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Liquid chromatographic isolation and structural elucidation of methoxymethylene dimethyl dodecatrienes catalytically synthesized from methanol and three moles of isoprene

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ABSTRACT

The palladium-catalysed reaction of isoprene with methanol yields methoxy dimethyl octadienes ("methoxy dimers") and dimers of isoprene. To obtain additional information about the mechanism of catalysis this paper is aimed at identifying the higher boiling side-products of this reaction. After distillation in high vacuum the residue of the reaction was separated by analytical and preparative reversed-phase and normal-phase high-performance liquid chromatography, yielding at least six compounds with the formula $C_{16}H_{28}O$ ("methoxy trimers") plus trimers and tetramers of isoprene, all proven by mass spectra. The structure of two methoxy trimers was elucidated by ^1H and ^{13}C NMR spectra. Up until now they have not been described in the literature and they show an unexpected position of the methoxy group.

INTRODUCTION

Palladium complex compounds catalyse the dimerization of isoprene in the presence of phosphines. Protic nucleophiles used as a co-catalyst can be added to the dimer with the elimination of one double bond. For example, in the presence of methanol and by means of palladium acetylacetonate and triphenylphosphine about 60% methoxy dimethyl octadienes (called methoxy dimers hereafter) plus isoprene dimers are obtained from isoprene at 80°C as well as at room temperature [1,2]. Isoprene is almost completely converted.

About 5 l of methoxy dimers per gram of palladium used can be obtained before the catalyst becomes ineffective [2]. 1-Methoxy-2,6-dimethyl-octa-2,7-diene (40%) and 1-methoxy-2,7-dimethyl-octa-2,7-diene (20%) are formed at room temperature [1]. Similar mixtures are obtained when using tri-*n*-butylphosphine [3,4]. In each case, however, the formation of higher boiling products was observed, which could not be analysed by gas chromatography up to 200°C [1,3,5].

The present paper is aimed at studying this higher boiling residue and answering the following questions:

(1) Do isoprene trimers form during the above catalysis?

(2) Does the reaction result in the formation of addition compounds of methanol to trimers of isoprene (called methoxy trimers hereafter, molecular empirical formula $C_{16}H_{28}O$)?

(3) What can be stated about the structure of these methoxy trimers?

Up until now only 1-methoxy-1-vinyl-1,5,9-tri-methyl-deca-4,8-diene [6], *i.e.*, nerolidole methyl ether, has been known beside 1-methoxy-3,7,11-trimethyl-dodeca-2,6,10-triene (farnesyl methyl ether), which is often mentioned in the literature.

EXPERIMENTAL

Reaction of isoprene with methanol for obtaining the starting mixture [1]

Under exclusion of oxygen and moisture 0.745 g of triphenylphosphine, 0.761 g of palladium acetyl-acetonate, 50 ml of isoprene and 80 ml of methanol were mixed and stirred. After allowing to stand at room temperature for 20 h in intervals of 2 h each, the following substances were added: two portions each of 150 ml of isoprene, one portion of 150 ml of isoprene and 100 ml of methanol, two portions each of 100 ml of isoprene and one portion of 70 ml of isoprene (total volumes 770 ml of isoprene and 180 ml of methanol, both free of moisture and oxygen and freshly distilled). After allowing to stand overnight and refluxing for 1 h, distillation yielded 381 g of methoxy dimers, b.p. 46–58°C at 270 Pa.

After taking two intermediate fractions at 58–95°C/270–470 Pa and 63–68°C/27–33 Pa, 7.45 g of crude mixture were obtained at 68–110°C/20–33 Pa. A 0.351-g amount of this high-vacuum distillate yielded 0.152 g of a mixture of methoxy trimers after the first liquid chromatographic group separation (see below). Therefore the yield of methoxy trimers is 0.53% relative to isoprene used. In repeated preparations the yields ranged from 0.5 to 2%.

Chemicals

Octadecyl silica gel for the preparative column was prepared according to ref. 7, but with the following modification: 61 g (0.176 mol) of *n*-octadecyl dimethyl chlorosilane (prepared from *n*-octadecyl magnesium bromide and dimethyldichlorosilane) were dissolved in 350 ml of *n*-hexane, and 50 ml of dry gaseous dimethylamine were introduced. After separation of the solid dimethylamine hydrochloride by filtration, the resulting solution was directly reacted (16 h at 50°C in hexane and 8 h at 80°C hexane-free) with 94.7 g of spherical ES silica gel (previously dried at 150°C for 30 h) from VEB Leuna Werke (particle size, d_p, 10 μm, 331 m^2/g; with 7.8 μmol SiOH/m^2 = 0.2445 mol SiOH). After

washing with toluene and methanol and drying *in vacuo* at 80°C, 123.5 g of octadecyl silica gel were obtained. Elementary analysis resulted in 17.55% carbon and 3.85% hydrogen. According to ref. 8, 3.64 μmol of octadecyl groups per m^2 can be calculated.

All eluents were purified and regenerated by means of fractional distillation using a Vigreux column. The mixtures of the eluents were prepared by weighing in the constituents and degassing the mixtures by ultrasound and *in vacuo*.

High-performance liquid chromatographic (HPLC) separations

The first group separation was made in a self-constructed apparatus by means of preparative reversed-phase (RP) chromatography. The apparatus consisted of an MC 300 micropump with a low-dead-volume filter and an L pump head (Mikrotechna, Prague, Czechoslovakia); PTFE tubing of 1.0 mm I.D. and 2.0 mm O.D. as an overpressure safety device; a manometer measuring up to 160 bar with a Bourdon tube —reconstructed to allow permanent passage of the eluent; a 1-m stainless-steel capillary of about 0.3 mm I.D. and 0.7 mm O.D.; a self-constructed six-way valve of stainless-steel and PTFE with a sample loop of 1.85 ml volume and about 1 mm I.D.; a self-constructed stainless-steel preparative column 400 × 22 mm I.D. (column A), filled with a slurry of the prepared octadecyl silica gel in 1,2-dichloroethane at about 200 bar by means of a Haskel pump (Haskel-Burbanks)[a] with a filling tube of 2000 × 22 mm I.D., an RIDK 101 differential refractometer (Laboratorni Přistroje, Prague, Czechoslovakia), the reference cell of which was passed by pure eluent by means of gravity flow, combined with a K201 recorder (VEB Carl Zeiss, Jena, Germany); and a 8300 Uvicord II UV detector (LKB, Sweden) with a 100-μl measuring cell (about 2.5 mm optical pathway), combined with an MK motor compensator (VEB Messgeraetewerk, Magdeburg, Germany).

Preparative samples were introduced into column A via the sample loop. All other injections were made directly into the column bed by means of the

stop-flow method. The fractions were collected manually.

In the following separations the MMC minipump with the 2 D pump head (Mikrotechna) was used and the Uvicord II UV detector was substituted by a Dukol UD UV detector (VEB Carl Zeiss). For recording the UV and refractive index (RI) signals the TZ 4620 line recorder (double line recorder) (Laboratorni Přistroje) was used.

The semipreparative separation of the methoxy trimer fraction from column A was carried out in a self-constructed column of 308 × 7.5 mm I.D. on LiChrospher SI 100 (Merck), d_p 10 μm (column B), filled in as a slurry in cyclohexanol at 200 bar using an SK 15 pump (Orlita, Giessen, Germany) and rinsing with n-heptane afterwards. This semipreparative separation was repeated 15 times. The fractions (1–3, Fig. 3) obtained in this way were separately rechromatographed in 5–8 portions of 2.5–5 μl after removing the eluent on a 15-cm Vigreux column and finally with a water jet pump.

The fractions were analysed in a self-constructed column 250 × 4 mm I.D. on RP-18 silica gel (Merck), d_p 10 μm (column C), and in a self-constructed column, 300 × 4.5 mm I.D., on LiChrospher SI 100, d_p 10 μm (column D), both being filled in as a slurry in cyclohexanol at about 250 bar and subsequently rinsed with methanol and heptane, respectively.

The dead volumes (V_0) were determined with deuterated methanol (CH_3O^2H) in methanol-containing eluents and with pentane in hexane-containing eluents (column A 90.1 ml, B 9.25 ml, C 1.93 ml, D 3.05 ml).

NMR

The ^1H and ^{13}C NMR spectra were recorded with a Varian XL-300 spectrometer in [^2H]chloroform solution. The δ values are referred to tetramethylsilane as standard. The assignments of the ^{13}C NMR signals to the primary, secondary, tertiary and quaternary carbon atoms were verified by means of the distortionless enhancement by polarisation transfer (DEPT) spectra [9].

RESULTS AND DISCUSSION

Using octadecyl silica gel (column A) and pure methanol a rapid group separation of the high-
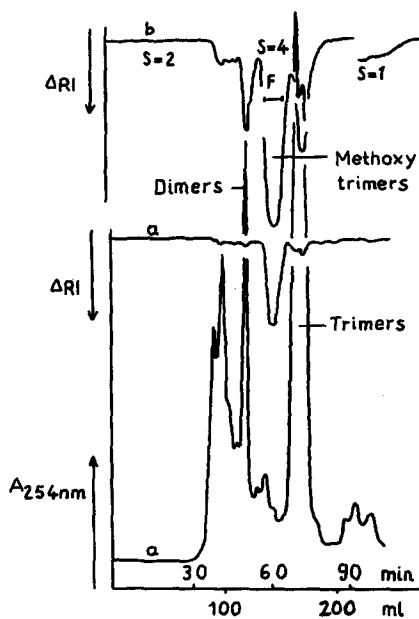

Fig. 1. Group separation of the high-vacuum distillate on 400 × 22 mm octadecyl silica gel (column A) in pure methanol. Pressure about 15 bar. (a) Sample of 40 μl. Detectors: RIDK 101, sensitivity 1, and Uvicord II. Injection into the column bed. (b) Sample of 500 μl + 500 μl of methanol. Detector: RIDK 101, sensitivity (S) 2, 4 and 1. Injection via sample loop. Retention volume of methoxy trimers 153 ml.
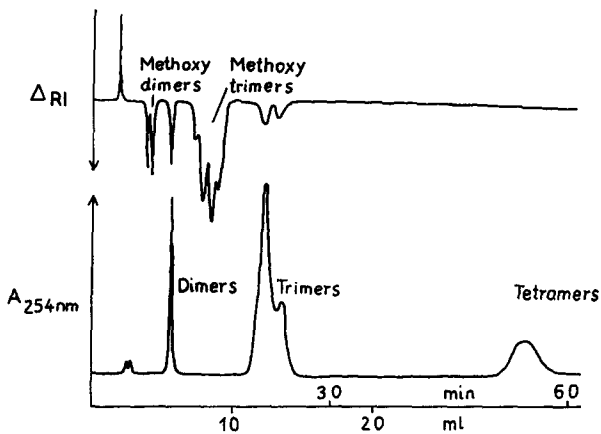

Fig. 2. Analytical separation of a synthetic mixture of appropriate amounts of methoxy dimers, methoxy trimers, dimers, trimers and tetramers of isoprene on 250 × 4 mm RP-18 silica gel (Merck), d_p 10 μm (column C), in methanol–water (85:15, w/w). Detectors: RIDK 101, sensitivity 1, and Dukol UD. Flow-rate 34.28 ml/h. Pressure about 20 bar.

vacuum distillate into dimers, methoxy trimers, trimers and tetramers of isoprene is possible (Fig. 1). At first the fractions were analysed on octadecyl silica gel (column C) with methanol–water (85:15, w/w) (Fig. 2).

The assignments of the peaks resulted from the molecular mass determined by mass spectrometry. It is advantageous that, unlike the methoxy compounds, the oligomers of isoprene contain a conjugated double bond and show intensive signals at 254 nm, while unlike the oligomers the methoxy compounds in the eluents employed show intensive signals in the differential refractometer.

As anticipated, the methoxy trimer fraction could be separated into distinct structural isomers more easily by adsorption chromatography than by RP chromatography. Therefore this fraction was first analytically separated on LiChrospher SI 100 with hexane–diethyl ether (99:1, w/w) (column D) and then preparatively (column B, Fig. 3).

Fractions 1, 2 and 3 (Fig. 3) were concentrated and then again purified on column B. Fraction 1 (compound I) could be shown to be a methoxy trimer (mass number 236) by mass spectrometry.

To elucidate the structure of compounds II (fraction 2) and III (fraction 3) the ^1H and ^{13}C NMR spectra were recorded. The interpretation of the ^1H spectra resulted in the following signal assignments:

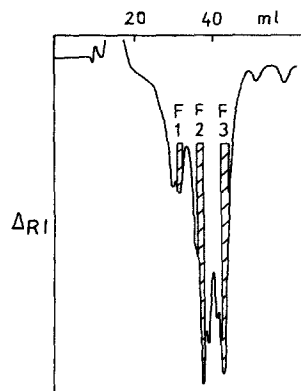Compound II: δ = 5.68 (m, 1 CH=); 5.40 (m,

1 CH=); 4.94 (m, 2 CH=); 4.69 (m, 2 CH=); 3.81 (s, 1 CH_2O); 3.21 (s, 1 CH_3O); 2.00 (m, 3 CH_2, 1 CH); 1.73 (s, 1 CH_3–C=); 1.52 (m, 1 CH_2); 1.35 (m, 1 CH_2); 0.98 (d, J = 6.5 Hz, 1 CH_3–CH=).

Compound III: δ = 5.93 (t, 1 CH=); 4.71 (m, 4 CH=); 3.81 (s, 1 CH_2O); 3.26 (s, 1 CH_3O); 2.01 (m, 4 CH_2); 1.71, 1.62 (2s, 2 CH_3–C=); 1.53 (m, 2 CH_2).

In the ^{13}C NMR spectra the following signals were found:

Compound II: δ = 145.8, 136.0 (2 C=); 144.7, 129.1 (2 CH=); 112.7, 109.9 (2 CH_2=); 76.9 (CH_2O); 57.4 (CH_3O); 37.5 (CH); 37.8, 36.6, 27.7, 26.3, 25.2 (5 CH_2); 22.4, 20.2 (2 CH_3).

Compound III: δ = 149.6, 145.9, 132.3 (3 C=); 128.2 (1 CH=); 109.9, 109.0 (2 CH_2=); 78.8 (CH_2O); 54.4 (CH_3O); 37.6, 35.8, 35.8, 27.7, 27.4, 25.9 (6 CH_2); 22.4, 13.8 (2 CH_3).

The NMR spectra of both substances prove the existence of the following structural elements:

Three C=C double bonds.

One CH_3–O–CH_2 group.

Five CH_2 groups (compound II), 6 CH_2 groups (compound III).

Two CH_3 groups.

In the case of II the structural element CH_3–CH– is unambiguously present.

On principle, several isomeric structures must be taken into consideration regarding the possible course of the reaction. From the NMR data, especially the ^{13}C chemical shifts, the structures in Fig. 4 can be assumed to be most likely for compounds II and III.

The ^{13}C chemical shifts of the olefinic carbon atoms are especially representative of the elucidation of the structure. By comparison with literature data of compounds containing similar structural
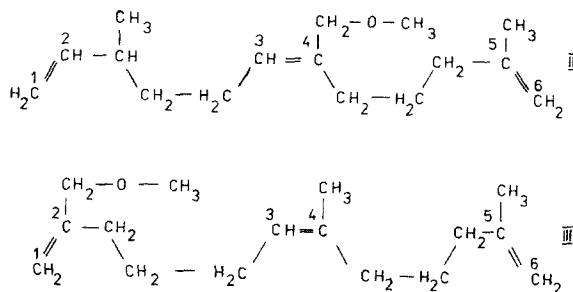

Fig. 3. Preparative separation of 25 μl of the fraction of methoxy trimers of Fig. 1 on a 308 × 7.5 mm LiChrospher SI 100 column (Merck), d_p 10 μm (column B), in hexane–diethyl ether (99:1, w/w). Detector: RIDK 101, sensitivity 4. Flow-rate 119.7 ml/h. Pressure about 18 bar. [F1, capacity factor (k') = 2.45; F2, k' = 3.0; F3, k' = 3.7].

Fig. 4. Proposed structures for compounds II and III.

TABLE I

ASSIGNMENTS OF THE ^{13}C NMR SIGNALS TO THE OLEFINIC CARBON ATOMS

	C-1	C-2	C-3	C-4	C-5	C-6
II	109.9	144.7	129.1	136.0	145.8	109.0
III	109.9	149.6	128.2	132.3	145.9	109.0

elements [10,11], an assignment of the signals can be made as shown in Table I.

The proposed structures for II and III are also in accordance with the elution behaviour of both substances, because III, with the methoxyl at the end-position, should be more strongly retained on a polar stationary phase than II. It should be pointed out that, beside the structures given here, one alternative structure for both II and III is also possible, in which the substituents at the central double bond (CH_3OCH_2 in II, CH_3 in III) would be positioned at carbon-3. It should be difficult to distinguish between them.

These data support the idea that all substances eluted between fractions 1, 2 and 3 (Fig. 3) are also methoxy trimers. This leads to the conclusion that in the above-mentioned reaction at least six different methoxy trimers with the formula $C_{16}H_{28}O$ (including Z–E isomers) are formed beside dimers, trimers and tetramers of isoprene and methoxy dimers. The position of the methoxy group is unexpected and important for elucidating the mechanism of the catalysis.

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