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STEREOCHEMICAL ASPECTS OF THE BECKMAN REARRANGEMENT OF OXIMES OF LEVOGLUCOSENONE AND ITS DIHYDRO DERIVATIVE. ENANTIOSELECTIVE SYNTHESIS OF (+)-γ-PELARGONOLACTONE

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Regiospecific C^5-halogenation with retention of configuration occurred upon Beckman fragmentation of levoglucosenone oxime using $SOCl_2$ or PBr_3. On the other hand, the oxime of its dihydro derivative gave under these conditions the C^6- substitution product. A stereoselective synthetic scheme for (+)-γ-pelargonolactone, an attractant for the rice and corn weevils Sitophiltus zeamais, *was developed from the fragmentation product of levoglucosenone oxime.*

Key words: levoglucosenone, second-order Beckman rearrangement, ketoximes, nitriles, nucleophilic substitution.

The great synthetic potential of levoglucosenone as a platform compound has been demonstrated repeatedly in the synthesis of complicated natural compounds [1]. The preparation of linear chiral chains using traditional methods is problematic for carbohydrate chemistry in the case of levoglucosenone. A promising approach to the synthesis of polyfunctional acyclic chiral moiety from levoglucosenone is Beckman fragmentation of levoglucosenone oxime, which is known to form nitriles in the case of α-aminoketoximes, their ethers, α-aldoximes, α-halo-, -hydroxy-, -oxo-, and -carboxyketoximes [2].

We studied the fragmentation of levoglucosenone oxime **1** and its dihydro derivative **2** and devised a synthesis of (+)-γ-pelargonolactone **15**, an attractant of rice and corn weevils *Sitophiltus zeamais*, in order to prove the configuration of the asymmetric center in the fragmentation product of **1**.

The oxime of **1** was prepared using $NH_2OH \cdot HCl$ in pyridine as a mixture of the *syn*- and *anti*-isomers **3a** and **b** in a 3:2 ratio. It should be noted that our attempts to carry out this reaction in MeONa—MeOH, KOH—EtOH, Et_3N, K_2CO_3—MeOH, and EtOH—Py formed the known aldol-cleavage products [2]. Pure oximes **3a** and **b** give rather quickly an equilibrium mixture of the same ratio upon storage.

Second-order Beckman rearrangement was performed using $SOCl_2$ and PBr_3 in CCl_4. Both the pure isomers and their mixture were reacted. This had no effect on the yields of nitriles **4** and **5**. Subsequent acid hydrolysis of **4** formed the functionally saturated chiral moiety **6** (Scheme 1).

The effect of the double bond on the rearrangement mechanism was evaluated by hydrogenating **1** over Pd/C (5%) to afford **2**. Formation of the oxime of **2** gave pure crystalline **8**. The structure of oxime **8** was established using ^{13}C NMR of the starting ketones and their oximes. Like oxime **3a**, C-3 of oxime **8** experiences a stronger coupling with the hydroxyl, shifting from 30.57 ppm in the starting dihydrolevoglucosenone to 27.41 ppm in the oxime.

The rearrangement occurs with predominant formation of nitrile **9a** upon reaction of oxime **8** with $SOCl_2$ (Scheme 1).

The C atoms bound to Cl in chloroformates **4** and **9** resonate in the ^{13}C NMR spectra taken in JMOD mode at 53.21 and 44.38 ppm, respectively, with a negative amplitude in the first instance (CH group); positive, in the second (CH_2 group).

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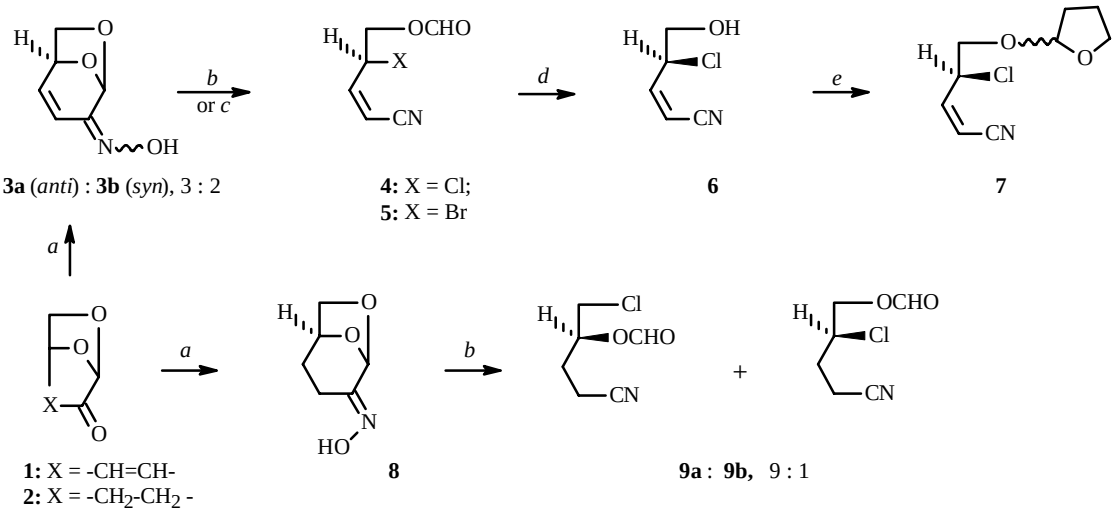
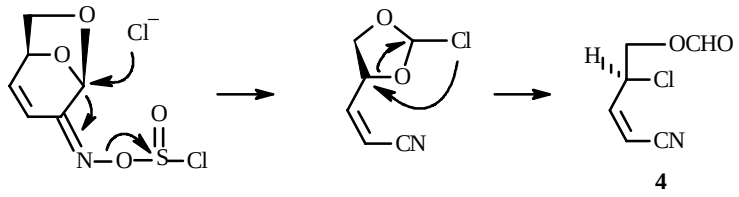


a. $NH_2OH \cdot HCl$, Py; *b*. $SOCl_2$, CCl_4; *c*. PBr_3, CCl_4; *d*. HCl-THF; *e*. DHF, CH_2Cl_2, *p*-TsOH

Scheme 1.

Ring opening is stereospecific in both instances. Protection of the hydroxyl with tetrahydrofuran gives only two diastereomers. The PMR spectrum using $Eu(camph)_3$ shift reagent also unambiguously indicates the presence of one enantiomer.

The proposed fragmentation mechanism consists of the cleavage of the C^1–C^2 bond and S_Ni substitution with retention of configuration at C^5:

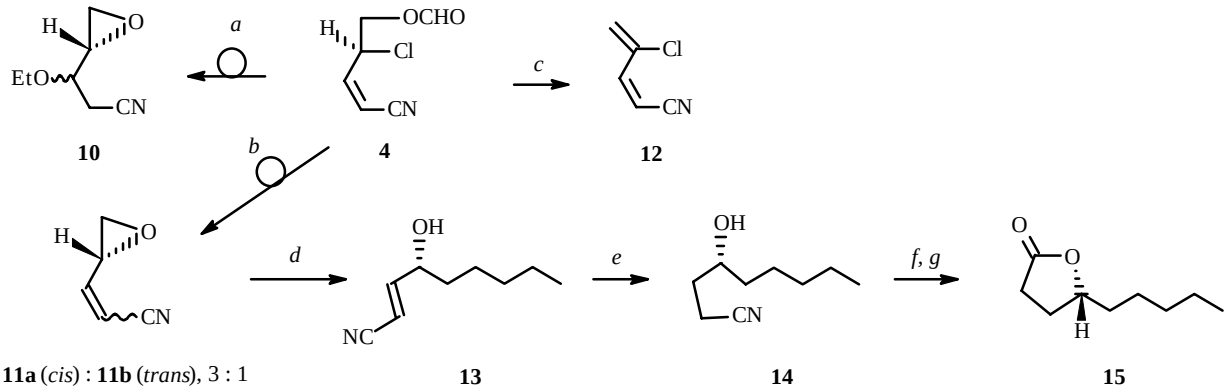


An attempt to prove the configuration of the asymmetric center of **4** by oxidative hydrolysis and cyclization into the known (*S*)-(-)-5-(hydroxymethyl)-2(5H)-furan [3] was unsuccessful. Mixtures of epimeric ethoxyoxiranes **10** formed. Hydrolysis of **4** under phase-transfer-catalysis conditions also gave only a mixture of the *cis*- and *trans*-isomeric epoxides **11a** and -**b** (85%). Storing **4** in pyridine gave diene **12** [4].

The configuration of the asymmetric center in the rearrangement product of the oxime of **4** was proved by synthesizing (+)-4(*R*)-pentyl-γ-lactone **15**, an attractant of the rice and corn weevils *Sitophiltus zeamais* [5].

Known schemes for synthesizing optically active γ-lactones for introducing chiral centers use L-glutamic acid or D-ribose [5]. One of the successful methods for forming the side chain in γ-lactones is based on regioselective opening of an oxirane ring using a cuprate reagent [6]. We used this method in the developed synthesis. Thus, opening of the oxirane ring in **11a** and -**b** by butylcuprate reagent occurs regiospecifically to afford **13**. Hydrogenation of the double bond with subsequent hydrolysis of the cyano group and work up with aqueous HCl (10%) gave the target lactone **15** (72%) with $[\alpha]_D^{20}$ +28.8° (*c* 1.0, MeOH).

The sign of the optical rotation angle of **15** agrees with the literature value {lit. $[\alpha]_D^{20}$ +47.2° (*c* 1.0, MeOH) [5]}. Taking into account the inversion of configuration in preparing the oxirane, the configuration of the C-4 asymmetric center in the fragmentation products of levoglucosenone (**4** and **5**) can be assigned to the *S*-type. This confirms the proposed Beckman fragmentation mechanism. The difference in the absolute value of the optical rotation angle is probably due to partial racemization in the early steps.



a. H_2O_2 - NaOH, EtOH; *b*. 50% KOH, CH_2Cl_2, TEBAC; *c*. Py; *d*. 1 eq. Bu_2CuLi; *e*. H_2-Pd/C; *f*. KOH, *t*-BuOH; *g*. 10% HCl

Scheme 2.

EXPERIMENTAL

IR spectra were recorded on UR-20 and Specord M-80 instruments (as films or in mineral oil). PMR and ^{13}C NMR spectra were recorded on an AM-300 (Bruker) spectrometer at working frequencies 300 and 75.47 MHz, respectively, with TMS internal standard and $CDCl_3$ solvent. Analytical TLC was performed on Sorbfil plates (PTLC-AF-A grade, ZAO "Sorbpolymer," Krasnodar). Optical rotation angles were measured on a Perkin—Elmer-141 instrument. Mass spectra were measured in an MX-1306 instrument (ionization potential 70 eV, ionization-chamber temperature 30-50°C).

Analytical data for all compounds agreed with those calculated.

1,6-Anhydro-β-D-glycerohexopyranos-2-ulose (2) was prepared as before [6]. ^{13}C NMR (δ_C, ppm): 29.33 (C-4), 30.57 (C-3), 66.99 (C-6), 72.68 (C-5), 100.99 (C-1), 200.08 (C-2).

***Syn*- and *anti*-oximes of 1,6-anhydro-3,4-dideoxy-β-D-glycerohex-3-enopyranos-2-ulose (3a and b).** A solution of **1** (1.8 g) in pyridine (20 mL) was stirred and treated with $NH_2OH \cdot HCl$ (2.2 g). After 30 min the reaction mixture was treated with ethylacetate (50 mL), washed with water (2 × 50 mL), dried over Na_2SO_4, filtered, and evaporated. The solid was chromatographed over silica gel. Yield 1.8 g (92%) of *syn*- and *anti*-isomers of oximes (**3a** and **b**) in a 3:2 ratio (PMR). R_f 0.38 (benzene—isopropanol, 9:1). $C_6H_7O_3N$, $[\alpha]_D^{20}$ -54.5° (*c* 1.0, $CHCl_3$). IR spectrum (ν, cm^{-1}): 840, 910, 1000, 1130, 1270, 1300, 1460, 1660, 1720, 1740, 2920, 3100, 3400.

3a. PMR (δ, ppm, J/Hz): 3.85 (2H, m, H-6), 4.87 (1H, dtt, J = 4.8, 1.6, H-5), 5.73 (1H, d, J = 1.6, H-1), 6.60 (1H, dd, J = 10.0, 4.8, H-4), 6.80 (1H, dd, J = 10.0, 1.6, H-3), 8.40-8.60 (1H, m, OH).

^{13}C NMR (δ_C, ppm): 70.22 (C-6), 72.10 (C-5), 100.09 (C-1), 115.57 (C-3), 137.90 (C-4), 150.06 (C-2).

3b. PMR (δ, ppm, J/Hz): 3.85 (1H, d, J = 6.6, H_a-6), 3.89 (1H, dd, J = 6.6, 4.8, H_b-6), 4.90 (1H, dt, J = 4.8, 1.6, H-5), 6.15 (1H, dd, J = 9.8, 1.6, H-3), 6.53 (1H, dd, J = 9.8, 4.8, H-4), 6.60 (1H, d, J = 1.6, H-1), 8.50-8.80 (1H, m, OH).

^{13}C NMR (δ_C, ppm): 69.09 (C-6), 71.35 (C-5), 93.07 (C-1), 122.30 (C-3), 135.70 (C-4), 152.60 (C-2).

4(*S*)-Chloro-5-formyloxypent-2-enonitrile (4). A cooled (0°C) solution of oxime **3** (1.9 g) in CCl_4 (10 mL) was treated dropwise with $SOCl_2$ (1.2 mL) in CCl_4 (10 mL), stirred at 0°C for 1 h, treated with saturated aqueous NaCl solution (20 mL), and extracted with CCl_4 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to afford **4** (1.4 g, 65%), $C_6H_6O_2NCl$. R_f 0.3 (heptane—ethylacetate, 1:1). $[\alpha]_D^{20}$ +116.9° (*c* 1.0, $CHCl_3$). IR spectrum (ν, cm^{-1}): 740, 830, 1160, 1650, 1740, 2220, 2950.

PMR (δ, ppm, J/Hz): 4.41 (1H, dd, J = 5.6, 1.6, H_a-5), 4.45 (1H, dd, J = 11.6, 6.7, H_b-5), 5.0 (1H, ddd, J = 10.2, 6.7, 5.6, H-4), 5.51 (1H, d, J = 10.9, H-2), 6.51 (1H, dd, J = 10.9, 10.2, H-3), 8.10 (s, 1H, –OCHO).

^{13}C NMR (δ_C, ppm): 53.21 (C-4), 64.47 (C-5), 103.27 (C-2), 113.98 (CN), 147.56 (C-3), 159.76 (–OCHO).

4(*S*)-Bromo-5-formyloxypent-2-enonitrile (5). A cooled (0°C) solution of oxime **3** (1.0 g) in CCl_4 (10 mL) was treated dropwise with PBr_3 (1.2 g) in CCl_4 (10 mL), stirred at 0°C for 2 h, treated with saturated aqueous NaCl solution

(20 mL), and extracted with CCl_4 (3 × 20 mL). The combined organic layers were dried over MgSO and evaporated to afford **5** (1.1 g, 70%), $C_6H_6O_2NBr$. IR spectrum (ν, cm^{-1}): 680, 830, 1150, 1650, 1740, 2210, 2960.

PMR (δ, ppm, J/Hz): 4.42 (1H, dd, J = 11.6, 7.6, H_a-5), 4.48 (1H, dd, J = 11.6, 5.5, H_b-5), 5.0 (1H, ddd, J = 10.6, 7.6, 5.5, H-4), 5.47 (1H, d, J = 10.9, H-2), 5.5 (1H, dd, J = 10.9, 10.6, H-3), 8.03 (1H, s, –OCHO).

^{13}C NMR (δ_C, ppm): 42.18 (C-4), 64.65 (C-5), 102.54 (C-2), 114.02 (CN), 148.09 (C-3), 159.70 (–OCHO).

4(*S*)-Chloro-5-hydroxypent-2-enonitrile (6). A solution of **4** (0.5 g) in THF was treated with aqueous HCl (5 mL, 5%) and stirred at room temperature for 1 h. The reaction mixture was neutralized by $NaHCO_3$ solution and extracted with ethylacetate (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, evaporated, and chromatographed over SiO_2 to afford **6** (0.3 g, 73.5%), C_5H_6ONCl. R_f 0.5 (benzene—isopropanol, 9:1). $[\alpha]_D^{20}$ +23.3° (*c* 1.0, $CHCl_3$). IR spectrum (ν, cm^{-1}): 740, 790, 830, 1060, 1100, 1645, 1740, 2250, 2900, 2970, 3090, 3450.

PMR (δ, ppm, J/Hz): 3.58 (1H, br.s, OH), 3.72 (1H, dd, J = 11.9, 5.6, H_a-5), 3.80 (1H, dd, J = 11.9, 5.5, H_b-5), 4.75 (1H, ddd, J = 11.0, 5.6, 5.5, H-4), 5.50 (1H, d, J = 10.8, H-2), 6.48 (1H, dd, J = 11.0, 10.8, H-3).

^{13}C NMR (δ_C, ppm): 57.69 (C-4), 65.15 (C-5), 102.25 (C-2), 114.45 (C-1), 149.34 (C-3). Mass spectrum (EI, *m/z*, I_{rel}, %): $[M]^+$ not observed, 103, 101 (25) $[M - CH_2OH]^+$, 52 (37) $[CH_2{=}CH{-}CN]^+$, 39 (65) $[C_3H_3]^+$, 31 (100) $[CH_2{=}OH]^+$.

4(*S*)-Chloro-5-tetrahydrofuranyloxypent-2-enonitrile (7a and b). A cooled (0°C) solution of **6** (0.127 g) in CH_2Cl_2 (5 mL) was treated with DHF (0.22 mL) and stirred at room temperature for 3 h with catalytic amounts of *p*-TsOH. After the starting material disappeared (TLC monitoring), the mixture was washed with water, dried over $MgSO_4$, and concentrated. Column chromatography isolated a diastereomeric mixture (55:45) of **7a** and **b** (0.108 g), $C_9H_{12}O_2NCl$, R_f 0.64 (hexane—ethylacetate, 3:1) in 56% yield.

PMR (δ, ppm, J/Hz): **7a**, 1.62-1.88 (4H, m, H_2-2′, H_2-3′), 3.50-3.81 (4H, m, H_2-5, H_2-4′), 4.75 (1H, m, H-4), 5.03 (1H, m, H-1′), 5.43 (1H, d, J = 10.5, H-2), 6.38 (1H, dd, J = 10.5, 3.6, H-3). **7b**, 1.62-1.88 (4H, m, H_2-2′, H_2-3′), 3.50-3.81 (4H, m, H_2-5, H_2-4′), 4.75 (1H, m, H-4), 5.03 (1H, m, H-1′), 5.42 (1H, d, J = 10.6, H-2), 6.34 (1H, dd, J = 10.5, 3.6, H-3).

^{13}C NMR (δ, ppm): **7a**, 22.48 (C-3′), 31.8 (C-2′), 54.6 (C-4), 68.61 (C-4′), 67.05 (C-5), 101.8 (C-2), 104.31 (C-1′), 114.18 (C-1), 149.36 (C-3). **7b**, 22.94 (C-3′), 31.95 (C-2′), 54.68 (C-4), 66.83 (C-4′), 69.49 (C-5), 101.94 (C-2′), 103.42 (C-1′), 114.18 (C-1), 149.51 (C-3).

1,6-Anhydro-β-D-glycerohexopyranos-2-ulose oxime (8). A solution of **2** (3.9 g) in Py (50 mL) was stirred and treated with $NH_2OH{\cdot}HCl$ (4.9 g) (TLC monitoring). After 30 min the reaction mixture was diluted with ethylacetate (130 mL), washed with water (2 × 130), dried over $MgSO_4$, and evaporated. The solid was chromatographed over silica gel to afford **8** (2.51 g, 57.7%), $C_6H_9O_3N$, R_f 0.3 (heptane—ethylacetate, 4:1), $[\alpha]_D^{20}$ -100.5° (*c* 1.0, $CHCl_3$).

PMR (δ, ppm, J/Hz): 1.75 (1H, ddd, J = 13.8, 8.0, 0.8, H^{eq}-4), 2.05 (1H, dddd, J = 13.8, 11.4, 7.2, 3.5, H^{ax}-4), 2.25 (1H, ddd, J = 16.8, 11.4, 3.4, H^{ax}-3), 3.05 (1H, ddd, J = 16.8, 7.2, 1.0, H^{eq}-3), 3.87 (1H, dd, J = 7.1, 5.3, H-6), 3.93 (1H, d, J = 7.1, H-6), 4.67 (1H, br.s, H-5), 5.51 (1H, s, H-1), 8.85 (1H, s, OH).

^{13}C NMR (δ_C, ppm): 15.86 (C-4), 27.41 (C-3), 67.15 (C-6), 73.16 (C-5), 100.08 (C-1), 153.95 (C-2).

5(*S*)-Chloro-4-formyloxypentonitrile (9a and b). A cooled (0°C) solution of the oxime (2.3 g) in CCl_4 (12 mL) was treated dropwise with $SOCl_2$ (1.45 mL) in CCl_4 (12 mL), stirred at 0°C for 1 h (TLC monitoring), treated with saturated aqueous NaCl solution (25 mL), and extracted with CCl_4 (3 × 25 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to afford **9a** and **b** (1.7 g, 65.4%), $C_6H_8O_2NCl$, R_f 0.3 (heptane—ethylacetate, 5:1), $[\alpha]_D^{20}$ -28.2° (*c* 1.0, $CHCl_3$).

PMR (δ, ppm, J/Hz): **9a**, 2.0 (2H, dt, J = 7.3, 6.4, 2H-3), 2.36 (2H, t, J = 7.3, 2H-2), 3.53 (1H, dd, J = 11.9, 4.7, H_a-6), 3.60 (1H, dd, J = 11.9, 5.0, H_b-6), 5.12 (1H, ddt, J = 6.4, 5.0, 4.7, H-5), 8.05 (1H, s, –OCHO). **9b**, 2.15 (2H, m, 2H-3), 2.6 (2H, m, 2H-2), 4.1 (1H, m, H-4), 4.28 (2H, m, 2H-5), 8.03 (1H, s, –OCHO).

^{13}C NMR (δ_C, ppm): **9a**, 12.94 (C-2), 26.79 (C-3), 44.38 (C-5), 70.32 (C-4), 118.50 (CN), 159.95 (–OCHO). **9b**, 14.01 (C-2), 29.73 (C-3), 56.51 (C-4), 59.86 (C-5), 118.50 (CN), 159.95 (–OCHO).

(1′*R*)-Oxiranyl-3-ethoxypropanonitrile (10). A solution of **6** (0.5 g, 3.8 mmol) in ethanol (7 mL) was treated with KOH solution (6.8 mL, 30%) and slowly dropwise with H_2O_2 (1.9 mL, 30%), heated to 80°C, and held at that temperature until the reaction was complete (TLC monitoring). The temperature was lowered to 55°C. The solution was treated slowly with finely ground KOH until the foaming stopped. The solution was acidified with HCl (6%) until the pH was 3 and extracted with ethylacetate (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and evaporated. The solid was chromatographed over SiO_2 using hexane—ethylacetate (1:1) to afford **10** (0.42 g, 78%), $C_7H_{11}O_2N$.

^{13}C NMR (δ, ppm): 14.94, 15.00 (CH_3), 20.89, 21.41 (C-1), 43.22, 45.87 (C-2′), 51.74, 52.98 (C-3), 65.88, 65.96 (CH_2O), 74.47, 75.48 (C-2), 116.79, 116.90 (CN).

(1′*R*)-3-Oxiranylprop-2(*Z*,*E*)-enonitriles (11a and b). A cooled (0°C) solution of **6** (1.2 g, 9.16 mmol) in CH_2Cl_2 (10 mL) was vigorously stirred with catalyatic amounts of TEBAC, treated slowly dropwise with KOH solution (3 mL, 10.1 mmol, 50%) (TLC monitoring), diluted with water (10 mL), and extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried over Na_2SO_4, and evaporated. Column chromatography over SiO_2 (hexane—ethylacetate, 1:1) afforded (R_f = 0.3) **11a** and **-b** (0.671 g, 85%, 3:1 ratio), C_5H_5ON.

PMR (δ, ppm, J/Hz): *Syn*-isomer **11a**, 2.80 (1H, dd, J = 5.4, 2.3, H_a-2′), 3.10 (1H, dd, J = 5.4, 4.3, H_b-2′), 3.82 (1H, ddd, J = 8.9, 4.3, 2.4, H-3), 5.60 (1H, d, J = 11.4, H-1), 6.08 (1H, dd, J = 11.4, 8.9, H-2).

^{13}C NMR (δ, ppm): 48.24 (C-2′), 49.51 (C-3), 103.21 (C-1), 114.96 (CN), 151.13 (C-2). *Anti*-isomer **11b**, 2.70 (1H, dd, J = 5.5, 2.5, H_a-2′), 3.05 (1H, dd, J = 5.5, 4.3, H_b-2′), 3.45 (1H, ddd, J = 6.6, 4.3, 2.5, H-3), 5.70 (1H, d, J = 16.4, H-1), 6.50 (1H, dd, J = 16.4, 6.6, H-2). ^{13}C NMR (δ, ppm): 49.80 (C-2′), 50.21 (C-3), 102.14 (C-1), 114.96 (CN), 151.04 (C-2).

(*Z*)-3-Chloro-1-cyanobuta-1,3-diene (12). A solution of **4** (0.1 g) in pyridine (2 mL) was held at 20°C for 24 h, treated with water (5 mL), and extracted with ethylacetate (3 × 3 mL). The organic layers were combined, washed with aqueous HCl (10%), dried over $MgSO_4$, and evaporated. The solid was chromatographed over SiO_2 to afford **12** (0.034 g, 86%). Spectral data corresponded with those published previously [4].

4(*R*)-Hydroxynon-2-(*E*)-enonitrile (13). A suspension of CuI (0.480 g, 2.3 mmol) in absolute Et_2O was stirred vigorously at -40°C, treated slowly dropwise with BuLi (1.74 mL, 4.58 mmol, 2.63 N), stirred at the same temperature for 30 min, cooled to -80°C, treated with a solution of **11** (0.200 g, 2.10 mmol) in ether (3 mL), and held at -80°C for 1 h. The temperature was slowly raised to 0°C. The mixture was hydrolyzed with NH_4Cl solution. The organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 25 mL). The organic layers were combined and dried over $MgSO_4$. Column chromatography over SiO_2 (hexane—ethylacetate, 2:1) afforded **13** (0.079 g, 66%), $C_9H_{15}ON$, $[\alpha]_D^{20}$ -21.4 (*c* 1.0, $CHCl_3$).

PMR (δ, ppm, J/Hz): 0.90 (3H, t, J = 6.7, H-9), 1.23-1.40 (6H, m, 2H-6,7,8), 1.54 (1H, quint., J = 6.7, H_a-5), 1.545 (1H, quint., J = 6.7, H_b-5), 1.8 (1H, br.s, OH), 4.29 (1H, ddt, J = 6.7, 4.3, 2.0, H-4), 5.67 (1H, dd, J = 16.1, 2.0, H-2), 6.76 (1H, dd, J = 16.1, 4.2, H-3).

^{13}C NMR (δ, ppm): 13.88 (CH_3), 22.41 (C-8), 24.69 (C-6), 31.48 (C-7), 36.27 (C-5), 70.87 (C-4), 98.48 (C-2), 117.37 (CN), 156.92 (C-3).

4(*R*)-Hydroxynononitrile (14). A solution of **13** (0.350 g, 2.3 mmol) in ethylacetate was treated with Pd/C (0.035 g, 5%) and stirred under a H_2 atomsphere (TLC monitoring). After 36 h the reaction mixture was filtered and evaporated. The solid was chromatographed over SiO_2 (hexane—ethylacetate, 3:1) to afford **14** (0.339 g, 97%), $C_9H_{17}ON$, $[\alpha]_D^{20}$ -18.3 (*c* 1.0, $CHCl_3$).

PMR (δ, ppm, J/Hz): 0.82 (3H, t, J = 6.3, H-9), 1.12-1.35 (4H, m, H_2-7, H_2-8), 1.38 (2H, m, H_2-6), 1.60 (2H, m, H_2-5), 1.6 (1H, m, OH), 1.61 (1H, quint., J = 6.7, H_a-5), 1.63 (1H, quint., J = 6.7, H_b-5), 1.75 (1H, ddt, J = 7.9, 7.6, 3.4, H_a-3), 1.80 (1H, ddt, J = 7.9, 7.6, 3.4, H_b-3), 2.44 (1H, t, J = 7.6, H_a-2), 2.45 (1H, t, J = 7.6, H_b-2), 3.65 (1H, ttt, J = 6.7, 3.4, H-4).

^{13}C NMR (δ, ppm): 13.68 (C-2), 13.98 (CH_3), 22.52 (C-8), 25.12 (C-6), 31.62 (C-7), 32.46 (C-3), 37.42 (C-5), 70.0 (C-4), 119.95 (CN).

4(*R*)-Pentyl-γ-lactone (15). A solution of **14** (0.30 g, 1.93 mmol) dissolved in *t*-BuOH (3 mL) was treated with finely ground KOH (0.38 g, 6.7 mmol), refluxed until the starting material disappeared (TLC monitoring), cooled to 0°C, diluted with saturated NaCl solution (10 mL), stirred, treated with HCl (12 N) until the pH reached 5, and extracted with $CHCl_3$ (3 × 5 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated. The solid was chromatographed over SiO_2 to afford **15**, (0.134 g, 72%), $C_9H_{16}O_2$, $[\alpha]_D^{20}$ +28.8° (*c* 1.0, MeOH).

PMR (δ, ppm, J/Hz): 0.9 (3H, t, J = 6.5, 3H-5′), 1.35 (4H, m, 2H-4′ and 2H-3′), 1.45 (2H, m, 2H-2′), 1.6 (1H, tdd, J = 9.8, 7.4, 5.4, H_a-1′), 1.72 (1H, tdd, J = 9.8, 7.4, 5.4, H_b-1′), 1.85 (1H, tdd, J = 12.5, 9.6, 8.9, H_a-3), 2.35 (1H, ddd, J = 12.5, 6.7, 6.4, H_b-3), 2.55 (2H, dd, J = 9.6, 6.7, 2H-2), 4.5 (1H, dddd, J = 8.9, 7.4, 6.4, 5.2, H-4).

^{13}C NMR (δ, ppm): 13.96 (C-5′), 22.50 (C-4′), 24.91 (C-2′), 28.02 (C-3), 28.89 (C-2), 31.51 (C-3′), 35.55 (C-1′), 81.18 (C-4), 177.4 (C-1).

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