Chemistry of Natural Compounds, Vol. 39, No. 2, 2003

SYNTHESIS OF A DITERPENE 1,3,4-OXADIAZOLIN-2′-ONE FROM DIMETHYLCYCLOPENTENONEPIMARATE

E. V. Tret′yakova, O. B. Flekhter, F. Z. Galin, L. V. Spririkhin, and G. A. Tolstikov

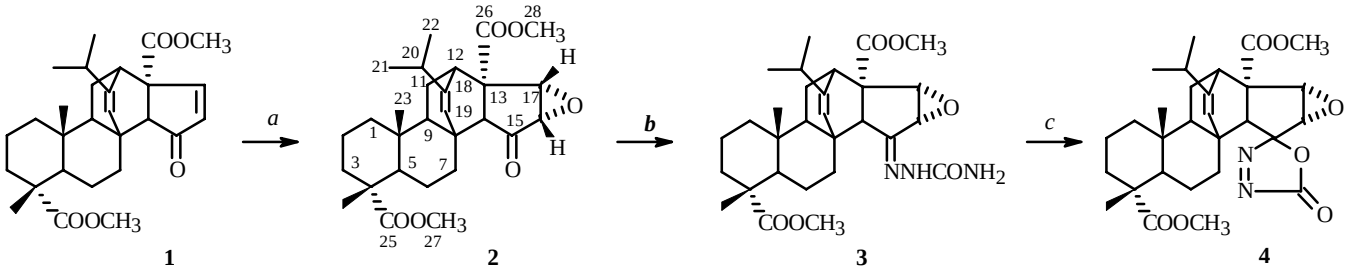
UDC 547.824:542.91:548.737

A diterpene 1,3,4-oxadiazolin-2′-one was synthesized by lead-tetraacetate oxidation of 16,17-epoxydimethylcyclpentenonepimarate. The structures of the synthesized compounds were confirmed by IR and NMR spectroscopies.

Key words: dimethylcyclopentanopimarate, 1,3,4-oxadiazolin-2′-one structure.

Oxadiazolinones typically have biological activity and are used as intermediates in the synthesis of acetylene—carbonyl compounds [1]. The latter property was used to synthesize several acetylenic secosteroids [2, 3], in the stereoselective synthesis of exobrevicomine, the principal sex attractant of the Western pine beetle (*Dendrocotnus brevicomis*) [4], and to prepare the synthon 8-methylprostanoid [5] etc.

We synthesized the diterpene 1,3,4-oxadiazolin-2′-one (**4**). Dimethylcyclopentenonepimarate (**1**), prepared from levopimaric acid [6], was oxidized by H_2O_2 solution (35%) to epoxide **2** in 80% yield. The signal for the double bond in the cyclopentenone disappeared and signals for the C-16 and C-17 epoxides appeared at δ 58.1 and 57.4 ppm in the ^{13}C NMR spectrum. In the PMR spectrum, H-16 resonated at δ 3.20 ppm as a singlet; H-17, at δ 3.65 ppm as a doublet. The through-space coupling constant (J = 1.8 Hz) between H-17 and H-12 is consistent with their mutual W-location. This indicates that H-17 has the endo-position (i.e., β-) and, therefore, the epoxide has the exo-position. The gauche position of H-16 and H-17 is confirmed by the lack of spin—spin coupling between them. The *cis*-fusion of rings D and E and the *syn*-position of rings C and E also indicate that the formation of one α-epoxide should be expected [7].



1 **2** **3** **4**

a: 35% H_2O_2, 60°C, 6M NaOH, MeOH; *b*: $NH_2NHCONH_2$ HCl, EtOH, NaOAc $3H_2O$; *c*: $Pb(OAc)_4$, CH_2Cl_2, 2.4N HCl

Reaction of **2** with semicarbazide hydrochloride in aqueous ethanol produced epoxysemicarbazone **3** in 69% yield after recrystallization from alcohol. The ^{13}C NMR spectrum exhibited a strong-field shift for C-15 to δ 157.9 ppm and a slight change of chemical shift for the epoxy group as a result of the formation of the new C=N bond.

Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, 450054, Ufa, pr. Oktyabrya, 71, fax (3472) 35 60 66, e-mail: obf@anrb.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 154-155, March-April, 2003. Original article submitted February 18, 2003.

 0009-3130/03/3902-0204$25.00

Oxidation of **3** by $Pb(OAc)_4$ in CH_2Cl_2 and subsequent hydrolysis of the intermediate imine produced the new diterpene 1,3,4-oxadiazolinon-2′-one (**4**) in 48% yield after purification by chromatography. The ^{13}C NMR spectrum shows a strong-field shift for C-15 (to δ 132.9 ppm) as a result of the formation of the new –N–C–O-bond. The carbonyl atom of the heterocyclic C=O fragment resonated at δ 152.1 ppm.

EXPERIMENTAL

IR spectra were recorded on Specord M80 and UR-20 spectrometers in mineral oil. ^{13}C NMR and PMR spectra were recorded on a Bruker AM-300 spectrometer (75.5 and 300 MHz, respectively) in $CDCl_3$ with $SiMe_4$ internal standard. Melting points were determined on a Boetius microstage.

TLC was performed on Silufol plates (Chemapol, Czech Rep.) using $CHCl_3$:CH_3OH (20:1). Compounds were developed by phosphotungstic acid in ethanol (10%) with subsequent heating at 100-120°C for 2-3 min. Dimethylcyclopentenonepimarate was prepared as before [6].

Elemental analyses of the compounds agreed with those calculated.

16,17-Epoxydimethylcyclopentenonepimarate (2). A solution of dimethylcyclopentenonepimarate (**1**, 1 mmol, 0.44 g) in CH_3OH (10 mL) was vigorously stirred and treated with aqueous H_2O_2 (0.35 mL, 35%) and then dropwise over 5 min with NaOH solution (0.1 mL, 6 M). The reaction mixture was stirred for 3 h at 60-65°C with a reflux condenser and poured into water (50 mL). The resulting precipitate was filtered off, washed with water, and dried. Yield 0.38 g (80%), mp 132-135°C. IR spectrum (ν, cm^{-1}): 1740, 1670, 1510, 1480, 1390, 1300, 1260, 1205, 1120, 1090, 1060, 1030, 900, 880, 840, 740. PMR spectrum (δ, ppm, J/Hz): 0.52 (3H, s, 23-H), 0.80 (3H, d, J = 6.8, 21-H/22-H), 0.85 (3H, d, J = 6.8, 22-H/21-H), 0.89-0.98 (2H, m, $1H_a$, $11\text{-}H_a$), 1.05 (3H, s, 24-H), 1.17-1.50 (8H, m, $1\text{-}H_e$, $2\text{-}H_{a,e}$, $3\text{-}H_e$, $6\text{-}H_{a,e}$, $7\text{-}H_{a,e}$), 1.51-1.72 (4H, m, $3\text{-}H_a$, $11\text{-}H_e$, 9-H, 5-H), 2.20 (1H, ddd, $^4J_{12,19}$ = 1.6, $^3J_{12/11a}$ = 2.2, $^3J_{12,11e}$ = 13.2, 12-H), 2.35 (1H, sept, J = 6.8, 20-H), 2.85 (1H, br.s, 14-H), 3.20 (1H, s, 16-H), 3.55 (3H, s, 28-H), 3.65 (1H, d, J = 1.8, 17-H), 3.75 (3H, s, 27-H), 5.19 (1H, br.s, 19-H).

^{13}C NMR (δ, ppm): 37.4 (C-1), 16.9 (C-2), 34.3 (C-3), 46.9 (C-4), 51.6 (C-5), 21.7 (C-6), 33.2 (C-7), 41.4 (C-8), 51.8 (C-9), 36.5 (C-10), 25.6 (C-11), 38.4 (C-12), 61.2 (C-13), 52.6 (C-14), 206.1 (C-15), 58.1 (C-16), 57.4 (C-17), 146.6 (C-18), 126.5 (C-19), 25.9 (C-20), 21.0 (C-21), 20.5 (C-22), 16.7 (C-23), 15.4 (C-24), 179.1 (C-25), 173.1 (C-26), 48.9 (C-27), 56.8 (C-28).

16,17-Epoxydimethylcyclopentenonepimarate Semicarbazone (3). A solution of **2** (0.47 g, 1 mmol) in ethanol (10 mL) was treated with aqueous $H_2NNHCONH_2 \cdot HCl$ (10 mL, 1.2 M) and $NaOAc \cdot 3H_2O$ (0.5 g), stirred for 6 h at 40°C with a reflux condenser, and poured into water (100 mL). The resulting precipitate was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 0.36 g (69%), mp 148-150°C. IR spectrum (ν, cm^{-1}): 3600-3300, 1730, 1470, 1380, 1310, 1260, 1200, 1150, 1110, 1090, 1020, 980, 820, 770. PMR spectrum (δ, ppm, J/Hz): 0.55 (3H, s, 23-H), 0.79 (3H, d, J = 6.8, 21-H/22-H), 0.87 (3H, d, J = 6.8, 22-H/21-H), 0.90-1.00 (2H, m, $1\text{-}H_a$, $11\text{-}H_a$), 1.03 (3H, s, 24-H), 1.15-1.45 (8H, m, $1\text{-}H_e$, $2\text{-}H_{a,e}$, $3\text{-}H_e$, $6\text{-}H_{a,e}$, $7\text{-}H_{a,e}$), 1.50-1.70 (4H, m, $3\text{-}H_a$, $11\text{-}H_e$, 9-H, 5-H), 2.22 (1H, ddd, $^4J_{12,19}$ = 1.6, $^3J_{12,11a}$ = 2.2, $^3J_{12,11e}$ = 13.2, 12-H), 2.36 (1H, sept, J = 6.8, 20-H), 2.88 (1H, br.s, 14-H), 3.15 (1H, s, 16-H), 3.52 (3H, s, 28-H), 3.73 (3H, s, 27-H), 3.89 (1H, d, J = 1.8, 17-H), 5.20 (1H, br.s, 19-H), 9.65 (3H, br.s, NH, NH_2).

^{13}C NMR (δ, ppm): 38.2 (C-1), 17.2 (C-2), 36.9 (C-3), 47.3 (C-4), 52.1 (C-5), 22.2 (C-6), 35.0 (C-7), 41.9 (C-8), 52.4 (C-9), 37.6 (C-10), 25.7 (C-11), 39.2 (C-12), 64.0 (C-13), 52.7 (C-14), 157.9 (C-15), 61.6 (C-16), 58.6 (C-17), 146.2 (C-18), 126.5 (C-19), 33.6 (C-20), 21.4 (C-21), 20.7 (C-22), 16.9 (C-23), 15.8 (C-24), 179.5 (C-25), 171.9 (C-26), 49.3 (C-27), 56.8 (C-28), 151.9 (C=O).

1,2,3-Oxadiazolin-2′-one of 16,17-Epoxydimethylcylopentenonepimarate (4). A suspension of **3** (0.53 g, 1 mmol) in dry CH_2Cl_2 (20 mL) was stirred at 0°C, treated with $Pb(OAc)_4$ (0.6 g, 1.36 mmol), held at room temperature for 4 h, treated with cold water (5 mL) and aqueous HCl (3 mL, 2.4 N), and stirred another 0.5 h until fully hydrolyzed. The precipitate was filtered off. The organic layer was extracted with CH_2Cl_2 (2×20 mL), washed with water (3×30 mL), dried over $CaCl_2$, and evaporated in vacuum. The solid was chromatographed over Al_2O_3 with elution by benzene. Yield 0.25 g (48%), mp 168-170°C. IR spectrum (ν, cm^{-1}): 1820, 1730, 1475, 1390, 1300, 1290, 1205, 1160, 1100, 1080, 1025, 990, 830, 760, 730. PMR spectrum (δ, ppm, J/Hz): 0.49 (3H, s, 23-H), 0.76 (3H, d, J = 6.8, 21-H/22-H), 0.81 (3H, d, J = 6.8, 22-H/21-H), 0.88-0.98 (2H, m, $1\text{-}H_a$, $11\text{-}H_a$), 1.05 (3H, s, 24-H), 1.15-1.48 (8H, m, $1\text{-}H_e$, $2\text{-}H_{a,e}$, $3\text{-}H_e$, $6\text{-}H_{a,e}$, $7\text{-}H_{a,e}$), 1.51-1.73 (4H, m, $3\text{-}H_a$, $11\text{-}H_e$, 9-H, 5-H), 2.18 (1H, ddd, $^4J_{12,19}$ = 1.6, $^3J_{12,11a}$ = 2.2, $^3J_{12,11e}$ = 13.2, 12-H), 2.34 (1H, sept, J = 6.8, 20-H), 2.85 (1H, br.s, 14-H), 3.19

(1H, s, 16-H), 3.53 (3H, s, 28-H), 3.60 (1H, d, J = 1.8, 17-H), 3.76 (3H, s, 27-H), 5.20 (1H, br.s, 19-H).

^{13}C NMR spectrum (δ, ppm): 38.1 (C-1), 17.3 (C-2), 36.9 (C-3), 47.3 (C-4), 52.1 (C-5), 22.2 (C-6), 35.0 (C-7), 41.9 (C-8), 52.4 (C-9), 37.6 (C-10), 25.7 (C-11),, 39.2 (C-12), 64.0 (C-13), 52.7 (C-14), 132.9 (C-15), 61.6 (C-16), 58.6 (C-17), 146.8 (C-18), 124.8 (C-19), 33.6 (C-20), 21.4 (C-21), 20.7 (C-22), 16.9 (C-23), 15.8 (C-24), 179.1 (C-25), 177.7 (C-26), 49.1 (C-27), 56.5 (C-28), 152.9 (C=O).

RFERENCES

1. G. A. MacAlpine and J. Warkentin, *Can. J. Chem.*, **56**, No. 3, 308 (1978).
2. M. Tanabe, D. F. Crowe, R. L. Dehn, and G. Detre, *Tetrahedron Lett.*, 3739 (1967).
3. M. Tanabe, D. F. Crowe, and R. L. Dehn, *Tetrahedron Lett.*, 3943 (1967).
4. P. J. Kosienski and R. W. Ostrow, *J. Org. Chem.*, **41**, 398 (1976).
5. E. J. Corey and H. S. Sachdev, *J. Org. Chem.*, **40**, 579 (1975).
6. E. V. Tret′yakova, O. B. Flekhter, F. Z. Galin, L. V. Spirikhin, and G. A. Tolstikov, *Khim. Prirod. Soedin.*, 206 (2002).
7. W. Herz, R. C. Blackstone, and M. G. Nair, *J. Org. Chem.*, **32**, No. 10, 2992 (1967).