Supporting Information for Angew. Chem. Int. Ed. Z17943

Novel Ene-like Cycloisomerization Reaction of Nitrile Oxides Tethered to Allyltrimethylsilane

Teruhiko Ishikawa,* Jin Urano, Shushiro Ikeda, Yasuhiro Kobayashi, and Seiki Saito*

Department of Bioscience and Biotechnology, Faculty of Engineering, Okayama University, Tsushima, Okayama, Japan 700-8530

e-mail: seisaito@biotech.okayama-u.ac.jp

Experimental Section

Instrumentation. IR spectra ware recorded on a Horiba Fourier transform infrared spectrophotometer Model FT-210 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Mercury-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) instrument. The chemical shifts are given in δ unit relative to internal $CHCl_3$ (7.26 ppm for ^{1}H) or $CDCl_3$ (77 ppm for ^{13}C). All NMR experiments were performed using deuteriochloroform as a solvent unless otherwise indicated. Mass spectra were obtained on a JEOL JMS-DX303 instrument relying on a JMA-DA5000 mass data system. Elemental analyses were made with a Perkin-Elmer 2400 CHN Elemental Analyzer.

Analytical Procedure and Data Presentation. Analytical thin layer chromatography was performed on Merck precoated silica gel 60 F-254 (0.25 mm thickness). ^{1}H NMR spectral data were indicated in the form: δ value of signal (peak multiplicity, integrated number of protons and coupling constant (if any)). Splitting patterns are abbreviated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad.

General Reaction Procedure. All reactions, unless otherwise noted, were conducted under a nitrogen or an argon atmosphere. Liquid reagents were transferred via a dry hypodermic syringe from sure seal bottles to a reaction flask through a rubber septum wired on to the reaction flask. The septum can also serve to permit evacuation to eliminate air and introduce the inert gas by means of a steady stream of inert gas flowing system. Organic

extracts were concentrated by evaporation with a rotary evaporator evacuated at around 60 mmHg. Column chromatography, unless otherwise specified, was performed on a Merck silica gel 60 7734 using an appropriate ratio of ethyl acetate (AcOEt)/hexane mixed solvent and abbreviated as CC.

Materials. Unless otherwise noted, materials were obtained from commercial suppliers and reagent grade materials were used without further purification. Aqueous Sodium hypochlorite (available chlorine 5 %) is purchased from the Kanto Chemical Company, Inc., and used as received. Toluene, dichloromethane (CH_2Cl_2), dimethylsulfoxide (DMSO), and dimethylformamide (DMF) were freshly distilled from CaH_2 prior to use. Ether was distilled from benzophenone/ketyl prior to use. Tetrahydrofuran (THF) purchased from Kanto Chemical Co., Inc is dehydrated and stabilizer-free grade and was used as received.

Carbon chain substrates **1a**–**d** and **1i** could be prepared from readily available compounds such as 5-pentanolide (**13** and **15**),[1] 6-hexanolide (**14**),[1] 1-*O*-(methoxy)carbonyl-2-(methylene)hexane-1,3,6-triol (**18**),[2] or 2-(iodomethyl)allyltrimethylsilane (**19**),[3] respectively. The oxa- or aza-chain substrates **1e**–**h** were obtained through the coupling of **19** with **21**–**23**, respectively.[4] These procedures were outlined in Scheme S1.

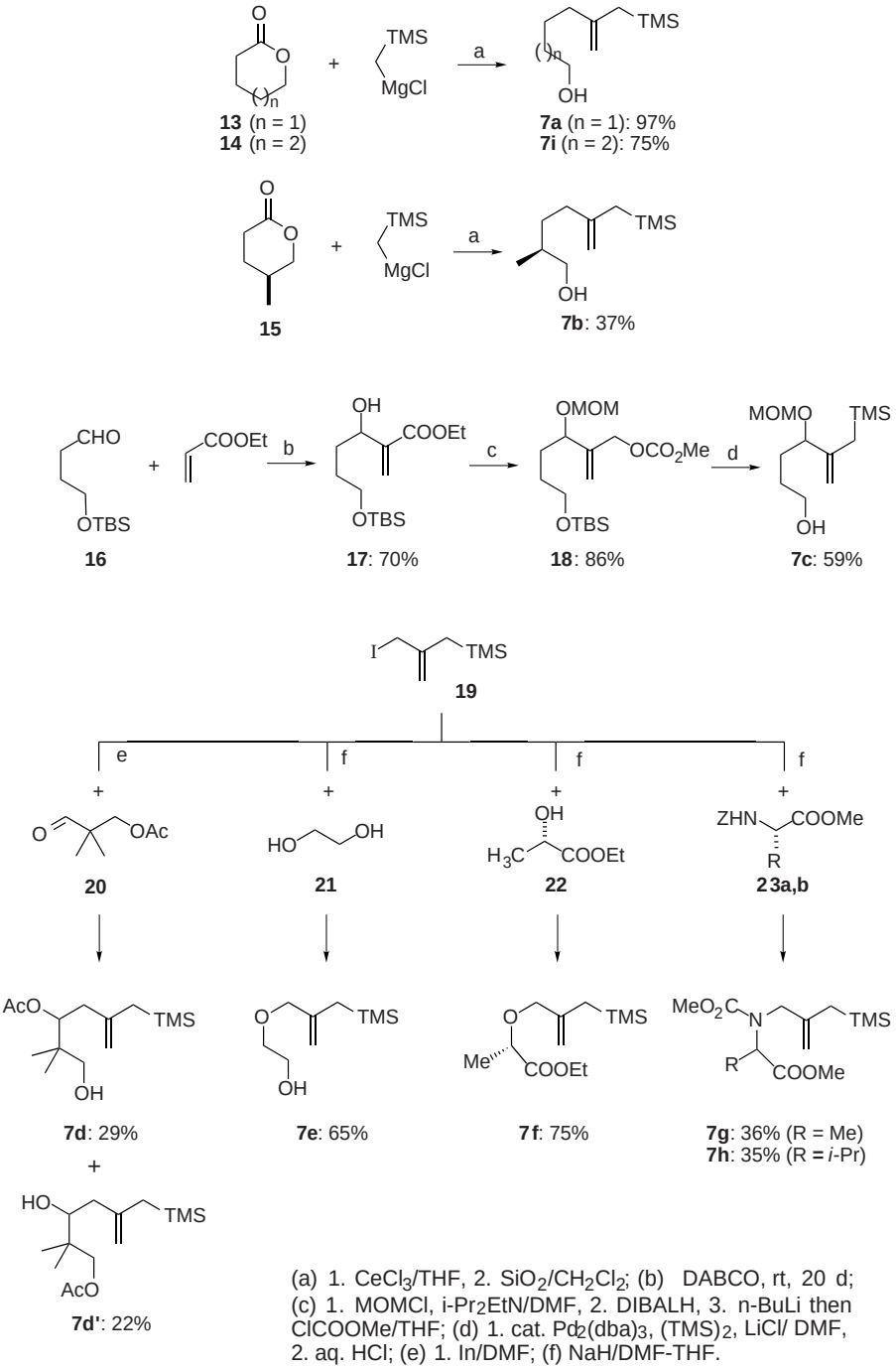
(1) These compounds were reacted with $(CH_3)_3SiCH_2MgCl$ (4 equiv) in the presence of $CeCl_3$ and the adducts were subjected to the Peterson olefination conditions: Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261–6264.

(2) Prepared through Baylis-Hillmann reaction between 4-(TBDMSO)butanal and acrylate ester followed by reduction and alkoxycarbonylation. For palladium(0) catalyzed silylation of allyl carbonate, see Tsuji, T.; Kajita, S.; Isobe, S.; Funato, M. *J. Org. Chem*. **1993**, *58*, 3607–3608.

(3) For **19**, see: Trost, B.; Chan, D.; Nanninga, T. *Org. Synth.* **1984**, *62*, 58–66. For indium-mediated allylation of **20** with **19** leading to **7d**, see: Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem*. **1988**, *53*, 1833–1835.

(4) Williamson ether synthesis was employed for the syntheses of these compounds.

Scheme S1



5-[(Trimethylsilyl)methyl]hex-5-en-1-ol (**7a**). A suspension of anhydrous $CeCl_3$ prepared from its hydrate (8.0 g, 21.5 mmol), by drying at 150 ˚C in vacuo for 2 h, in THF (50 mL) was stirred at room temperature for 2 h. To this slurry was added trimethylsilylmethylmagnesium chloride (1 M in ether, 22 mL) at –78 ˚C, thus-obtained milky suspension was stirred at –78 ˚C for 1 h followed by the addition of δ-valerolactone **13** (0.5 mL, 5.4 mmol) at –78 ˚C. The reaction was allowed to warm to room temperature, stirred

for 21 h, and quenched by the addition of water. The mixture was filtered through a Celite pad, the filter cake being thoroughly rinsed with AcOEt. The combined organic solutions were dried with Na_2SO_4 and concentrated to give a crude bis(silylmethyl)alcohol. The crude product was dissolved in CH_2Cl_2 (40 mL), and silica gel (5 g) was added. The suspension was stirred for 2 h, filtered, and concentrated to give an oil, which, on CC (5 : 1 hexane/AcOEt), gave **7a** (976 mg, 97 %); ^{1}H NMR δ 0.01 (s, 9H), 1.44–1.64 (m, 6H), 1.94–2.00 (m, 2H), 3.61–3.67 (m, 2H), 4.50–4.52 (m, 1H), 4.57–4.60 (m, 1H); ^{13}C NMR –1.4, 23.7, 26.5, 32.2, 37.7, 62.3, 106.8, 147.1; IR (film) 3338, 2952, 1633 cm^{-1}.

(2*S*)-2-Methyl-5-[(trimethylsilyl)methyl]hex-5-en-1-ol (**7b**). This compound was prepared from (4*R*)-4-methyl-δ-valerolactone **15** by the similar procedure as that for **7a**. **7c** (37 %): $[\alpha]^{24}_D$ + 7.72 (c 1.01, $CHCl_3$); ^{1}H NMR δ 0.01 (s, 9H), 0.93 (d, 3H, *J* = 6.8 Hz), 1.19–1.31 (m, 3H), 1.50–1.69 (m, 4H), 1.88–2.08 (m, 1H), 3.40–3.58 (m, 2H), 4.51–4.52 (m, 1H), 5.90–6.00 (m, 1H); ^{13}C NMR δ –1.4, 16.4, 26.7, 31.2, 35.3, 35.4, 67.9, 106.7, 147.5; IR (film) 3338, 1633 cm^{-1}.

6-[(Trimethylsilyl)methyl]hept-6-en-1-ol (**7i**). This compound was prepared from ε-caprolactone **14** by the similar procedure as that for **7a**. **7i** (75 %); ^{1}H NMR δ 0.07 (s, 9H), 1.28–1.70 (m, 9H), 1.99–2.05 (m, 2H), 3.68–3.74 (m, 2H), 4.56–4.58 (m, 1H), 4.63–4.65 (m, 1H); ^{13}C NMR δ –1.3, 25.4, 26.6, 27.5, 32.6, 38.0, 62.8, 106.7, 147.5; IR (film) 3338, 1633 cm^{-1}.

Ethyl 3-methylene-6-*O*-*tert*-buthyldimetylsilyl-3,6-dihydroxyhexanoate (**17**). 4-*O*-(*tert*-butyldimethylsilyl)-3-hydroxybutanal (2.63 g, 0.0131 mol) was mixed with ethyl acrylate (2.83 mL, 0.0260 mol) and 1,4-diazabicyclo[2.2.2]octane (0.732 g, 6.53 mmol) at room temperature and the mixture was stirred for 20 days and concentrated to give an oil, which, on CC (10 : 1 hexane/AcOEt), gave **17** (2.75 g, 70 %); ^{1}H NMR δ 0.07 (s, 6H), 0.89 (s, 9H), 1.30 (t, 3H, *J* = 7.1 Hz), 1.61–1.69 (m, 2H), 1.78–1.90 (m, 2H), 3.56 (d, 1H), 3.65–3.69 (m, 2H), 4.22 (q, 2H, *J* = 7.1 Hz), 4.42–4.49 (m, 1H), 5.85 (dd, 1H, *J* = 1.4, 1.3 Hz), 6.24 (dd, 1H, *J* = 1.4, 0.6 Hz); ^{13}C NMR δ –5.5, 14.0, 18.1, 25.7, 28.8, 33.4, 60.4, 63.1, 70.5, 124.3, 142.8, 166.3; IR (film) 3400, 1719 cm^{-1}.

Methyl 2-methylene-3-(methoxy)methyloxy-6-(*tert*-butyldimethylsiloxy)hexyl carbonate (**18**). To a solution of **17** (4.38 g, 14.5 mmol) in DMF (30 mL) were added *N*,*N*-

Diisopropylethylamine (7.4 mL, 43.5 mmol) and chloromethyl methyl ether (2.7 mL, 36.2 mmol) at room temperature, and the mixture was stirred at 70 °C for 24 h. The reaction was quenched by the addition of water and extracted with three portions of AcOEt. The combined extracts were dried over Na_2SO_4 and concentrated to afford an oil, which was purified by CC to give ethyl 2-methylene-3-*O*-(methoxy)methyl-6-*O*-*tert*-butyldimethylsilyl-3,6-dihydroxyhexanoate (4.97 g, 99 %). To a solution of this ester (1.72 g, 4.96 mmol) in THF (20 mL) was added DIBALH (1M in toluene, 11 mL, 11 mmol) at –78 °C, and the mixture was stirred at –78 °C for 1 h. The reaction was quenched by the addition of water and filtered through a Celite pad. The combined filtrates were dried over Na_2SO_4 and concentrated to give an oil, which, on CC, gave 2-methylene-3-*O*-(methoxy)methyl-6-*O*-(*tert*-butyldimethylsilyl)hexane-1,3,6-triol (1.33 g, 88 %); ^{1}H NMR δ 0.04 (s, 6H), 0.88 (s, 9H), 1.46–1.73 (m, 4H), 1.95–2.00 (m, 1H), 3.37 (s, 3H), 3.58–3.67 (m, 2H), 4.07–4.26 (m, 3H), 4.54 & 4.68 (ABq, 2H, *J* = 6.7 Hz), 5.10–5.12 (m, 1H), 5.25–5.26 (m, 1H); ^{13}C NMR δ –5.4, 18.2, 25.8, 28.9, 30.3, 55.4, 62.3, 62.6, 78.4, 93.9, 113.4, 147.2. To a solution of this triol (1.10 g, 3.6 mmol) in THF (10 mL) were added n-BuLi (1.56 M in hexane 3.1 mL, 4.8 mmol) and methyl chloroformate (0.42 mL, 5.4 mmol) at –78 °C. The mixture was stirred at –78 °C for 30 min, followed by the addition of water. The mixture was extracted with three portions of AcOEt, and the combined extracts were dried over Na_2SO_4 and concentrated to give an oil, which, on CC (15 : 1 hexane/AcOEt), gave **18** (1.27 g, 97 %); ^{1}H NMR δ 0.04 (s, 6H), 0.88 (s, 9H), 1.48–1.72 (m, 4H), 3.37 (s, 3H), 3.60–3.65 (m, 1H), 3.79 (s, 3H), 4.11–4.16 (m, 1H), 4.51 & 4.64 (ABq, 2H, *J* = 6.8 Hz), 4.63–4.65 (m, 2H), 5.20–5.22 (m, 1H), 5.27–5.29 (m, 1H); ^{13}C NMR δ –5.4, 18.1, 25.7, 28.8, 30.3, 54.6, 55.4, 62.5, 66.2, 77.4, 93.6, 115.6, 142.2, 155.4; IR (film) 2955, 1754 cm^{-1}.

2-[(Trimethylsilyl)methyl]-3-*O*-[(methoxy)methyl]-1-hexene-3,6-diol (**7c**). To a solution of **18** (800 mg, 2.2 mmol) in DMF (7 mL) were added successively LiCl (46 mg, 1.1 mmol), hexamethyldisilane (0.9 mL, 4.4 mmol), and $Pd_2(dba)_3$ (100 mg, 0.01 mmol). The mixture was heated at 100 °C for 10 h and filtered through florisil pad, and the combined filtrates were concentrated to give an oil, which, on CC, gave 2-[(Trimethylsilyl)methyl]-3-*O*-[(methoxy)methyl]-6-*O*-*tert*-butyldimethylsilyl-1-hexene-3,6-diol (591 mg, 75 %); ^{1}H NMR δ 0.03 (s, 9H), 0.04 (s, 6H), 0.89 (s, 9H), 1.33–1.75 (m, 6H), 2.45–2.50 (m, 1H), 3.37 (s, 3H),

3.58–3.65 (m, 2H), 3.88–3.93 (m, 1H), 4.49 & 4.64 (ABq, 2H, J = 6.6 Hz), 4.73–4.75 (m, 1H), 4.88–4.90 (m, 1H); ^{13}C NMR δ –5.3, –1.0, 18.2, 21.2, 25.9, 29.1, 30.2, 55.4, 62.8, 79.6, 93.7, 109.9, 145.9. To a solution of this diol (520 mg, 1.44 mmol) in MeOH (5 mL) was added 1N-HCl (0.36 mL, 0.36 mmol) at 0 °C, and the mixture was stirred at 0 °C for 20 min followed by the addition of aqueous solution of $NaHCO_3$. The mixture was extracted with three portions of AcOEt. The combined extracts were dried over Na_2SO_4 and concentrated to give an oil, which, on CC (3 : 1 hexane/AcOEt), gave **7d** (280 mg, 79 %); ^{1}H NMR δ 0.04 (s, 9H), 1.32–1.55 (m, 2H), 1.59–1.76 (m, 4H), 3.38 (s, 3H), 3.64–3.69 (m, 2H), 3.92–3.97 (m, 1H), 4.51 & 4.65 (ABq, 2H, J = 6.6 Hz), 4.75–4.77 (m, 1H), 4.89–4.91 (m, 1H); ^{13}C NMR δ –1.1, 21.3, 28.9, 30.3, 55.5, 62.5, 79.4, 93.7, 109.8, 145.6; IR (film) 3210, 1636 cm^{-1}.

3-Hydroxy-2-(trimethylsilyl)methyl-1-propene. An oven-dried flask was charged with n-BuLi (1.55 M in hexane, 100 mL, 155 mmol) and the bulk of the hexane was removed at reduced pressure. The flask is carefully recharged with nitrogen, and diethyl ether (70 mL) was added. To this solution was added tetramethylethylenediamine (23.4 mL, 155 mmol) at 0 °C. The mixture was stirred at 0 °C for 10 min, and 2-methyl-2-propen-1-ol (5 ml, 59.4 mmol) was slowly added, followed by the addition of THF (45 mL). The mixture was allowed to warm to room temperature during 4 h. The reaction mixture was vigorously stirred for 45 h. The reaction mixture was recooled to –30 °C, and chlorotrimethylsilane was added. The mixture was stirred at room temperature for 30 min, quenched with saturated aqueous sodium bicarbonate, and extracted with three portions of AcOEt. The combined extracts were dried over Na_2SO_4, filtered, and concentrated to afford an oil. The crude product was distilled at reduced pressure to give 2-(trimethylsiloxymethyl)allyltrimethylsilane as a colorless oil: bp 57–59 °C (4 mmHg). The product was dissolved in THF (50 mL), and the mixture was cooled to 0 °C followed by the addition of 1N-H_2SO_4 (5 mL). The mixture was stirred at 0 °C for 30 min, neutralized by the addition of aqueous solution of $NaHCO_3$, and extracted with three portions of AcOEt. The combined extracts were dried over Na_2SO_4, filtered, and concentrated to give an oil, which, on CC, gave 3-hydroxy-2-trimethylsilylmethyl-1-propene (5.45 g, 65 %).

3-Iodo-2-(trimethylsilyl)methyl-1-propene (**19**). To a solution of 3-hydroxy-2-trimethylsilylmethyl-1-propene (1.27 g, 8.8 mmol) and Et_3N (7.4 mL 52.8 mmol) in CH_2Cl_2

(20 mL) was added methanesulufonyl chloride (2.0 mL 26.4 mmol) at 0 °C. The mixture was stirred at room temperature for 40 min, quenched by the addition of water, and extracted with several portions of AcOEt. The combined extracts were dried over Na_2SO_4, filtered, and concentrated to afford an oil. The crude product was dissolved in 3–pentanone (50 mL) and NaI (3.96 g 26.4 mmol) was added. The mixture was stirred at room temperature for 1.5 h, quenched by the addition of water, and extracted with several portions of AcOEt. The combined extracts were dried over Na_2SO_4, filtered, and concentrated to give an oil, which, on CC (10 : 1 hexane/AcOEt), gave **19** (1.67 g 75 %); ^{1}H NMR δ 0.04 (s, 9H), 1.72 (s, 2H), 3.88 (s, 2H), 4.70–4.72 (m, 1H), 5.10–5.14 (m, 1H); ^{13}C NMR δ –1.47, 13.7, 24.8, 111.9, 144.5; IR (film) 1621 cm^{-1}.

3-Acetoxy-2,2-dimethyl-5-[(trimethylsilyl)methyl]hex-5-en-1-ol (**7d**). To a suspension of indium metal (321 mg 2.8 mmol) in DMF (5 mL) was added a solution of **19** (720 mg 2.8 mmol) and 3-acetoxy-2,2-(dimethyl)propanal **20** (272 mg 1.9 mmol) in DMF (5 mL) at room temperature under vigorous stirring. The reaction mixture was stirred for 2 h and filtered through a florisil pad, the filter cake being thoroughly rinsed with several portions of AcOEt. The combined filtrates were concentrated to give an oil, which, on CC (8 : 1 hexane/AcOEt), gave **7d** (152 mg 29 %) and **7d'** (115 mg, 22 %) as a colorless oil for both; Data for **7d**: ^{1}H NMR δ 0.02 (s, 9H), 0.81 (s, 3H), 0.99 (s, 3H), 1.48&1.58 (ABq, 2H, *J* = 13.5, Hz), 2.06 (s, 3H), 2.12–2.21 (m, 2H), 2.72 (dd, 1H, *J* = 4.7, 9.9 Hz), 3.11 (dd, 1H, *J* = 9.9, 11.8 Hz), 3.33 (dd, 1H, *J* = 4.7, 11.8 Hz), 4.61–4.63 (m, 2H), 5.05 (dd, 1H, *J* = 4.7, 8.5 Hz); ^{13}C NMR δ –1.5, 18.6, 20.8, 21.9, 26.3, 37.6, 39.0, 69.1, 74.8, 109.6, 143.5, 172.2; IR (film) 3312, 1709 cm^{-1}.

5-[(Trimethylsilyl)methyl]-3-oxa-5-hexen-1-ol (**7e**). To a solution of ethylene glycol **21** (1.22 g 19.7 mmol) in THF (20 mL) and DMF (10 mL) was added NaH (60 % in oil 292 mg, 7.3 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 h. To the mixture was added a solution of **19** (1.67 g 6.6 mmol) in DMF (5 mL) at 0 °C, and the mixture was stirred at room temperature for 15 h. The reaction was quenched by the addition of water and extracted with several portions of AcOEt. The combined extracts were dried over Na_2SO_4 and concentrated to give an oil, which, on CC (5 : 1 hexane/AcOEt), gave **7e** (804 mg, 65 %); ^{1}H NMR δ 0.02 (s, 9H), 1.54–1.62 (m, 2H), 2.01–2.07 (m, 1H), 3.17–3.24 (m, 2H), 3.75–3.78 (m,

2H), 3.9 (s, 2H), 4.72–4.77 (m, 1H), 4.82–4.91 (m, 1H); ^{13}C NMR δ –1.4, 23.1, 61.8, 71.1, 75.1, 109.2, 143.6; IR (film) 3112, 1645 cm^{-1}.

Ethyl (2*S*)-2-methyl-5-(trimethylsilyl)methyl-3-oxa-5-hexenoate (**7f**). This compound was prepared from ethyl (*s*)-(-)-lactate **22** by the similar procedure as that for **7e**. **7f**: (430 mg, 75 %); $[\alpha]^{24}_{D}$ –24.17 (c 1.01, $CHCl_3$); ^{1}H NMR δ 0.01 (s, 9H), 1.33 (t, 3H, *J* = 7.1 Hz), 1.42 (d, 3H, *J* = 6.9 Hz), 1.52–1.56 (m, 2H), 3.82 & 3.96 (ABq, 2H, *J* = 12.6 Hz), 4.02 (q, 2H, *J* = 6.9 Hz), 4.68–4.74 (m, 1H), 4.78–4.89 (m, 1H); ^{13}C NMR δ –1.5, 14.2, 18.6, 23.0, 73.6, 109.6, 111.9, 143.1, 173.3; IR (film) 2991, 1751 cm^{-1}.

***N*-Methoxycarbonyl-*N*-[(3-trimethylsilyl)-2-(methylene)propyl]alanine methyl ester** (**7g**). This compound was prepared from **23a** by the similar procedure as that for **7f. 7g**: (36 %); ^{1}H NMR δ 0.04 (s, 9H), 1.41 (d, 3H, *J* = 7.1 Hz), 1.46–1.55 (m, 2H), 3.70 (s, 3H), 3.75 (br, 2H), 4.40 (q, 1H, *J* = 7.1 Hz), 4.64–4.70 (m, 1H), 4.72–4.81 (m, 1H); ^{13}C NMR δ –1.6, 14.7, 23.49, 51.9, 52.4, 53.4, 54.3, 108.14, 143.0, 156.5, 172.3; IR (film) 2954, 1749, 1708 cm^{-1}.

***N*-Methoxycarbonyl-*N*-[(3-trimethylsilyl)-2-(methylene)propyl]valine methyl ester** (**7h**). This compound was prepared from **23b** by the similar procedure as that for **7f**. **7h** (35 %); ^{1}H NMR δ 0.05 (s, 9H), 0.72–0.98 (br, 6H), 1.37–1.59 (br, 2H), 2.15–2.37 (br, 1H), 3.42–3.91 (br, 7H), 4.0–4.19 (br, 1H), 4.31–4.45 (br, 1H), 4.48–4.61 (br, 2H); ^{13}C NMR δ –1.6, 18.5, 19.8, 24.4, 27.6, 49.7, 51.5, 52.8, 63.7, 106.1, 142.4, 157.4, 170.9; IR (film) 2956, 1745, 1708 cm^{-1}.

General Procedure for the Synthesis of Allyltrimethylsilane-oximes (method A for **7a–e** and **7i**). To a solution of **7** and Et_3N (10 equiv) in DMSO was added pyridine sulfur trioxide (4 equiv) in one portion at 0 °C. The mixture was stirred at 0 °C to room temperature for 30 min. The reaction was quenched by the addition of water and extracted with several portions of AcOEt. The combined organic solutions were dried with Na_2SO_4 and concentrated to give a crude aldehyde. To a solution of the crude aldehyde in EtOH were added NH_2OH-HCl (6 equiv) and Et_3N (8 equiv) at 0 ˚C, and the mixture was stirred at room temperature for 1 h. The reaction was diluted with water and extracted with several portions

of AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to afford an oil, which, on CC, gave aldoximes (**1a–e** and **1i**).

General Procedure for the Synthesis of Allyltrimethylsilane-oximes (method B for **7f–h**). To a solution of **7** in THF, cooled to –78 °C, was slowly added DIBAL (1.0 equiv). The mixture was stirred at –78 °C for 30 min, quenched by the addition of water, and filtered through a Celite pad. The combined organic solutions were concentrated to give the corresponding aldehyde. To a solution of the crude aldehyde in EtOH were added NH_2OH-HCl (6 equiv) and Et_3N (8 equiv) at 0 ˚C, and the mixture was stirred at room temperature for 1 h. The reaction was diluted with water and extracted with several portions of AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to afford an oil, which, on CC, gave aldoximes (**1f– h**)

5-(Trimethylsilyl)methyl-5-hexenal oxime (**1a**). 91 % yield from **7a** as a colorless oil. ^{1}H NMR (for the major geometric isomer) δ 0.04 (s, 9H), 1.49–1.52 (m, 2H), 1.59–1.69 (m, 2H), 1.96–2.05 (m, 2H), 2.17–2.24 (m, 2H), 4.52–4.56 (m, 1H), 4.59–4.62 (m, 1H), 7.44 (t, 1H), 7.52–7.55 (br, 1H); ^{13}C NMR (for the major geometric isomer) δ –1.3, 24.1, 26.5, 29.0, 37.4, 107.4, 146.5, 151.9; IR (film) 3261, 1633 cm^{-1}. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; Found: C, 60.10; H, 10.43.

(2*S*)-2-methyl-5-[(trimethylsilyl)methyl]-5-hexenal oxime (**1b**). 49 % yield from **7b** as a colorless oil; $[\alpha]^{25}_D$ –10.78 (c 1.03, $CHCl_3$); ^{1}H NMR (for the major geometric isomer) δ 0.01 (s, 9H), 1.09 (d, 3H, *J* = 6.5 Hz), 1.46–1.65 (m, 4H), 1.97 (t, 2H, *J* = 7.9 Hz), 2.30–2.43 (m, 1H), 4.51–4.54 (m, 1H), 4.57–4.60 (m, 1H), 7.12–7.21 (br, 1H), 7.30 (d, 1H); ^{13}C NMR (for the major geometric isomer) δ –1.3, 17.8, 26.7, 32.6, 34.0, 35.4, 107.2, 146.8, 156.0; IR (film) 3230, 1630 cm^{-1}.

4-*O*-(Methoxy)methyl-4-hydroxy-5-[(trimethylsilyl)methyl]-5-hexenal oxime (**1c**). 91 % yield from **7c** as a colorless oil; ^{1}H NMR (for the major geometric isomer) δ 0.02 (s, 9H), 1.33 (dd, 1H, *J* = 1.2, 14.4 Hz), 1.51 (dd, 1H, *J* = 1.2, 14.4 Hz), 1.67–1.79 (m, 2H), 2.20–2.35 (m, 2H), 3.37 (s, 3H), 3.93 (t, 1H, *J* = 6.5 Hz), 4.49 & 4.63 (ABq, 2H, *J* = 6.6 Hz), 4.75–4.78 (m, 1H), 4.90–4.93 (m, 1H), 6.76 (t, 1H, *J* = 5.5 Hz), 8.21–8.36 (br, 1H); ^{13}C NMR

(for the major geometric isomer) δ –1.0, 21.6, 25.9, 30.7, 55.6, 79.0, 93.8, 110.3, 145.2, 152.1; IR (film) 3365, 1669 cm^{-1}.

3-Acetoxy-2,2-dimethyl-5-(trimethylsilyl)methyl-5-hexenal oxime (**1d**). 82 % yield from **7d** as a colorless oil; ^{1}H NMR (for the major geometric isomer) δ –0.1 (s, 9H), 0.98 (s, 3H), 0.99 (s, 3H), 1.38–1.41 (m, 2H), 1.9 (s, 3H), 2.0–2.02 (m, 2H), 4.48–4.52 (m, 2H), 4.95 (dd, 2H, *J* = 2.8, 10.4 Hz);^{13}C NMR (for the major geometric isomer) δ –1.5, 20.8, 21.8, 22.2, 26.1, 38.8, 40.8, 75.7, 110.5, 143.0, 155.5, 170.5; IR (film) 3415, 2956, 1739 cm^{-1}.

5-(Trimethylsilyl)methyl-3-oxa-5-hexenal oxime (**1e**). 73 % yield from **7e** as a colorless oil; ^{1}H NMR (for the major geometric isomer) δ 0.02 (s, 9H), 1.54–1.65 (m, 2H), 3.82–3.91 (m, 2H), 4.08 (d, 1H, *J* = 5.8 Hz), 4.74–4.88 (m, 1H), 4.91–5.01 (m, 1H), 7.50 (t, 1H, *J* = 5.8 Hz), 7.79 (br, 1H); ^{13}C NMR (for the major geometric isomer) δ –1.4, 23.1, 63.9, 74.6, 109.8, 143.1, 148.6; IR (film) 3544, 1677 cm^{-1}. Anal. Calcd for $C_9H_{19}O_2Si$: C, 53.69; H, 9.51; Found: C, 53.54; H, 9.39.

(2*S*)-2-Methyl-5-(trimethylsilyl)methyl-3-oxa-5-hexenal oxime (**1f**). 52 % yield from **7f** as a colorless oil; $[\alpha]^{24}_{D}$ –24.27 (c 1.01, $CHCl_3$); ^{1}H NMR δ 0.02 (s, 9H), 1.34 (d, 3H, *J* = 6.32 Hz), 1.50–1.54 (m, 2H), 3.82 & 3.87 (ABq, 2H, *J* = 6.3 Hz), 4.01 (dq, 1H, *J* = 6.32 Hz), 4.64–4.71 (m, 1H), 4.83–4.92 (m, 1H), 7.07–7.10 (br, 1H), 7.31 (d, 1H, *J* = 7.42 Hz); ^{13}C NMR δ –1.4, 19.3, 23.2, 71.8, 73.4, 109.3, 143.4, 152.8; IR (film) 3447, 2952, 1444 cm^{-1}.

2-Methyl-3-methoxycarbonyl-5-(trimethylsilyl)methyl-3-aza-5-hexenal oxime (**1g**). 36 % yield from **7g** as a colorless oil; ^{1}H NMR δ 0.04 (s, 9H), 1.35 (d, 3H), 1.41–1.46 (m, 2H), 3.6–3.81 (m, 4H), 4.64–4.70 (m, 1H), 4.72–4.78 (m, 1H), 7.13–7.15 (m, 1H) 7.48–7.54 (m, 1H); ^{13}C NMR δ –1.5, 23.6, 23.9, 51.8, 52.7, 53.3, 142.9, 151.2, 151.9, 156.7; IR (film) 3367, 2954, 1708 cm^{-1}.

2-Isopropyl-3-methoxycarbonyl-5-(trimethylsilyl)methyl-3-aza-5-hexenal oxime (**1h**). 24 % yield from **7h** as a colorless oil; ^{1}H NMR δ 0.04 (s, 9H), 0.90 (d, 3H), 0.92 (d, 3H), 1.44 (m, 2H), 2.21–2.44 (br, 1H), 3.55–3.80 (br, 6H), 4.65–4.71 (m, 2H), 7.0–7.05 (br, 1H), 7.48–7.58 (br, 1H); ^{13}C NMR δ –1.5, 19.3, 23.3, 28.4, 63.5, 109.5, 142.6, 149.9, 156.6; IR (film) 3320, 2922, 1752 cm^{-1}.

6-[(Trimethylsilyl)methyl]-6-heptenal oxime (**1i**). 85 % yield from **7i** as a colorless oil. ^{1}H NMR (for the major geometric isomer) δ 0.00 (s, 9H), 1.46–1.53 (m, 6H), 1.92–2.00

(m, 2H), 2.17–2.25 (m, 1H), 2.35–2.43 (m, 1H), 4.50–2.52 (m, 1H), 4.56–4.58 (m, 1H), 6.72 (t, 1H, *J* = 5.5 Hz), 7.90–8.0 (br, 1H); ^{13}C NMR (for the major geometric isomer) δ –1.3, 24.8, 25.7, 26.6, 29.4, 37.7, 107.0, 147.2, 152.2; IR (film) 3230, 1630 cm^{-1}.

General Procedure for Ene-type Cyclizations.

To a solution of oxime **1a-i** (0.36 mmol) in CH_2Cl_2 (7 mL) was slowly added an aqueous solution of NaOCl (available chlorine 5 %, 1.0 mL) at 0 °C during 1 h. The mixture was stirred vigorously at 0 °C to room temperature for 1 h. The reaction was diluted with water and extracted with several portions of AcOEt. The combined extracts were dried over Na_2SO_4 and concentrated to give an oil, which was purified by column chromatography on silica gel, to afford the cyclic oxime **2a-i** .

(1*Z*,3*Z*)-3-[(Trimethylsilyl)methylene]cyclohexanone oxime (**2a**) 82 % yield from **1a** as a colorless oil; ^{1}H NMR δ 0.13 (s, 9H), 1.65–1.75 (m, 2H), 2.28–2.37 (m, 4H), 3.36 (d, 2H, *J* = 1.1 Hz), 5.25–5.28 (m, 1H), 8.92–9.10 (br, 1H); ^{13}C NMR δ –0.04, 26.1, 31.3, 32.7, 39.2, 124.8, 152.7, 158.6; IR (film) 3335, 1621 cm^{-1}. Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; Found: C, 60.51; H, 9.51. NOE experiment for **2a**: The NOE (9.3%) was observed between the exocyclic olefinic proton and C(4) methylene protons when the olefinic proton was irradiated.

(2*S*)-2-Methyl-(1*Z*,5*Z*)-5-[(trimethysilyl)methylene]cyclohexanone oxime (**2b**). 82 % yield from **1b** as a colorless oil; $[\alpha]^{24}_D$ +21.9 (c 1.05, $CHCl_3$); ^{1}H NMR δ 0.13 (s, 9H), 1.14 (d, 3H, *J* = 6.8 Hz), 1.31–1.44 (m, 1H), 1.83–1.93 (m, 1H), 2.26–2.49 (m, 3H), 2.82 & 3.90 (ABq, 2H, *J* = 15.3 Hz), 5.25–5.26 (m, 1H), 9.16–9.25 (br, 1H); ^{13}C NMR δ –0.06, 16.6, 31.9, 34.4, 36.3, 37.9, 124.5, 153.0, 160.9; IR (film) 3335, 2961, 1621 cm^{-1}.

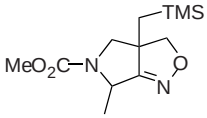
4-*O*-(Methoxy)methyl-4-hydroxy-(1*Z*,3*E*)-3-[(trimethylsilyl)methylene]-cyclohexanone oxime (**2c**). 78 % yield from **1c** as a colorless oil; ^{1}H NMR δ 0.15 (s, 9H), 1.77–1.99 (m, 2H), 2.28 (dt, 1H, *J* = 4.9, 14.5 Hz), 2.51–2.62 (m, 1H), 3.08 & 3.72 (ABq, 2H, *J* = 15.3 Hz), 3.38 (s, 3H), 4.12–4.18 (m, 1H), 4.60 & 4.68 (ABq, 2H, *J* = 6.6 Hz), 5.53–5.54 (m, 1H), 7.20–7.35 (br, 1H); ^{13}C NMR δ –0.17, 26.7, 29.3, 31.6, 55.4, 77.9, 93.6, 127.8, 149.9, 157.8; IR (film) 3198, 1723 cm^{-1}.

3-Acetoxy-2,2-dimethyl-(1*Z*,5*E*)-5-[(trimethylsilyl)methylene]cyclohexanone oxime. (**2d**). 55 % yield from **1d** as a colorless oil; ^{1}H NMR δ 0.14 (s, 9H), 1.21 (s, 3H), 1.19 (s, 3H), 2.05 (s, 3H), 2.4–2.75 (m, 2H), 3.42 & 3.50 (ABq, 2H, *J* = 15.3 Hz), 4.7 (dd, 1H, *J* = 3.9 Hz), 5.28 (m, 1H), 8.1 (br, 1H); ^{13}C NMR δ –0.2, 21.1, 21.5, 24.2, 30.0, 39.6, 40.7, 77.5, 127.9, 147.0, 161.1, 170.5; IR (film) 3434, 2973, 1739 cm^{-1}.

(1*E*,3*E*)-3-[(trimethylsilyl)methylene]-5-oxacyclohexanone oxime (**2e**). 41 % yield from **1e** as a colorless oil; ^{1}H NMR δ 0.16 (s, 9H), 3.48–3.51 (m, 2H), 4.18 (s, 2H), 4.2–4.28 (m, 2H), 5.4–5.5 (m, 1H), 7.8 (br, 1H); ^{13}C NMR δ –0.3, 29.3, 68.0, 75.2, 126.5, 146.6, 154.7; IR (film) 3330, 2952, 1633 cm^{-1}. Anal. Calcd for $C_9H_{17}NO_2Si$: C, 54.23; H, 8.60; Found: C, 54.18; H, 8.39.

(2*S*)-2-methyl-(1*E*,5*E*)-5-[(trimethylsilyl)methylene]-3-oxacyclohexanone oxime (**2f**). 75 % yield from **1f** as a colorless oil; $[\alpha]^{24}_D$ +3.09 (c 1.01, $CHCl_3$); ^{1}H NMR δ 0.21 (s, 9H), 1.43 (d, 3H, *J* = 6.3 Hz), 3.24 & 3.7 (ABq, 2H, *J* = 17.8 Hz), 4.12–4.23 (m, 1H), 4.18 & 4.31 (ABq, 2H, *J* = 13.4 Hz), 5.38–5.42 (m, 1H), 7.39–7.54 (br, 1H); ^{13}C NMR δ –0.3, 17.2, 28.8, 72.9, 73.7, 125.3, 147.4, 157.7; IR (film) 3344, 2954, 1625 cm^{-1}.

2-Methyl-3-(methoxycarbonyl)-(1*E*,5*E*)-5-[(trimethylsilyl)methylene]-3-aza-cyclohexanone oxime (**2g**). 33 % yield from **1g** as a colorless oil; ^{1}H NMR δ 0.15 (s, 9H), 1.3 (d, 3H, *J* = 6.9 Hz), 3.31–3.90 (m, 3H), 3.69 (s, 3H), 4.20–4.42 (br, 1H), 4.75–5.01 (br, 1H), 5.52–5.58 (m, 1H), 8.16 (br, 1H); ^{13}C NMR δ –0.4, 19.2, 28.8, 50.2, 50.8, 52.8, 127.7, 145.1, 155.5, 157.6; IR (film) 3376, 2956, 1712 cm^{-1}.

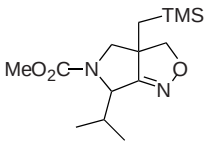


[3+2]cycloadduct of **1g**

7-(Metoxycarbonyl)-8-methyl-5-(trimethylsilyl)methyl-2,7-diaza-3-oxabicyclo-[3.3.0]oct-1-ene ([3+2] cycloadduct of **1g**). 48 % yield from **1g** as a colorless oil. ^{1}H NMR (for 1:1 mixture of diastereomers) δ (0.086 and 0.097 (2s, 9H)), 0.98 and 1.05 (ABq, 2H, *J* = 14.8 Hz), (1.47 and 1.50 (2d, 3H, *J* = 6.3 Hz)), 3.22–3.29 (m, 1H), (3.73 and 3.77 (2s, 3H)), 3.86–4.30 (m, 3H), (4.54 and 4.63 (2q, 1H, *J* = 6.6 Hz)).

2-Isopropyl-3-(methoxycarbonyl)-(1*E*,5*E*)-5-[(trimethylsilyl)methylene]-3-aza-cyclohexanone oxime (**2h**). 40 % yield from **1h** as a colorless oil; ^{1}H NMR δ 0.14 (s, 9H),

0.77–0.9 (m, 6H), 1.87–2.08 (m, 1H), 3.22–3.88 (m, 3H), 3.68 (s, 3H), 4.16–4.54 (m, 2H), 5.5–5.58 (m, 1H), 7.8–8.1 (br 1H); ^{13}C NMR δ –0.3, 19.1, 19.3, 29.0, 29.5, 50.7, 52.8, 108.3, 127.8, 145.3, 155.8; IR (film) 3368, 2901, 1721 cm^{-1}.



[3+2]cycloadduct of **1h**

7-(Methoxycarbonyl)-8-isopropyl-5-(trimethylsilyl)methyl-2,7-diaza-3-oxabicyclo-[3.3.0]oct-1-ene ([3+2] cycloadduct of **1h**). 43 % yield from **1h** as a colorless oil. ^{1}H NMR (for 6:5 mixture of diastereomers) δ (0.085 and 0.095 (2s, 9H)), (0.9 and 1.0 (2d, 3H, *J* = 6.9 Hz), 0.82–1.10 (m, 2H), 2.38–2.58 (m, 1H), 3.18–3.21 (m, 1H), (3.73 and 3.77 (2s, 3H)), 3.85–4.25 (m, 3H), (4.47 and 4.58 (2d, 1H, *J* = 4.4 Hz)).

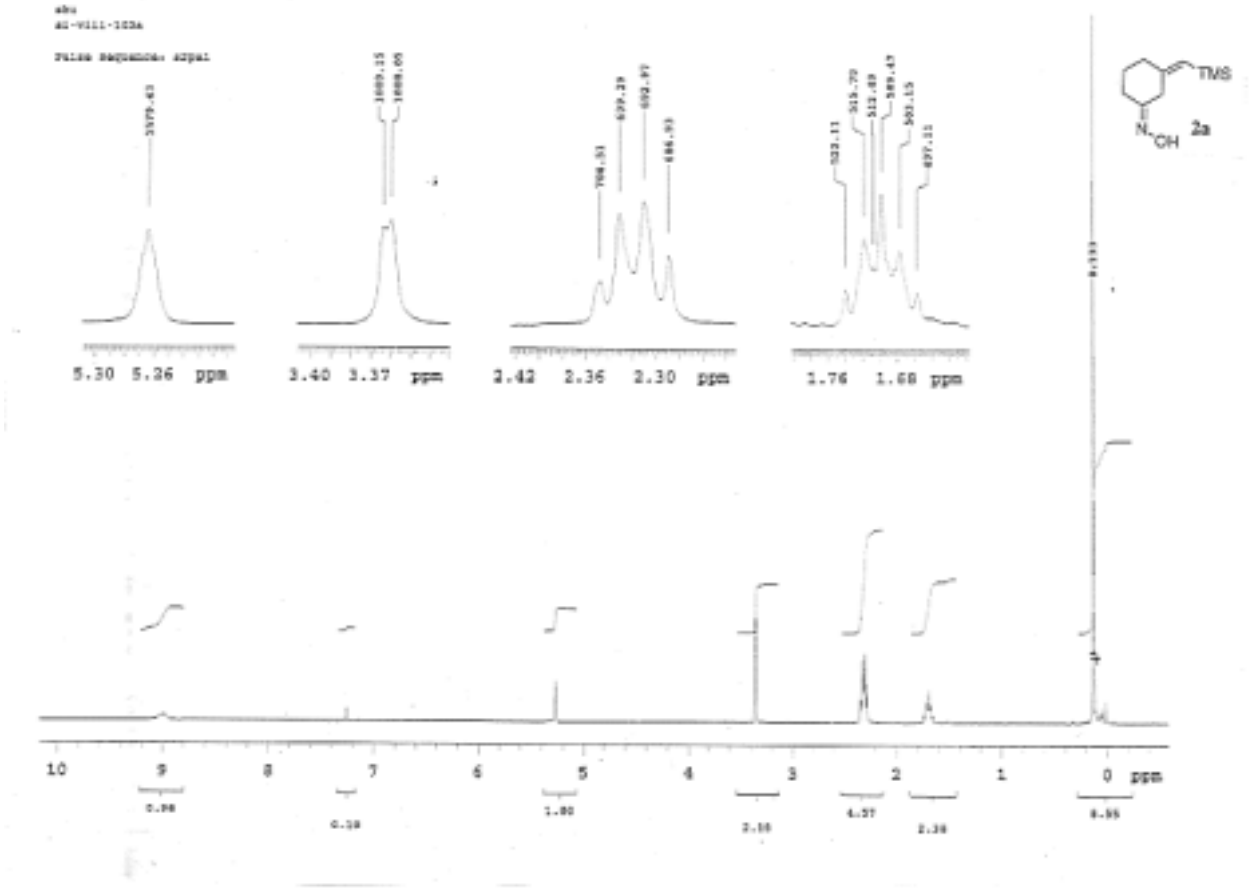
(1*Z*)-3-[(Trimethylsilyl)methyl]-2-cycloheptenone oxime (**2i**). 28 % yield from **1i** as a colorless oil; ^{1}H NMR δ 0.05 (s, 9H), 1.69–1.74 (m, 6H), 2.20–2.26 (m, 2H), 2.42–2.48 (m, 2H), 6.30 (s, 1H), 8.40–9.00 (br, 1H); ^{13}C NMR δ –1.2, 25.1, 26.1, 32.1, 33.4, 34.6, 114.2, 153.9, 157.2; IR (film) 3215, 1664 cm^{-1}.

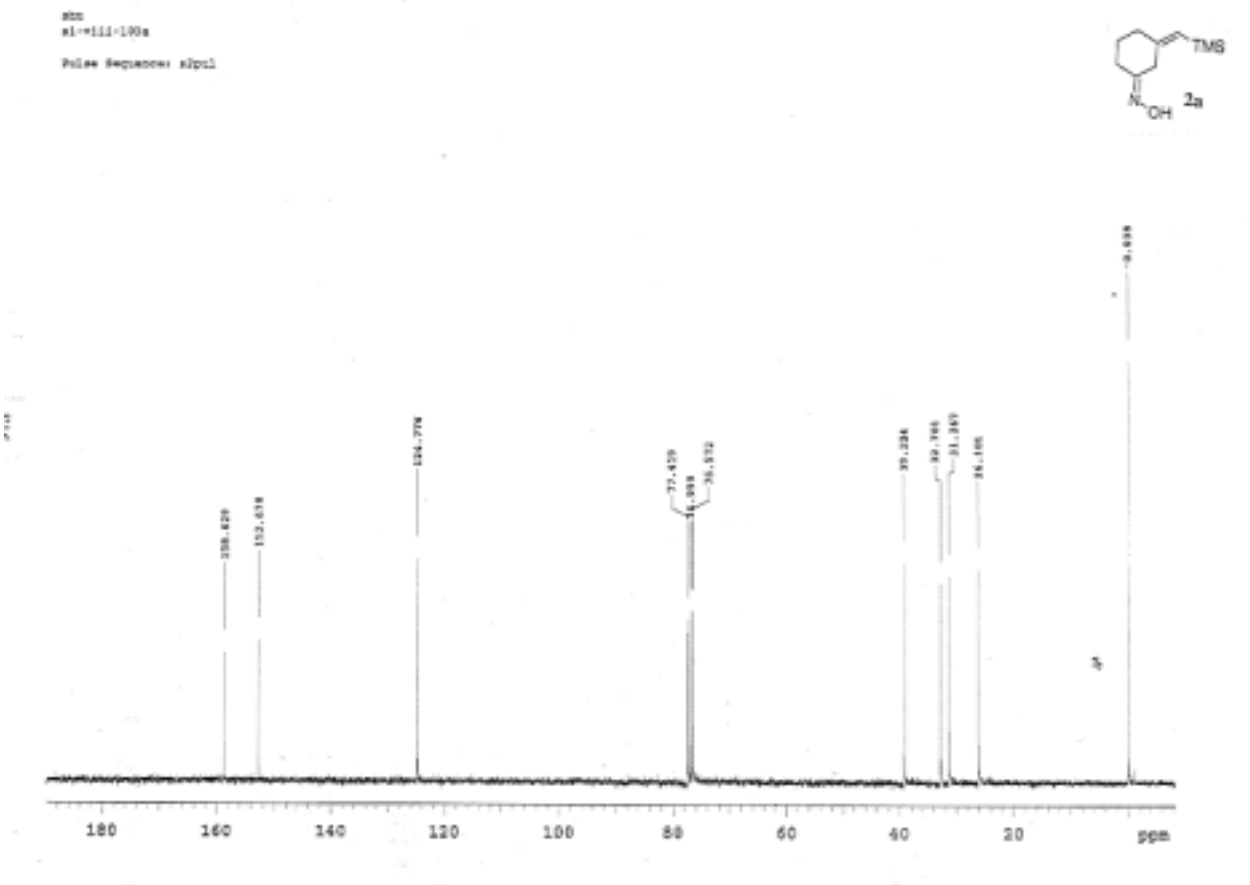
(1*Z*,3*Z*)-3-[(Trimethylsilyl)methylene]cycloheptanone oxime (**2i'**). 12 % yield from **1i** as a colorless oil; ^{1}H NMR δ 0.08 (s, 9H), 1.62–1.72 (m, 4H), 2.18–2.23 (m, 2H), 2.26–2.32 (m, 2H), 3.35 (s, 2H), 5.47 (s, 1H), 8.30–8.45 (br, 1H); ^{13}C NMR δ –0.1, 28.1, 31.2, 33.4, 36.2, 42.6, 128.7, 155.2, 161.1; IR (film) 3425, 1751 cm^{-1}.

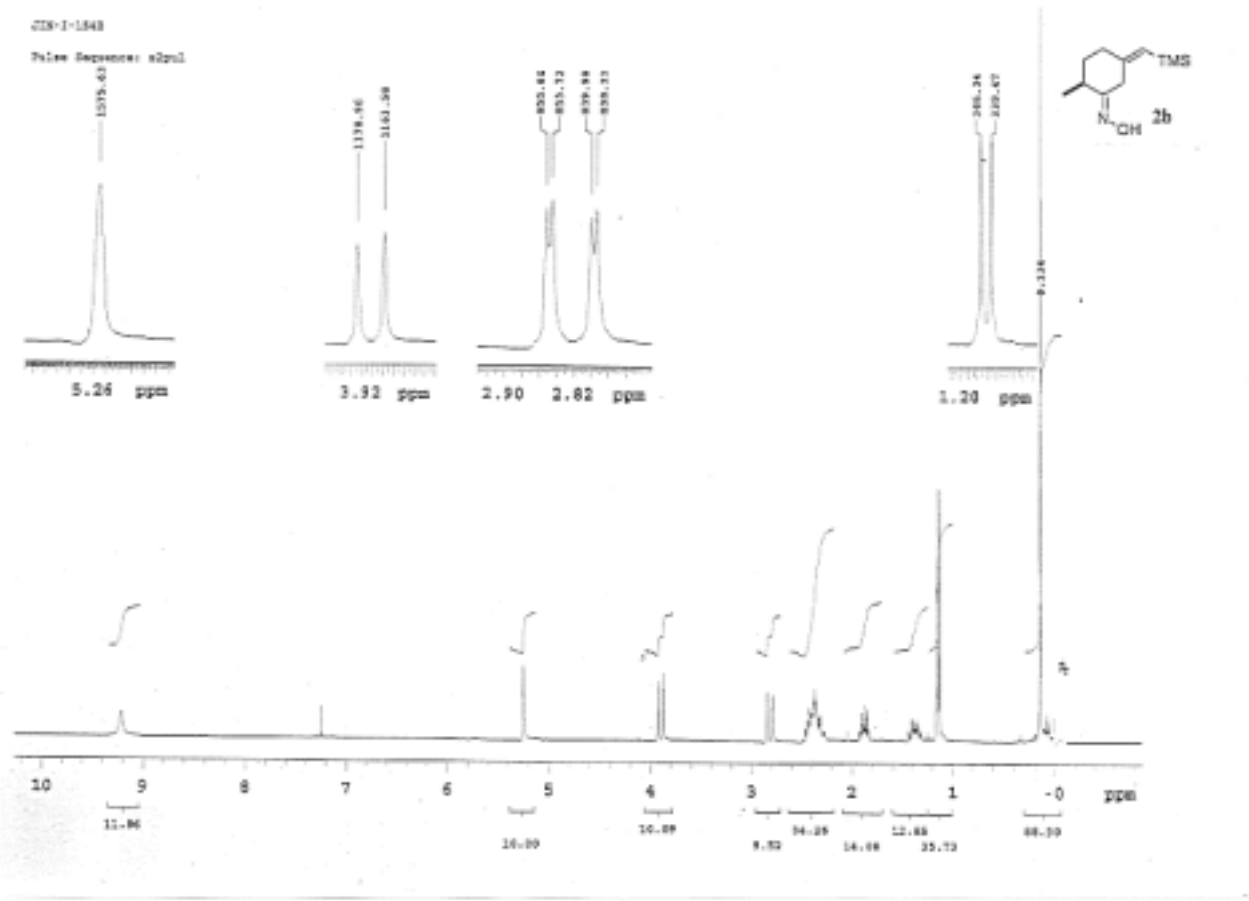
(3*Z*)-(Trimethylsilyl)methylene-6-hexanelactam (**8**). To a solution of the oxime **2a** (70 mg, 0.35 mmol) and pyridine (0.28 mL, 3.5 mmol) in CH_2Cl_2 was added methanesulfonyl chloride (0.05 mL, 0.7 mmol) at 0 °C. The mixture was stirred at room temperature for 1.5 h. The reaction was diluted with water and extracted with CH_2Cl_2. The combined extracts were dried with Na_2SO_4 and concentrated to give an oil which, on CC (2 : 1 hexane/AcOEt), gave **11** (33 mg, 48 %): ^{1}H NMR δ 0.16 (s, 9H), 1.74–1.84 (m, 2H), 2.45 (t, 2H, *J* = 6.0 Hz), 3.27 (s, 2H), 3.26–3.37 (m, 2H), 5.42 (s, 1H), 5.70–5.78 (br, 1H); ^{13}C NMR δ 0.04, 30.6, 42.3, 43.3, 43.6, 129.6, 148.7, 174.3; IR (film) 3209, 2950, 1654 cm^{-1}. Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; Found: C, 60.60; H, 9.53.

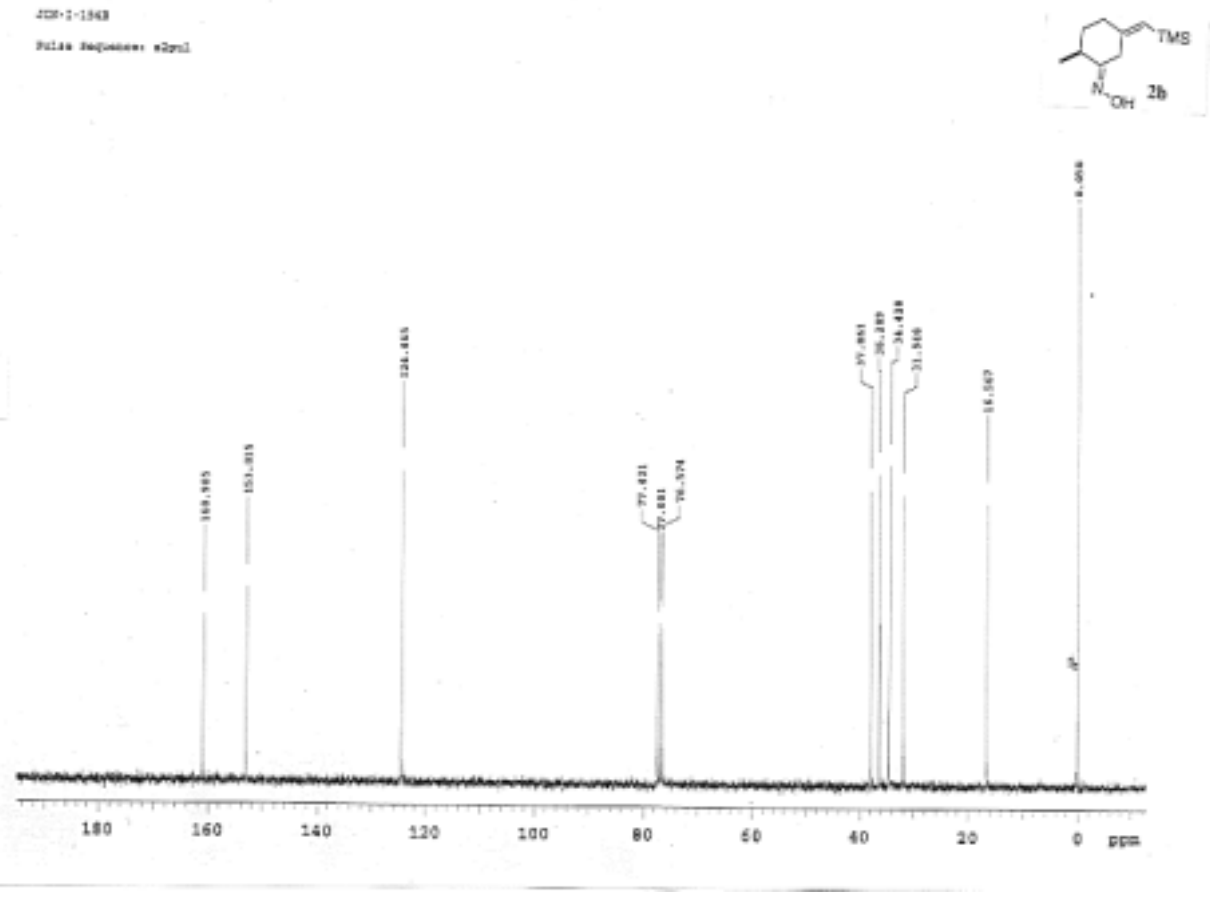
(6*S*)-3-(Trimetylsilyl)methyl-2-hexenelactam (**9**). This compound was prepared by the similar procedure as that for **8**. **9:** (99%); $[\alpha]^{20}_{D}$ +54.0 (c 0.20, MeOH); ^{1}H NMR δ 0.06 (s,

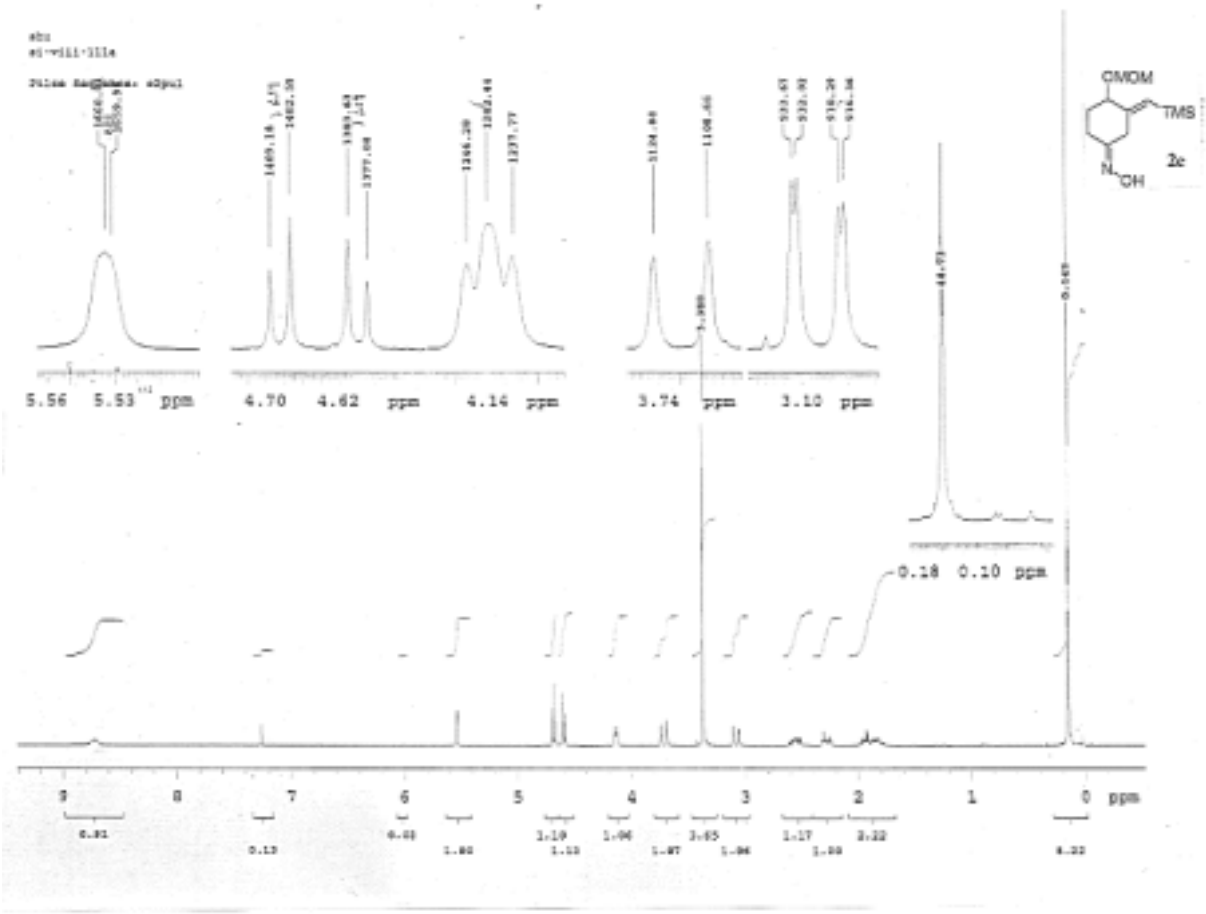
9H), 1.21 (d, 3H, J = 6.6 Hz), 1.69 (s, 2H), 1.72–1.96 (m, 2H), 2.12–2.23 (m, 1H), 2.38–2.51 (m, 1H), 3.42–3.55 (m, 1H), 5.58 (s, 1H), 5.80–5.90 (br, 1H); ^{13}C NMR δ –1.3, 21.3, 31.9, 34.2, 35.9, 47.6, 119.4, 154.4, 170.3; IR (film) 3434, 1648 cm^{-1}. Anal. Calcd for $C_{11}H_{21}NOSi$: C, 62.50; H, 10.01; Found: C, 62.37; H, 9.88.

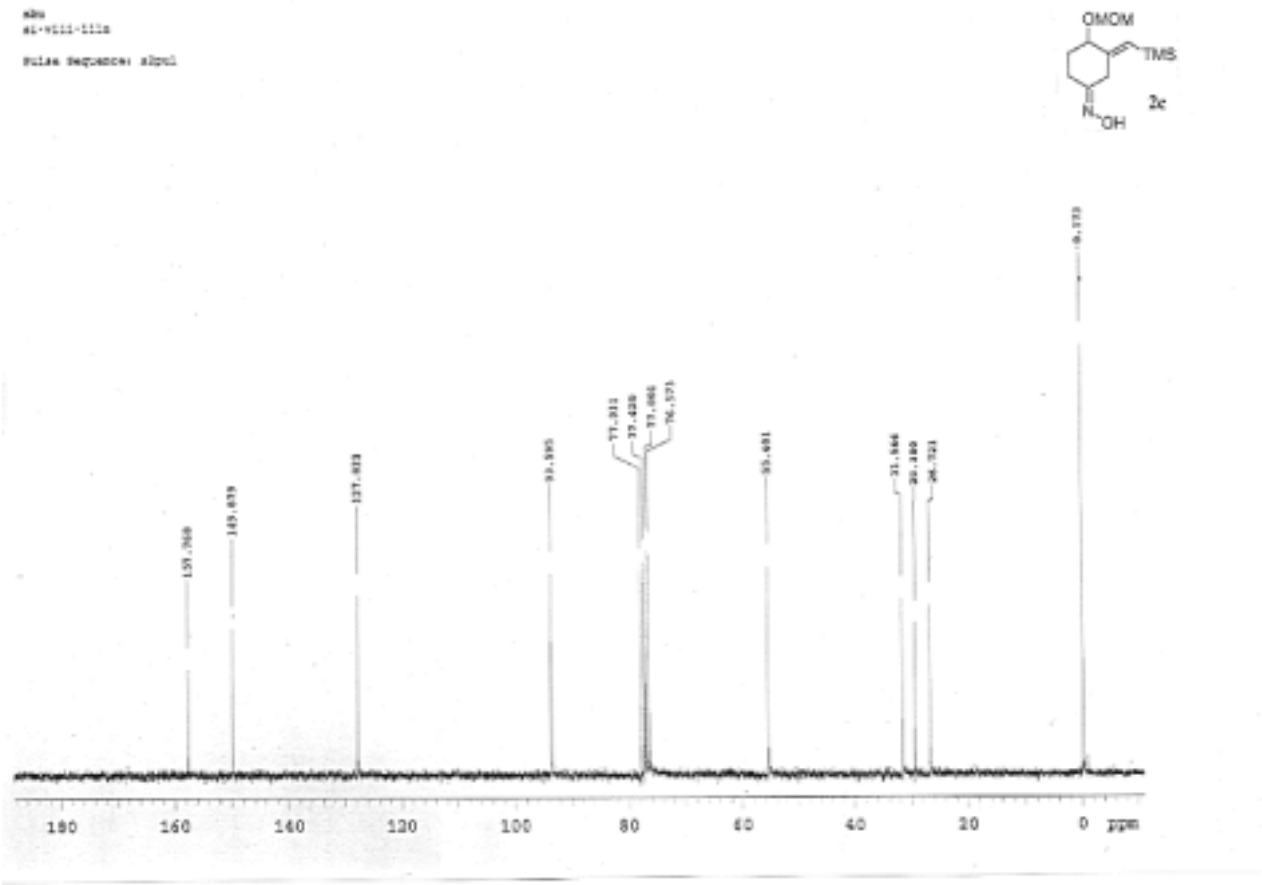

TMS
N
OH
2a
5.30 5.26 ppm
3.40 3.37 ppm
2.42 2.36 2.30 ppm
1.76 1.68 ppm
10 9 8 7 6 5 4 3 2 1 0 ppm

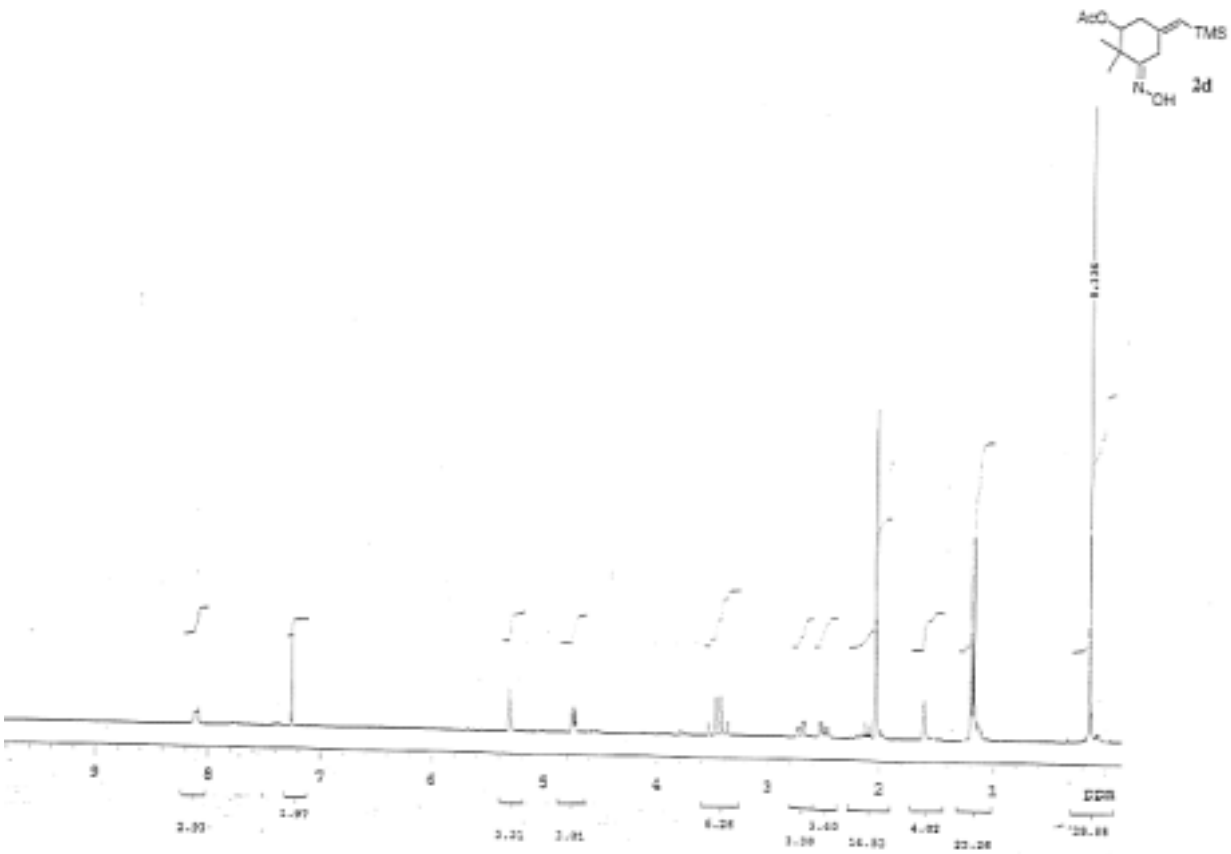

TMS
N
OH
2a
180 160 140 120 100 80 60 40 20 ppm

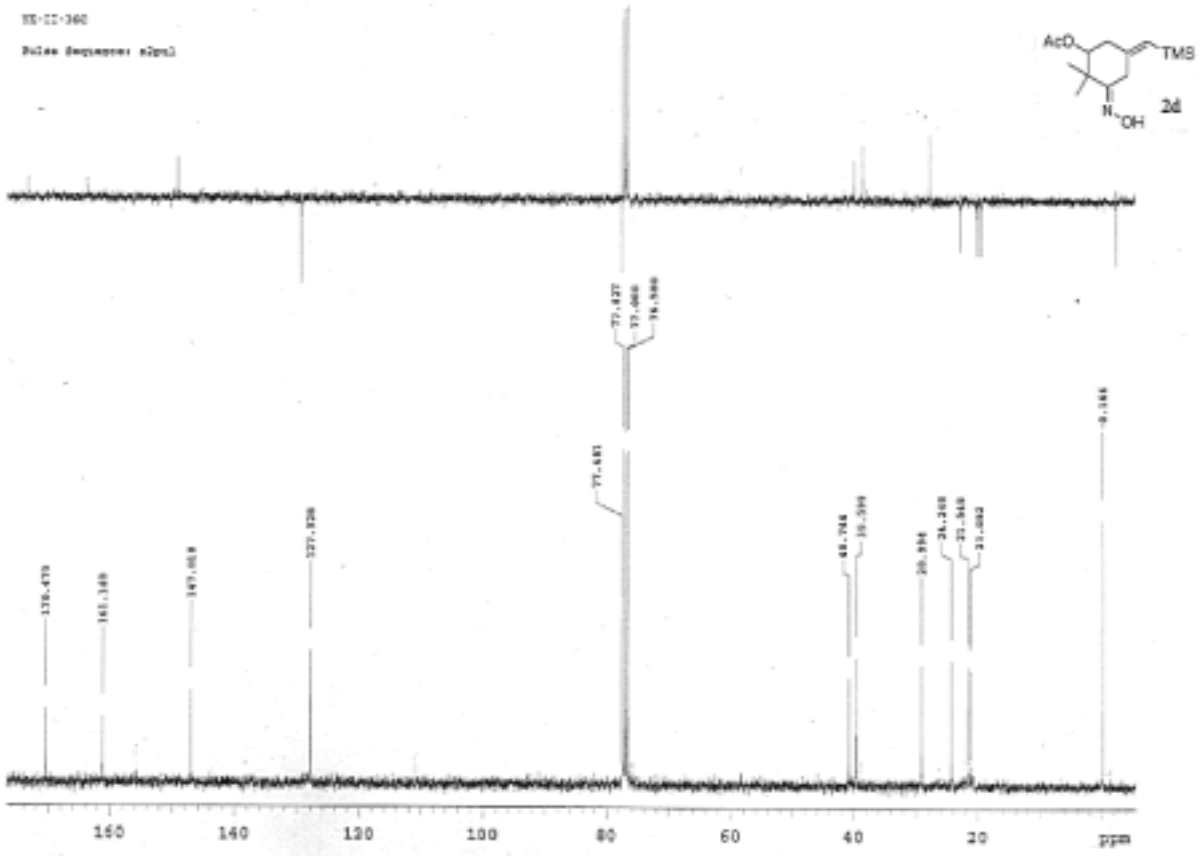

TMS
N
OH
2b
5.26 ppm
3.92 ppm
2.90 2.82 ppm
1.20 ppm
10 9 8 7 6 5 4 3 2 1 -0 ppm

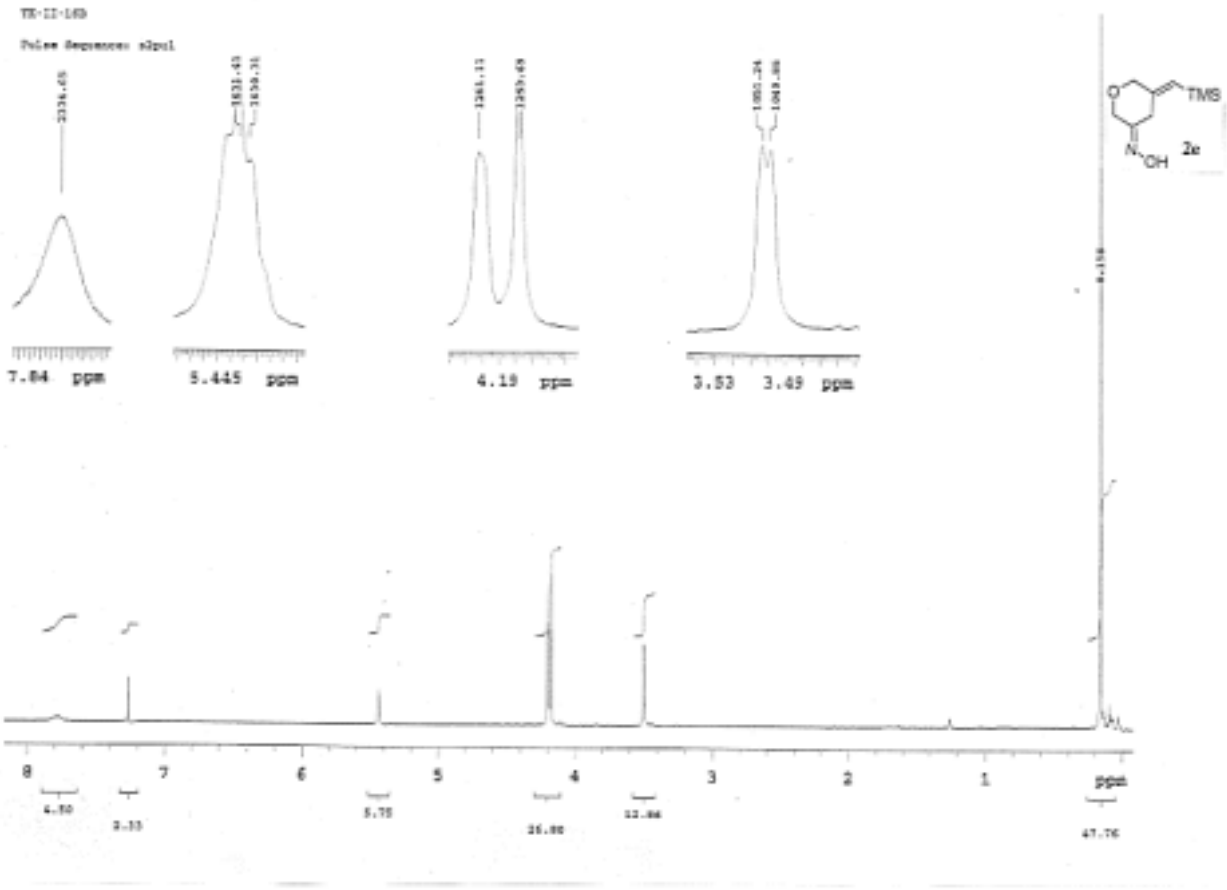

TMS
N
OH
2b
180 160 140 120 100 80 60 40 20 0 ppm

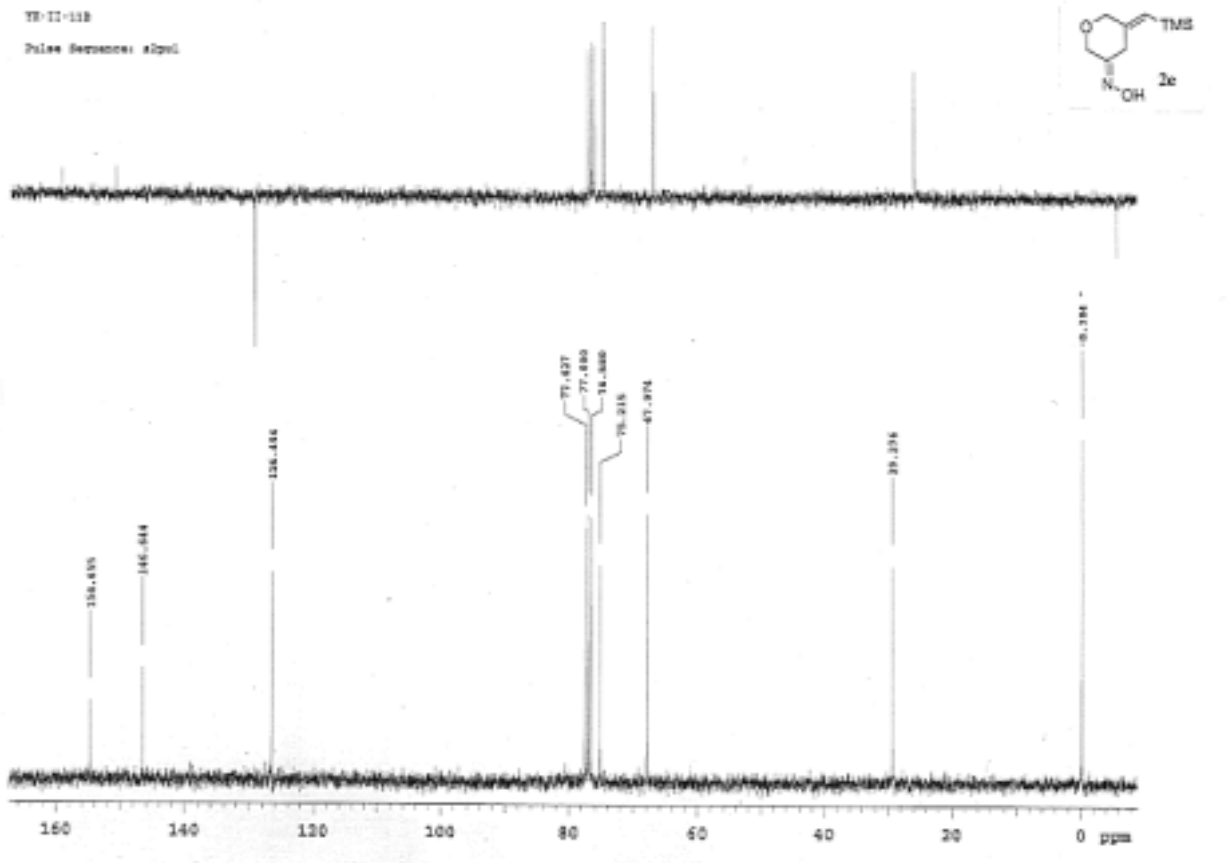

OMOM
TMS
2c
N
OH
5.56 5.53 ppm
4.70 4.62 ppm
4.14 ppm
3.74 ppm
3.10 ppm
0.18 0.10 ppm
9 8 7 6 5 4 3 2 1 0 ppm

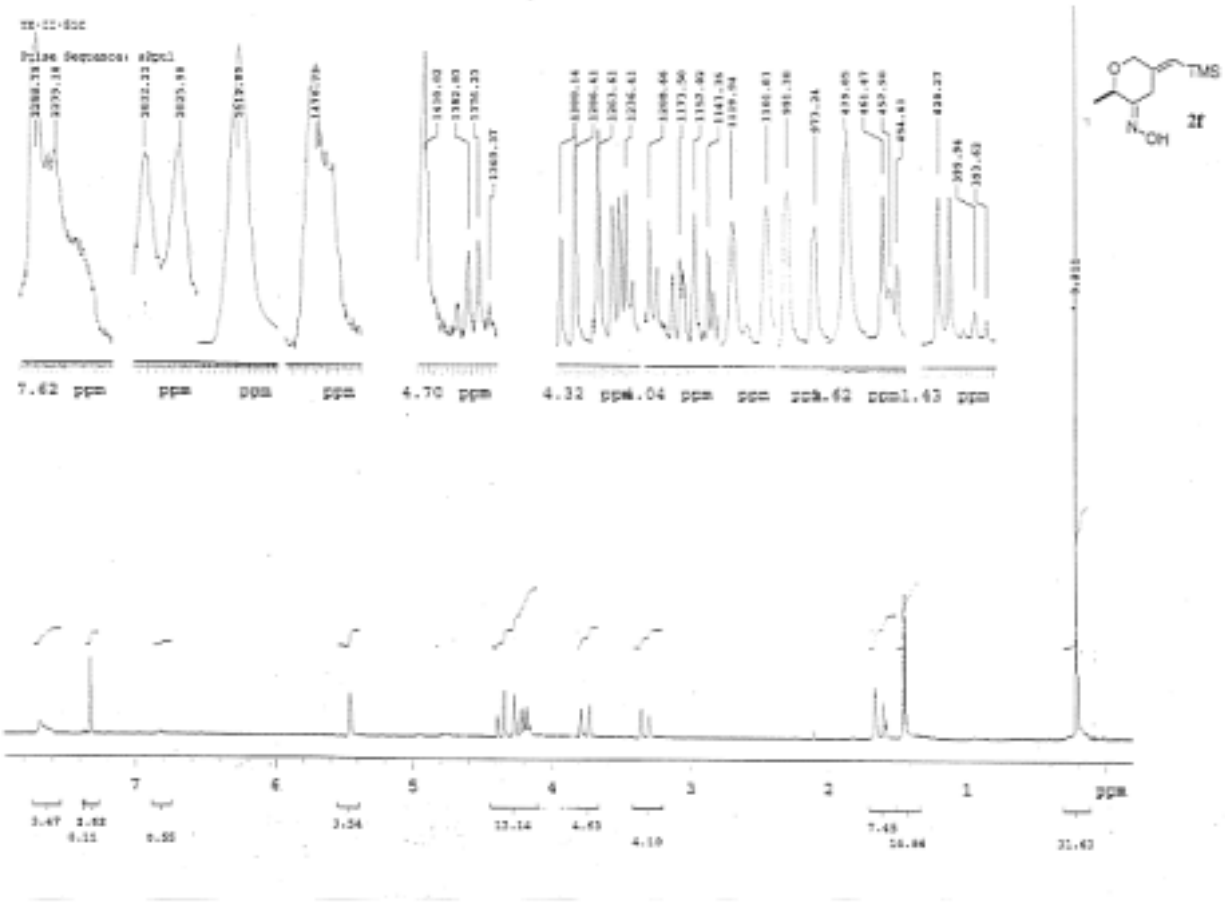

OMOM
TMS
2c
N
OH
190 160 140 120 100 80 60 40 20 0 ppm

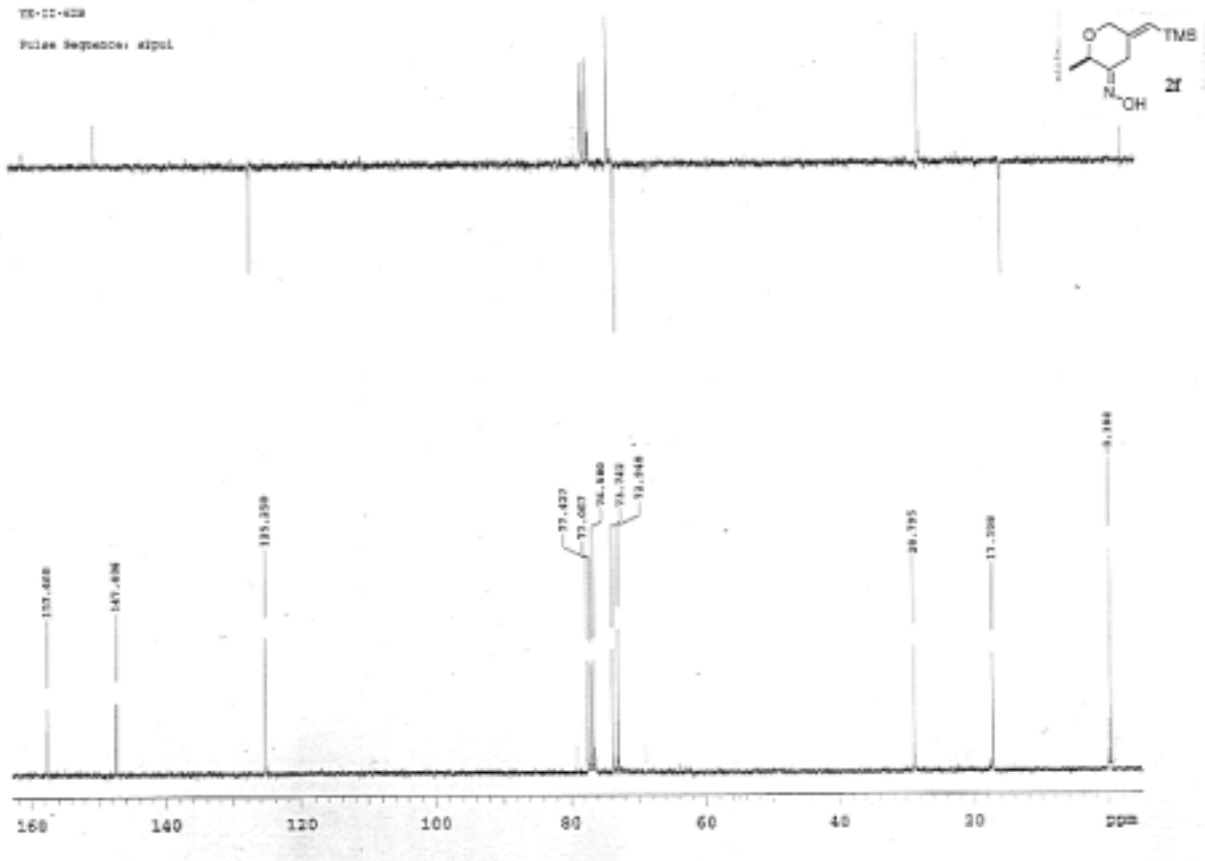

AcO
TMS
N
OH
2d
ppm

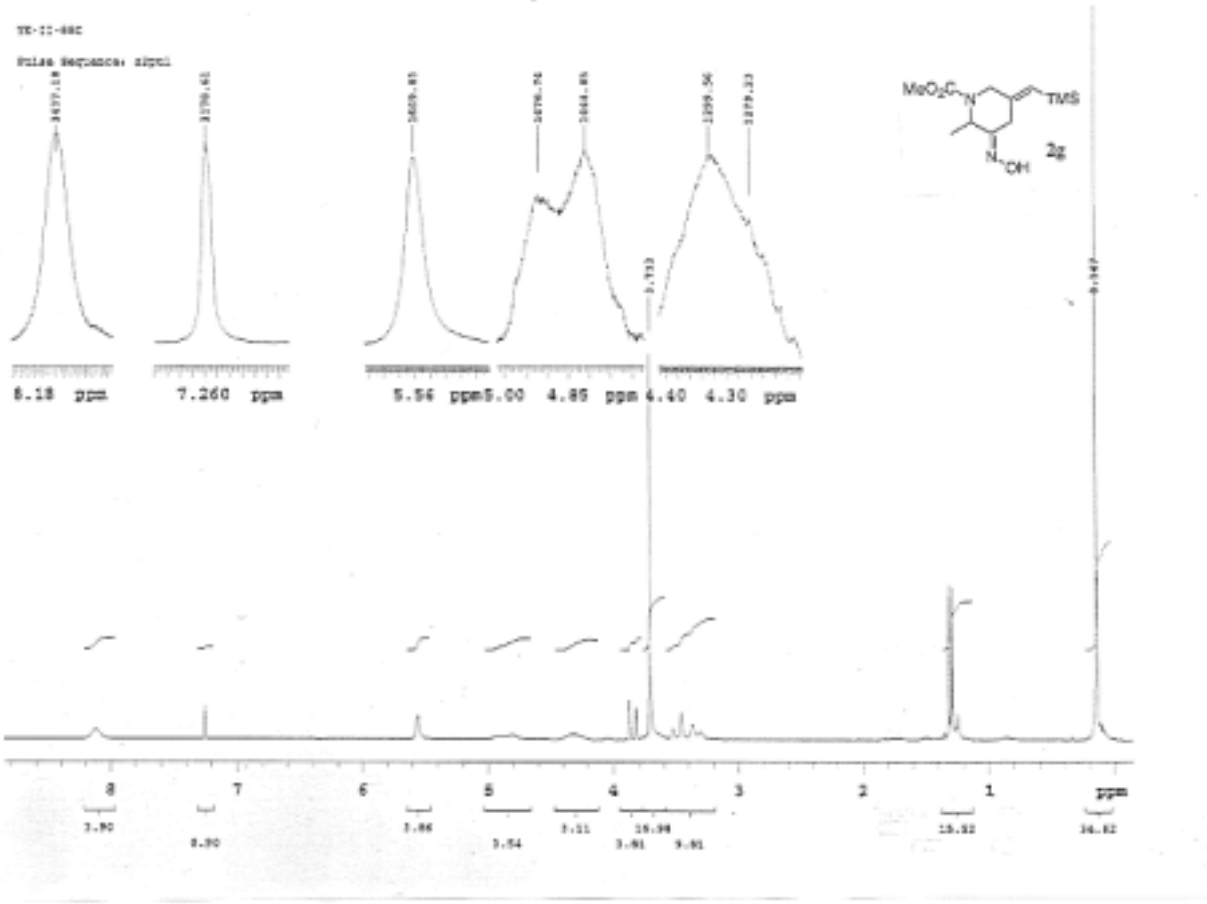

AcO
TMS
N
OH
2d
160
140
120
100
80
60
40
20
ppm

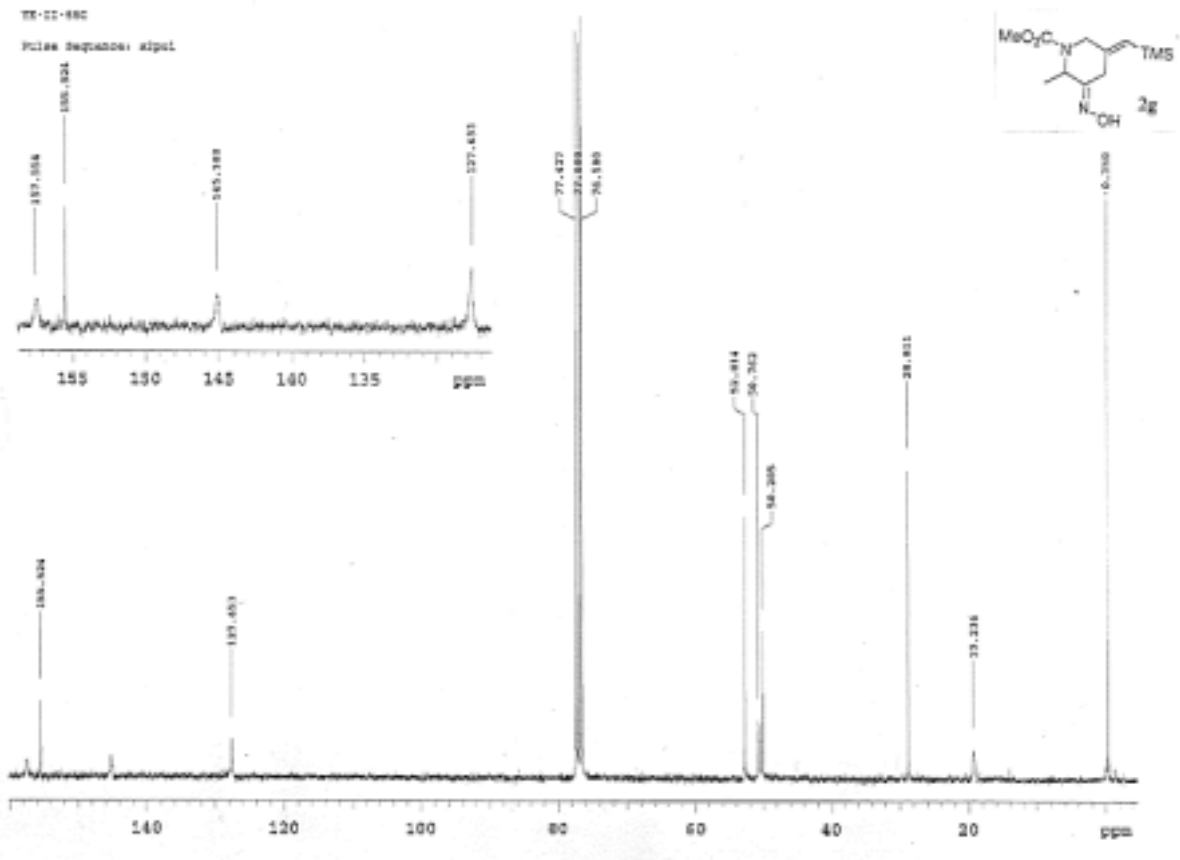

TMS
2e
7.84 ppm
5.445 ppm
4.19 ppm
3.53 3.49 ppm
ppm

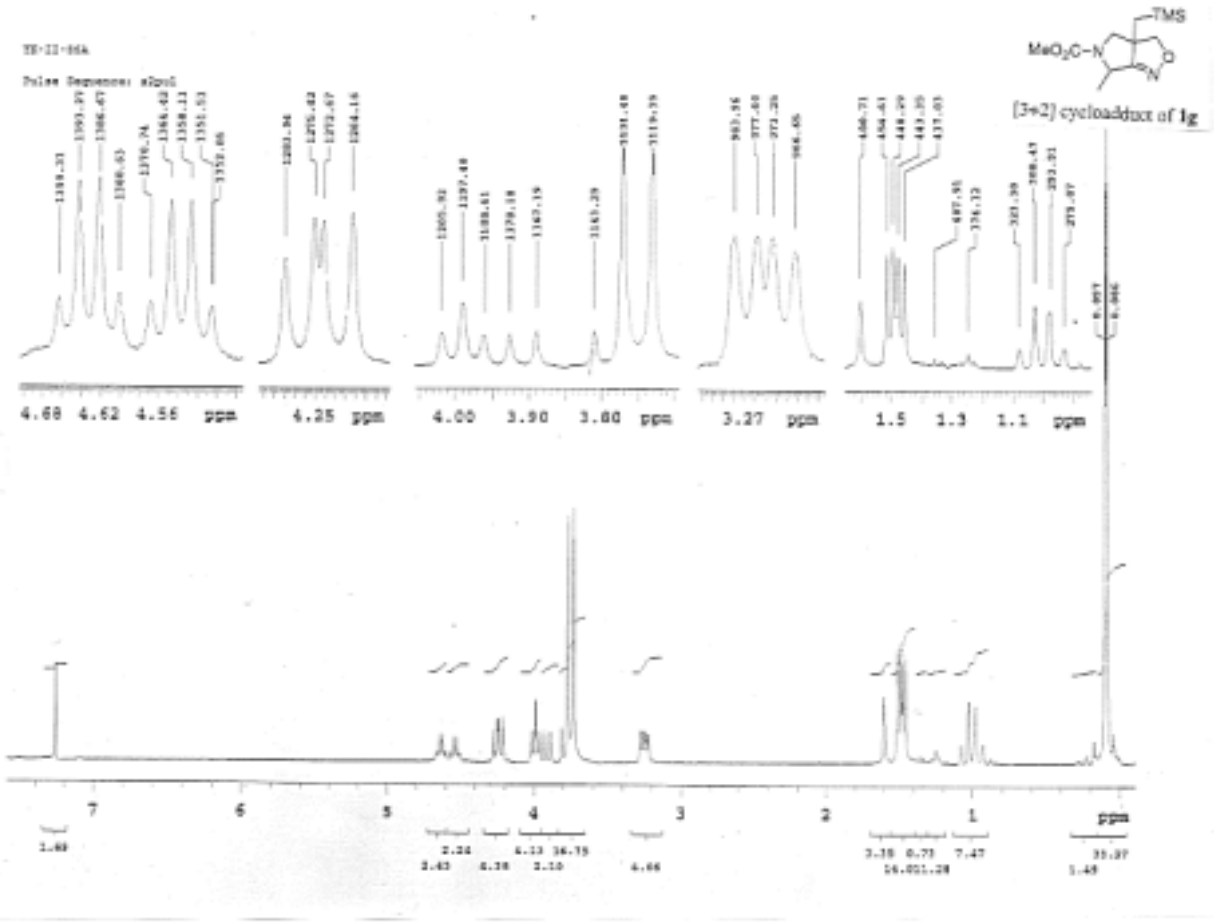

TMS
2e
160
140
120
100
80
60
40
20
0 ppm

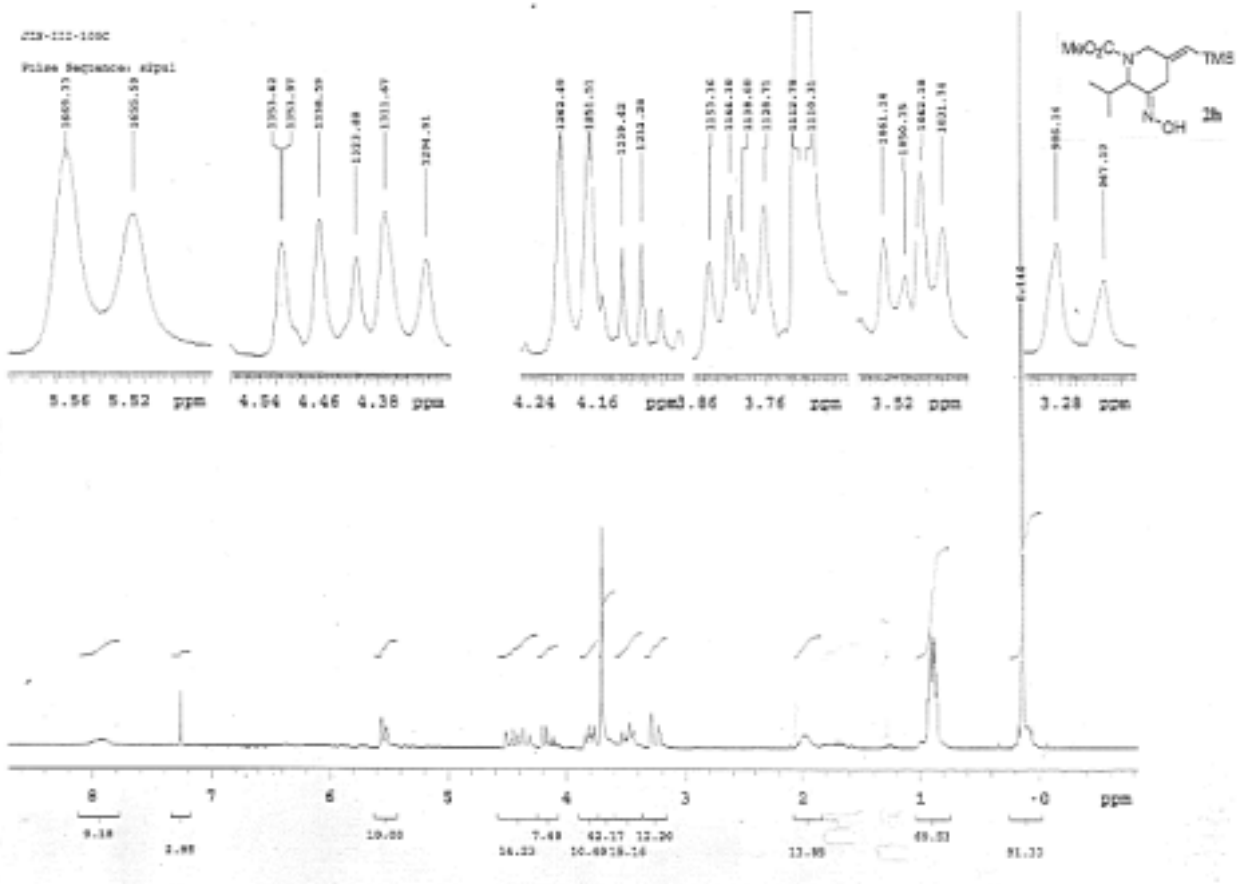

TMS
2f
N
OH
ppm

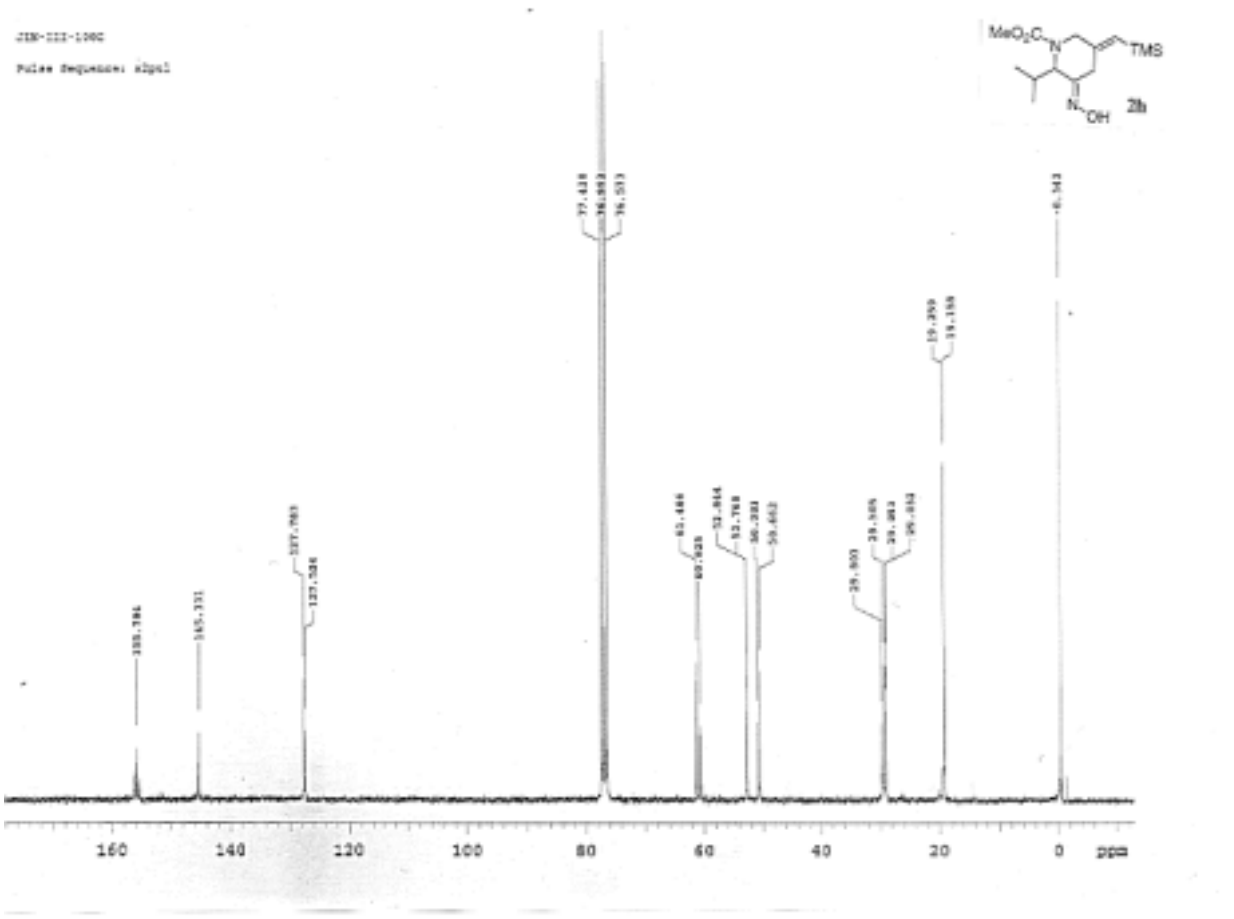

Pulse Sequence: s2pul
TMS
2f
N
OH
ppm

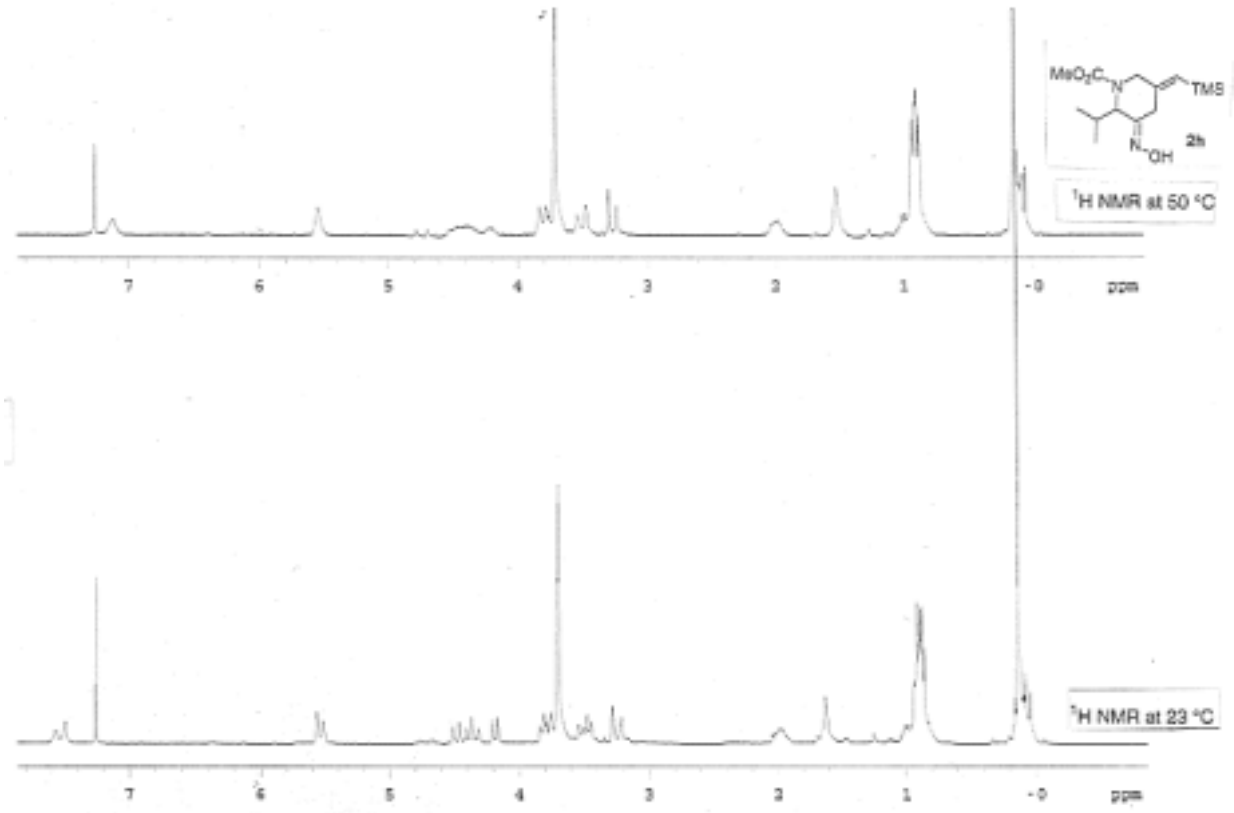

MeO2C
TMS
N
OH
2g
8.18 ppm
7.260 ppm
5.56 ppm
5.00
4.85 ppm
4.40
4.30 ppm
ppm


MeO2C
TMS
N
OH
2g
155
150
145
140
135
ppm
140
120
100
80
60
40
20
ppm

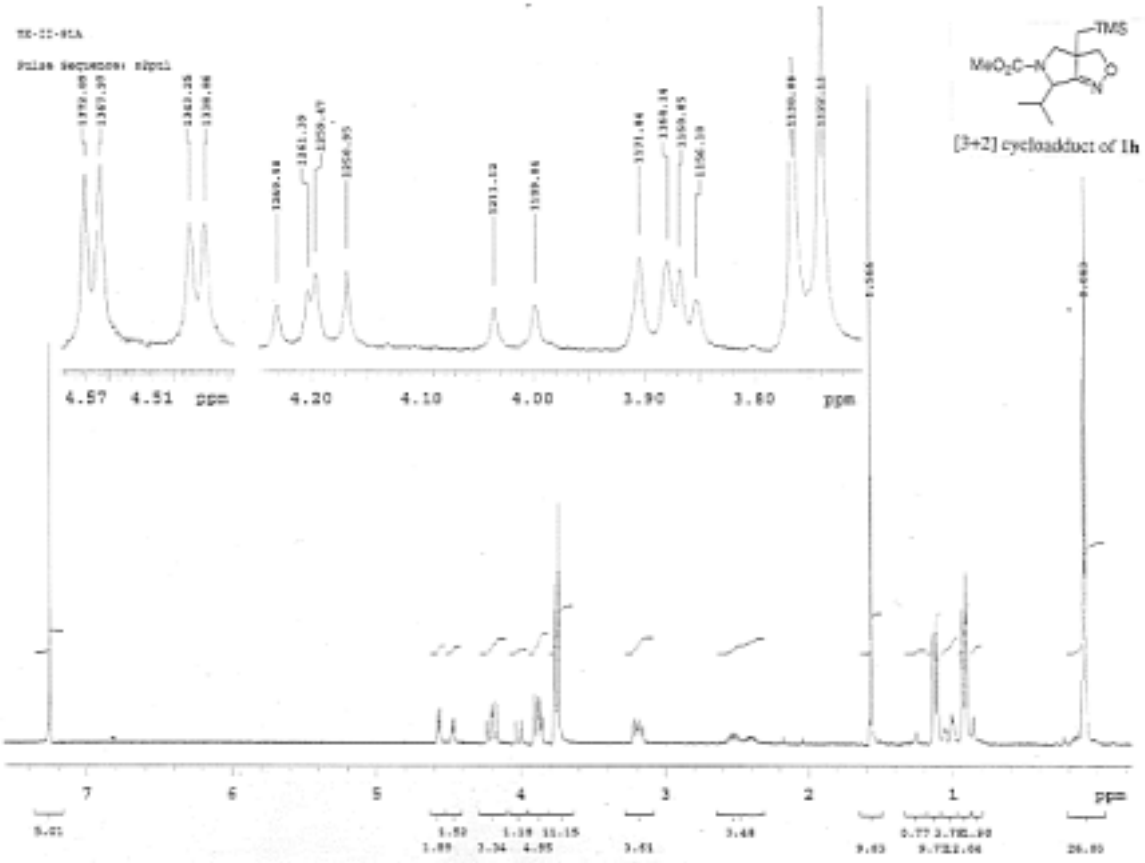

TMS
MeO2C–N
[3+2] cycloadduct of 1g

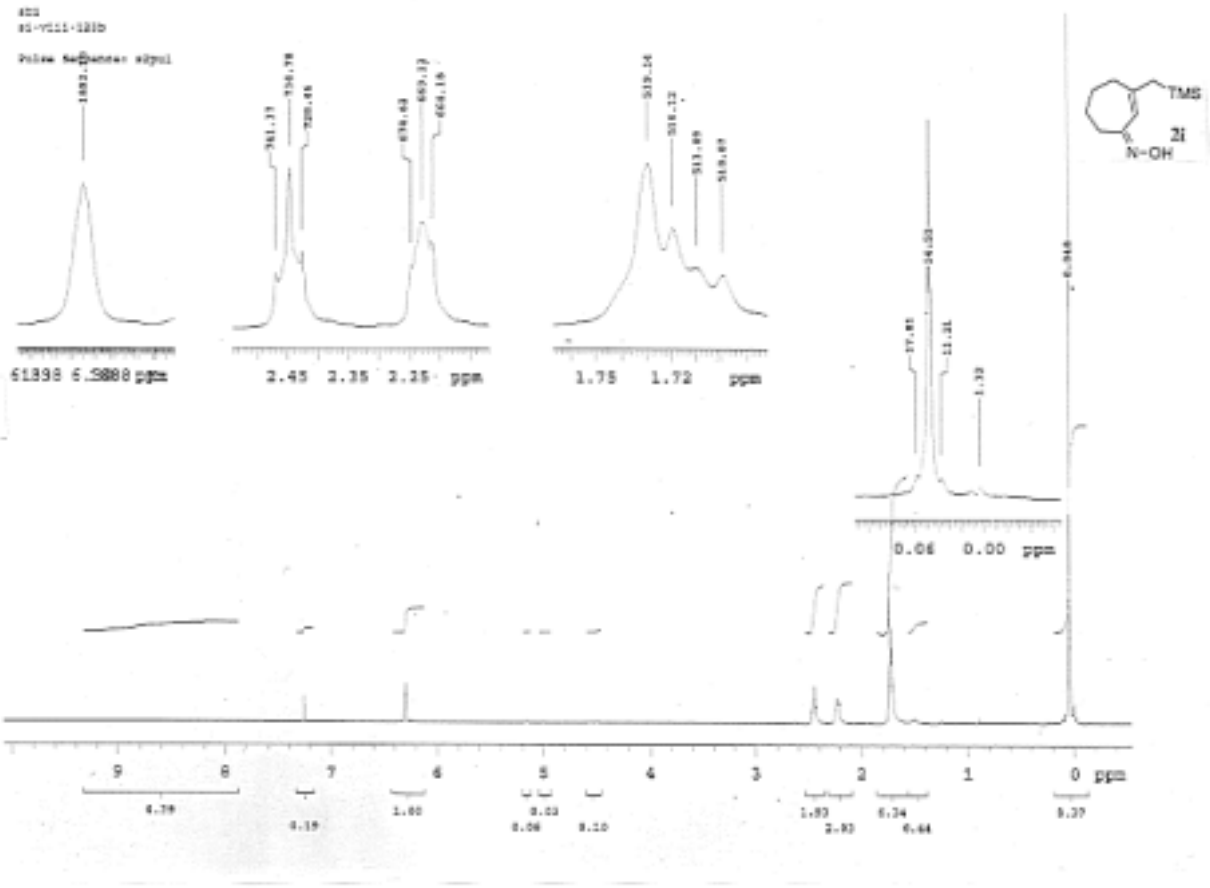

MeO2C–N
TMS
N–OH
2h

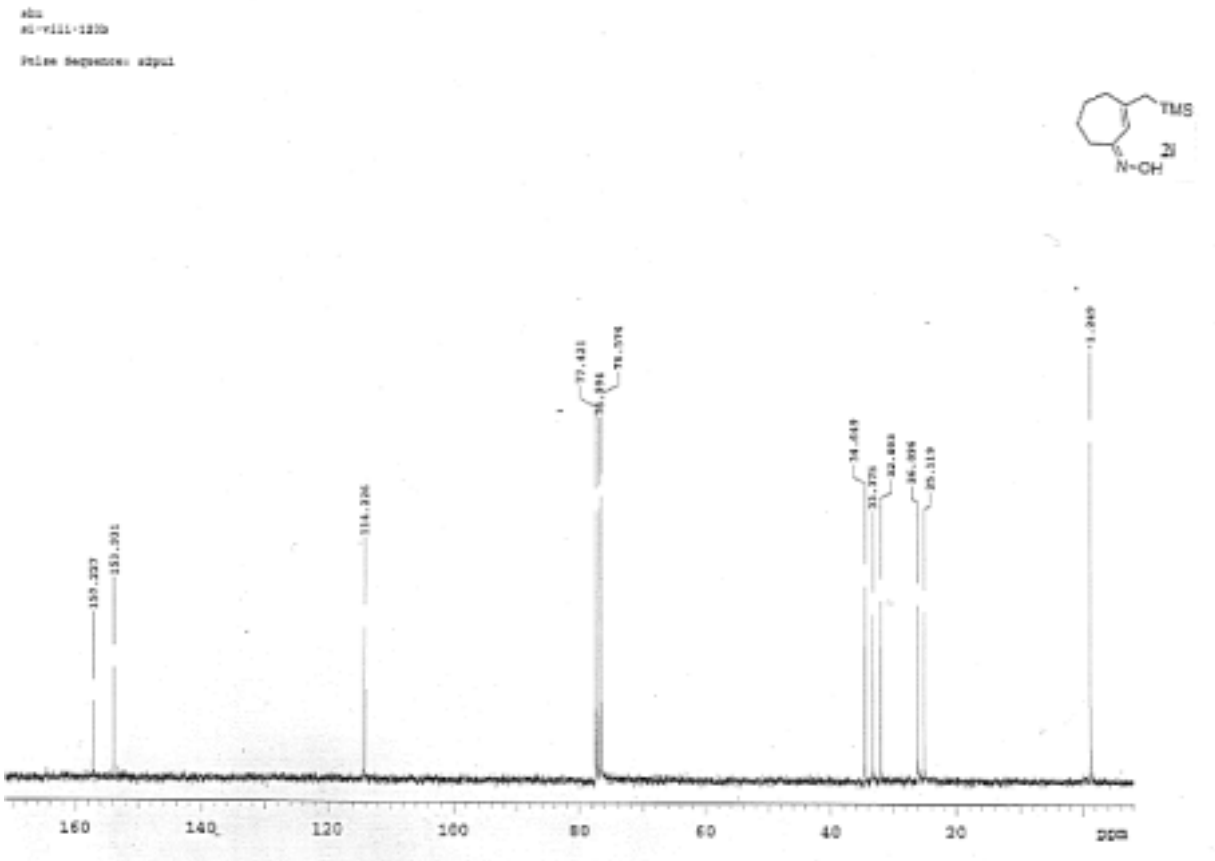

MeO2C
TMS
N
OH
2h
160
140
120
100
80
60
40
20
0
ppm

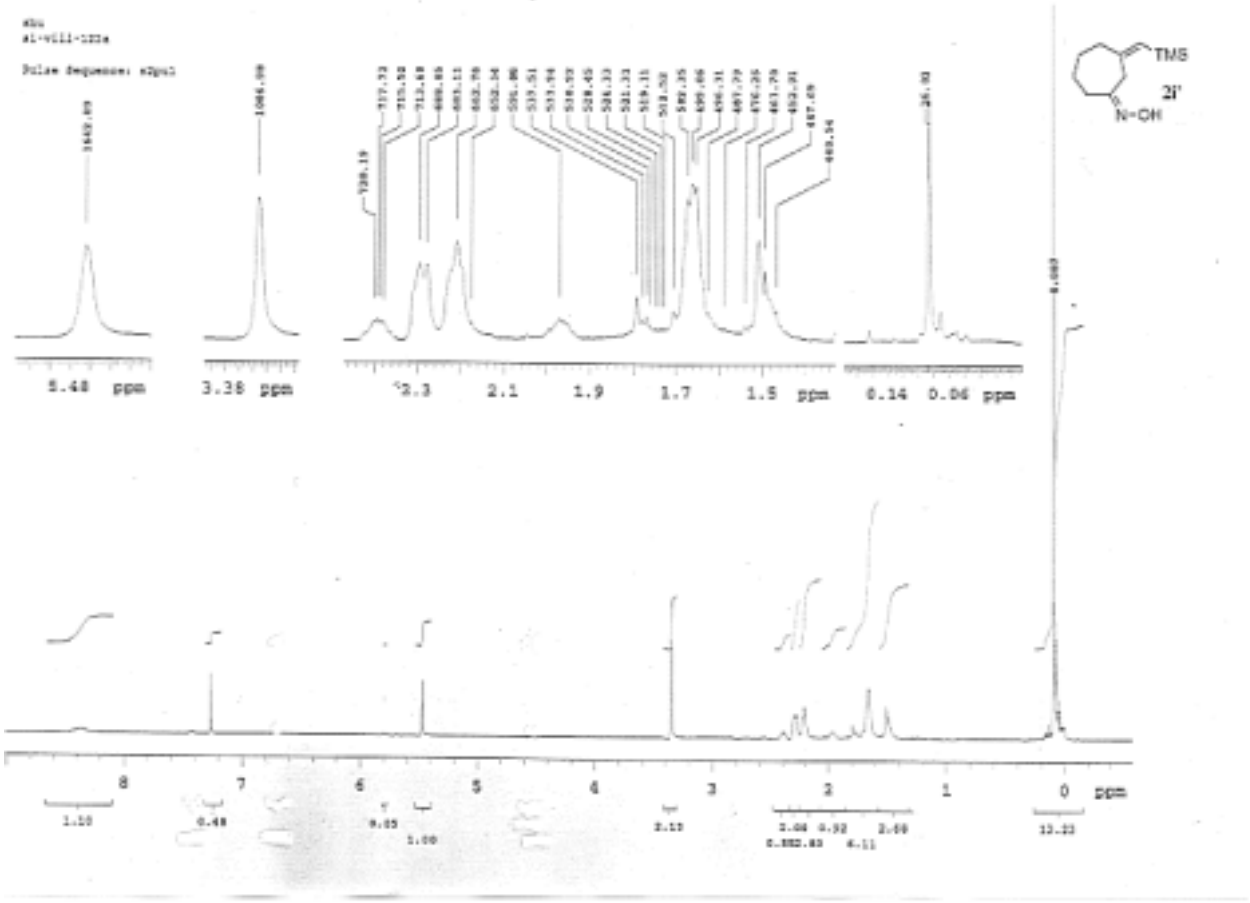

MeO2C
TMS
N
OH
2h
1H NMR at 50 °C
7
6
5
4
3
2
1
-0
ppm

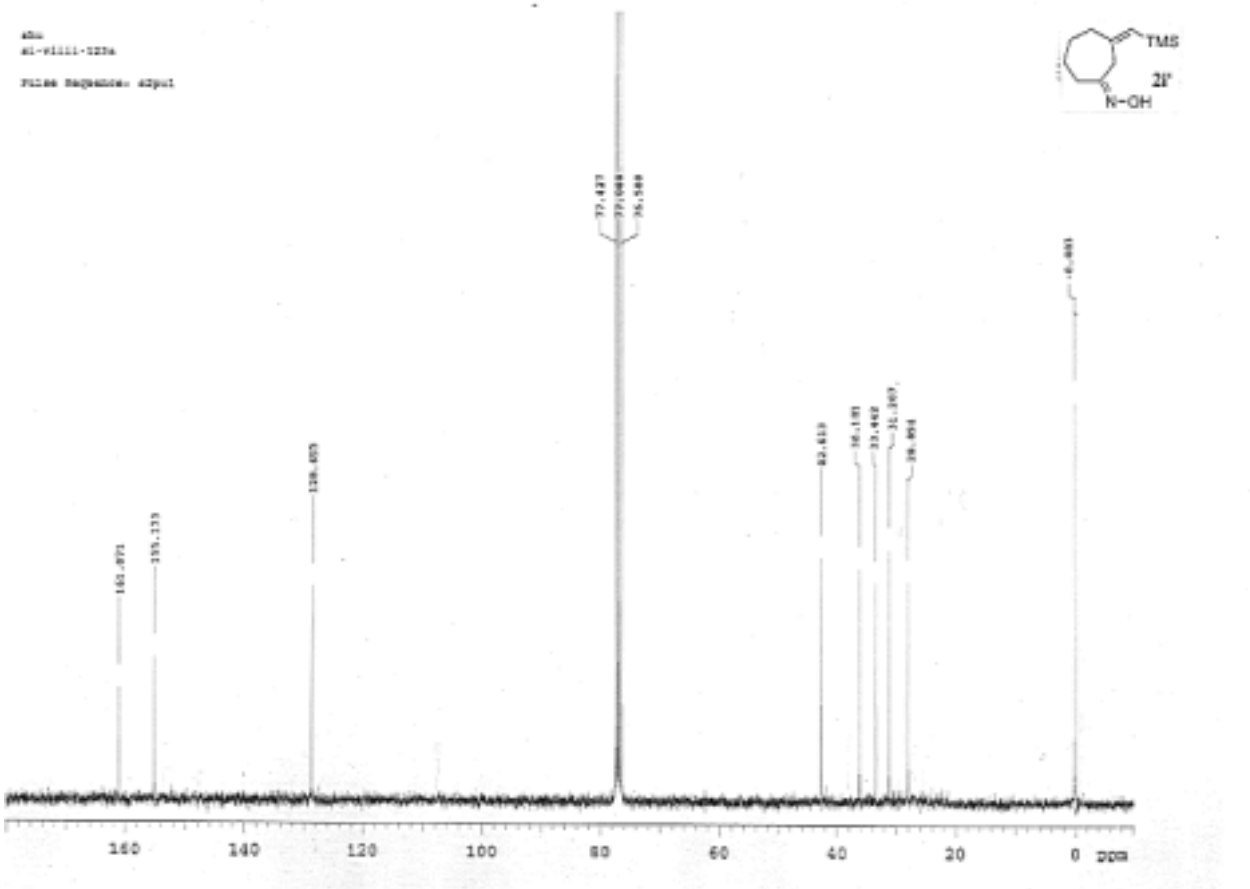
1H NMR at 23 °C
7
6
5
4
3
2
1
-0
ppm

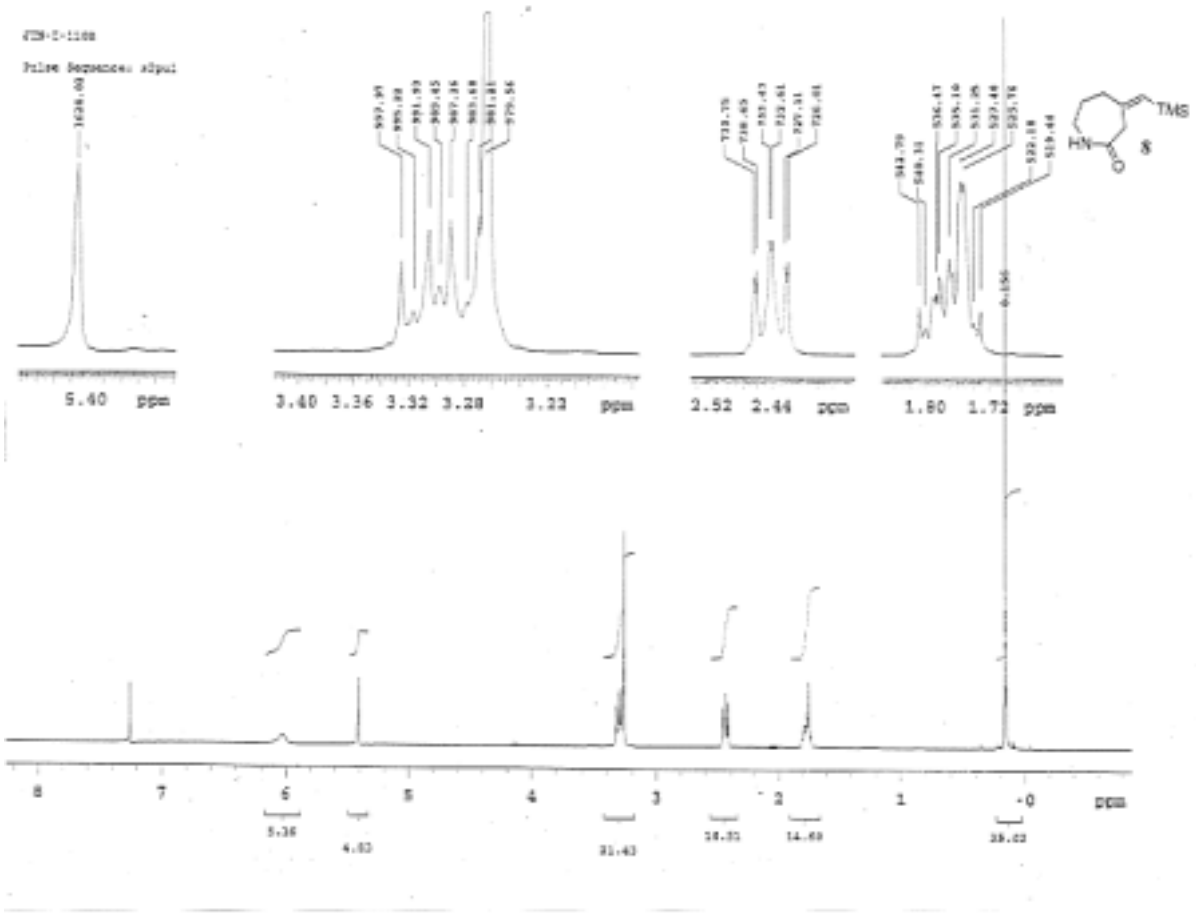

TMS
MeO2C–N
[3+2] cycloadduct of 1h
4.57 4.51 ppm
4.20 4.10 4.00 3.90 3.80 ppm
7 6 5 4 3 2 1 ppm

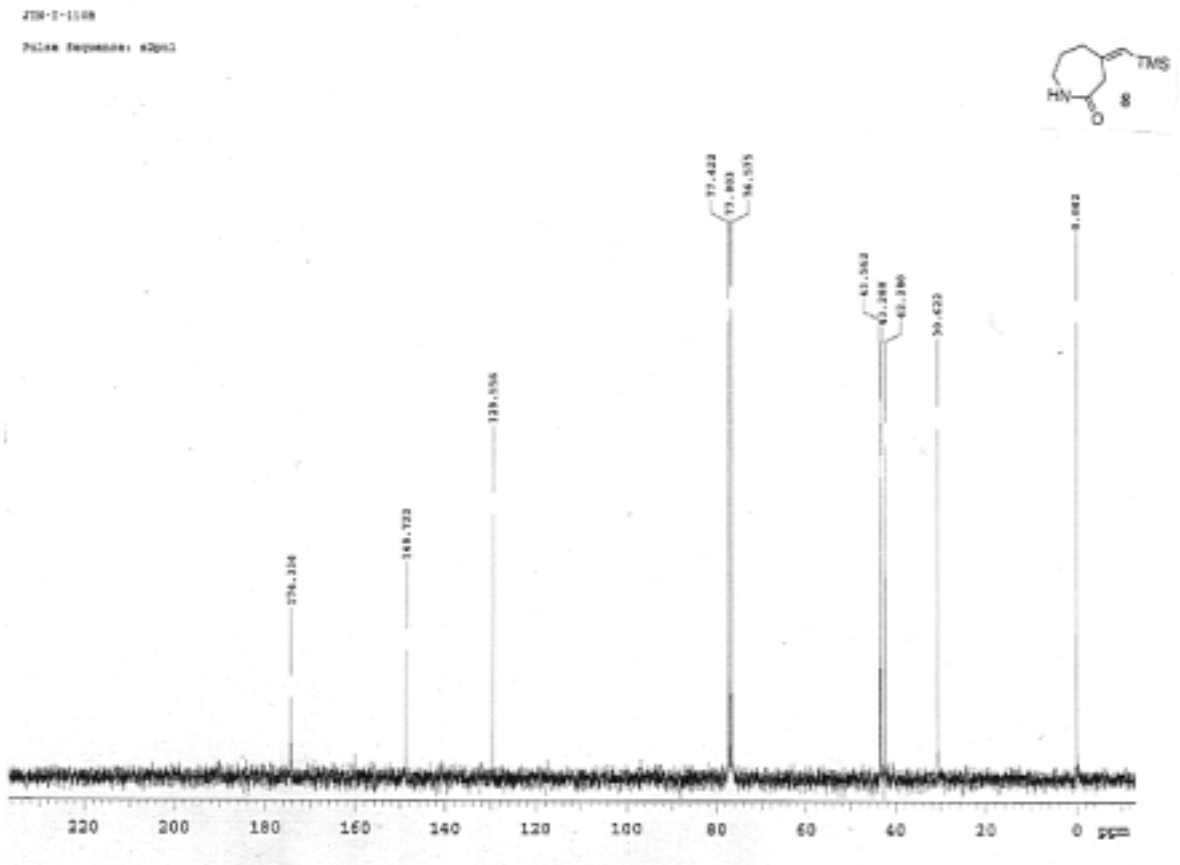

TMS
2i
N-OH
0.06 0.00 ppm
9 8 7 6 5 4 3 2 1 0 ppm

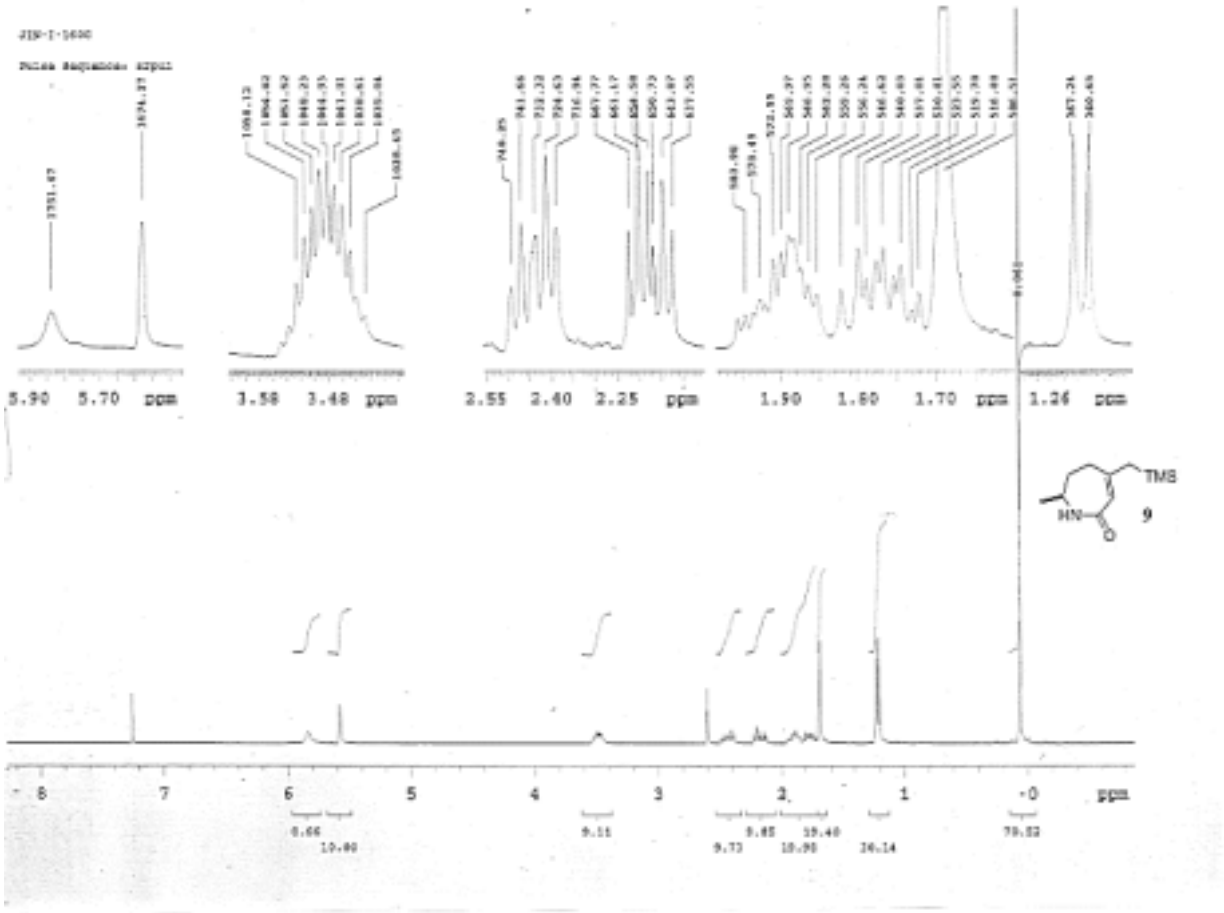

TMS
2i
N-OH
160 140 120 100 80 60 40 20 ppm

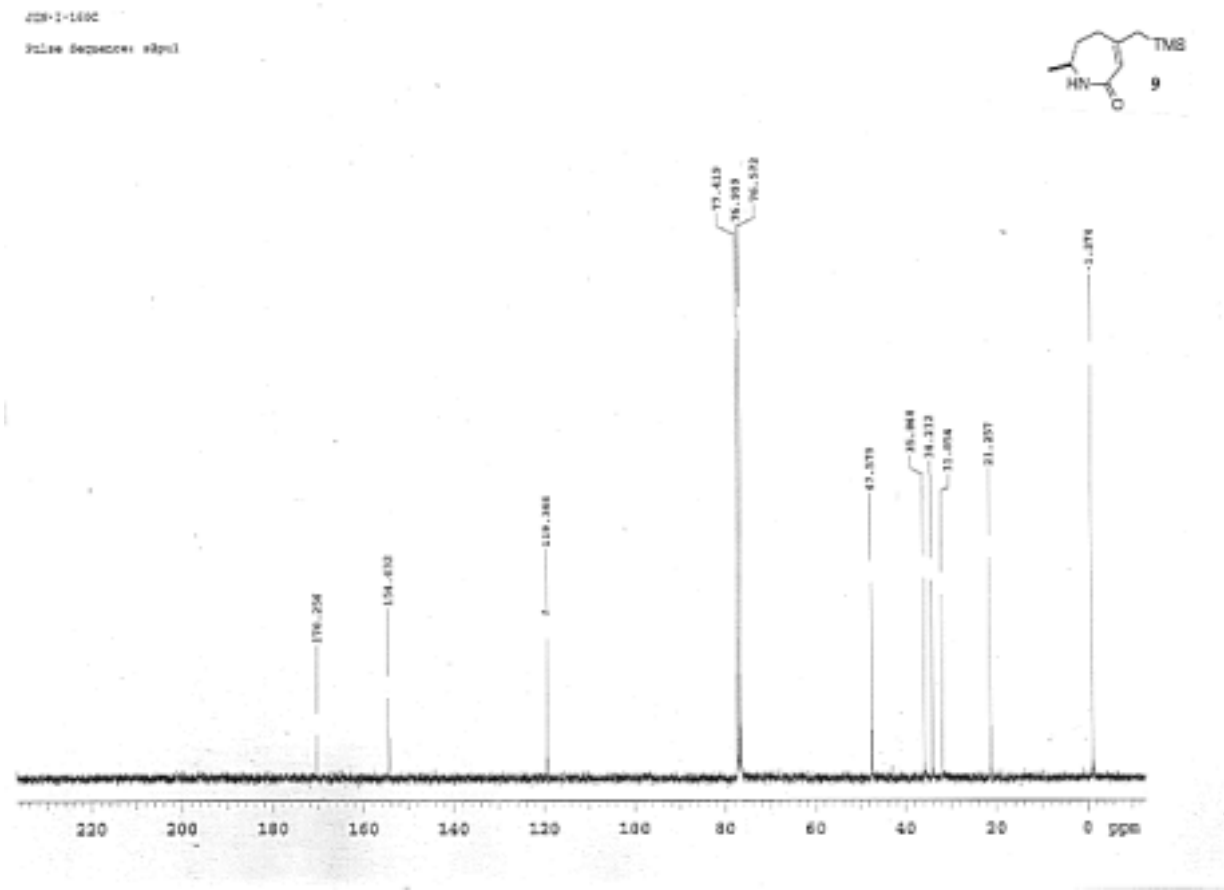

TMS
2f'
N-OH
5.48 ppm
3.38 ppm
2.3
2.1
1.9
1.7
1.5 ppm
0.14
0.06 ppm
8
7
6
5
4
3
2
1
0 ppm


TMS
2f'
N-OH
160
140
120
100
80
60
40
20
0 ppm


TMS
8
5.40 ppm
3.40 3.36 3.32 3.28 3.22 ppm
2.52 2.44 ppm
1.80 1.72 ppm
8 7 6 5 4 3 2 1 +0 ppm
5.36
4.02
31.43
18.31
14.69
28.02


TMS
8
220 200 180 160 140 120 100 80 60 40 20 0 ppm


TMS
HN
O
9
ppm


TMS
HN
O
9
ppm