Stereoretentive O to C Rearrangement of Vinyl Acetals. Solvent Cage Effects as a Stereocontrol Element.

Yongda Zhang, Nathan T. Reynolds, Kavita Manju and Tomislav Rovis*

Department of Chemistry, Colorado State University
Fort Collins, Colorado 80523

Supporting Information

General Methods. All reactions were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring. Tetrahydrofuran, diethyl ether, and dichloromethane were degassed with argon and passed through two columns of neutral alumina. Toluene was degassed with argon and passed through one column of neutral alumina and one column of Q5 reactant. Column chromatography was performed on EM Science silica gel 60 (230-400 mesh). Thin layer chromatography was performed on EM Science 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light, $KMnO_4$, aqueous ceric ammonium molybdate, or bromocresol green dips followed by heating.

Melting points were measured with a MelTemp II melting point apparatus outfitted with a Fluke 51 thermocouple and are uncorrected. Infrared spectra were obtained on a Nicolet Avatar 320 FT-IR spectrometer. ^{1}H NMR and spectra were recorded on a Varian 300, 400, or 500 MHz spectrometer at ambient temperature. Data are reported as follows: chemical shift in parts per million (δ, ppm) from an internal standard [tetramethylsilane (TMS) or deuterated chloroform ($CDCl_3$)], multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, and coupling constant (Hz). ^{13}C NMR were recorded on a Varian 300, 400, or 500 MHz spectrometer at ambient temperature. Chemical shifts are reported in ppm from $CDCl_3$ taken as 77.0 ppm. Mass spectra were obtained on Fisons VG Autospec.

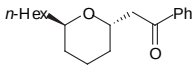
Vinyl acetals **1, 3, 5, 7, 9, 11, 13, 15, 19** were prepared according to literature methods.[1,2]

Procedure A: General procedure for the BF_3•OEt_2 mediated rearrangement of vinyl acetals: A flame-dried round bottom flask containing a magnetic stir bar was charged with the vinyl acetal (0.11 mmol). Under an atmosphere of argon, toluene was added *via* syringe (0.5 mL) and the reaction cooled to the desired temperature. BF_3•OEt_2 (16 μL, 0.12 mmol, neat) was added to the solution *via* syringe and the reaction allowed to stir 30 min. Saturated Na_2CO_3 (2 mL) was added and the mixture allowed to warm to ambient temperature. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Diastereoselectivity was determined by ^{1}H NMR of the unpurified reaction mixture. Analytically pure material was obtained by column chromatography on silica gel.

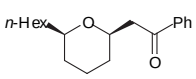
---

1 Dixon, D. J.; Ley, S. V.; Tate, E. W. *J. Chem. Soc.: Perkin Trans 1* **2000**, 2385.
2 Rychnovsky, S. D.; Dahanukar, V. H. *J. Org. Chem.* **1996**, *61*, 7648

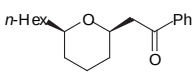
Procedure B: General procedure for the $Me_3Al/BF_3{\bullet}OEt_2$ mediated rearrangement of vinyl acetals: A flame-dried round bottom flask containing a magnetic stir bar was charged with the vinyl acetal (0.11 mmol). Under an atmosphere of argon, toluene was added *via* syringe (0.5 mL) and the reaction cooled to the desired temperature. Me_3Al (0.22 mL, 0.44 mmol, 2.0 M in hexanes) was added dropwise *via* syringe and the reaction allowed to stir 2 min at that temperature. $BF_3{\bullet}OEt_2$ (16 μL, 0.12 mmol, neat) was then added to the solution *via* syringe and the reaction allowed to stir 30 min. Saturated Na_2CO_3 (2 mL) was added and the mixture allowed to warm to ambient temperature. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Diastereoselectivity was determined by ^{1}H NMR of the unpurified reaction mixture. Analytically pure material was obtained by column chromatography on silica gel.



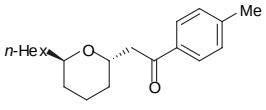
***trans*-6-hexyl-2-(2-oxo-2-phenylethyl)tetrahydropyran (*trans*-2).**[1] According to general procedure **A**, vinyl acetal **1** (30.0 mg, 0.11 mmol) and $BF_3{\bullet}OEt_2$ (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**2** (27.9 mg, 93%), a white solid.



***cis*-6-hexyl-2-(2-oxo-2-phenylethyl)tetrahydropyran (*cis*-2).**[1] According to general procedure **B**, vinyl acetal **1** (30.0 mg, 0.11 mmol), Me_3Al (0.22 mL, 0.44 mmol) and $BF_3{\bullet}OEt_2$ (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 7:93 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**2** (25.8 mg, 86%), a white solid.

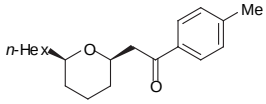


***cis*-6-hexyl-2-(2-oxo-2-phenylethyl)tetrahydropyran (*cis*-2).**[1] According to general procedure **B**, vinyl acetal **1** (0.5 g, 1.7 mmol), Me_3Al (3.5 mL, 6.8 mmol), $BF_3{\bullet}OEt_2$ (0.23 mL, 1.8 mmol, neat) and Toluene (8.5 mL) at –78 °C produced the product as a 3:97 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**2** (0.46 g, 92%).

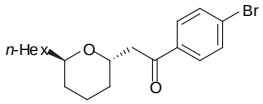


***trans*-6-hexyl-2-(2-oxo-2-p-tolylethyl)tetrahydropyran (*trans*-4).** According to general procedure **A**, vinyl acetal **3** (60.0 mg, 0.22 mmol) and $BF_3{\bullet}OEt_2$ (28 μL, 0.22 mmol, neat) at –78 °C produced the product as a 93:7 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**4** (54.0 mg, 90%), a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.24 (m, 2H), 4.34 (dddd, 1H, *J* = 3.6, 6.7, 6.7, 6.7 Hz), 3.71 (m, 1H), 3.27 (dd, 1H, *J* = 6.6, 15.3 Hz), 3.00 (dd, 1H, *J* = 6.5, 15.5 Hz), 2.40 (s, 3H), 1.81-1.60 (m, 5H), 0.86 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$)δ 198.1, 143.6, 134.7, 129.1, 128.2, 72.0, 67.8, 43.4, 32.8, 31.9, 30.4, 29.7, 29.3, 25.7, 22.7, 21.7, 18.6, 14.2; IR (NaCl, neat)

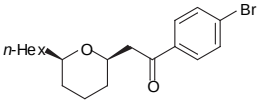
2931, 2856, 1684, 1606, 1458, 1286, 1180, 1041 cm^{-1}; HRMS $[C_{20}H_{30}O_2+H]^+$ calcd 330.2324. Found 303.2328 (FAB+).



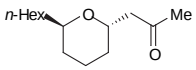
***cis*-6-hexyl-2-(2-oxo-2-p-tolylethyl)tetrahydropyran (*cis*-4).** According to general procedure **B**, vinyl acetal **3** (30.0 mg, 0.11 mmol), Me_3Al (0.22 mL, 0.44 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 4:96 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**4** (27.6 mg, 92%), a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (2H,m), 7.23 (2H, m), 3.91 (1H, dddd, *J* = 1.8, 6.4, 6.7, 12.7 Hz), 3.27 (1H, m), 3.27 (1H, dd, *J* = 15.6, 6.4 Hz), 2.91 (1H, dd, *J* = 6.1, 15.6 Hz), 2.40 (3H, s), 1.81 (1H, m), 1.72 (1H, m), 1.13-1.60 (14H, m), 0.85 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 198.2, 143.5, 134.9, 129.0, 128.3, 78.1, 74.7, 45.5, 36.6, 31.9, 31.9, 31.5, 29.4, 25.5, 23.7, 22.7, 21.7, 14.2; IR (NaCl, neat) 2929, 2858, 1684, 1606, 1070, 802 cm^{-1}; HRMS $[C_{20}H_{30}O_2+H]^+$ calcd 330.2324. Found 303.2324 (FAB+).



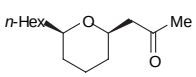
***trans*-6-hexyl-2-(2-oxo-2-[4-bromophenyl])ethyl tetrahydropyran (*trans*-6).** According to general procedure **A**, vinyl acetal **5** (40.0 mg, 0.11 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**5** (36.0 mg, 90%), a white solid: Rf = 0.19 (1:9 EtOAc/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.59 (m, 2H), 4.31 (dddd, 1H, *J* = 7.4 Hz, *J* = 7.1 Hz, *J* = 7.1 Hz, *J* = 3.6 Hz), 3.71 (m, 1H), 3.26 (dd, 1H, *J* = 15.4, 6.8 Hz), 2.94 (dd, 1H, *J* = 15.4 Hz, *J* = 6.4 Hz), 1.80-1.60 (m, 5H), 1.45-1.10 (m, 11H), 0.86 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 135.9, 131.7, 129.7, 128.0, 72.1, 67.6, 43.5, 32.6, 31.9, 30.5, 29.5, 29.3, 25.7, 22.7, 18.6, 14.2; IR (NaCl, neat) 2931, 2856, 1686, 1585, 1396, 1286, 1070 cm^{-1}; HRMS $[C_{19}H_{29}O_2Br]^+$ calcd 369.1252. Found 369.1251 (FAB+).



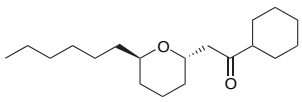
***cis*-6-hexyl-2-(2-oxo-2-[4-bromophenyl])ethyltetrahydropyran (*cis*-6).** According to general procedure **B**, vinyl acetal **5** (40.0 mg, 0.11 mmol), Me_3Al (0.22 mL, 0.44 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 10:90 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**6** (32.0 mg, 80%), a white solid: Rf = 0.27 (1:9 EtOAc/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.57 (m, 2H), 3.88 (dddd, 1H, *J* = 12.8, 7.5, 5.4, 2.5 Hz), 3.26 (dd, 1H, *J* = 15.5, 7.0 Hz), 3.25 (m, 1H), 2.85 (dd, 1H, *J* = 15.4, 5.7 Hz), 1.83 (m, 1H), 1.70 (m, 1H) 1.10-1.60 (m, 14H), 0.83 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 136.2, 131.6, 129.9, 129.9, 78.1, 74.7, 45.6, 36.5, 31.9, 31.9, 31.4, 29.3, 25.5, 23.6, 22.7, 14.2; IR (NaCl, neat) 2929, 2856, 1685, 1585, 1396, 1286, 1070 cm^{-1}; HRMS $[C_{19}H_{29}O_2Br]^+$ calcd 369.1252. Found 369.1253 (FAB+).



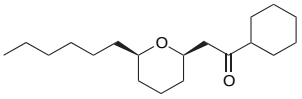
***trans*-6-hexyl-2-(2-oxo-propyl)tetrahydropyran (*trans*-8).**[1] According to general procedure **A**, vinyl acetal **7** (30.0 mg, 0.133 mmol) and BF_3•OEt_2 (20 μL, 0.14 mmol, neat) at –78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**8** (27.0 mg, 90%), a white solid.



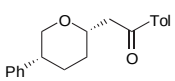
***cis*-6-hexyl-2-(2-oxo-propyl)tetrahydropyran (*cis*-8).**[1] According to general procedure **B**, vinyl acetal **7** (35.0 mg, 0.155 mmol), Me_3Al (0.30 mL, 0.60 mmol) and BF_3•OEt_2 (20 μL, 0.16 mmol, neat) at –55 °C produced the product as a 12:88 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**8** (25.0 mg, 71%), a white solid.



***trans*-6-hexyl-2-(2-oxo-2-cyclohexylethyl)tetrahydropyran (*trans*-10).** According to general procedure **A**, vinyl acetal **9** (30.0 mg, 0.10 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**10** (27.0 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.22 (dddd, 1H, *J* = 3.6, 6.0, 6.0, 6.0 Hz), 3.68 (m, 1H), 2.78 (dd, 1H, *J* = 7.8, 15.9 Hz), 2.47 (dd, 1H, *J* = 5.4, 15.9 Hz), 2.39 (m, 1H), 1.86-1.57 (m, 10H), 1.39-1.16 (m, 16H), 0.88 (t, 3H, *J* = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 212.5, 72.0, 67.7, 51.4, 45.5, 33.2, 32.1, 30.6, 29.9, 28.6, 28.5, 26.2, 20.0, 26.0, 23.0, 18.8, 14.4; IR (NaCl, neat) 2929, 2854, 1708, 1451, 1377, 1039 cm^{-1}; HRMS $[C_{19}H_{35}O_2]^+$ calcd 295.2637. Found 295.2640 (FAB+).

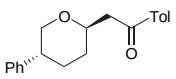


***cis*-6-hexyl-2-(2-oxo-2-cyclohexylethyl)tetrahydropyran (*cis*-10).** According to general procedure **B**, vinyl acetal **9** (30 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –32 °C produced the product as a 10:90 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**10** (25.0 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (dddd, 1H, *J* = 2.8, 5.1, 7.5, 12.6 Hz), 3.25 (m, 1H), 2.73 (dd, 1H, *J* = 7.2, 15.0 Hz), 2.38 (dd, 1H, *J* = 5.4, 15.0 Hz), 2.39 (m, 1H), 1.86-1.43 (m, 10H), 1.42-1.12 (m, 16H), 0.88 (t, 3H, *J* = 6.3 Hz) ^{13}C NMR (75 MHz, $CDCl_3$) 212.9, 78.2, 74.9, 51.8, 47.8, 36.8, 32.1, 32.0, 31.7, 29.6, 28.6, 28.3, 26.2, 26.0, 25.9, 25.8, 23.9, 22.9, 14.4; IR (NaCl, neat) 2930, 2855, 1709, 1450, 1373, 1082 cm^{-1}; HRMS $[C_{19}H_{35}O_2]^+$ calcd 295.2637. Found 295.2637 (FAB+).

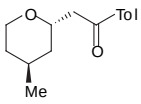


***cis*-5-phenyl-2-(2-oxo-2-p-tolylethyl)tetrahydropyran (*cis*-12).** According to general procedure **A**, vinyl acetal 11 (8.0 mg, 0.027 mmol) and BF_3•OEt_2 (60 μL, 0.03 mmol, 0.5 M in PhMe) at –78 °C produced the product as a 5:95 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**12** (7.6 mg, 95%), a white solid: Rf = 0.44 (1:4 EtOAc/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (m, 2H), 7.46 (m, 2H), 7.19-7.34 (m, 5H), 4.21 (m, 1H), 4.18 (m, 1H), 3.89 (dd, 1H, *J* = 11.9, 3.8 Hz), 3.34 (dd, 1H, *J* = 16.1,

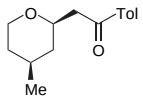
6.4 Hz), 3.02 (dd, 1H, *J* = 16.0, 6.1 Hz), 2.85 (m, 1H), 2.41 (s, 3H), 2.10 (m, 1H), 1.98 (m, 1H), 1.48-1.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.7, 144.0, 134.6, 129.1, 128.4, 128.3, 128.2, 128.0, 125.8, 73.5, 70.1, 44.2, 38.6, 29.4, 27.2, 21.7; IR (NaCl, neat) 2931, 1681, 1606, 1180, 1107, 1058, 701 cm^{-1}; HRMS $[C_{19}H_{29}O_2Br]^+$ calcd 295.1698. Found 295.1700 (FAB+).



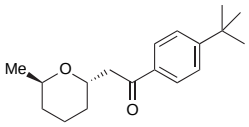
***trans*-5-phenyl-2-(2-oxo-2-p-tolylethyl)tetrahydropyran (*trans*-12).** According to general procedure **B**, vinyl acetal **11** (30 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –25 °C produced the product as a 90:10 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**12**(25.5 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.33-7.19 (m, 7H), 4.09-3.97 (m, 2H), 3.48 (dd, 1H, *J* = 11.1, 11.1 Hz), 3.34 (dd, 1H, *J* = 16.2, 6.6 Hz), 2.99 (dd, 1H, *J* = 16.2, 6.0 Hz), 2.89-2.78 (m, 1H), 2.42 (s, 3H), 2.09-1.76 (m, 2H), 1.64-1.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.8, 144.2, 142.4, 135.0, 129.5, 128.8, 128.6, 127.4, 126.8, 74.4, 74.1, 45.2, 42.9, 32.2, 30.7, 21.9; IR (NaCl, neat) 2926, 1682, 1605, 1181, 1108, 1083, 754, 700 cm^{-1}; HRMS $[C_{19}H_{23}O_2]^+$ calcd 295.1698. Found 295.1703 (FAB+).



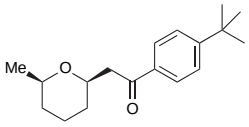
***trans*-4-methyl-2-(2-oxo-2-p-tolylethyl)tetrahydropyran (*trans*-14).** According to general procedure **A**, vinyl acetal **13** (30.0 mg, 0.130 mmol) and BF_3•OEt_2 (15 μL, 0.16 mmol, neat) at –78 °C produced the product as a 5:95 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**14** (28.0 mg, 93%), a white solid: Rf = 0.xx (1:4 EtOAc/hex);
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (m, 2H), 7.25 (m, 2H), 4.29 (dddd, 1H, *J* = 9.3, 6.9, 6.6, 3.1 Hz), 3.76-3.88 (m, 2H), 3.28 (dd, 1H, *J* = 15.9, 6.9 Hz), 2.91 (dd, 1H, *J* = 15.9, 6.1 Hz), 2.40 (s, 3H), 2.05 (m, 1H), 1.80 (dddd, 1H, *J* = 13.2, 7.5, 7.5, 4.7 Hz), 1.62 (ddd, 1H, *J* = 13.8, 9.1, 4.7 Hz), 1.49 (dddd, 1H, *J* = 13.6, 4.7, 3.1, 1.6 Hz), 1.26 (m, 1H), 1.09 (d, 3H, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 143.7, 134.6, 129.1, 128.2, 68.9, 62.8, 44.0, 37.6, 32.0, 25.0, 21.7, 18.6; IR (NaCl, neat) 2957, 2923, 1682, 1606, 1181, 1080 cm^{-1}; HRMS $[C_{15}H_{21}O_2]^+$ calcd 233.1542. Found 233.1538 (FAB+).



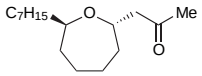
***cis*-4-methyl-2-(2-oxo-2-*p*-tolylethyl)tetrahydropyran (*cis*-14).** According to general procedure **B**, vinyl acetal **13** (23.2 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –25 °C produced the product as a 11:89 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**14** (18.0 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.26 (m, 2H), 3.99-3.90 (m, 2H), 3.46 (ddd, 1H, *J* = 2.1, 11.7, 11.7 Hz), 3.28 (dd, 1H, *J* = 6.0, 15.9 Hz), 2.91 (dd, 1H, *J* = 6.3, 15.9 Hz), 2.41 (s, 3H), 1.80-1.08 (m, 5H), 0.94 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 144.0, 134.9, 129.3, 128.5, 74.3, 68.4, 45.4, 40.8, 34.7, 30.5, 22.6, 22.0; IR (NaCl, neat) 2951, 2924, 1682, 1607, 1258, 1177, 1090 cm^{-1}; HRMS $[C_{15}H_{21}O_2]^+$ calcd 233.1542. Found 233.1540 (FAB+).



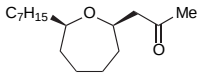
***trans*-6-methyl-2-(2-oxo-2-[4-*tert*-butylphenyl])tetrahydropyran (*trans*-16).** According to general procedure **A**, vinyl acetal **15** (30.0 mg, 0.11 mmol) and BF_3•OEt_2 (16 μL, 0.12 mmol, neat) at –78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**16** (27.6 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (m, 2H), 7.47 (m, 2H), 4.44 (dddd, 1H, *J* = 3.6, 6.6, 6.6, 6.6 Hz,), 3.99 (dqd, 1H, *J* = 3.3, 6.6, 12.6, 12.6 Hz), 3.30 (dd, 1H, *J* = 6.3, 15.9 Hz), 3.08 (dd, 1H, *J* = 6.6, 15.9 Hz), 1.82 -1.62 (m, 4H), 1.47-1.09 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.2, 156.8, 137.7, 128.3, 125.6, 68.0, 67.9, 43.2, 35.4, 31.5, 31.4, 30.3, 19.7, 18.6; IR (NaCl, neat) 2965, 2933, 1681, 1606, 1286, 1192, 1047 cm^{-1}; HRMS $[C_{18}H_{27}O_2]^+$ calcd 275.2011. Found 275.2020 (FAB+).



***cis*-6-methyl-2-(2-oxo-2-[4-*tert*-butylphenyl])tetrahydropyran (*cis*-16).** According to general procedure **B**, vinyl acetal **15** (30 mg, 0.11 mmol), Me_3Al (0.21 mL, 0.44 mmol) and BF_3•OEt_2 (16.6 μL, 0.13 mmol, neat) at – 78 °C produced the product as a 14:86 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**16** (24.0 mg, 80 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.47 (m, 2H), 3.99 (dddd, 1H, *J* = 1.8, 5.4, 7.2, 12.9 Hz), 3.51 (dqd, 1H, *J* = 1.8, 6.0, 12.6, 12.6 Hz), 3.30 (dd, 1H, *J* = 5.1, 16.2 Hz), 2.98 (dd, 1H, *J* = 7.2, 16.2 Hz), 1.85-1.54 (m, 4H), 1.38-1.11 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.0, 156.8, 134.9, 128.3, 125.6, 74.5, 74.30, 45.8, 35.4, 33.4, 31.7, 31.4, 23.8, 22.5; IR (NaCl, neat) 2965, 2932, 1683, 1606, 1218, 1107, 1085, 1067, 990cm^{-1}; HRMS $[C_{18}H_{27}O_2]^+$ calcd 275.2011. Found 275.2008 (FAB+).

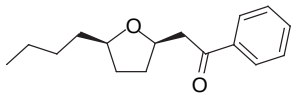


***trans*-7-heptyl-2-(2-oxopropyl)tetrahydrooxepane (*trans*-20).** According to general procedure **A**, vinyl acetal **19** (25 mg, 0.10 mmol) and BF_3•OEt_2 (16.0 μL, 0.12 mmol, neat) at – 78 °C produced the product as a 95:5 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**20** (23.0 mg, 92 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.17-4.13 (m, 1H), 3.55 (m, 1H), 2.72 (dd, 1H, *J* = 7.8, 15.6 Hz), 2.38 (dd, 1H, *J* = 5.1, 15.6 Hz), 2.18 (s, 3H), 1.80-1.77 (m, 4H), 1.46-1.19 (m, 16H), 0.88 (t, 3H, *J* = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 207.6, 75.6, 70.5, 50.8, 36.6, 36.3, 36.2, 32.1, 31.4, 29.9, 29.6, 27.8, 27.2, 26.7, 23.0, 14.4; IR (NaCl, neat) 2926, 2854, 1717, 1456, 1356, 1101 cm^{-1}; HRMS $[C_{16}H_{31}O_2]^+$ calcd 255.2324. Found 255.2323 (FAB+).



***cis*-7-heptyl-2-(2-oxopropyl)tetrahydrooxepane (*cis*-20).** According to general procedure **B**, vinyl acetal **19** (25 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16.0 μL, 0.12 mmol, neat) at – 78 °C produced the product as a 14:86 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**20** (21.0 mg, 84 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.17-4.13 (m, 1H), 3.55 (m, 1H), 2.72 (dd, 1H, *J* = 7.8, 15.6 Hz), 2.38 (dd, 1H, *J* = 5.1, 15.6 Hz), 2.18 (s, 3H), 1.80-1.77 (m, 4H), 1.46-1.19 (m, 16H), 0.88 (t, 3H, *J* = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 207.6, 75.6, 70.5, 50.8, 36.6, 36.3, 36.2, 32.1, 31.4, 29.9, 29.6, 27.8, 27.2, 26.7, 23.0, 14.4; IR (NaCl, neat)

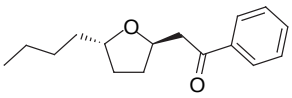
2926, 2854, 1717, 1456, 1356, 1101 cm^{-1}; HRMS $[C_{16}H_{31}O_2]^+$ calcd 255.2324. Found 255.2315 (FAB+).



***cis*-2-(5-butyl-tetrahydo-furan-2-yl)-1-phenyl-ethanone (cis-22)**

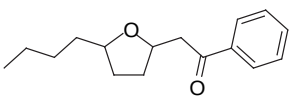
According to general procedure **B**, vinyl acetal *cis*-**21** (25 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16.0 μL, 0.12 mmol, neat) at – 78 °C produced the product as an 8:92 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *cis*-**22** (21.0 mg, 85 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99-7.94 (m, 2H), 7.58-7.52 (m, 1H), 7.48-7.42 (m, 2H), 4.42-4.33 (m, 1H), 3.86-3.77 (m, 1H), 3.43 (dd, 1H, *J* = 5.7, 15.9 Hz), 3.03 (dd, 1H, *J* = 7.5, 15.8Hz), 2.22-2.09 (m, 1H), 2.06-1.93 (m, 1H), 1.62-1.23 (m, 8H), 0.89 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 198.5, 137.2, 133.2, 128.6, 128.3, 79.8, 75.5, 45.5, 36.1, 31.7, 31.3, 28.6, 23.1, 14.4; IR (NaCl, neat) 2956, 2930, 2859, 1685, 1597, 1449, 1376, 1278, 1209, 1076, 1001, 753, 690 cm^{-1}; HRMS $[C_{16}H_{23}O_2]^+$ calcd 247.1698. Found 247.1698 (FAB+).

The stereochemistry of the starting material **21** was assigned by literature methods.[2] The stereochemistry of the products was determined based on one dimensional difference nOe experiments. The methine protons alpha to oxygen were irradiated. Qualitative enhancement of the nOe was observed only for *cis*-**22**.



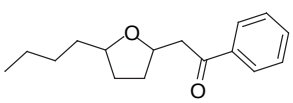
***trans*-2-(5-butyl-tetrahydo-furan-2-yl)-1-phenyl-ethanone (*trans-22*)**

According to general procedure **B**, vinyl acetal *trans*-**21** (25 mg, 0.10 mmol), Me_3Al (0.21 mL, 0.40 mmol) and BF_3•OEt_2 (16.0 μL, 0.12 mmol, neat) at – 78 °C produced the product as a 96:4 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded *trans*-**22** (21.0 mg, 85 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2H), 7.59-7.54 (m, 1H), 7.49-7.43 (m, 2H), 4.57-4.48 (m, 1H), 4.02-3.93 (m, 1H), 3.42 (dd, 1H, *J* = 5.7, 16.2 Hz), 3.04 (dd, 1H, *J* = 7.8, 16.2 Hz), 2.30-2.16 (m, 1H), 2.11-1.98 (m, 1H), 1.66-1.22 (m, 8H), 0.90 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 198.6, 137.2, 133.2, 128.7, 128.3, 79.2, 75.0, 45.3, 35.9, 32.6, 32.2, 28.6, 23.1, 14.4; IR (NaCl, neat) 2957, 2930, 2859, 1684, 1449, 1279, 1209, 1064, 1000, 753, 690 cm^{-1}; HRMS $[C_{16}H_{22}O_2]^+$ calcd 247.1698. Found 247.1699 (FAB+).



2-(5-butyl-tetrahydo-furan-2-yl)-1-phenyl-ethanone (*cis* and *trans-22*)

According to general procedure **A**, vinyl acetal *cis*-**21** (12 mg, 0.05 mmol) and BF_3•OEt_2 (8.0 μL, 0.06 mmol, neat) at – 78 °C produced the product as a 1:2 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexane[3]s) afforded a mixture of *trans and cis*-**22** (11.0 mg, 92 %).



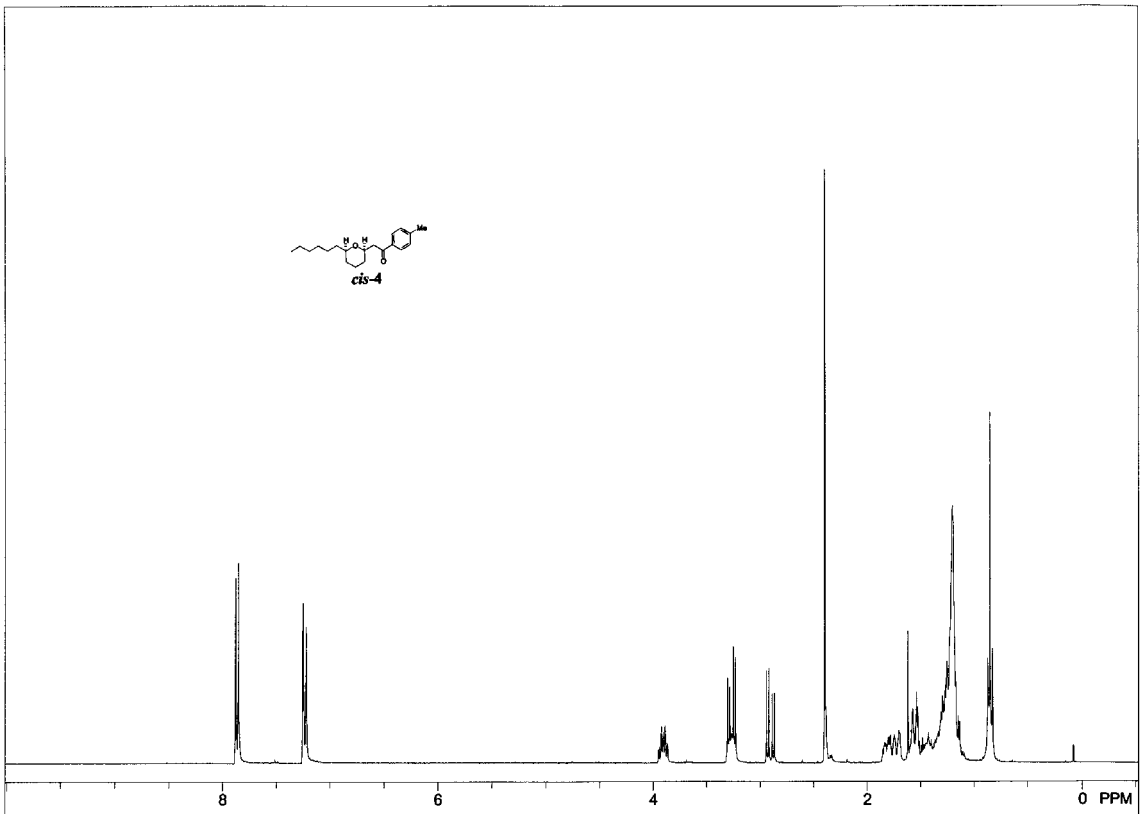
2-(5-butyl-tetrahydo-furan-2-yl)-1-phenyl-ethanone (*cis* and *trans-22*)

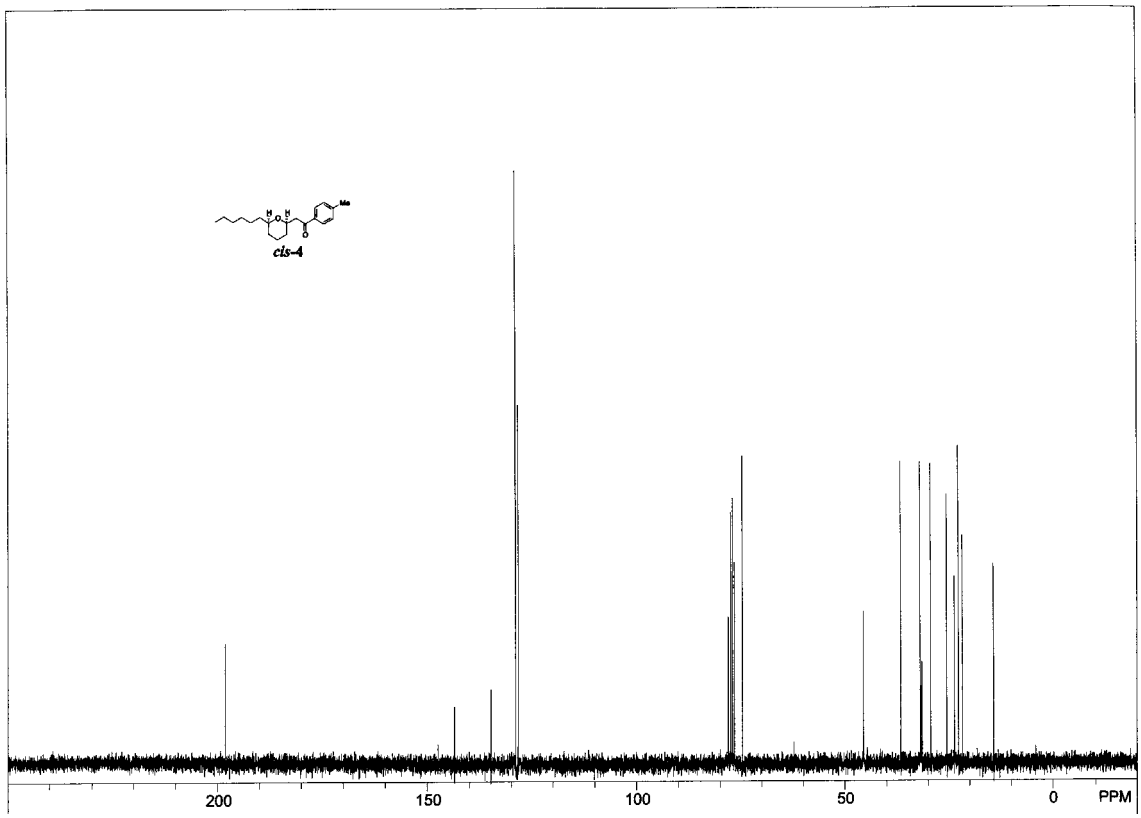
According to general procedure **A**, vinyl acetal *trans*-**21** (12 mg,

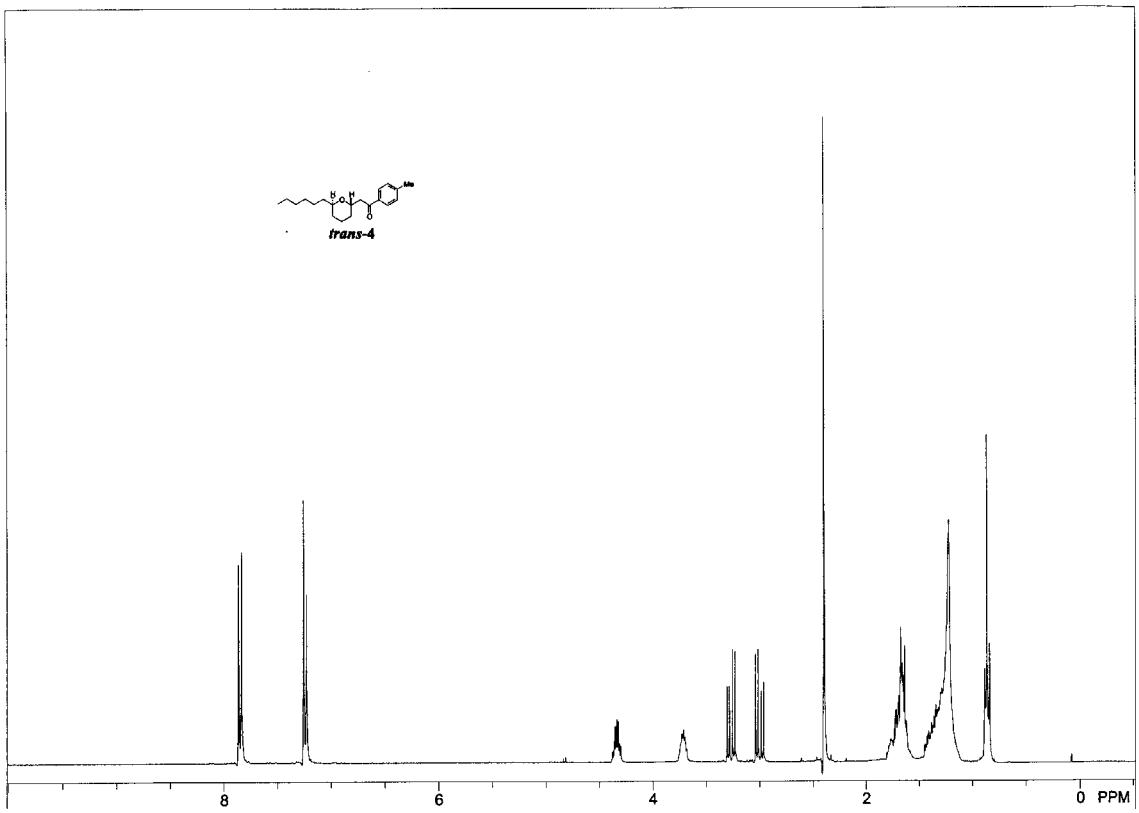
0.05 mmol) and BF_3•OEt_2 (8.0 μL, 0.06 mmol, neat) at – 78 °C produced the product as a 1:2 mixture of isomers (*trans/cis*). Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded a mixture of *trans and cis*-**22** (10.8 mg, 90 %).

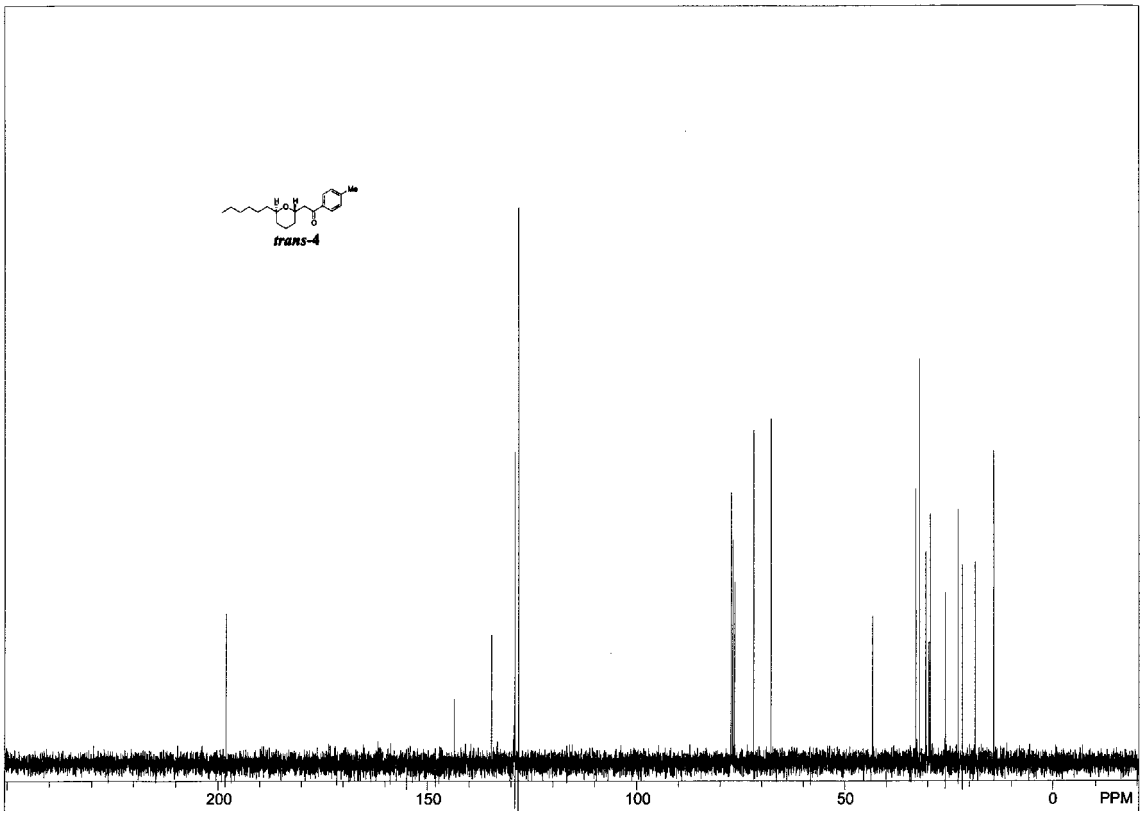
^{1}H and ^{13}C NMR spectra of new compounds are attached:

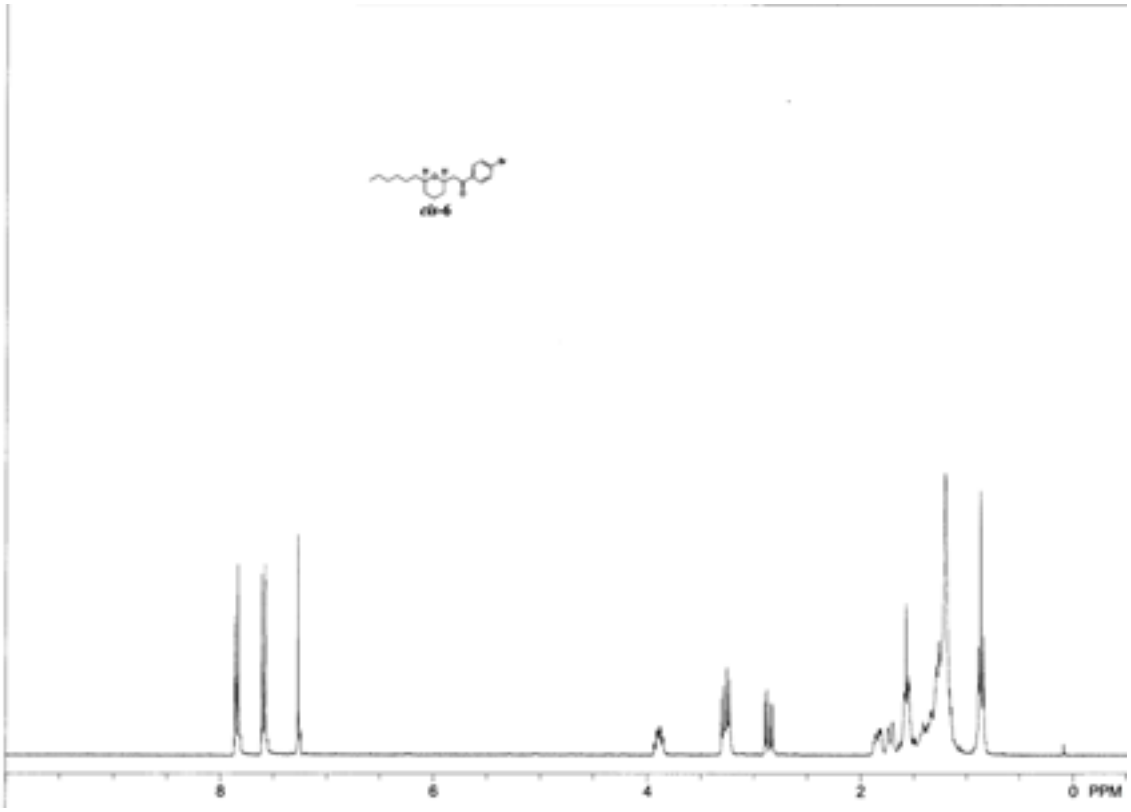
Spectra for New Compounds:

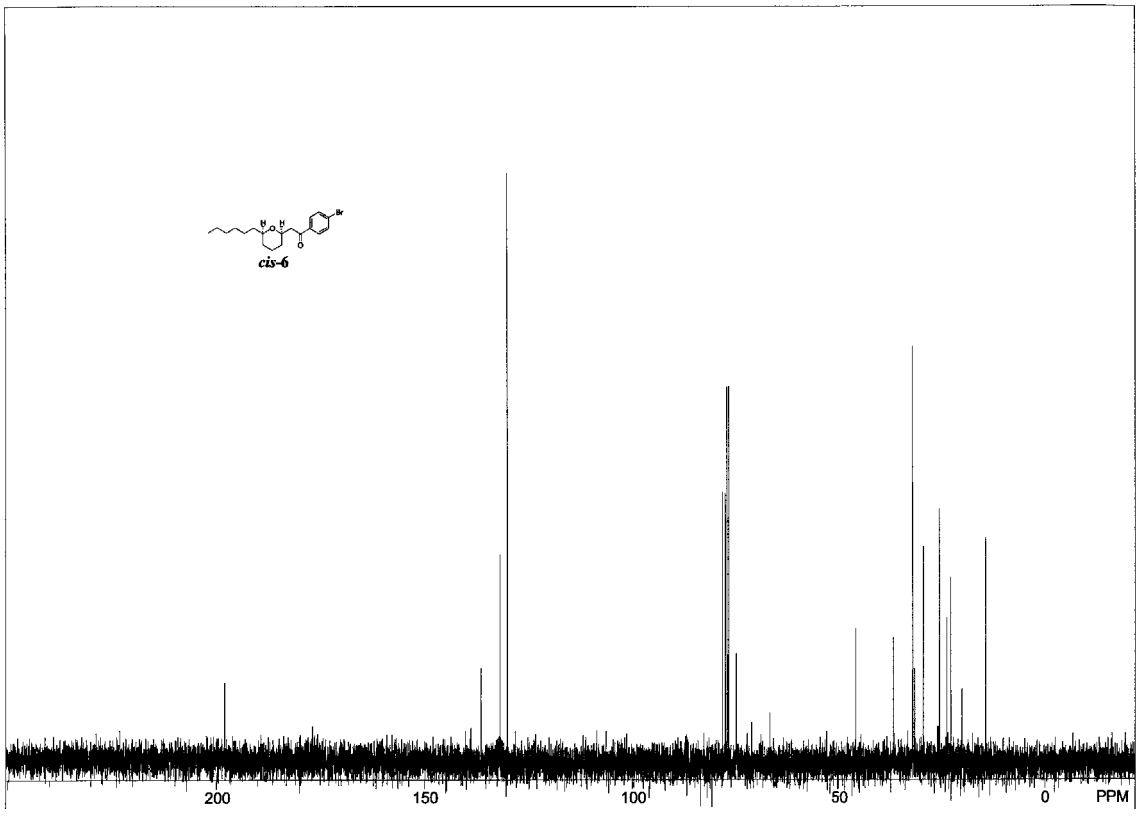


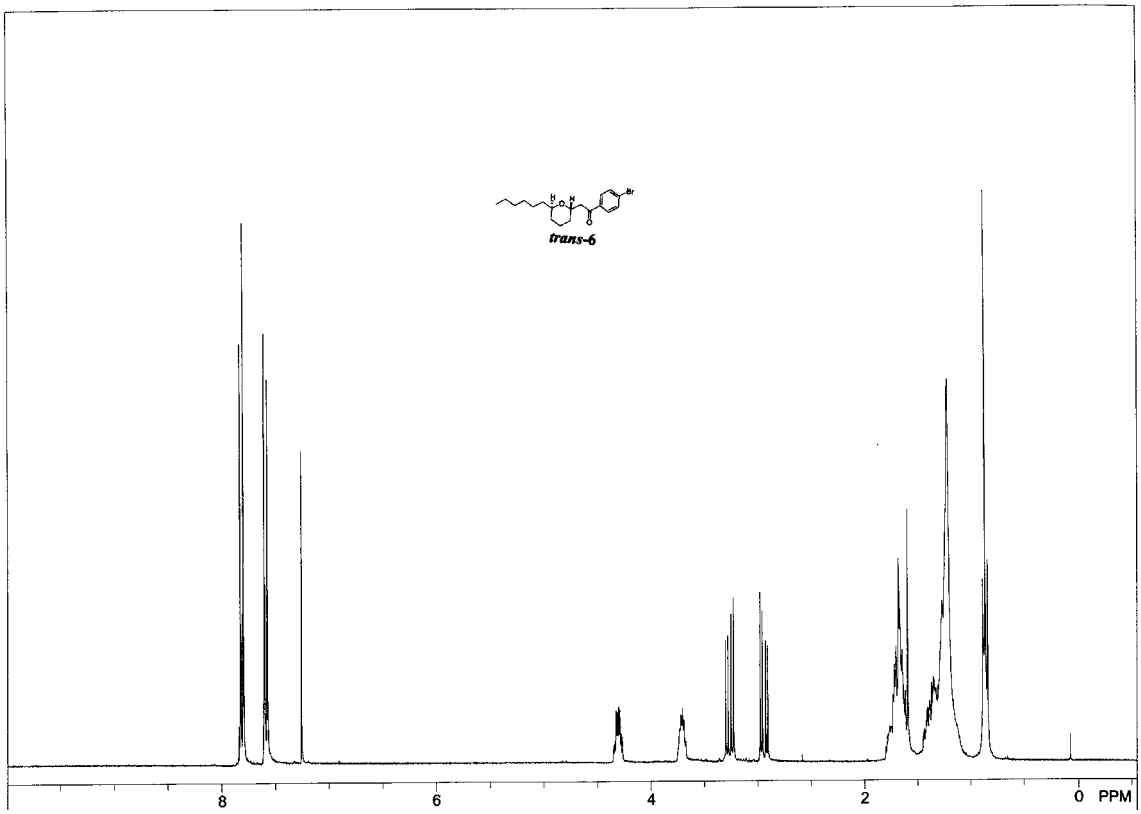


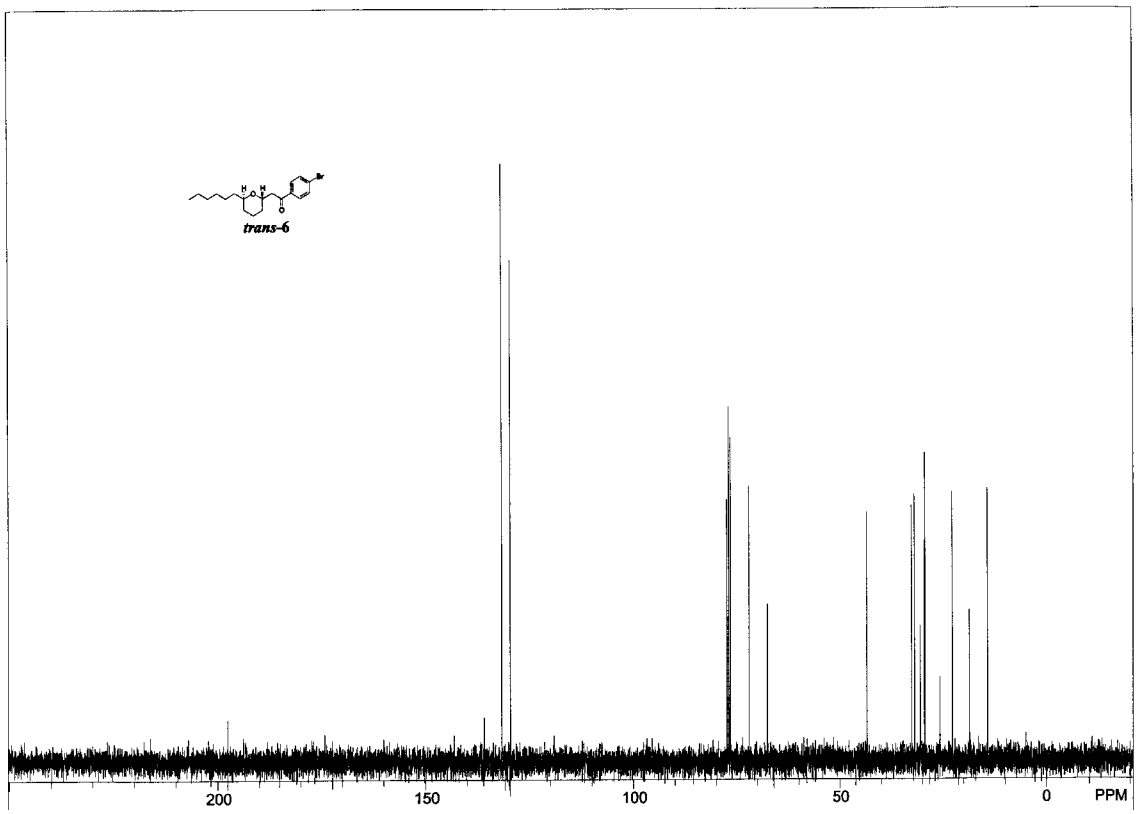

trans-4
8
6
4
2
0 PPM

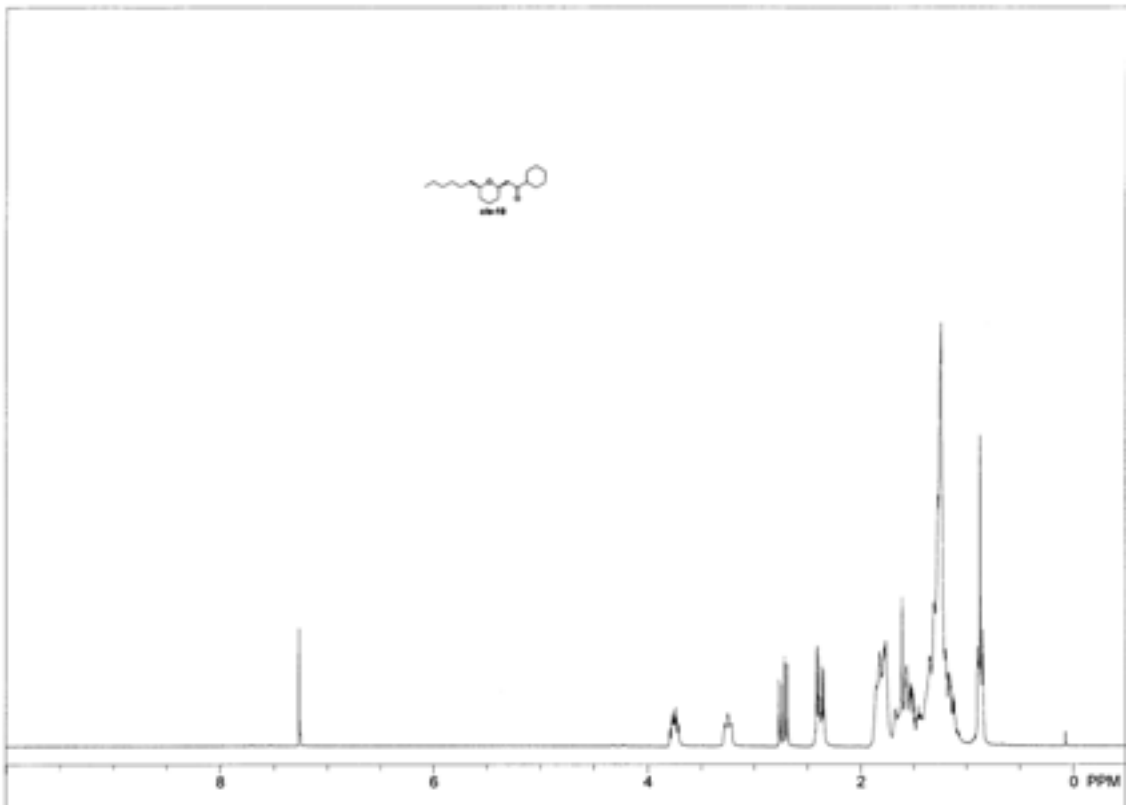

trans-4
200
150
100
50
0 PPM

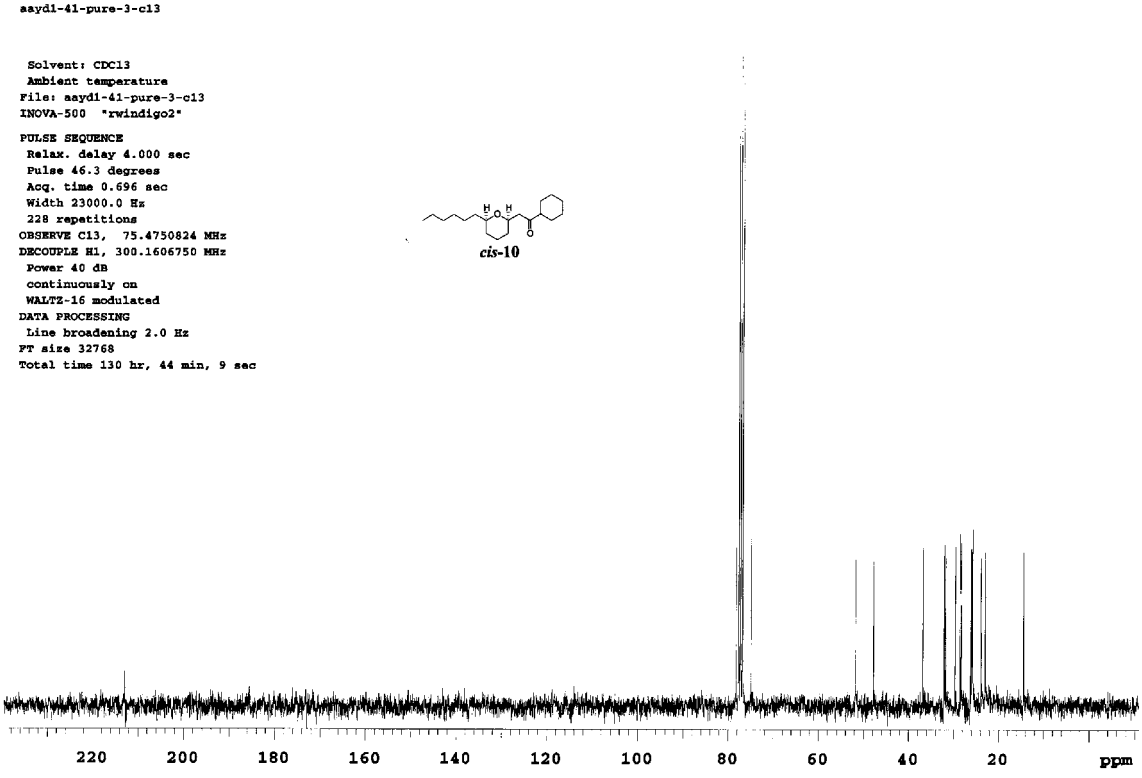

8
6
4
2
0 PPM

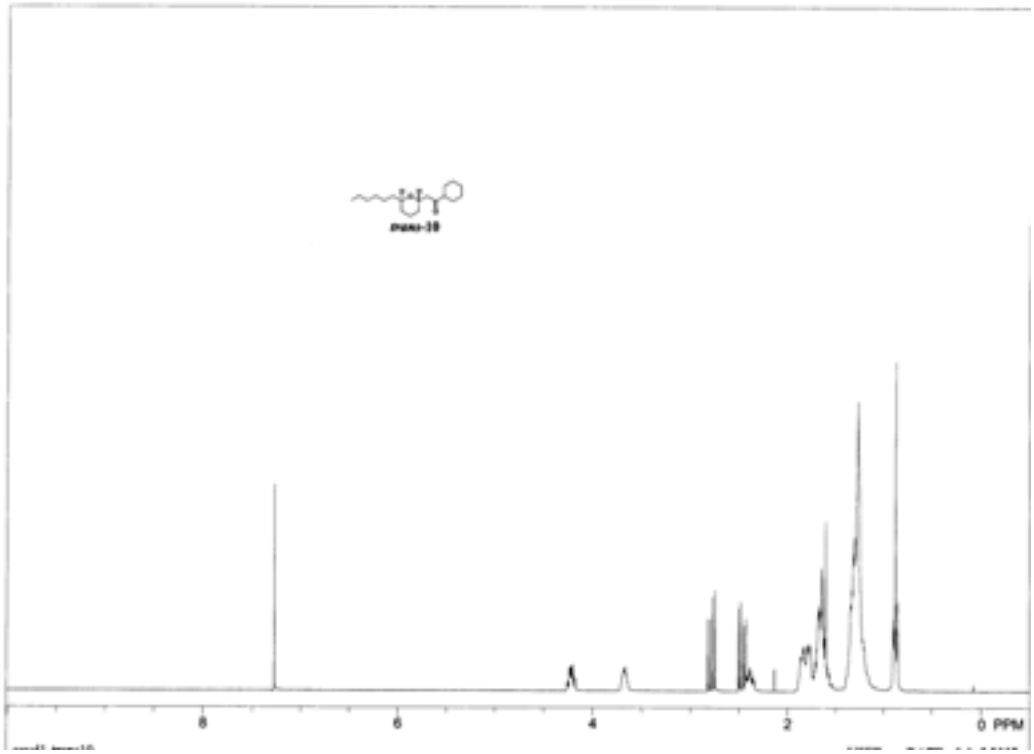

cis-6
200
150
100
50
0
PPM


trans-6
8
6
4
2
0 PPM


trans-6
200
150
100
50
0 PPM


8
6
4
2
0 PPM

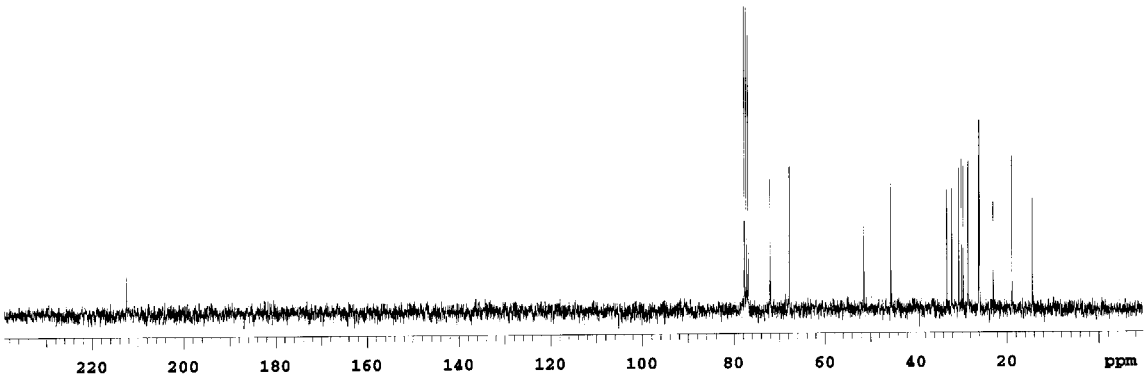

asyd1-41-pure-3-c13
Solvent: CDCl3
Ambient temperature
File: asyd1-41-pure-3-c13
INOVA-500 "rwindigo2"
PULSE SEQUENCE
Relax. delay 4.000 sec
Pulse 46.3 degrees
Acq. time 0.696 sec
Width 23000.0 Hz
228 repetitions
OBSERVE C13, 75.4750824 MHz
DECOUPLE H1, 300.1606750 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 32768
Total time 130 hr, 44 min, 9 sec
cis-10
220
200
180
160
140
120
100
80
60
40
20
ppm

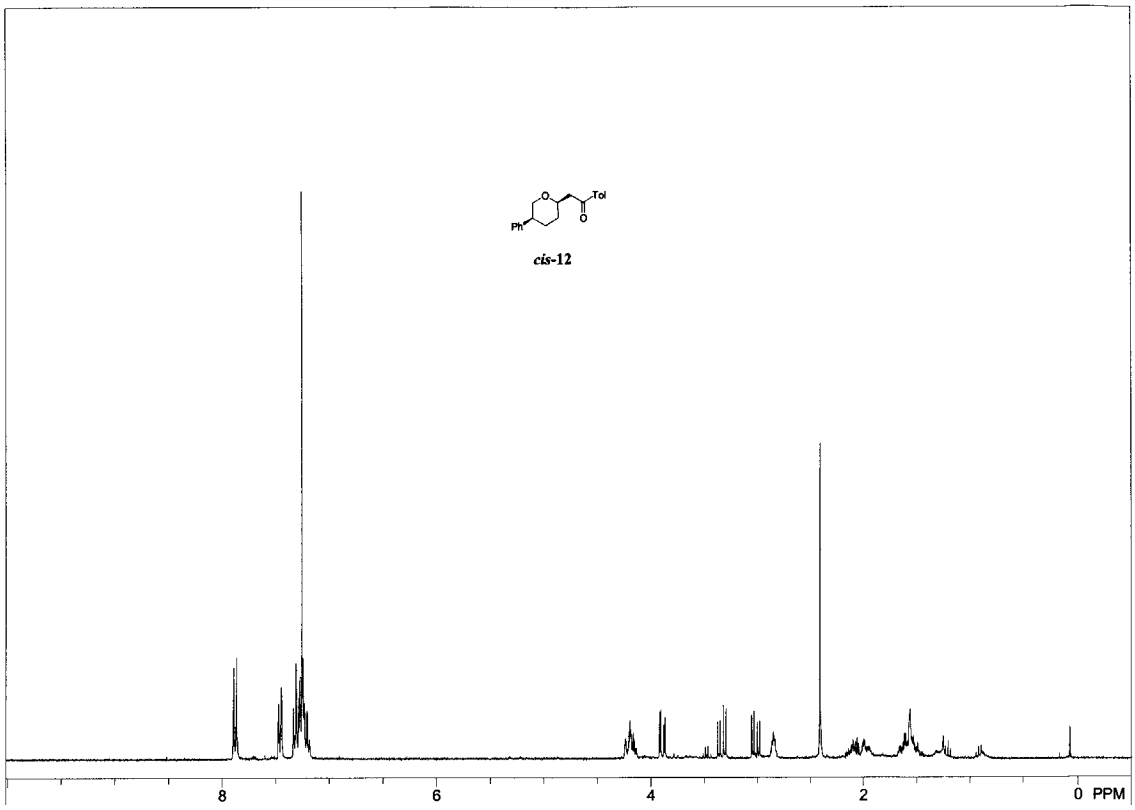


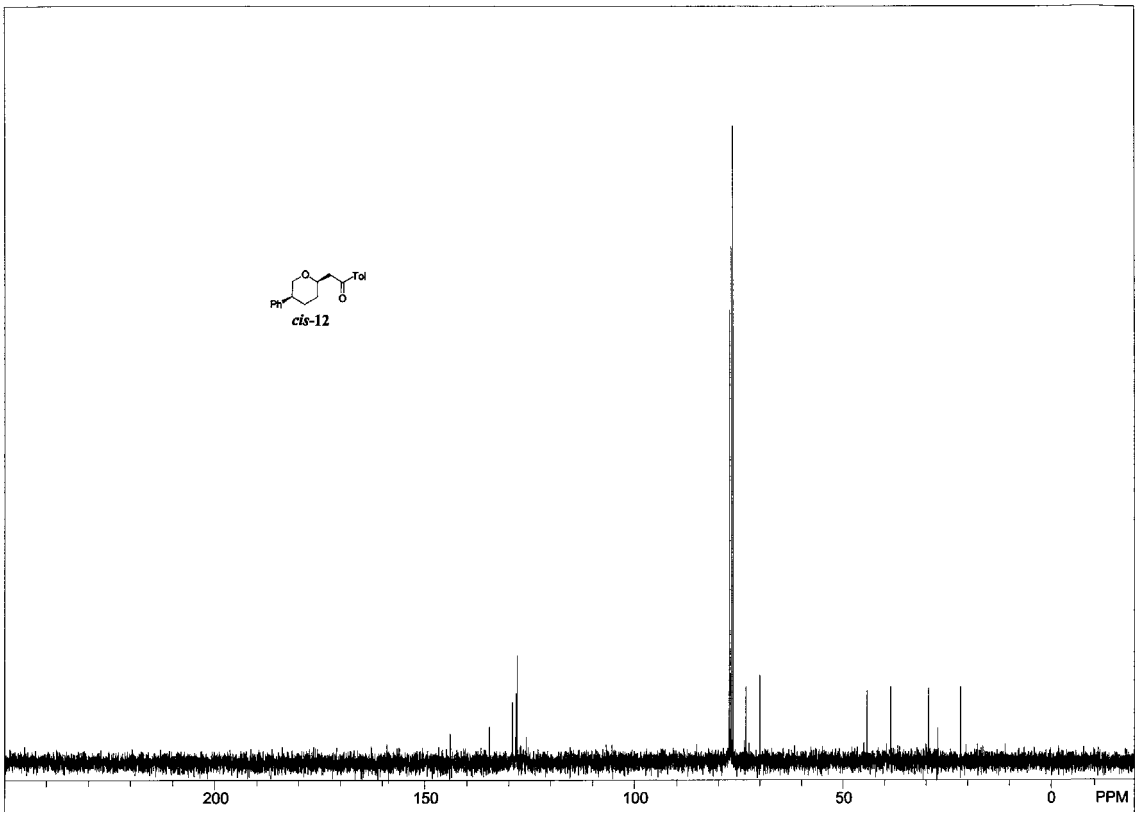
aaydl-translo-cl3

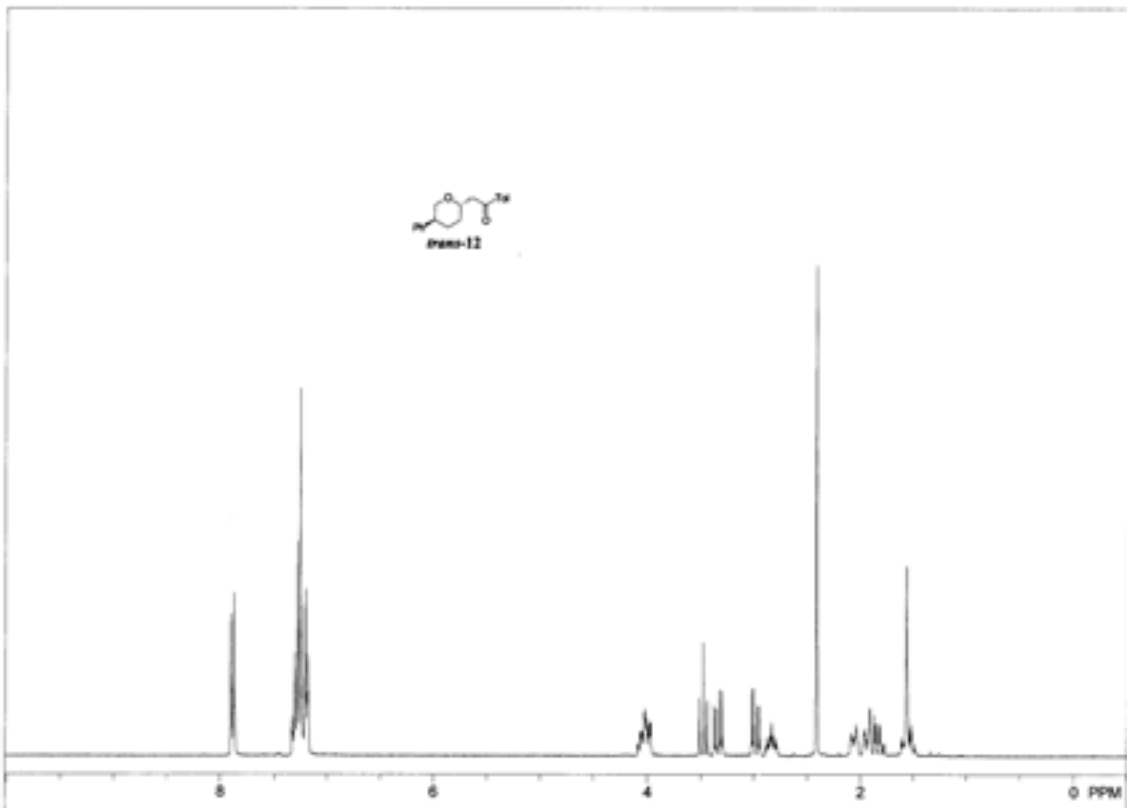
Solvent: CDCl3
Ambient temperature
File: aaydl-transl0-cl3
INOVA-500 "rwindigo2"

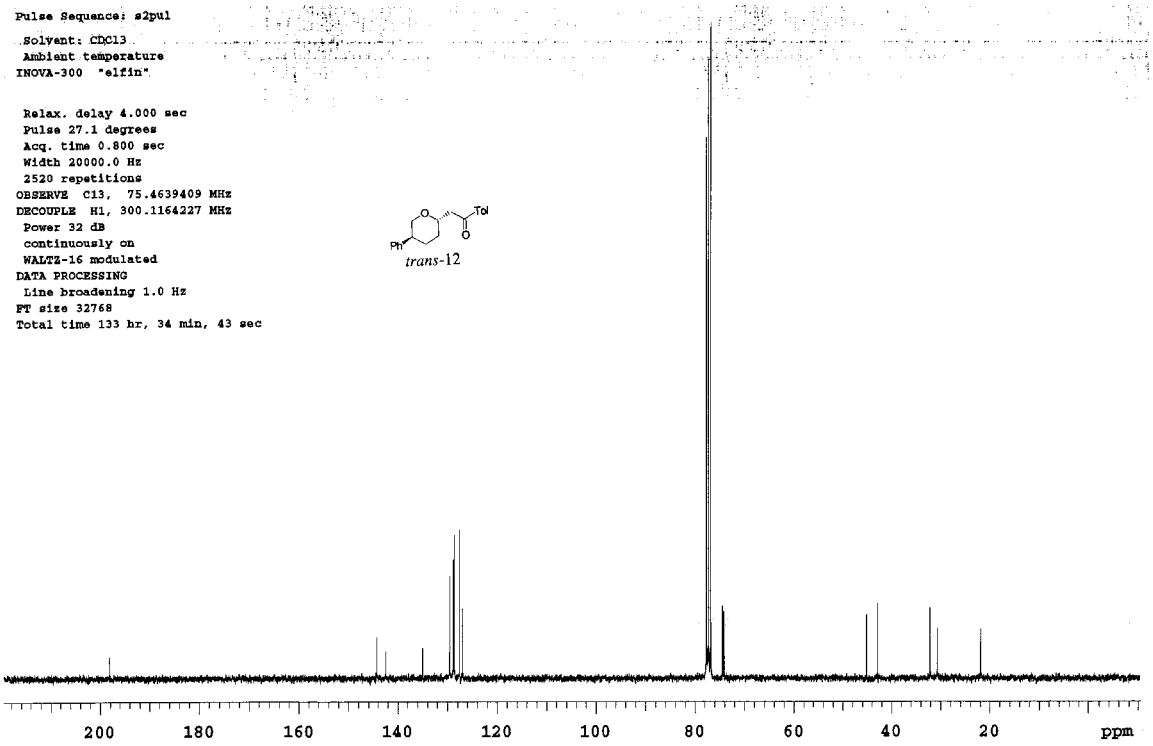
PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 46.3 degrees
Acq. time 0.696 sec
Width 23000.0 Hz
348 repetitions
OBSERVE C13, 75.4750824 MHz
DECOUPLE H1, 300.1606750 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 32768
Total time 47 hr, 24 min, 9 sec

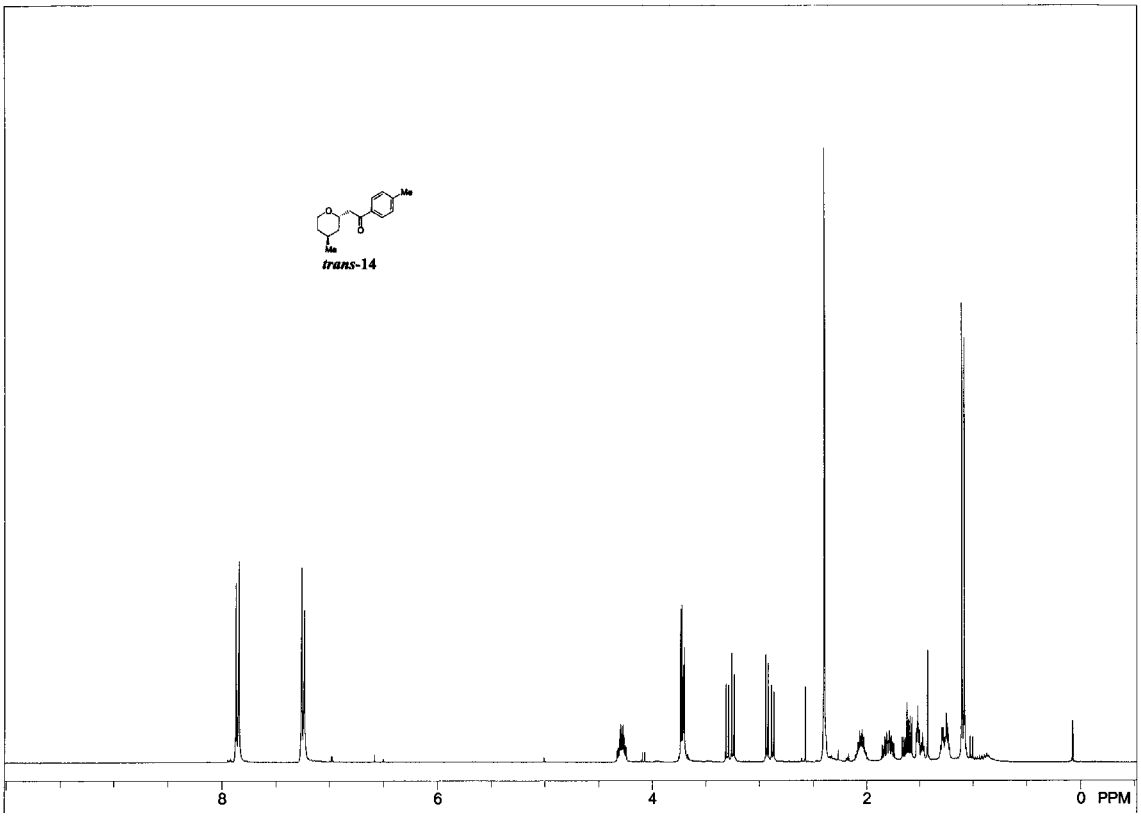


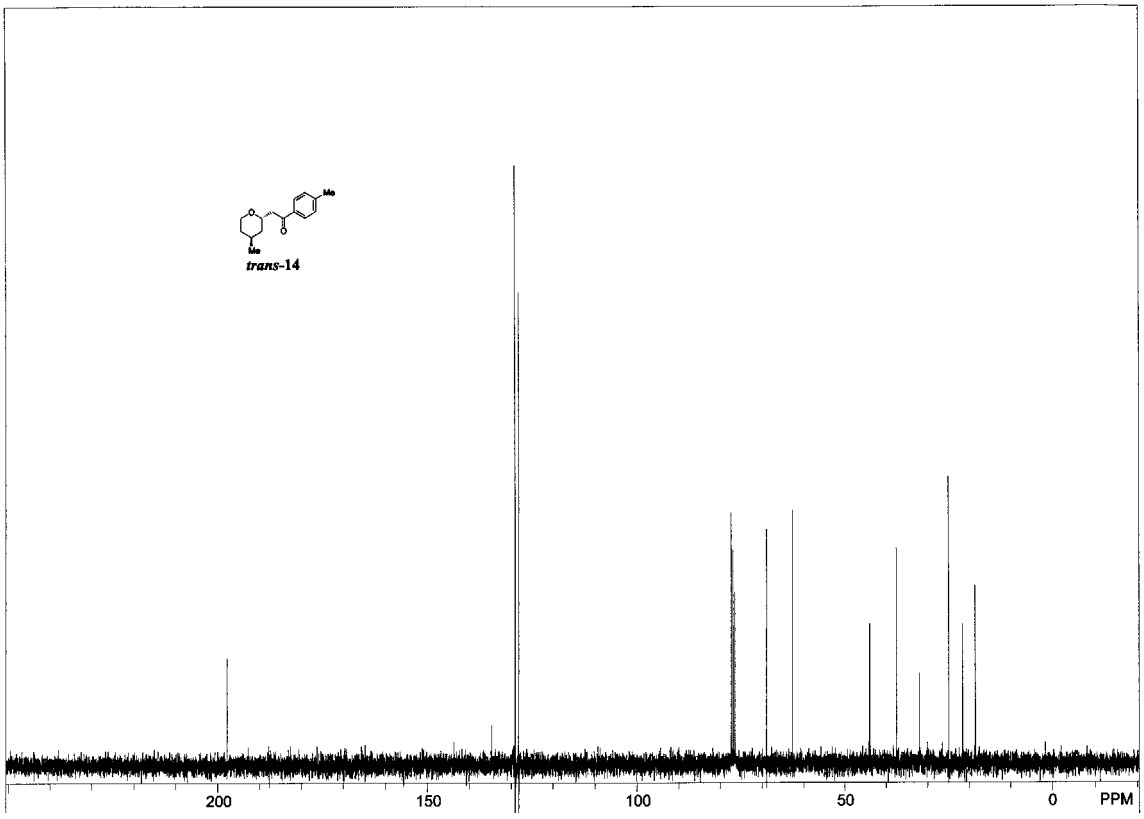

Ph
O
Tol
O
cis-12
8
6
4
2
0 PPM

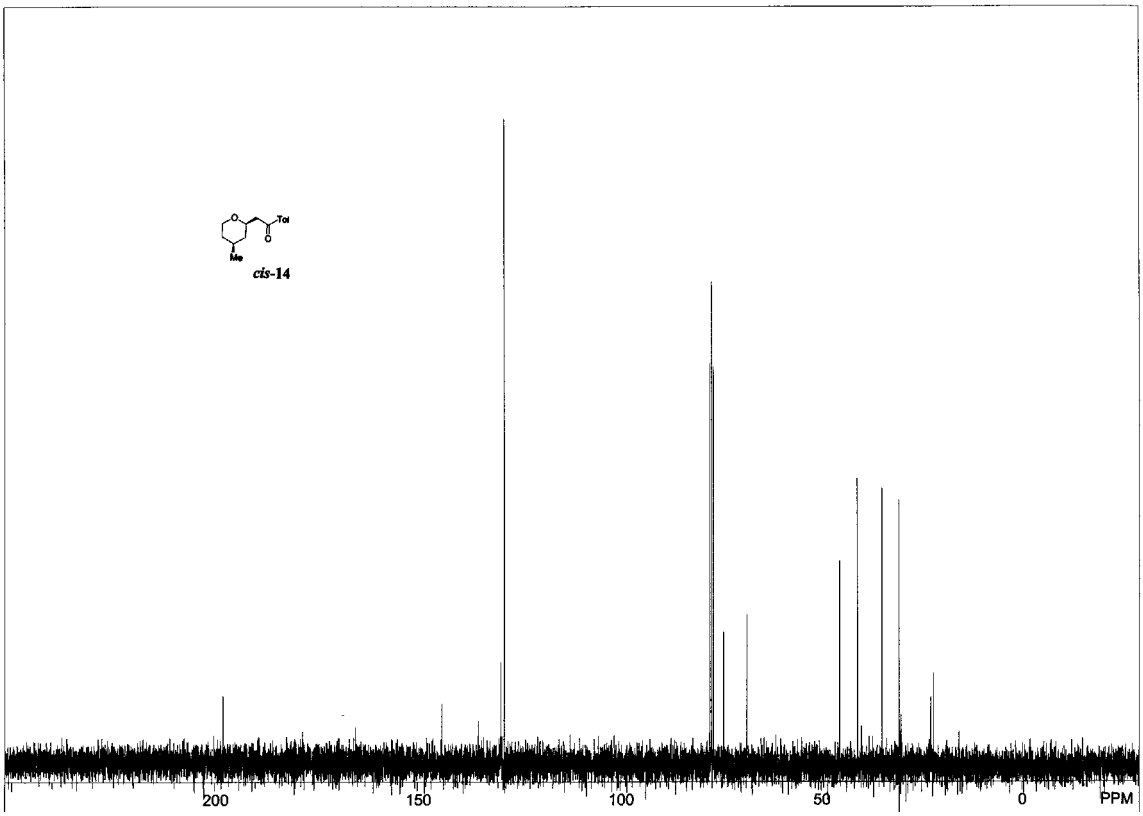

Ph
O
Tol
O
cis-12
200
150
100
50
0 PPM

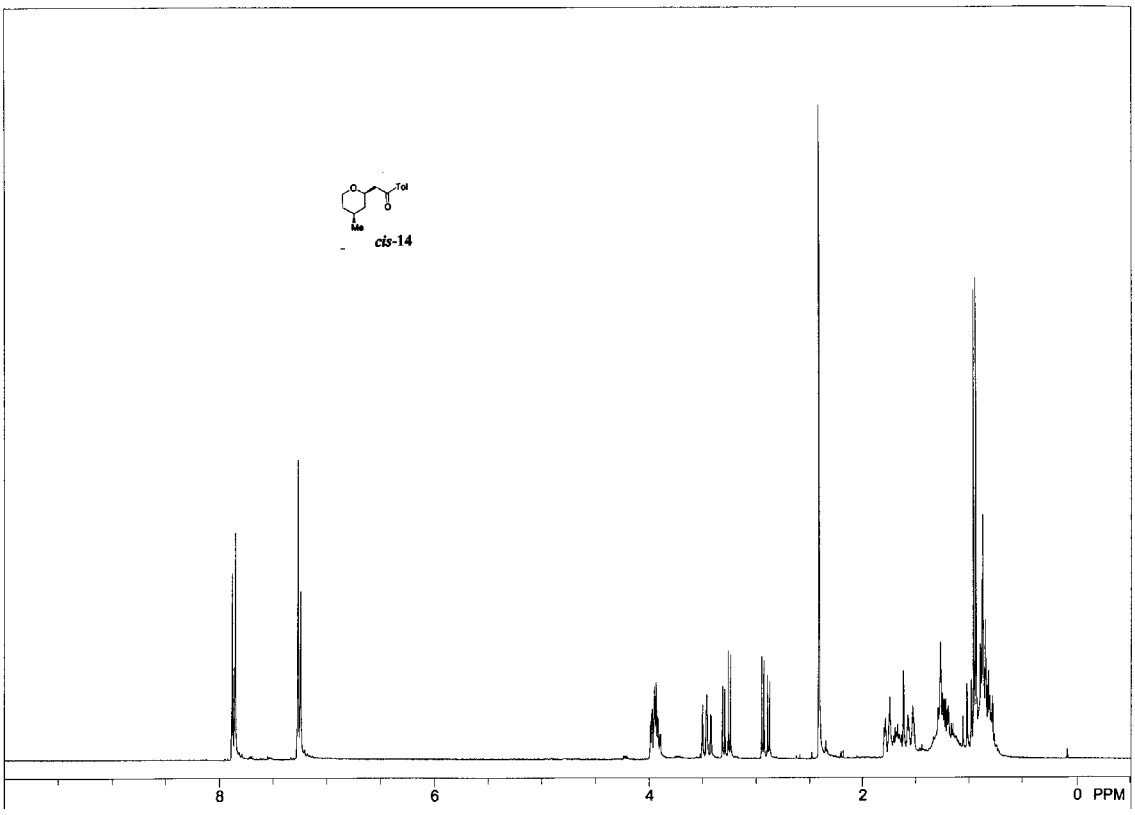

trans-12
8
6
4
2
0 PPM

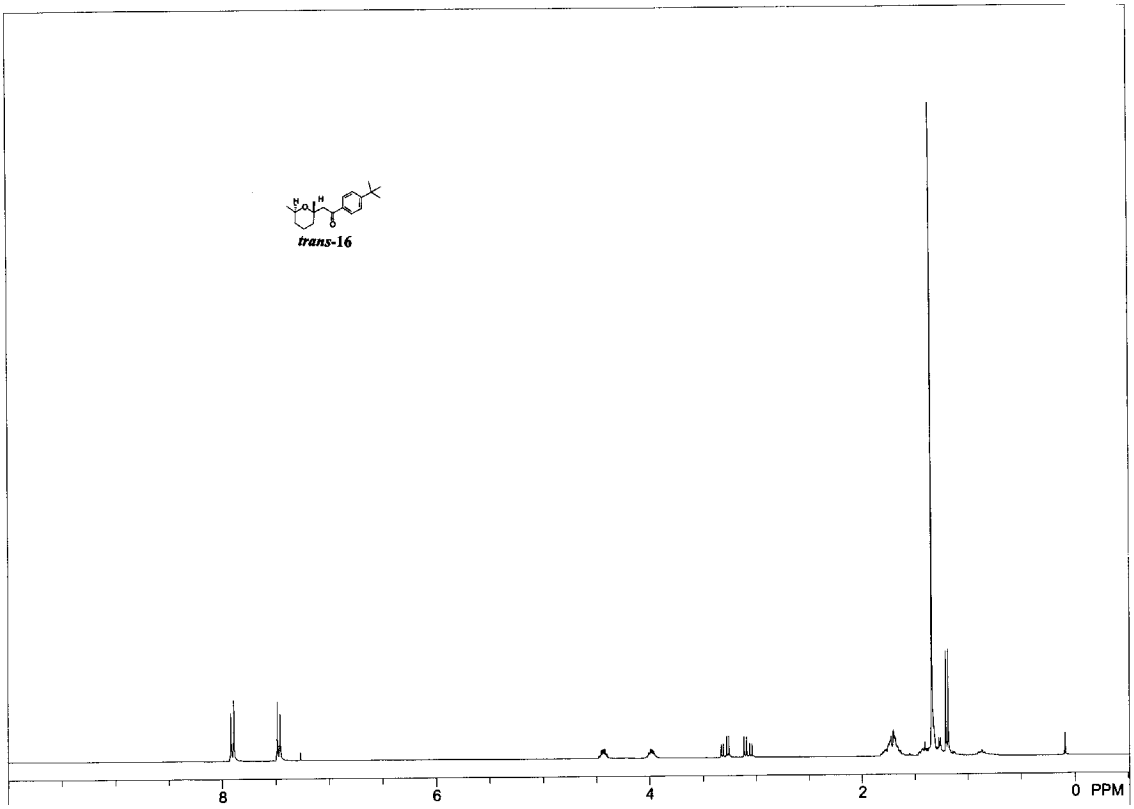

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "elfin"
Relax. delay 4.000 sec
Pulse 27.1 degrees
Acq. time 0.800 sec
Width 20000.0 Hz
2520 repetitions
OBSERVE C13, 75.4639409 MHz
DECOUPLE H1, 300.1164227 MHz
Power 32 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 32768
Total time 133 hr, 34 min, 43 sec
trans-12
200
180
160
140
120
100
80
60
40
20
ppm

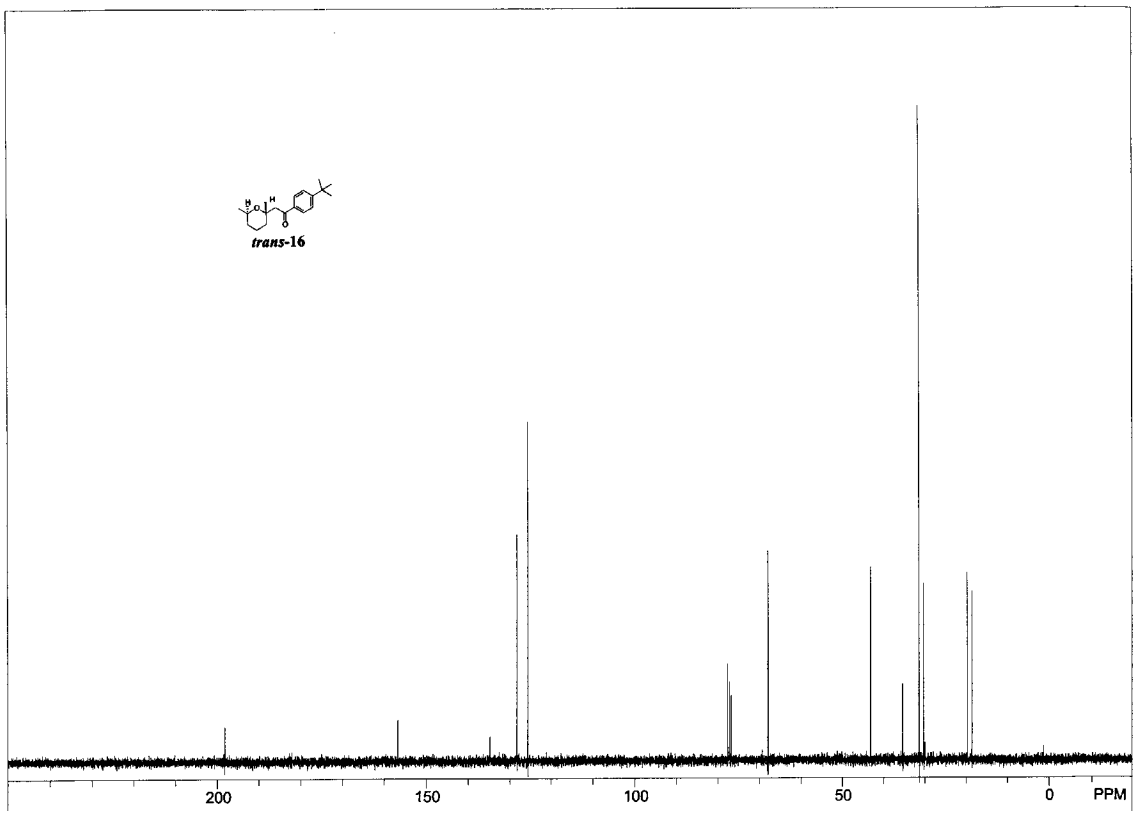

trans-14
8
6
4
2
0 PPM

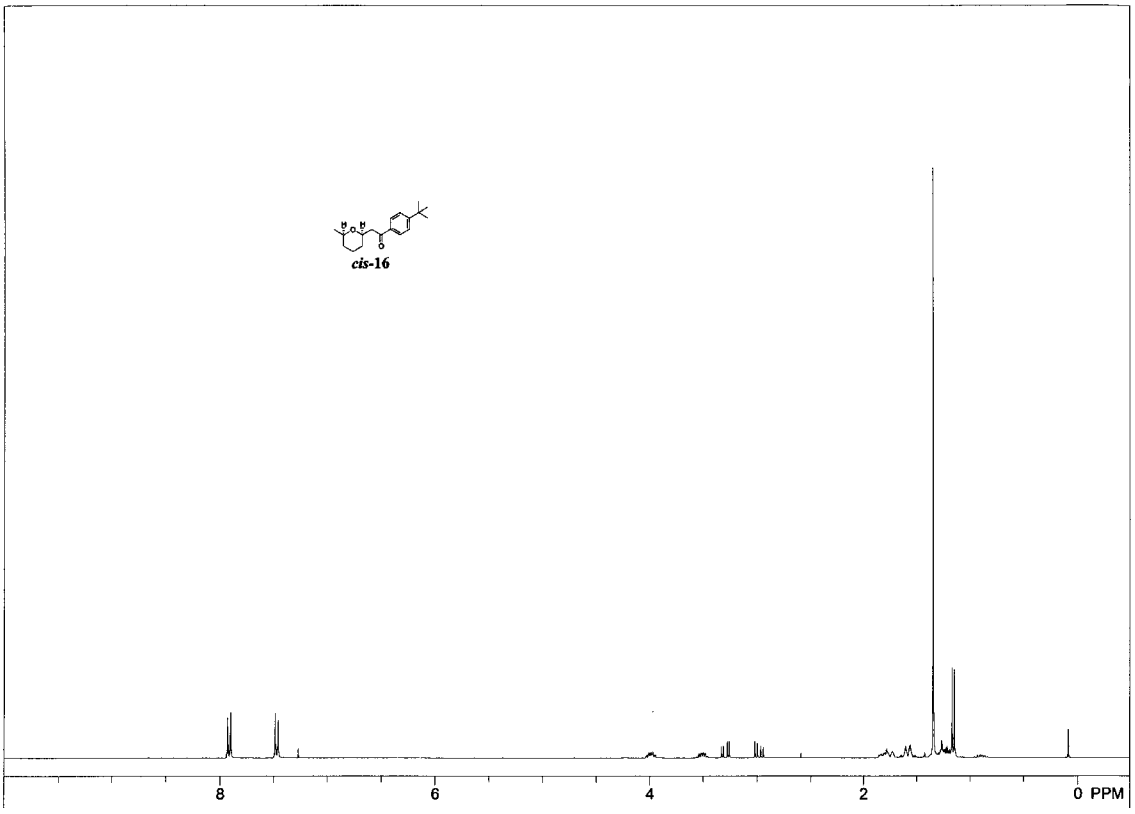

trans-14
200
150
100
50
0 PPM

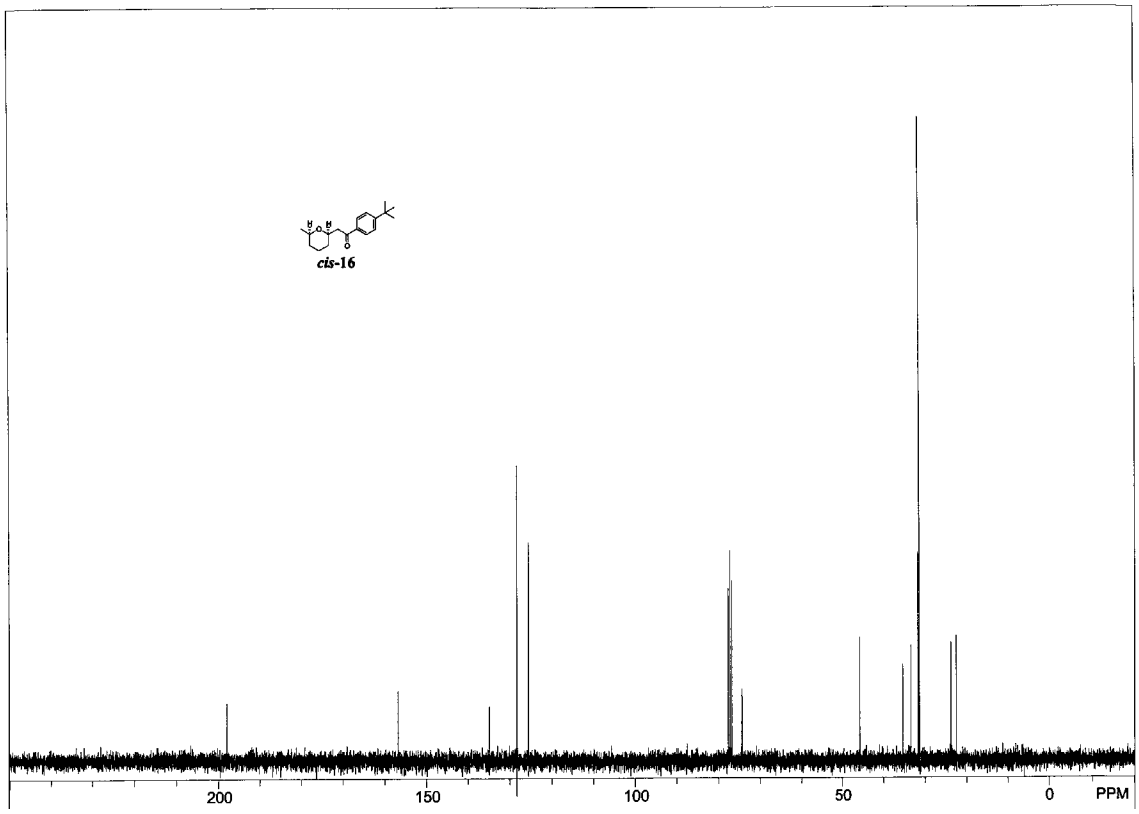

Tol
Me
cis-14
200
150
100
50
0
PPM

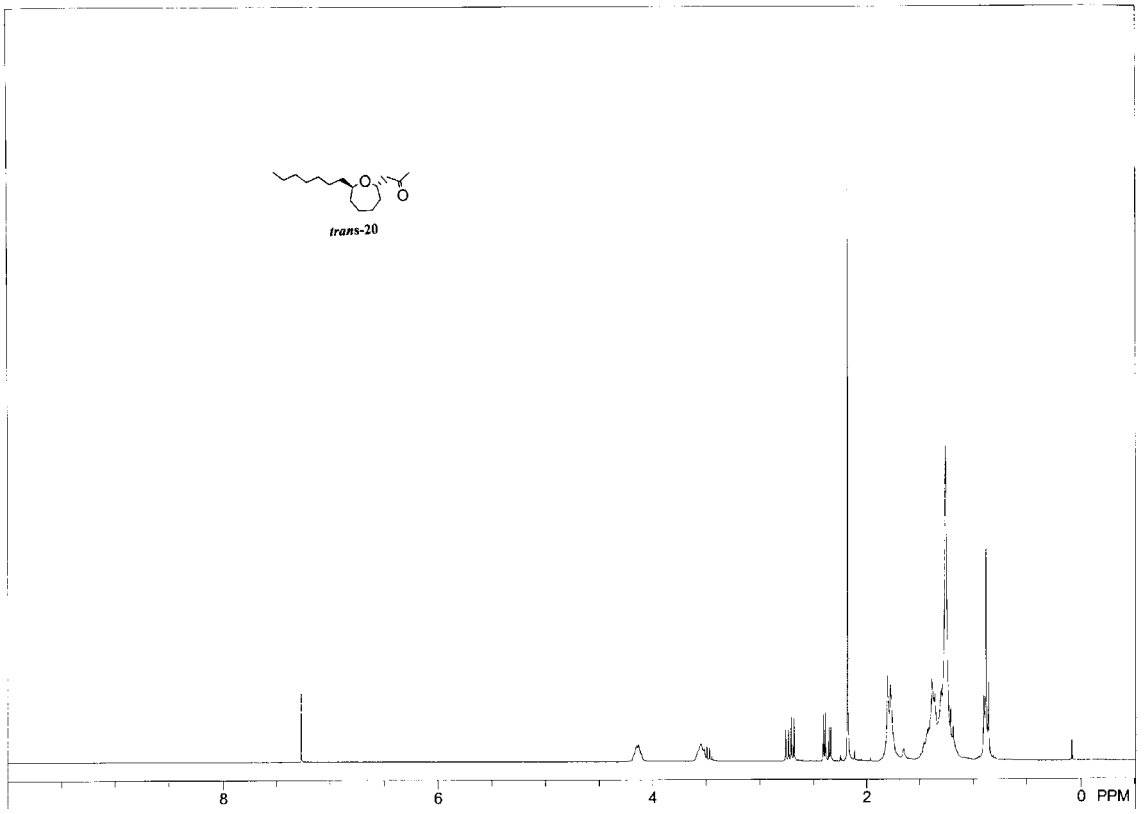

Tol
Me
cis-14
8
6
4
2
0 PPM

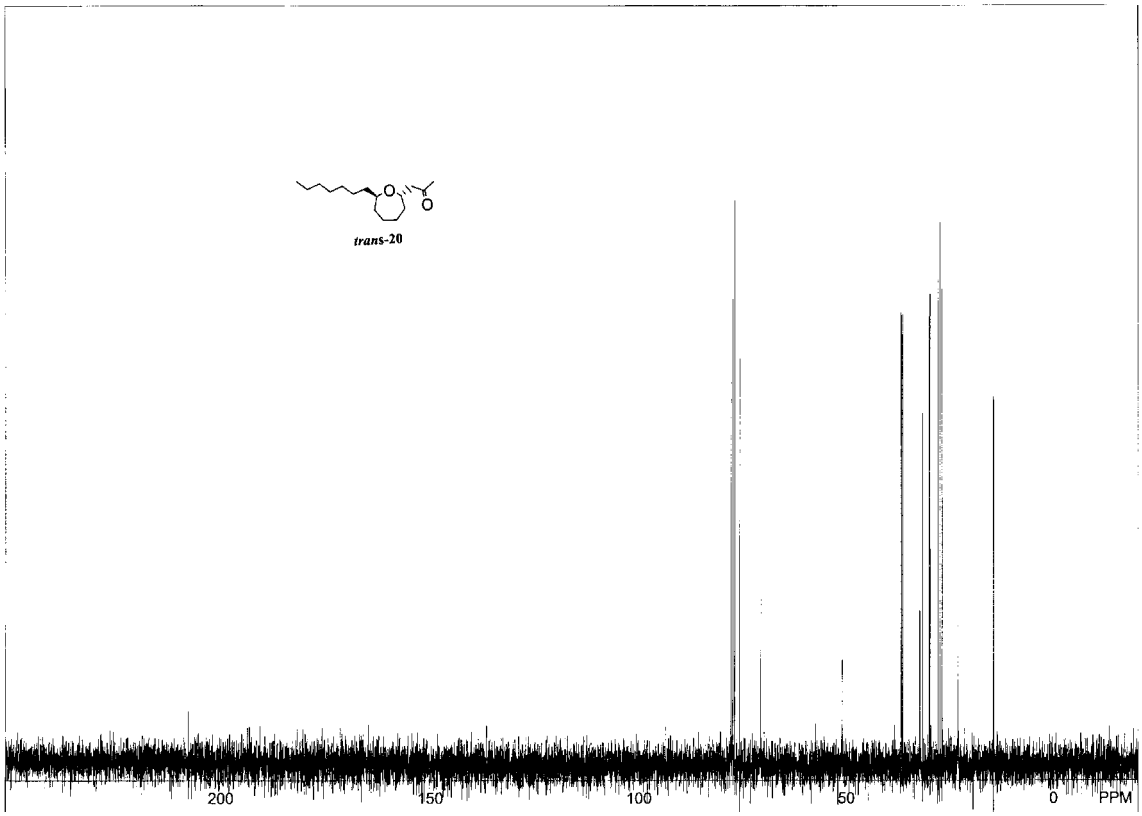

trans-16
8
6
4
2
0 PPM

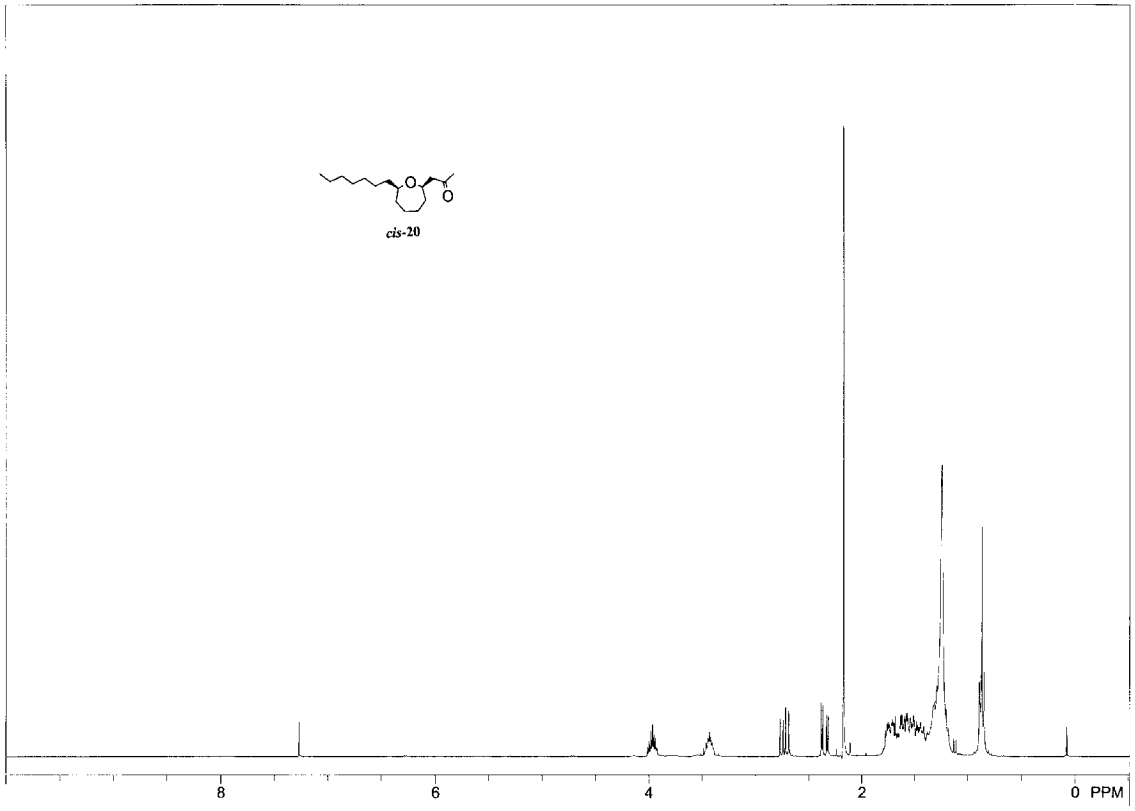

trans-16
200
150
100
50
0
PPM

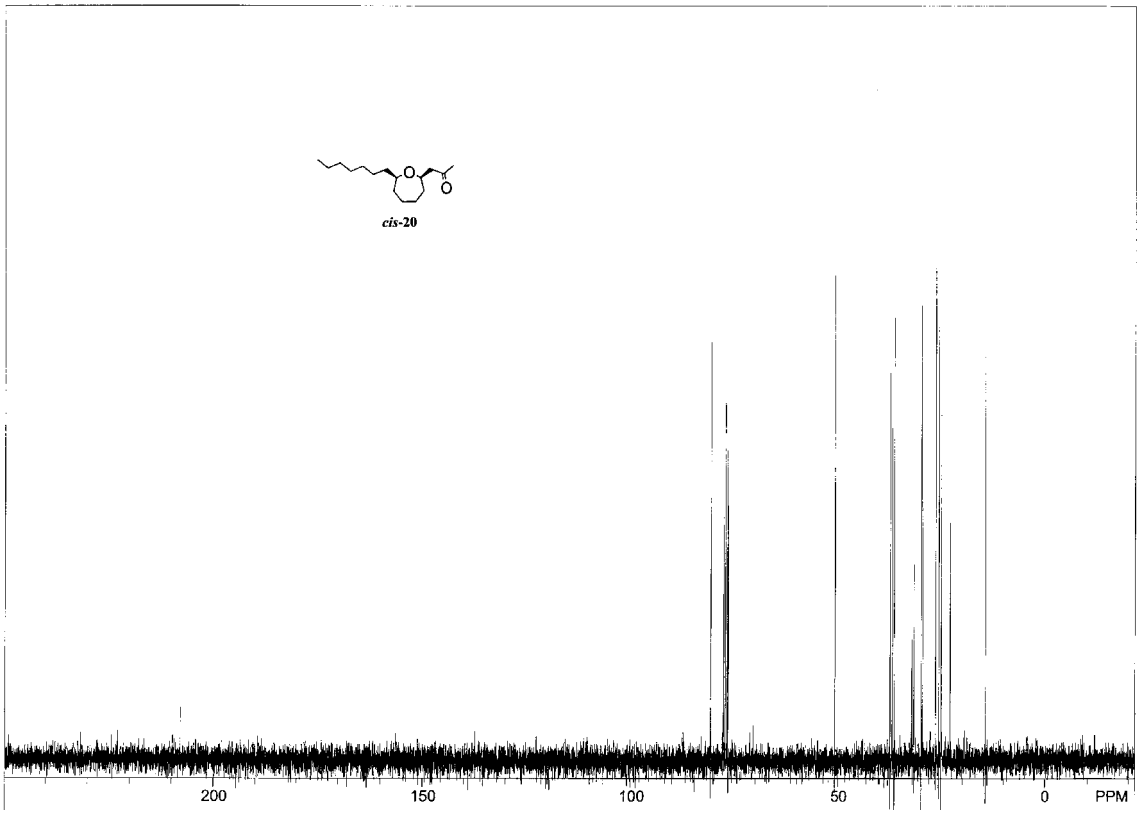

cis-16
8
6
4
2
0 PPM

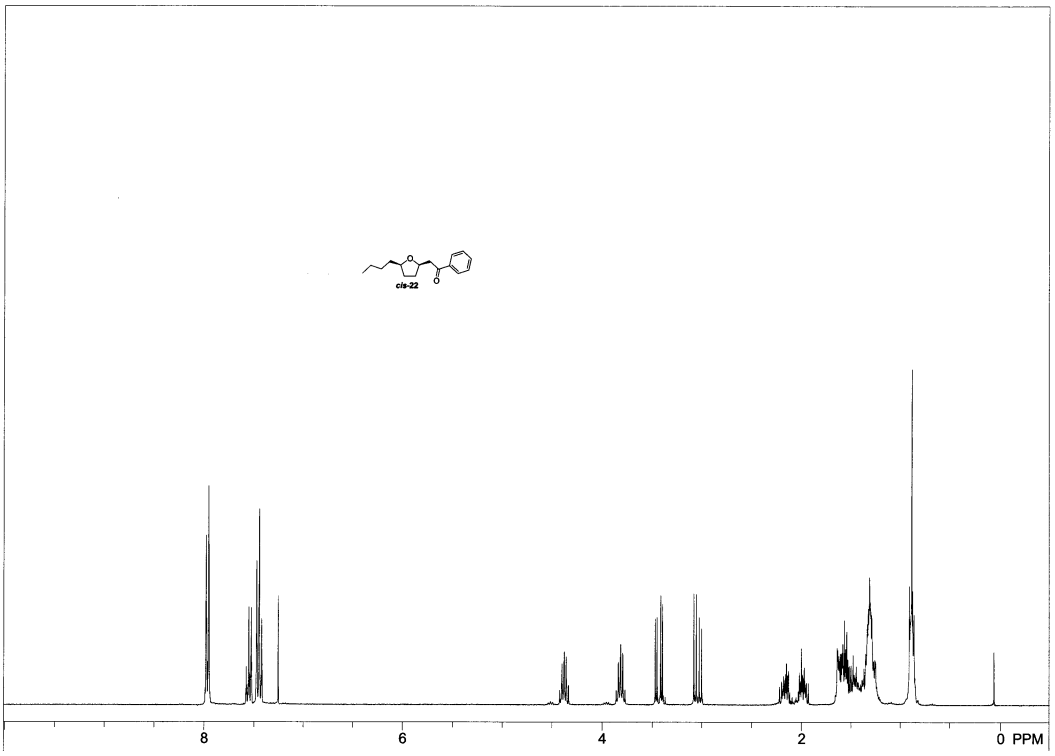

cis-16
200
150
100
50
0
PPM

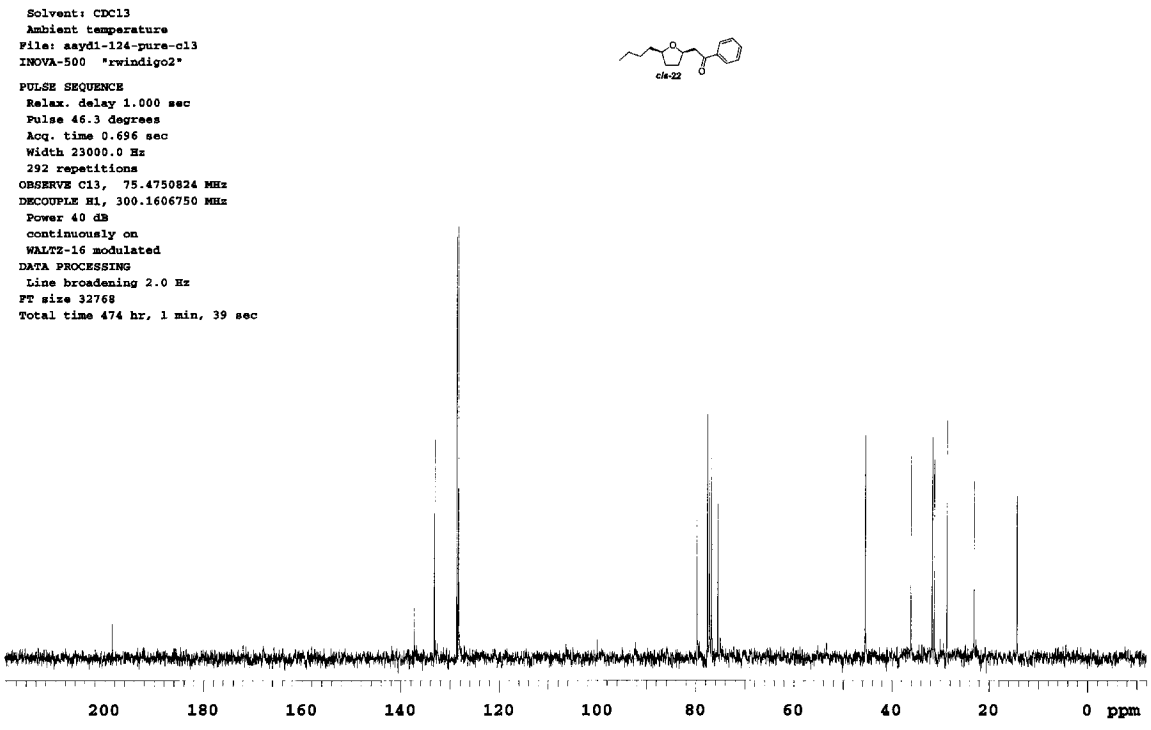

trans-20
8
6
4
2
0 PPM

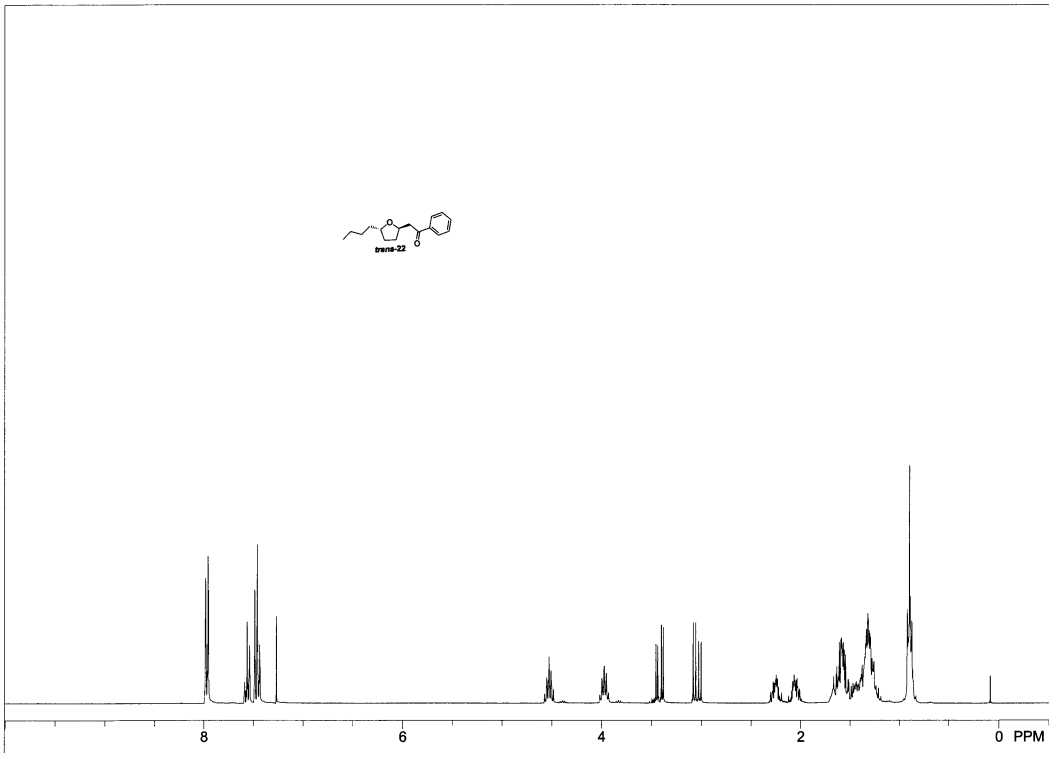

trans-20
200
150
100
50
0
PPM

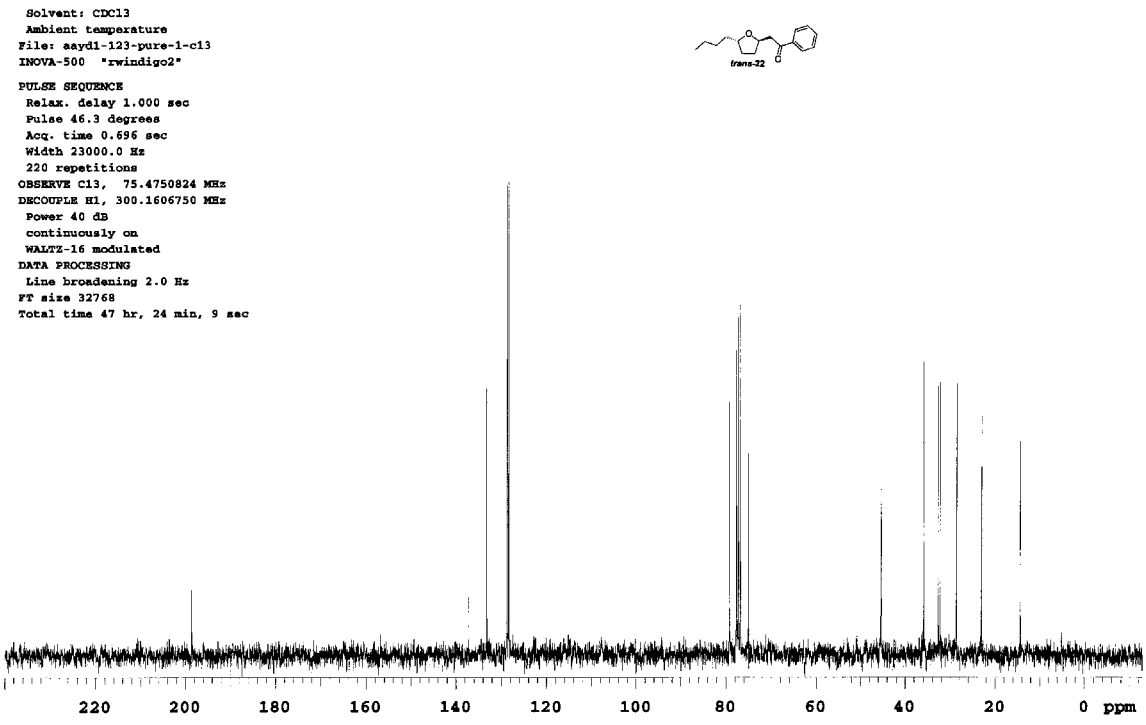

cis-20
8
6
4
2
0 PPM


cis-20
200
150
100
50
0 PPM


cis-22
8
6
4
2
0 PPM


Solvent: CDCl3
Ambient temperature
File: aaydi-124-pure-c13
INOVA-500 "rwindigo2"
PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 46.3 degrees
Acq. time 0.696 sec
Width 23000.0 Hz
292 repetitions
OBSERVE C13, 75.4750824 MHz
DECOUPLE H1, 300.1606750 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 32768
Total time 474 hr, 1 min, 39 sec
cis-22
200
180
160
140
120
100
80
60
40
20
0 ppm


trans-22
8
6
4
2
0 PPM


Solvent: CDCl3
Ambient temperature
File: aayd1-123-pure-1-c13
INOVA-500 "rwindigo2"
PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 46.3 degrees
Acq. time 0.696 sec
Width 23000.0 Hz
220 repetitions
OBSERVE C13, 75.4750824 MHz
DECOUPLE H1, 300.1606750 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 32768
Total time 47 hr, 24 min, 9 sec
trans-22
220
200
180
160
140
120
100
80
60
40
20
0 ppm