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Hydroboration–Oxidation of Ricinoleic Acid Derivatives

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Abstract—The regioselectivity in the hydroboration–oxidation of ricinoleic acid derivatives only slightly depends on the configuration of the optically active center: the fraction of the resulting 1,3-diol is larger by 6–10% than that of the 1,4-isomer. The new asymmetric center has preferentially *S* configuration, as follows from the formation of the corresponding stereoisomeric 1,3-dioxane from the 1,3-diol and of 2,5-dialkyltetrahydrofuran from the 1,4-diol.

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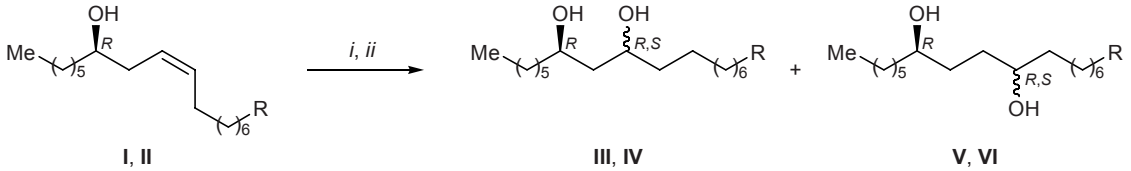
Hydroboration of double bond and subsequent oxidation of organoboranes thus formed with hydrogen peroxide, which occurs with retention of the initial configuration, provides a convenient method for preparative hydration of various olefins, including natural unsaturated compounds. It is known [1] that internal olefins readily undergo hydroboration to trialkylboranes in such a way that the boron atom adds at both carbon atoms at the double bond with equal probabilities.

In the present work we examined hydroboration–oxidation of unsaturated compounds **I** and **II** isolable from castor oil [2]; specifically, we were interested in the regio- and stereoselectivity of the process and asymmetric induction with participation of the optically active center, which are determined by the presence of a hydroxy group in the homoallylic position. As hydroborating agent we used a solution of diborane in tetrahydrofuran [3]. Hydroboration of the olefinic bond in compounds **I** and **II**, followed by oxidation of organoboron intermediates with an alkaline solution of hydrogen peroxide, gave the corresponding regio- and diastereoisomeric 1,3- and 1,4-diols **III**/**IV** and **V**/**VI** (Scheme 1). According to the HPLC data, the fractions of regioisomers **III** and **V** obtained by hydroboration–oxidation of enol **I** were 55 and 45%, respectively. Compound **V**, (7*R*,10*RS*)-octadecane-7,10-diol, was a mixture of diastereoisomers at a ratio of 7 : 3 (^{1}H NMR data). The structure of 1,4-diol **V** and configuration of the newly formed asymmetric center (C^{10}) was determined by its quantitative cyclization to the corresponding *cis*- and *trans*-2,5-dialkyltetrahydrofurans **VII** on heating in boiling benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid [4]. This reaction followed intramolecular S_N2 mechanism [5] with inversion of configuration of only one asymmetric center in the initial 1,4-diol (Scheme 2).

In the ^{13}C NMR spectra of stereoisomeric tetrahydrofurans **VII**, signals from C^2 and C^5, as well as from two α-methylene groups on C^2 and C^5 in the *trans*

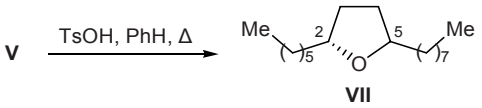
Scheme 1.



I, **II** **III**, **IV** **V**, **VI**

III, **V**, R = Me; **IV**, **VI**, R = CH_2OH; *i*: $NaBH_4$, $BF_3 \cdot Et_2O$, THF; *ii*: H_2O_2, NaOH.

Scheme 2.



stereoisomer are displaced downfield relative to the corresponding signals of the *cis* isomer. The observed differences in the chemical shifts of *cis* and *trans* isomers are typical of 1,3-dialkylcyclopentane derivatives [6], 2,5-disubstituted tetrahydrofurans [7], and some analogous derivatives of silacyclopentane and sulfolanes [8] and are widely used for stereochemical assignments.

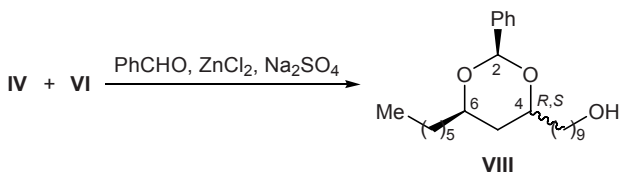
In keeping with the ^{13}C NMR data, the ratio of stereoisomeric tetrahydrofurans **VII** coincides with that found for initial diol **V**, and the *trans* (*dl*) stereoisomer prevails (7:3). While assigning the configuration of the newly formed asymmetric center we proceeded from the following considerations. If the (7*R*)-center in the (7*R*,10*S*)- and (7*R*,10*R*)-diastereoisomers of **V** is inverted, the resulting stereoisomeric tetrahydrofurans would have (2*S*,5*S*)-*trans* and (2*S*,5*R*)-*cis* configurations, respectively. Inversion of the new C^{10} center would give rise to (2*R*,5*R*)-*trans* and (2*R*,5*S*)-*cis* isomers. It is seen that spectrally indistinguishable (2*S*,5*S*)- and (2*R*,5*R*)-*trans*-enantiomer couple should be formed from (7*R*,10*S*)-diol **V** and that the (2*S*,5*R*)/(2*R*,5*S*)-*cis*-**VII** couple should originate from (7*R*,10*R*)-**V**. Taking into account that the asymmetric center in initial compound **I** has *R* configuration, inversion of any asymmetric center in diol **V** should lead to a stereoisomer having *S* configuration of the new asymmetric carbon atom. Thus the hydroboration–oxidation product obtained from compound **I** contains 70% of *meso*-diol and 30% of *dl*-diol. Likewise, the hydroboration–oxidation of unsaturated diol **II** gives a mixture of 53% of (10*RS*,12*R*)-octadecane-1,10,12-triol (**IV**) and 47% of (9*RS*,12*R*)-octadecane-1,9,12-triol (**VI**) (HPLC data).

Selective protection of 1,3-diol **IV** by treatment with benzaldehyde [9] led to the formation of *cis*,*cis*- and *trans*,*trans*-stereoisomers of 4,6-dialkyl-2-phenyl-1,3-dioxane **VIII** (Scheme 3). By benzylidenation of a mixture of *cis*-hydration products of compound **II** we succeeded in separating 1,3- and 1,4-diols by chromatography and identifying them. It is known that cyclization to 1,3-dioxane **VIII** upon benzylidene protection is not accompanied by inversion of the asymmetric center [9, 10] and that alkyl-substituted 1,3-dioxanes in neutral medium exist as stable *chair* conformers where internal rotation of the heteroring is hindered [11]. The chemical shift of the 2-H proton in both stereoisomers (δ 5.56 ppm) indicates conformational stability and equatorial orientation of the phenyl substituent in both stereoisomers [12]. In the ^{13}C NMR spectrum of dioxane **VIII** we observed two sets of signals corresponding to a couple of diastereoisomers, the major component being that with more downfield chemical shifts of C^2 (d, δ_C 100.57 ppm), C^4, and C^6 (d, δ_C 77.10 ppm) [equatorial orientation of both alkyl substituents, *cis*,*cis* or *eee* isomer]. If the C^{12} atom in triol **IV** has *R* configuration, the asymmetric C^4 center in the *cis*(*ee*)-C^4,C^6-stereoisomer should have *S* configuration. More upfield signals [δ_C, ppm: 99.1 d (C^2), 71.34 d (C^4), 77.92 d (C^6)] belong to the *trans*(*ea*)-C^4,C^6-stereoisomer in which the axial alkyl substituent interacts with the 2-H atom. In this case, axial orientation of the substituent on C^4 corresponds to *R* configuration. The fractions of the *cis*,*cis* (*eee*) and *trans*,*trans* (*eae*) stereoisomers are 75 and 25%, respectively, i.e., (10*S*,12*R*)-triol **IV** is the major isomer.

According to the HPLC data, 1,3-diol **III** is a mixture of diastereoisomers at a ratio of 66:34, while the diastereoisomer ratio of triol **VI** is 61:39. Comparison of the NMR spectra of 1,3- and 1,4-diols **III** and **V** with those of compounds **IV** and **VI** with a terminal hydroxy group indicates that in all cases the major diastereoisomers are those having *S* configuration of the newly formed asymmetric center.

Thus our results show that the hydroxy group at the asymmetric carbon atom only slightly affects the regioselectivity in the hydroboration–oxidation of ricinoleic acid derivatives but gives rise to asymmetric induction at each carbon atom at the double bond.

Scheme 3.



EXPERIMENTAL

The IR spectra were recorded from samples prepared as thin films on a Specord M-82 spectrometer. The ^1H and ^{13}C NMR spectra were measured on a Bruker AMX-300 instrument at 300.13 MHz for ^1H and 75.47 MHz for ^{13}C using tetramethylsilane as

internal reference; signals were assigned with the aid of two-dimensional correlation techniques (H–H and C–H COSY). The diastereoisomer ratios were determined from the NMR spectra recorded with a 10-s pulse delay. HPLC analysis was performed on a Du Pont liquid chromatograph (USA) equipped with a refractometric detector and a 300×3.9-mm stainless steel column; stationary phase μ-Porasil (Waters, grain size 5 μm), eluent hexane–isopropyl alcohol (92:8), room temperature. Sorbfil silica gel (Russia) was used for thin-layer chromatography. Column chromatography was performed on silica gel (Lancaster, UK, 70–230 μm). The elemental analyses of the isolated compounds were consistent with the calculated values.

Hydroboration–oxidation of (7*R*,9*Z*)-octadec-9-en-7-ol (I). A solution of 0.8 ml of $BF_3 \cdot Et_2O$ in 16 ml of anhydrous tetrahydrofuran was added dropwise to a suspension of 2.0 g (7.5 mmol) of unsaturated alcohol **I** and 0.18 g (4.4 mmol) of $NaBH_4$ in 43 ml of anhydrous tetrahydrofuran (argon, 20°C). The mixture was stirred for 3.5 h, 1.5 ml of water was added, the mixture was stirred for 10 min, 1.6 ml of a 3 N solution of NaOH and 1.6 ml of 30% hydrogen peroxide were added, and the mixture was stirred for 16 h. The mixture was then diluted with 200 ml of methyl *tert*-butyl ether, the organic phase was separated, washed with a saturated solution of sodium chloride, dried over Na_2SO_4, and evaporated, and the residue, 2.09 g (98%), was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent to isolate 1.15 g of (7*R*,9*RS*)-octadecane-7,9-diol (**III**, R_f 0.11) and 0.94 g of (7*R*,10*RS*)-octadecane-7,10-diol (**V**, R_f 0.10).

(7*R*,9*RS*)-Octadecane-7,9-diol (III). IR spectrum, ν, cm^{-1}: 1110 (C–O), 3340 (OH). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 0.80 m (6H, CH_3), 1.20–1.30 m (18H, CH_2), 1.35–1.45 m (4H, 5-H, 12-H), 1.50–1.65 m (2H, 8-H), 1.70 t (4H, 6-H, 10-H, ^3J = 7.0), 2.90 br.s (2H, OH), 3.90 m and 4.00 m (1H each, 7-H, 9-H). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 13.35 q (C^1, C^{18}), 22.33 t (C^2, C^{17}), 25.30 t (C^5, C^{12}), 29.09 t and 29.35 t (C^4, C^{11}, C^{13}, C^{14}, C^{15}), 31.63 t (C^3, C^{16}), 35.74 t (C^6, C^{10}), 38.65 t (C^8), 68.84 d and 68.49 d (C^7, C^9).

(7*R*,10*RS*)-Octadecane-7,10-diol (V). IR spectrum, ν, cm^{-1}: 1110 (C–O), 3340 (OH). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 0.80 m (6H, CH_3), 1.20 m (18H, CH_2), 1.35 m (4H, 5-H, 12-H), 1.50 t and 1.55 t (2H each, 6-H, 11-H, ^3J = 7.0), 3.50 br.s and 3.65 br.s (1H, 7-H, 10-H). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 13.35 q (C^1, C^{18}), 22.33 t (C^2, C^{17}), 24.62 t and 24.76 t (C^5, C^{12}), 29.09 t and 29.35 t (C^4, C^{13}, C^{14}, C^{15}), 31.63 t (C^3, C^{16}), 36.54 t and 36.40 t (C^8, C^9), 37.29 t (C^6, C^{11}), 71.83 d (C^7, C^{10}).

2-Hexyl-5-octyltetrahydrofuran (VII). A mixture of 0.15 g (0.6 mmol) of diol **V** and 0.01 g of *p*-toluenesulfonic in 5 ml of benzene was heated for 18 h under reflux in a flask equipped with a Dean–Stark trap. The solvent was distilled off, 30 ml of methyl *t*-butyl ether was added to the residue, and the solution was washed with water, dried over Na_2SO_4, and evaporated. Yield 0.13 g (96%). IR spectrum: ν 1070 cm^{-1} (C–O). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 0.80 m (6H, CH_3), 1.20 m (16H, CH_2), 2.85 m (4H, 3-H, 4-H, *trans*), 2.80 m (4H, 3-H, 4-H, *cis*), 3.85 m (2H, 2-H, 5-H, *trans*), 3.80 m (2H, 2-H, 5-H, *cis*). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 13.40 q ($C^{6'}$, $C^{8''}$), 22.35 t ($C^{5'}$, $C^{7''}$), 26.06 t ($C^{2'}$, $C^{2''}$), 29.23–29.56 t (other C aroms), 31.91 t (C^3, C^4, *trans*), 30.84 t (C^3, C^4, *cis*), 31.66 t ($C^{4'}$, $C^{6''}$), 36.06 t ($C^{1'}$, $C^{1''}$, *trans*), 35.97 t ($C^{1'}$, $C^{1''}$, *cis*), 78.95 d (C^2, C^5, *trans*), 78.68 d (C^2, C^5, *cis*).

Hydroboration–oxidation of (9*Z*,12*R*)-octadec-9-ene-1,12-diol (II). As described above for the hydroboration–oxidation of compound **I**, from 2.0 g (7.0 mmol) of diol **II** we obtained 2.1 g (99%) of a mixture of (10*RS*,12*R*)-octadecane-1,10,12-triol (**IV**) and (9*RS*,12*R*)-octadecane-1,9,12-triol (**VI**) at a ratio of 53:47 (according to the HPLC data), which was subjected to subsequent cyclization without additional purification.

Cyclization of triol IV. A mixture of 1.5 g (5 mmol) of isomeric triols **IV** and **VI** (53:47), 1.5 ml (15 mmol) of freshly distilled benzaldehyde, 0.45 g (3.3 mmol) of anhydrous $ZnCl_2$, and 0.45 g (3.0 mmol) of anhydrous Na_2SO_4 was stirred for 12 h at room temperature under argon. The mixture was then treated with 7.3 ml of a 10% aqueous solution of Na_2SO_3 and stirred for 10 min, the precipitate of $Zn(OH)_2$ was filtered off and washed first with water and then with diethyl ether, the aqueous phase was extracted with diethyl ether (3×20 ml), and the extracts were combined, washed with water, dried over Na_2SO_4, and evaporated. The residue, 1.55 g, was subjected to chromatography on silica gel using petroleum ether–methyl *tert*-butyl ether (10:1) as eluent to isolate 0.90 g of 1,3-dioxane **VIII** (R_f 0.50), 0.10 g of triol **IV** (R_f 0.11), and 0.55 g of triol **VI** (R_f 0.10).

9-[(6*R*)-Hexyl-2-phenyl-1,3-dioxan-4-yl)nonan-1-ol (VIII). IR spectrum, ν, cm^{-1}: 1040, 1125, 1155 (O–C–O); 1643 (C=C_{arom}); 3410 (OH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.80 (3H, CH_3, ^3J = 7.0), 1.20 m (16H, CH_2), 1.30–1.70 m (11H, 5-H, 6-H, 8-H, 10-H, 11-H, OH), 3.65 t (2H, 1-H, ^3J = 6.6), 3.95 m (4H, 7-H, 9-H), 5.56 s (1H, PhCH), 7.30–7.60 m (5H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.15 q ($C^{6'}$); 22.68 t ($C^{5'}$); 25.14 t (C^8); 26.27 t ($C^{2'}$); 25.80 t (C^3); 29.12 t ($C^{3'}$); 29.46–29.61 t (C^4–C^7); 31.90 t ($C^{4'}$); 32.86 t (C^2); 36.09 t (C^9, $C^{1'}$, *cis*,*cis*); 34.68 t and 37.17 t (C^9, $C^{1'}$, *trans*,*trans*); 36.70 t ($C^{5''}$, *cis*,*cis*); 34.35 t ($C^{5''}$, *trans*,*trans*); 63.07 t (C^1); 77.10 d ($C^{4''}$, $C^{6''}$, *cis*,*cis*); 71.34 d and 77.92 d ($C^{4''}$, $C^{6''}$, *trans*,*trans*); 100.57 d ($C^{2''}$, *cis*,*cis*); 99.11 d ($C^{2''}$, *trans*,*trans*); 126.17, 126.72, 128.17, 139.24 (C_{arom}).

(10*RS*,12*R*)-Octadecane-1,10,12-triol (IV). IR spectrum, ν, cm^{-1}: 1050, 1110 (C–O); 3340 (OH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.90 t (3H, CH_3, ^3J = 7.0), 1.20–1.45 m (20H, CH_2), 1.45–1.65 m (8H, 2-H, 9-H, 11-H, 13-H), 2.25 br.s (3H, OH), 3.65 t (2H, 1-H, ^3J = 6.5), 3.95 m (2H, 10-H, 12-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.16 q (C^{18}), 22.66 t (C^{17}), 25.62 t (C^8), 25.83 t (C^3, C^{14}), 29.39 t (C^7), 29.44 t (C^{15}), 29.55 t (C^5, C^6), 29.65 t (C^4), 31.90 t (C^2), 32.65 t (C^{16}), 37.57 t (C^9), 37.61 t (C^{13}), 42.40 t (C^{11}), 63.13 t (C^1), 69.56 d and 69.53 d (C^{10}, C^{12}).

(9*RS*,12*R*)-Octadecane-1,9,12-triol (VI). IR spectrum, ν, cm^{-1}: 1050, 1110 (C–O); 3340 (OH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.90 t (3H, CH_3, ^3J = 7.2), 1.20–1.45 m (18H, CH_2), 1.46 m (2H, 2-H), 1.45–1.70 m (8H, 8-H, 10-H, 11-H, 13-H), 2.25 br.s (3H, OH), 3.40 m (2H, 9-H, 12-H), 3.64 t (2H, 1-H, ^3J = 6.6). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.14 q (C^{18}), 22.68 t (C^{17}), 25.76 t (C^7, C^{14}), 29.42 t (C^6, C^{15}), 29.62 t (C^3–C^6), 31.90 t (C^2), 32.84 t (C^{16}), 33.35 t (C^{10}), 34.08 t (C^{11}), 37.62 t and 37.57 t (C^{13}), 37.87 t and 37.82 t (C^8), 63.07 t (C^1), 72.38 d and 72.02 d (C^9, C^{12}).

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