Synthesis of substituted cyclopentanes based on intramolecular [3+2] cycloaddition of trimethylsilyl nitronates generated from 6-nitrohex-1-ene derivatives

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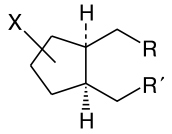
A method for the stereoselective synthesis of substituted 4a*S**,7a*S**-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one, promising synthon of isoprostanes, has been developed based on the intramolecular dipolar [3+2] cycloaddition of silyl nitronates generated from 6-nitrohex-1-ene derivative.

Key words: 6-nitrohex-1-enes, cyclopentanes, [3+2] cycloaddition, silyl nitronates, perhydrocyclopenta[*c*]isoxazoles, hexahydrocyclopenta[*c*]pyran-3(1*H*)-ones, isoprostanes.

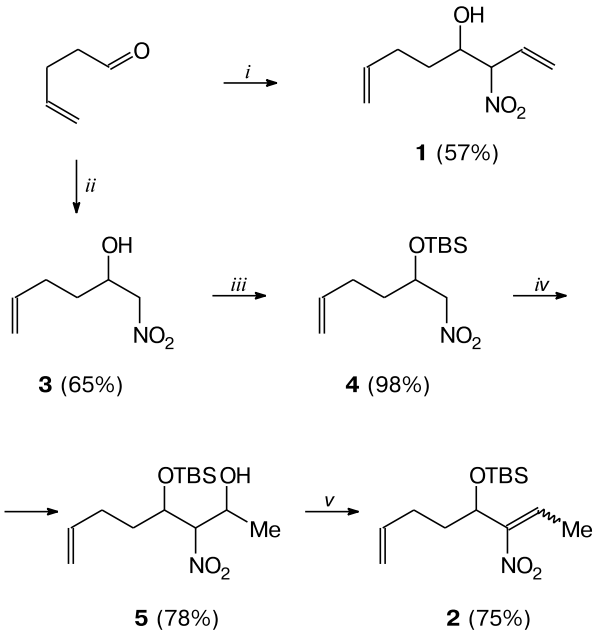
Earlier,[1] we have reported that intramolecular dipolar [3+2] cycloaddition of silyl nitronates generated from unsaturated nitro compounds can be efficiently used in the synthesis of cyclopentane monoisoprenoids. The present study deals with the application of this methodology in the synthesis of other representatives of natural cyclopentanoids, in particular, isoprostanes,[2] differing from the well studied prostaglandins by *cis*-arrangement of the side chains on the cyclopentane ring. These compounds, discovered in 1990, are formed *in vivo* as racemates by nonenzymatic free-radical cyclization of arachidenic acid.[2] Taking this into account, it seemed interesting to study a possibility to obtain compounds of the isoprostane series using the indicated above intramolecular [3+2] reaction of easily available 6-nitrohex-1-ene derivatives **1** and **2**, whose substitution pattern has been chosen based on the data obtained earlier.[1]



Isoprostanes

A mixture of approximately equal amounts of diastereomers **1**, which is unseparable by chromatography on SiO_2, was obtained in one step by the nitroaldol condensation of 3-nitropropene with pent-4-enal (Scheme 1). Nitrodienes **2** were synthesized in four steps (see Scheme 1), that allowed us, in particular, avoid the use of poorly available and unstable 3-nitropropene. The first step of the synthesis of **2** included condensation of pentenal with nitromethane, followed by transformation of the thus formed nitro alcohol **3** to the TBS derivative **4**, which further was involved into the second nitroaldol condensation with acetaldehyde. The thus obtained mixture of diastereomers **5** was subjected to dehydration to yield nitrodienes **2** (*Z*-**2** : *E*-**2** ≈ 2 : 1).

Scheme 1



Reagents and conditions: *i*. CH_2=$CHCH_2NO_2$, 0.025 *M* NaOH, *n*-$C_{16}H_{33}(CH_3)_3NBr$ (cat.), 0 °C; *ii*. 1) $MeNO_2$, 10 *M* NaOH, EtOH, 0 °C; 2) AcOH; *iii*. TBSCl, imidazole, DMF, 20 °C; *iv*. 1) MeCHO, 10 *M* NaOH, EtOH, 0 °C; 2) AcOH; *v*. DCC, CuCl (cat.), Et_2O, 20 °C.

The unsaturated nitro compounds **1** and **2** were subjected to silylation under conditions described earlier.[1c] In the case of allylic nitro derivatives **1**, the generation of silyl nitronate **6** is accompanied by stereospecific cycloaddition to form *cis*-annulated perhydrocyclopentaisoxazole **7**

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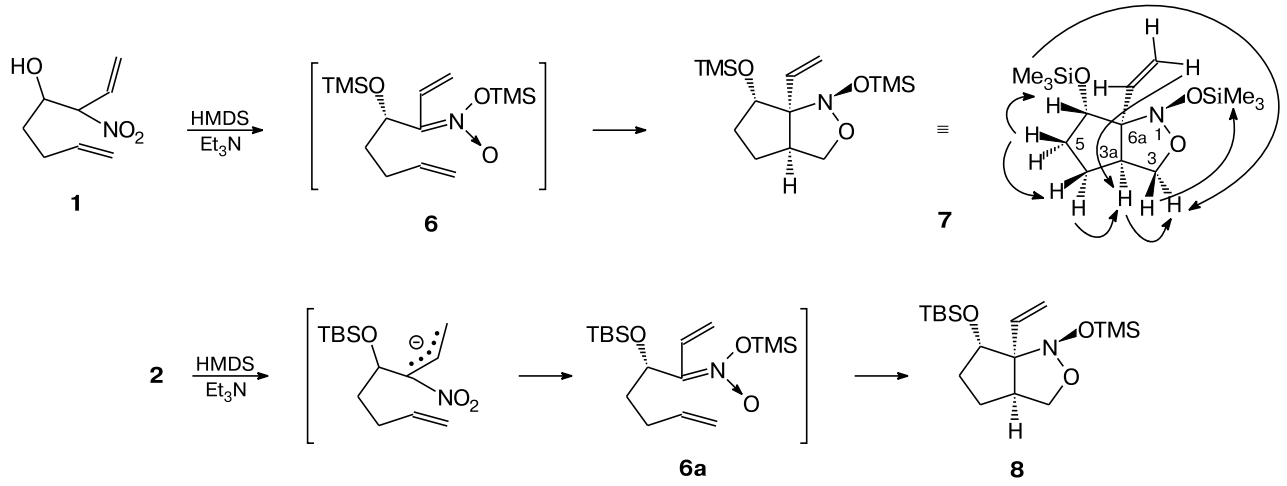
Scheme 2

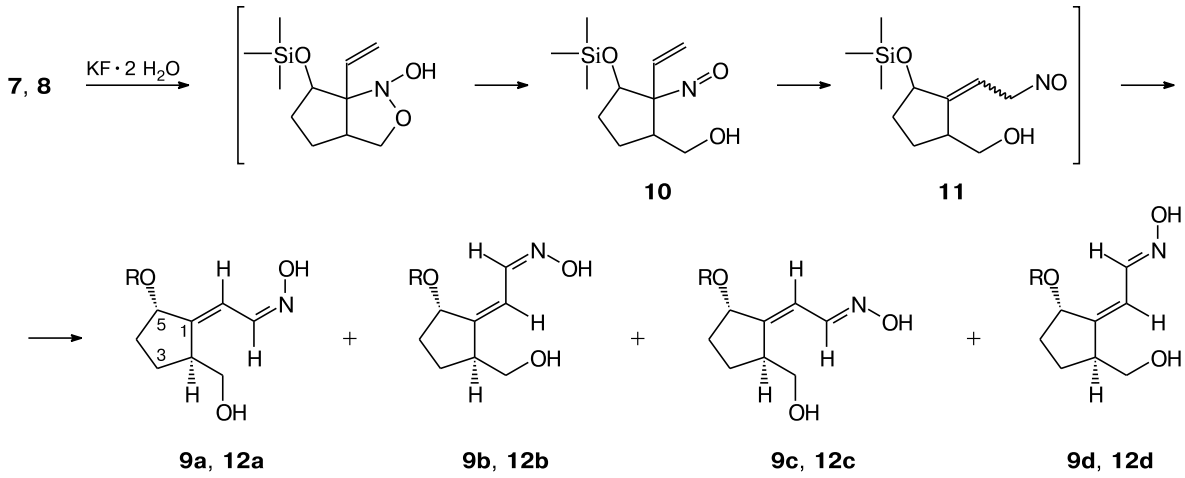


in virtually quantitative yield (Scheme 2). Its configuration was confirmed by NOE in the ^{1}H NMR spectrum. Transformation of a mixture of nitrodienes **2** to isoxazolidine **8**, which suggests formation of nitronate **6a** through the step of allylic deprotonation, occurs with the same degree of stereoselectivity. Spectroscopic characteristics (^{1}H, ^{13}C NMR) of compound **8** are close to those of isoxazolidine **7**.

Further transformations of perhydrocyclopentaisoxazoles **7** and **8** are based on the method for the isoxazolidine fragment opening upon the action of fluoride ion described earlier for related compounds.[1,3] Thus, treatment of compound **7** with the solution of $KF \cdot 2H_2O$ in methanol results in good total yield of a mixture of isomeric oximes **9** in the ratio (^{1}H NMR data) **9a** : **9b** : **9c** : **9d** ≈ ≈ 2 : 1 : 1 : 1 (Scheme 3). Formation of isomers **9** suggests initial generation of tertiary nitroso compound **10** and its allylic rearrangement to a mixture of unstable primary ones **11**, which then isomerize to the corresponding oximes **9** (see Ref. 1b). Separation of this mixture on SiO_2 gives only enriched fractions of stereoisomers **9** because of their close chromatographic mobility. In Scheme 3, isomers **9** are given in the order of increasing polarity. Their stereochemistry was established by NMR spectroscopy. Thus, configuration of the double bond for the *E*-isomers **9a** and **9c** and *Z*-isomers **9b** and **9d** was assigned based on the NOESY experimental data, which exhibit the cross-peaks between the olefinic proton and, respectively, the protons HC(5) of cyclopentane ring or CH_2O group.

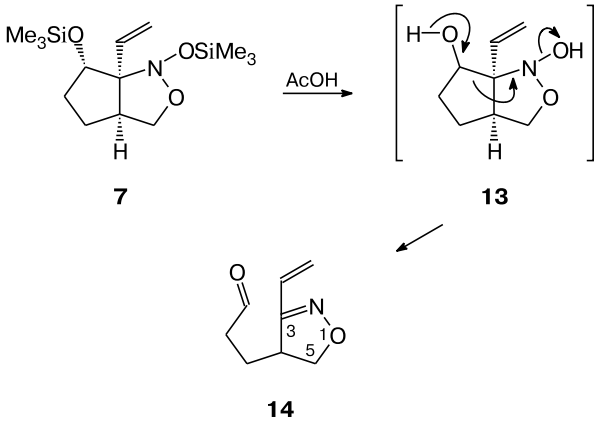
Assignment of oximes **9** to *syn*- or *anti*-series was made based on the literature data,[4] which show that in the pairs of *syn*- and *anti*-isomers the first have lower CH constant

Scheme 3



9a—**d:** R = H; **12a**—**d:** R = TBS

Scheme 4



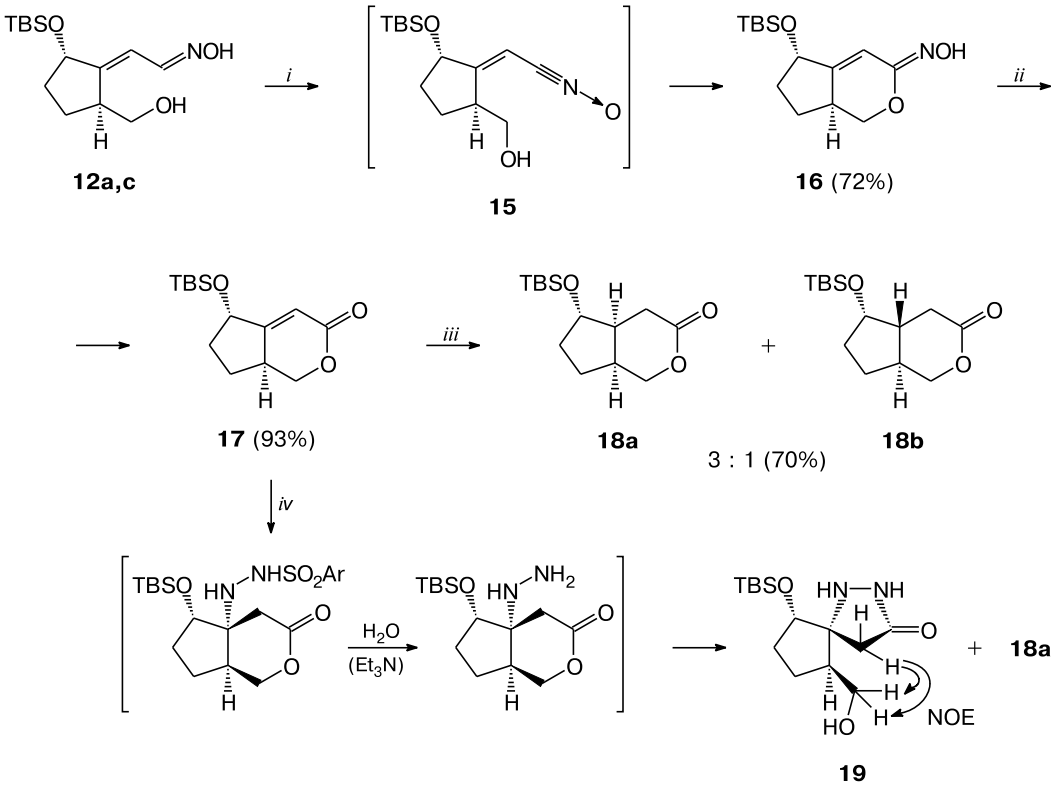
$J_{H-C=N}$. It is equal to 163.3 Hz for *syn*-isomers **9a**,**b** and to 173.3 and 175.8 Hz for *anti*-isomers **9c**,**d**, respectively.

Transformation of TBSO-substituted derivative **8** under the action of $KF \cdot 2H_2O$ proceeds similarly, however, in this case the process is characterized by higher differentiation of the mixture formed (**12a** : **12b** : **12c** : **12d** ≈ ≈ 26 : 12 : 20 : 7) in favor of *E*-isomers **12a** and **12c** (see Scheme 3). The structures of crystalline compounds **12**, isolated in the individual state by chromatography, were established by ^1H and ^{13}C NMR spectroscopy with account for the regularities found for oximes **9a**—**c**.

It is interesting to note that desilylation of isoxazolidine **7** under the action of AcOH takes another direction (Scheme 4). Obviously, in this case simultaneous acetolysis of both trimethylsilyloxy groups occurs to yield unstable dihydroxy derivative **13**, which further undergoes cleavage with the formation of isoxazoline **14**.

It may be stated that the presence of bulky *tert*-butyldimethylsilyl substituent in the molecule of the starting substrate **2** finally leads to the increase in the content of monocyclic compounds **12a,c**, the products of cleavage of intermediate isoxazolidine **8**, whose structure meets the purpose of this study. Thus, treatment of a mixture of **12a**,**c** with *N*-chlorosuccinimide (Scheme 5) led through a possible intermediate **15** to bicyclic oxime **16**, whose mild deoximation under the action of iodoxybenzoic acid (IBX) gave rise to cyclopentatetrahydropyranone **17**. Catalytic hydrogenation of the latter yielded the desired saturated lactone **18a** in satisfactory stereoselectivity with *cis*-annulation of the cyclopentane and perhydropyranone rings together with *trans*-stereoisomer **18b** (~25%). Both

Scheme 5



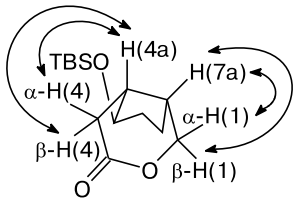
Reagents and conditions: *i*. NCS, Et_3N, $CHCl_3$, 0 °C; *ii*. IBX, DMF, THF, 20 °C; *iii*. H_2, 10% Pd/C, 20 °C; *iv*. *o*-nitrophenylsulfonyl hydrazide, Et_3N, CH_2Cl_2, 20 °C.

components of this mixture were quantitatively separated by column chromatography on SiO_2.

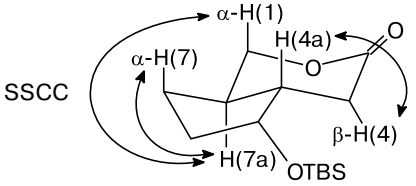
Hydrogenation of lactone **17** with diimide proceeds stereoselectively, however, the desired compound **18a** was obtained only in 8% yield, with spirohydrazide **19** being the main reaction product (33%). The latter results apparently from the Michael addition of *o*-nitrophenylsulfonyl hydrazide, the starting material for the *in situ* generation of diimide. Aqueous treatment of the reaction mixture results in hydrolysis of the sulfonylhydrazide residue of the intermediate Michael adduct, and the thus formed alkylhydrazine intramolecularly opens the lactone ring giving compound **19**, whose stereochemistry was confirmed by Overhauser effects.

Catalytic hydrogenation of unsaturated oxime **16** is characterized by about the same degree of stereoselectivity as in the case of unsaturated lactone **17**. Chromatographic separation of the reaction products along with a mixture of isomeric saturated oximes **20a**,**b** (58%, **20a** : **20b** 2 : 1, the ^{1}H NMR data) also gave lactones **18a**,**b** (15%, **18a** : **18b** 3 : 2, the ^{1}H NMR data), which, apparently, are formed through partial deoximation of the corresponding oximes on the silica gel surface (Scheme 6). In addition, a small amount (12%) of hydrogenolysis product **21** was isolated from the reaction mixture.

Structures of lactones **18a,b** were confirmed by analysis of the ^{1}H-^{1}H spin-spin coupling constants in the ^{1}H NMR spectra, since no any nontrivial cross-peaks were found in the NOESY spectra of these isomers. Thus, for the main isomer **18a** with the *cis*-annulation of the cyclopentane and perhydropyranone rings, the spin-spin coupling constants (SSCC) between the protons at C(1) and C(7a), as well as between C(4) and C(4a) are within the range 5.1—6.5 Hz, which corresponds to the eclipsed arrangement of these hydrogen atoms. At the same time, in the spectrum of minor isomer **18b** only one spin-spin coupling constant is observed for each pair of protons HC(1), HC(7a) and HC(4), HC(4a) (10.6 and 12.4 Hz, respectively). This suggests their axial-axial interaction in the chair conformation in the six-membered ring and indicates that the minor isomer is a *trans*-annulated structure. The eclipsed arrangement of substituents in the *cis*-isomer **18a** also exists in the boat-type conformation of the lactone ring. It is interesting to note that the spin-spin coupling constants between HC(4a) and HC(7a) in both isomers **18** have approximately the same values, however, in the case of lactone **18a** it suggests an axial-axial interaction, whereas for **18b** a dihedral angle H(4a)—C(4a)—C(7a)—H(7a) is equal to 0°. The regularities found are also characteristic of saturated oximes **20a**,**b**.



18a



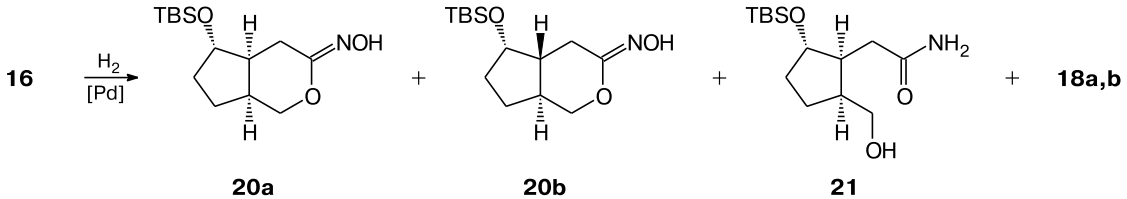
18b

In conclusion, a method for the synthesis of promising synthon for natural cyclopentanoids of the isoprostane series, *viz.*, cyclopentalerolactone **18a**, with satisfactory stereoselectivity has been developed based on available starting compounds. Further development of the present study suggests a search for possibilities to increase stereoselectivity of this synthetic scheme, as well as for the ways of its application in the synthesis of some representatives of iso- and neuroprostanes.

Experimental

Melting points were measured on a Kofler apparatus. IR spectra were recorded on a Bruker ALPHA-T spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200, Bruker AM-300, and Bruker AVANTE II-600 spectrometers in $CDCl_3$ (unless otherwise is stated) at 298 K relatively to the signals of the solvent (δ_H 7.27 and δ_C 77.0, respectively). Mass spectra (EI, 70 eV) were recorded on a Finigan MAT ITD-700 instrument. High-resolution mass spectra (ESI) were obtained on a Bruker micrOTOF II spectrometer at capillary potential 4.5 kV with the direct inlet (*via* a syringe) of the sample solution in methanol (3 μL min^{-1}) in the positive ions mode (the range of

Scheme 6



20a **20b** **21**

masses 300—2000 Da), the main flow of nitrogen was 4 L min^{-1} (180 °C). Column chromatography was performed on Silica gel 60 (0.04—0.06 mm, Fluka). The R_f values were measured on Silufol plates with the fixed layer. Solvents, including light petroleum with b.p. 40—70 °C, were purified and dried according to standard procedures. We used in our work commercially available n-$C_{16}H_{33}(CH_3)_3NBr$, HMDS, Et_3N, nitromethane, imidazole, TBSCl, acetaldehyde, DCC, NCS (Acros Organics). 3-Nitropropene,[5] pent-4-enal,[6] and *o*-nitrophenylsulfonyl hydrazide[7] were obtained according to the known procedures.

3-Nitroocta-1,7-dien-4-ol (1), a mixture of diastereomers. The catalyst n-$C_{16}H_{33}(CH_3)_3NBr$ (0.2 g, 0.57 mmol) was added to a mixture of 3-nitropropene (0.5 g, 5.74 mmol), 4-pentenal (0.48 g, 5.71 mmol), and aqueous NaOH (0.025 *M*, 15 mL) with vigorous stirring at 20 °C. The mixture was stirred for 2 h at room temperature, then saturated with NaCl and extracted with $MeOBu^t$ (3×50 mL). The combined organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 using gradient elution with the light petroleum—$MeOBu^t$ mixture (up to 20% of the latter) to obtain a mixture of diastereomers (**1**) (~1 : 1, 0.56 g, 57%) as a light yellow oil, R_f 0.30 (light petroleum—$MeOBu^t$, 1 : 1). MS (ESI), m/z: $[M + Na]^+$, found 194.0796, calculated 194.0788. IR (neat), ν/cm^{-1}: 920, 948, 992, 1084, 1276, 1372, 1428, 1524, 1560, 1644, 2856—2980, 3080, 3436, 3550. ^{1}H NMR (200.13 MHz), δ: 1.4—1.68 (m, 2 H, $H_2C(5)$); 2.06—2.34 (m, 2 H, $H_2C(6)$); 4.13 (ddd, 0.5 H, CHO, J = 2.9 Hz, J = 9.2 Hz, J = 11.6 Hz); 4.27 (ddd, 0.5 H, CHO, J = 4.0 Hz, J = 4.0 Hz, J = 8.3 Hz); 4.80 (dd, 0.5 H, $CHNO_2$, J = 3.4 Hz, J = 9.8 Hz); 4.86 (dd, 0.5 H, $CHNO_2$, J = 9.2 Hz, J = 9.2 Hz); 5.01 (d, 1 H, *E*-HC(8), J = 10.2 Hz); 5.06 (d, 1 H, *Z*-HC(8), J = 13.7 Hz); 5.45 (d, 0.5 H, *E*-HC(1), J = 9.9 Hz); 5.50 (d, 0.5 H, *Z*-HC(1), J = 17.4 Hz); 5.53 (d, 0.5 H, *Z*-HC(1), J = 17.1 Hz); 5.57 (d, 0.5 H, *E*-HC(1), J = 9.7 Hz); 5.96 (ddd, 0.5 H, HC(2), J = 17.1 Hz, J = 9.7 Hz, J = 9.7 Hz); 6.18 (ddd, 0.5 H, HC(2), J = 9.2 Hz, J = 9.9 Hz, J = 17.4 Hz). ^{13}C NMR (50.03 MHz), δ: 29.25 and 29.50 (C(5)); 31.76 and 32.03 (C(6)); 71.36 and 71.50 (C(4)); 93.20 and 95.31 (C(3)); 115.82 (C(8)); 124.14 and 124.53 (C(1)), 127.74 and 129.32 (C(7)), 137.11 and 137.25 (C(2)).

(±)-1-Nitrohex-5-en-2-ol (3). Aqueous NaOH (10 *M*, 1.5 mL, 15 mmol) was added dropwise to a mixture of 4-pentenal (1.26 g, 15 mmol) and nitromethane (0.98 g, 16 mmol) at 0 °C with vigorous stirring over 10 min. The reaction mixture was heated to 20 °C, stirred for 10 min, neutralized with AcOH (0.9 g, 15 mmol), then diluted with ethyl acetate (50 mL) and water (10 mL). The organic layer was separated, washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 using gradient elution, starting from light petroleum to 15% of EtOAc in light petroleum, to obtain nitro alcohol **3** (1.41 g, 65%) as a colorless oil, R_f 0.42 (light petroleum—$MeOBu^t$, 2 : 1), b.p. 87—89 °C (0.1 Torr). Found (%): C, 49.71; H, 7.42; N, 9.70. $C_6H_{11}NO_3$. Calculated (%): C, 49.65; H, 7.64; N, 9.65. IR (neat), ν/cm^{-1}: 1092, 1156, 1212, 1244, 1380, 1404, 1436, 1468, 1556, 1584, 1640, 2928, 3100—3300. MS (EI), m/z (I_{rel} (%)): 84 $[M - HNO_2]^+$ (25); 85 $[M - NO_2]^+$ (6); 83 (35); 81 (43); 80 (50); 57 (49); 56 (67); 55 (100). ^{1}H NMR (200.13 MHz), δ: 1.50—1.80 (m, 2 H, $H_2C(3)$); 2.10—2.40 (m, 2 H, $H_2C(4)$); 2.63 (s, 1 H, OH); 4.28—4.52 (m, 3 H, CHOH, $CHNO_2$); 5.00—5.16 (m, 2 H, H_2C=); 5.70—5.92 (dddd, 1 H, HC=, J = 6.7 Hz, J = 6.7 Hz, J = 10.2 Hz, J = 13.4 Hz). ^{13}C NMR (50.03 MHz), δ: 29.30 (C(3)), 32.61 (C(4)), 67.97 (C(2)), 80.49 (C(1)), 115.97 (C(5)), 137.00 (C(6)).

(±)-5-(*tert*-Butyldimethylsilyloxy)-6-nitrohex-1-ene (4). Imidazole (5.10 g, 75 mmol) was added to a stirred solution of nitro alcohol **3** (4.35 g, 30 mmol) and TBSCl (5.42 g, 36 mmol) in DMF (15 mL) at 20 °C under argon. The reaction mixture was stirred for 7 h at 20 °C, then diluted with water and extracted with $MeOBu^t$. The organic layer was washed with water and brine, dried with Na_2SO_4 and concentrated *in vacuo*. The residue was distilled to obtain silyl ether **4** (7.61 g, 98%) as a colorless liquid, b.p. 82—85 °C (0.08 Torr). Found (%): C, 55.70; H, 10.00; N, 5.59. $C_{12}H_{25}NO_3Si$. Calculated (%): C, 55.56; H, 9.71; N, 5.4. IR (neat), ν/cm^{-1}: 1004, 1072, 1112, 1256, 1364, 1388, 1420, 1476, 1560, 1644, 1724. MS (EI), m/z (I_{rel} (%)): 202 $[M - C_4H_9]^+$ (16), 168 (37), 118 (87), 104 (43), 75 (100). ^{1}H NMR (200.13 MHz), δ: 0.05 (s, 3 H, MeSi); 0.10 (s, 3 H, MeSi); 0.9 (s, 9 H, Me_3CSi); 1.55—1.75 (m, 2 H, $H_2C(4)$); 2.03—2.20 (m, 2 H, $H_2C(3)$); 4.30—4.52 (m, 3 H, CHOTBS, $CHNO_2$); 4.97—5.14 (m, 2 H, H_2C=); 5.70—5.92 (dddd, 1 H, HC=, J = 6.5 Hz, J = 6.5 Hz, J = 10.2 Hz, J = 16.8 Hz). ^{13}C NMR (50.03 MHz), δ: –4.71 and –5.22 (MeSi); 17.85 and 25.55 ($Me_3\underline{C}Si$); 28.66 (C(4)); 34.21 (C(3)); 69.48 (C(5)); 80.34 (C(6)); 115.47 (C(1)); 131.14 (C(2)).

4-(*tert*-Butyldimethylsilyloxy)-3-nitrooct-7-en-2-ols (5). Aqueous NaOH (10 *M*, 1 mL) was added to a vigorously stirred solution of nitro compound **4** (2.59 g, 10 mmol) and acetaldehyde (0.58 g, 13 mmol) in EtOH (3 mL) at 0 °C. The reaction mixture was stirred for 3 h at this temperature, then neutralized with acetic acid (0.60 g, 10 mmol), heated to 20 °C, diluted with water, and extracted with $MeOBu^t$. The extract was washed with water and brine, dried with Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 eluting with the light petroleum—$MeOBu^t$ mixture (4 : 1) to yield a mixture of diastereomeric nitro alcohols **5** (2.36 g, 78%) as a colorless oil, R_f 0.3 (light petroleum—$MeOBu^t$, 4 : 1). Found (%): C, 55.58; H, 9.64; N, 4.65. $C_{14}H_{29}NO_4Si$. Calculated (%): C, 55.41; H, 9.63; N, 4.62. IR (neat), ν/cm^{-1}: 1004, 1076, 1124, 1280, 1332, 1364, 1384, 1412, 1464, 1476, 1644, 2860—3000, 3528. MS (EI), m/z (I_{rel} (%)): 246 $[M - C_4H_9]^+$ (0.4); 199 $[M - C_3H_6NO_3]^+$ (19); 184 (11); 162 (14); 75 (100). ^{1}H NMR (200.13 MHz), δ: 0.13, 0.15, 0.16, 0.18 (all s, 6 H, Me_2Si); 0.91, 0.93 (both s, 9 H, Me_3C); 1.30 (d, 3 H, $H_3C(1)$, J = 6.3 Hz); 1.32 (d, 3 H, $H_3C(1)$, J = 6.5 Hz); 1.60—1.9 (m, 2 H, $H_2C(5)$); 2.1—2.5 (m, 2 H, $H_2C(6)$); 2.90 (s, 1 H, OH); 4.28—4.50 (m, 3 H, C<u>H</u>OH, CHOTBS, $CHNO_2$); 4.97—5.11 (m, 2 H, H_2C=); 5.68—5.90 (m, 1 H, HC=). ^{13}C NMR (50.03 MHz), δ: –4.77 and 4.50 (Me_2Si); 17.9 ($Me_3\underline{C}$); 19.55 and 20.02 (C(1)); 25.71 (Me_3C); 28.11 and 28.37 (C(5)); 32.83 and 34.13 (C(6)); 64.98 and 67.37 (C(2)); 69.94 and 72.72 (C(4)); 94.17 and 94.60 (C(3)); 115.46 and 115.64 (C(8)); 137.08 and 137.50 (C(7)).

4-(*tert*-Butyldimethylsilyloxy)-3-nitroocta-2,7-diene (2), a mixture of 2*E*- and 2*Z*-isomers. The reagents DCC (2.68 g, 13.0 mmol) and CuCl (50 mg, 0.5 mmol) were added to a stirred solution of a mixture of diastereomers **5** (3.0 g, 9.9 mmol) in Et_2O (10 mL) under argon at 20 °C. The reaction mixture was stirred for 3 h, then diluted with light petroleum (50 mL). A precipitate formed was filtered off, washed with light petroleum on the filter, the combined filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 eluting with the light petroleum—$MeOBu^t$ (95 : 5) to

yield a mixture of isomers **2** (2.08 g, 75%) (*Z*-**2** : *E*-**2** ≈ 2 : 1, the ^{1}H NMR data) as a colorless oil, b.p. 75—78 °C (0.09 Torr). Found (%): C, 58.97; H, 9.52; N, 4.88. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (neat), ν/cm^{-1}: 1100, 1260, 1332, 1364, 1388, 1444, 1464, 1472, 1644, 1668, 2124, 2860—3000, 3080. MS (EI), *m*/*z* (I_{rel} (%)): 255 $[M - NO]^+$ (0.7), 230 $[M - C_4H_7]^+$ (24), 228 $[M - C_4H_9]^+$ (38), 198 (34), 183 (66), 157 (49), 143 (56), 104 (91), 75 (100).

Diene *Z*-**2**. ^{1}H NMR (200.13 MHz), δ: 0.04 and 0.10 (both s, 3 H each, Me_2Si); 0.91 (s, 9 H, Me_3C); 1.58—2.21 (m, 4 H, 2 CH_2); 1.98 (dd, 3 H, $H_3C(1)$, *J* = 1.06 Hz, *J* = 7.38 Hz); 4.67 (m, 1 H, CH(4)); 4.95—5.11 (m, 2 H, H_2C=); 5.68—5.92 (m, 1 H, HC=); 6.11 (q, 1 H, HC(2), *J* = 7.38 Hz). ^{13}C NMR (50.03 MHz), δ: −5.14 and −4.96 (Me_2Si); 13.58 (C(1)); 25.67 (Me_3C); 28.89 (C(5)); 36.04 (C(6)); 70.11 (C(4)); 114.93 (C(8)); 126.64 (C(2)); 137.67 (C(7)); 154.44 (C(3)).

Diene *E*-**2**. ^{1}H NMR (200.13 MHz), δ: 0.0 and 0.09 (both s, 3 H each, Me_2Si); 0.89 (s, 9 H, Me_3C); 2.07 (d, 3 H, $H_3C(1)$, *J* = 7.73 Hz); 1.58—2.21 (m, 4 H, 2 CH_2); 4.67 (m, 1 H, CH(4)); 4.95—5.11 (m, 2 H, H_2C=); 5.68—5.92 (m, 1 H, HC=); 7.16 (q, 1 H, HC(2), *J* = 7.73 Hz). ^{13}C NMR (50.03 MHz), δ: −5.36 and −5.03 (Me_2Si); 12.93 (C(1)); 17.97 (Me_3C); 29.79 (C(5)); 36.10 (C(6)); 68.34 (C(4)); 115.11 (C(8)); 134.11 (C(2)); 154.27 (C(3)).

(3a*S,6*S**,6a*S**)-1,6-Bis(trimethylsilyloxy)-6a-vinylperhydrocyclopenta[*c*]isoxazole (7).** A mixture of nitrodiene **1** (0.39 g, 2.28 mmol), hexamethyldisilazane (6 mL) and Et_3N (0.23 g, 2.28 mmol) was heated for 5 h at 110 °C under argon, then concentrated *in vacuo*. The residue was distilled to obtain isoxazolidine **7** (0.51 g, 72%) as a colorless liquid, b.p. 85 °C (bath temperature, 0.06 Torr). Found (%): C, 53.24; H, 9.28; Si, 17.63. $C_{14}H_{29}NO_3Si_2$. Calculated (%): C, 53.29; H, 9.26; Si, 17.80. IR (neat), ν/cm^{-1}: 844, 896, 912, 1116, 1136, 1252, 1384, 1420, 1552, 2900, 2960, 3084. MS (EI), *m*/*z* (I_{rel} (%)): 315 $[M]^+$ (3), 299 (11), 284 (10), 208 (13), 191 (17), 181 (13), 135 (42), 118 (40), 103 (47), 72 (100). ^{1}H NMR (200.13 MHz), δ: 0.14 (s, 9 H, TMSO); 0.18 (s, 9 H, TMSO—N); 1.38 (m, 1 H, β-HC(4)); 1.53 (m, 1 H, β-HC(5)); 1.68 (m, 1 H, α-HC(5)); 2.04 (m, 1 H, α-HC(4)); 2.95 (m, 1 H, HC(3a)); 3.60 (dd, 1 H, β-HC(3), *J* = 2.1 Hz, *J* = 7.7 Hz); 3.91 (dd, 1 H, HC(6), *J* = 6.0 Hz, *J* = 10.4 Hz); 4.40 (dd, 1 H, α-HC(3), *J* = 8.3 Hz, *J* = 8.3 Hz); 5.07 (d, 1 H, *E*-HC=C, *J* = 17.9 Hz); 5.21 (d, 1 H, *Z*-HC=C, *J* = 11.3 Hz); 5.95 (dd, 1 H, C—HC=, *J* = 11.3 Hz, *J* = 17.9 Hz). ^{13}C NMR (50.03 MHz), δ: −0.30 and 0.09 (CH_3Si), 27.09 (C(4)), 31.56 (C(5)), 42.19 (C(3a)), 75.28 (C(3)), 78.49 (C(6)), 90.88 (C(6a)), 114.35 (H_2C=), 134.52 (HC=).

(3a*S,6*S**,6a*S**)-6-(*tert*-Butyldimethylsilyloxy)-1-trimethylsilyloxy-6a-vinylperhydrocyclopenta[*c*]isoxazole (8).** A mixture of nitrodienes **2** (2.28 g, 8 mmol), hexamethyldisilazane (20 mL), and Et_3N (0.81 g, 8 mmol) was heated for 5 h at 110 °C under argon, then concentrated *in vacuo*. The residue was distilled to obtain isoxazolidine **8** (2.17 g, 76%) as a colorless oil, b.p. 96—98 °C (0.08 Torr). Found (%): C, 57.43; H, 9.94. $C_{17}H_{35}NO_3Si_2$. Calculated (%): C, 57.09; H, 9.86. IR (neat), ν/cm^{-1}: 1072, 1116, 1140, 1252, 1360, 1392, 1472, 1556, 1648, 2124, 2850—3000, 3084. MS (EI), *m*/*z* (I_{rel} (%)): 300 $[M - C_4H_9]^+$ (19), 268 $[M - OTMS]^+$ (29), 171 (45), 147 (64), 115 (38), 101 (49), 75 (100). ^{1}H NMR (200.13 MHz), δ: 0.06 and 0.10 (both s, 3 H each, Me_2Si); 0.18 (s, 9 H, TMSO—N); 0.89 (s, 9 H, Me_3C); 1.2—2.2 (m, 4 H, $H_2C(4)$ and $H_2C(5)$); 2.95 (m, 1 H, HC(3a)); 3.60 (dd, 1 H, β-HC(3), *J* = 2.1 Hz, *J* = 8.1 Hz); 3.91 (dd, 1 H, HC(6), *J* = 6.0 Hz, *J* = 10.4 Hz); 4.40 (dd, 1 H, α-HC(3), *J* = 8.0 Hz, *J* = 8.0 Hz); 5.05 (dd, 1 H, *E*-HC=C, J_1 = 1.1 Hz, J_2 = 17.6 Hz); 5.21 (dd, 1 H, *Z*-HC=C, J_1 = 1.1 Hz, J_2 = 11.3 Hz); 5.96 (dd, 1 H, C—C(H)=, *J* = 11.3 Hz, *J* = 17.6 Hz). ^{13}C NMR (50.03 MHz), δ: −4.81 ($C\underline{Me}_3$), −0.34 (Me_3Si), 18.02 ($Me_3\underline{C}$), 25.74 (Me_2Si), 27.10 (C(4)), 31.65 (C(5)), 42.14 (C(3a)), 75.26 (C(3)), 78.62 (C(6)), 91.17 (C(6a)), 113.94 (H_2C=), 134.8 (HC=).

***syn*-2-[(2*S**,5*S**)-2-Hydroxy-5-hydroxymethyl-*E*-cyclopentylidene]ethanaldoxime (9a), *syn*-2-[(2*S**,5*S**)-2-hydroxy-5-hydroxymethyl-*Z*-cyclopentylidene]ethanaldoxime (9b), *anti*-2-[(2*S**,5*S**)-2-hydroxy-5-hydroxymethyl-*E*-cyclopentylidene]-ethanaldoxime (9c), and *anti*-2-[(2*S**,5*S**)-2-hydroxy-5-hydroxymethyl-*Z*-cyclopentylidene]ethanaldoxime (9d).** A solution of $KF \cdot 2H_2O$ (0.1 g, 1.1 mmol) in MeOH (4 mL) was added to a stirred solution of isoxazolidine **7** (0.29 g, 0.92 mmol) in THF (1 mL) at −70 °C under argon. The reaction mixture was heated to −5 °C, kept for 1.5 h, then concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 using gradient elution from light petroleum to ethyl acetate to obtain a mixture of oximes **9a** : **9b** : **9c** : **9d** = 2 : 1 : 1 : 1 (the ^{1}H NMR data) (0.14 g, 60%) as a colorless oil. Found (%): C, 55.59; H, 8.04; N, 8.60. $C_8H_{13}NO_3$. Calculated (%): C, 56.13; H, 7.65; N, 8.18. IR (neat), ν/cm^{-1}: 968, 1032, 1104, 1180, 1388, 1552, 1648, 2876, 2952, 2960, 3300. MS (EI), *m*/*z* (I_{rel} (%)): 154 $[M - OH]^+$ (29), 140 $[M - CH_2OH]^+$ (13), 124 (29), 122 (30), 108 (31), 96 (64), 78 (60), 67 (64), 58 (100). ^{13}C NMR (50.03 MHz), δ: 23.8, 23.9, 24.1, 25.1, (C(4′)); 32.7, 32.8, 33.5, 34.0 (C(3′)); 41.5, 41.7, 45.6 (C(5′)); 63.1, 64.3, 65.4, 65.5 ($\underline{C}H_2OH$); 72.0, 74.0, 74.2 (C(2′)); 110.5, 112.3, 116.1, 117.7 (C(1)); 145.0, 145.1, 148.1 (C=NOH); 155.4, 157.3, 158.4 (C(1′)).

A mixture of oximes **9** (64 mg) was chromatographed on SiO_2 (10 g) eluting with the light petroleum—EtOAc (4 : 1) mixture. The following fractions enriched (up to 90%) with individual isomers were isolated: **9a** (18.4 mg, R_f 0.26, EtOAc), **9b** (16 mg, R_f 0.22, EtOAc), **9c** (4 mg, R_f 0.19, EtOAc), **9d** (3 mg, R_f 0.13, EtOAc).

Oxime **9a**. ^{1}H NMR (300.13 MHz, $CDCl_3$: CD_3OD : : CD_3COCD_3 = 8 : 1 : 1), δ: 1.34—1.78 (m, 2 H, $H_2C(4′)$); 1.85—2.10 (m, 2 H, $H_2C(3′)$); 2.75—3.18 (m, 1 H, HC(5′)); 3.45—3.65 (m, 2 H, H_2CO); 4.30—4.91 (m, 1 H, HCO); 6.08 (d, 1 H, HC(2), *J* = 9.2 Hz); 7.87 (d, 1 H, HC=N, *J* = 9.2 Hz).

Oxime **9b**. ^{1}H NMR (300.13 MHz, $CDCl_3$: CD_3OD : : CD_3COCD_3 = 8 : 1 : 1), δ: 1.34—1.78 (m, 2 H, $H_2C(4′)$); 1.85—2.10 (m, 2 H, $H_2C(3′)$); 2.75—3.18 (m, 1 H, HC(5′)); 3.45—3.65 (m, 2 H, H_2CO); 4.30—4.91 (m, 1 H, HCO); 5.95 (d, 1 H, HC(2), *J* = 10.2 Hz); 8.03 (d, 1 H, HC=N, *J* = 10.2 Hz).

Oxime **9c**. ^{1}H NMR (300.13 MHz, $CDCl_3$: CD_3OD : : CD_3COCD_3 = 8 : 1 : 1), δ: 1.34—1.78 (m, 2 H, $H_2C(4′)$); 1.85—2.10 (m, 2 H, $H_2C(3′)$); 2.75—3.18 (m, 1 H, HC(5′)); 3.45—3.65 (m, 2 H, H_2CO); 4.30—4.91 (m, 1 H, HCO); 6.67 (d, 1 H, HC(2), *J* = 10.2 Hz); 7.20 (d, 1 H, HC=N, *J* = 10.2 Hz).

Oxime **9d**. ^{1}H NMR (300.13 MHz, $CDCl_3$: CD_3OD : : CD_3COCD_3 = 8 : 1 : 1), δ: 1.34—1.78 (m, 2 H, $H_2C(4′)$); 1.85—2.10 (m, 2 H, $H_2C(3′)$); 2.75—3.18 (m, 1 H, HC(5′)); 3.45—3.65 (m, 2 H, H_2CO); 4.30—4.91 (m, 1 H, HCO); 6.60 (d, 1 H, HC(2), *J* = 9.8 Hz); 7.50 (d, 1 H, HC=N, *J* = 9.8 Hz).

***syn*-2-[(2*S**,5*S**)-2-(*tert*-Butyldimethylsilyloxy)-5-hydroxymethyl-*E*-cyclopentylidene]ethanaldoxime (12a), *syn*-2-[(2*S**,5*S**)-2-(*tert*-butyldimethylsilyloxy)-5-hydroxymethyl-*Z*-cyclopentylidene]ethanaldoxime (12b), *anti*-2-[(2*S**,5*S**)-2-(*tert*-butyldimethylsilyloxy)-5-hydroxymethyl-*E*-cyclopentylidene]-**

ethanaldoxime (12c), and *anti*-2-[(2*S,5*S**)-2-(*tert*-butyldimethylsilyloxy)-5-hydroxymethyl-*Z*-cyclopentylidene]ethanaldoxime (12d).** A solution of $KF \cdot 2H_2O$ (0.16 g, 1.7 mmol) in MeOH (8 mL) was added to a stirred solution of isoxazolidine **8** (0.57 g, 1.58 mmol) in THF (8 mL) at −70 °C under argon. The reaction mixture was heated to 20 °C, kept for 1 h, then diluted with $MeOBu^t$ (50 mL) and filtered. The filtrate was concentrated *in vacuo* and the residue was subjected to column chromatography on SiO_2 using gradient elution from light petroleum to $MeOBu^t$. The following compounds were isolated in the order of elution: oxime **12a** (128 mg, 28.4%), oxime **12b** (62 mg, 13.8%), oxime **12d** (35 mg, 7.8%), and oxime **12c** (105 mg, 23.3%).

Oxime **12a**. R_f 0.66 ($MeOBu^t$—light petroleum, 4 : 1), colorless crystals, m.p. 116—121 °C ($MeOBu^t$—light petroleum, 1 : 2). Found (%): C, 58.84; H, 9.73; N, 4.87. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (KBr), ν/cm^{-1}: 628, 680, 776, 835, 868, 896, 956, 992, 1032, 1124, 1252, 1332, 1388, 1436, 1472, 1628, 1660, 2860—3056. MS (EI), *m/z* (I_{rel} (%)): 285 $[M]^+$ (0.7), 268 (9), 254 (5), 236 (5), 212 (13), 192 (54), 182 (21), 165 (10), 153 (27), 135 (50), 122 (39), 118 (57), 106 (60), 91 (30), 75 (100) ^{1}H NMR (300.13 MHz), δ: −0.08 and 0.11 (both s, 3 H each, Me_2Si); 0.92 (s, 9 H, Me_3C); 1.40—1.50 (m, 2 H, $H_2C(4')$); 1.93—2.10 (m, 2 H, $H_2C(3')$); 3.07 (m, 1 H, CH(5′)); 3.53—3.60 (m, 2 H, CH_2O); 4.46 (dd, 1 H, HC(2′), *J* = 8.3 Hz, *J* = 10.7 Hz); 6.17 (ddd, 1 H, HC=C, *J* = 1.8 Hz, *J* = 1.8 Hz, *J* = 9.8 Hz); 7.99 (d, 1 H, HC=N, *J* = 9.8 Hz); 9.34 (br.s 1 H, OH). ^{13}C NMR (50.03 MHz), δ: −4.9 and −4.6 (Me_2Si); 18.0 ($Me_3\underline{C}Si$); 23.7 (C(3′)); 25.7 ($C\underline{Me}_3$); 33.4 (C(4′)); 40.9 (C(5′)); 66.4 ($\underline{C}H_2OH$); 74.8 (C(2′)); 115.1 (C=$\underline{C}$H), 148.2 (C=NOH); 155.9 (C(1′)).

Oxime **12b**. R_f 0.60 ($MeOBu^t$—light petroleum, 4 : 1), colorless crystals, m.p. 102—105 °C ($MeOBu^t$—light petroleum, 1 : 2). Found (%): C, 59.09; H, 9.78; N, 5.00. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (KBr), ν/cm^{-1}: 520, 654, 752, 776, 848, 872, 972, 1016, 1108, 1132, 1204, 1256, 1304, 1380, 1436, 1444, 1476, 1544, 1580, 1628, 2812—3208, 3388. MS (EI), *m/z* (I_{rel} (%)): 268 $[M - OH]^+$ (5), 252 (5), 210 (16), 192 (6), 183 (6), 165 (15), 153 (33), 135 (28), 118 (13), 105 (10), 96 (12), 91 (10), 75 (100). ^{1}H NMR (300.13 MHz), δ: −0.11 and 0.13 (both s, 3 H each, Me_2Si); 0.89 (s, 9 H, Me_3C); 1.40—1.75 (m, 2 H, $H_2C(4')$); 1.90—2.10 (m, 2 H, $H_2C(3')$); 2.85 (m, 1 H, CH(5′)); 3.70 (m, 2 H, CH_2O); 4.82 (ddd, 1 H, HC(2′), *J* = 2.5 Hz, *J* = 5.6 Hz, *J* = 8.3 Hz); 6.69 (ddd, 1 H, HC=C, *J* = 1.8 Hz, *J* = 1.8 Hz, *J* = 9.9 Hz); 7.70 (d, 1 H, HC=N, *J* = 9.9 Hz); 9.38 (br.s 1 H, OH). ^{13}C NMR (50.03 MHz), δ: −4.7 and −3.7 (Me_2Si); 17.9 ($Me_3\underline{C}Si$); 25.0 (C(3′)); 25.8 ($C\underline{Me}_3$); 34.9 (C(4′)); 45.6 (C(5′)); 64.7 ($\underline{C}H_2OH$); 74.2 (C(2′)); 111.8 (C=$\underline{C}$H), 145.4 (C=NOH); 157.1 (C(1′)).

Oxime **12c**. R_f 0.36 ($MeOBu^t$—light petroleum, 4 : 1), colorless crystals, m.p. 123—128 °C ($MeOBu^t$—light petroleum, 1 : 1). Found (%): C, 58.93; H, 9.74; N, 4.88. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (KBr), ν/cm^{-1}: 668, 676, 776, 836, 876, 1028, 1132, 1176, 1256, 1328, 1360, 1464, 1472, 1628, 1652, 2856—3068, 3200. MS (EI), *m/z* (I_{rel} (%)): 268 $[M - OH]^+$ (4), 254 (3), 236 (7), 211 (16), 192 (46), 182 (15), 165 (15), 153 (47), 135 (19), 118 (76), 106 (27), 91 (90), 75 (100). ^{1}H NMR (300.13 MHz), δ: −0.11 and 0.14 (both s, 3 H each, Me_2Si); 0.94 (s, 9 H, Me_3C); 1.40—1.75 (m, 2 H, $H_2C(4')$); 1.90—2.10 (m, 2 H, $H_2C(3')$); 3.11 (m, 1 H, CH(5′)); 3.60 (d, 2 H, CH_2O, *J* = 17.0 Hz); 4.48 (ddd, 1 H, HC(2′), *J* = 2.5 Hz, *J* = 5.6 Hz, *J* = 8.3 Hz); 6.80 (ddd, 1 H, HC=C, *J* = 1.8 Hz, *J* = 1.8 Hz, *J* = 10.3 Hz); 7.35 (d, 1 H, HC=N, *J* = 10.3 Hz); 9.00 (br.s, 1 H, OH). ^{13}C NMR (50.03 MHz), δ: −4.8 and −4.6 (Me_2Si); 18.2 ($Me_3\underline{C}Si$); 23.9 (C(3′)); 25.8 ($C\underline{Me}_3$); 33.6 (C(4′)); 41.0 (C(5′)); 66.5 (CH_2OH); 75.0 (C(2′)); 110.6 (C=$\underline{C}$H), 145.7 (C=NOH); 158.3 (C(1′)).

Oxime **12d**. R_f 0.45 ($MeOBu^t$—light petroleum, 4 : 1), colorless crystals, m.p. 102—105 °C ($MeOBu^t$—light petroleum, 1 : 2). Found (%): C, 59.26; H, 9.62; N, 5.13. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (KBr), ν/cm^{-1}: 668, 680, 776, 836, 856, 940, 980, 1028, 1096, 1184, 1252, 1316, 1360, 1460, 1472, 1652, 1700, 2856—3076, 3250. MS (EI), *m/z* (I_{rel} (%)): 267 $[M - OH_2]^+$ (2), 254 (2), 238 (4), 228 (23), 210 (48), 194 (7), 182 (13), 153 (90), 135 (44), 122 (25), 106 (35), 94 (27), 75 (100). ^{1}H NMR (300.13 MHz), δ: −0.12 and 0.17 (both s, 3 H each, Me_2Si); 0.91 (s, 9 H, Me_3C); 1.40—1.70 (m, 2 H, $H_2C(4')$); 1.90—2.10 (m, 2 H, $H_2C(3')$); 2.86 (m, 1 H, CH(5′)); 3.68 (d, 2 H, CH_2O, *J* = 17.0 Hz); 4.79 (ddd, 1 H, HC(2′), *J* = 2.5 Hz, *J* = 5.6 Hz, *J* = 8.3 Hz); 6.10 (ddd, 1 H, HC=C, *J* = 1.8 Hz, *J* = 1.8 Hz, *J* = 10.4 Hz); 8.30 (d, 1 H, HC=N, *J* = 10.4 Hz); 9.00 (br.s 1 H, OH). ^{13}C NMR (50.03 MHz), δ: −4.6 and −3.8 (Me_2Si); 17.8 ($Me_3\underline{C}Si$); 25.2 (C(3′)); 25.8 ($C\underline{Me}_3$); 34.9 (C(4′)); 45.4 (C(5′)); 64.8 (CH_2OH); 74.1 (C(2′)); 117.5 (C=$\underline{C}$H), 149.0 (C=NOH); 155.1 (C(1′)).

(±)-4-(3-Oxopropyl)-3-vinyl-4,5-dihydroisoxazole (14). Acetic acid (0.1 g, 1.67 mmol) was added to a stirred solution of isoxazolidine **7** (0.12 g, 0.32 mmol) in THF (2 mL) at −30 °C under argon. The reaction mixture was heated to 20 °C over 30 min, kept for 1 h, diluted with EtOAc (10 mL), washed with saturated aq. $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 eluting with the ethyl acetate—light petroleum (1 : 1) mixture to obtain isoxazoline **14** (40 mg, 73%) as a colorless oil, R_f 0.33 (ethyl acetate—light petroleum, 1 : 1). Found (%): C, 62.67; H, 7.50; N, 9.60. $C_8H_{11}NO_2$. Calculated (%): C, 62.73; H, 7.24; N, 9.14. IR (neat), ν/cm^{-1}: 892, 928, 992, 1096, 1192, 1376, 1620, 1720, 2732, 2884, 2932, 3096, 3400. MS (EI), *m/z* (I_{rel} (%)): 153 $[M]^+$ (21), 124 (18), 109 (71), 108 (80), 96 (64), 79 (86), 55 (100). ^{1}H NMR (200.13 MHz), δ: 1.80—2.02 (m, 2 H, HC(1′)), 2.52 (m, 1 H, HC(2′)); 3.47 (m, 1 H, HC(4)); 4.15—4.35 (m, 2 H, HC(5)); 5.62 (d, 1 H, HC=C, *J* = 10.0 Hz); 5.73 (d, 1 H, H′C=C, *J* = 15.0 Hz); 6.63 (dd, 1 H, C—C(H)=, *J* = 15.0 Hz, *J* = 10.0 Hz); 9.80 (s, 1 H, HC(3′)). ^{13}C NMR (50.03 MHz), δ: 22.99 (C(1′)), 40.40 (C(2′)), 45.22 (C(4)), 74.30 (C(5)), 122.33 (H_2C=), 125.60 (HC=), 160.5 (C(3)), 200.72 (C=O).

(5*S,7a*S**)-5-(*tert*-Butyldimethylsilyloxy)-5,6,7,7a-tetrahydrocyclopenta[*c*]pyran-3(1*H*)-one oxime (16).** *N*-Chlorosuccinimide (0.29 g, 2.2 mmol) was added to a stirred solution of a mixture of oximes **12a,c** (**12a** : **12c** = 3 : 2, 0.57 g, 2 mmol) in $CHCl_3$ (30 mL) at 0 °C under argon, followed by addition of Et_3N (0.22 g, 2.2 mmol) after 5 h. The reaction mixture was kept for 12 h at 20 °C, then concentrated *in vacuo*. The residue was dissolved in $MeOBu^t$ (20 mL), washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 using gradient elution with the light petroleum—$MeOBu^t$ (3 : 1 → 1 : 1) mixture to obtain oxime **16** (0.41 g, 72%) as colorless crystals, m.p. 103—105 °C (light petroleum). Found (%): C, 59.41; H, 9.04; N, 5.06. $C_{14}H_{25}NO_3Si$. Calculated (%): C, 59.32; H, 8.89; N, 4.94. IR (KBr), ν/cm^{-1}: 668, 760, 776, 840, 852, 864, 952, 960, 1040, 1080, 1096, 1108, 1164, 1252, 1284, 1320, 1344, 1356,

1392, 1440, 1468, 1520, 1652, 1664, 1716, 2340, 2856, 2864, 2928, 2956, 3144—3300. ^{1}H NMR (200.13 MHz), δ: 0.08 and 0.09 (both s, 6 H, Me_2Si); 0.88 (s, 9 H, Me_3C); 1.16 (dddd, 1 H, α-HC(7), J = 7.3 Hz, J = 8.2 Hz, J = 10.0 Hz, J = 12.0 Hz); 1.72 (dddd, 1 H, α-HC(6), J = 6.2 Hz, J = 8.3 Hz, J = 12.2 Hz, J = 13.6 Hz); 1.94—2.16 (m, 2 H, β-HC(6), β-HC(7)); 2.99 (m, 1 H, HC(7a)); 3.62 (dd, 1 H, α-HC(1), J = 10.0 Hz, J = 11.8 Hz); 4.56 (dd, 1 H, β-HC(1), J = 6.1 Hz, J = 10.0 Hz); 4.63 (dddd, 1 H, HC(5), J = 1.3 Hz, J = 1.3 Hz, J = 5.8 Hz, J = 5.8 Hz); 5.95 (dd, 1 H, HC(4), J = 1.2 Hz, J = 2.7 Hz); 7.98 (br.s 1 H, OH). ^{13}C NMR (50.03 MHz), δ: –4.72 and –4.62 (Me_2Si), 18.09 ($Me_3\underline{C}$), 24.43 (C(7)), 25.69 ($\underline{Me}_3C$), 34.60 (C(6)), 36.92 (C(7a)), 71.08 (C(1)), 73.59 (C(5)), 111.28 (C(4)), 152.35 (C(4a)), 155.29 (C(3)).

(5*S,7a*S**)-5-(*tert*-Butyldimethylsilyloxy)-5,6,7,7a-tetrahydrocyclopenta[*c*]pyran-3(1*H*)-one (17).** Iodoxybenzoic acid (317 mg, 1.2 mmol) was added to a stirred solution of oxime **16** (283 mg, 1 mmol) in the mixture of DMF (1 mL) and THF (3 mL) at 20 °C. The suspension obtained was stirred for 1 h, then diluted with light petroleum (20 mL) and water (5 mL). The organic layer was separated, washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 eluting with the MeOBu^t—light petroleum (1 : 4) mixture to obtain lactone **17** (249 mg, 93%) as colorless crystals, m.p. 41—43 °C (light petroleum). Found (%): C, 62.69; H, 8.98. $C_{14}H_{24}O_3Si$. Calculated (%): C, 62.64; H, 9.01. IR (KBr), ν/cm^{-1}: 672, 704, 736, 776, 836, 856, 864, 936, 952, 980, 1024, 1032, 1100, 1124, 1148, 1164, 1208, 1260, 1280, 1304, 1340, 1360, 1392, 1464, 1472, 1516, 1616, 1648, 1668, 1712, 2856, 2888, 2928, 2960, 3316, 3436. ^{1}H NMR (200.13 MHz), δ: 0.10 (s, 6 H, Me_2Si); 0.89 (s, 9 H, Me_3C); 1.17 (dddd, 1 H, α-HC(7), J = 6.3 Hz, J = 9.8 Hz, J = 11.2 Hz, J = 12.3 Hz); 1.75 (dddd, 1 H, α-HC(6), J = 7.1 Hz, J = 7.1 Hz, J = 11.2 Hz, J = 13.6 Hz); 2.28 (m, 2 H, β-HC(6), β-HC(7)); 3.06 (m, 1 H, HC(7a)); 3.91 (dd, 1 H, α-HC(1), J = 10.4 Hz, J = 12.9 Hz); 4.51 (dd, 1 H, β-HC(1), J = 6.2 Hz, J = 10.4 Hz); 4.66 (ddd, 1 H, HC(5), J = 2.5 Hz, J = 6.4 Hz, J = 6.4 Hz); 5.88 (dd, 1 H, HC(4), J = 1.2 Hz, J = 2.5 Hz). ^{13}C NMR (50.03 MHz), δ: –4.68 (Me_2Si), 18.06 ($Me_3\underline{C}$), 24.06 (C(7)), 25.66 ($\underline{Me}_3C$), 34.81 (C(6)), 37.18 (C(7a)), 71.42 (C(1)), 73.44 (C(5)), 113.08 (C(4)), 169.01 (C(4a)), 220.54 (C(3)).

(4a*S,5*S**,7a*S**)-5-(*tert*-Butyldimethylsilyloxy)-4,4a,5,6,7,7a-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (18a) and (4a*R**,5*S**,7a*S**)-5-(*tert*-butyldimethylsilyloxy)-4,4a,5,6,7,7a-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (18b).** A suspension of 10% Pd/C (0.1 g) in EtOH (3 mL) was stirred in the atmosphere of H_2 at 20 °C, followed by addition of a solution of lactone **17** (0.2 g, 0.74 mmol) in EtOH (3 mL) and stirring for another 72 h until the starting compound completely disappeared (TLC monitoring). The catalyst was filtered off, the filtrate was concentrated *in vacuo*, and the residue was subjected to column chromatography on SiO_2 eluting with the light petroleum—MeOBu^t (4 : 1) to yield a mixture of lactones **18a**,**b** in the ratio **18a** : **18b** = 3 : 1 (the ^{1}H NMR data) (140 mg, 70%). Additional chromatography of this mixture with gradient elution from light petroleum to the light petroleum—MeOBu^t (4 : 1) gave individual compounds **18a** and **18b**.

Lactone **18a**. A colorless oil, R_f 0.50 (light petroleum—MeOBu^t, 4 : 1). MS (ESI), m/z: $[M + H]^+$, found 271.1726, calculated 271.1735; $[M + Na]^+$, found 293.1546, calculated 293.1554. IR (neat), ν/cm^{-1}: 672, 776, 808, 836, 864, 900, 940, 968, 1004, 1032, 1060, 1096, 1128, 1216, 1256, 1320, 1360, 1384, 1432, 1464, 1472, 1652, 1748, 2856, 2896, 2928, 2950. ^{1}H NMR (600.13 MHz), δ: 0.06 and 0.08 (both s, 3 H each, Me_2Si); 0.89 (s, 9 H, Me_3C); 1.45 (dddd, 1 H, β-HC(7), J = 6.8 Hz, J = 7.0 Hz, J = 8.8 Hz, J = 12.0 Hz); 1.57 (dddd, 1 H, β-HC(6), J = 6.8 Hz, J = 6.9 Hz, J = 9.0 Hz, J = 12.0 Hz); 1.81 (dddd, 1 H, α-HC(6), J = 5.0 Hz, J = 5.1 Hz, J = 7.0 Hz, J = 12.2 Hz); 2.01 (dddd, 1 H, α-HC(7), J = 5.0 Hz, J = 6.6 Hz, J = 9.1 Hz, J = 12.0 Hz); 2.34 (dddd, 1 H, HC(4a), J = 5.1 Hz, J = 5.7 Hz, J = 6.5 Hz, J = 12.6 Hz); 2.37 (dd, 1 H, α-HC(4), J = 5.7 Hz, J = 14.6 Hz); 2.59 (ddddd, 1 H, HC(7a), J = 4.9 Hz, J = 6.1 Hz, J = 6.6 Hz, J = 8.8 Hz, J = 12.6 Hz); 2.62 (dd, 1 H, β-HC(4), J = 6.5 Hz, J = 14.6 Hz); 3.81 (ddd, 1 H, HC(5), J = 5.1 Hz, J = 5.1 Hz, J = 6.9 Hz); 3.99 (dd, 1 H, β-HC(1), J = 6.1 Hz, J = 11.5 Hz); 4.24 (dd, 1 H, α-HC(1), J = 4.9 Hz, J = 11.5 Hz). ^{13}C NMR (50.03 MHz), δ: –4.80 and –4.57 (Me_2Si), 17.94 ($Me_3\underline{C}$), 25.76 ($\underline{Me}_3C$), 25.77 (C(7)), 32.43 ((C4)), 34.13 (C(6)), 34.65 (C(7a)), 43.15 (C(4a)), 70.13 (C(1)), 79.64 (C(5)), 173.30 (C(3)).

Lactone **18b**. A colorless oil, R_f 0.45 (light petroleum—MeOBu^t, 4 : 1). MS (ESI), m/z: $[M + H]^+$, found 271.1730, calculated 271.1735; $[M+Na]^+$, found 293.1551, calculated 293.1554. IR (neat), ν/cm^{-1}: 668, 720, 776, 808, 836, 968, 1004, 1040, 1064, 1084, 1120, 1224, 1260, 1280, 1348, 1388, 1432, 1448, 1472, 1652, 1748, 2340, 2364, 2864, 2952. ^{1}H NMR (600.13 MHz), δ: 0.06 and 0.07 (both s, 3 H each, Me_2Si); 0.90 (s, 9 H, Me_3C); 1.21 (dddd, 1 H, α-HC(7), J = 7.0 Hz, J = 7.0 Hz, J = 9.0 Hz, J = 12.0 Hz); 1.66 (dddd, 1 H, HC(4a), J = 4.8 Hz, J = 5.4 Hz, J = 12.2 Hz, J = 12.4 Hz); 1.77 (ddd, 1 H, β-HC(6), J = 7.0 Hz, J = 9.2 Hz, J = 11.0 Hz); 1.95 (dddd, 1 H, β-HC(7), J = 3.5 Hz, J = 7.5 Hz, J = 9.2 Hz, J = 11.0 Hz); 2.17 (dddd, 1 H, α-HC(6), J = 3.5 Hz, J = 5.0 Hz, J = 9.0 Hz, J = 11.0 Hz); 2.24 (ddddd, 1 H, HC(7a), J = 5.1 Hz, J = 7.5 Hz, J = 10.6 Hz, J = 12.0 Hz, J = 12.2 Hz); 2.64 (dd, 1 H, α-HC(4), J = 5.4 Hz, J = 17.9 Hz); 2.71 (dd, 1 H, β-HC(4), J = 12.4 Hz, J = 17.9 Hz); 4.04 (dd, 1 H, α-HC(1), J = 10.6 Hz, J = 11.0 Hz); 4.20 (dd, 1 H, HC(5), J = 4.8 Hz, J = 5.0 Hz); 4.62 (dd, 1 H, β-HC(1), J = 5.1 Hz, J = 11.0 Hz). ^{13}C NMR (50.03 MHz), δ: –4.56 (Me_2Si), 18.87 ($Me_3\underline{C}$), 25.73 ($\underline{Me}_3C$, C(7)), 29.61 (C(4)), 34.56 (C(6)), 34.61 (C(7a)), 36.52 (C(4a)), 70.23 (C(1) and C(5)), 173.82 (C(3)).

(5*R,6*S**,9*S**)-7-(*tert*-Butyldimethylsilyloxy)-10-hydroxymethyl-1,2-diazaspiro[4.4]nonan-3-one (19).** *o*-Nitrophenylsulfonyl hydrazide (434 mg, 2 mmol) and Et_3N (404 mg, 4 mmol) were added to a stirred solution of lactone **17** (134 mg, 0.5 mmol) in CH_2Cl_2 (1 mL) at 20 °C under argon. The reaction mixture was stirred for 4 h, then diluted with EtOAc, washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on SiO_2 eluting with the MeOBu^t—light petroleum (2 : 3) mixture to yield lactone **18a** (11 mg, 8%) (^{1}H NMR). Further elution with the EtOAc—MeOH mixture yielded spiro compound **19** (50 mg, 33%) as colorless crystals, m.p. 119—121 °C (EtOAc). MS (ESI), m/z: $[M + H]^+$, found 301.1938, calculated 301.1942. IR (KBr), ν/cm^{-1}: 668, 720, 776, 836, 916, 940, 984, 1004, 1032, 1068, 1080, 1112, 1144, 1180, 1252, 1360, 1376, 1416, 1436, 1472, 1540, 1696, 2368, 2856, 2880, 2928, 2956, 3044, 3172, 3240, 3388. ^{1}H NMR (200.13 MHz), δ: 0.09 and 0.10 (both s, 3 H each, Me_2Si); 0.91 (s, 9 H, Me_3C); 1.20, 1.64 and 191 (all m, 4 H, 2 CH_2); 2.33 (m, 1 H, HC(9)); 2.28 and 2.63 (both d, 1 H each, $H_2C(4)$, J = 16.5 Hz); 3.60 (dd, 1 H, HCOH, J = 8.2 Hz, J = 11.0 Hz); 3.70 (dd, 1 H, H´COH, J = 4.8 Hz, J = 11.0 Hz);

3.95 (dd, 1 H, HC(6), J = 6.2 Hz, J = 6.2 Hz). ^{13}C NMR (50.03 MHz), δ: –4.89 and –4.47 (Me_2Si), 17.99 ($Me_3\underline{C}$), 22.62, 25.72 ($\underline{Me}_3C$), 30.66, 34.96, 44.22 64.27 (CH_2O), 72.96 (C(5)), 75.25 (C(7)), 176.46 (C(3)).

(4a*S,5*S**,7a*S**)-5-(*tert*-Butyldimethylsilyloxy)-4,4a,5,6,7,7a-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one oxime (20a), (4a*R**,5*S**,7a*S**)-5-(*tert*-butyldimethylsilyloxy)-4,4a,5,6,7,7a-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one oxime (20b), and (1*S**,2*S**,3*S**)-1-(*tert*-butyldimethylsilyloxy)-3-hydroxymethyl-2-carbamoylmethylcyclopentane (21).** A suspension of 5% $Pd/BaSO_4$ (80 mg) containing unsaturated oxime **16** (0.2 g, 0.7 mmol) in EtOAc (10 mL) was vigorously stirred for 6 h at 20 °C in the atmosphere of H_2, followed by addition of the catalyst (40 mg) and stirring for another 4 h until the starting compound completely disappeared (TLC monitoring). The catalyst was filtered off, washed with EtOAc on the filter, the combined filtrate was concentrated *in vacuo*, and the residue was subjected to column chromatography on SiO_2. Gradient elution with the light petroleum—$MeOBu^t$ (2 : 1 → 2 : 3) mixture gave a mixture of lactones **18a,b** (**18a** : **18b** ≈ 3 : 2, the ^{1}H NMR data) (28 mg, 15%), a mixture of saturated oximes **20a,b** (**20a** : **20b** ≈ 3 : 2, the ^{1}H NMR data) (120 mg, 58%), and amide **21** (24 mg, 12%).

A mixture of oximes **20a,b**. Amorphous powder, m.p. 95—120 °C (light petroleum). Found (%): C, 58.89; H, 9.43; N, 4.86. $C_{14}H_{27}NO_3Si$. Calculated (%): C, 58.91; H, 9.53; N, 4.91. IR (KBr), ν/cm^{-1}: 668, 748, 776, 836, 856, 896, 908, 928, 960, 1004, 1040, 1056, 1104, 1116, 1156, 1188, 1208, 1252, 1292, 1304, 1340, 1360, 1380, 1436, 1472, 1672, 1692, 2856, 2896, 2928, 2992, 3280, 3304.

Oxime **20a**. ^{1}H NMR (600.13 MHz), δ: 0.06 and 0.07 (both s, 3 H each, Me_2Si); 0.88 (s, 9 H, Me_3C); 1.45 (dddd, 1 H, β-HC(7), J = 6.8 Hz, J = 7.0 Hz, J = 8.0 Hz, J = 13.0 Hz); 1.57 (dddd, 1 H, β-HC(6), J = 5.3 Hz, J = 6.0 Hz, J = 7.0 Hz, J = 11.7 Hz); 1.81 (dddd, 1 H, α-HC(6), J = 5.3 Hz, J = 6.0 Hz, J = 6.0 Hz, J = 11.7 Hz); 1.96 (dddd, 1 H, α-HC(7), J = 6.0 Hz, J = 6.0 Hz, J = 7.0 Hz, J = 13.0 Hz); 2.34 (m, 1 H, HC(4a)); 2.24 (dd, 1 H, α-HC(4), J = 7.0 Hz, J = 18.0 Hz); 2.58 (m, 1 H, HC(7a)); 2.54 (dd, 1 H, β-HC(4), J = 9.0 Hz, J = 18.0 Hz); 3.86 (ddd, 1 H, HC(5), J = 5.3 Hz, J = 5.3 Hz, J = 5.3 Hz); 3.91 (dd, 1 H, β-HC(1), J = 6.8 Hz, J = 11.5 Hz); 4.21 (dd, 1 H, α-HC(1), J = 5.1 Hz, J = 11.5 Hz); 7.69 (br.s 1 H, OH). ^{13}C NMR (150.03 MHz), δ: –4.77 and –4.60 (Me_2Si), 17.90 ($Me_3\underline{C}$), 25.09 ($\underline{Me}_3C$), 25.77 (C(7)), 26.25 (C(3)), 34.12 (C(6)), 35.41 (C(7a)), 42.28 (C(4a)), 69.06 (C(1)), 79.09 (C(5)), 155.72 (C(3)).

Oxime **20b**. ^{1}H NMR (600.13 MHz), δ: 0.04 and 0.05 (both s, 3 H each, Me_2Si); 0.88 (s, 9 H, Me_3C); 1.41 (m, 1 H, α-HC(7)); 1.64 (m, 1 H, HC(4a)); 1.72 (m, 1 H, β-HC(6)); 1.91 (m, 1 H, β-HC(7)); 2.09 (m, 1 H, α-HC(6)); 2.20 (m, 1 H, HC(7a)); 2.48 (dd, 1 H, α-HC(4), J = 6.6 Hz, J = 20.0 Hz); 2.48 (dd, 1 H, β-HC(4), J = 10.4 Hz, J = 20.0 Hz); 3.76 (dd, 1 H, α-HC(1), J = 10.8 Hz, J = 11.4 Hz); 4.24 (ddd, 1 H, HC(5), J = 1.0 Hz, J = 4.5 Hz, J = 4.5 Hz); 4.63 (dd, 1 H, β-HC(1), J = 5.0 Hz, J = 10.0 Hz); 7.88 (br.s 1 H, OH). ^{13}C NMR (50.03 MHz), δ: –5.05 and –4.86 (Me_2Si), 17.82 ($Me_3\underline{C}$), 25.60 ($\underline{Me}_3C$), 24.70 (C(7)), 27.12 (C(3)), 34.55 (C(6)), 37.93 (C(7a)), 46.45 (C(4a)), 75.81 (C(1)), 72.99 (C(5)), 153.98 (C(3)).

Amide **21**. Colorless crystals, m.p. 107—109 °C (EtOAc). MS (ESI), m/z: $[M + H]^+$, found 288.1989, calculated 288.1989; $[M + Na]^+$, found 310.1820, calculated 310.1809. IR (KBr), ν/cm^{-1}: 672, 700, 776, 836, 868, 888, 912, 972, 992, 1004, 1024, 1068, 1092, 1112, 1188, 1256, 1276, 1308, 1332, 1364, 1384, 1424, 1444, 1472, 1632, 1672, 2332, 2360, 2856, 2896, 2928, 2932, 3168, 3350. ^{1}H NMR (200.13 MHz), δ: 0.02 (s, 6 H, Me_2Si); 0.86 (s, 9 H, Me_3C); 1.19—1.41 (m, 1 H, HC(4)); 1.47—1.61 (m, 1 H, HC(5)); 1.72 (ddd, 1 H, HC(5), J = 5.0 Hz, J = 8.4 Hz, J = 13.1 Hz); 1.80—1.99 (m, 2 H, HC(3), H´C(4)); 1.99—2.11 (m, 1 H, HC(2)); 2.25 (dd, 1 H, HCC=O, J = 7.4 Hz, J = 15.7 Hz); 2.47 (dd, 1 H, H´CC=O, J = 7.4 Hz, J = 15.7 Hz); 3.58—3.42 (m, 2 H, H_2CO); 3.69 (s, 1 H, OH); 4.18 (q, 1 H, HC(1), J = 4.4 Hz); 6.11 and 6.19 (both br.s, 1 H each, H_2N). ^{13}C NMR (50.03 MHz), δ: –4.99 and –4.50 (Me_2Si), 18.02 ($Me_3\underline{C}$), 25.63 (C(4)), 25.82 ($\underline{Me}_3C$), 33.79 (C(5)), 35.28 ($\underline{C}H_2C$=O), 43.37 (C(3)), 44.92 (C(2)), 65.33 (CH_2OH), 75.90 (C(1)), 176.58 (C=O).

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