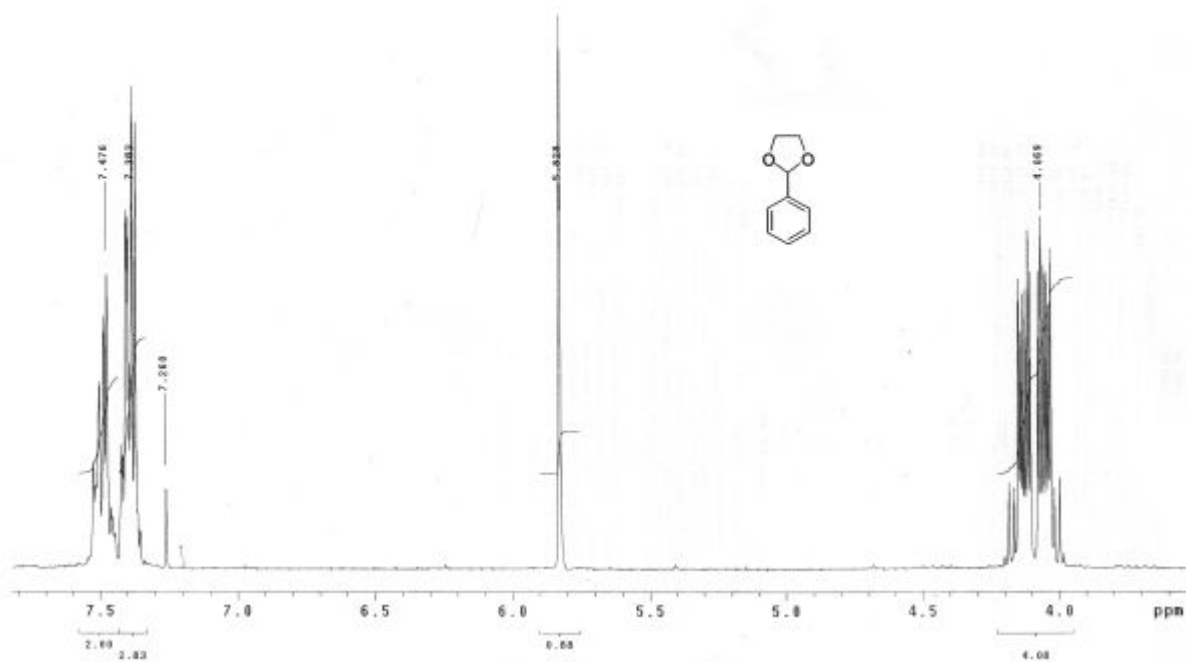
MS-1014aH
Pulse Sequence: s2pu1



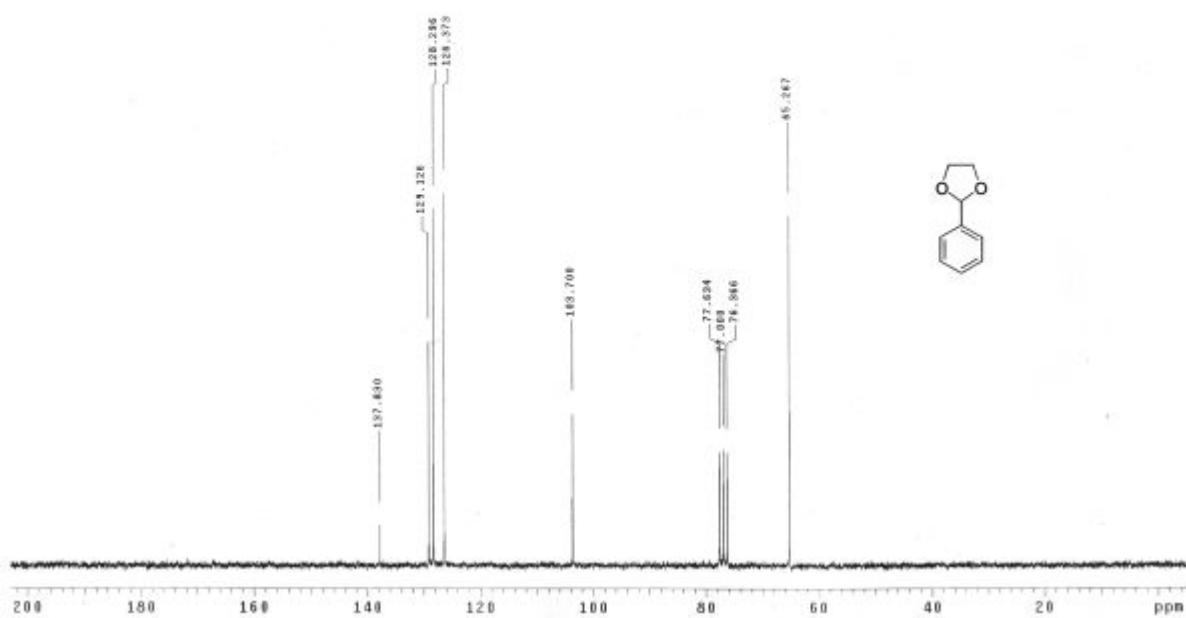
MS-1014aC
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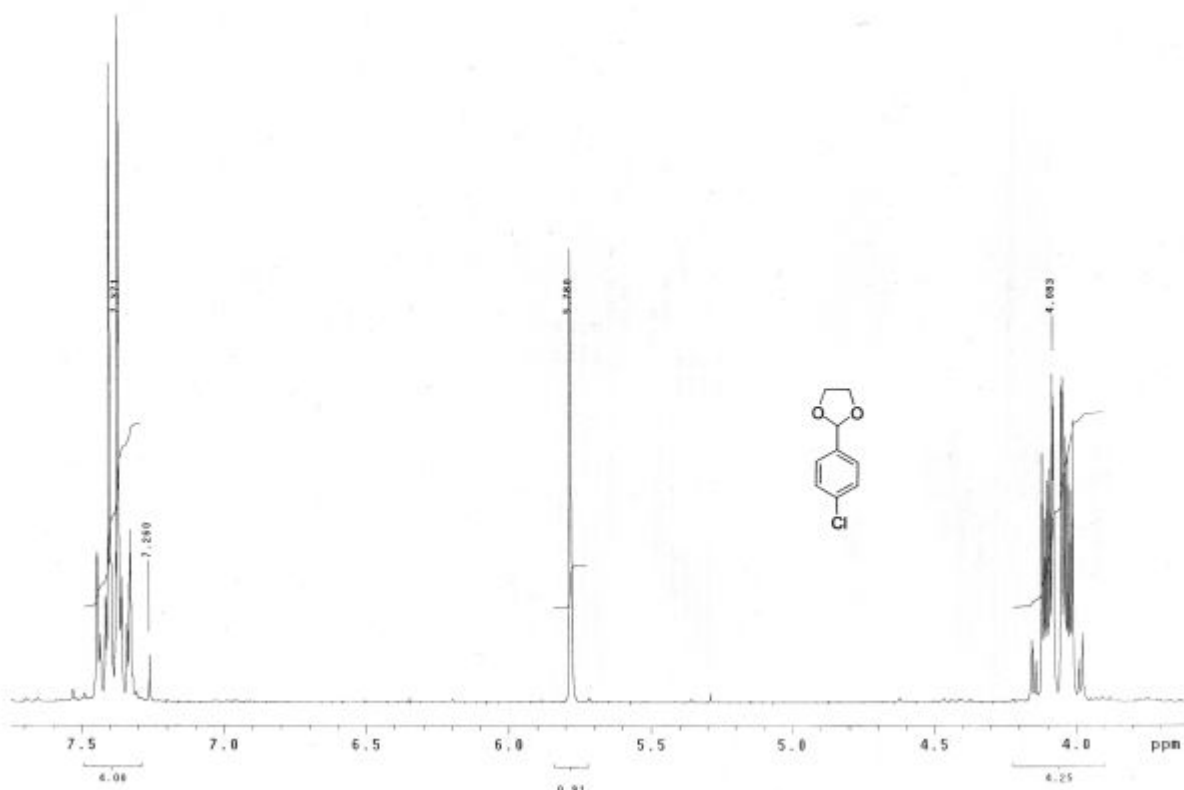
MS-1013KH
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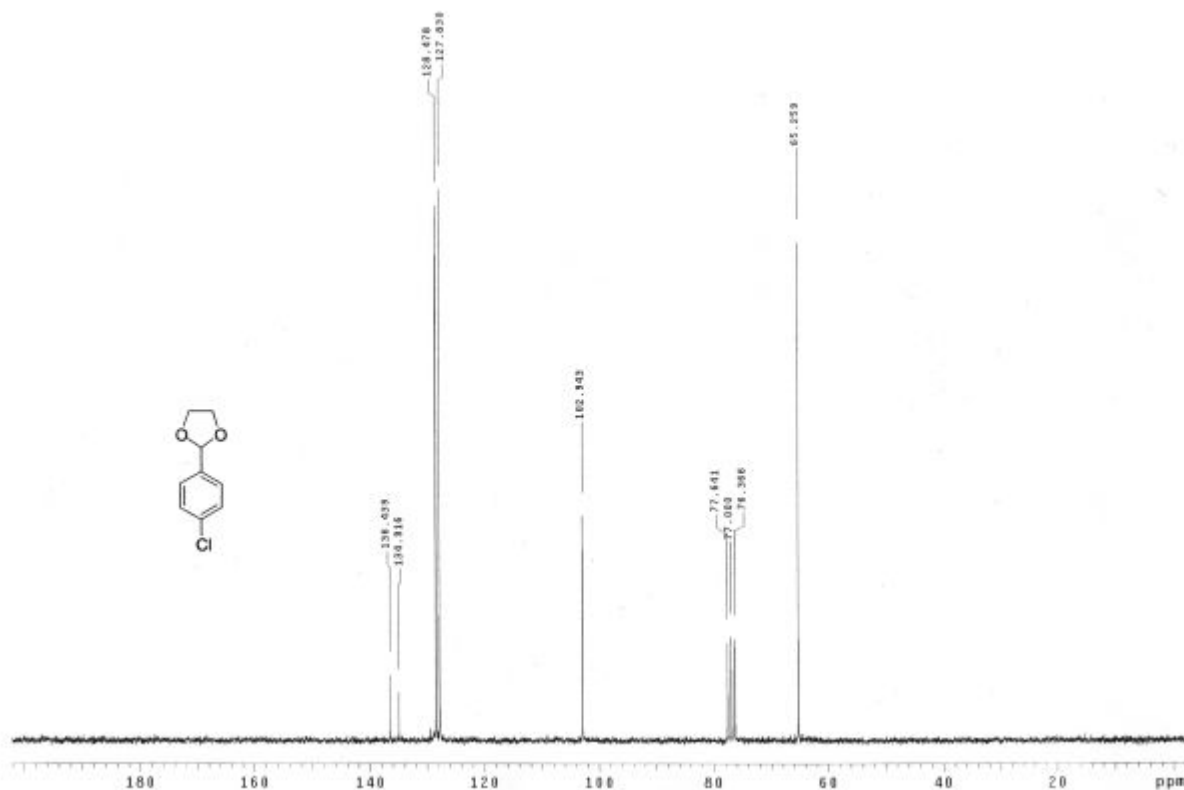
MS-1013KH
Pulse Sequence: s2pu1



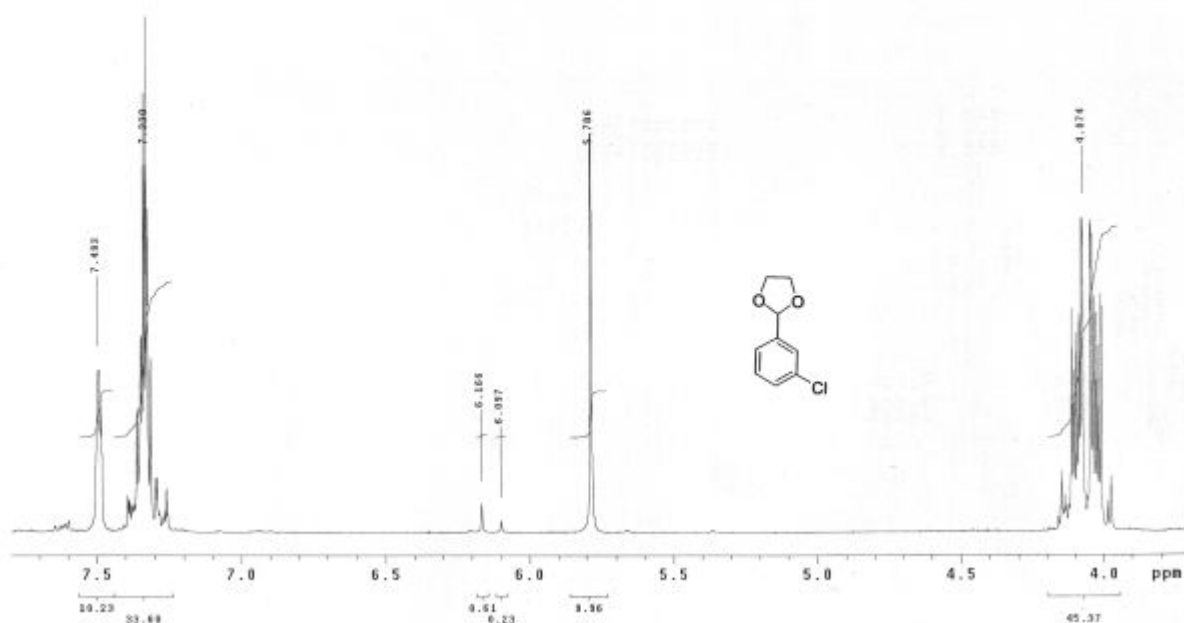
M8-1016K6
 Pulse Sequence: zgpg1



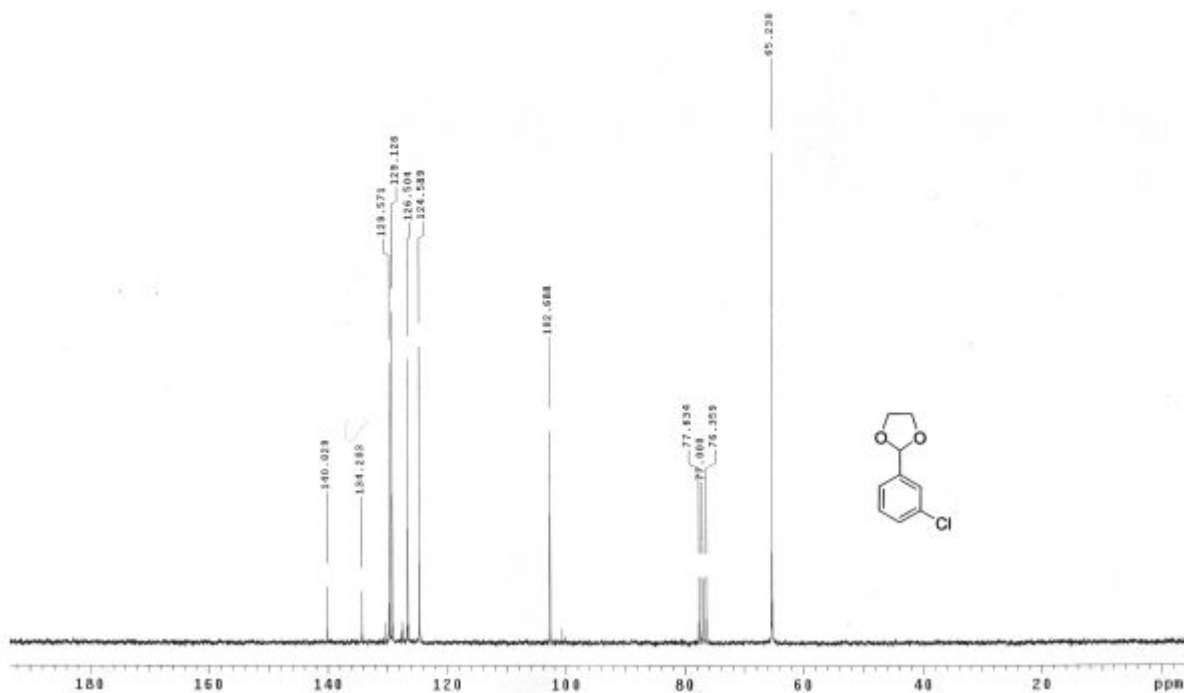
M8-1016K6
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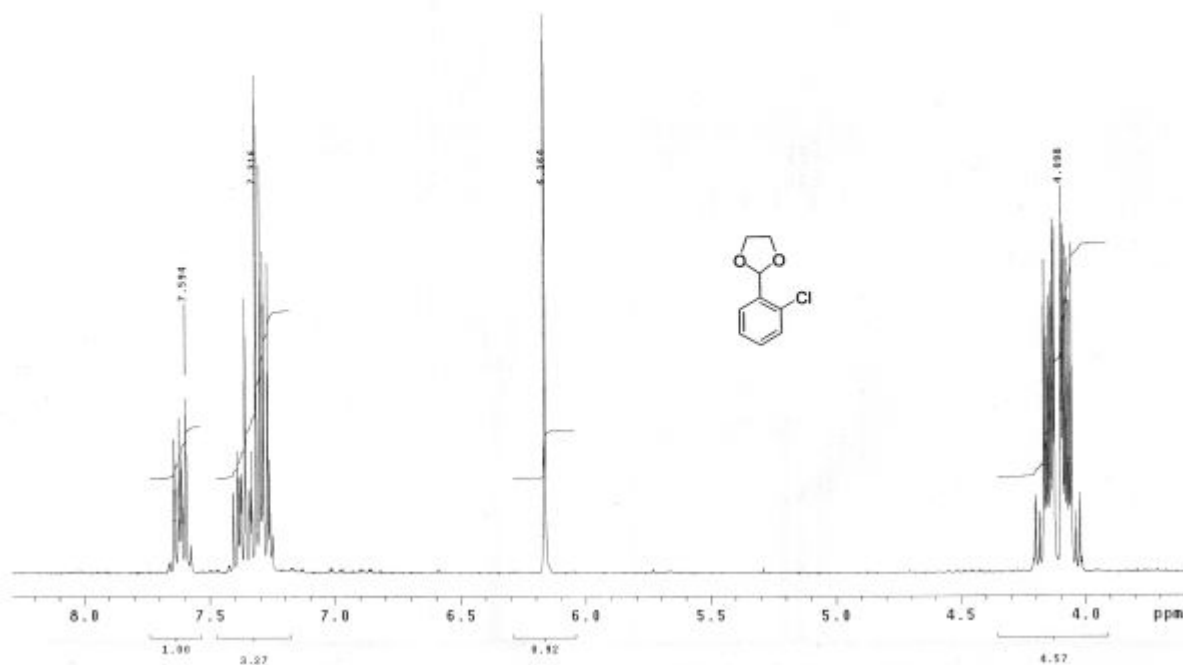
MS-1026xH
Pulse Sequence: s2pu1



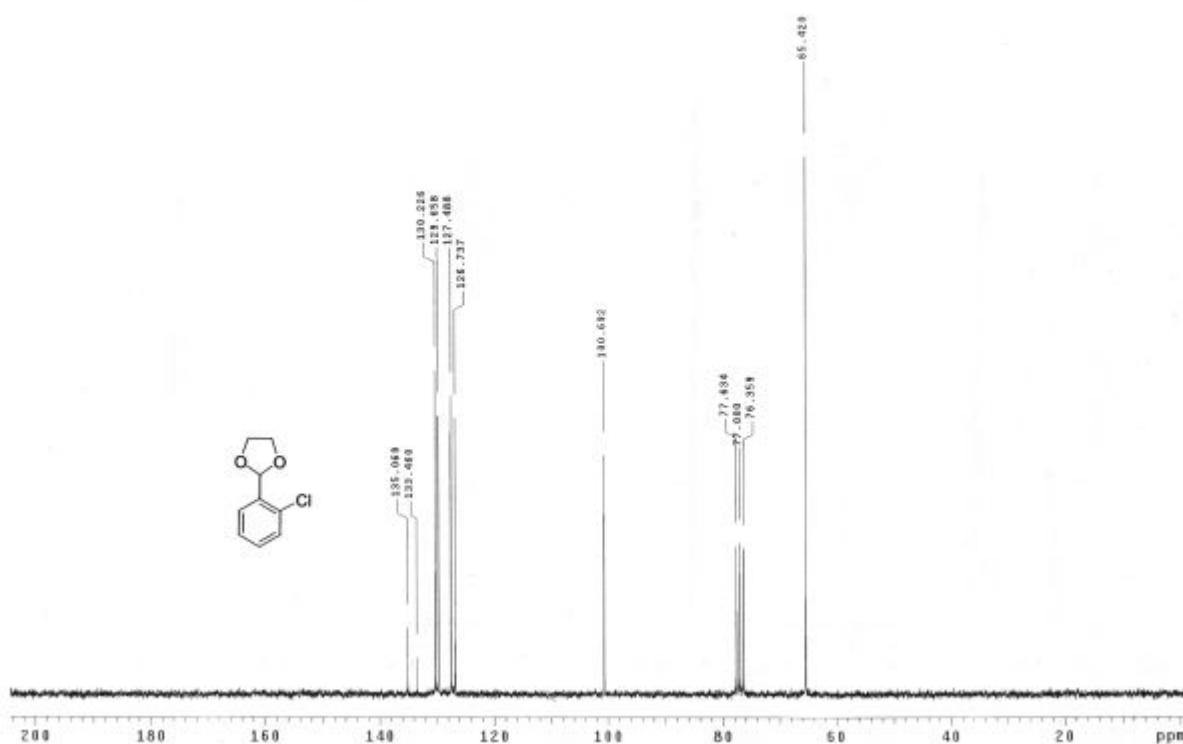
MS-1026xC
Pulse Sequence: s2pu1



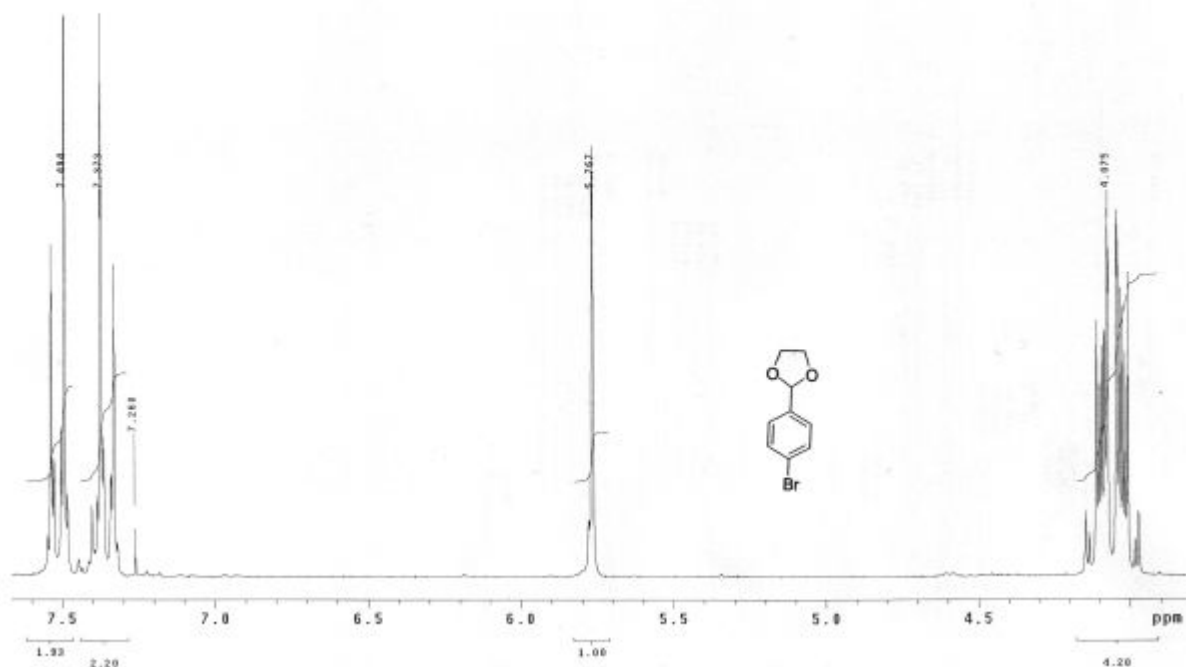
MS-1017xH
Pulse Sequence: s2pu3



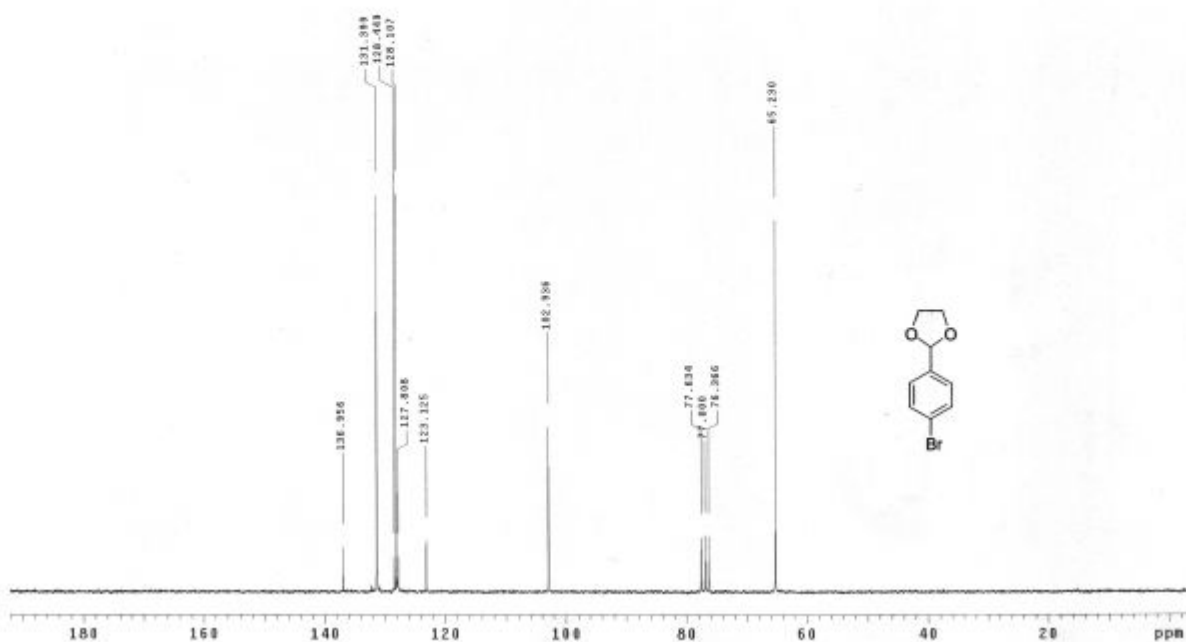
MS-1017xG
Pulse Sequence: s2pu1



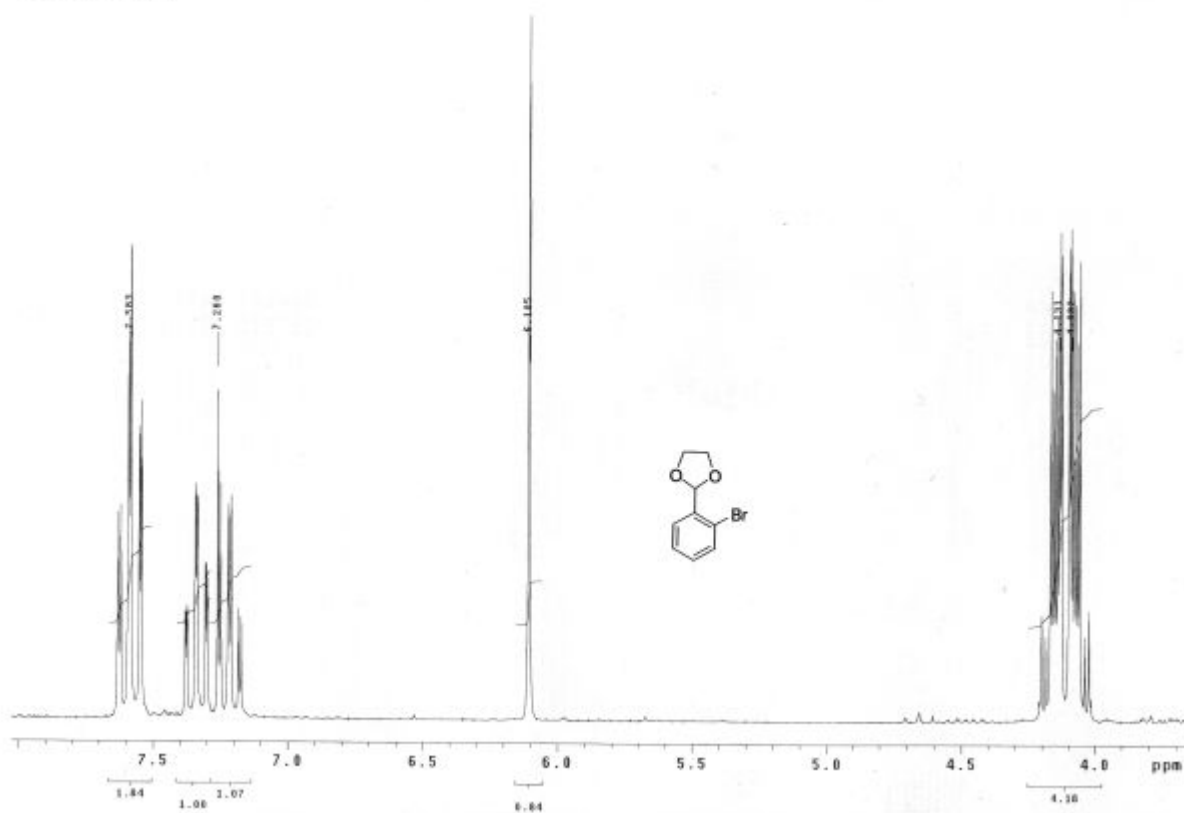
MS-1025KH
Pulse Sequence: zgpg1



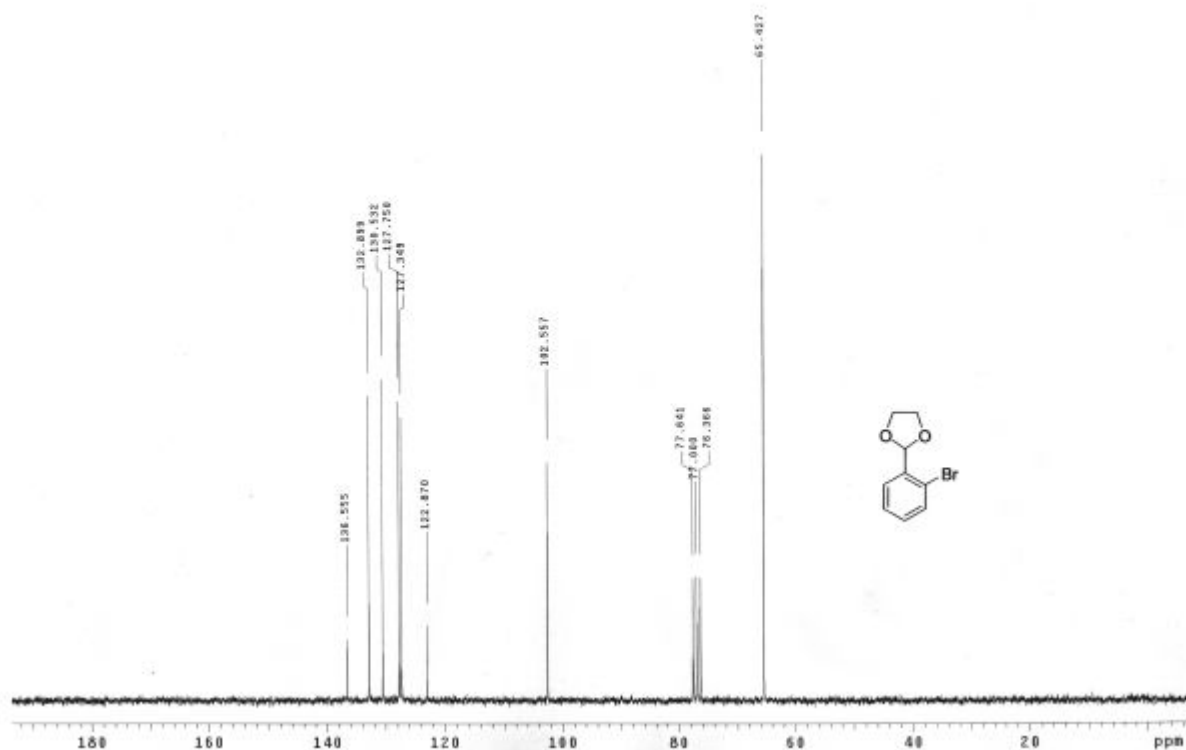
MS-1025KH
Pulse Sequence: zgpg1



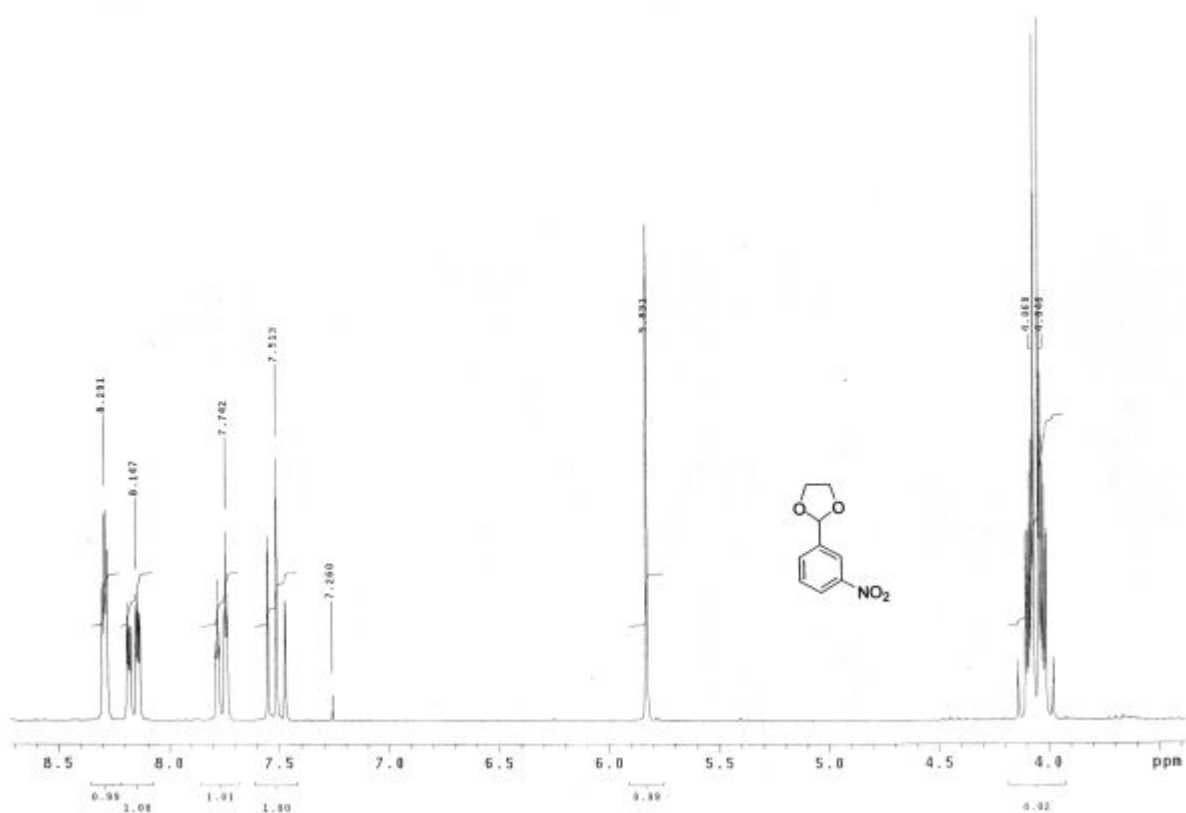
MB-1024xH
Pulse Sequence: zgpg1



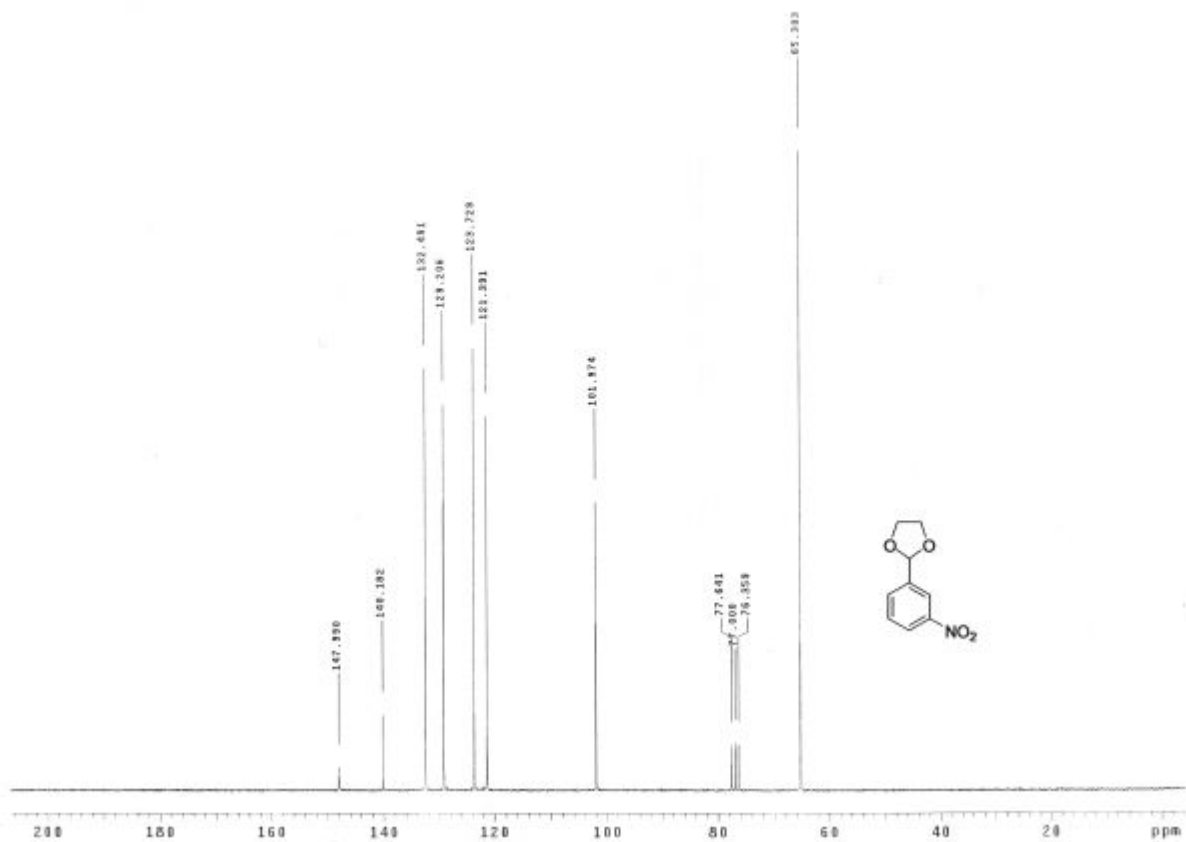
MB-1024xG
Pulse Sequence: zgpg1



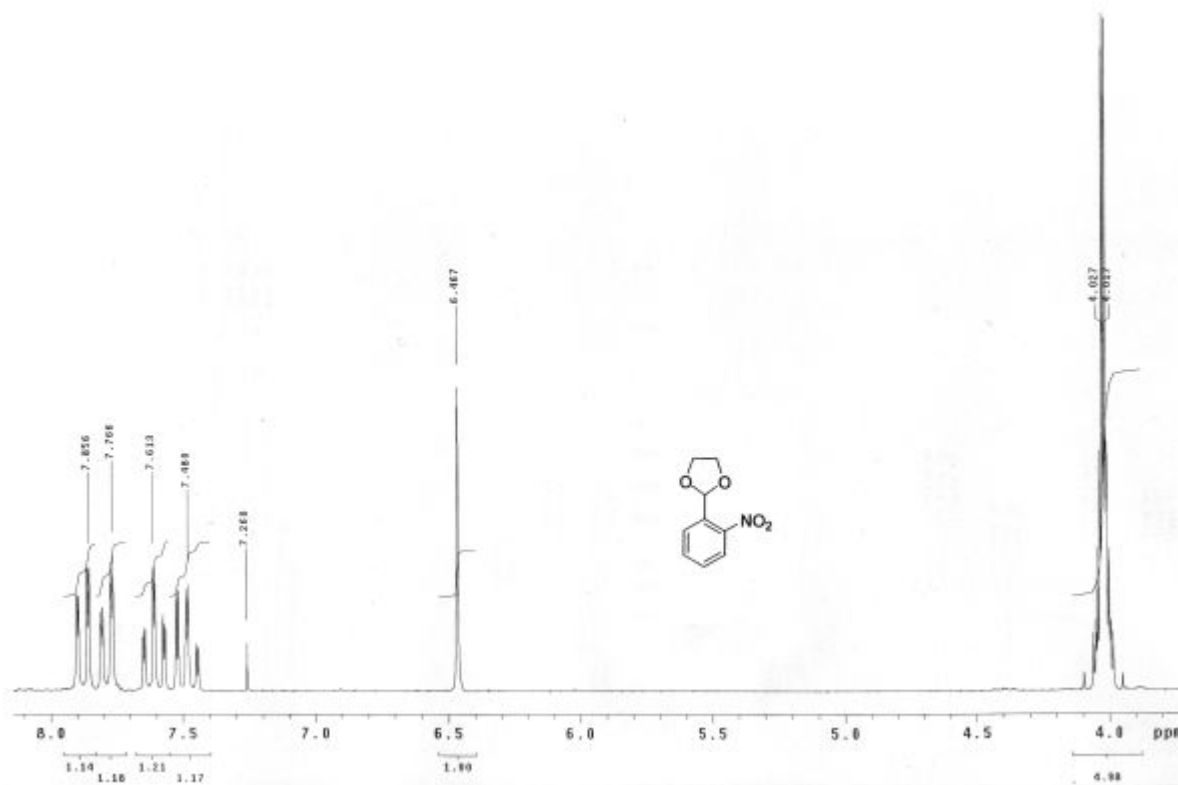
MS-1926wH
Pulse Sequence: s2pt1



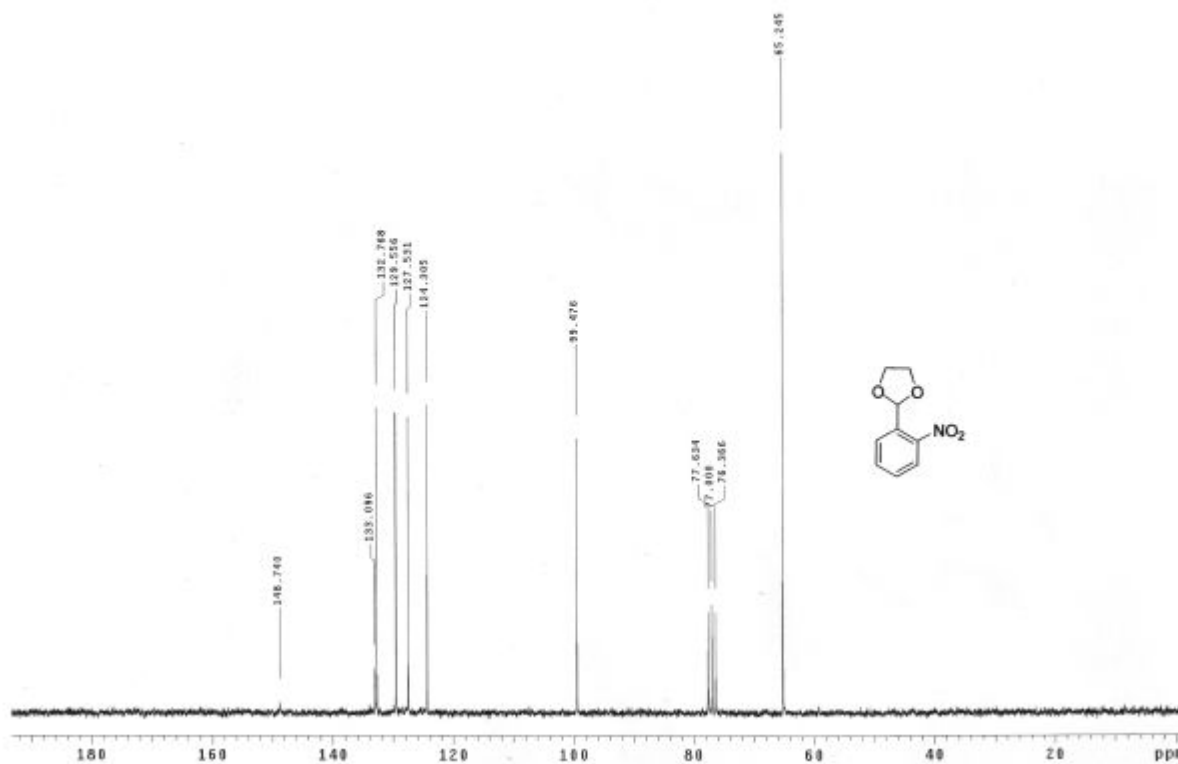
MS-1926wG
Pulse Sequence: s2pt1



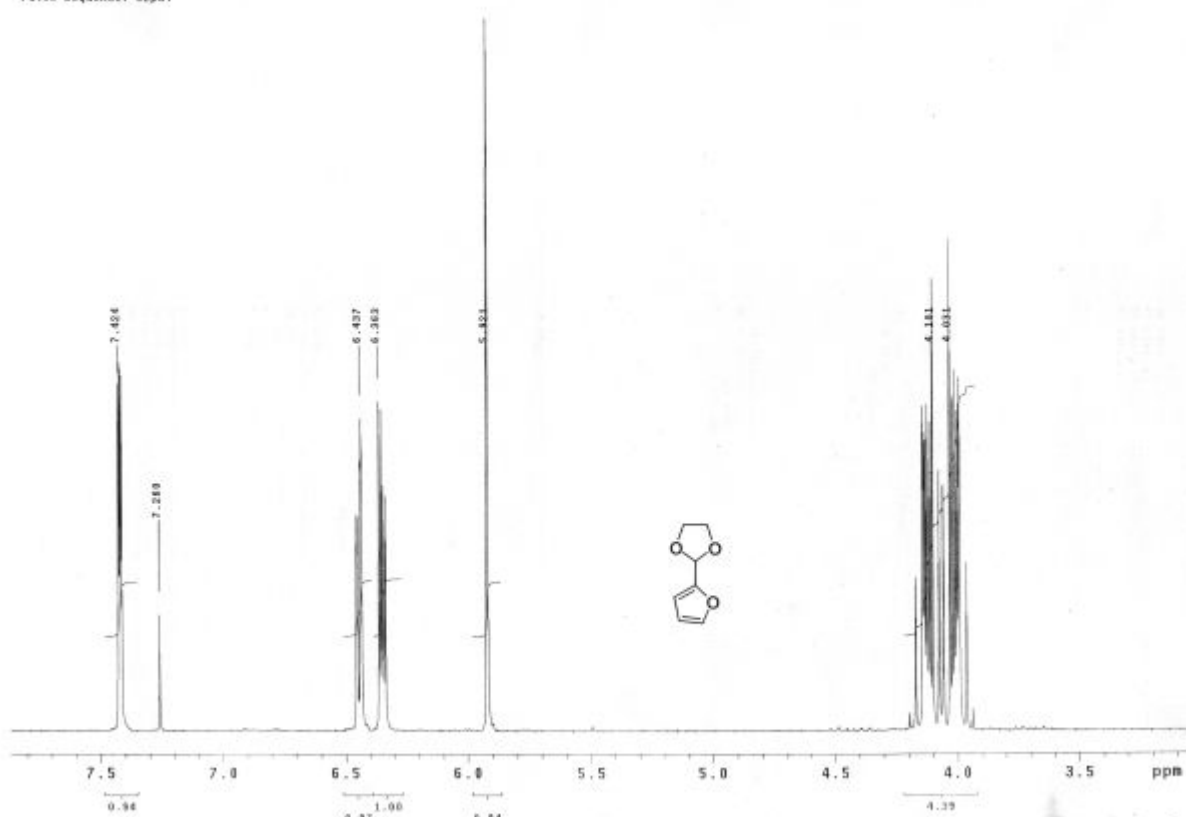
RB-1621xH
Pulse Sequence: zgpg30



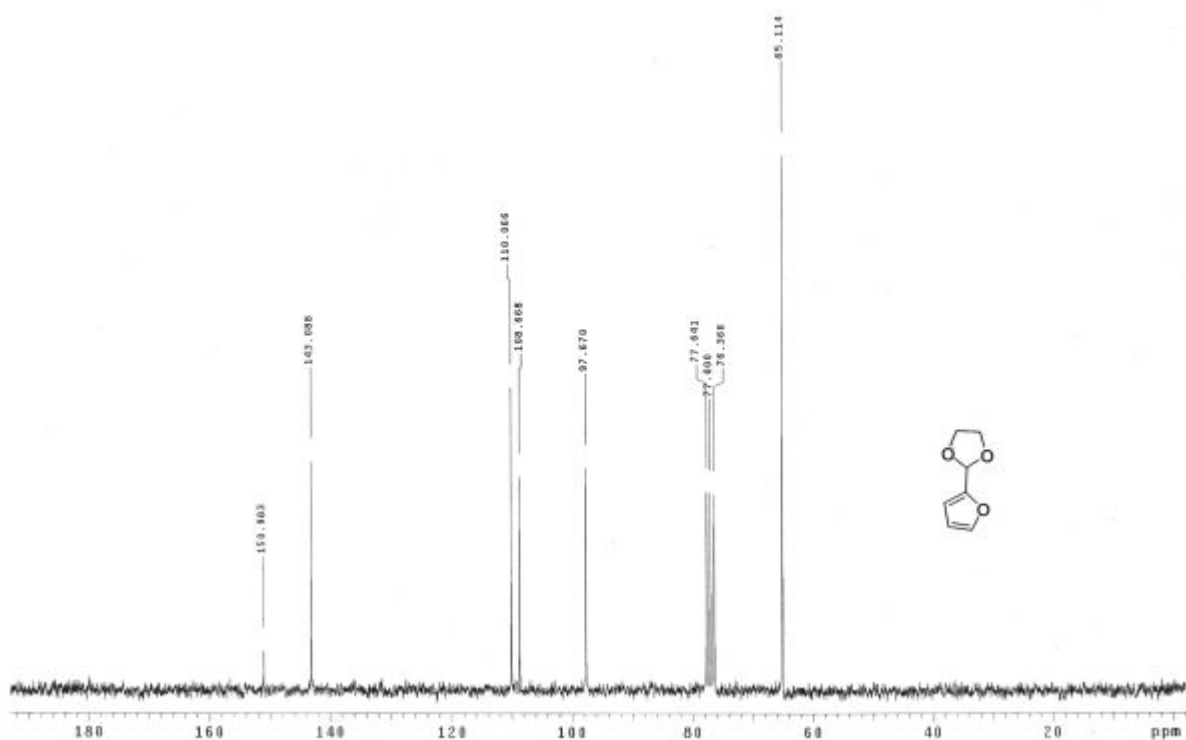
RB-1621xG
Pulse Sequence: zgpg30



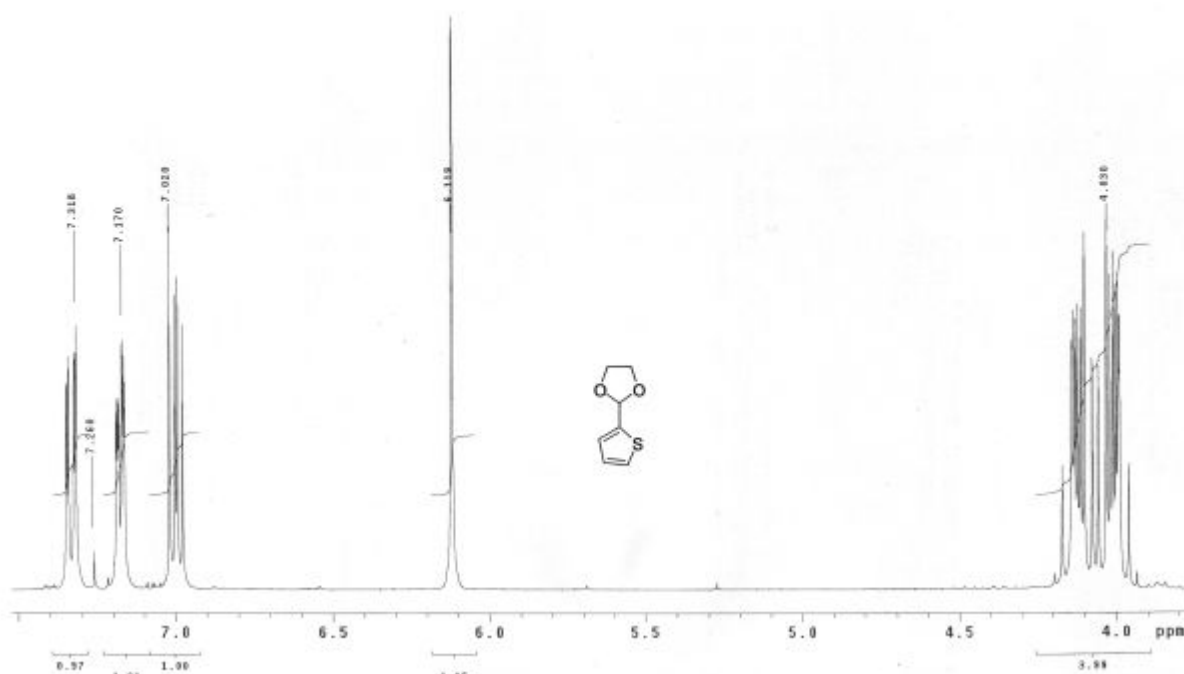
MS-1010xH
Pulse Sequence: zgpg1



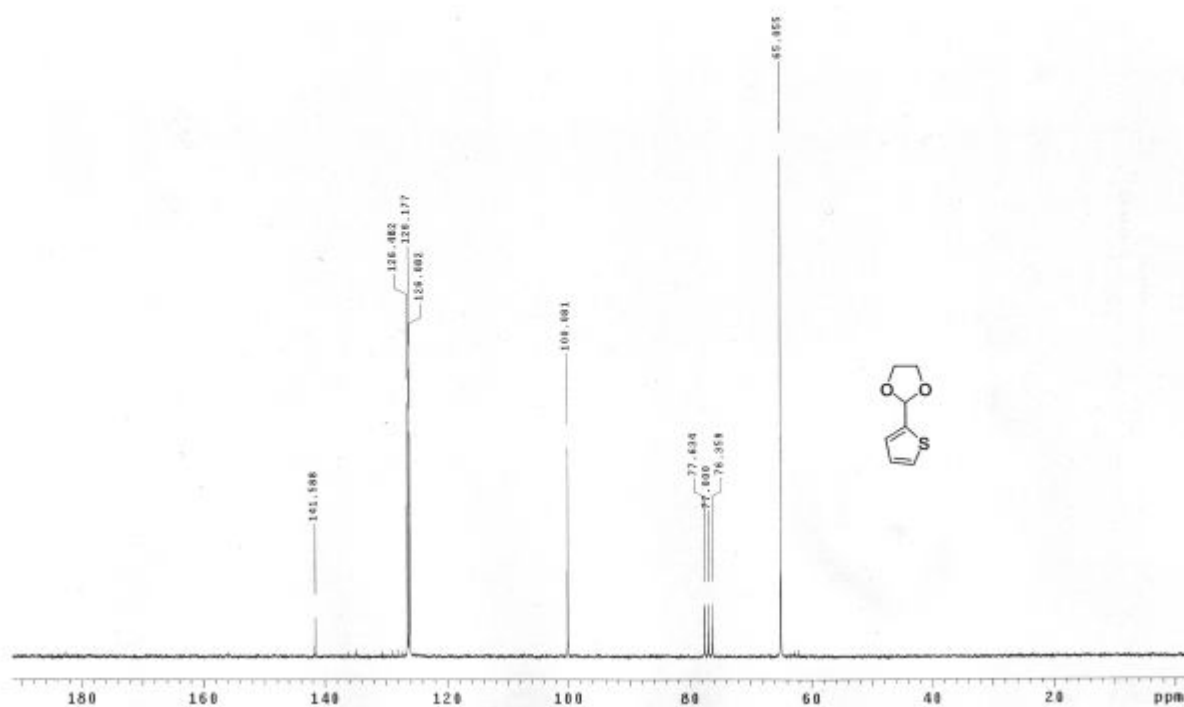
MS-1010xH
Pulse Sequence: zgpg1



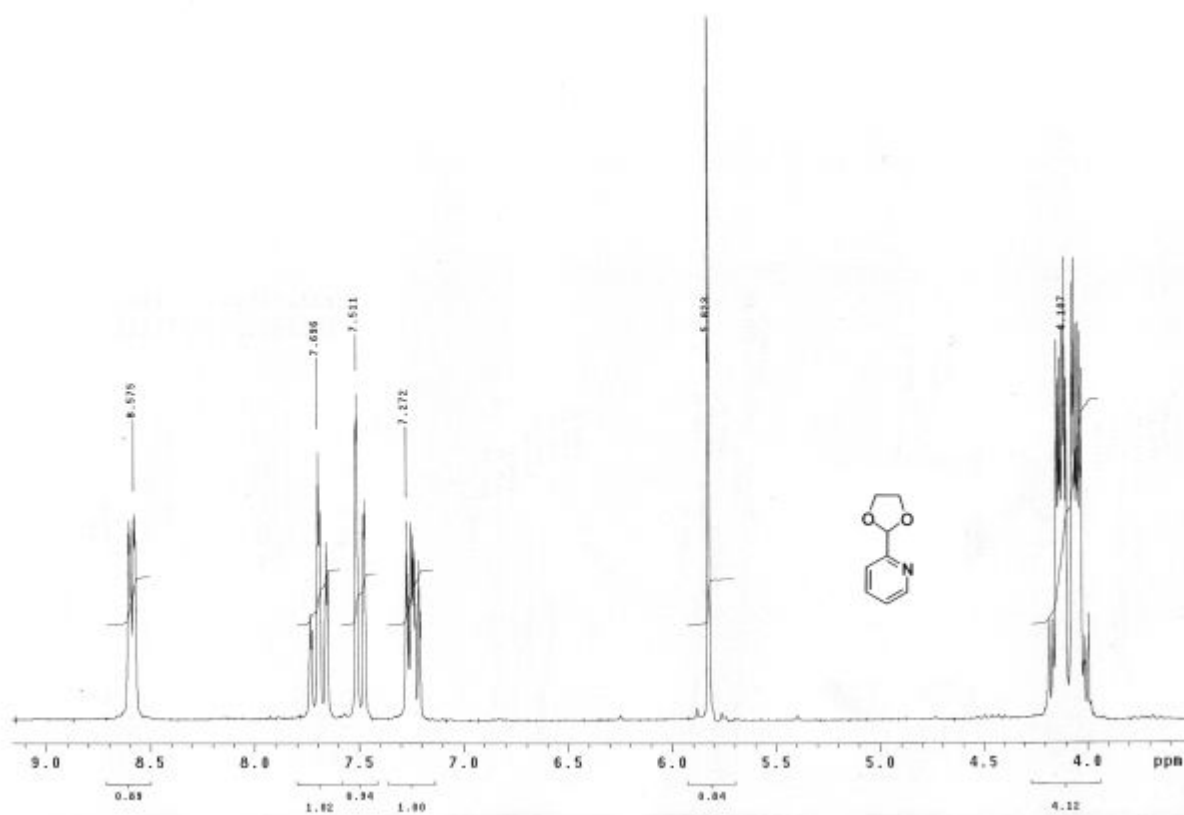
MB-1023aH
Pulse Sequence: zgpg30



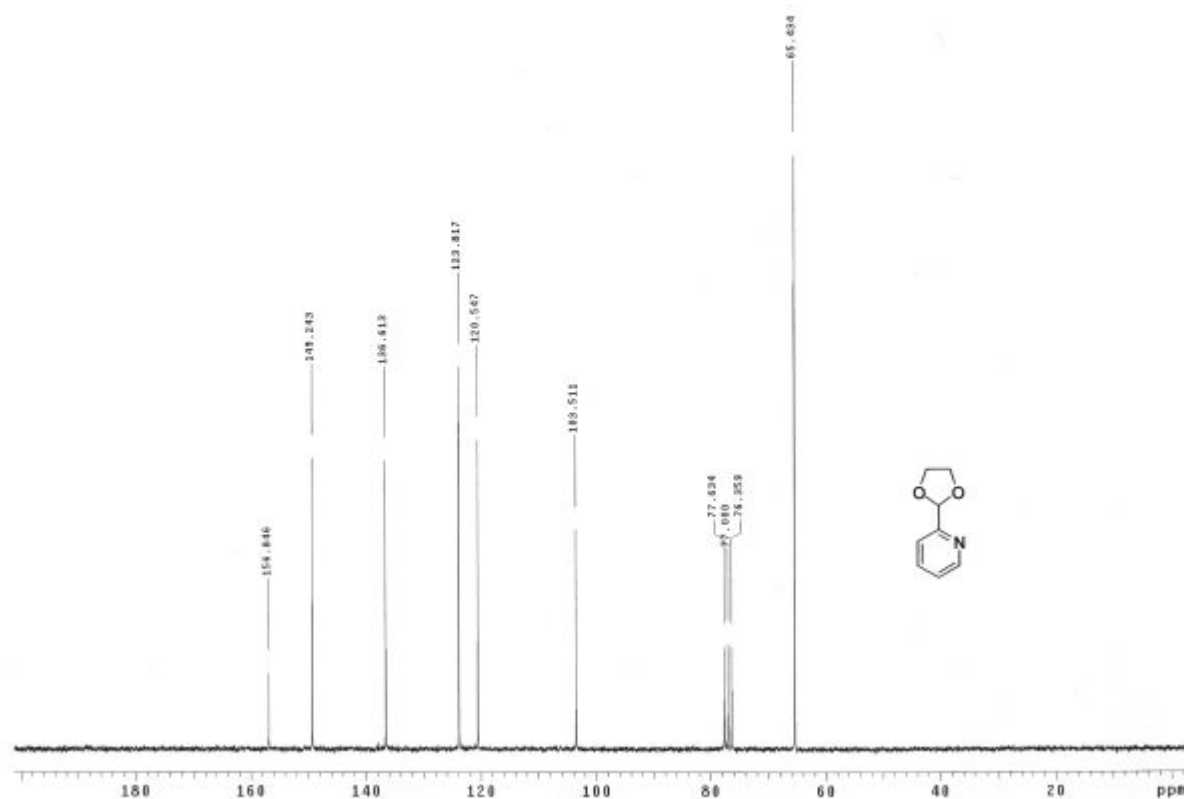
MB-1023aC
Pulse Sequence: zgpg30



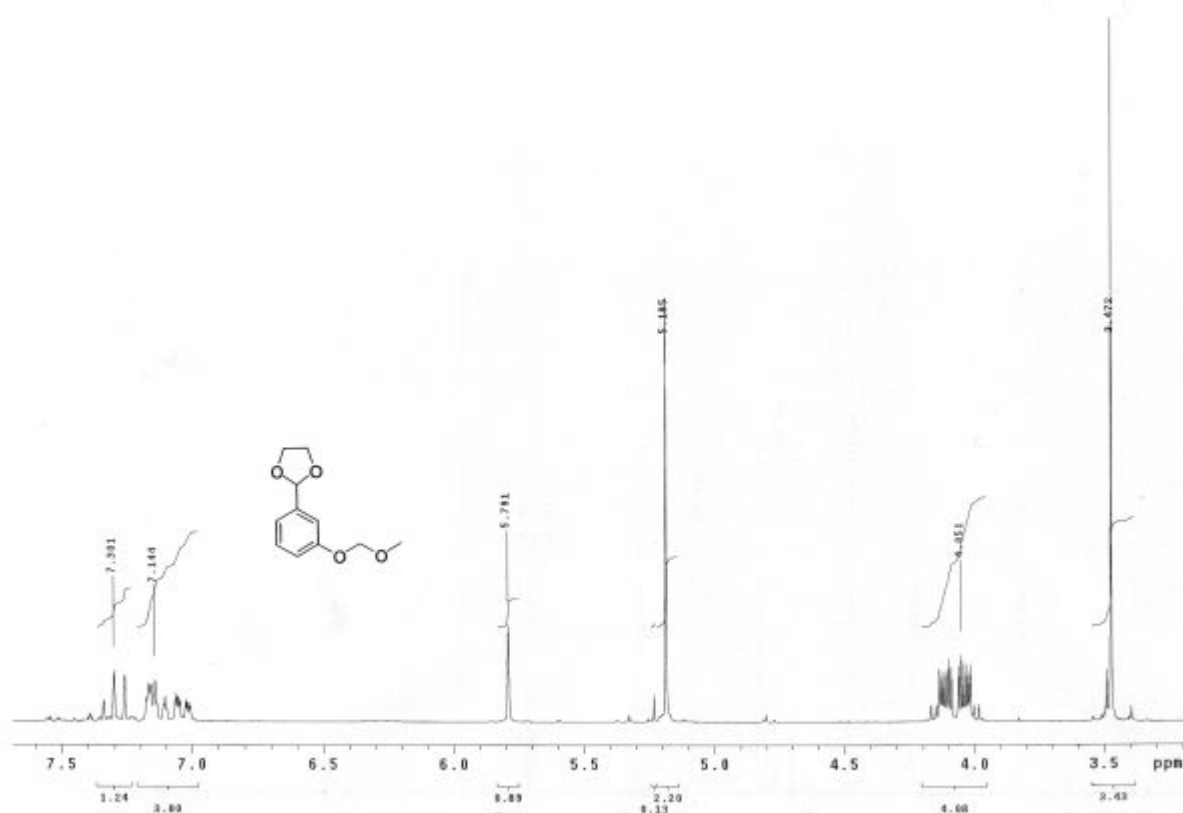
MS-1027MR
Pulse Sequence: zgpg1



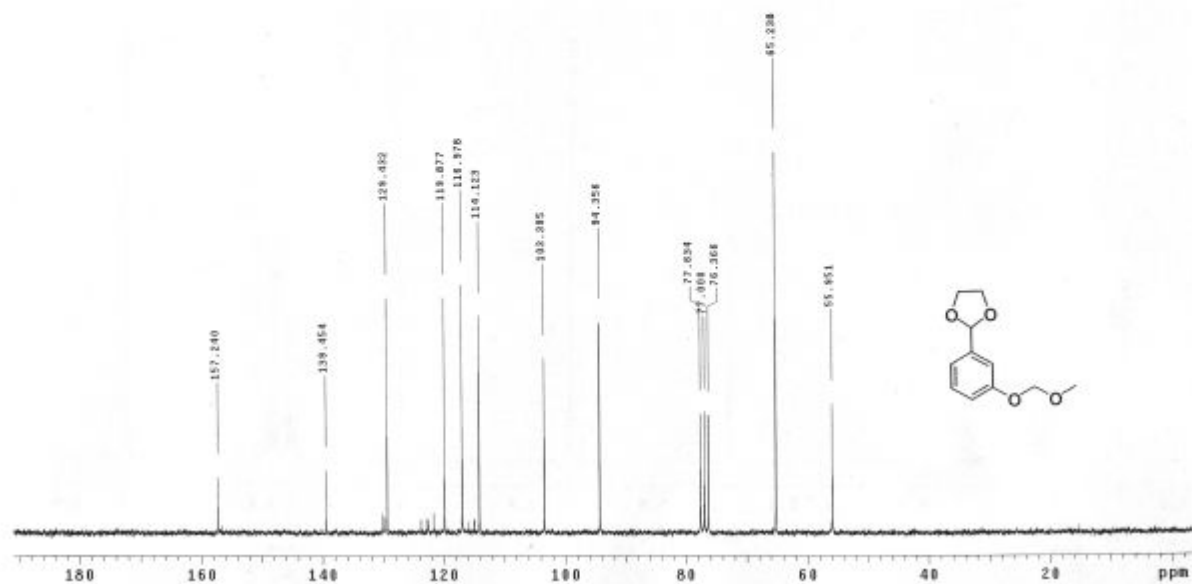
MS-1027KC
Pulse Sequence: zgpg1

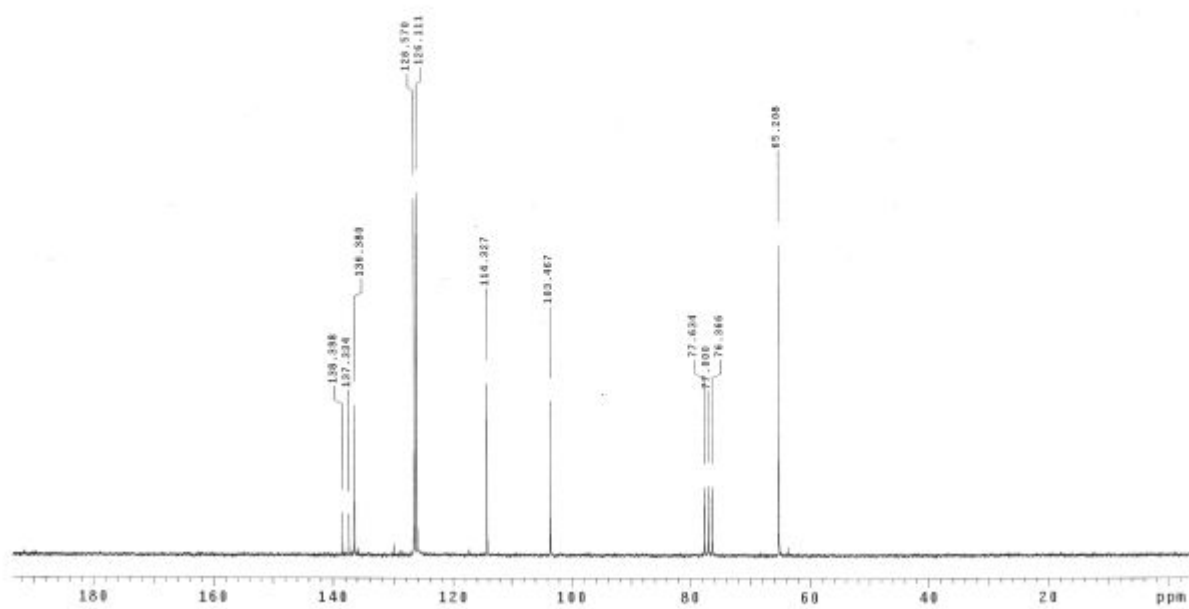
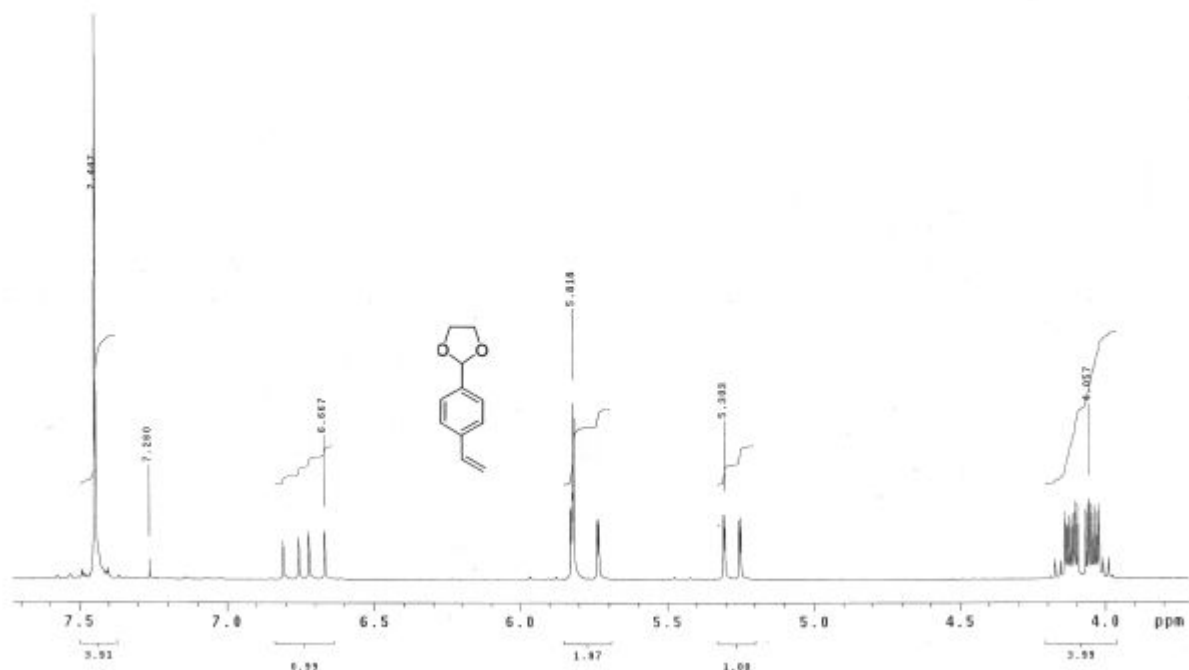


MS-1036v08
Pulse Sequence: zgpg30

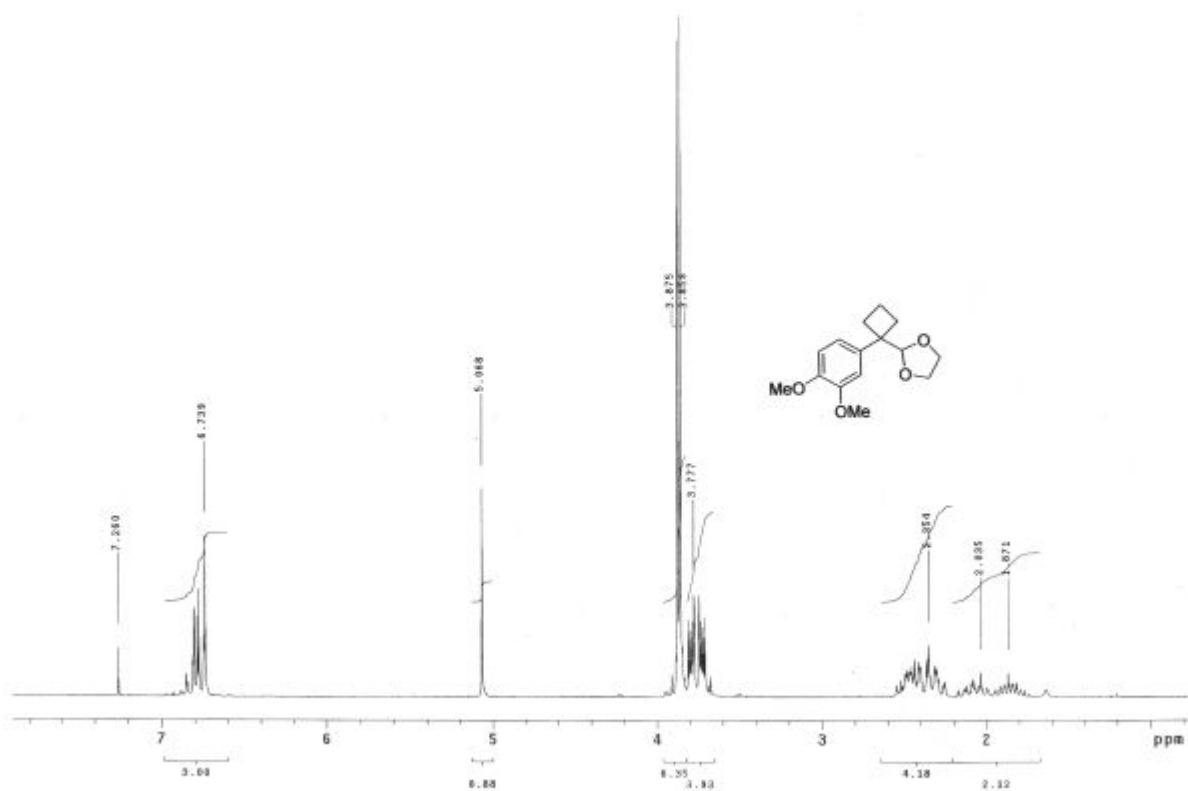


MS-1636v08
Pulse Sequence: zgpg30

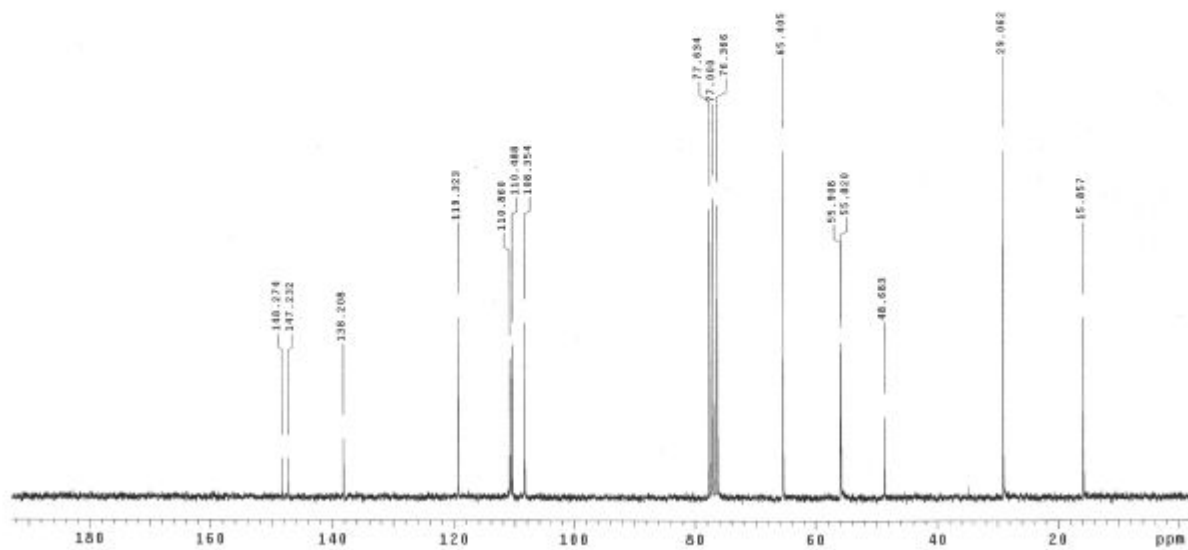




100 MHz, CDCl₃, TMS



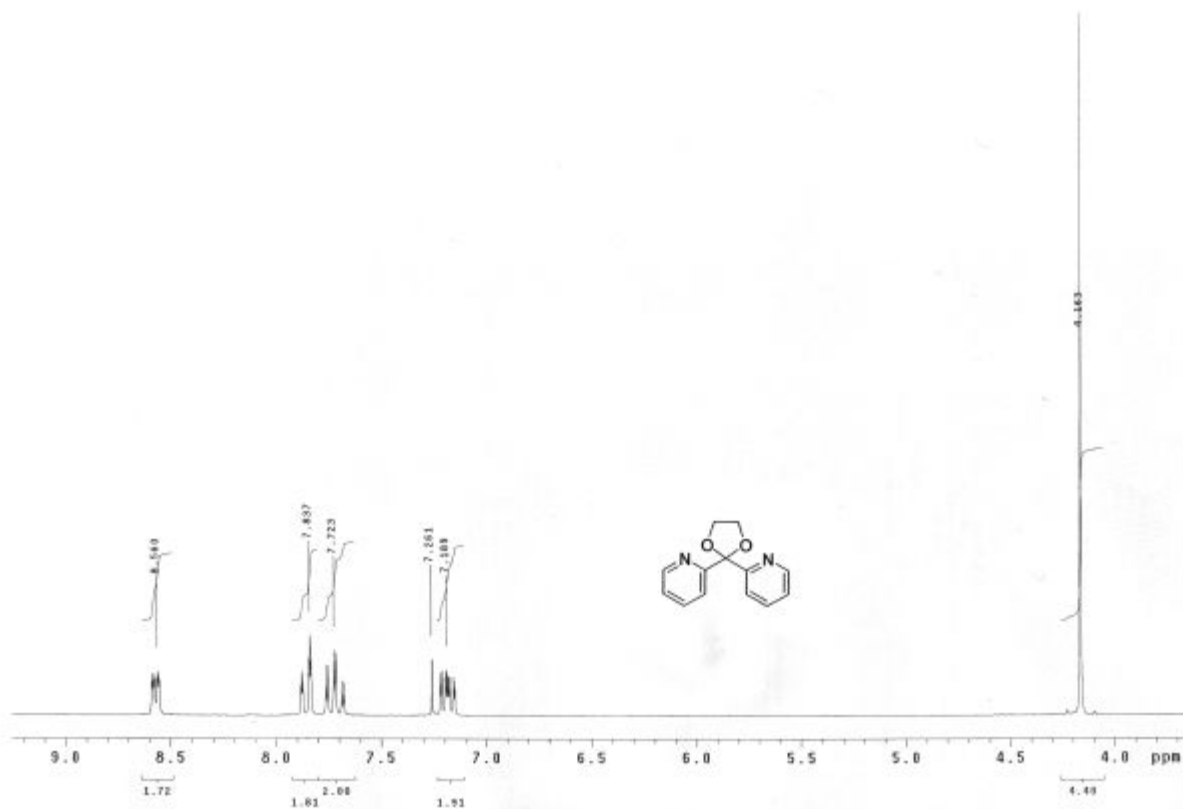
100 MHz, CDCl₃, TMS



Spectra of the described compounds (Table 2 in article)

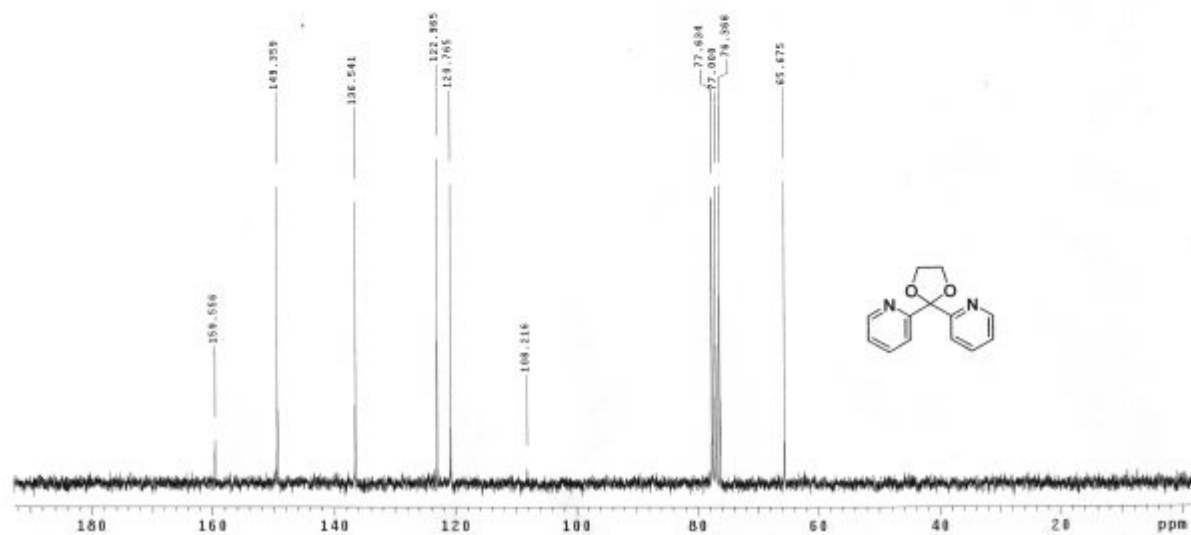
MS-1040aH

Pulse Sequence: s2pu1

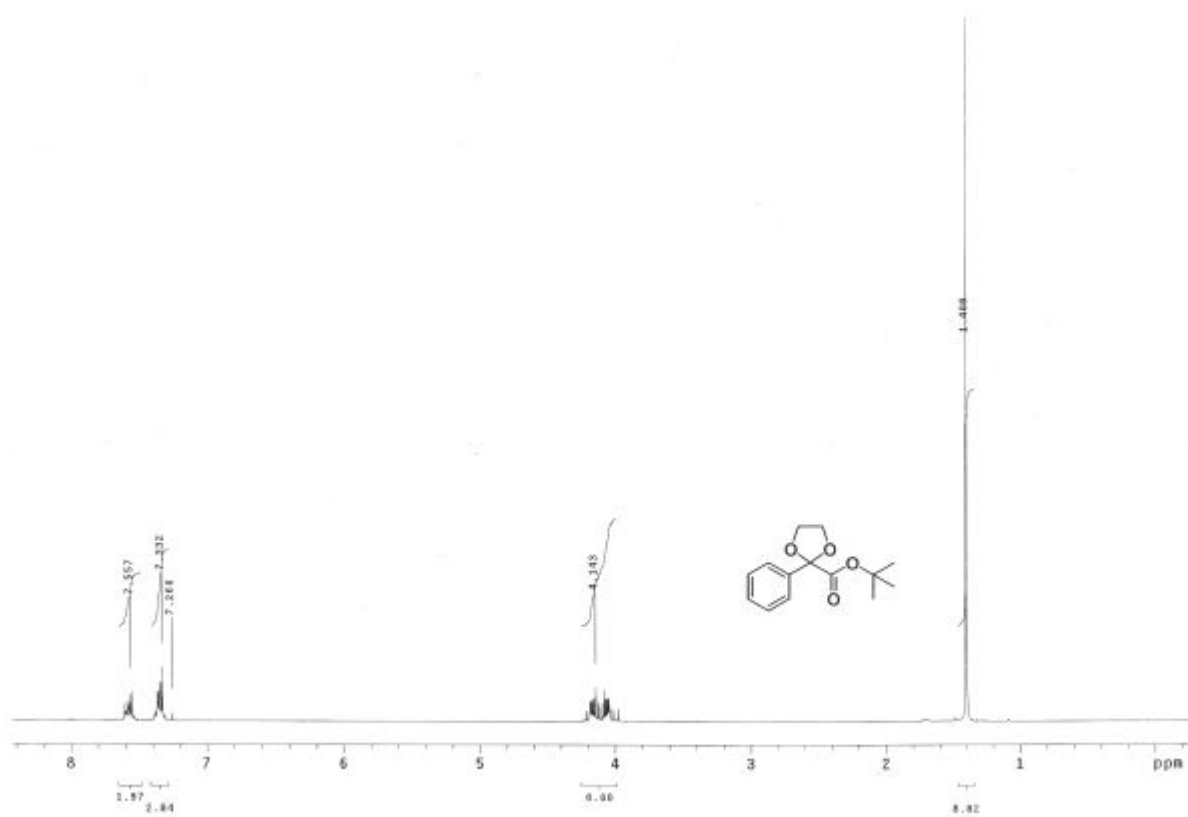


MS-1040xC

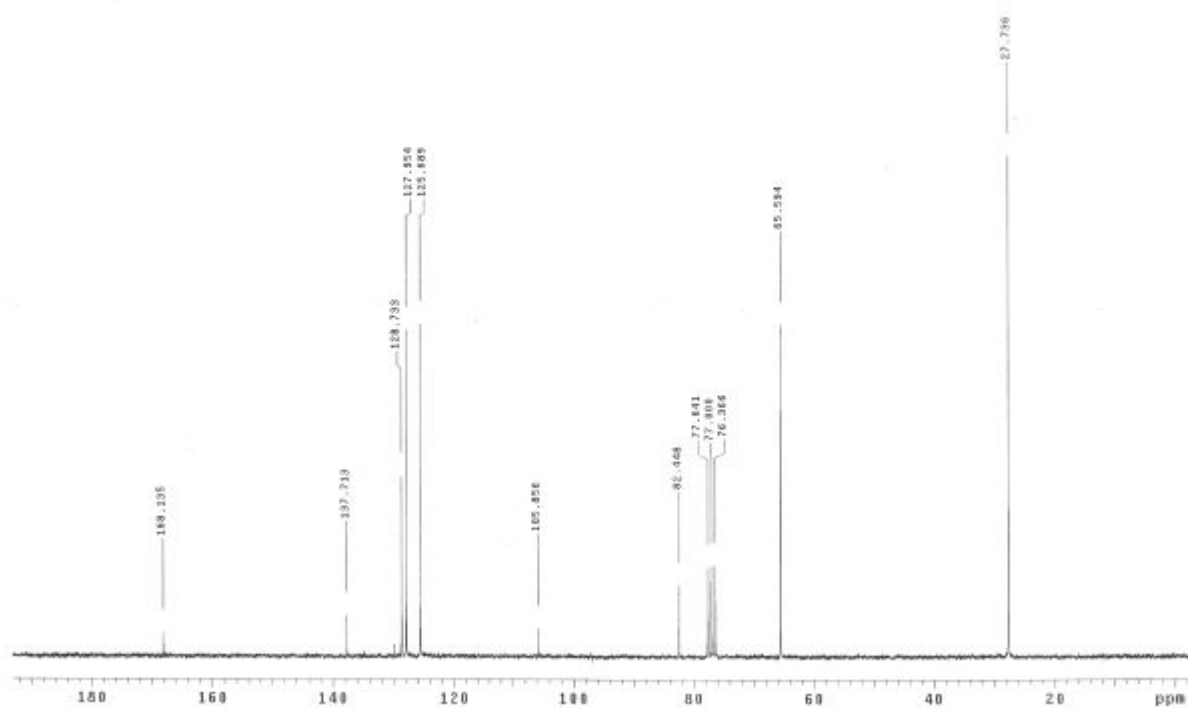
Pulse Sequence: s2pu1



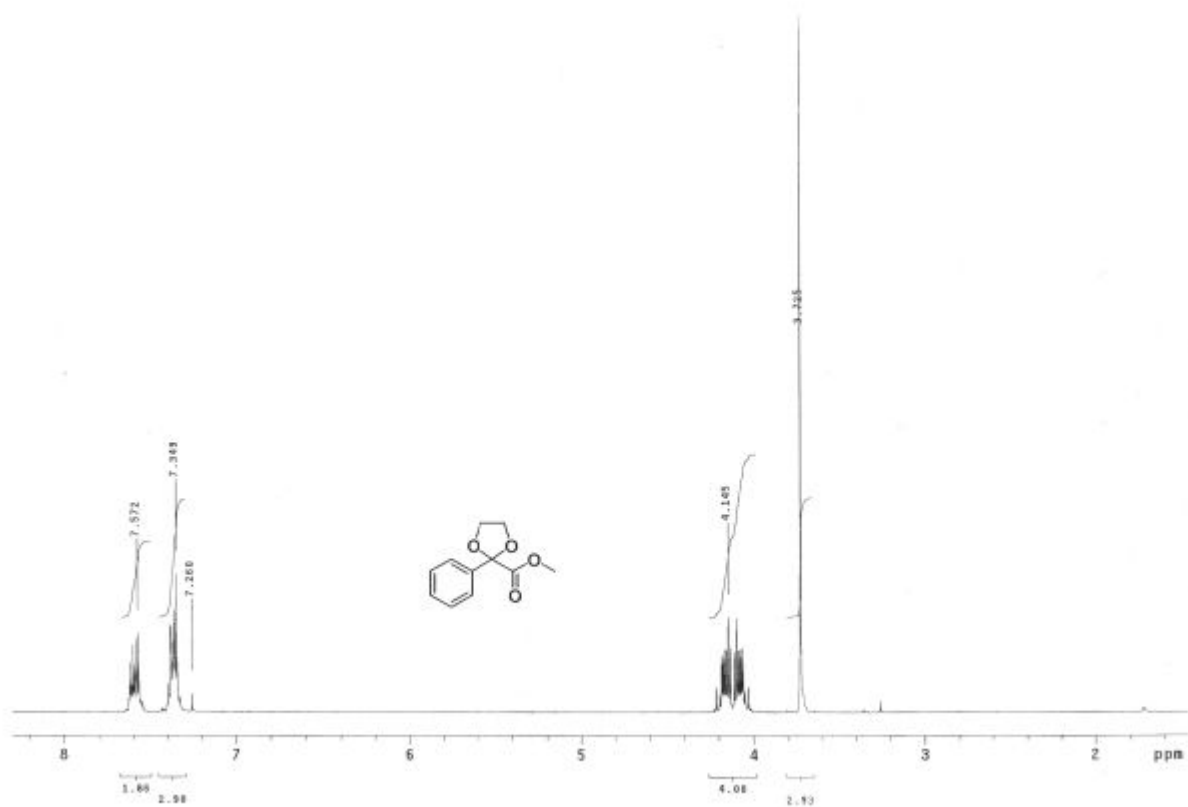
Pulse Sequence: zgpg30



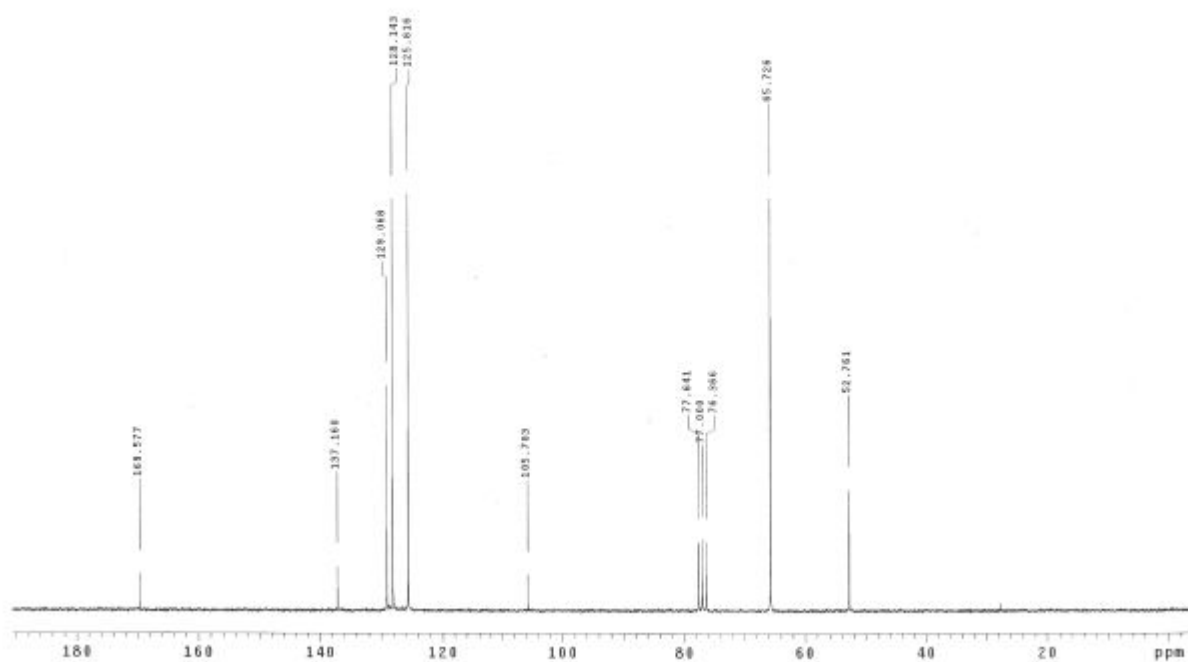
Pulse Sequence: zgpg30



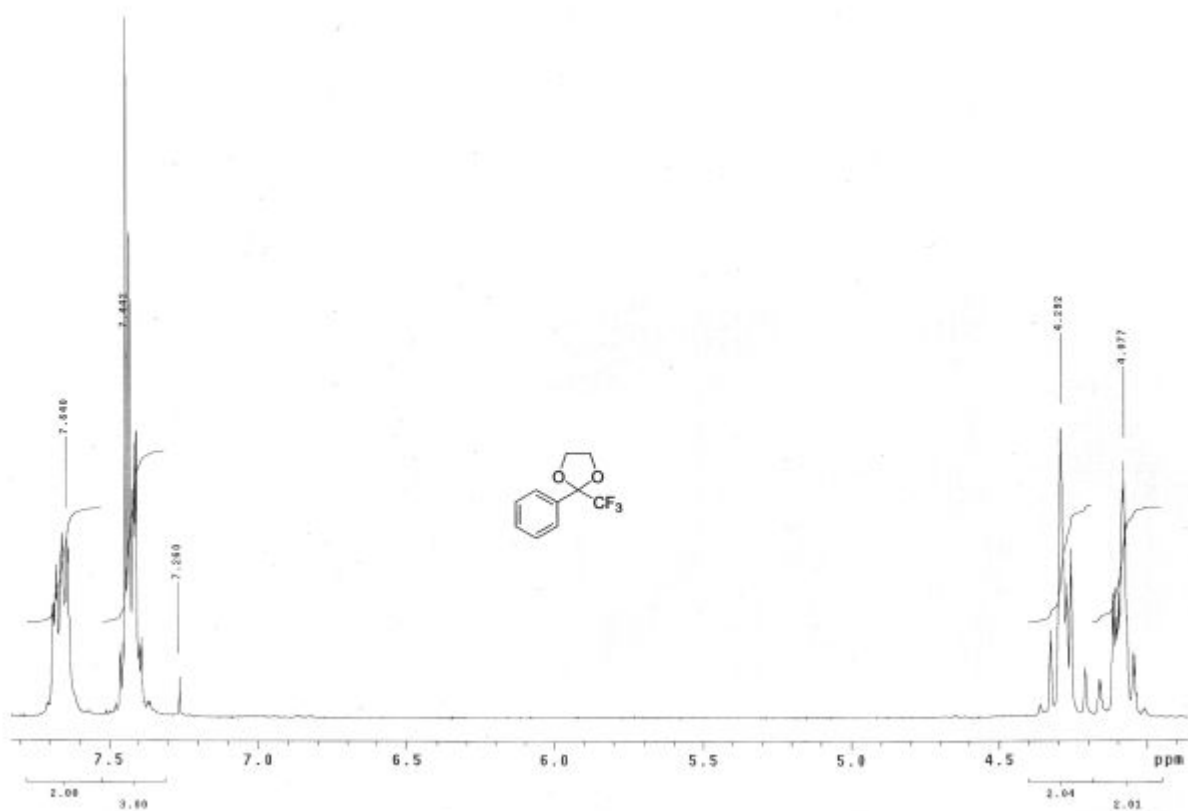
Pulse Sequence: zgpg30



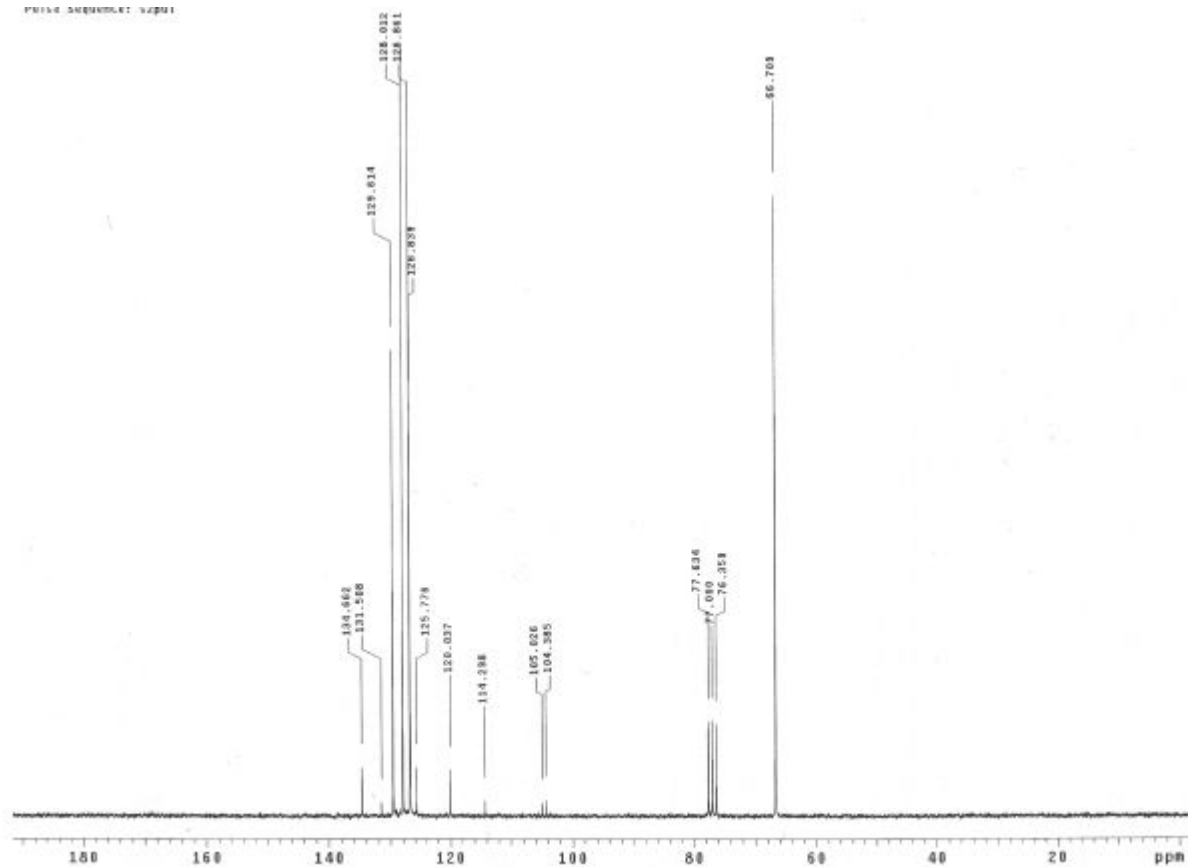
Pulse Sequence: zgpg30



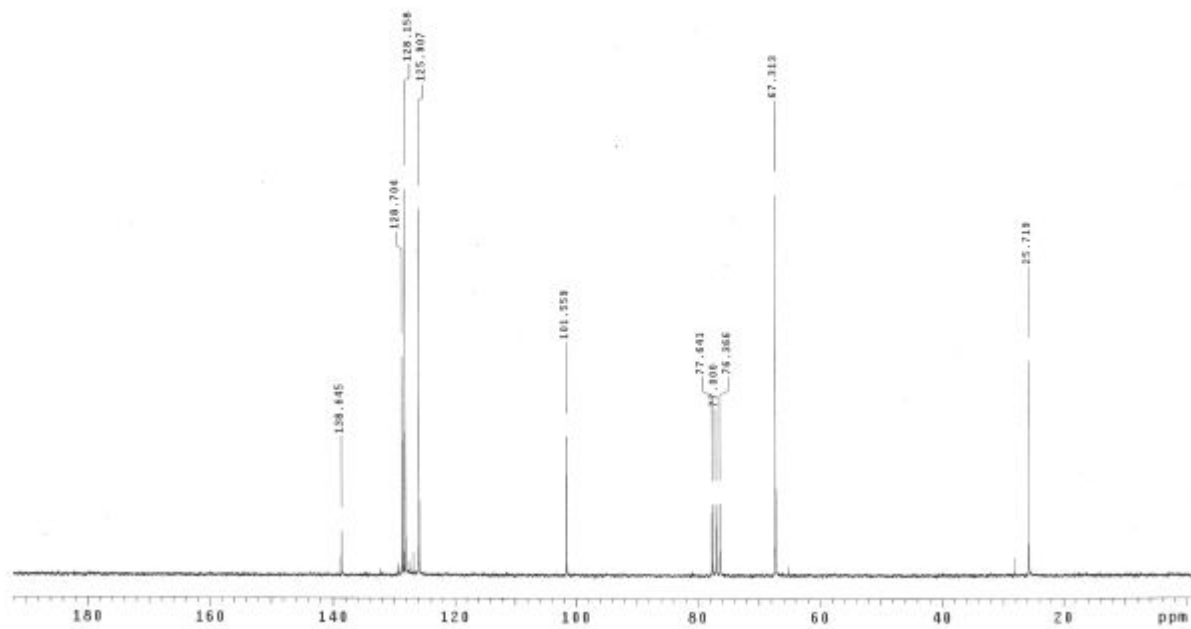
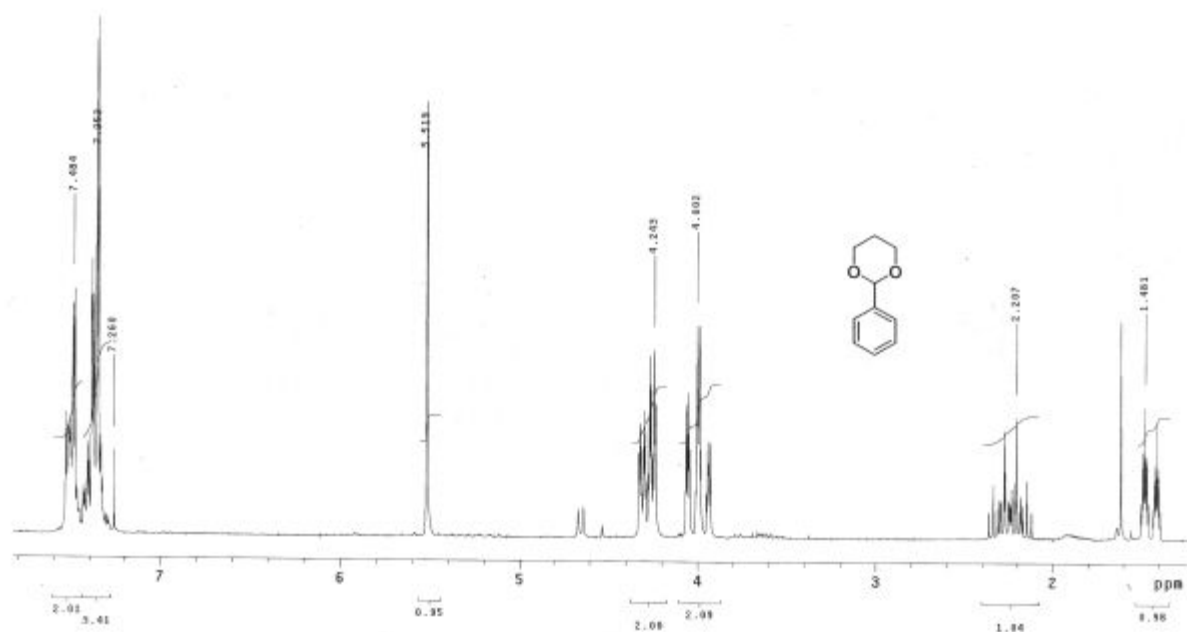
Pulse Sequence: zgpg30

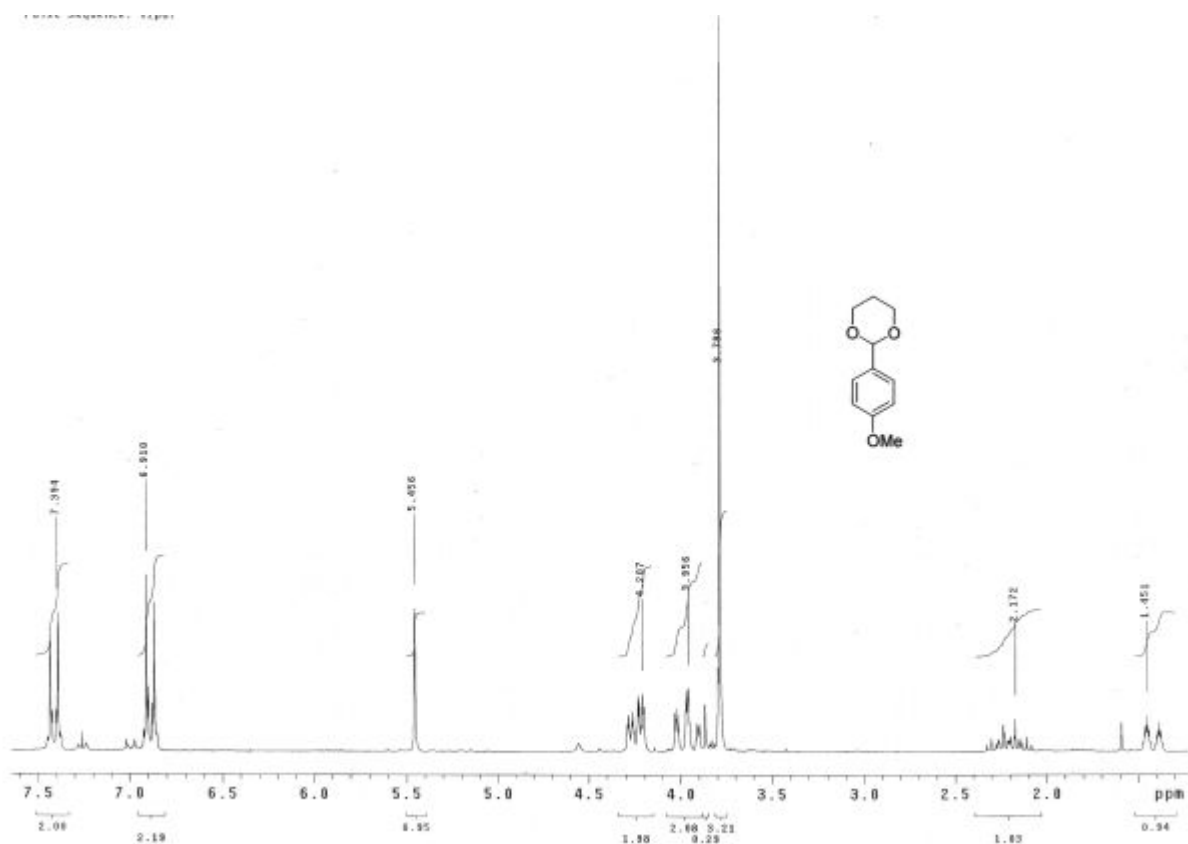


Pulse Sequence: zgpg30

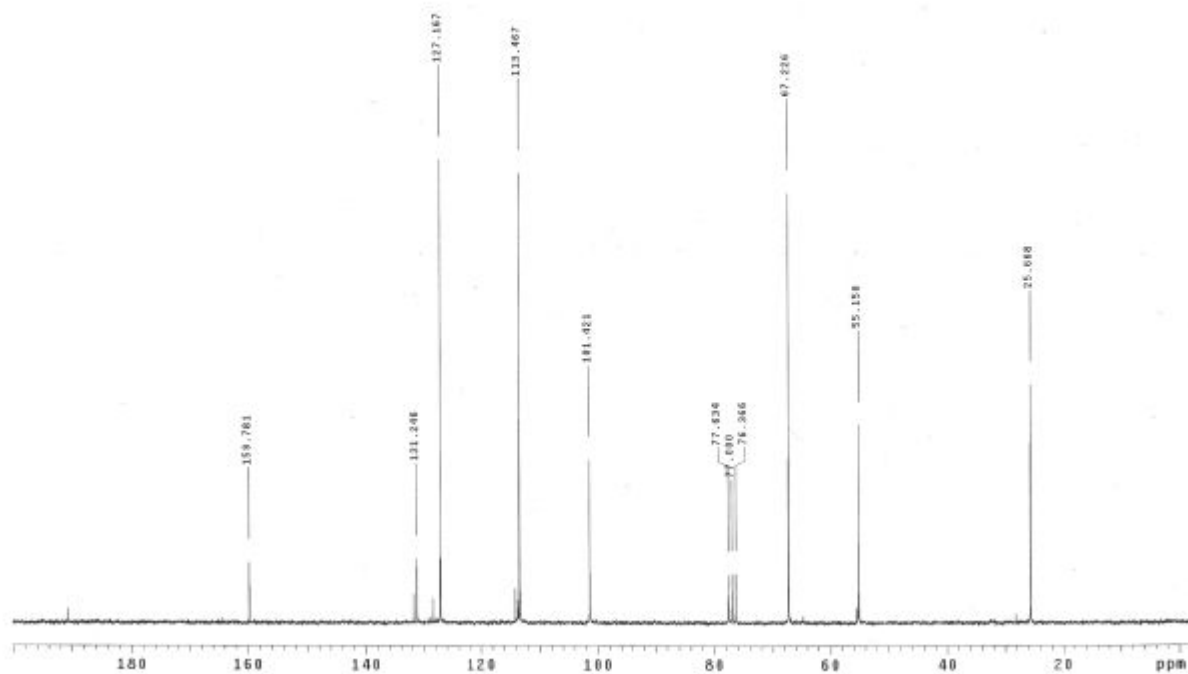


Spectra of the described compounds (Table 3 in article)

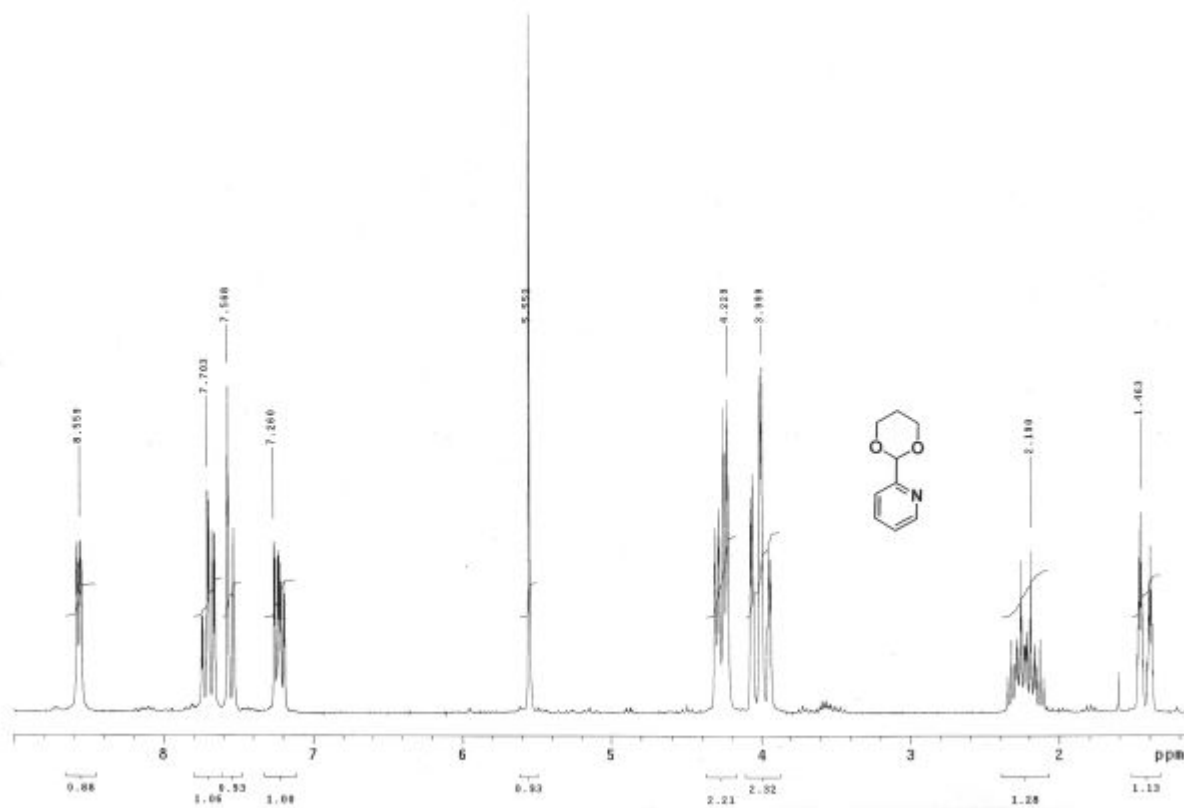




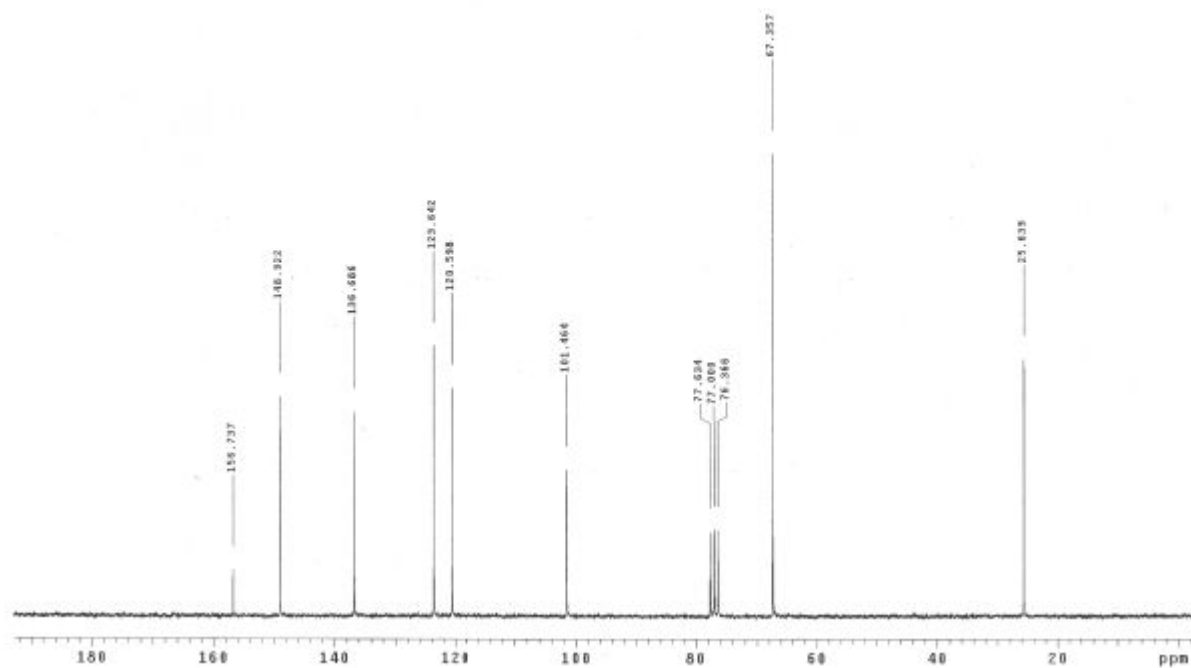
Pulse Sequence: szpsf

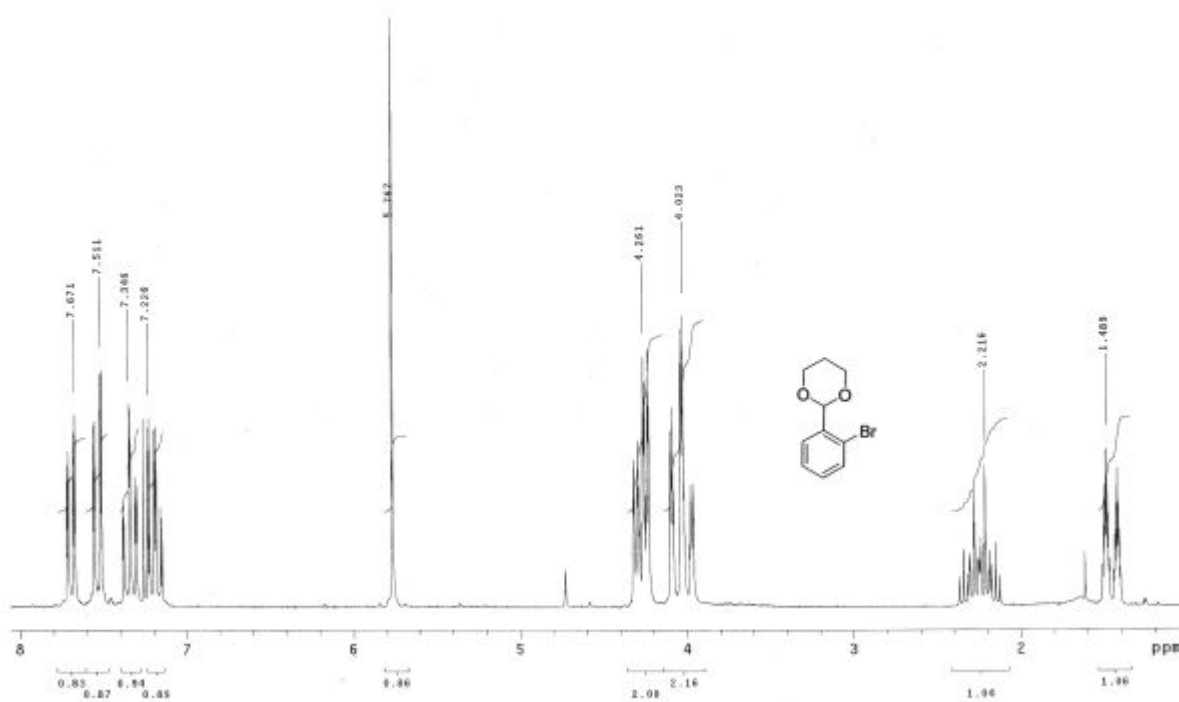


Pulse Sequence: s2pu1

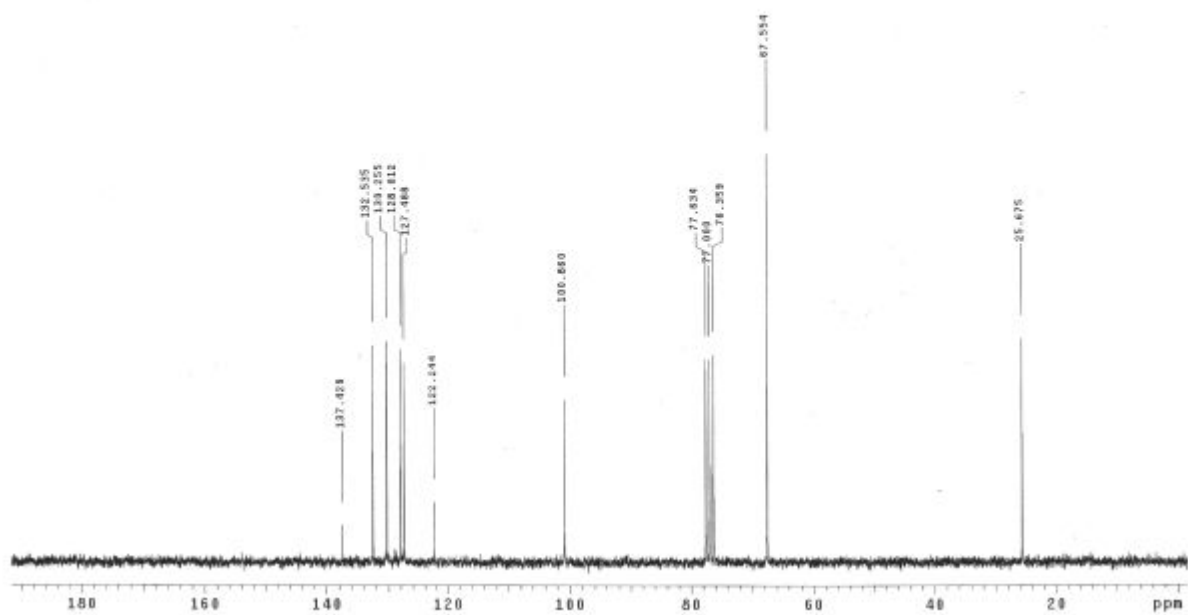


Pulse Sequence: s2pu1



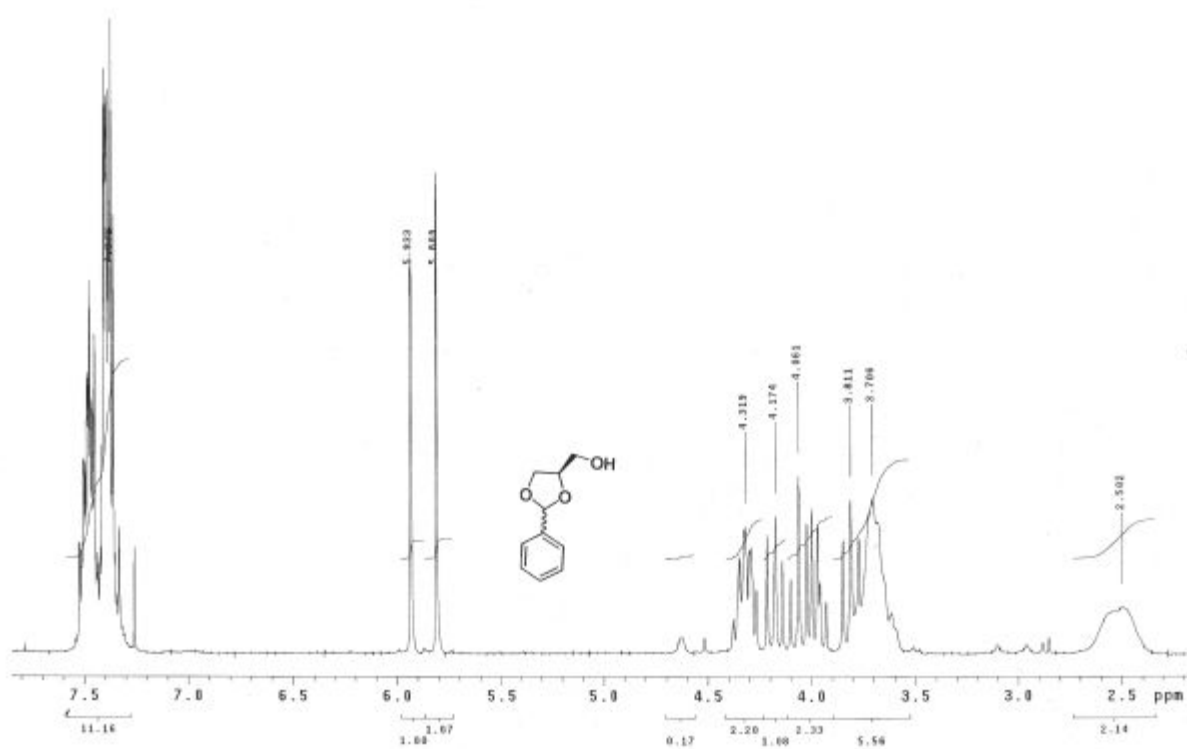


1H NMR spectrum

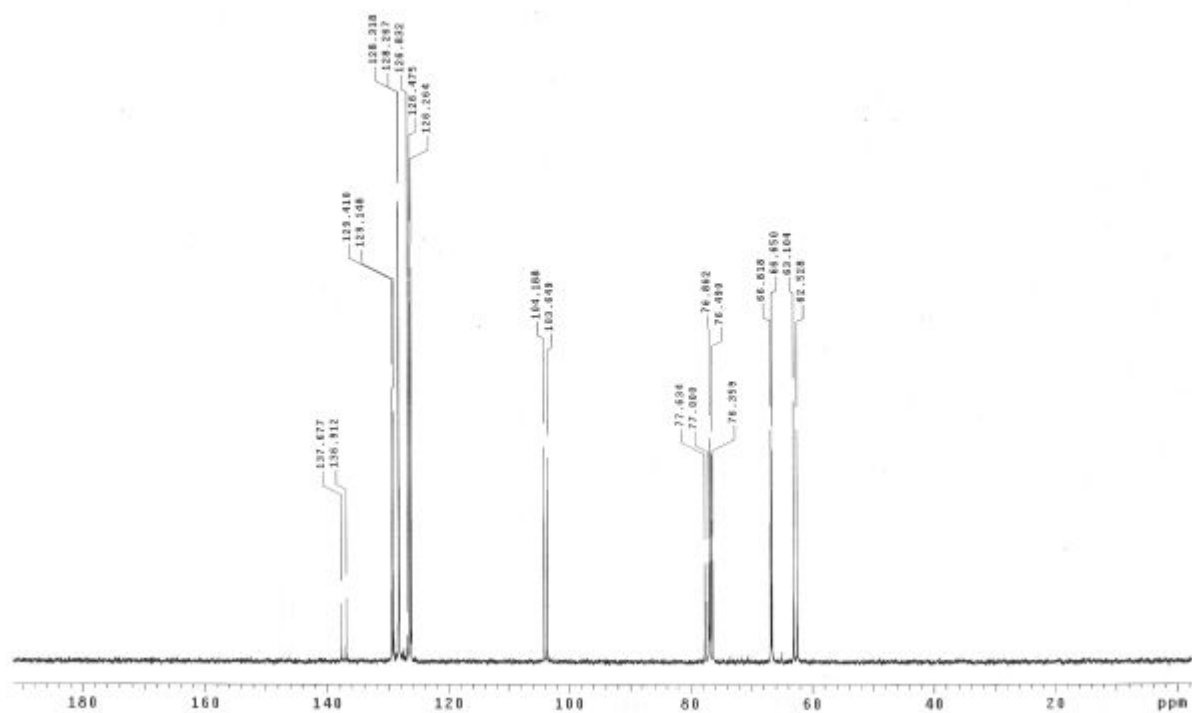


Spectra of the described compounds (Scheme 2 in article, mixture of diastereoisomers)

Pulse Sequence: zgpg30

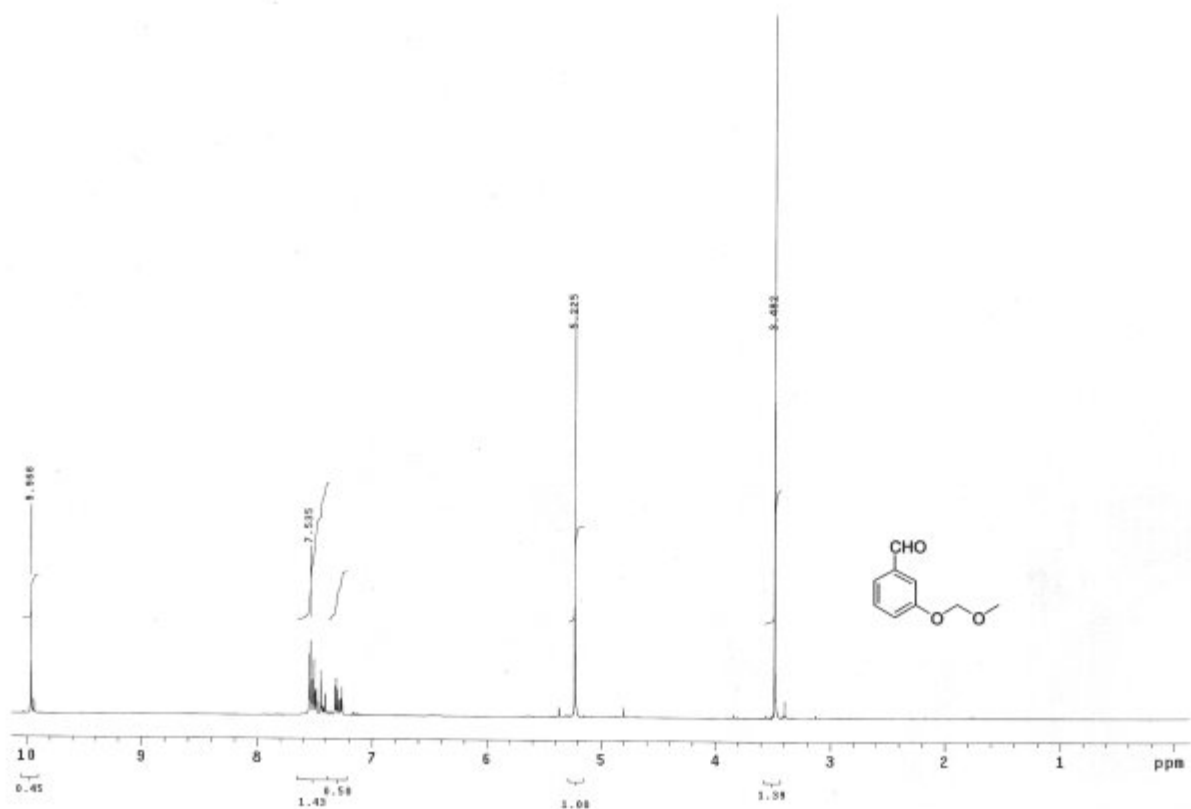


Pulse Sequence: zgpg30



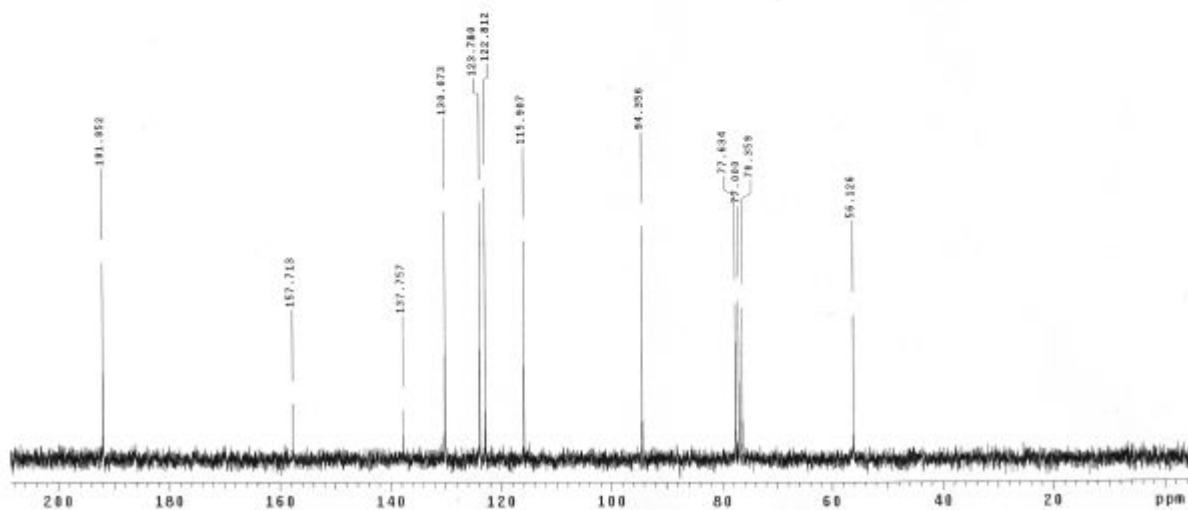
Spectra of the described compounds (aldehydes)

Pulse Sequence: zgpg1

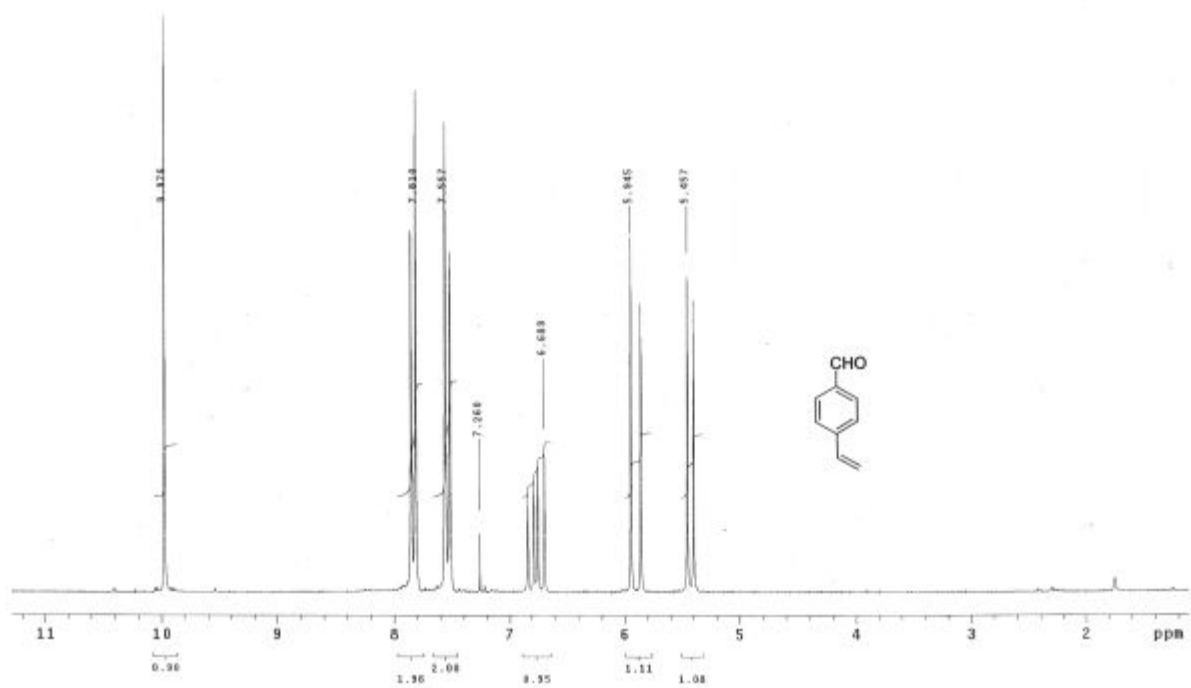


MS-1053HC

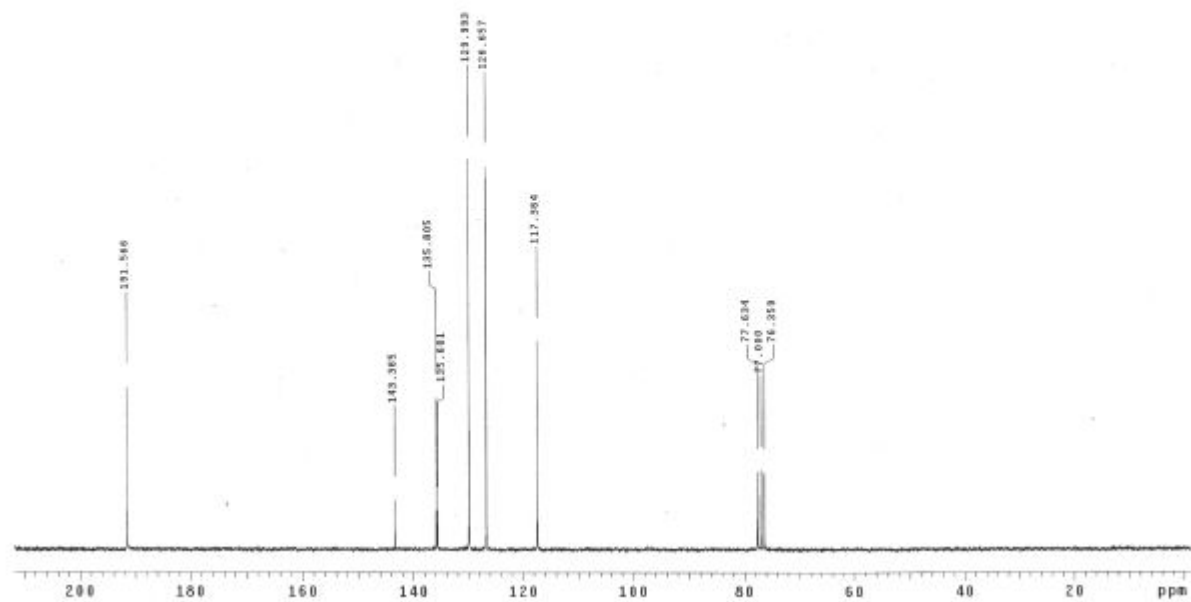
Pulse Sequence: zgpg1



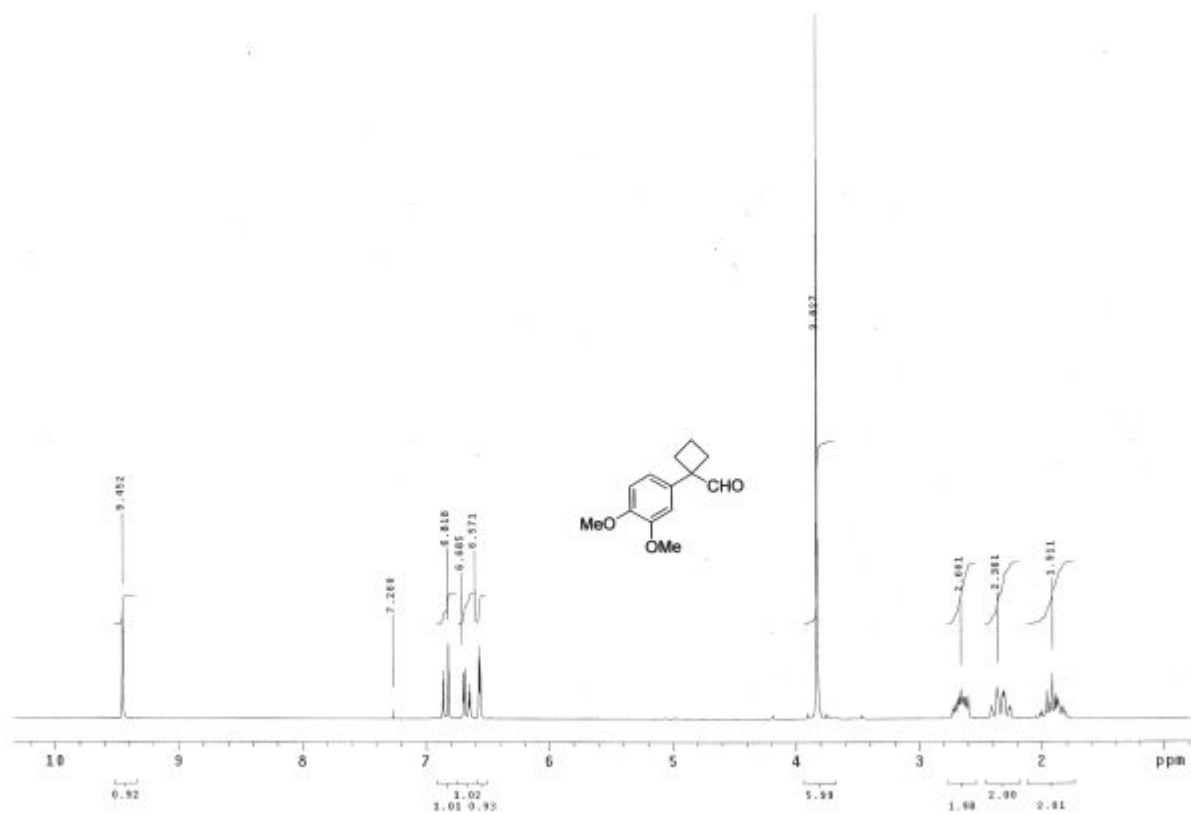
Pulse Sequence: szp01



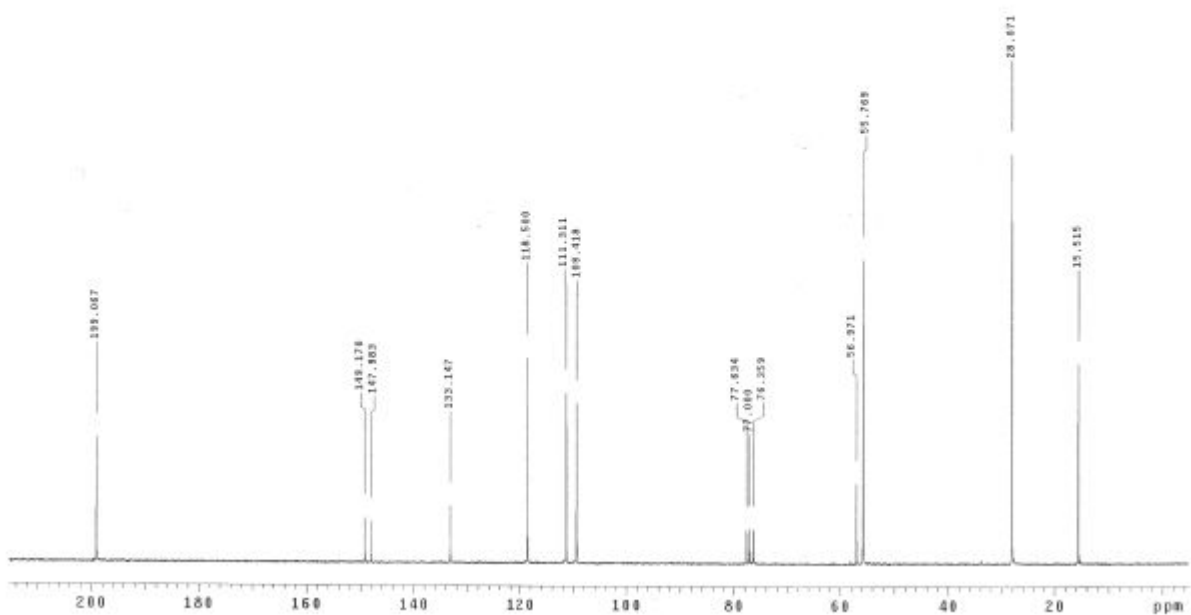
13C NMR Spectrum: szp01



Pulse Sequence: zgpg30

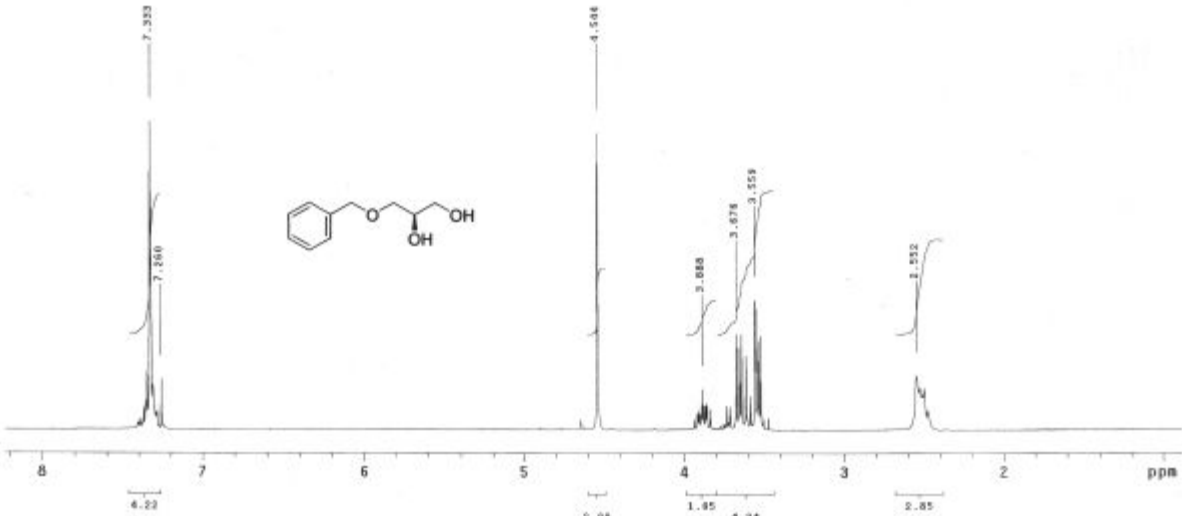


Pulse Sequence: zgpg30



Spectra of 1-O-benzylglycerol

Pulse Sequence: zgpg30



Pulse Sequence: zgpg30

