REACTIONS OF DITERPENOIDS ON SOLID SUPPORTS
II. BEHAVIOR OF DI- AND TRICYCLIC DITERPENOIDS ON
ALUMINA CONTAINING OXIDANTS

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The behavior of epimanool (1), epimanool oil, larixol (2), cis-abienol (3) and methyl dehydroabietate (4) on alumina impregnated with oxidants (H_2CrO_4 and $KMnO_4$) has been studied. This has led to the methyl ketone (5) and norambrenolide (8) — precursors of the perfume substances 14,15,17-trinorlabdane-8,13-dione (6), 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (7), and methyl 7-oxodehydroabietate (14). α-Levantenolide (11) has been synthesized in one stage from cis-abienol (3) for the first time.
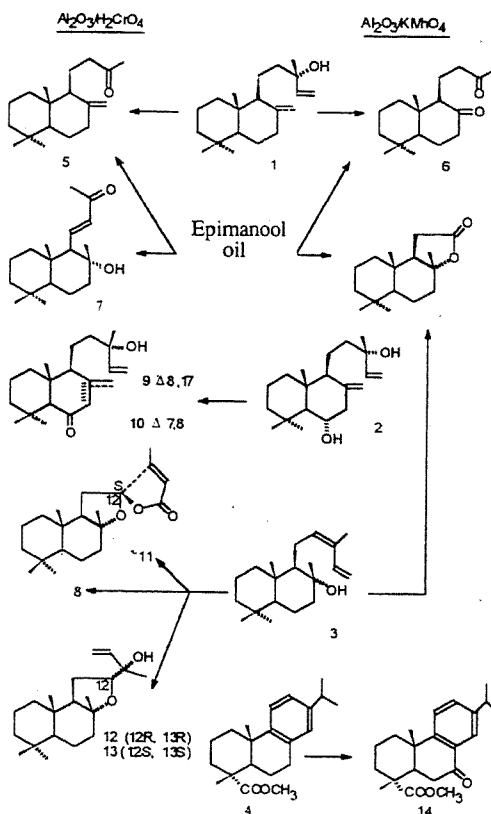
Over a number of years, oxidation reactions of labdane diterpenoids and resin acids have aroused great interest in scientists. These natural compounds form unique material and find wide practical use in the synthesis of a whole series of perfume components and biologically active substances [2, 3]. In spite of the enormous amount of experimental material on the oxidative transformation of diterpenoids, the search for the optimum conditions of oxidation that will increase the yield of desired products and decrease the amount of wastes remains an urgent one. Recently, interest has risen in reactions on solid supports impregnated with various oxidants. There have been reports on the oxidation of terpenoids with $KMnO_4$, H_2CrO_4, and $K_2Cr_2O_7$ deposited on Al_2O_3 and SiO_2 [4-6].

Continuing an investigation of reactions of diterpenoids on solid supports [1], we have studied the behavior of the bicyclic labdane alcohols epimanool (1), epimanool oil (a mixture of diterpene alcohols), larixol (2), and cis-abienol (3), and also a tricyclic diterpenoid — methyl dehydroabietate (4) — on alumina impregnated with $KMnO_4$ or H_2CrO_4. In both cases we investigated only the neutral reaction products (the amount of acids was less than 10%). The sorbent/oxidant and substrate/sorbent ratios corresponded to those given in the literature [4, 5]. As solvent we used acetone, since it gave the highest conversion of the substrate.

After a solution of epimanool (1) in acetone with the addition of acetic acid had been kept over the sorbent Al_2O_3/H_2CrO_4 at room temperature for 5 days, we eluted the mixture of reaction products (65% yield), of which 90% was the methyl ketone (5). Compound (5) is the main intermediate in the synthesis of perfume substances with the odor of ambergris [2]. The methyl ketone (2) has previously been obtained by the oxidation of manool with CrO_3 in acetic acid with a yield of 25% [7], and on oxidation with $KMnO_4$ with a yield of 30-45% [8, 9].

The conversion of epimanool (1) on $Al_2O_3/KMnO_4$ led to a reaction mixture (yield 25-30%) 90% of which was 4,15,17-trinorlabdane-8,13-diol (6). Previously, compound (6) has been obtained from manool either by ozonization (yield 50%) [10] or by two-stage oxidation (yield about 80%) [11].

Epimanool oil is an industrial by-product in the production of neutral larch resin and consists of a mixture of diterpene alcohols the epimanool content of which ranges from 30 to 80%. In the samples of the oil that were tested in reactions on sorbents, in addition to compound (1), we identified neoabienol. After the oil had been kept on the sorbent Al_2O_3/H_2CrO_4, a reaction mixture (yield 70%) consisting of two main components (GLC) was formed. By chromatography we isolated the methyl ketone (5) and 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (7) (yield 35%). This method of oxidizing the diol enables compound (7) to be obtained preparatively.

Al₂O₃/H₂CrO₄   Al₂O₃/KMnO₄

5   1   6

Epimanool oil

7

9 Δ8,17
10 Δ 7,8

2

12

8

3

11

12 (12R, 13R)
13 (12S, 13S)

4   14

When epimanool oil was oxidized on $Al_2O_3/KMnO_4$, in addition to the diketone (**6**), we obtained 12-norambrenolide (**8**) — one of the most important substances for obtaining perfume materials. The interaction of larixol (**2**) with Al_2O_3/H_2CrO_4 led to a reaction mixture consisting of 6-oxoepimanool (**9**), its $\Delta^{7,8}$ isomer (**10**), and unchanged larixol (**2**). After the interaction of compound (**2**) with $Al_2O_3/KMnO_4$, the yield of the mixture of reaction products eluted from the sorbent with a polar solvent amounted to less than 10%, which was probably due to the adsorption of the oxidation products on the Al_2O_3 and MnO_2.

We also studied the chemical behavior of *cis*-abienol (**3**). The interaction of compound (**3**) with Al_2O_3/H_2CrO_4 gave a reaction mixture (yield 70%) consisting of three components (GLC). After the separation of the mixture into individual compounds, we isolated and identified α-levantenolide (**11**), norambrenolide (**8**), and a mixture of two isomers: (12R,13R)- and (12S,13S)-8,12-epoxylabd-14-en-13-ol (**12** and **13**, respectively) in a ratio of 6:1 (according to the PMR spectrum).

α-Levantenolide (**11**) and its β- isomer have been isolated previously from tobacco leaves [12] and, later, from *Cistus ladaniferus* L. [13]. Known attempts to synthesize the lactone (**11**) from monocyclic and labdane compounds were connected with the possible biological activity of the levantolides [14-16]. However, all these methods are fairly laborious and with many stages. We have for the first time succeeded in obtaining α-levantenolide (**11**) from *cis*-abienol (**3**) in one stage. The mechanism of the formation of compound (**11**) from (**3**) falls within the generally accepted scheme of the oxidation of olefins by chromium salts [17].

The isomeric epoxylabdanes (**12**) and (**13**) isolated from the reaction mixture have been found in *Nicotiana tabacum* L., and the authors proposed a possible route for the biosynthesis of compounds (**11**), (**12**), and (**13**) from *cis*-abienol (**3**) [18]. The epoxides (**12**) and (**13**) have been obtained synthetically by the epoxidation [19] and photooxidation [20] of the latter.

After the interaction of *cis*-abienol (**3**) with $Al_2O_3/KMnO_4$, the main component of the reaction mixture was norambrenolide (**8**).

We studied the behavior of the tricylcic diterpenoid methyl dehydroabietate (**4**) on sorbents with oxidants. On the interaction of compound (**4**) with $Al_2O_3/KMnO_4$, the main reaction products was methyl 7-oxodehydroabietate (**14**), which was obtained with a yield of 85%. Previously, the maximum yield of ketone (**14**) on the oxidation of methyl dehydroabietate had been 65% [3].

The oxidation of compound (**4**) on Al_2O_3/H_2CrO_4 formed a multicomponent mixture from which it was possible to separate and identify only 15% of methyl 7-oxodehydroabietate (**14**).

Thus, by using sorbents with oxidants deposited on them we have succeeded in performing the oxidation of the diterpenoids (1–4) selectively in one stage without the formation of waste waters in the working up of the reaction mixtures and have obtained a number of important polyfunctional compounds.

EXPERIMENTAL

Melting points were determined on a Kofler block, and optical rotations on a Polamat A polarimeter at 580 nm in $CHCl_3$ solutions. IR spectra were taken in CCl_4 solutions on a UR-20 instrument, and PMR spectra on Bruker WP-200 (200.13 MHz) and AC-200 (200.13 MHz) instruments (δ scale, internal standard $CHCl_3$, the signal of which was taken as 7.24 ppm). ^{13}C NMR spectra were recorded in $CDCl_3$ solutions on a AC-200 (50.32 MHz) instrument (δ scale, the solvent as internal standard, 76.9 ppm).

The gas—liquid chromatography of the reaction mixtures and the checking of the individuality of the compounds were performed on a Chrom-5 instrument under the following recording conditions: glass column with the stationary phase SE-30 deposited on Chromaton N-Super, length 2 m, diameter 3 mm, column temperature 180°C, carrier gas nitrogen, 30 ml/min. For separating the reaction mixtures and isolating individual compounds we used adsorption chromatography on silica gel with a grain size of 71-100 μm.

The eluents used were mixtures of petroleum ether (PE) and diethyl ether (DE) (% shows the percentage of DE in the mixture). The course of the reactions and the progress of column chromatography were followed on Silufol plates. The epimanool oil was a product of the Experimental Factory of TsNILKhI [Central Scientific—Research Laboratory of Wood Chemistry] (Novgorod); clear liquid with n_D 1.5196-1.5280.

Preparation of the Sorbent Al_2O_3/H_2CrO_4 (in a similar way to [4]). To a solution of 1.5 g of CrO_3 in 50 ml of water were added 20 g of neutral Al_2O_3 and 20 ml of water. The mixture was stirred for 30 min, and the water was eliminated in a rotary evaporator. The sorbent with the oxidant was heated at 80°C for 2 h.

Preparation of the Sorbent $Al_2O_3/KMnO_4$ in a similar way to [5]. To a solution of 15 g of $KMnO_4$ in 100 ml of water was added 15 g of Al_2O_3. Further treatment was as described above.

Oxidation of Epimanool (1) on Al_2O_3/H_2CrO_4. A solution of 0.15 g of compound (1) in a mixture of 3 ml of acetone and 0.5 ml of acetic acid was deposited on 2 g of the sorbent and left at room temperature for 5 days (monitoring by TLC). Then the reaction mixture was eluted from the sorbent with DE and, after treatment with saturated Na_2CO_3 solution, the eluate was dried and the solvent was distilled off. This gave 0.095 g (65%) of a mixture of products containing 90% of the methyl ketone (5) and 5% of epimanool (1). The reaction mixture was chromatographed, and elution with a 5% DE mixture yielded 14,15-bisnorlabd-8(17)-en-13-one (5), $[\alpha]$ +19° (c 1.92), the spectral characteristics (IR and NMR spectra) of which coincided with those given in the literature [9]: $[\alpha]_D$ +38° (c 1.0).

Oxidation of Epimanool (1) on $Al_2O_3/KMnO_4$. A solution of 1 g of compound (1) in 10 ml of acetone was deposited on 10 g of the sorbent and was left for 2 days. The solvent was evaporated off, the dry residue was deposited on a column of SiO_2, the products were eluted with DE, and the eluent was evaporated off. Yield 0.25 g (25%). By chromatography (15% DE) 0.16 g (65%) of 14,15,17-trisnorlabddan-8,13-dione (6), $[\alpha]$ −30.7° (c 0.91), was isolated. Its spectra characteristics (IR and PMR spectra) were identical with those given in the literature [21]: $[\alpha]_D$ −10.3 (c 2.1).

Interaction of Epimanool Oil with Al_2O_3/H_2CrO_4. A solution of 2 g of epimanool oil (ratio of epimanool (1) and neoabienol 2.7:1 acording to PMR results) in a mixture of 10 ml of acetone and 1 ml of acetic acid was deposited on 20 g of the sorbent and left for 8 days. The reaction mixture was worked up as described above. The product contained 30% of the methyl ketone (5), 50% of the hydroxy ketone (7), and 10% of epimanool (1) (GLC). By chromatography (5% DE) we isolated 0.2 g of compound (5) and (100% DE) 0.5 g (35%) of 8α-hydroxy-14,15-bisnorlabd-11-en-13-one (7), mp 124-127°C (DE), $[\alpha]$ +10° (c 1.0); lit. [22]: mp 126°C, $[\alpha]_D$ 0; lit. [23]: mp 126-127°C, $[\alpha]_D$ +15.8° (c 0.43). ^{13}C NMR spectrum: 15.82 (q), 18.18 (t), 20.01 (t), 21.43 (q), 24.85 (q), 27.48 (q), 33.21 (q + s), 37.71 (s), 40.86 (t), 41.66 (t), 42.86 (t), 55.40 (d), 65.73 (d), 72.17 (s), 135.27 (d), 144.52 (d), 197.40 (s) ppm.

Interaction of Epimanool Oil with $Al_2O_3/KMnO_4$. A solution of 1.2 g of the oil in 10 ml of acetone was deposited on 10 g of the sorbent and was left for 2 days. After the reaction mixture had been worked up as described above, 0.3 g (25%) of a mixture of products was obtained the chromatography (10% DE) of which led to the isolation of 0.05 g of 12-norambrenolide (8), mp 123-126°C (hexane), $[\alpha]$ +40° (c 0.3); lit. [24]: mp 122-123°C (PE), $[\alpha]_D$ +42° (c 0.25), and (15% DE) 0.07 g of compound (6).

Oxidation of Larixol (2) on Al_2O_3/H_2CrO_4. A solution of 0.13 g of compound (2) in 2 ml of acetone and 0.5 ml of acetic acid was deposited on 1.7 g of the sorbent and was left for 5 days. The reaction products (0.1 g, 75%) were chromatographed, with the isolation of (15% DE) 0.045 g of 13-hydroxylabd-8(17),14-dien-6-one (9) and (20% DE) 0.015 g of 13-hydroxylabd-7,14-dien-6-one (10), identical according to TLC, GLC, and spectral characteristics with an authentic sample [25].

Reaction of *cis*-Abienol (3) with Al_2O_3/H_2CrO_4. A solution of 0.8 g of compound (3) in 10 ml of acetone and 1 ml of acetic acid was deposited on 20 g of the sorbent and left for 5 days. The yield of reaction mixture after working up was 0.55 g (70%). According to GLC, it contained 30% of α-levantenolide (11), 40% of norambrenolide (8), and 15% of a mixture of the isomers (12) and (13). It was chromatographed and yielded (10% DE) 0.1 g of norambrenolide (8); (20% DE) 0.04 g of a mixture of compounds (12) and (13) in a ratio of 6:1, their PMR and ^{13}C NMR spectra being identical with those decribed in the literature [19]; (25% DE) 0.07 g of α-levantenolide (11), mp 209-212°C (hexane), [α] +50° (*c* 0.9); lit. [16]: mp 210°C (hexane), $[α]_D$ +60° (*c* 0.7). PMR spectrum, ppm: 0.83 (3H, s), 0.87 (3H, s), 0.89 (3H, s), 1.38 (3H-17, s), 1.98 (3H-16, d, J = 1.5 Hz), 5.70 (H-14, q, J = 1.5 Hz); lit. [16]: PMR spectrum (C_6D_6) [sic]. The ^{13}C NMR spectrum (for a solution in $CDCl_3$) coincided with that described in the literature [26].

Reaction of *cis*-Abienol (3) with $Al_2O_3/KMnO_4$. A suspension of 0.07 g of compound (3), 3 ml of acetone, and 1 g of the sorbent was left overnight. After working up, 0.03 g (43%) of 12-norambrenolide (8) was obtained.

Oxidation of Methyl Dehydroabietate (4) on $Al_2O_3/KMnO_4$. A solution of 2.2 g of compound (4) in 20 ml of acetone was deposited on 20 g of the sorbent and was left for 5 days. After working up, 2 g (90%) of reaction mixture was obtained, and its chromatography (10% DE) led to the isolation of 1.8 g (85%) of methyl 7-oxodehydroabietate (14), the IR and PMR spectra of which coincided with those of an authentic specimen.

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