

# Nitrosochlorination of cembrene

Alexey V. Tkachev<sup>\*a</sup> and Alexey V. Vorobjev<sup>b</sup>

<sup>a</sup> Department of Natural Sciences, Novosibirsk State University, 630090 Novosibirsk, Russian Federation.

Fax: +7 3832 34 4855; e-mail: atkachev@nioch.nsc.ru

<sup>b</sup> N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation

10.1070/MC2000v010n03ABEH001240

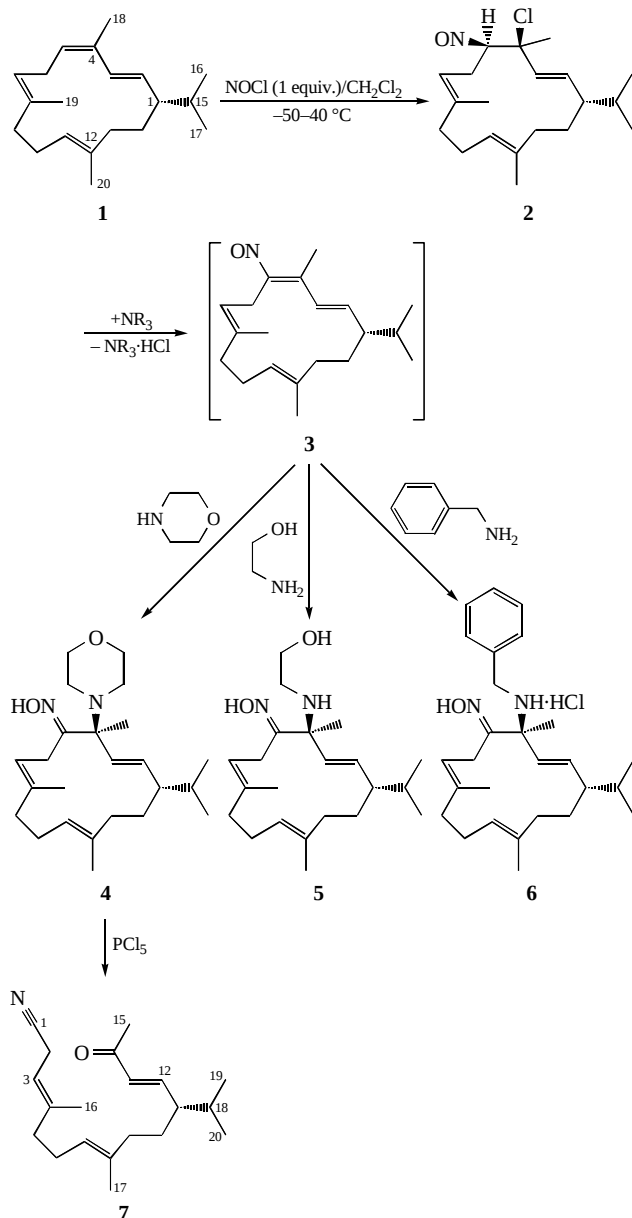
The reaction of NOCl with cembrene at  $-50\text{ }^{\circ}\text{C}$  in  $\text{CH}_2\text{Cl}_2$  results in 1,2-addition to the conjugated system of double bonds.

Cembrene **1** is the most widespread representative of cembrane-type diterpenoids.<sup>1,2</sup> Of the chemical properties of this natural compound, electrophilic cyclizations and oxidative transformations (Jones oxidation, oxidation by ozone and per acids, autoxidation, etc.) were studied.

As a rule, reactions of NOCl with conjugated dienes result in tar-like products or complex mixtures of derivatives. We used the nitrosochlorination of cembrene at the system of conjugated double bonds for preparation of nitrogen-containing derivatives.

Cembrene **1** does not form crystalline nitrosochlorides with alkyl nitrites in acidic media or with a solution of NOCl; a

complex mixture resulted from the reaction in both cases. A cembrene molecule has two conjugated double bonds and is very reactive towards electrophilic addition. The reaction of cembrene with an NOCl solution completed in a second at  $-5-0\text{ }^{\circ}\text{C}$  to form a tar. At a lower temperature, adduct **2** was formed, as evidenced by a bluish colour of the reaction mixture. The colour became dark brown on heating to  $-5-0\text{ }^{\circ}\text{C}$ . The formation of adduct **2** was supported by the isolation of corresponding  $\alpha$ -amino oximes after treatment of the reaction mixture with amines (Scheme 1). The amino oximes can be prepared in good yields as described below. A solution of NOCl in  $\text{CH}_2\text{Cl}_2$  (1.1 ml,  $1.8\text{ mmol cm}^{-3}$ ) was added to a solution of **1** (0.545 g, 2.0 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (20 ml) with stirring at  $-50\text{ }^{\circ}\text{C}$ . A blue colour appeared immediately and disappeared after adding morpholine (0.52 g, 6.0 mmol) at the specified temperature. The reaction mixture was allowed to heat spontaneously to room temperature, and a crystalline precipitate was formed. The reaction mixture was heated and allowed to stand at reflux for 5 min. The mixture was diluted with light petroleum (40 ml) and extracted with 1 M aqueous HCl ( $2\times 10\text{ ml}$ ). The combined acidic extracts were washed with *tert*-butyl methyl ether (10 ml), neutralised with concentrated aqueous ammonia and extracted with *tert*-butyl methyl ether ( $2\times 10\text{ ml}$ ). The combined extracts were dried over  $\text{MgSO}_4$  and concentrated at reduced pressure to give 0.82 g of the crude product as viscous yellow oil, which became solid at staying for several hours. Crystallization from hexane affords morpholine derivative **4** (0.46 g, 59%).<sup>†</sup> Derivatives of ethanolamine **5**<sup>‡</sup> and

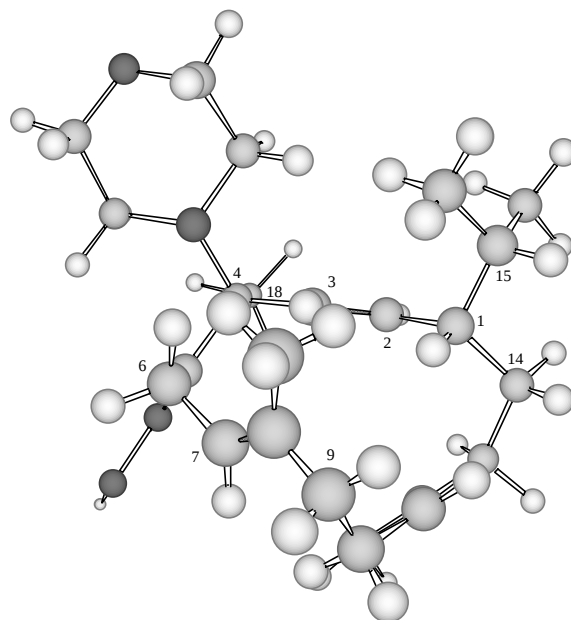


Scheme 1

<sup>†</sup> (1*S*,2*E*,4*S*,7*E*,11*E*)-4-(Morpholin-4-yl)cembra-2,7,11-trien-5-one (E)-oxime **4**: white crystals (yield 59%) from hexane, mp  $141-142\text{ }^{\circ}\text{C}$ ;  $[\alpha]_{\text{D}}^{20} +305$  (c 1.0,  $\text{CHCl}_3$ ). NMR spectra were measured on a Bruker AM-400 spectrometer, 400.13 and 100.61 MHz for  $^1\text{H}$  and  $^{13}\text{C}$ , respectively ( $0.32\text{ mmol cm}^{-3}$  in  $\text{CCl}_4\text{-C}_6\text{D}_6$ , 4:1 v/v,  $25\text{ }^{\circ}\text{C}$ ).  $^1\text{H}$  NMR (hereafter,  $^1\text{H}$  chemical shifts put in square brackets were taken from the 2D heteronuclear  $^{13}\text{C}$ - $^1\text{H}$  chemical shift correlation spectra),  $\delta$ : 1.70 (dddd, H-1,  $J$  9.3, 9.3, 4.4 and 4.3 Hz), 5.20 (dd, H-2,  $J$  15.7 and 9.3 Hz), 5.32 (d, H-3,  $J$  15.7 Hz), 3.44 (dd, H-6,  $J$  13.5 and 10.8 Hz), 3.10 (dm, H-6,  $J$  13.5 Hz,  $W_{1/2}$  7 Hz), 5.47 (dd, H-7,  $J$  10.8 and 3.0 Hz), [2.09, 2.04] (H-9), [2.10, 2.04] (H-10), 4.92 (br. s, H-11,  $W_{1/2}$  11 Hz), [1.90, 1.84] (H-13), [1.47, 1.23] (H-14), 1.49 (dqq, H-15,  $J$  4.3, 6.8 and 6.7 Hz), 0.80 (d, H-16,  $J$  6.7 Hz), 0.78 (d, H-17,  $J$  6.8 Hz), 1.24 (s, H-18), 1.62 (t, H-19,  $J$  1.3 Hz), 1.43 (d, H-20,  $J$  0.8 Hz), 3.56 (dd,  $\text{CH}_2\text{OCH}_2$ ,  $J$  4.6 and 4.6 Hz), 2.51 and 2.20 (2dt,  $\text{CH}_2\text{NCH}_2$ ,  $J$  11.7 and 4.6 Hz), 9.48 (br. s, =NOH).  $^{13}\text{C}$  NMR,  $\delta$ : 46.59 (C-1), 133.86 (C-2,  $^1J_{\text{C-H}}$  151.5 Hz), 134.74 (C-3,  $^1J_{\text{C-H}}$  156.6 Hz,  $^2,3J_{\text{C-H}}$  3.7, 3.7 and 3.7 Hz), 66.16 (C-4,  $^2,3J_{\text{C-H}}$  2.9, 2.9, 2.9 and 2.9 Hz), 162.97 (C-5), 24.69 (C-6,  $^1J_{\text{C-H}}$  129.2 Hz,  $^2,3J_{\text{C-H}}$  3.3 Hz), 122.10 (C-7,  $^1J_{\text{C-H}}$  157.5 Hz), 133.46 (s, C-8 or C-12), 38.87 (C-9,  $^1J_{\text{C-H}}$  127.8 Hz), 23.63 (C-10,  $^1J_{\text{C-H}}$  125.3 Hz), 124.92 (C-11,  $^1J_{\text{C-H}}$  152.3 Hz), 132.16 (C-12 or C-8), 36.33 (C-13,  $^1J_{\text{C-H}}$  126.3 Hz), 28.05 (C-14,  $^1J_{\text{C-H}}$  126.4 Hz), 33.86 (C-15,  $^1J_{\text{C-H}}$  126.8 Hz), 20.98 (C-16,  $^1J_{\text{C-H}}$  124.7 Hz,  $^2,3J_{\text{C-H}}$   $5\times 4.8$  Hz), 19.68 (C-17,  $^1J_{\text{C-H}}$  124.5 Hz,  $^2,3J_{\text{C-H}}$   $5\times 4.7$  Hz), 11.49 (C-18,  $^1J_{\text{C-H}}$  127.0 Hz,  $^2,3J_{\text{C-H}}$  4.2 Hz), 15.65 (C-19,  $^1J_{\text{C-H}}$  125.0 Hz,  $^2,3J_{\text{C-H}}$  8.0, 3.9 and 3.9 Hz), 15.84 (C-20,  $^1J_{\text{C-H}}$  124.2 Hz,  $^2,3J_{\text{C-H}}$  8.4, 5.2 and 2.8 Hz), 67.79 ( $\text{CH}_2\text{OCH}_2$ ,  $^1J_{\text{C-H}}$  142.6 Hz,  $^2,3J_{\text{C-H}}$  3.6 and 3.6 Hz), 47.31 ( $\text{CH}_2\text{NCH}_2$ ,  $^1J_{\text{C-H}}$  132.6 Hz,  $^2,3J_{\text{C-H}}$  4.2 and 4.2 Hz). IR ( $\text{CHCl}_3$ ,  $\nu/\text{cm}^{-1}$ ): 3590 ( $\nu_{\text{N-O}}$ ). IR (KBr,  $\nu/\text{cm}^{-1}$ ): 1105 ( $\delta_{\text{O-C}}$ ), 980 ( $\delta_{\text{CH=CH}}$ ), 955 ( $\nu_{\text{N-O}}$ ). MS,  $m/z$  (%): 388.30856 ( $\text{M}^+$ , 8), 371 ( $\text{M}^+ - \text{OH}$ , 100), 303 (8), 301 (10), 286 (21), 284 (20), 260 (11), 258 (19), 208 (20), 166 (16), 140 (10), 107 (9), 95 (10), 93 (10), 86 (14), 81 (22), 79 (12), 69 (17), 67 (14), 57 (10), 55 (18). Found (%): C, 74.5; H, 10.5; N, 7.3. Calc. for  $\text{C}_{24}\text{H}_{40}\text{N}_2\text{O}_2$  (%): C, 74.18; H, 10.37; N, 7.21.

benzylamine **6**<sup>8</sup> were prepared in the same manner. The amino oximes **4–6** exhibit the same properties as other  $\alpha$ -amino oximes of terpenic nature:<sup>3</sup> they are soluble in dilute aqueous solutions of inorganic acids and can be easily extracted back after neutralization with aqueous ammonia; they lose a tertiary amino group upon heating to 100 °C in toluene (compound **4**) to form a mixture of unsaturated ketoximes; they easily undergo the Beckmann-type fragmentation. Thus, the treatment<sup>4</sup> of a solution of morpholino derivative **4** (0.33 g, 0.85 mmol) in CH<sub>2</sub>Cl<sub>2</sub> with PCl<sub>5</sub> (0.21 g, 1.0 mmol) at 10 °C resulted in 0.36 g of a pale yellow oil, which was purified by column chromatography on a silica gel column to give keto nitrile **7** (0.22 g, 86%).<sup>†</sup>

The formation of amino oximes **4–6** proceeds *via* nitroso olefin **3** (as was found for other amino oximes<sup>3</sup>), which can be



**Figure 1** Molecular structure of the most stable conformation of compound **4**. The characteristic dihedral angles and calculated and experimental spin-spin coupling constants are as follows: H1–C1–C2–H2 +158°,  $^3J_{\text{calc.}}$  10.3 Hz ( $^3J_{\text{exp.}}$  9.3 Hz); H1–C1–C14–H14 $\alpha$  –160°,  $^3J_{\text{calc.}}$  11.5 Hz ( $^3J_{\text{exp.}}$  9.3 Hz); H1–C1–C14–H14 $\beta$  –49°,  $^3J_{\text{calc.}}$  2.3 Hz ( $^3J_{\text{exp.}}$  4.3 Hz); H6 $\alpha$ –C6–C7–H7 +63°,  $^3J_{\text{calc.}}$  3.4 Hz ( $^3J_{\text{exp.}}$  3.0 Hz); H6 $\beta$ –C6–C7–H7 +163°,  $^3J_{\text{calc.}}$  10.8 Hz ( $^3J_{\text{exp.}}$  10.8 Hz); H1–C1–C15–H15 +65°,  $^3J_{\text{calc.}}$  3.4 Hz ( $^3J_{\text{exp.}}$  4.4 Hz).

considered as a stereochemical analogue of starting cembrene **1**. Thus, the conformational behaviour of the molecule of nitroso olefin **3** in a solution should resemble that of the molecule of cembrene **1**, which is conformationally homogeneous, having the same conformation in a solution<sup>5</sup> and in the crystal state.<sup>6</sup> In such a form, double bonds are practically perpendicular to an imaginary plane of the macrocycle. Thus, addition reactions to the double bonds proceed stereoselectively to give products arising from an attack of a reagent from the outside plane of the double bond.<sup>7</sup> Therefore, the addition of amines to nitroso olefin **3** should proceed stereochemically similar to the addition of electrophiles to the 4,5-double bond in **1** and lead to the *S*-configuration of carbon in the 4-position. This reaction stereochemistry was supported by NMR spectroscopy and calculated data. A comparison of chemical shifts and coupling constants for compounds **4–6** shows that all of the compounds have the same conformation of the macrocycle and the same configuration of the C4-carbon. An analysis of the spin-spin couplings  $^3J_{\text{H-H}}$  for compounds **4–6** allows one to believe that in these molecules the conformation of the fragment containing C1–C4 atoms resembles that of a cembrene molecule: pseudoequatorial isopropyl, protons at C1–C3 and methyl at C-4 are almost in the same plane; H1 and H2 are antiperiplanar. An insignificant difference in the chemical shifts of H6 $\alpha$  and H6 $\beta$  protons for

<sup>†</sup> (1*S*,2*E*,4*S*,7*E*,11*E*)-4-(2-Hydroxyethylamino)cembra-2,7,11-trien-5-one (E)-oxime **5**. White crystals (55% yield) from hexane–CHCl<sub>3</sub>, mp 139–141 °C;  $[\alpha]_{\text{D}}^{20}$  +336 (c 1.0, CHCl<sub>3</sub>). NMR data (0.30 mmol cm<sup>–3</sup> in C<sub>5</sub>D<sub>5</sub>N). <sup>1</sup>H NMR (60 °C)  $\delta$ : 1.81 (dddd, H-1, *J* 9.9, 9.9, 4.7 and 4.7), 5.46 (dd, H-2, *J* 15.5 and 9.5 Hz), 5.83 (d, H-3, *J* 15.5 Hz), 3.68 (dm, H-6, *J* 13.2 Hz, *W*<sub>1/2</sub> 9 Hz), 3.62 (dd, H-6, *J* 13.2 and 10.2 Hz), 5.84 (dd, H-7, *J* 10.2 and 3.1 Hz), [2.17, 2.11] (H-9), [2.19, 2.05] (H-10), 5.14 (dd, H-11, *J* 4.4 and 4.4 Hz), [1.98] (H-13), [1.58] (H-14), 1.31 (dddd, H-14, *J* 13.6, 10.0, 4.9 and 4.9 Hz), [1.55] (H-15), 0.90 (d, H-16, *J* 6.8 Hz), 0.87 (d, H-17, *J* 6.9 Hz), 1.76 (br. s, H-18), 1.71 (br. s, H-19), 1.53 (br. s, H-20), 3.90 (dd, NCH<sub>2</sub>CH<sub>2</sub>O, *J* 5.5 and 5.5 Hz), 3.01 and 2.78 (2dt, NCH<sub>2</sub>CH<sub>2</sub>O, *J* 11.7 and 5.5 Hz), 12.00 (s, =NOH), 3.9 (br. s, CH<sub>2</sub>OH). <sup>13</sup>C NMR (30 °C)  $\delta$ : 46.63 (C-1,  $^1J_{\text{C-H}}$  128.6 Hz), 130.67 (C-2,  $^1J_{\text{C-H}}$  147.5 Hz), 136.96 and 156.2 (C-3), 61.17 (C-4), 161.65 (C-5), 25.08 (C-6,  $^1J_{\text{C-H}}$  131.2 and 128.4 Hz,  $^2,3J_{\text{C-H}}$  2.5 Hz), 123.35 (C-7,  $^1J_{\text{C-H}}$  156.4 Hz), 133.40 (C-8 or C-12), 39.04 (C-9,  $^1J_{\text{C-H}}$  125.2 Hz), 23.59 (C-10,  $^1J_{\text{C-H}}$  126.3 Hz), 125.18 (C-11,  $^1J_{\text{C-H}}$  152.2 Hz), 132.59 (C-12 or C-8), 36.57 (C-13,  $^1J_{\text{C-H}}$  125.5 Hz,  $^2,3J_{\text{C-H}}$  7.3, 3.8 and 3.3 Hz), 28.16 (C-14,  $^1J_{\text{C-H}}$  124.8 Hz), 33.50 (C-15,  $^1J_{\text{C-H}}$  128.8 Hz), 20.83 (C-16,  $^1J_{\text{C-H}}$  124.6 Hz,  $^2,3J_{\text{C-H}}$  5 $\times$ 4.1 Hz), 19.40 (C-17,  $^1J_{\text{C-H}}$  124.6 Hz,  $^2,3J_{\text{C-H}}$  5 $\times$ 5.1 Hz), 20.56 (C-18,  $^1J_{\text{C-H}}$  127.2 Hz,  $^2,3J_{\text{C-H}}$  4.0 Hz), 14.99 (C-19,  $^1J_{\text{C-H}}$  125.2 Hz,  $^2,3J_{\text{C-H}}$  4.4 and 3.2 Hz), 15.07 (C-20,  $^1J_{\text{C-H}}$  125.0 Hz,  $^2,3J_{\text{C-H}}$  4.5 and 3.5 Hz), 62.44 (NCH<sub>2</sub>CH<sub>2</sub>O,  $^1J_{\text{C-H}}$  140.2 Hz,  $^2,3J_{\text{C-H}}$  6.9, 4.0 and 4.0 Hz), 46.08 (NCH<sub>2</sub>CH<sub>2</sub>O,  $^1J_{\text{C-H}}$  132.2 Hz). IR (CCl<sub>4</sub>,  $\nu/\text{cm}^{-1}$ ): 3599 ( $\nu_{\text{OH}}$ ), 3309 ( $\nu_{\text{N-H}}$ ), 949 ( $\nu_{\text{N-O}}$ ). MS, *m/z* (%): 362.29333 (M<sup>+</sup>, 2), 346 (23), 345 (M<sup>+</sup> – OH, 100), 317 (4), 303 (5), 302 (8), 301 (5), 286 (5), 285 (4), 284 (3), 274 (6), 258 (10), 182 (15), 140 (13), 114 (31), 95 (10), 86 (13), 81 (17), 79 (10), 69 (14), 67 (12), 55 (12), 41 (13). Found (%): C, 73.0; H, 10.5; N, 7.4. Calc. for C<sub>22</sub>H<sub>38</sub>N<sub>2</sub>O<sub>2</sub> (%): C, 72.7; H, 10.5; N, 7.7.

<sup>§</sup> (1*S*,2*E*,4*S*,7*E*,11*E*)-4-Benzylaminocembra-2,7,11-trien-5-one (E)-oxime hydrochloride **6**. A solvate with 0.5 mol of acetonitrile. White crystals (68% yield) from acetonitrile, mp 131.5–133.0 °C (decomp.);  $[\alpha]_{\text{D}}^{20}$  +90 (c 1.0, CHCl<sub>3</sub>). NMR data (0.25 mmol cm<sup>–3</sup> in CDCl<sub>3</sub>, 30 °C). <sup>1</sup>H NMR,  $\delta$ : 1.78 (ddd, H-1, *J* 8.9, 8.9, 4.8 and 3.7 Hz), 6.08 (dd, H-2, *J* 16.0 and 8.9 Hz), 5.67 (d, H-3, *J* 16.0 Hz), 3.16 (dd, H-6, *J* 15.5 and 7.9 Hz), 3.03 (dd, *J* 15.5 and 5.3 Hz), 4.97 (dd, H-7, *J* 7.9 and 5.3 Hz), [2.09, 2.03] (H-9), [2.23, 2.05] (H-10), 4.81 (dd, H-11, *J* 8.9 and 3.5 Hz), [1.99] (H-13), [1.55] (H-14), 1.42 (dddd, H-14, *J* 14.1, 9.5, 4.8 and 4.3 Hz), [1.68] (H-15), 0.89 (d, H-16, *J* 7.0 Hz), 0.91 (d, H-17, *J* 7.0 Hz), 1.69 (br. s, H-18), 1.57 (br. s, H-19), 1.50 (br. s, H-20), 3.92 and 3.89 (PhCH<sub>2</sub>N, AB-system, *J*<sub>AB</sub> 13.7 Hz), 7.60 (d, 2H, PhCH<sub>2</sub>N, *J* 7.2 Hz), 7.22 (m, 2H, PhCH<sub>2</sub>N), 7.20 (m, 1H, PhCH<sub>2</sub>N), 10.21 (s, =NOH), 10.1 and 8.6 (2br. s, NH<sub>2</sub><sup>+</sup>), 1.94 (s, MeCN). <sup>13</sup>C NMR,  $\delta$ : 47.08 (C-1,  $^1J_{\text{C-H}}$  127.0 Hz), 141.13 (C-2,  $^1J_{\text{C-H}}$  149.1 Hz), 126.29 (C-3,  $^1J_{\text{C-H}}$  157.3 Hz), 65.85 (C-4), 155.97 (C-5), 24.70 (C-6,  $^1J_{\text{C-H}}$  129.5 Hz,  $^2,3J_{\text{C-H}}$  3.5 Hz), 118.72 (C-7,  $^1J_{\text{C-H}}$  153.8 Hz), 133.07 (C-8 or C-12), 38.25 (C-9,  $^1J_{\text{C-H}}$  125.0 Hz), 23.66 (C-10,  $^1J_{\text{C-H}}$  129.0 and 124.5 Hz), 124.93 (C-11,  $^1J_{\text{C-H}}$  150.8 Hz), 131.12 (C-12 or C-8), 36.32 (C-13,  $^1J_{\text{C-H}}$  125.0 Hz), 26.50 (C-14,  $^1J_{\text{C-H}}$  125.9 Hz), 32.18 (C-15,  $^1J_{\text{C-H}}$  125.5 Hz), 20.05 (C-16,  $^1J_{\text{C-H}}$  124.4 Hz,  $^2,3J_{\text{C-H}}$  5 $\times$ 5.1 Hz), 19.83 (C-17,  $^1J_{\text{C-H}}$  124.8 Hz,  $^2,3J_{\text{C-H}}$  5 $\times$ 4.4 Hz), 23.35 (C-18,  $^1J_{\text{C-H}}$  129.7 Hz), 15.33 (C-19,  $^1J_{\text{C-H}}$  125.2 Hz,  $^2,3J_{\text{C-H}}$  8.0, 3.9 and 3.9 Hz), 14.85 (C-20,  $^1J_{\text{C-H}}$  125.2 Hz,  $^2,3J_{\text{C-H}}$  8.5, 5.2 and 3.2 Hz), 47.60 (t, PhCH<sub>2</sub>N,  $^1J_{\text{C-H}}$  143.5 Hz), 131.01 (d, PhCH<sub>2</sub>N,  $^1J_{\text{C-H}}$  158.8 Hz,  $^2,3J_{\text{C-H}}$  6.4 and 6.4 Hz), 128.51 (d, PhCH<sub>2</sub>N,  $^1J_{\text{C-H}}$  160.4 Hz,  $^2,3J_{\text{C-H}}$  7.6 Hz), 128.75 (d, PhCH<sub>2</sub>N,  $^1J_{\text{C-H}}$  160.6 Hz,  $^2,3J_{\text{C-H}}$  7.6 and 7.6 Hz), 136.64 (s, PhCH<sub>2</sub>N), 1.57 (q, MeCN,  $^1J_{\text{C-H}}$  135.9 Hz), 116.09 (s, MeCN,  $^2,3J_{\text{C-H}}$  10.2 Hz). IR (KBr,  $\nu/\text{cm}^{-1}$ ): 1575 ( $\delta_{\text{N-H}}$ ), 1455 ( $\nu_{\text{C=CA}}$ ), 977 ( $\nu_{\text{N-O}}$ ). MS, *m/z* (%): 408.31425 (M<sup>+</sup>, 4), 392 (30), 391 (M<sup>+</sup> – OH, 98), 317 (15), 303 (17), 286 (13), 284 (15), 260 (11), 258 (12), 228 (12), 160 (21), 148 (8), 107 (21), 106 (47), 95 (8), 92 (10), 91 (100), 81 (14), 79 (15), 69 (10), 67 (11), 55 (12), 41 (18), 36 (11), 32 (11). Found (%): C, 72.2; H, 9.1; Cl, 7.5; N, 7.1. Calc. for C<sub>27</sub>H<sub>41</sub>ClN<sub>2</sub>O<sup>–</sup>·0.5CH<sub>3</sub>CN (%): C, 72.23; H, 9.20; Cl, 7.61; N, 7.52.

<sup>†</sup> (3*E*,7*E*,11*S*,12*E*)-11-Isopropyl-4,8-dimethyl-14-oxopentadeca-3,7,12-trienenitrile **7**. Viscous yellowish oil,  $[\alpha]_{\text{D}}^{20}$  –10 (c 1.0, CHCl<sub>3</sub>). NMR data (0.73 mmol cm<sup>–3</sup> in CDCl<sub>3</sub>, 30 °C). <sup>1</sup>H NMR,  $\delta$ : 2.93 (dq, H-2, *J* 7.0 and 0.7 Hz), 5.05 (ttq, H-3, *J* 7.0, 1.3 and 1.3 Hz), [1.95] (H-5), [1.98] (H-6), 4.94 (ttq, H-7, *J* 6.7 and 1.2 Hz), [1.82, 1.73] (H-9), [1.52] (H-10), 1.30 (dtd, H-10, *J* 13.5, 9.6 and 5.3 Hz), [1.84] (H-11), 6.49 (dd, H-12, *J* 15.9 and 9.6 Hz), 5.89 (d, H-13, *J* 15.9 Hz), 2.14 (s, H-15), 1.56 (br. s, H-16), 1.46 (d, H-17, *J* 1.2 Hz), [1.60] (H-18), 0.80 (d, H-19, *J* 6.7 Hz), 0.75 (d, H-20, *J* 6.7 Hz). <sup>13</sup>C NMR,  $\delta$ : 118.04 (C-1), 15.70 (C-2), 111.49 (C-3), 134.83 (C-4), 38.70 (C-5), 25.57 (C-6), 123.35 (C-7), 141.60 (C-8), 37.00 (C-9), 29.29 (C-10), 48.40 (C-11), 150.20 (C-12), 131.90 (C-13), 197.79 (C-14), 26.49 (C-15), 15.89 (C-16), 15.52 (C-17), 31.21 (C-18), 20.20 (C-19), 18.76 (C-20). IR (CCl<sub>4</sub>,  $\nu/\text{cm}^{-1}$ ): 2245 ( $\nu_{\text{C}\equiv\text{N}}$ ), 1690, 1675, 1630 ( $\nu_{\text{C=O}}$ ,  $\nu_{\text{C=C}}$ ), 1250, 980 ( $\delta_{\text{CH=CH}}$ ). UV [EtOH,  $\lambda_{\text{max}}/\text{nm}$  (lg  $\epsilon$ ): 227 (3.83). MS, *m/z* (%): 301.24041 (M<sup>+</sup>, 7), 286 (2), 258 (14), 243 (4), 216 (2), 207 (4), 189 (8), 163 (7), 149 (15), 139 (23), 126 (14), 123 (12), 121 (16), 109 (21), 107 (22), 97 (35), 95 (28), 93 (24), 81 (53), 79 (16), 71 (38), 69 (24), 68 (15), 67 (27), 55 (28), 53 (12), 43 (100), 41 (28).

compounds **4–6** ( $\Delta\delta_{\text{H}} = 0.05\text{--}0.3$  ppm), as compared to known amino oximes with six-membered carbocycles (0.7–1.4 ppm),<sup>8</sup> indicates that there is another type of orientation of the methylene group adjacent to the oxime moiety. Such a disposition is possible in the case of a synclinal position of protons of the methylene group and the oxime moiety. The methyl C-18 group is antiperiplanar to H-2 [nuclear Overhauser effect (3H18 $\Rightarrow$ H2)]. Conformational analysis by molecular mechanics (MM2) and quantum-chemical semiempirical calculations (MNDO, PM3) show that there are at least six stable low-energy conformations ( $\Delta\Delta H_f^\circ = 0.0, 1.7, 3.4, 3.5, 3.6$  and  $5.4$  kcal mol<sup>-1</sup>), which differ in the orientation of endocyclic carbon–carbon double bonds. The calculated couplings  $^3J_{\text{H-C}(\text{sp}^2)\text{--C}(\text{sp}^3)\text{--H}}$  (obtained by a known equation<sup>9</sup>) for the least strained conformation of morpholino derivative **4** are in good agreement with the experimental values (Figure 1).

This work was supported by the Russian Foundation for Basic Research (grant no. 96-15-97017) and INTAS (grant no. 97-0217).

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Received: 1st December 1999; Com. 99/1566