Synthesis of (5*S**,4a*S**,7a*S**)-5-hydroxyhexahydrocyclopenta[*c*]pyran-3(1*H*)-one*

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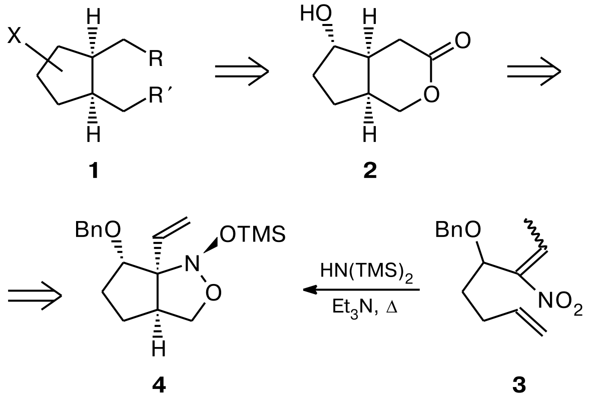
(5*S**,4a*S**,7a*S**)-5-Hydroxyhexahydrocyclopenta[*c*]pyran-3(1*H*)-one, the promising isoprostane building block, was synthesized using intramolecular [3+2] cycloaddition of silyl nitronate generated from 4-benzyloxy-3-nitroocta-2,7-diene on the key step.

Key words: 5*S**,4a*S**,7a*S**-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one, silyl nitronates, dipolar [3+2] cycloaddition, isoprostanes, nitroalkenes.

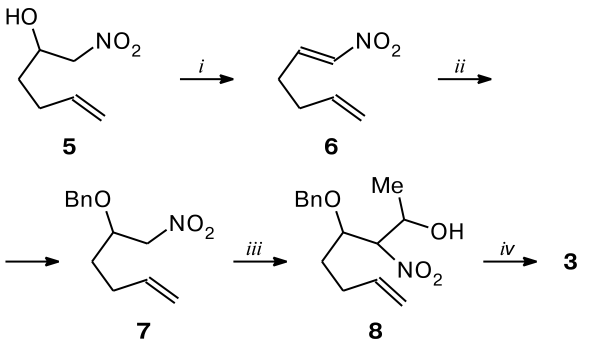
Isoprostanes of general formula **1** differing from prostaglandins by *cis*-configuration of the side chains at the cyclopentane ring and forming *in vivo* as racemates in non-enzymatic free radical ring closure of arachidenic acid[1] are of great interest owing to their biological properties, for example, they could serve as biomarkers of oxidative stress *in vivo*.[2] In continuation of our research on the synthesis of natural cyclopentanoids involving dipolar [3+2] cycloaddition of silyl nitronates generated from unsaturated nitro compounds,[3] we describe here the application of this approach for the synthesis of (5*S**,4a*S**,7a*S**)-5-hydroxyhexahydrocyclopenta[*c*]pyran-3(1*H*)-one **2** (Scheme 1), the promising precursor for isoprostanes (*cf.* Ref. 4).

Scheme 1



The starting material for the synthesis of lactone **2** was a mixture of isomeric nitrodienes **3**. The latter was prepared from the known product **5** of nitroaldol condensation of pent-4-enal with nitromethane[3d] (Scheme 2). It was found that the attempted traditional benzylation of alcohol **5** with benzyl halide in the presence of base ((KOH, NaH)[5] does not proceed properly due apparently to the competing α-deprotonation of the starting nitro compound.

Scheme 2



Reagents and conditions: *i*. Bu$_2$SnO (20—30 mol.%), PhH, reflux (*cf.* Ref. 6); *ii*. BnONa, THF, 10 °C; *iii*. MeCHO, Bu^{t}OK, THF—Bu^{t}OH (1 : 1), 10 °C; *iv*. DCC, cat. CuCl, Et$_2$O, 20 °C.

Benzyl ether **7** was synthesized by two-step procedure including dehydration of alcohol **5** by treatment with Bu$_2$SnO under previously described conditions[6] and subsequent conjugate addition of sodium benzylate to nitroalkene **6**. Nitroaldol condensation of compound **7** with acetaldehyde afforded a mixture of diastereomeric nitro alcohols **8** with nearly identical chromatographic mobility. This mixture was dehydrated to give nitrodienes **3** (*Z*/*E* ~2 : 1, ^{1}H NMR data).

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* Dedicated to Academician of the Russian Academy of Sciences O. M. Nefedov in occasion of his 80th birthday.

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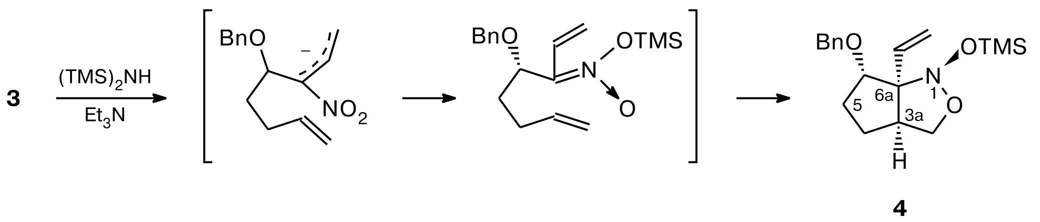
Scheme 3

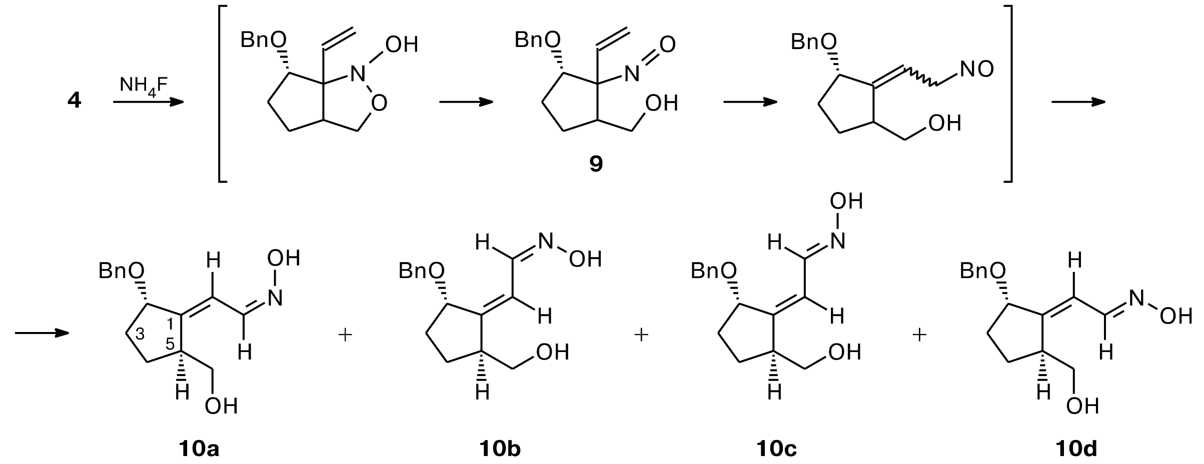


Under conditions described earlier,^{3} nitrodienes **3** smoothly underwent silylation to yield cyclopentaisoxazolidine **4** formed by intramolecular dipolar [3+2] cycloaddition with selectivity known for the relative example^{3d} (Scheme 3).

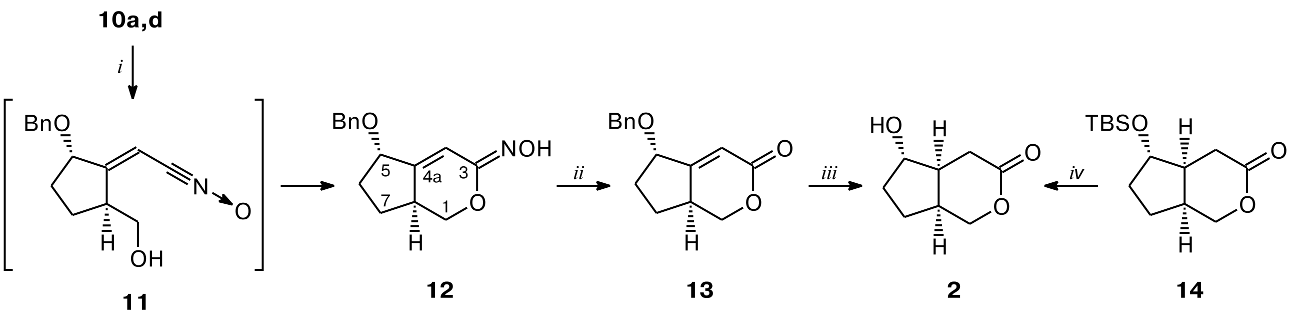
Desilylation isoxazolidine ring opening in compound **4** under the action of NH_4F (Scheme 4) proceeded *via* tertiary nitroso intermediate **9** and resulted in a mixture of approximately equal amounts of isomeric oximes **10a—d** (*cf.* Ref. 3d). This mixture was quantitatively separated by SiO_2 column chromatography and compounds **10a** and **10d** with suitable side chain configuration were used for the further transformations into target cyclopentavalerolactone **2**.

Treatment of the mixture of oximes **10a**,**d** with *N*-chlorosuccinimide *via* probable intermediate **11** provided cyclic product **12**, which was deoximated with 2-iodoxybenzoic acid (IBX) to give unsaturated lactone **13** (Scheme 5). Pd-Catalyzed hydrogenation of the double bond in the latter proceeded stereospecifically and was accompanied by hydrogenolysis of the benzyl ether bond to give the target product **2**. The structure and stereochem-

Scheme 4



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.* $Bu_4NF \cdot 3H_2O$, THF, 20 °C.

ical homogeneity of **2** were confirmed by comparison of its physicochemical parameters with those for the product obtained by desilylation of the synthesized earlier[3d] TBS-ether **14**.

Hitherto unknown compounds **2**, **4**, **7**, **10**, **12**, and **13** were characterized by means of spectroscopy. Thus, the configuration of the double bond of unsaturated oximes **10** (*E*-**10a**,**d** and *Z*-**10b**,**c**) was determined by the NOESY experiments, which revealed the cross peaks for couplings of the olefinic proton with the HC(5) cyclopentane ring proton or the proton of the CH_2O group, respectively. It is of note that physicochemical parameters of compounds **2**, **4**, **7**, **8**, **10**, **12**, and **13** correlates with those of the closely related compounds previously synthesized.[3d]

In summary, the herein described transformations are the next example of the application of intramolecular [3+2] cycloaddition of unsaturated silyl nitronate towards the synthesis of the building blocks of natural cyclopentanoids (see Ref. 3). Using this strategy, (5*S**,4a*S**,7a*S**)-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (**2**) was synthesized. Application of this compound as the synthon for isoprostanes will be the subject of our further investigations.

Experimental

Melting points were determined on a Koefler apparatus. IR spectra were recorded on a Bruker ALPHA-T instrument. ^1H and ^{13}C NMR spectra were run on Bruker AC-200, Bruker AM-300, and Bruker AVANCE II-600 spectrometers in $CDCl_3$ at 298 K, the chemical shifts are given in the δ-scale relative to the residual solvent signals (δ_H 7.27 and δ_C 77.0, respectively). High resolution mass spectra (ESI) were run on a Bruker micrOTOF II instrument at capillary potential 4.5 kV using direct inlet (*via* syringe pump) with MeOH as a solvent (a flow rate of 3 μL min^{-1}) operating on a positive ions mode (the mass range 500—3000 Da), rate of the main nitrogen flow is 4 L min^{-1} (180 °C). Mass spectra (EI, 70 eV) were obtained on a Finnigan MAT ITD-700 mass spectrometer. Column chromatography was performed on a Silica gel 60 (0.04—0.06 mm, Fluka); R_f values were measured using the precoated plates Silufol. Solvents, including petroleum ether with b.p. 40—70 °C, were purified and dried using standard procedures. Commercially available Bu_2SnO, Bu^tOK, BnOH, HMDS, Et_3N, acetaldehyde, DCC, NCS, NH_4F, $Bu_4NF \cdot 3H_2O$ (Acros Organics) were used. 2-Iodoxybenzoic acid (IBX) was synthesized by the known procedure.[7]

(±)-5-Benzyloxy-6-nitrohex-1-ene (7). To a stirred solution of benzyl alcohol (1.17 g, 10.9 mmol) in THF (7 mL), NaH (0.42 g of ~60% dispersion in mineral oil, ~11 mmol,) was added by portions at 20 °C under argon. After 40 min of stirring, a solution of nitrodiene **6** (see Ref. 6) (0.46 g, 3.6 mmol) in THF (15 mL) was added over a period of 5 min. The reaction mixture was stirred at 20 °C for 2 h and cooled to –30 °C, excess of NaH was decomposed by addition of AcOH (1 mL) and the mixture was diluted with $MeOBu^t$ (20 mL). The resulting solution was washed with water, brine, dried with Na_2SO_4, and the solvent was removed *in vacuo*. The residue was subjected to column chromatography (SiO_2, elution with petroleum ether—$MeOBu^t$, 5 : 1). The eluates containing product were combined, concentrated *in vacuo*, and distilled to give benzyl ether **7** in a yield of 0.76 g (89%), colorless liquid, b.p. 104—106 °C (0.08 Torr). Found (%): C, 66.30; H, 7.58; N, 5.81. $C_{13}H_{17}NO_3$. Calculated (%): C, 66.36; H, 7.28; N 5.90. IR (neat), ν/cm^{-1}: 627, 642, 699, 741, 916, 996, 1028, 1058, 1101, 1209, 1309, 1385, 1420, 1454, 1497, 1556, 1641, 2869, 2930, 2978, 3005, 3033, 3067. ^1H NMR (200.13 MHz), δ: 1.60—1.90 (m, 2 H, $H_2C(4)$); 2.13—2.27 (m, 2 H, $H_2C(3)$); 4.21 (dddd, 1 H, $C\underline{H}OBn$, *J* = 4.27 Hz, *J* = 5.73 Hz, *J* = 6.66 Hz, *J* = 7.73 Hz); 4.39—4.56 (m, 2 H, $CHNO_2$); 4.59 (br.s, 2 H, $C\underline{H}_2Ph$); 5.00—5.13 (m, 2 H, H_2C=); 5.80 (dddd, 1 H, HC=, *J* = 6.5 Hz, *J* = 6.5 Hz, *J* = 10.3 Hz, *J* = 16.9 Hz); 7.28—7.39 (m, 5 H, HC_{arom}).

4-Benzyloxy-3-nitrooct-7-en-2-ols 8 (mixture of diastereomers). At 10 °C, to a stirred solution of nitro compound **7** (4.30 g, 18.2 mmol) and acetaldehyde (1.36 g, 31 mmol) in THF—Bu^tOH (18 mL, 1 : 1), was added Bu^tOK (336 mg, 3 mmol) by portions over a period of 5 min under nitrogen. The reaction mixture was then stirred at 20 °C for 1 h, diluted with $MeOBu^t$ (30 mL), washed with saturated aqueous NH_4Cl solution, water, and brine, the organic layer was dried with Na_2SO_4, and the solvent was removed *in vacuo*. Column chromatorgaphy of the residue (SiO_2, elution with petroleum ether—$MeOBu^t$, 3 : 2) afforded 4.58 g (90%) of a mixture of diastereomers **8** as a colorless oil, R_f 0.55 (petroleum ether—$MeOBu^t$, 1 : 1). HR MS (ESI), *m/z*: found 280.1540, calculated for $C_{15}H_{21}NO_4$, $[M + H]^+$ 280.1543; found 302.1352, calculated for $[M + Na]^+$ 302.1363. IR (neat), ν/cm^{-1}: 699, 745, 916, 954, 995, 1028, 1070, 1091, 1210, 1281, 1332, 1372, 1455, 1497, 1550, 1641, 2873, 2933, 2978, 3033, 3067, 3426. ^1H NMR (200.13 MHz), δ: 1.29, 1.30, 1.31 (all d, 3 H, Me, *J* = 6.5 Hz); 1.58—1.95 (m, 2 H, HC(5)); 2.07—2.38 (m, 2 H, HC(6)); 4.00—4.82 (m, 5 H, HC(2), HC(3), HC(4), CH_2O); 4.94—5.14 (m, 2 H, H_2C=C); 5.78 (m, 1 H, HC=C), 7.22—7.43 (m, 5 H, HC_{arom}).

5-Benzyloxy-6-nitroocta-1,6-dienes (3), a mixture of 6*Z*- and 6*E*-isomers. To a stirred solution of a mixture of diastereomers **8** (4.48 g, 16 mmol) in Et_2O (20 mL), DCC (4.32 g, 21 mmol) and CuCl (100 mg, 1 mmol) were added at 20 °C under argon. The reaction mixture was stirred for 1 h, diluted with petroleum ether (100 mL). The precipitate that formed was filtered off and washed with petroleum ether. The combined filtrates were concentrated *in vacuo*. The column chromatography of the residue (SiO_2, elution with petroleum ether—$MeOBu^t$, 95 : 5) afforded 3.69 g (88%) of a mixture of isomers **3** (*Z*-**3** : *E*-**3** ≈ 1 : 2, ^1H NMR data) as a colorless oil, R_f 0.81 (petroleum ether—$MeOBu^t$, 2: 1). HR MS (ESI), *m/z*: found 262.1441, calculated for $C_{15}H_{19}NO_3$, $[M + H]^+$ 262.1438; found 284.1259, calculated for $[M + Na]^+$ 284.1257. IR (neat), ν/cm^{-1}: 699, 739, 845, 916, 995, 1028, 1097, 1208, 1453, 1522, 1641, 1664, 2124, 2857, 2931, 3032, 3066. ^1H NMR (200.13 MHz), δ: 1.74—1.95 (m, 2 H, 2 HC(5)); 2.01 (dd, ~0.3 H, $H_3C(1)$, *J* = 0.7 Hz, *J* = 7.3 Hz, *Z*-**3**); 2.04 (br.d, ~0.7 H, $H_3C(1)$, *J* = 7.7 Hz, *E*-**3**); 4.36—4.62 (m, 2 H, CH_2O); 4.63—4.76 (m, 1 H, HC(4)); 4.93—5.08 (m, 2 H, H_2C=C); 5.66—5.91 (m, 1 H, HC=C); 6.11 (q, ~0.3 H, HC(2), *J* =7.3 Hz, *Z*-**3**); 7.24—7.4 (m, ~5.7H, HC_{arom}, HC(2), *E*-**3**).

(3a*S,6*S**,6a*S**)-6-Benzyloxy-1-trimethylsilyloxy-6a-vinylperhydrocyclopenta[*c*]isoxazole (4).** A mixture of nitrodienes **3** (4.50 g, 17.2 mmol), hexamethyldisilazane (11.08 g, 68.8 mmol), and Et_3N (1.76 g, 17.4 mmol) was heated at 110 °C for 5 h under argon, concentrated *in vacuo*, and the residue was distilled. Compound **4** was obtained in a yield of 5.22 g (91%) as colorless oil, b.p. 130 °C (bath temperature, 0.08 Torr). HR MS (ESI), *m/z*:

found 334.1840, calculated for $C_{18}H_{27}NO_3Si$, $[M + H]^+$ 334.1833. IR (neat), ν/cm^{-1}: 1072, 1116, 1140, 1252, 1360, 1392, 1472, 1556, 1648, 2124, 2850—3000, 3084. MS (EI), *m/z* (I_{rel} (%)): 333 $[M]^+$ (49), 314 (22), 301 (21), 288 (9), 273 (73), 246 (19), 243 (31), 241 (59), 234 (7), 226 (20), 223 (21), 219 (13), 213 (20), 200 (11), 198 (24), 195 (31), 186 (22), 182 (33), 181 (49), 170 (22), 169 (24), 168 (38), 157 (11), 155 (21), 154 (37), 150 (16), 149 (48), 148 (39), 143 (22), 138 (23), 134 (24), 120 (51), 126 (30), 124 (15), 123 (25), 118 (19), 116 (54), 115 (47), 110 (17), 108 (43), 106 (55), 105 (54), 102 (44), 98 (37), 96 (40), 95 (34), 94 (42), 91 (61), 90 (100). ^{1}H NMR (200.13 MHz), δ: 0.23 (s, 9 H, TMSO); 0.99—2.31 (m, 4 H, $H_2C(4)$ and $H_2C(5)$); 3.03 (dddd, 1H, HC(3a), *J* = 2.0 Hz, *J* = 6.2 Hz, *J* = 7.9 Hz, *J* = 9.4 Hz); 3.62 (dd, 1 H, β-HC(3), *J* = 2.0 Hz, *J* = 8.1 Hz); 3.80 (dd, 1 H, HC(6), *J* = 6.3 Hz, *J* = 11.1 Hz); 4.40 (dd, 1 H, α-HC(3), *J* = 7.9 Hz, *J* = 8.1 Hz); 4.63 and 4.80 (both d, 1 H each, $\underline{H}_2$CPh, *J* = 12.1 Hz); 5.16 (dd, 1 H, *E*-HC=C, *J* = 0.6 Hz, *J* = 17.5 Hz); 5.30 (dd, 1 H, *Z*-HC=C, *J* = 0.8 Hz, *J* = 11.1 Hz); 6.12 (dd, 1 H, HC=C, *J* = 11.1 Hz, *J* = 17.5 Hz); 7.27—7.42 (m, 5 H, HC_{arom}).

***syn*-2-[(2*S**,5*S**)-2-Benzyloxy-5-hydroxymethyl-*E*-cyclopentylidene]ethanealdoxime (10a), *syn*-2-[(2*S**,5*S**)-2-benzyloxy-5-hydroxymethyl-*Z*-cyclopentylidene]ethanealdoxime (10b), *anti*-2-[(2*S**,5*S**)-2-benzyloxy-5-hydroxymethyl-*Z*-cyclopentylidene]ethanealdoxime (10c) and *anti*-2-[(2*S**,5*S**)-2-hydroxy-5-hydroxymethyl-*E*-cyclopentylidene]ethanealdoxime (10d).** To stirred suspension of NH_4F (0.17 g, 4.62 mmol) in MeOH (7 mL) cooled to −50 °C, a solution of compound **4** (1.1 g, 3.30 mmol) in THF (10 mL) was added under argon. The mixture was allowed to warm up to ambient temperature, kept for 1 h, and concentrated *in vacuo*. Column chromatography of the residue (SiO_2, gradient elution from petroleum ether to ethyl acetate) afforded 0.6 g (70%) of a mixture of oximes **10** as viscous oil. HR MS (ESI), *m/z*: found 262.1436, calculated for $C_{15}H_{19}NO_3$, $[M + H]^+$ 262.1438; found 284.1252, calculated for $[M + Na]^+$ 284.1257. Subsequent column chromatography gave eluates enriched with individual isomers, which with the exception of **10a** (see below) were purified by crystallization.

Oxime **10a**. R_f 0.66 (MeOBu^t—petroleum ether, 4 : 1). No crystals were obtained due to ready isomerization into the corresponding *anti*-isomer **10d** (the transformation half-time is ~36 h). ^{1}H NMR (300.13 MHz), δ: 1.47—1.69 (m, 2 H, $H_2C(4')$); 1.91—2.12 (m, 2 H, $H_2C(3')$); 3.04 (m, 1 H, CH(5′)); 3.48 (m, 2 H, CH_2O); 4.27 (br.t, 1 H, HC(2′), *J* = 5.8 Hz); 4.59 (m, 1 H, H_2CPh); 6.30 (br.d, 1 H, HC=C, *J* = 10.4 Hz); 7.21—7.41 (m, 5 H, HC_{arom}); 7.99 (d, 1 H, HC=N, *J* = 10.4 Hz). ^{13}C NMR (50.03 MHz), δ: 24.9 (C(3′)); 30.1 (C(4′)); 42.1 (C(5′)); 65.8 (CH_2OH); 71.2 (C(2′)); 81.1 ($\underline{C}H_2$Ph), 117.7 (C=$\underline{C}$H), 127.6, 128.4, 138.3 (Ph), 148.5 (C=NOH); 153.0 (C(1′)).

Oxime **10b**. Colorless crystals, m.p. 112—114 °C (MeOBu^t). IR (KBr), ν/cm^{-1}: 694, 731, 860, 929, 986, 1036, 1069, 1107, 1147, 1170, 1209, 1273, 1319, 1350, 1374, 1395, 1453, 1497, 1629, 1655, 2837—3256. ^{1}H NMR (300.13 NHz), δ: 1.37—1.62 (both m, 1 H each, $H_2C(4')$); 1.87—2.12 (m, 2 H, $H_2C(3')$); 2.82 (m, 1 H, CH(5′)); 3.44—3.71 (m, 2 H, CH_2O); 4.42 and 4.54 (both d, 1 H each, $\underline{H}_2$CPh, *J* = 12.1 Hz); 4.58 (m, 1 H, HC(2′)); 6.76 (br.d, 1 H, HC=C, *J* = 9.6 Hz); 7.23—7.34 (m, 5 H, HC_{arom}); 7.42 (d, 1 H, HC=N, *J* = 9.6 Hz). ^{13}C NMR (50.03 MHz), δ: 25.6 (C(3′)); 30.3 (C(4′)); 45.6 (C(5′)); 64.3 (CH_2OH); 70.4 (C(2′)); 78.8 ($\underline{C}H_2$Ph), 113.3 (C=$\underline{C}$H), 127.8, 127.9, 128.4, 137.7 (Ph), 145.4 (C=NOH); 154.4 (C(1′)).

Oxime **10c**. Colorless crystals, m.p. 108—110 °C (MeOBu^t). IR (KBr), ν/cm^{-1}: 578, 632, 701, 752, 854, 905, 936, 986, 1033, 1064, 1155, 1228, 1310, 1347, 1391, 1422, 1456, 1474, 1604, 2880—3216. ^{1}H NMR (300.13 MHz), δ: 1.37 and 1.60 (both m, 1 H each, $H_2C(4')$); 1.84—2.11 (m, 2 H, $H_2C(3')$); 2.78 (m, 1 H, CH(5′)); 3.42—3.72 (m, 2 H, CH_2O); 4.45 and 4.54 (both d, 1 H each, $\underline{H}_2$CPh, *J* = 11.3 Hz); 4.55 (m, 1 H, HC(2′)); 6.20 (br.d, 1 H, HC=C, *J* = 10.3 Hz); 7.20—7.41 (m, 5 H, HC_{arom}); 8.10 (d, 1 H, HC=N, *J* = 10.3 Hz). ^{13}C NMR (50.03 MHz), δ: 25.8 (C(3′)); 30.4 (C(4′)); 45.4 (C(5′)); 64.4 (CH_2OH); 70.5 (C(2′)); 78.8 ($\underline{C}H_2$Ph), 119.3 (C=$\underline{C}$H), 127.8, 128.1, 128.5, 137.8 (Ph), 148.9 (C=NOH); 152.4 (C(1′)).

Oxime **10d**. Colorless crystals, m.p. 123—125 °C (MeOBu^t). IR (KBr), ν/cm^{-1}: 594, 626, 699, 744, 857, 882, 912, 999, 1074, 1118, 1211, 1260, 1334, 1359, 1423, 1453, 1651, 2841—3213. ^{1}H NMR (300.13 MHz), δ: 1.45—1.72 (m, 2 H each, $H_2C(4')$); 1.87—2.15 (m, 2 H, $H_2C(3')$); 3.08 (m, 1 H, CH(5′)); 3.36—3.59 (m, 2 H, CH_2O); 4.28 (br.t, 1 H, HC(2′), *J* = 6.5 Hz); 4.60 (m, 2 H, $\underline{H}_2$CPh); 6.90 (dt, 1 H, HC=C, *J* = 1.9 Hz, *J* = 10.1 Hz); 7.20—7.41 (m, 6 H, HC_{arom}, HC=N). ^{13}C NMR (50.03 MHz), δ: 24.8 (C(3′)); 30.1 (C(4′)); 42.1 (C(5′)); 65.8 (CH_2OH); 71.2 (C(2′)); 81.3 ($\underline{C}H_2$Ph), 112.3 (C=$\underline{C}$H), 127.6, 127.7, 128.4, 138.3 (Ph), 145.7 (C=NOH); 155.3 (C(1′)).

(5*S,7a*S**)-5-Benzyloxy-5,6,7,7a-tetrahydrocyclopenta-[*c*]pyran-3(1*H*)-one oxime (12).** At 0 °C, to a stirred under argon solution of a mixture of oximes **10a,d** (**10a** : **10d** = 2 : 3, 313 mg, 1.2 mmol) in $CHCl_3$ (40 mL), *N*-chlorosuccinimide (0.2 g, 1.5 mmol) was added followed by the addition of Et_3N (152 mg, 1.5 mmol) 4 h after. The reaction mixture was kept at 20 °C for 12 h and concentrated *in vacuo*. The residue was dissolved in MeOBu^t (20 mL), washed with water, brine, dried with Na_2SO_4, and the solvent was removed *in vacuo*. Column chromatography of the residue (SiO_2, elution with MeOBu^t) afforded oxime **12** in a yield of 218 mg (70%) as colorless crystals, m.p. 112—113 °C (MeOBu^t—petroleum ether). HR MS (ESI), *m/z*: found 260.1281, calculated for $C_{15}H_{17}NO_3$, $[M + H]^+$ 260.1281. IR (KBr), ν/cm^{-1}: 701, 750, 762, 832, 863, 953, 1035, 1068, 1149—1275, 1322, 1385, 1400, 1455, 1470, 1640, 2859—3298. ^{1}H NMR (200.13 MHz), δ: 1.13—1.35 (m, 1 H, HC(7)); 1.82—2.27 (m, 3 H, $H_2C(6)$, H′C(7)); 3.02 (m, 1 H, HC(7a)); 3.64 (dd, 1 H, α-HC(1), *J* = 10.0 Hz, *J* = 11.7 Hz); 4.38 (m, 1 H, HC(5)); 4.48 and 4.57 (both d, 1 H each, H_2CPh, *J* = 11.4 Hz); 4.60 (dd, 1 H, β-HC(1), *J* = 6.4 Hz, *J* = 10.0 Hz); 6.10 (br.d, 1 H, HC(4), *J* = 2.5 Hz); 7.26—7.41 (m, 5 H, HC_{arom}); 8.42 (br.s, 1 H, OH). ^{13}C NMR (50.03 MHz), δ: 24.7 (C(7)), 31.70 (C(6)), 36.20 (C(7a)), 70.6 (C(1)), 79.6 (C(5)), 113.1 (C(4)), 127.8, 128.5, 137.9 (Ph), 152.0 (C(4a)), 152.4 (C(3)).

(5*S,7a*S**)-5-Benzyloxy-5,6,7,7a-tetrahydrocyclopenta-[*c*]pyran-3(1*H*)-one (13).** To a stirred solution of oxime **12** (0.27 g, 1.04 mmol) in DMF—THF (4 mL, 1 : 3), 2-iodoxybenzoic acid (IBX, 0.33 g, 1.25 mmol) was added at 20 °C. The resulting suspension was stirred for 1 h, diluted with petroleum ether (20 mL). The precipitate that formed was filtered off, washed with petroleum ether—MeOBu^t, 4 : 1. The combined filtrates were washed with water, brine, dried with Na_2SO_4, and concentrated *in vacuo*. Column chromatography (SiO_2, elution with MeOBu^t—petroleum ether, 3 : 2) afforded lactone **13** in a yield of 224 mg (88%) as colorless oil, R_f 0.50 (petroleum ether—MeOBu^t). HR MS (ESI), *m/z*: found 245.1174, calculated for $C_{15}H_{16}O_3$, $[M + H]^+$ 245.1172; found 267.0994, calculated for $[M + Na]^+$ 267.0992. IR (neat), ν/cm^{-1}: 700, 743, 840, 871, 956, 1031, 1067, 1091, 1109, 1143, 1165, 1209, 1239, 1278, 1306, 1332, 1392, 1454, 1467, 1496, 1727, 2873, 2940, 2972, 3031, 3063, 3087. ^{1}H NMR (200.13 MHz), δ: 1.13—1.38 (m, 1 H, α-HC(7)); 1.83—2.04 (m, 1 H, β-HC(7)); 2.04—2.29 (m, 2 H, H_2C(6)); 2.98—3.24 (m, 1 H, HC(7a)); 3.93 (dd, 1 H, α-HC(1), *J* = 10.9 Hz, *J* = 12.6 Hz); 4.42 (m, 1 H, HC(5)); 4.36—4.66 (m, 3 H, β-HC(1), H_2CPh); 6.00 (br.s, 1 H, HC(4)); 7.20—7.51 (m, 5 H, HC_{arom}). ^{13}C NMR (50.03 MHz), δ: 24.3 (C(7)), 31.9 (C(6)), 36.5 (C(7a)), 71.2 (C(1)), 71.7 (C(5)), 114.6 (C(4)), 127.9, 128.6, 137.5 (Ph), 166.1 (C(4a)), 218.5 (C(3)).

(5*S,4a*S**,7a*S**)-5-Hydroxyhexahydrocyclopenta[*c*]pyran-3(1*H*)-one (2).** ***A.*** A suspension of 10% Pd/C (0.33 mg) in EtOH (1 mL) was stirred for 20 min at ambient temperature under hydrogen atmosphere, then a solution of lactone **13** (102 mg, 0.42 mmol) in EtOH (1.5 mL) was added and the stirring was continued for 21 h until complete consumption of the starting compound (TLC monitoring). The catalyst was filtered off, the filtrate was concentrated *in vacuo*, the column chromatography of the residue (SiO_2, gradient elution form petroleum ether—MeOBu^t (1 : 1) to MeOBu^t) afforded lactone **2** in a yield of 52 mg (79%) as colorless oil, R_f 0.52 (MeOBu^t). HR MS (ESI), *m/z*: found 157.0858, calculated for $C_8H_{12}NO_3$, $[M + H]^+$ 157.0859; found 179.0673, calculated for $[M + Na]^+$ 179.0679. IR ($CHCl_3$), ν/cm^{-1}: 828, 948, 980, 1024, 1084, 1160, 1244, 1260, 1336, 1388, 1428, 1452, 1480, 1741, 2876, 2940, 2964, 3012, 3608. ^{1}H NMR (600.13 MHz), δ: 1.44 (m, 1 H, β-HC(7); 1.59 (m, 1 H, β-HC(6)); 1.85 (m, 1 H, α-HC(6)); 2.00 (m, 1 H, α-HC(7)); 2.34 (dddd, 1 H, HC(4a), *J* = 6.2 Hz, *J* = 6.3 Hz, *J* = 11.5 Hz, *J* = 11.8 Hz); 2.40 (dd, 1 H, α-HC(4), *J* = 6.2 Hz, *J* = 15.1 Hz); 2.60 (m, 1 H, HC(7a)); 2.61 (dd, 1 H, β-HC(4), *J* = 6.3 Hz, *J* = 15.1 Hz); 3.83 (dd, 1 H, HC(5), *J* = 5.7 Hz, *J* = 11.5 Hz); 3.98 (dd, 1 H, β-HC(1), *J* = 6.0 Hz, *J* = 11.7 Hz); 4.22 (dd, 1 H, α-HC(1), *J* = 4.8 Hz, *J* = 11.7 Hz). ^{13}C NMR (150.03 MHz), δ: 25.79 (C(7)), 32.25 (C4)), 33.60 (C(6)), 34.91 (C(7a)), 42.61 (C(4a)), 70.03 (C(1)), 78.83 (C(5)), 173.47 (C(3)).

B. To a stirred solution of lactone **14** (see Ref. 3d, 0.39 g, 1.44 mmol) in THF (15 mL), $Bu_4NF \cdot 3H_2O$ (0.6 g, 1.9 mmol) was added at 20 °C. The reaction mixture was stirred for 30 min, diluted with EtOAc, washed with water, brine, and the solvent was removed *in vacuo*. Column chromatography of the residue (SiO_2, gradient elution from petroleum ether—MeOBu^t, 1 : 1, to MeOBu^t) afforded lactone **2** in a yield of 200 mg (89%), which is nearly identical to the sample described above.

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