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> SHORT COMMUNICATIONS

Reaction of Levoglucosenone with (±)-α-Terpineol and Its Acetate

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In continuation of our studies [1, 2], we focused on the potential of levoglucosenone in the synthesis of menthane derivatives as a separate problem and examined the possibility for direct introduction of a menthane fragment into levoglucosenone molecule via reaction with (\pm) - α -terpineol.

A short synthetic route to (\pm) - α -terpineol is the twostep procedure utilizing large-scale initial compounds, isoprene and methyl acrylate [3]. The transformation of (\pm) - α -terpineol into a chiral subunit requires its preliminary optical resolution and introduction of functional groups that could ensure subsequent transformations.

It is known that dehydration of α -terpineol leads to the formation of a number of isomeric dienes, including α -terpinene whose yield in some cases attains 25% [4]. The use of such a mixture of menthane derivatives as diene component and of levoglucosenone as dienophile is attractive from the viewpoint of simultaneous solution of both problems. For this purpose, a toluene solution of levoglucosenone and diene mixture obtained from (±)- α -terpineol according to the procedure described in [4] was heated at 160°C in a sealed glass ampule (metohd *a*). In fact, after 9 h, we succeeded in isolating from the reaction mixture Diels–Alder adduct V in 3% yield [calculated on the initial (\pm) - α -terpineol]. Increase of the reaction time reduced the yield of V, and we failed to detect it in the reaction mixture after 30 h, presumably because of its decomposition.

We also tried to use as starting compounds (\pm) - α -terpineol (I) and (\pm) - α -terpinyl acetate (II), expecting generation of α -terpinene (III) *in situ* under the given Diels–Alder reaction conditions. In the first case, no cycloaddition products were detected in the reaction mixture, and in the second case adduct V was formed in 4% yield in 28 h (method *b*).

The structure of V was determined on the basis of the ¹H and ¹³C NMR data. The coupling constant between 5a-H and 9a-H equal to 8.6 Hz indicates *cis* junction of the bicyclo[2.2.2]octane and pyran fragments. The signal assignment was confirmed by the HMBC technique. The 9a-H proton (δ 1.87 ppm) showed couplings with C² ($\delta_{\rm C}$ 68.29 ppm), C^{5a} (49.29), C⁵ (200.96), C⁸ (138.26), and C⁹ (35.59), and cross-peaks of 5a-H (δ 2.90 ppm) with C⁵, C⁶ ($\delta_{\rm C}$ 44.98 ppm), C⁷ (135.53), and C¹¹ (20.80) were



Pressure, atm	Ratio IV:I	Temperature, °C	Reaction time, h	Yield of V , ^a %
6000	1:2.5	100	6	4
6000	1:2	100	1.5	0
10000	1:2	100	3	5
10000	1:2	150	3	Tarry material
10000	2:1	100	3	5 ^b

Table 1. Reaction of (\pm) - α -terpineol (I) with levoglucosenone (IV) in toluene (method *c*)

^a Calculated on the initial levoglucosenone.

^b Calculated on the initial (\pm)- α -terpineol.

Table 2. Reaction of (\pm) - α -terpinyl acetate (II) with levoglucosenone (IV) in toluene (method *d*; reaction time 3 h)

Pressure, atm	Ratio IV: II	Temperature, °C	Yield of V , ^a %
6000	1:1	100	0
6000	1:1	150	11
10000	1.5:1	150	22
10000	2:1	150	35
10000	3:1	150	37
6000	1:2	200	Tarry material

^a Calculated on the initial (\pm) - α -terpinyl acetate.

observed. The position of the double C=C bond and orientation of the methyl and isopropyl substituents were determined using NOESY technique. The NOESY spectrum revealed correlations between the 9a-H proton, on the one hand, and $2-H_4$ (δ 3.75 ppm), 5a-H, 10-H (1.40), and 9-CH₃ (1.3), on the other, while the 5a-H proton displayed correlations with 9a-H, $2-H_A$, and methyl protons in the isopropyl fragment (δ 0.88 ppm). Nuclear Overhauser effects were also observed for 1-H and 2-H_B (δ 3.87 ppm) and 1-H and 9-CH₃. Furthermore, protons of the 9-CH₃ group were coupled with 8-H (δ 6.03 ppm), and 7-H (δ 5.92 ppm) was coupled with the CH proton of the isopropyl group (δ 2.97 ppm). These findings allowed us to assign *endo* position to the double bond and R and S configurations to C^6 and C^9 , respectively.

Further optimization of the reaction conditions for (\pm) - α -terpineol (I) and its acetate II was performed at pressures of 6000 and 10000 atm (methods *c* and *d*; Tables 1, 2). It is seen that the optimum conditions for the formation of Diels-Alder adduct (V) containing a menthane fragment are as follows: pressure 10000 atm, temperature 150°C, levoglucosenone- (\pm) - α -terpinyl acetate ratio 3:1.

2-(4-Methylcyclohex-3-en-1-yl)propan-2-yl acetate (II). A solution of 0.200 g (1.3 mmol) of (\pm) - α -terpineol (I) in 2.0 mL of isopropenyl acetate was cooled to 0°C, and a catalytic amount of *p*-toluenesulfonic acid (10%) was added. When the reaction was complete (TLC), the mixture was evaporated under reduced pressure on a rotary evaporator, and the residue was purified by silica gel column chromatography. Yield 0.232 g (91%), colorless liquid, R_f 0.65 (petroleum ether–EtOAc, 1:1). ¹H NMR spectrum, δ , ppm: 1.22 m (1H, CH₂), 1.38 s (3H, CH₃), 1.40 s (3H, CH₃), 1.62 br.s (3H, CH₃), 1.70–1.82 m (2H, CH₂), 1.94 s (3H, CH₃), 1.90–2.12 m (4H, CH, CH₂), 5.38 br.s (1H, CH). ¹³C NMR spectrum, δ_C , ppm: 22.45 (CH₃), 23.08 (CH₃), 23.29 (CH₃), 23.83 (C⁶), 26.34 (C²), 30.86 (C⁵), 42.53 (C¹), 84.81 (CHO), 120.30 (C³), 133.91 (C⁴), 170.48 (C=O). Found, %: C 73.42; H 10.36. C₁₂H₂₀O₂. Calculated, %: C 73.43; H 10.27.

(1S,4R,5aS,6R,9S,9aR)-1,4-Epoxy-6-isopropyl-9methyl-6,9-ethano-1,2,5a,6,9,9a-hexahydrobenzo[*d*]oxepin-5(4*H*)-one (V). *a*. α -Terpineol (I), 0.6 g (3.9 mmol), was added to a solution of 2.45 g (27.2 mmol) of oxalic acid in 5.0 mL of water, and the mixture was heated under reflux until the reaction was complete (TLC). The mixture was cooled and extracted with petroleum ether (3×10 mL), and the combined extracts were dried over MgSO₄ and evaporated under reduced pressure on a rotary evaporator. The residue was dissolved in 3.0 mL of toluene, 0.231 g (1.84 mmol)

of levoglucosenone (IV) was added, and the mixture was heated for 9 h in a sealed glass ampule at 160°C. The ampule was cooled and opened, the mixture was evaporated under reduced pressure on a rotary evaporator, and the residue was subjected to silica gel column chromatography. Yield 0.031 g (3%), colorless crystals, mp 61°C, $[\alpha]_D^{20} = -167.2^\circ$ (*c* = 1.0, CHCl₃), $R_{\rm f}$ 0.5 (benzene). IR spectrum, v, cm⁻¹: 2963, 1725, 1465, 1372, 1120, 992, 676, 501. ¹H NMR spectrum, δ, ppm: 0.88 d (6H, CH₃, J = 6.9 Hz), 1.10 d.d (1H, $12-H_4$, J = 3.1, 9.1 Hz), 1.30 s (3H, CH_3), 1.25-1.33 m $(2H, 11-H), 1.42 \text{ t.d} (1H, 12-H_B, J = 2.5, 9.1 \text{ Hz}),$ 1.87 d.d (1H, 9a-H, J = 0.9, 8.6 Hz), 2.90 d (1H, 5a-H, J = 8.6 Hz), 2.97 s (1H, 1'-H), 3.75 d (1H, 2-H₄, J =7.3 Hz), 3.87 d.d (1H, 2-H_B, J = 4.6, 7.3 Hz), 4.77 d.d (1H, 1-H, J = 0.9, 4.6 Hz), 4.79 s (1H, 4-H), 5.92 d(1H, 7-H, J = 8.4 Hz), 6.03 d (1H, 8-H, J = 8.4 Hz).¹³C NMR spectrum, δ_{C} , ppm: 16.76 (C^{1"}), 18.70 (C^{2"}), 20.80 (C¹¹), 22.76 (CH₃), 29.97 (C^{1'}), 35.59 (C⁹), 38.13 (C¹⁰), 44.98 (C⁶), 48.58 (C^{9a}), 49.29 (C^{5a}), 68.29 (C²), 73.12 (C^1), 100.61 (C^4), 135.53 (C^7), 138.26 (C^8), 200.96 (C=O). Mass spectrum: m/z 262.2 $[M]^+$. Found, %: C 73.28; H 8.47. C₁₆H₂₂O₃. Calculated, %: C 73.25; H 8.45. M 262.34.

b. α -Terpinyl acetate (II), 0.135 g (0.69 mmol), was added to a solution of 0.260 g (2.06 mmol) of levo-glucosenone (IV) in 3.0 mL of toluene. The mixture was heated in a sealed glass ampule for 28 h at 160°C and was then treated as described above in *a*. Yield 0.007 g (4%).

c. α -Terpineol (I), 0.240 g (1.58 mmol), was added to a solution of 0.100 g (0.79 mmol) of levoglucosenone (IV) in 1.3 mL of toluene. The mixture was heated for 3 h in a high-pressure reactor at 100°C and 10000 atm and was then treated as described above in *a*. Yield 0.011 g (5%). *d*. α -Terpinyl acetate (II), 0.080 g (0.4 mmol), was added to a solution of 0.154 g (1.2 mmol) of levoglucosenone (IV) in 1.3 mL of toluene. The mixture was heated for 3 h in a high-pressure reactor at 150°C and 10000 atm and was then treated as described above in *a*. Yield 0.040 g (37%).

The spectral and analytical data were obtained using the equipment of the Khimiya Joint Center at the Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences. The ¹H and ¹³C NMR spectra were recorded on Bruker AM-300 (300 MHz for ¹H and 75.47 MHz for ¹³C) and Bruker Avance III (500 MHz) instruments from solutions in CDCl₃. The IR spectra were measured on Shimadzu IR Prestige-21 and Bruker Tensor 27 spectrometers from films or Nujol mulls. The mass spectra were obtained on a Hewlett Packard 6890 chromatograph coupled with an HP 5973 mass-selective detector. The optical rotations were measured on a Perkin Elmer 341 polarimeter. Analytical TLC was performed on Sorbfil PTSKh-AF-A plates. The melting points were determined on a Boetius PHMK 05 melting point apparatus.

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