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SHORT COMMUNICATIONS

Stereospecific Reduction of 6-Oxo Group and Hydogenolysis of 14 -Hydroxy Group in 20-Hydroxyecdysone 20,22-Acetonide at Treating with Sodium in Liquid Ammonia

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Reaction of α,β-unsaturated ketones with alkali metals solutions in liquid ammonia is widely applied to selective reduction of a conjugated double bond [1, 2]. We found unexpectedly that in reaction of 20-hydroxyecdysone 20,22-acetonide (**I**) with sodium in liquid ammonia instead of reduction of the Δ^7-bond occurred a stereospecific reduction of the 6-oxo group and hydrogenolysis of 14α-hydroxy group accompanied by the shift of the Δ^7-bond in the direction of the departing group and by epimerization at the C^5 atom. As a result (20R,22R)-2β,3β,6α,25-tetrahydroxy-20,22-isopropylidenedioxy-5α-cholest-8(14)-ene (**II**) was obtained.

The conversion of ketone **I** into alcohol **II** is unambiguously demonstrated by the observed displacement in the ^{13}C NMR spectrum of C^6 atom signal from δ 203.3 ppm [3] to δ 66.4 ppm and its transformation from a singlet into a doublet. Unique signals of C^6 atom in the ^{13}C NMR spectrum and of H^6 proton (δ 4.16 ppm) in the ^1H NMR spectrum testify to the unique configuration of the new asymmetric center. The formed alcohol **II** is 6α-epimer as shows the position of H^6 proton signal at δ 4.16 ppm and that of C^6 atom at δ 66.4 ppm in the ^1H and ^{13}C NMR spectra whereas in the 6β-epimer alcohols the H^6 signal appears in a stronger field (δ 3.6–3.8 ppm), and that of C^6, downfield (δ 70.0–70.5 ppm) [4, 5].

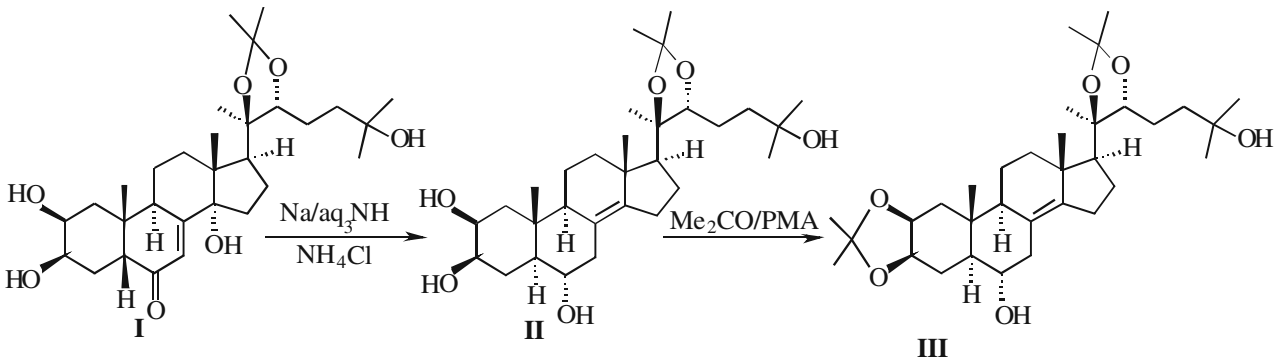
The formation of tetra-substituted $\Delta^{8,14}$-bond is confirmed by singlets of sp^2-atoms C^8 and C^{14} in the ^{13}C NMR spectrum at δ 125.3 and 142.4 ppm respectively. The structure of compound **II** was also proved by a high-resolution mass spectrum.

By treatment with acetone in the presence of phosphomolybdic acid monoacetonide **II** was converted into diacetonide **III** whose ^1H and ^{13}C NMR spectra are similar (except for the chemical shifts of atoms H^6 and C^6) to the spectra of previously described 6β-epimer [5].

Thus in reaction of 20-hydroxyecdysone 20,22-acetonide with sodium solution in liquid ammonia occurred a conversion previously never observed in steroid series of a γ-hydroxy-α,β-conjugated ketone into a β,γ-unsaturated alcohol.

(20R,22R)-2β,3β,6α,25-Tetrahydroxy-20,22-isopropylidenedioxy-5α-choles-8(14)-ene (II). To a solution of 0.13 g (5.7 mmol) of Na in 10 ml of ammonia

Scheme.



distilled over Na at –33°C while stirring was added a solution of 1.0 g (1.9 mmol) of compound **I** in 5 ml of anhydrous THF, the mixture was maintained for 25 min at this temperature, then 1.0 g of NH_4Cl was added, and the reaction mixture was left standing at room temperature till complete evaporation of ammonia. The crude product was extracted with ethyl acetate (3×100 ml), the extract was evaporated, and the solid residue was subjected to column chromatography (40 g of SiO_2, eluent $CHCl_3$–MeOH, 20:1), yield 0.69 g (72%), mp135–137°C, R_f 0.32 ($CHCl_3$–MeOH, 7:1), $[\alpha]_D^{23}$ +43.7° (*C* 1.83, CH_3OH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 s (3H, H_3C^{19}), 1.13 s (3H, H_3C^{18}), 1.27 s (3H, H_3C^{21}), 1.39 s (6H, H_3C^{26}, H_3C^{27}), 1.41 s and 1.50 s (6H, $M\varepsilon_2C$),1.55–2.80 m (21H, CH, CH_2), 4.00 m (1H, HC^{22}, $w_{1/2}$ 15.0 Hz), 4.16 m (1H, HC^6, $w_{1/2}$ 25.0 Hz), 4.39 m (1H, HC^2, $w_{1/2}$ 25.0 Hz), 4.55 m (1H, HC^3, $w_{1/2}$ 6.0 Hz). ^{13}C NMR spectrum (C_5D_5N), δ, ppm: 19.2 q (C^{18}), 19.4 t (C^{11}), 21.7 q (C^{21}), 22.3 t (C^{23}), 23.7 t (C^{16}), 24.1 q (C^{19}), 24.9 t (C^4), 25.9 t (C^7), 26.4 q and 28.9 q ($\underline{M\varepsilon_2}C$), 28.7 q and 29.6 q ($C^{26}$, C^{27}), 34.0 t (C^{15}), 35.5 d (C^9), 37.1 t (C^{12}), 38.3 t (C^1), 38.4 s (C^{10}), 41.4 t (C^{24}), 42.6 d (C^5), 42.9 s (C^{13}), 55.3 d (C^{17}), 66.4 d (C^6), 67.5 d (C^3), 68.7 s (C^{25}), 69.1 d (C^2), 81.6 d (C^{22}), 83.7 s (C^{20}), 106.2 s ($Me_2\underline{C}$), 125.3 s (C^8), 142.4 s (C^{14}). High resolution mass spectrum: *m*/*z* 506.35940 $[M]^+$. $C_{30}H_{50}O_6$. Calculated *M* 506.36071. Mass spectrum, *m*/*z* (I_{rel}, %): 506 (3.5), 488 (2.9), 430 (9.0), 413 (4.1), 397 (5.5), 349 (4.7), 331 (35.3), 300 (2.2), 287 (8.6), 263 (7.2), 201 (18.7), 183 (6.3), 159 (7.5), 145 (10.1), 143 (70.5), 125 (58.5), 119 (11.1), 117 (11.6), 109 (11.9), 107 (16.6), 102 (84.8), 97 (11.3), 93 (17.3), 85 (14.1), 81 (24.4), 69 (24.0), 59 (100), 43 (76.4).

(20R,22R)-6α,25-Dihydroxy-2β,3β:20,22-bis(isopropylidenedioxy)-5α-cholest-8(14)-ene (III). A dispersion of 0.2 g (0.4 mmol) of monoacetonide **II** and 4 mg of phosphomolybdic acid in 40 ml of aetone was stirred at room temperature till the reaction mixture became homogeneous (~10 min), then the solution was evaporated to the volume of ~5 ml, and 15 ml of 0.2% solution of $NaHCO_3$ was added. The reaction product was extracted with ethyl acetate (3×60 ml), the extract was evaporated, and the solid residue was subjected to column chromatography (20 g of SiO_2, eluent $CHCl_3$–MeOH, 20:1). Yield 0.19 g (86%), mp 86°C, R_f 0.3 ($CHCl_3$–MeOH, 9:1), $[\alpha]_D^{20}$ –2.0° (*C* 0.57, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.82 s (3H, H_3C^{18}), 0.96 s (3H, H_3C^{19}), 1.17 s (3H, H_3C^{21}), 1.22 s (6H, H_3C^{26}, H_3C^{27}), 1.31 s, 1.35 s, 1.42 s and 1.51 s (12H, Me_2C), 1.60–2.50 m (21H, CH, CH_2), 3.79 m (1H, HC^{22}, $w_{1/2}$ 7.0 Hz), 4.11 m (2H, HC^2, HC^6, $w_{1/2}$ 11.0 Hz), 4.37 m (1H, HC^3, $w_{1/2}$ 6.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 19.5 t (C^{11}), 19.7 t (C^4), 19.7 q (C^{18}), 21.5 q (C^{21}), 21.9 t (C^{16}), 22.5 t (C^{23}), 23.9 q (C^{19}), 24.2 t (C^{15}), 26.4 q, 26.7 q, 28.6 q and 29.0 q ($\underline{Me_2}C$), 29.1 q (C^{27}), 29.6 q (C^{26}), 32.8 t (C^7), 35.8 (C^9), 37.3 t (C^{12}), 37.3 s (C^{10}), 38.2 t (C^1), 41.4 t (C^{24}), 43.1 d (C^5), 43.5 s (C^{13}), 55.7 d (C^{17}), 67.6 d (C^6), 70.3 s (C^{25}), 72.8 d (C^3), 72.3 d (C^2), 81.7 d (C^{22}), 84.1 s (C^{20}), 106.9 s (2,3-$Me_2\underline{C}$), 107.5 s (20,22-$Me_2\underline{C}$), 123.7 d (C^8), 144.3 s (C^{14}).

^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-300 (operating frequencies 300.13 and 75.46 MHz respectively), internal reference TMS. Carbon signals were assigned using ^{13}C NMR spectra recorded in the mode of J-modulation. Mass spectra were measured on Finnigan MAT 8200E instrument (electron impact, 70 eV). The melting points were estimated on a heating block of Boëtius type. The specific rotation was measured on a polarimeter Perkin-Elmer 141. TLC was performed on Silufol plates, development with ethanolic vanillin solution acidified with sulfuric acid.

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REFERENCES

1. Caine, D., *Organic Reactions. Reduction and Related Reactions of α,β-Unsaturated Carbonil Compounds with Metals in Liquid Ammonia*, Dauben, W.G. Ed., New York: Wiley, 1976, vol. 23, p. 1.
2. Dryden, H.L. Jr., *Organic Reactions in Steroid Chemistry Reduction of Steroids By Metal-Ammonia Soltions*, Fried, J., and Edwards, J.A., Eds., New York: Van Nostrand Reinhold, 1972, vol. 1, p. 27.
3. Odinokov, V.N., Galyautdinov, I.V., Nedopekin, D.V., and Khalilov, L.M., *Izv. Akad. Nauk, Ser.Khim.,* 2003, 220.
4. Odinokov, V.N., Savchenko, R.G., Shafikov, R.V., Afon'kina, S.R., Khalilov, L.M., Kachala, V.V., and Shashkov, A.S., *Zh. Org. Khim.,* 2005, vol. 41, p. 1323.
5. Shafikov, R.V., Afon'kina, S.R., Savchenko, R.G., Galyautdinov, I.V., and Odinokov, V.N., *Zh. Org. Khim.,* 2007, vol. 43, p. 310.