Supplementary Information

Mechanochemical synthesis, simultaneous double cycloaddition reactions of bisnitrones and potential anticancer activities of the bis cycloadducts

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1 General Methods

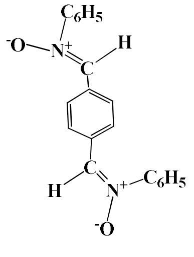
Unless otherwise stated, all reagents were obtained from commercial sources and used without further purification. Progress of all the reactions were monitored by TLC using 0.25 mm silica gel plates (Merck 60F$_{254}$, UV indicator). Column chromatography was performed with silica gel (E.Merck, Germany) with 60–200 mesh. All other reagents and solvents were purified before starting reactions or column chromatography.^{1}H NMR spectra were recorded on a Bruker DRX 300 (300 Hz)spectrometer at ambient temperature.^{13}C NMR spectra were recorded on a Bruker DRX 300 (75 Hz) spectrometer at ambient temperature. The coupling constants (J) are expressed in Hz. Infra-red spectra were recorded on a Perkin-Elmer RX 1-881 machine as a film or KBr pellets. Mass-spectrometry data was recorded using a Joel SX-102 (FAB).

The ball mill used was a Retsch MM500 mixer mill digital GmbH,42781Haan, Germany. Reactions were carried out using stainless steel jars from Retsch. Milling balls were purchased from Germany.

2 Experimental Procedures

2.1 General procedure 1–Mechanochemical synthesis of terepthalaldehyde derived bis nitrones

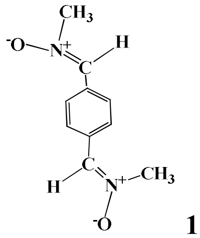
To a 25 mL stainless steel milling vessel (Retsch MM500 mixer mill digital GmbH,42781 Haan, Germany) was added 2 stainless steel balls, terepthalaldehyde (309mg, 5.3127 mmol),N-phenylhydroxylamine hydrochloride (500mg, 2 equivalent) and NaHCO3 (1 mmol). A stainless steel milling ball was added and the mixture milled at 60 Hz for 30 min. The formation of bisnitrone was monitored by TLC (Rf = 0.40).After the completion of reaction, CH2Cl2 was added. The mixture was then filtered on cotton to remove NaCl. The filtrate was evaporated under vacuum to afford the desired product terepthalaldehyde derived bisnitrone 1) as white crystals (90%; m.p: 1120C) without need for further purification. Same methodology was followed for the synthesis of other bisnitrones (R=C6H5). Both the bisnitrones were found to be stable and were reacted with various activated alkenes & alkynes in 1,3-dipolar cycloaddition reaction.



1a (*N*-phenyl terepthalaldehyde derived nitrone)

Spectroscopic data for nitrone **1a**(R = C_6H_5): UV λ_{max} 244 nm.IR (KBr): υ_{max} 3115 (m). 1640 (m), 1615 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.20 (s, 4H, aromatic carbons), 7.70-6.90 (m, 2x5H), 1.30 (s, 2x1H, -CH=N$^+$). ^{13}CNMR (75 MHz, $CDCl_3$): δ ppm 145.50 (2 x CH=N$^+$), 137.44, 137.30, 137.14, 136.97, 135.77, 135. 62 (aromatic carbons), 129.67, 129.52, 128.06 (phenyl carbons linking 2-C-atoms). FAB-MS (m/z): 316 (M^+), 239, 196, 77.

2.1

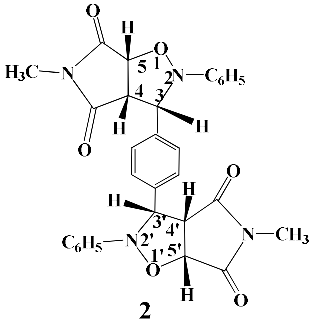


1a (*N*-methyl terepthalaldehyde derived nitrone)

Spectroscopic data for nitrone **1a** (R = CH_3): UV λ_{max} 238 nm.IR (KBr): υ_{max} 3096 (m). 1650 (m), 1625 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ ppm 6.90 (s, 4H, aromatic protons), 4.10 (s, 2x1H, -CH=N^+), 2.34 (s, 2x6H, N-CH_3). ^{13}CNMR (75 MHz, $CDCl_3$): δ ppm 142.30 (2 x CH=N^+),129.44, 129.25 (phenyl carbons), 24.46 (2xCH_3 carbons). FAB-MS (m/z): 192 (M^+), 134 (BP), 133.

2.2 General procedure II–Mechanochemical synthesis of bis(isoxazolidine) derivatives from terepthalaldehyde derived nitrones (Table 1; entry 1)

To a 25 mL stainless steel milling vessel containing terepthalaldehyde derived nitrone **1a** (R=C_6H_5; 1 equivalent) was added *N*-methylmaleimide (2 equivalent 500 mg; 1 mmol) and the mixture was milled at 60 Hz for 30 min. After the completion of reaction, as indicated by TLC (R_f= 0.66), CH_2Cl_2 was added and the mixture was filtered on cotton for the removal of NaCl. The filtrate was evaporated under vacuum to afford pure bisisoxazolidines **2** (Table **1**, entry **1**, 95%) as white crystals (MP: 152^0C). Same methodology was followed for other substrates depicted in Table **1**.



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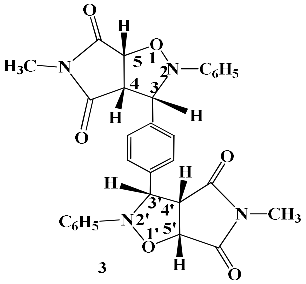
(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3'*S*, 3'a*S*, 6a*R*)--2,5-diphenyl-4,6-dioxo-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2', 5'-dimethyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*) dione 2

2 (entry 1, Table 1): White crystals, Yield 95%; R_f= 0.66; FT-IR (KBr): υ_{max}3006 (m), 1760 (s), 1670 (s), 1470 (m), 1230 (m), 784 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ ppm 7.88-7.50 (m, 2x5H), 7.20 (s, 4H, aromatic protons), 6.42 (d, *J* = 3.00 Hz, C_5H protons), 6.42 (d, *J* = 3.20 Hz, C_3H protons), 3.80 (s, 6H, 2xN-CH$_3$), 2.3 (dd, *J* = 3.00 Hz, 2x1H, C$_4$H protons). ^{13}C NMR (CDCl$_3$): δ ppm 176.70, 175.10 (carbonyl carbons), 135.77, 133.60, 133.42, 133.15, 133.00 (2xC$_6$H$_5$, aromatic carbons), 127.55, 127.14 (2x4 aromatic carbons), 73.54 (C$_5$, C$_{5'}$), 68.60 (C$_3$, C$_{3'}$), 55.34 (C$_4$, C$_{4'}$), 24.70, 24.52 (methyl carbons). FAB - MS (*m/z*):534 (M$^+$), 305, 229 (BP), 154, 90, 77.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3'*S*, 3'a*S*, 6a*R*)--2,5-diphenyl-4,6-dioxo-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2', 5'-dimethyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*) dione 3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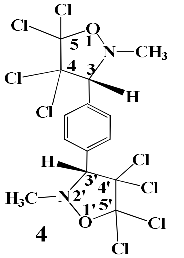
3. (entry 2, Table 1): White crystals, Yield 95%; R$_f$= 0.66;; FT-IR (KBr): υ$_{max}$3030 (m), 1765 (s), 1680 (s), 1474 (m), 1235 (m), 780 (s) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ ppm 7.88-7.50 (m, 2x5H), 7.20 (s, 4H, aromatic protons), 6.42 (d, *J* = 3.00 Hz, C$_5$H protons), 6.42 (d, *J* = 3.20 Hz, C$_3$H protons), 3.80 (s, 6H, 2xN-CH$_3$), 2.3 (dd, *J* = 3.00 Hz, 2x1H, C$_4$H protons). ^{13}C NMR (CDCl$_3$): δ ppm 173.50, 173.25 (carbonyl carbons), 134.60, 134.15, 133.40, 133.00, 132.80 (2xC$_6$H$_5$, aromatic carbons), 128.35, 128.40 (2x4 aromatic carbons), 75.20 (C$_5$, C$_{5'}$), 67.30 (C$_3$, C$_{3'}$), 57.30 (C$_4$, C$_{4'}$), 26.55 (methyl carbons). FAB-MS (m/z) : 534 (M$^+$), 305, 229 (BP), 154, 90, 77.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3'*S*, 3'a*S*, 6a*R*)-2,5-dimethyl-3,4-dichloro-6-dioxo-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2',5'-dimethyl-3',4'-dichloro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*) dione 4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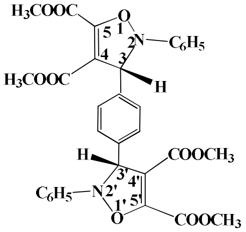
(entry **3**, Table **1**):White solid, Yield 92%; R$_f$= 0.72; FT-IR (KBr): υ$_{max}$3026 (m), 1768 (s), 1677 (s), 1455 (m), 1250 (m), 778 (s) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ ppm 7.58-7.30 (2xdd,4H, aromatic protons), 3.80 (2x3H, N-CH$_3$), 1.80 (s, 1H, C$_3$H), 1.40 (s,1H, C$_{3'}$H). ^{13}C NMR (CDCl$_3$): δ ppm 125.76, 125.40 (2x4 aromatic carbons), 72.43 (C$_5$, C$_{5'}$), 67.30 (C$_3$, C$_{3'}$), 54.68 (C$_4$, C$_{4'}$), 27.26 (CH$_3$ carbons). FAB - MS (*m/z*):528 (M$^+$), 300, 228, 154.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3’*S*,3’a*S*,6a*R*)-(S)-2-phenyl-2,3-dihydroisoxazole-4,5-methyldicarboxylate-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2-2’-diphenyl-4’5’-dimethyl-dicarboxylate-2*H*-pyrrolo[3,4-*d*]isoxazole) 5



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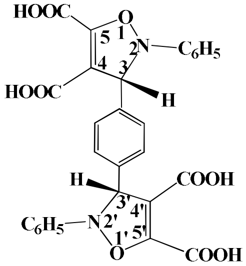
5. (entry **4**, Table **1**): White gummy mass, Yield 90%; R_f= 0.68; FT-IR (KBr): υ_{max}3036 (m), 1770 (s), 1685 (s), 1440 (m), 1235 (m), 788 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ ppm 7.95-7.50 (m, 2x5H), 7.20 (dd, 2x2H, 4H, aromatic protons), 3.35 (br, s, 12H, $COOCH_3$ protons), 2.80 (s, H, C_3H proton), 1.30 (s,1H,$C_{3'}H$). ^{13}C NMR ($CDCl_3$): δ ppm 168.70, 168.54 (carbonyl carbons), 135.45, 133.20, 133.13, 133.00, 132.66 (2xC_6H_5, aromatic carbons), 128.48, 128.34 (4 aromatic carbons), 74.40 (C_5, $C_{5'}$), 65.48 (C_3, $C_{3'}$), 53.90 (C_4, $C_{4'}$), 25.40 (CH_3 carbons of $COOCH_3$). FAB - MS (*m/z*):600 (M$^+$), 446, 338, 262 (BP), , 154, 77.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3’*S*,3’a*S*,6a*R*)-(S)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylic acid-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2’-diphenyl-4’5’-dicarboxylic acid-2*H*-pyrrolo[3,4-*d*]isoxazole) 6



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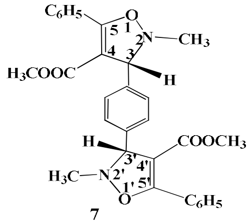
(entry **5**, Table **1**):White viscous liquid, Yield 90%; R_f= 0.72; FT-IR (KBr): υ_{max}3020 (m), 1766 (s), 1675 (s), 1450 (m), 1260 (m), 776 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ ppm 10.10 (s, 4x1H, COOH protons), 7.90 (dd, 2x2H, 4H0, 7.70-7.45 (m,2x5H), 3.28 (s, 1H, C_3H), 2.70 (s, 1H, $C_{3'}H$). ^{13}C NMR ($CDCl_3$): δ ppm 167.55, 167.43 (carbonyl carbons), 137.55, 137.40, 137.32, 137.00, 136.76 (2xC_6H_5, aromatic carbons), 126.30, 126.18 (4 aromatic carbons), 73.65 (C_5, $C_{5'}$), 64.80 (C_3, $C_{3'}$), 52.90 (C_4, $C_{4'}$), 22.17 (C_3 & $C_{3'}$carbons). FAB - MS (*m/z*):544 (M$^+$), 390, 310 (BP), 154.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3'*S*,3'a*S*,6a*R*)-(S)-2-methyl-2,3-dihydroisoxazole-4,5-phenyl,methyldicarboxylate-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2'-methyl-4'5'- phenyl, methyl dicarboxylate 2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl) 7



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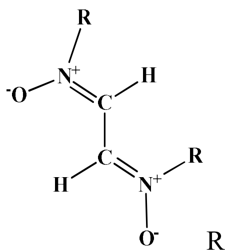
7. (entry **6**, Table **1**):White gummy liquid, Yield 90%; R_f= 0.70; FT-IR (KBr): υ_{max}3010 (m), 1760 (s), 1680 (s), 1440 (m), 1255 (m), 788 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ ppm 7.90 (dd, 2x2H, 4H), 7.70-7.45 (m, 2x5H), 3.35 (s, 6H, $2xCOOCH_3$), 3.20 (s, 2x1H, C_3H & $C_{3'}$H),, 2.70 (s, 6H, N-CH_3 protons). ^{13}C NMR ($CDCl_3$): δ ppm 169.55, 168.43 (carbonyl carbons), 137.55, 137.40, 137.32, 137.00, 136.76 ($2xC_6H_5$, aromatic carbons), 126.30, 126.18 (4 aromatic carbons), 73.65 (C_5, $C_{5'}$), 64.80 (C_3, $C_{3'}$), 52.90 (C_4, $C_{4'}$), 37.80 (s, 2x3H, $COOCH_3$), 30.15 (s, 6H, N-CH3 protons),22.17 (C_3 & $C_{3'}$carbons). FAB - MS (*m/z*): 512 (M^+), 358, 294 (BP), 218, 154.

General procedure II–Mechanochemical synthesis of glyoxal derived nitrones

To a 25 mL stainless steel milling vessel (Retsch MM500 mixer mill digital GmbH,42781 Haan, Germany) was added 2 stainless steel balls, glyoxal (220mg, 3.246mmole), *N*-substitutedhydroxylamines hydrochloride (500mg, 2 equivalent) and $NaHCO_3$ (1 mmol). A stainless steel milling ball was added and the mixture milled at 30 Hz for 40 min. The formation of bisnitrone was monitored by TLC (R_f = 0.36).After the completion of reaction, CH_2Cl_2 was added. The mixture was then filtered on cotton to remove NaCl. The filtrate was evaporated under vacuum to afford the desired product bisnitrone as white gummy mass (86%). The bisnitrone was found to be unstable and decomposes at room temperature if kept for more than 48 hours. Therefore, cycloadditions were performed without further delay once the bisnitrone is isolated. Same methodology was followed for the synthesis of other bisnitrones (R = CH_3; C_6H_5 ; $CH_2C_6H_5$).

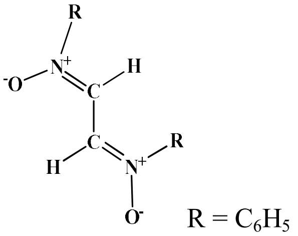
***N*-methyl-bis(nitrone) 1b**



R = CH_3

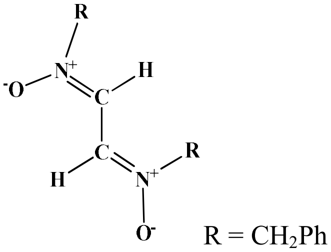
Spectroscopic data for nitrone **1b** (R = CH_3):UV λ_{max} 233 nm.IR (KBr): υ_{max} 1635 (m), 1610 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$):δ ppm 3.36 (d, 1H, *J* = 3.00 Hz, -CH=N^+), 3.00 (s, 6H, $2xCH_3$, N^+-CH_3), 2.84(d, J = 2.20 Hz, -CH=N$^+$), ^{13}CNMR (75 MHz, $CDCl_3$):δ ppm 141.60 (CH=N$^+$), 140.94 (CH=N$^+$), 24.74, 24.70 (N$^+$-CH_3).

***N*-phenyl-bis(nitrone) 1b**



Spectroscopic data for nitrone **1b** (R = C_6H_5):UV λ_{max} 242 nm.IR (KBr): υ_{max} 3110 (m). 1630 (m), 1610 (s) cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$):δ ppm 7.90-7.25 (m, 2x5H), 6.58 (d, 1H, J = 3.10 Hz, -CH=N$^+$), 6.48(d, J = 2.20 Hz, -CH=N$^+$).^{13}CNMR (75 MHz, $CDCl_3$):δ ppm 148.27 (CH=N$^+$), 131.48 (CH=N$^+$), 130.44, 130.24, 129.58, 129.30, 128.36 (2xaromatic carbons).

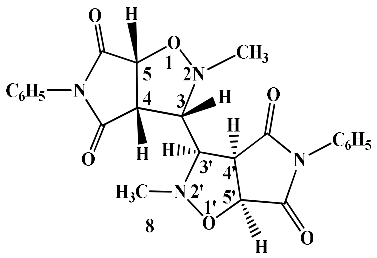
***N*-benzyl-bis(nitrone) 1b**



Spectroscopic data for nitrone **1b** (R = $CH_2C_6H_5$): UV λ_{max} 246 nm.IR (KBr): υ_{max} 3113 (m). 1615 (m), 1625 (s) cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$):δ ppm 7.65-7.50 (m, 2x5H), 6.14 (d, 1H, J = 4.30 Hz, -CH=N$^+$), 6.12(d, J = 4.70 Hz, -CH=N$^+$), 2.54 (s, 2x2H, CH_2 protons). ^{13}CNMR (75 MHz, $CDCl_3$):δ ppm 140.60 (CH=N$^+$), 139.30 (CH=N$^+$), 131.75, 130.42, 128.50, 128.22, 127.16 (2xaromatic carbons).

General procedure II–Mechanochemical synthesis of bis(isoxazolidine & isoxazoline) derivatives from glyoxal derived nitrones (Table 2; entry 1)

To a 25 mL stainless steel milling vessel containing glyoxal derived nitrone **1a** (R=CH_3; 1 equivalent) was added *N*-methylmaleimide (2 equivalent 500 mg) and the mixture was milled at 40 Hz for 40 min. After the completion of reaction, as indicated by TLC (R_f= 0.68), CH_2Cl_2 was added and the mixture was filtered on cotton for the removal of NaCl. The filtrate was evaporated under vacuum to afford pure bisisoxazolidines **8** (Table **2**, entry **1**, 94%) as yellowish white crystals. Same methodology was followed for other substrates depicted in Table **2**.



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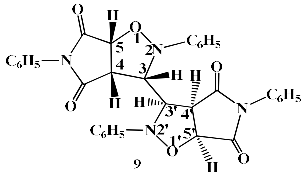
(*3R*, 3a*R*, 6a*S*)-dihydro-3-(3'*S*, 3'a*S*, 6a*R*)-hexahydro-2-methyl-5-phenyl-4,6-dioxo-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2'-methyl-5'-phenyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*) dione 8 (entry 1, Table 2): White crystals, Yield 94%; R_f= 0.68; FT-IR (KBr): υ_{max}2820 (m), 1760 (s), 1675 (s), 1465 (m), 1230 (m), 1125 (s) cm^{-1}. ^{1}H NMR (CDCl$_3$): δ ppm 7.40-7.18 (m, 2x5H), 3.26 (s, 6H, 2xN-CH$_3$), 2.20 (dd, *J* = 2.10, 2.10 Hz, C$_4$H & C$_{4'}$H), 1.90 (d, *J* = 2 Hz, 2xC$_5$H & C$_{5'}$H), 1.66 (dd, *J* = 2.00, 2.00 Hz, C$_3$H & C$_{3'}$H)). ^{13}C NMR (CDCl$_3$): δ ppm 174.78, 173.12 (carbonyl carbons), 75.80 (C$_5$, C$_{5'}$), 69.94 (C$_3$, C$_{3'}$), 56.77 (C$_4$, C$_{4'}$), 26.63, 26.58 (methyl carbons). FAB - MS (*m/z*): 462 (M$^+$), 231(BP), 154, 77.

(*3R*, 3a*R*, 6a*S*)-dihydro-3-((3'*S*, 3'a*S*, 6a*R*)-hexahydro-4,6-dioxo-2,5-diphenyl-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2',5'-diphenyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*)dione 9



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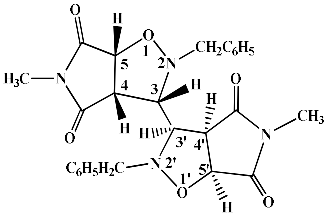
(entry **2**, Table 2): White crystals, Yield 94%; R_f= 0.70; FT-IR (KBr): υ_{max}3025 (m), 2830 (m), 1764 (s), 1660 (s), 1485 (m), 1345 (m), 784 (s) cm^{-1} . ^{1}H NMR (CDCl$_3$): δ ppm 7.60-7.46 (m, 2x5H), 7.40-7.32 (m,2x5H), 3.90 (dd, *J* = 2.20, 2.16 Hz, 2H, 2xC$_4$H & C$_{4'}$H), 2.20 (dd, *J* = 2.10, 2.10 Hz, 2x1H, C$_3$H & C$_{3'}$H), 1.90 (d, *J* = 3.00 Hz, C$_5$H), 1.82 (d, *J* = 3.00 Hz, C$_{5'}$H).^{13}C NMR (CDCl$_3$):δ ppm 172.40, 172.26 (carbonyl carbons), 138.83, 138.12, 137.94, 137.71, 129.74, 129.70, 129.33, 129.04 (aromatic carbons), 76.15 (C$_5$, C$_{5'}$), 66.47 (C$_3$, C$_{3'}$), 55.80 (C$_4$, C$_{4'}$). FAB - MS (*m/z*):586 (M$^+$), 293, 292, 216, 154, 77.

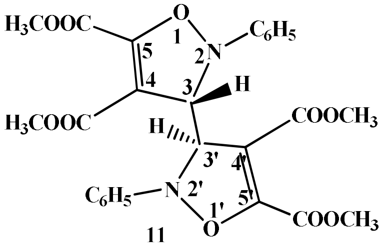
(*3R*, 3a*R*, 6a*S*)-2-benzyl-3-((3'*S*, 3'a*S*, 6a*R*)-2'-benzyl-hexahydro-5-methyl-4,6-dioxo-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-dihydro-5-methyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*)dione 10



10

(entry **3;** Table **2):** White crystals, Yield 92%; R_f= 0.62; FT-IR (KBr): υ_{max}3010 (m), 2900 (m), 1760 (s), 1660 (s), 1482 (m), 1340 (m), 780 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ ppm 7.46-7.26 (m, 10H, $2xCH_2\underline{C_6H_5}$), 4.37 (d, 2H, *J* = 7.16 Hz, $2xC_5H$ &$C_{5'}H$)), 3.24 (d, 2H, *J* = 7.14 Hz, $2xC_3H$ & $C_{3'}H$), 2.89 (dd, br, 2H, $2xC_4H$ & $C_{4'}H$), 2.60 (s, 6H, 2xN-CH_3 protons), 2.15 (s, 4H, $2x\underline{CH_2}C_6H_5$). ^{13}C NMR ($CDCl_3$): δ ppm 177.18, 176.04 (carbonyl carbons), 136.22, 133.12, 130.90, 127.70 (aromatic carbons), 78.67 (C_5, $C_{5'}$), 67.80 (C_3, $C_{3'}$), 56.77 (C_4, $C_{4'}$), 32.05 (benzyl carbons), 30.20 (N-Me carbons). FAB - MS (*m/z*): 490 (M^+), 308, 245, 244, 182, 91, 77.

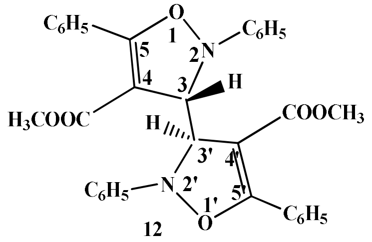
(*3R*, 3a*R*, 6a*S*)-2,5-diphenyl-2*H*-pyrrolo[3,4-*d*]isoxazol-3-yl)-2', 5'-diphenyl-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6-dimethyldicarboxylate(5*H*, 6a*H*)dione 11



11

Colourless gummy liquid, Yield 92%; R_f= 0.70; FT-IR (KBr): υ_{max}3030 (m), 2815 (m), 1760 (s), 1665 (s), 1480 (m), 1340 (m), 788 (s) cm^{-1} . ^{1}H NMR ($CDCl_3$): δ ppm 7.50-7.30 (m, 10H, 2x(O=C)NC_6H_5), 3.30 (br, s, 12H, $4xCOOCH_3$). 1.67 (d, 2H, *J* = 6.10 Hz, $2xC_3H$ & $C_{3'}H$). ^{13}C NMR($CDCl_3$):δ ppm 172.40, 172.26, 171.78, 170.60 (carbonyl carbons), 138.83, 138.12, 137.94, 137.71, 129.74, 129.70, 129.33, 129.04 (aromatic carbons), 76.15 (C_5, $C_{5'}$), 66.47 (C_3, $C_{3'}$), 55.80 (C_4, $C_{4'}$), 23.22, 22.58, 22.12, 21.43 (ester methyl carbons); FAB - MS (*m/z*): 572 (M^+), 418, 262 (BP), 154, 77.

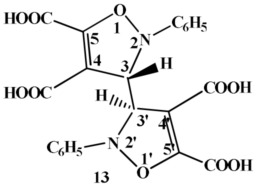
(3R, 3aR, 6aS)-2,5-diphenyl-2H-pyrrolo[3,4-d]isoxazol-3-yl)-2’, 5’-diphenyl-2H-pyrrolo[3,4-d]isoxazole-4,6-phenylmethylcarboxylate(5H, 6aH)dione 12



12

(entry **5**, Table 2): Pale yellow liquid, Yield 92%; R_f= 0.74; FT-IR (KBr): υ_{max}3010 (m), 2810 (m), 1755 (s), 166\0 (s), 1485 (m), 1342 (m), 780 (s) cm^{-1} . ^1H NMR ($CDCl_3$): δ ppm 7.80-7.55 (m, 10H, 2x(O=C)NC_6H_5), 7.50-7.15 (m, 10H), 6.70 (d, 1H, *J* = 6.06 Hz, C_3H), 6.60 (d, 1H, *J* = 5.00 Hz, $C_{3'}H$), 3.30 (br, s, 6H, 2x$COOCH_3$). ^{13}C NMR($CDCl_3$):δ ppm 172.80, 172.58 (carbonyl carbons), 137.60, 137.33, 137.14, 136.90, 136.47, 129.45, 129.30, 128.48 (aromatic carbons), 75.50(C_5, $C_{5'}$), 65.40(C_3, $C_{3'}$), 57.74(C_4, $C_{4'}$), 22.90 (ester methyl carbons), 20.12 (N-methyl carbons) ; FAB - MS (*m/z*): 560 (M^+), 280, 154, 77.

(3R, 3aR, 6aS)-2,5-diphenyl-2H-pyrrolo[3,4-d]isoxazol-3-yl)-2’, 5’-diphenyl-2H-pyrrolo[3,4-d]isoxazole-4,6-dicarboxylic acid(5H, 6aH)dione 13

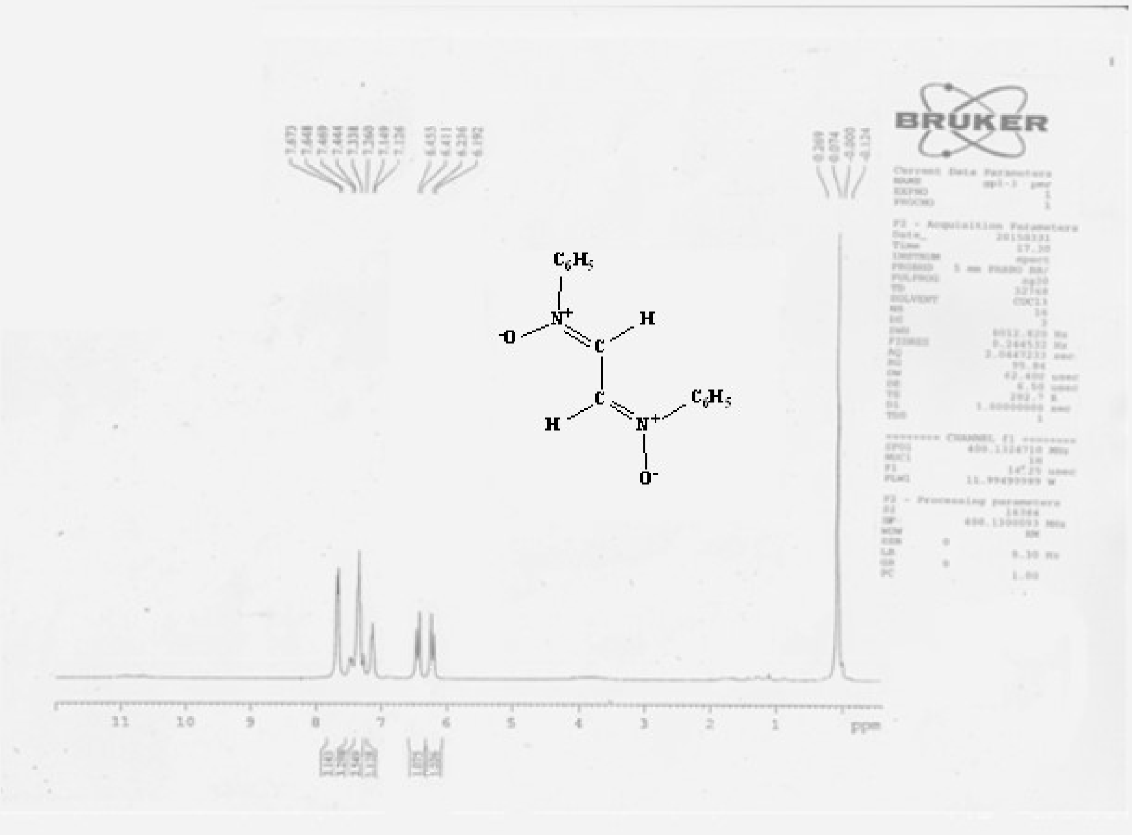


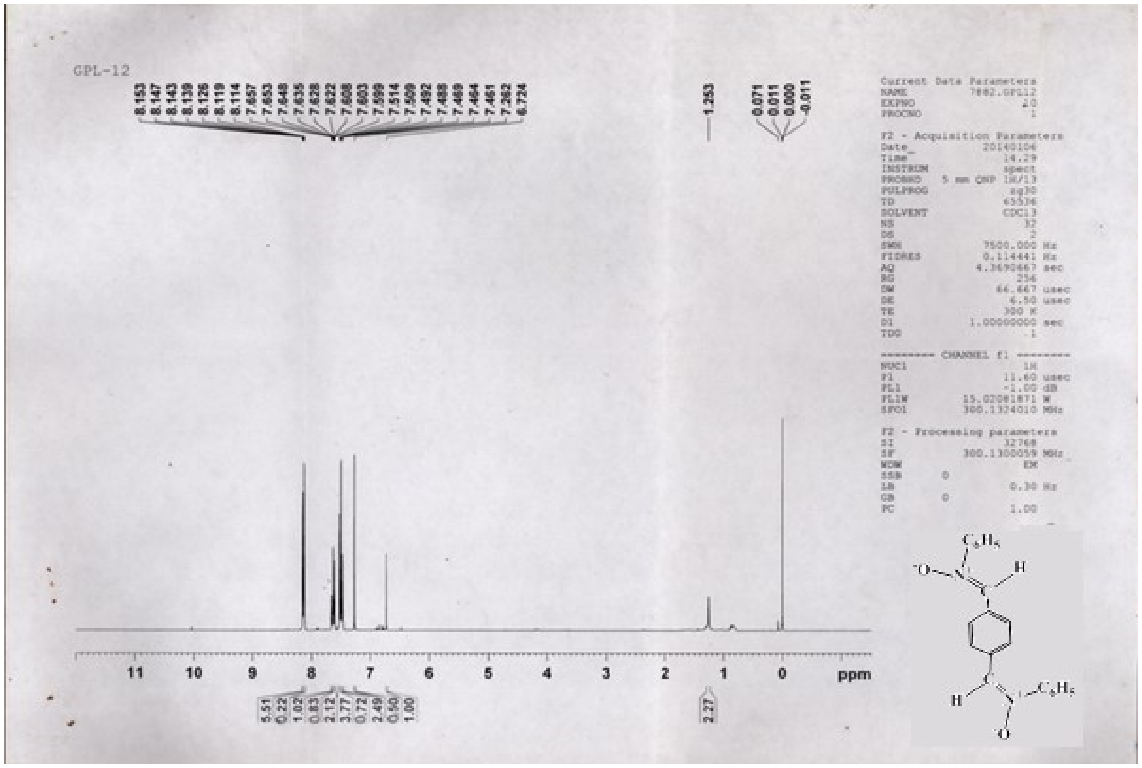
13

(Table **2;** entry **6):** Pale yellow liquid, Yield 92%; R_f = 0.74; FT-IR (KBr): υ_{max}3010 (m), 2810 (m), 1755 (s), 166\0 (s), 1485 (m), 1342 (m), 780 (s) cm^{-1} . ^1H NMR ($CDCl_3$): δppm 10.80 (br, s, 4H, COOH), 7.74-7.25 (m, 2x5H, phenyl protons), 6.54 (d, 1H, *J* = 3.06 Hz, C_3H), 6.30 (d, 2H, *J* = 2.00 Hz, $C_{3'}H$). ^{13}C NMR ($CDCl_3$):δ ppm 172.80, 172.58(carbonyl carbons), 137.60, 137.33, 137.14, 136.90, 136.47, 129.45, 129.30, 128.48 (aromatic carbons), 75.50(C_5, $C_{5'}$), 65.40(C_3, $C_{3'}$), 57.74(C_4, $C_{4'}$). FAB - MS (*m/z*): 468 (M^+), 314, 234, 154, 90, 77.

1H NMR & 13C NMR Spectra

Spectra as received in hard copy from CSIR-CDRI, Lucknow) were scanned and structures inserted. Hard copies as obtained is of light shade therefore scanning appeared in light shade.





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TD0                      1

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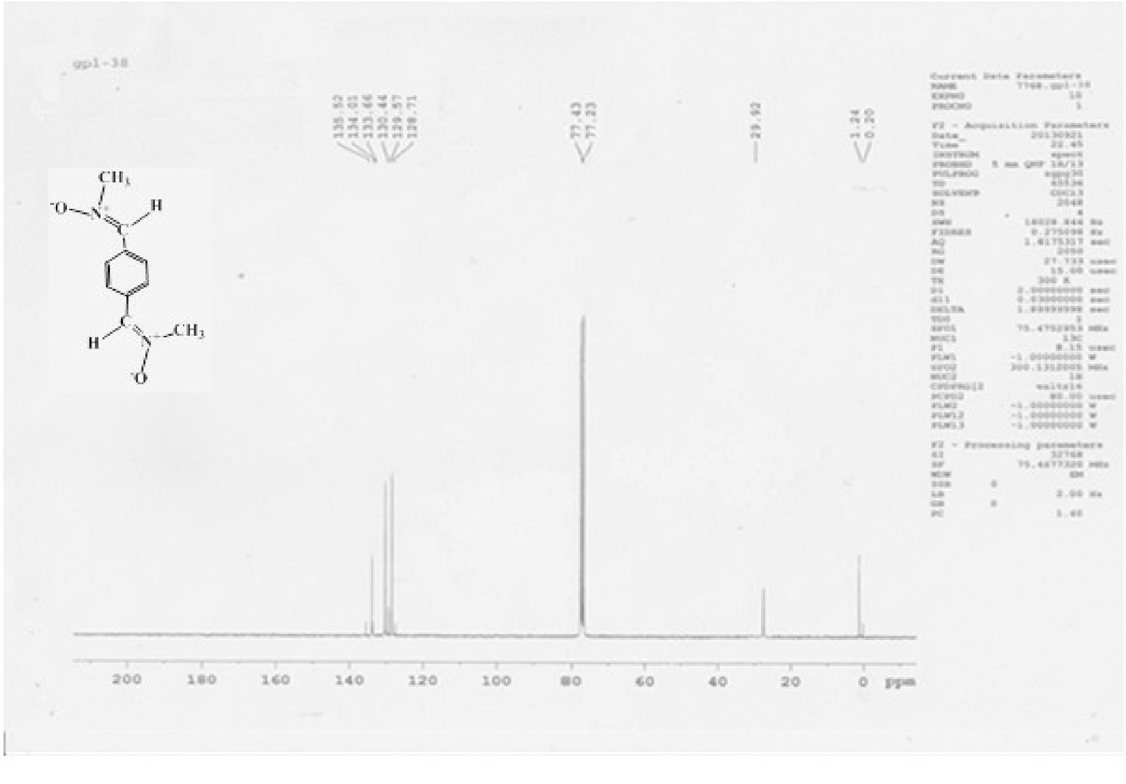

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PROCNO                   1

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TD                   65536
SOLVENT              CDCl3
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DS                       4
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FIDRES        0.275098 Hz
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PLW1       -1.00000000 W
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PCPD2            80.00 usec
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PLW12      -1.00000000 W
PLW13      -1.00000000 W

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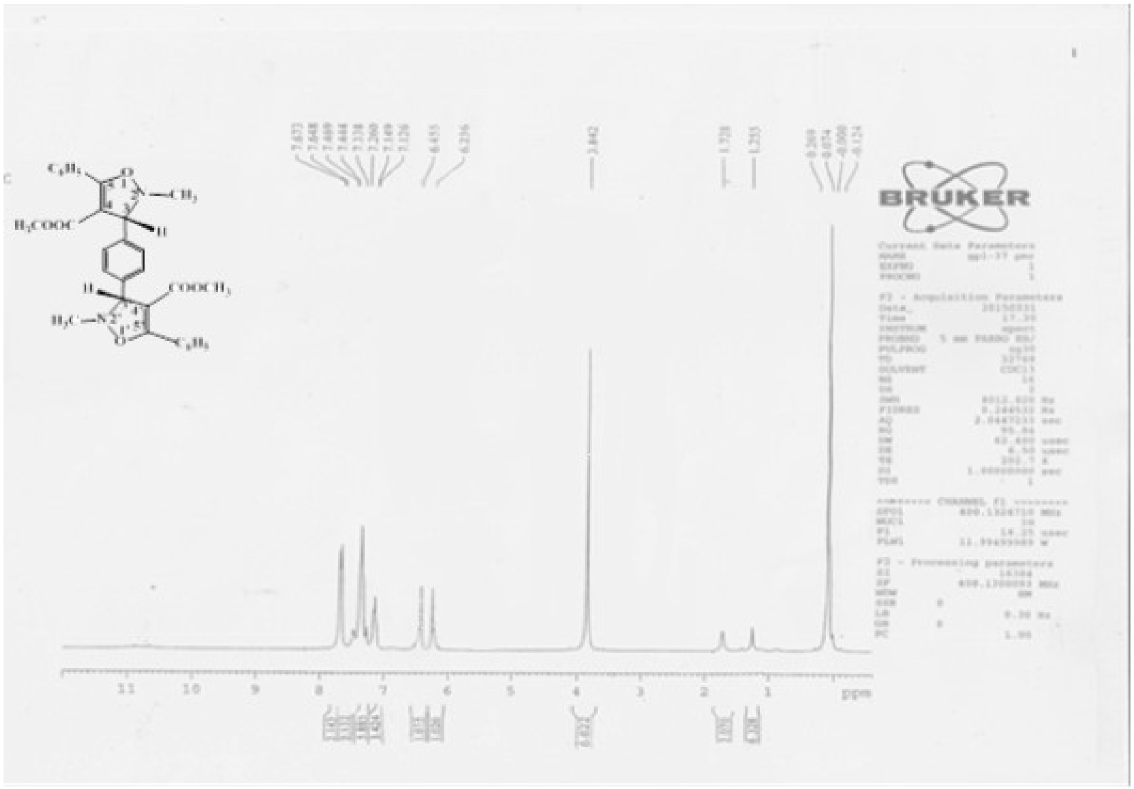
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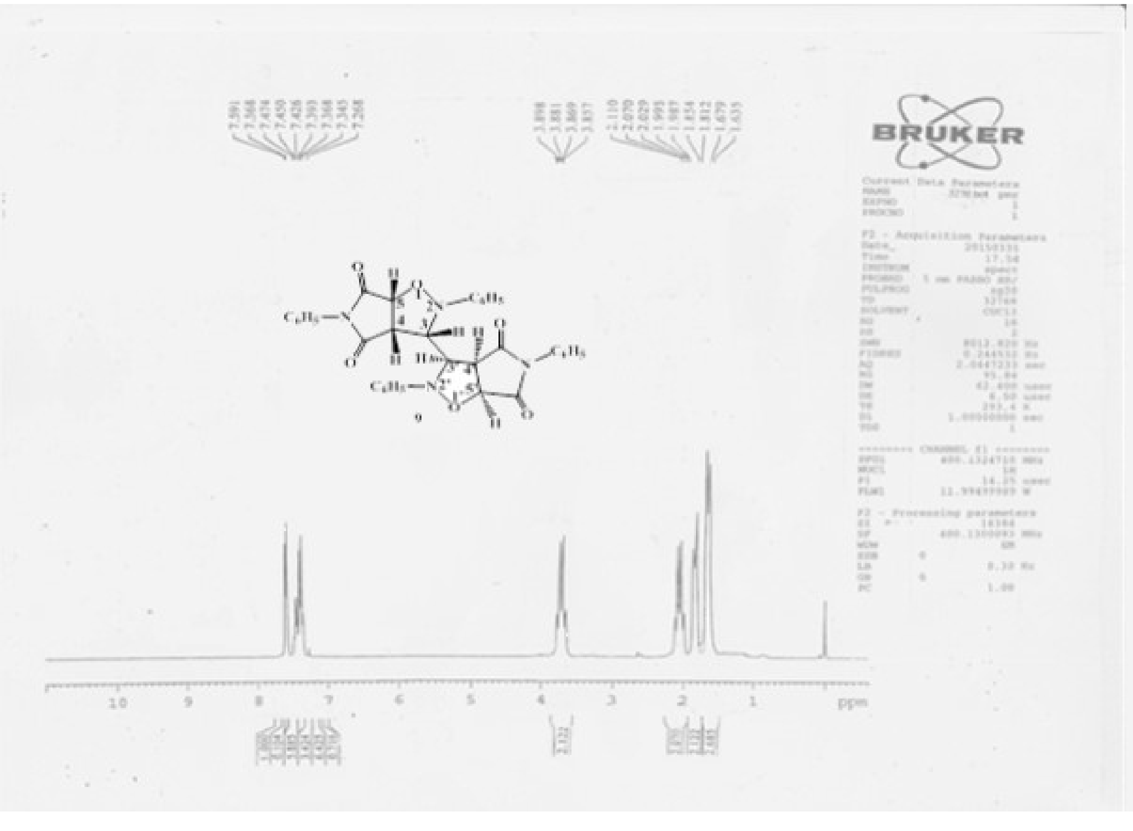
ppm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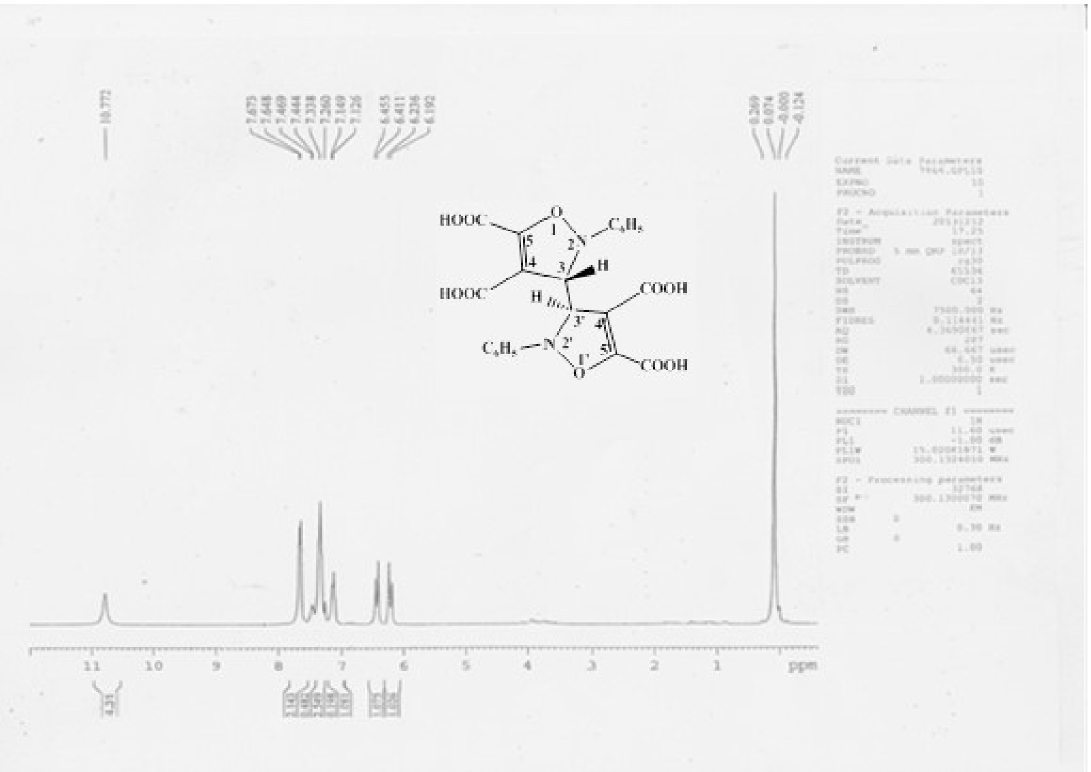
1
ppm



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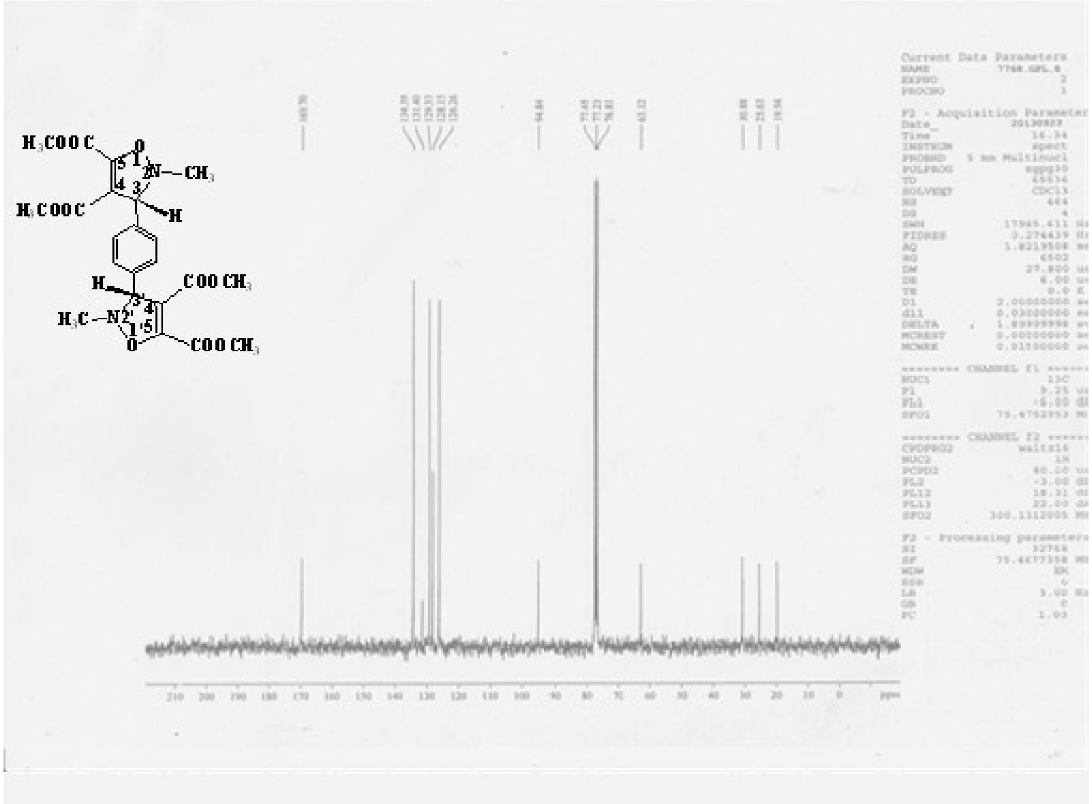

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PROCNO                1

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NS                  464
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MCWRK        0.01500000 se

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PL1               -6.00 dB
SFO1         75.4752953 M

======== CHANNEL f2 =====
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PL13              22.00 dB
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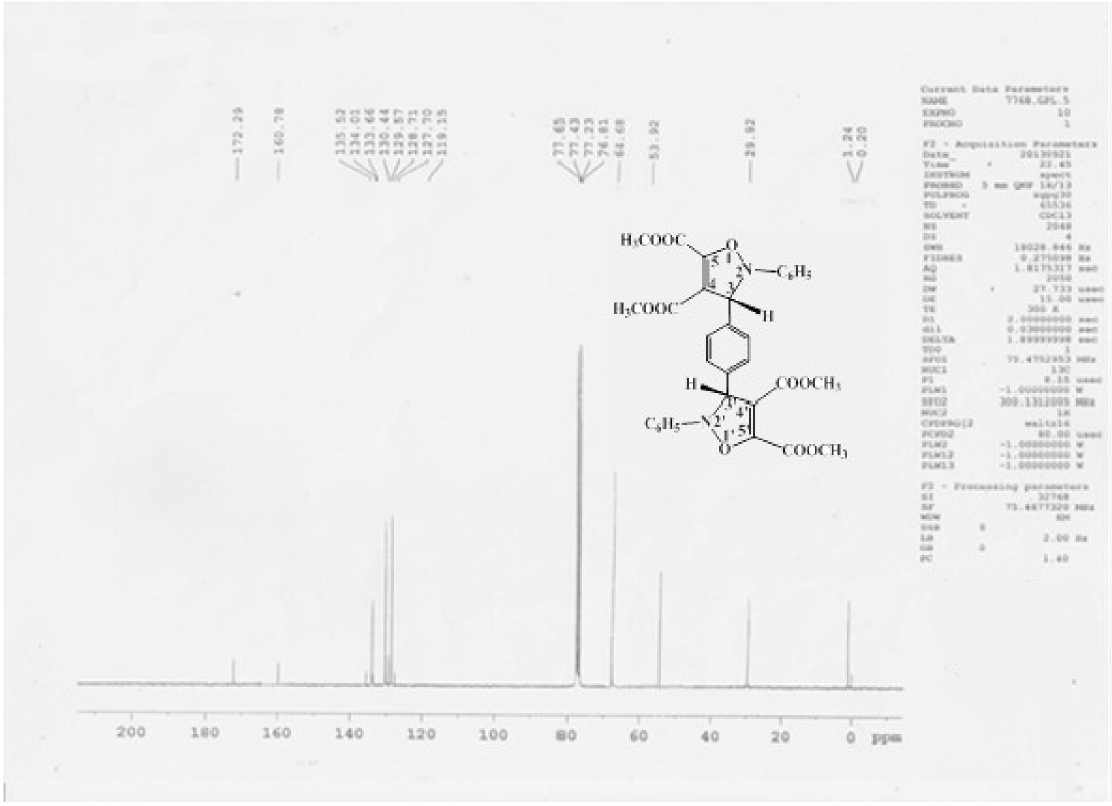

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PROCNO                    1

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SOLVENT               CDCl3
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SWH              18028.846 Hz
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RG                     2050
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DE                    15.00 usec
TE                    300 K
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d11             0.03000000 sec
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PLW12         -1.00000000 W
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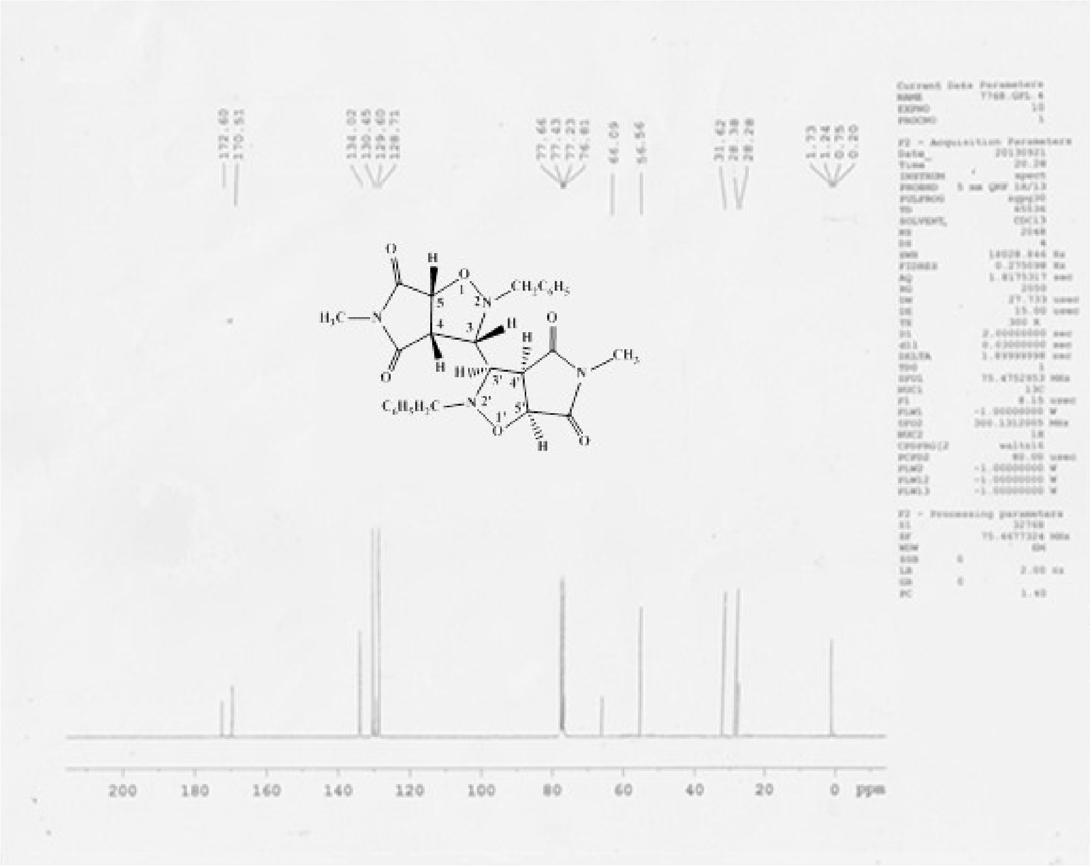

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TD                    65536
SOLVENT               CDCl3
NS                     2048
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RG                     2050
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NUC1                    13C
P1                     8.15 usec
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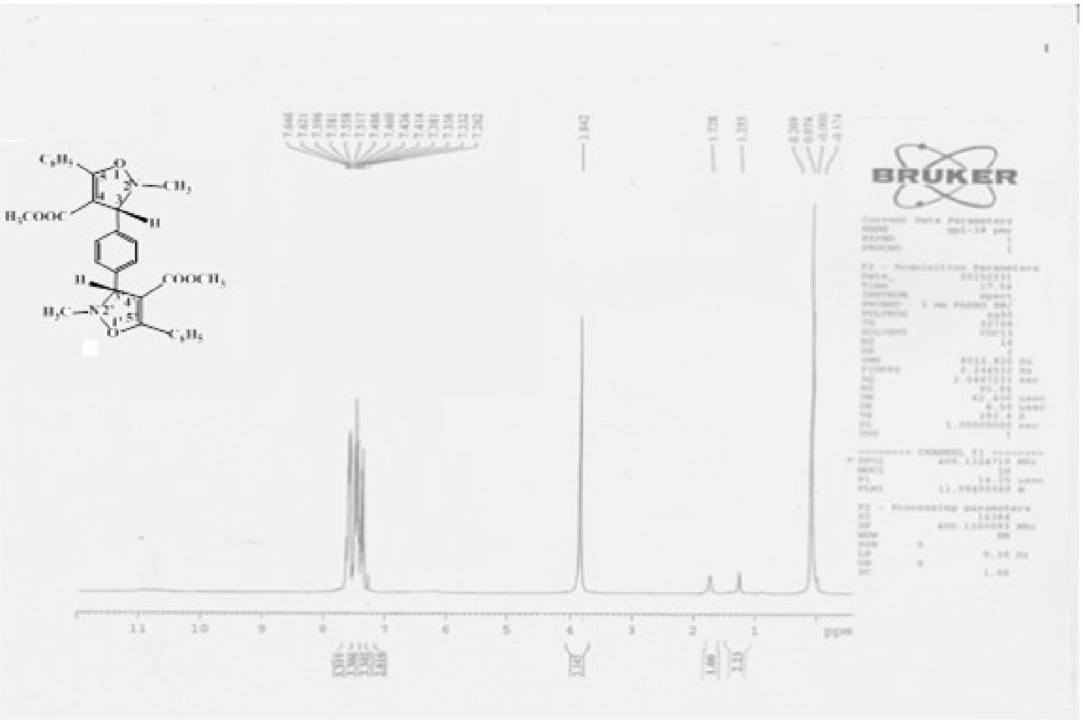

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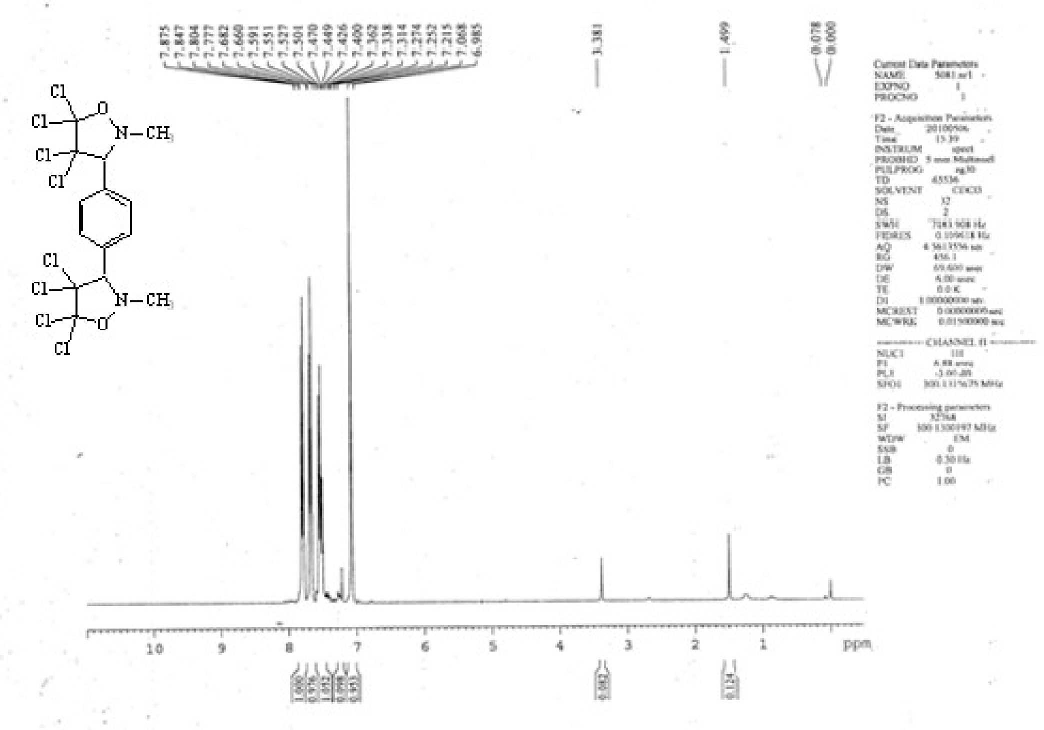

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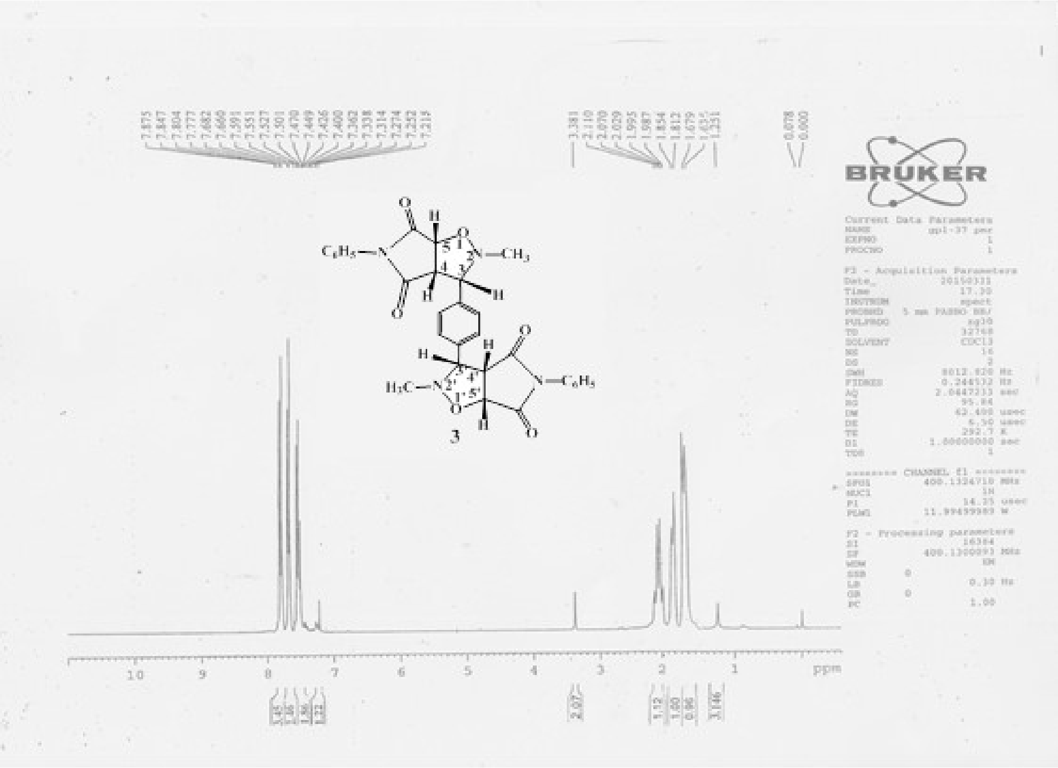
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PROCNO 1
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LB 0.30 Hz
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2
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4
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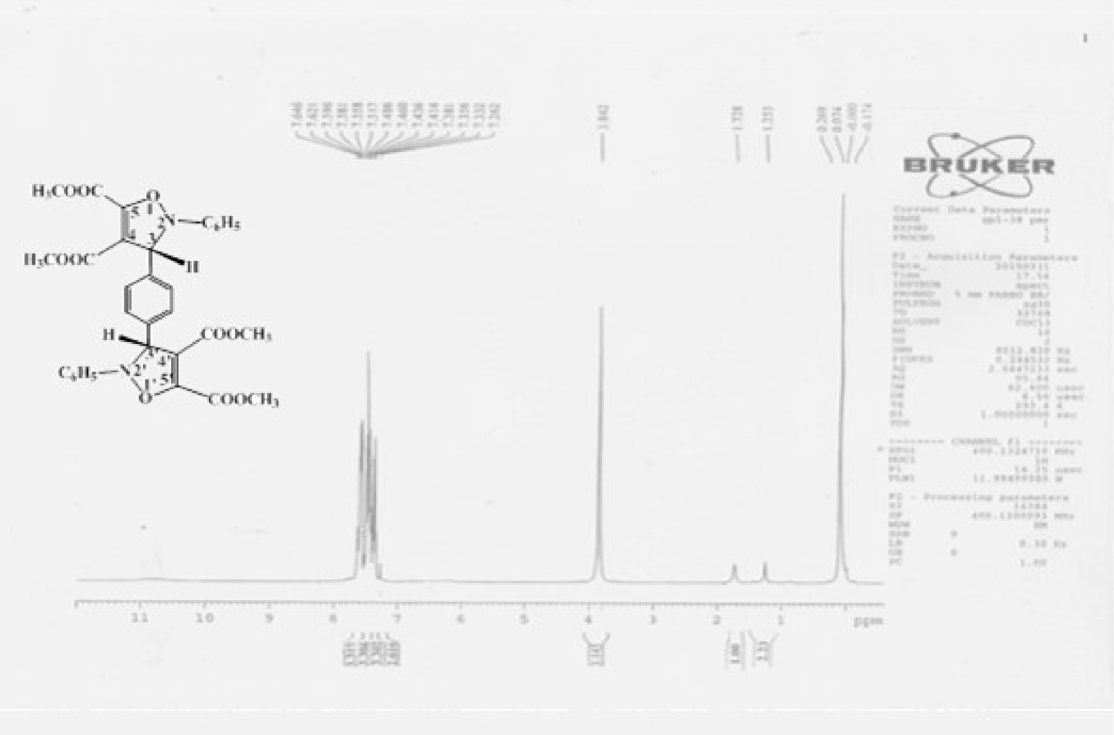
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PROCNO 1
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FIDRES 0.244532 Hz
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RG 95.84
DW 62.400 usec
DE 6.50 usec
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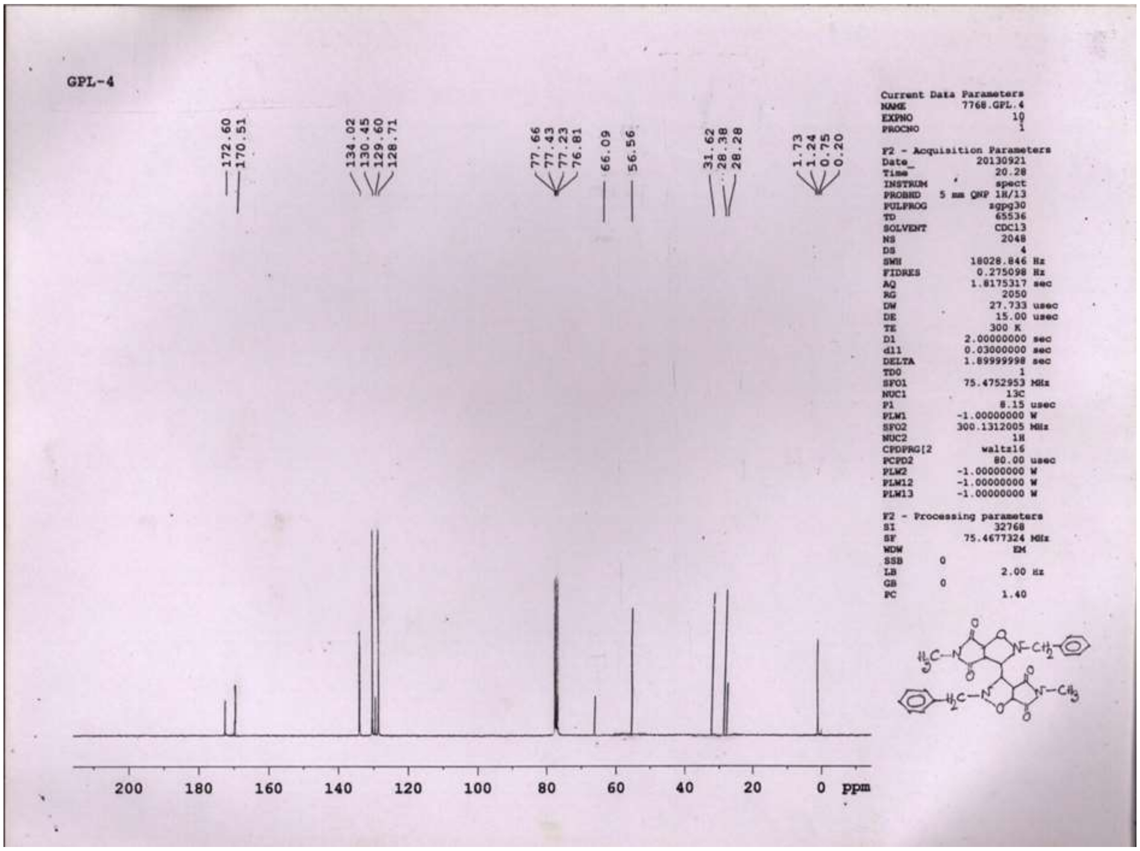

GPL-4

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FIDRES          0.275098 Hz
AQ             1.8175317 sec
RG                   2050
DW                 27.733 usec
DE                  15.00 usec
TE                 300 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                     1
SFO1          75.4752953 MHz
NUC1                  13C
P1                   8.15 usec
PLW1         -1.00000000 W
SFO2         300.1312005 MHz
NUC2                   1H
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PCPD2               80.00 usec
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PLW12        -1.00000000 W
PLW13        -1.00000000 W

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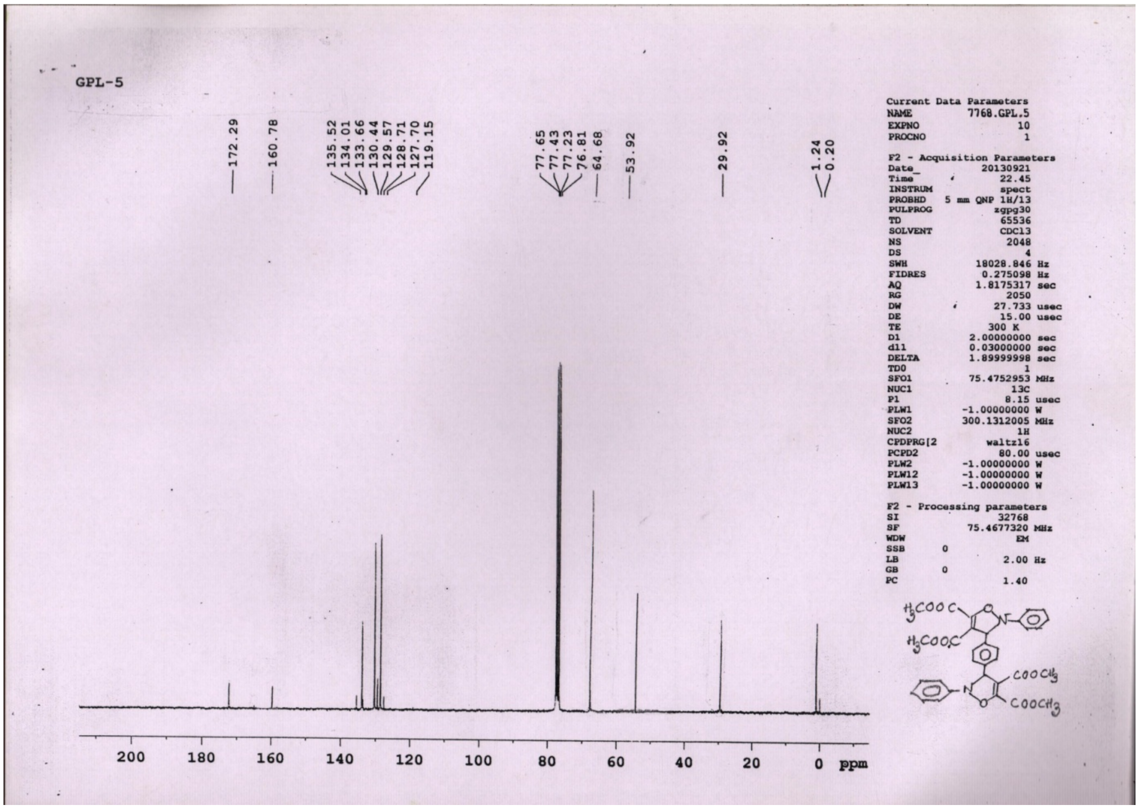

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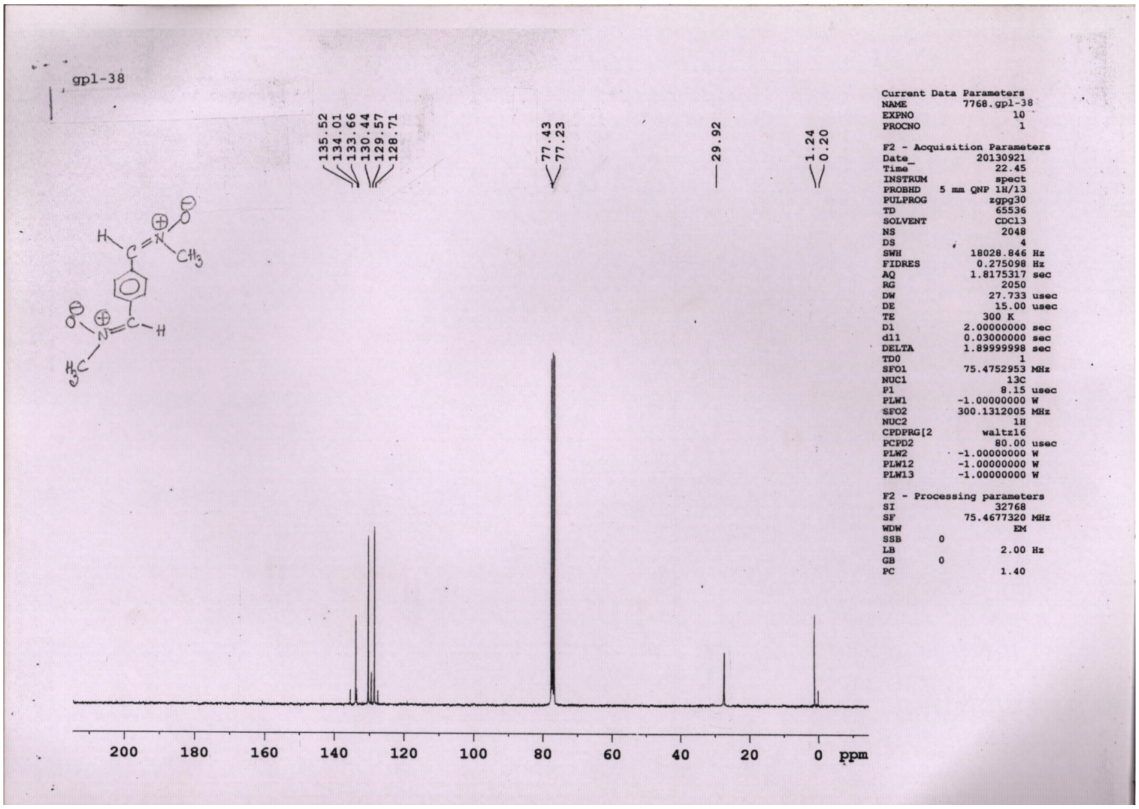
DS                     4
SWH            18028.846 Hz
FIDRES          0.275098 Hz
AQ             1.8175317 sec
RG                  2050
DW                27.733 usec
DE                 15.00 usec
TE                300 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                    1
SFO1          75.4752953 MHz
NUC1                 13C
P1                  8.15 usec
PLW1         -1.00000000 W
SFO2         300.1312005 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2              80.00 usec
PLW2         -1.00000000 W
PLW12        -1.00000000 W
PLW13        -1.00000000 W

F2 - Processing parameters
SI                 32768
SF            75.4677320 MHz
WDW                   EM
SSB        0
LB                  2.00 Hz
GB         0
PC                  1.40
```



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Current Data Parameters
NAME          7768.gpl-38
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130921
Time               22.45
INSTRUM            spect
PROBHD   5 mm QNP 1H/13
PULPROG          zgpg30
TD                 65536
SOLVENT            CDC13
NS                  2048
DS                     4
SWH            18028.846 Hz
FIDRES          0.275098 Hz
AQ             1.8175317 sec
RG                  2050
DW                27.733 usec
DE                 15.00 usec
TE                300 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                    1
SFO1          75.4752953 MHz
NUC1                 13C
P1                  8.15 usec
PLW1         -1.00000000 W
SFO2         300.1312005 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2              80.00 usec
PLW2         -1.00000000 W
PLW12        -1.00000000 W
PLW13        -1.00000000 W

F2 - Processing parameters
SI                 32768
SF            75.4677320 MHz
WDW                   EM
SSB        0
LB                  2.00 Hz
GB         0
PC                  1.40
```

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