ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 9, pp. 1392–1394. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © V.N. Odinokov, R.V. Shafikov, R.G. Savchenko, S.R. Afon'kina, A.S. Shashkov, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 9, pp. 1409–1411.

SHORT COMMUNICATIONS

Regio- and Stereoselectivity of Peracid Oxidation of 20-Hydroxy-2,3 : 20,22-di-*O*-isopropylidene-7,8-dihydroecdysone

V. N. Odinokov[a], R. V. Shafikov[a], R. G. Savchenko[a], S. R. Afon'kina[a], and A. S. Shashkov[b]

[a] *Institute of Petroleum Chemistry and Catalysis, Russian Academy of Sciences, pr. Oktyabrya 14, Ufa, 1450075 Bashkortostan, Russia*
e-mail: ink@anrb.ru

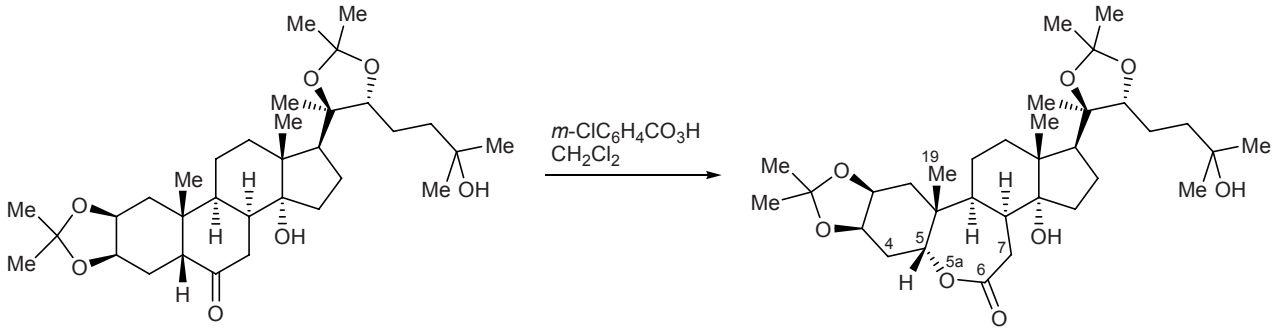
[b] *Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii pr. 47, Moscow, 119991 Russia*

Received January 9, 2008

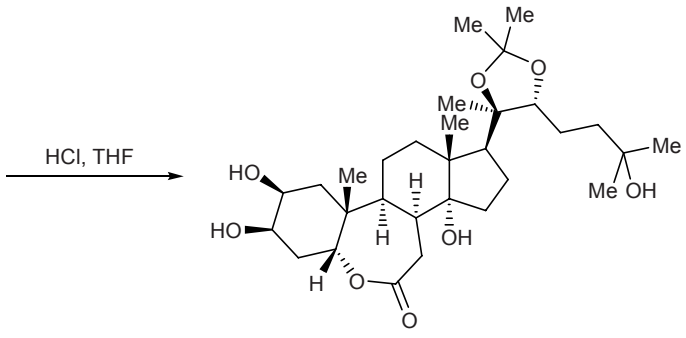
DOI: 10.1134/S107042800809025X

Oxidation of 7,8-dihydro analogs of ecdysteroids with peroxy acids (Baeyer–Villiger reaction) provides a method for the transformation of the steroid **B** ring into seven-membered lactone ring typical of brassinolide (plant growth and development hormone isolated from the *Brassica napus* rape pollen) [1]. The reaction of 7,8-dihydro-20-hydroxyecdysone 2β,3β:20,22-diacetonide (**I**) [2] with *m*-chloroperoxybenzoic acid in methylene chloride gave 20-hydroxy-7,8α-dihydro-5a-oxa-5a-homoecdysone 2β,3β:20,22-diacetonide (**II**) with high regio- and stereoselectivity.

The formation of lactone ring is confirmed by the presence in the ^{13}C NMR spectrum of compound **II** of a signal at δ_C 173.4 ppm which is typical of lactone carbonyl carbon atom (the C^6 signal of initial steroid **I** is located at δ_C 212 ppm [3]). Insofar as the C^5 atom in



I **II**



III

molecule **II** is linked to the lactone oxygen atom, its signal is displaced downfield (δ_C 77.9 ppm) relative to the corresponding signal in the spectrum of **I** (δ_C 50.5 ppm). The downfield region of the ^{1}H NMR spectrum of compound **II** contains a doublet from 5-H at δ 4.78 ppm ($w_{1/2}$ = 5 Hz; $J_{5,4} = J_{5,4'}$ = 3 Hz), indicating equatorial (β) orientation of that proton. This is also confirmed by observation of nuclear Overhauser effect for 5-H and β-C^{19}H$_3$ protons in the ROESY spectrum. The large coupling constant (J = 13 Hz) in the doublet of triplets arising from 8-H suggests its *trans* orientation with respect to the axial 7-H proton; this means that the 8-H proton occupies axial position (α-orientation) in the seven-membered lactone ring. The α-9-H proton occupies equatorial position in the **B** ring and is coupled with 8-H through a constant of 4 Hz. Removal of the acetal protection [4] from compound **II** gave 20,22-acetonide **III**.

Thus the transformation of the **B** ring in compound **I** into seven-membered lactone ring is not accompanied by change of configuration of the chiral centers and is characterized by regioselectivity typical of Baeyer–Villiger reaction.

(20*R*,22*R*)-14α,25-Dihydroxy-2β,3β:20,22-bis(isopropylidenedioxy)-5a-oxa-5a-homo-5β,8α-cholestan-6-one (II). A solution of 0.10 g (0.18 mmol) of compound **I** in 2 ml of methylene chloride was cooled to 0°C, a solution of 0.05 g (0.18 mmol) of *m*-chloroperoxybenzoic acid in 2 ml of methylene chloride was added under stirring, the mixture was stirred for a week at 20°C and cooled to 0°C, an additional portion of *m*-chloroperoxybenzoic acid, 0.05 g (0.18 mmol), in 2 ml of methylene chloride was added, and the mixture was left to stand for two weeks at 20°C. The mixture was then cooled to 0°C, 2 ml of water and 2 ml of a saturated solution of sodium hydrogen carbonate were added in succession, and the mixture was extracted with ethyl acetate (3×10 ml). The extracts were combined and evaporated under reduced pressure, and the residue was subjected to chromatography on 4 g of silica gel using chloroform–methanol (20:1) as eluent. Yield 0.053 g (52%), R_f 0.49 ($CHCl_3$–MeOH, 10:1), mp 153–155°C, $[\alpha]_D^{20}$ = 15.1° (c = 0.9, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1360, 1440 (C–O); 1700 (C=O). ^{1}H NMR spectrum (500.13 MHz, DMSO-d_6), δ, ppm: 0.86 s (3H, C^{18}H$_3$), 1.01 s (3H, C^{21}H$_3$), 1.07 s (3H, C^{27}H$_3$), 1.08 s (3H, C^{26}H$_3$), 1.12 s (3H, C^{19}H$_3$), 1.23 m and 1.90 m (1H each, 15-H), 1.23 s and 1.31 s (3H each, 20,22-Me$_2$C), 1.23 s and 1.39 s (3H each, 2,3-Me$_2$C), 1.34 m and 1.55 m (1H each, 24-H), 1.36 m and 1.40 m (1H each, 23-H), 1.40 m and 2.01 m (1H each, 1-H), 1.44 m and 1.46 m (1H each, 11-H), 1.55 m and 1.72 m (1H each, 12-H), 1.63 s and 2.07 s (1H each, 4-H), 1.70 m and 1.86 m (1H each, 16-H), 2.03 d.t (1H, 8-H, $J_{8,9}$ = 4.0 Hz), 2.14 d.d (1H, 7α-H, $J_{7\alpha,8}$ = 4.0 Hz), 2.15 m (1H, 17-H), 2.17 d.t (1H, 9-H, J = 11.0, 4.0 Hz), 2.98 t (1H, 7β-H, $^2J = {}^3J$ = 13.0 Hz), 3.55 m (1H, 22-H), 4.02 s (1H, 14-OH), 4.11 s (1H, 25-OH), 4.28 m (1H, 3-H), 4.35 m (1H, 2-H), 4.78 br.d (1H, 5-H, $w_{1/2}$ = 5 Hz). ^{13}C NMR spectrum (125.76 MHz, DMSO-d_6), δ_C, ppm: 17.0 (C^{11}), 17.1 (C^{18}), 21.1 (C^{16}), 21.3 (C^{21}), 23.1 (C^{23}), 24.9 and 27.7 (2,3-**Me**$_2$C), 25.1 (C^{19}), 26.7 and 29.0 (20,22-**Me**$_2$C), 29.0 (C^{27}), 29.5 (C^{26}), 30.4 (C^{15}), 32.2 (C^4), 32.2 (C^7), 32.6 (C^1), 33.8 (C^{12}), 36.3 (C^{10}), 39.2 (C^8), 41.0 (C^{24}), 43.6 (C^9), 46.0 (C^{13}), 49.2 (C^{17}), 68.4 (C^{25}), 70.6 (C^3), 72.3 (C^2), 77.9 (C^5), 81.2 (C^{22}), 83.5 (C^{14}), 84.0 (C^{20}), 105.8 (20,22-Me$_2$**C**), 106.6 (2,3-Me$_2$**C**), 173.4 (C^6); ^{13}C NMR spectrum (75.46 MHz, $CDCl_3$, JMOD), δ_C, ppm: 17.3 t (C^{11}), 17.6 q (C^{18}), 21.2 t (C^{16}), 21.4 q (C^{21}), 23.6 t (C^{23}), 24.9 q and 27.8 q (2,3-**Me**$_2$C), 26.7 q (C^{19}), 26.7 q and 29.6 q (20,22-**Me**$_2$C), 29.0 q (C^{26}, C^{27}), 32.1 t (C^{15}), 32.4 t (C^4), 32.7 t (C^7), 33.0 t (C^1), 34.2 t (C^{12}), 37.1 s (C^{10}), 40.1 d (C^8), 41.3 t (C^{24}), 44.2 d (C^9), 46.6 s (C^{13}), 49.8 d (C^{17}), 70.3 s (C^{25}), 71.2 d (C^3), 72.9 d (C^2), 79.2 d (C^5), 81.8 d (C^{22}), 84.3 s (C^{14}), 85.4 s (C^{20}), 106.8 s (20,22-Me$_2$**C**), 107.5 s (2,3-Me$_2$**C**), 173.6 s (C^6).

(20*R*,22*R*)-2β,3β,14α,25-Tetrahydroxy-20,22-isopropylidenedioxy-5α-oxa-5a-homo-5β,8α-cholestan-6-one (III). Compound **II**, 0.053 g (0.09 mmol), was dissolved in 9.6 ml of THF, 4.8 ml of 0.5 N hydrochloric acid was added at ~25°C under argon, and the mixture was stirred for 7 h, diluted with 10 ml of chloroform, and washed with a 5% solution of sodium hydrogen carbonate until neutral reaction. The organic phase was evaporated under reduced pressure, and the residue was subjected to chromatography on 2 g of silica gel using chloroform–methanol (20:1) as eluent. Yield 0.01 g (20%), R_f 0.70 ($CHCl_3$–MeOH, 3:1), mp 121–123°C, $[\alpha]_D^{20}$ = 14.9° (c = 1.0, $CHCl_3$). ^{1}H NMR spectrum (300.13 MHz, $CDCl_3$), δ, ppm: 0.96 s (3H, C^{18}H$_3$), 1.10 s (3H, C^{21}H$_3$), 1.19 s (6H, C^{26}H$_3$, C^{27}H$_3$), 1.29 s (3H, C^{19}H$_3$), 1.37 s and 1.48 s (3H each, Me$_2$C), 1.68–2.76 m (21H, CH, CH$_2$), 3.54 m (1H, 22-H), 3.67 m (1H, 2-H, $w_{1/2}$ = 15 Hz), 4.11 m (3-H, $w_{1/2}$ = 14 Hz), 4.73 m (1H, 5-H). ^{13}C NMR spectrum (75.46 MHz, $CDCl_3$), δ_C, ppm: 18.2 (C^{11}), 19.0 (C^{18}), 22.2 (C^{16}), 22.6 (C^{21}), 24.7 (C^{23}), 26.1 (C^{19}), 27.2 and 29.1 (20,22-**Me**$_2$C), 29.4 (C^{26},

C^{27}), 32.0 (C^{15}), 34.7 (C^{7}), 35.2 (C^{4}), 35.4 (C^{1}), 35.8 (C^{12}), 37.5 (C^{10}), 41.7 (C^{8}), 42.3 (C^{24}), 44.1 (C^{9}), 47.9 (C^{13}), 51.1 (C^{17}), 68.7 (C^{3}), 69.9 (C^{2}), 71.2 (C^{25}), 79.5 (C^{5}), 83.2 (C^{22}), 85.9 (C^{20}), 86.2 (C^{14}), 107.9 (20,22-Me_2**C**), 177.3 (C^{6}).

The IR spectrum was recorded in KBr on a Specord 75IR spectrometer. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AM-300 instrument. Homo- and heteronuclear COSY, TOCSY, ROESY, HSQC, and HBMC experiments for compound **II** were performed on a Bruker DRX-500 spectrometer. The chemical shifts were measured relative to tetramethylsilane (internal reference). The melting points were determined on Boetius melting point apparatus. The specific optical rotations were determined on a Perkin–Elmer 141 polarimeter. Thin-layer chromatography was performed on Silufol plates; spots were visualized by treatment with a solution of vanillin in ethanol acidified with sulfuric acid.

The authors thank Prof. L.M. Khalilov for helpful discussion of the NMR spectra.

This study was performed under financial support by the Academy of Sciences of Bashkortostan.

REFERENCES

1. Akhrem, A.A. and Kovganko, N.V., *Ekdisteroidy: Khimiya i biologicheskaya aktivnost'* (Ecdysteroids: Chemistry and Biological Activity), Minsk: Nauka i Tekhnika, 1989.
2. Odinokov, V.N., Afon'kina, S.R., Shafikov, R.V., Savchenko, R.G., Galyautdinov, I.V., Khalilov, L.M., and Shashkov, A.S., *Russ. J. Org. Chem*., 2007, vol. 43, p. 825.
3. Odinokov, V.N., Galyautdinov, I.V., Nedopekin, D.V., and Khalilov, L.M., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2003, p. 220.
4. Canonica, L., Danieli, B., Lesma, G., and Polmisano, G., *Helv. Chim. Acta*, 1987, vol. 70, p. 701.