PRILEZHAEV DIHYDROXYLATION OF (*R*)-OCTADEC-9*Z*-EN-7-0L

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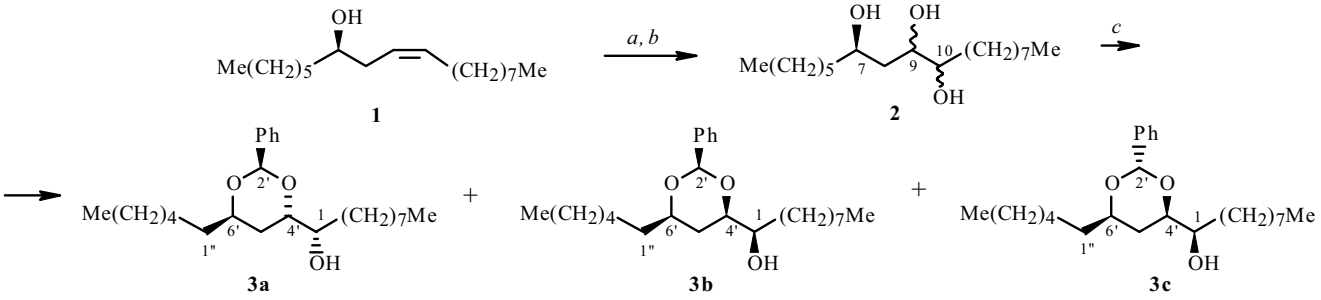
*Formation of new asymmetric centers with primarily the (*S*)-configuration was induced by the optically active center of (*R*)-octadec-9Z-en-7-ol upon Prilezhaev dihydroxylation. This was proved by cyclization of a 1,3-glycol system (de 26%) into the corresponding 1,3-dioxane stereoisomers.*

Key words: (*R*)-octadec-9*Z*-en-7-ol, Prilezhaev dihydroxylation, asymmetric induction.

We have previously shown that the hydroxyl at the optically active center of (*R*)-ricinoleic acid had a slight influence on the regioselectivity during hydroboration and oxidation of its derivatives [1]. This was indicated by the predominance by 6–10% of the 1,3-diol over its 1,4-isomer. However, the hydroxyl did induce formation of new asymmetric centers of primarily the (*S*)-configuration. This was demonstrated by cyclization of 1,3-glycols (up to 32–50%) into the corresponding stereoisomeric 1,3-dioxanes; 1,4-diols (up to 22–40%), into 2,5-dialkyl-substituted tetrahydrofurans.

Our goal was to study Prilezhaev dihydroxylation (asymmetric induction due to the influence of the homoallyl hydroxyl) of (*R*)-octadec-9*Z*-en-7-ol (**1**), which is available from castor oil [2].



a. H_2O_2, HCOOH; *b*. NaOH, H_2O; *c*. PhCHO, $ZnCl_2$, Na_2SO_4

Prilezhaev oxidation of non-terminal olefins is known to occur exclusively with formation of *cis*-epoxides [3]. This was demonstrated earlier using ricinoleic acid methyl ester as an example [4]. Further opening of the epoxide ring occurs under both acidic and basic conditions [5] with complete inversion of only one of the C atoms to form *trans*-diols.

Prilezhaev dihydroxylation of homoallyl alochol **1** was performed using H_2O_2 (30%) in the presence of formic acid with subsequent treatment by NaOH solution [3].

The configuration of the newly formed asymmetric centers on C-9 and C-10 of the product triol **2** was determined by cyclization using benzaldehyde of the 1,3-diol system into stereoisomeric 2,4,6-tri-substituted 1,3-dioxanes **3**. The cyclization to form a benzylidene group is known to occur quantitatively without inversion of the optically active center [6–8]. Alkyl-substituted 1,3-dioxanes in neutral media have a stable chair conformation with an equatorially oriented phenyl group in both stereoisomers [7]. Triol **2** produced a mixture of dialkylphenyl-substituted 1,3-dioxanes **3** that was separated by chromatography into three diastereoisomers **3a**, **3b**, and **3c** in high (>90%) purity. They were identified by NMR spectroscopy. The ^{13}C NMR spectrum of the reaction mixture from benzylation contained a set of resonances corresponding to three of the four possible diastereomers with the (*R*)-configuration at the dioxane C-6′ atom. The contents of the diastereomers were dominated by one of them (63.0, 23.5, and 13.5% according to quantitative ^{13}C NMR spectroscopy).

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Overlap of methylene proton resonances at 1.50–1.80 ppm and unresolved multiplets and overlap of resonances of the three protons on C-4′, C-6′, and C-1 in addition to the α-methylenes of substituents and C-5′ protons made it practically impossible to analyze and assign the stereochemistry of resonances in PMR spectra of **3a-c**. Nevertheless, analysis of COSY (C–H) and COSY (H–H) one- and two-dimensional spectra enabled resonances of C atoms and the C-6′, C-4′, and C-1 protons to be assigned, the mutual orientation of the substituents on C-6′ and C-4′ of the ring to be established, and the configuration of C-4′ of **3a-c** to be determined for the known (*R*)-configuration at C-6′.

NMR resonances of stereoisomers were assigned using literature data [9, 10] for stereoisomeric 2,4,6-trialkyl-1,3-dioxanes and proton spectra of 2-ethynyl-1,3-dioxane conformers.

Of three doublets in the range 67.0–83.0 ppm, the one at weakest field in ^{13}C spectra of **3a-c** was assigned to C-4′ of the ring. The proton resonance on this C atom in spectra of **3a-c** was a resolved doublet of doublets of doublets and was determined from COSY (C–H) and COSY (H–H) correlation spectra. The proton–proton SSCC were determined using double resonance of three protons in the range 3.5–4.0 ppm. Similar chemical shifts of C-6′ and C-1′′ α-methylene protons and the large ^3J SSCC (H_a-6′–H_a-5′) (12.3 Hz) indicated that the alkyl substituent on C-6′ had the equatorial orientation.

The ^3J SSCC (H_a-4′–H_a-5′) (11.7 Hz) and the weak-field shift of the resonance for C-1 (72.51 ppm) in the PMR spectrum for the dominant diastereomer **3a** compared with those for **3b** and **3c** (67.66 and 67.70, respectively) indicated that the substituent on C-4′ also had the equatorial orientation. Asymmetric C-4′ had the (*S*)-configuration for the diequatorial orientation of the substituents and the known (*R*)-configuration of asymmetric C-6′ in the *cis*,*cis*-(*eee*)-diastereomer. Resonances for C-1 in ^{13}C spectra of **3b** and **3c** were located at stronger field. This indicated that the substituent on C-4′ had the axial orientation. The vicinal SSCC (^3J = 5.7, 4.2, and 3.1 Hz) also were consistent with the equatorial orientation of proton H-4′ and, therefore, the axial orientation of the C-4′ substituent. Chiral C-4′ in *trans*-(*ea*)-(C-6′,C-4′) diastereomers **3b** and **3c** had the (*R*)-configuration because of the known (*R*)-configuration of optically active C-6′.

The similar chemical shifts for the heterocyclic C atoms in ^{13}C NMR spectra of **3b** and **3c** with a small strong-field shift for C-4′ of **3c** (81.43 ppm) compared with **3b** (82.61 ppm) and a noticeable weak-field shift of the C-2′ proton (5.84 ppm) in the spectrum of **3c** indicated that the Ph group was oriented axially and, therefore, asymmetric center C-2′ of **3c** had the (*S*)-configuration. Similar chemical shifts for the C-2′ protons of **3a** and **3b** (5.51 and 5.54, respectively), which appeared at stronger field compared with **3c**, indicated that the Ph group was oriented equatorially and, therefore, that asymmetric center C-2′ had the (*R*)-configuration.

Considering the (*S*)-configuration of C-4′ in the dominant diastereomer **3a** that was determined from spectra of the 1,3-dioxanes, it can be concluded that the dominant diastereomer triol **2a** had the (7*R*,9*S*,10*S*)-configuration.

EXPERIMENTAL

IR spectra were recorded as thin layers using a Specord M-82 instrument; NMR spectra, in $(CD_3)_2C{=}O$ solution on a Bruker AM-300 spectrometer (operating frequency 300.13 MHz for ^1H and 75.47 MHz for ^{13}C) with TMS internal standard. Resonances were assigned using two-dimensional COSY (C–H) and (H–H) correlation spectroscopy. The quantitative ratio of diastereomers was determined from NMR spectra recorded with a delay of 10 sec between pulses. HPLC was carried out on a Du Pont (USA) liquid chromatograph with a refractive-index detector, stainless steel column (300 × 3.9), μ-Porasil (Waters, 5 μm), and mobile phase hexane:isopropanol (92:8) at room temperature. TLC monitoring used Sorbfil (Russia) SiO_2.

Octadecan-7(*R*),9,10-triol (2). A cooled mixture that was prepared by adding H_2O_2 (30%, 1.1 mL, 10.5 mmol) to HCOOH (88%, 4.5 mL, 102.8 mmol) was treated over 30 min with **1** (2.00 g, 7.5 mmol) at a rate such that the temperature remained below 40°C. The resulting mixture was held at 40°C for 1 h and 20°C for 12 h. HCOOH was distilled at reduced pressure. The remainder was diluted with an ice-cold NaOH solution (0.60 g, 15.0 mmol) in H_2O (1.1 mL) at a rate such that the temperature remained below 45°C. The organic layer was separated. The aqueous layer was extracted with methyl-*t*-butylether (MTBE, 3 × 50 mL), dried over Na_2SO_4, and evaporated to afford **2** (2.14 g, 95%). IR spectrum (ν, cm^{-1}): 1110 (C–O), 3304 (OH).

PMR spectrum (δ, ppm): 0.90 (6H, m, H-1, H-18), 1.20–1.38 (20H, m, H-2–H-5, H-12–H-17), 1.40–1.68 (6H, m, H-6, H-8, H-11), 3.30–3.45 (1H, m, H-10), 3.60–3.73 (1H, m, H-9), 3.72–3.85 (1H, m, H-7), 3.80 (3H, br.s, OH).

^{13}C NMR spectrum: 14.28 (q, C-1, C-18), 23.07 (t, C-2, C-17), 25.19 (t, C-12), 25.46 (t, C-5), 29.07-29.61 (all t, C-4, C-13–C-15), 32.33 (t, C-3, C-16), 33.89 (33.74) (t, C-11), 38.66 (38.05) (t, C-6), 39.98 (39.71) (t, C-8), 72.62 (69.39), (d, C-7), 75.16 (72.24) (d, C-9), 75.49 (74.95) (d, C-10).

1-(6*R*-Hexyl-2-phenyl-1,3-dioxan-4-yl)nonan-1-ols (3a-c). A mixture of octadecan-7*R*,9,10-triol (**2**, 1.50 g, 5.0 mmol), freshly distilled benzaldehyde (1.5 mL, 15.0 mmol), anhydrous $ZnCl_2$ (0.45 g, 3.3 mmol), and anhdyrous Na_2SO_4 (0.45 g, 3.0 mmol) was stirred under Ar at room temperature until the reaction was finished (TLC monitoring), diluted with aqueous Na_2CO_3 solution (7.3 mL), and stirred for 10 min. The precipitate of $Zn(OH)_2$ was filtered off and washed with Et_2O. The aqueous layer was extracted with Et_2O (3 × 50 mL). The combined extracts were washed with H_2O, dried over $MgSO_4$, and evaporated to afford a mixture (1.63 g, 86%) of two stereoisomers in a 63:37 ratio that were separated by column chromatography (SiO_2, PE:EtOAc, 20:1).

1-(6*R*-Hexyl-2*R*-phenyl-1,3-dioxan-4*S*-yl)nonan-1*S*-ol (3a). $[\alpha]_D^{20}$ +1.6° (*c* 3.5, CH_2Cl_2).

PMR spectrum (δ, ppm, J/Hz): 0.83 (6H, t, CH_3), 1.20–1.41 (22H, m, H-3–H-8, H-1″–H-5″), 1.43-1.60 (3H, m, H-2, H_a-5′), 1.64 (1H, dt, ^{2}J = 12.1, ^{3}J = 2.4, H_e-5′), 2.80 (1H, br.s, OH), 3.51–3.62 (1H, m, H-1), 3.73 (1H, ddd, J = 6.9, 2.4, 11.7, H_a-4′), 3.78–3.86 (1H, m, H-6′), 5.51 (s, H_a-2′), Ph: 7.30–7.43 (3H, m), 7.51 (2H, d, J = 7.1).

^{13}C NMR spectrum: 13.15 (q, C-9, C-6″), 22.05 (t, C-8, C-5″), 24.55 (t, C-2″), 25.19 (t, C-3), 28.04-29.38 (all t, C-4–C-6, C-3″), 31.37 (t, C-7, C-4″), 31.77 (t, C-2), 35.62 (t, C-1″), 38.63 (t, C-5′), 72.51 (d, C-1), 75.93 (d, C-6′), 79.52 (d, C-4′), 99.91 (d, C-2′), Ph: 125.85, 127.32, 127.76 (all d), 139.21 (s).

1-(6*R*-Hexyl-2*R*-phenyl-1,3-dioxan-4*R*-yl)nonan-1*R*-ol (3b). $[\alpha]_D^{20}$ –15.5° (*c* 5.5, MTBE).

PMR spectrum (δ, ppm, J/Hz): 0.91 (6H, t, CH_3), 1.19–1.50 (16H, m, H-3–H-7, H-2″–H-4″), 1.40–1.51 (4H, m, H-8, H-5″), 1.52–1.61 (4H, m, H-2, H-1″), 1.60–1.81 (2H, m, H-5′), 3.10 (1H, br.s, OH), 3.55–3.85 (2H, m, H-1, H-6′), 4.01 (1H, ddd, ^{3}J = 5.7, 4.2, 3.2, H_e-4′), 5.54 (s, H_a-2′), Ph: 7.35–7.42 (3H, m), 7.52 (2H, d, J = 7.9).

^{13}C NMR spectrum: 13.35 (q, C-9, C-6″), 22.30 (t, C-8, C-5″), 25.32 (t, C-2″), 25.83 (t, C-3), 28.06-29.60 (all t, C-4–C-6, C-3″), 31.61 (t, C-7, C-4″), 32.38 (t, C-2), 38.28 (t, C-1″), 40.73 (t, C-5′), 78.39 (d, C-6′), 67.66 (d, C-1), 82.61 (d, C-4′), 102.16 (d, C-2′), Ph: 126.14, 127.87, 128.66 (all d), 139.25 (s).

1-(6*R*-Hexyl-2*S*-phenyl-1,3-dioxan-4*R*-yl)nonan-1*R*-ol (3c). $[\alpha]_D^{20}$ –4.0° (*c* 1.5, MTBE).

PMR spectrum (δ, ppm, J/Hz): 0.88 (6H, t, CH_3), 1.21–1.48 (16H, m, H-3–H-7, H-2″–H-4″), 1.40–1.51 (4H, m, H-8, H-5″), 1.52–1.61 (4H, m, H-2, H-1″), 1.63–1.80 (m, 2H, H-5′), 2.90 (1H, br.s, OH), 3.54–3.85 (2H, m, H-1, H-6′), 4.05 (1H, ddd, ^{3}J = 5.8, 4.3, 3.2, H_e-4′), 5.84 (s, H_e-2′), Ph: 7.30–7.39 (3H, m), 7.45 (2H, d, J = 7.8).

^{13}C NMR spectrum: 13.37 (q, C-9, C-6″), 22.30 (t, C-8, C-5″), 25.31 (t, C-2″), 25.85 (t, C-3), 28.57-29.61 (all t, C-4–C-6, C-3″), 31.61 (t, C-7, C-4″), 32.38 (t, C-2), 38.24 (t, C-1″), 40.67 (t, C-5′), 67.70 (d, C-1), 79.81 (d, C-6′), 81.43 (d, C-4′), 102.25 (d, C-2′), Ph: 126.60, 127.91, 128.89 (all d), 139.12 (s).

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