

Ozonolysis of Alkenes and Study of Reactions of Polyfunctional Compounds: LXIV.* Synthesis of Ambreinolide and 8 α ,13-Epoxy-14,15,16-trisnorlabd-12-ene Proceeding from Isoabienol Ozonolysis

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Received March 16, 1999

Abstract—The ozonolysis of isoabienol in MeOH followed by hydrogenation of the peroxide ozonolysis products on Lindlar catalyst afforded ambreinolide that under treatment with diisobutylaluminum hydride furnished 8 α ,13-epoxy-14,15,16-trisnorlabd-12-ene.

The ambreinolide is an important intermediate compound in the synthesis of perfumes with amber odor [3]. The most convenient among the known procedures for its synthesis is oxidation with potassium permanganate of the isoabienol. The latter substance became available when it was found in large amounts in the needles of an ordinary pine (*Pinus silvestris* L.) [3]. We established that ambreinolide (**II**) formed in over 90% yield at isoabienol (**I**) ozonolysis in methanol at -78°C followed by catalytic hydrogenation of the peroxide ozonolysis products.

The reduction of δ -lactone **II** with lithium aluminum hydride is known [4] to afford the corresponding diol, ambreinolol. We developed a method for quantitative conversion of compound **II** into unsaturated epoxide 8 α ,13-epoxy-14,15,16-trisnorlabd-12-ene (**III**) with a strong amber odor [5]. This conversion is attained by treating lactone **II** with diisobutylaluminum hydride at low temperature.

We presume that the most probable path of ozonolytic conversion of diene **I** into trisnorlabdane lactone **II** is as follows. The prevailing initial attack of ozone occurs at C¹³-methylene group, more substituted than vinyl group (cf. [6]); as a result arises zwitterion A, mesomeric to ion B. The subsequent addition of MeOH to zwitterion B affords vinyl hydroperoxide C that at further ozonization is either converted in peracid D or in zwitterion E which is stabilized by its own hydroxy group providing α -bishydroperoxide F. The peroxy compounds D and F are hydrogenated

into lactone **II**. In the course of its hydride reduction arises an intermediate semiacetal G that under acid treatment of the reaction mixture suffers dehydration and transforms into ambroxide **III**.

The alternative path may consist in an attack of a hydroxy group directly on the primary zwitterion A, and then after the ozonolysis of the remaining double bond in the intermediate compound H and the reduction of the ozonolysis peroxy products should form compound **I**. The decarbonylation of the latter to afford lactone **II** is dubious under the given reaction conditions.

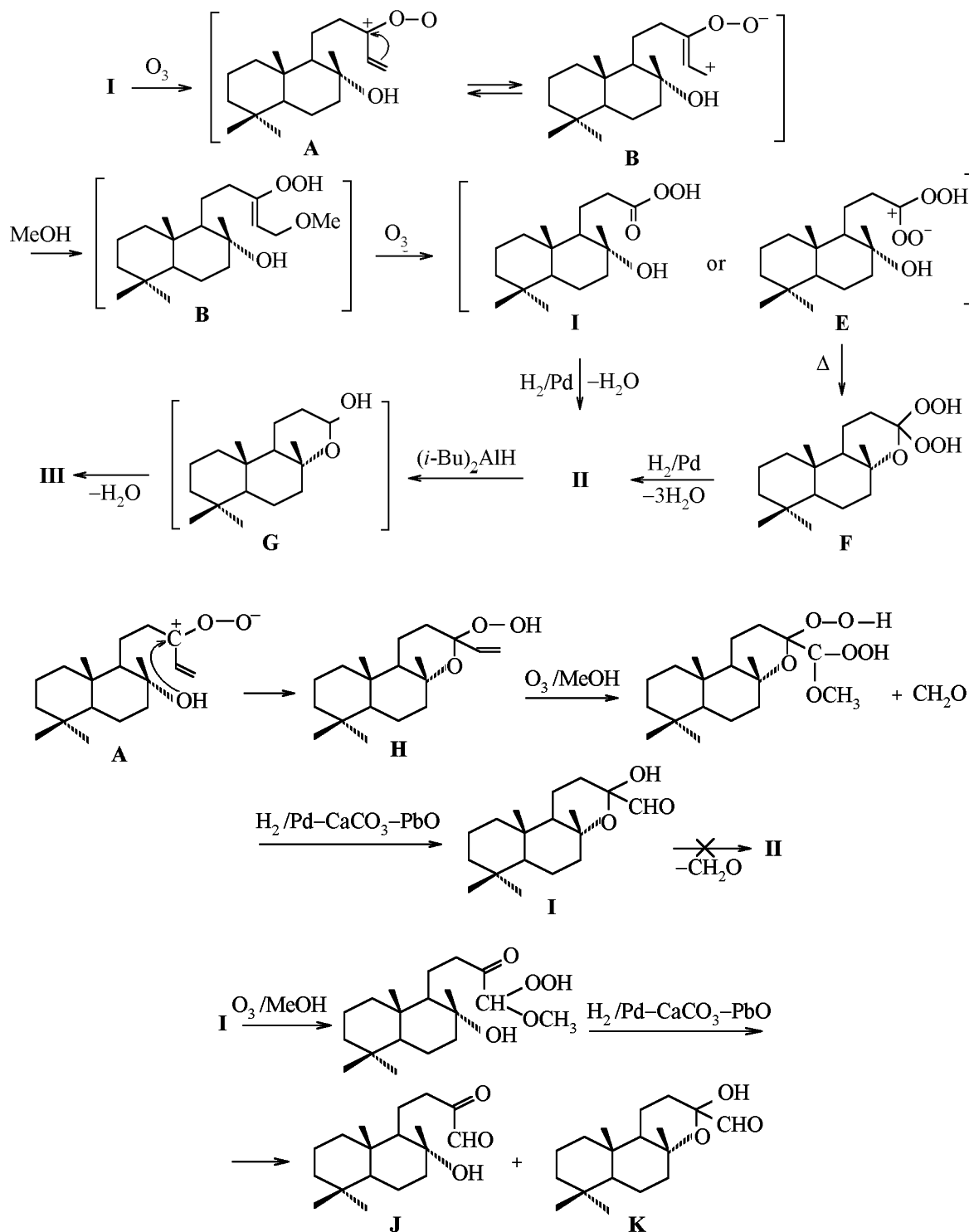
The simultaneous attack of ozone of both double bonds in isoabienol (**I**) cannot explain the facts observed since in the reaction products were neither detected ketoaldehyde (J) nor compound (K) originating from intermolecular reaction between hydroxy and keto groups.

The most probable reaction mechanism via intermediates A–G is in agreement with the published data [7]. The reduction of ambreinolide (**II**) by diisobutylaluminum hydride accompanied with dehydration results in high yield of 8 α ,13-epoxy-14,15,16-trisnorlabd-12-ene (**III**), ambroxide with a strong amber odor.

EXPERIMENTAL

IR spectra were recorded on UR-20 spectrophotometer from thin film. ¹H NMR spectra were run on spectrometer Tesla BS-576 (100 MHz), solvent CDCl₃, internal reference TMS. GLC was performed

* Communication LXIII see [1].



on Chrom-5 chromatograph (column 1200×4 mm, stationary phase 5% SE-30 on Chromaton N-AW-DMCS), oven temperature $50-300^\circ C$, carrier gas helium. Mass spectrum was measured on MKh-1320 instrument at ionizing electrons energy 70 eV.

(8R)-14,15,16-Trisnorlabdan-13,8-olide (II).

Through a solution of 1 g (3.4 mmol) of isoabieryl alcohol (I) in 40 ml of anhydrous MeOH was passed at $-78^\circ C$ a stream of ozone-oxygen mixture (5.5 wt% of O_3) till the solution became blue. Then the reaction mix-

ture was flushed with argon, warmed to 20°C, and 0.1 g of Lindlar catalyst was added. Then the reaction mixture was stirred under hydrogen atmosphere till the negative test for peroxides with acid water solution of KI. The catalyst was filtered off, the filtrate was evaporated in vacuo, and the residue crystallized. We obtained 0.85 g (93%) of compound **II**, mp 138.5–140°C (from hexane). Published data for ambreinolide (**II**) [8]: mp 140–141°C (from petroleum ether). IR spectrum (ν , cm^{-1}): 970, 1130, 1725. ^1H NMR spectrum (CDCl_3 , δ , ppm): 0.78 s (2H, H_2C^1), 0.82 s (3H, $\alpha\text{-CH}_3\text{C}^4$), 0.89 s (3H, CH_3C^{10}), 0.94 s (3H, $\beta\text{-CH}_3\text{C}^4$), 1.31–2.77 m (12H, CH, CH_2), 1.32 s (3H, CH_3C^8), 2.48 m (2H, CH_2CO_2). Mass spectrum, m/z , (I_{rel} , %): 264 $[M]^+$ (4.6), 249 $[M-\text{CH}_3]^+$ (23), 235 $[M-\text{CHO}]^+$ (1.3), 220 $[M-\text{CO}_2]^+$ (8.8), 192 $[M-\text{C}_3\text{H}_4\text{O}_2]^+$ (100), 177 (48), 149 (11.5), 137 (28.8).

8 α ,13-Epoxy-14,15,16-trisnorlabd-12-ene (**III**).

To a solution of 0.32 g (1.21 mmol) of ambreinolide **II** in 20 ml of anhydrous ethyl ether at -70°C within 3.5 h was added a solution of *i*-Bu₂AlH (1.2 ml, 70%) in 10 ml of ether. The reaction mixture was poured into 300 ml of water, was added 0.7 ml of CH_3COOH and 10 ml of CHCl_3 , and the mixture was stirred for 30 min, and again was added 50 ml of CHCl_3 . The organic layer was separated, washed with saturated aqueous NaHCO_3 , and dried on MgSO_4 . The drying agent was filtered off, the solvent was distilled off. We obtained 0.3 g (99%) of compound **III** mp 87–89°C, published data for ambroxide (**III**) [5]: mp 84–85°C (from ethanol). $[\alpha]_D^{20}$ -5.1° (*c*

2.6, $\text{C}_2\text{H}_5\text{OH}$). IR spectrum (ν , cm^{-1}): 1080, 1120, 1650. ^1H NMR spectrum (CDCl_3 , δ , ppm): 0.64–2.53 m (14H, CH, CH_2), 0.78 s (3H, CH_3C^{10}), 0.84 s (3H, $\alpha\text{-CH}_3\text{C}^4$), 0.97 s (3H, $\beta\text{-CH}_3\text{C}^4$), 1.20 s (3H, CH_3C^8), 4.62 m (1H, $\text{HC}^{12}=\text{C}^{13}$), 6.12 m (1H, $\text{HC}^{13}=\text{C}^{12}$). Mass spectrum, m/z (I_{rel} , %): 248 $[M]^+$ (30), 233 $[M-\text{CH}_3]^+$ (1.5), 230 $[M-\text{H}_2\text{O}]^+$ (1.2), 215 $[M-\text{CH}_3-\text{H}_2\text{O}]^+$ (1.4), 191 $[M-\text{C}_4\text{H}_9]^+$ (7), 95 $[\text{C}_6\text{H}_7\text{O}]^+$ (100).

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