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# 241. Geijerone (3-Isopropenyl-4-methyl-4-vinylcyclohexanone), a New, Naturally Occurring $C_{12}$ Terpenoid

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(28. VIII. 72)

*Summary.* In the essential oil of *Juniperus communis* L. (fruit), the title compound (*trans*-isomer) has been identified; its structure being confirmed by synthesis from elemol. The optical rotation of the natural compound was nearly the same as the synthetic sample, suggesting that it is not an artefact formed from a ten-membered ring precursor during the isolation.

In the course of an analysis of the essential oil of *Juniperus communis* L.[1]), a ketone, $C_{12}H_{18}O$, was isolated from the fraction with bp 81–86°/0.1 mm Torr, by combined chromatography on silica gel and gas chromatography (glpc.). The NMR.-spectrum of this ketone showed the typical signals for the *trans*-1-vinyl-2-isopropenyl-2-methyl structure associated with the elemenes and elemol[2]) and treatment with deuterium oxide under basic conditions [3] revealed the presence of four protons adjacent to the carbonyl group. There were thus two structures possible (not considering the stereochemistry), one of which (**1**) has already been described [4] [5]. Direct comparison of **1**, prepared from germacrone (**2**) [4], with the natural ketone showed them to be different, so there was a strong presumption that the new compound was represented by **3**.

It was found that elemol (**4**) is cleanly dehydrated to a mixture of $\beta$- (**5**) and $\gamma$-elemene (**6**) by phosphorus oxychloride in pyridine (pyrolysis of various esters is known to give complex mixtures [5]), and the two hydrocarbons can be separated by careful distillation. Epoxidation of $\gamma$-elemene (**6**) gave a mixture of two epoxides (**7a**, **7b**) which were separately characterized, but not separated for the next step. Treatment of the epoxides with dilute sulfuric acid in dioxan led to a mixture of glycols (**8**) that was converted to the desired ketone (**3**) with periodic acid. Treatment of the epoxide mixture (**7**) with periodic acid in aqueous dioxan also led directly to the ketone (**3**), for which the name '*geijerone*' is proposed.

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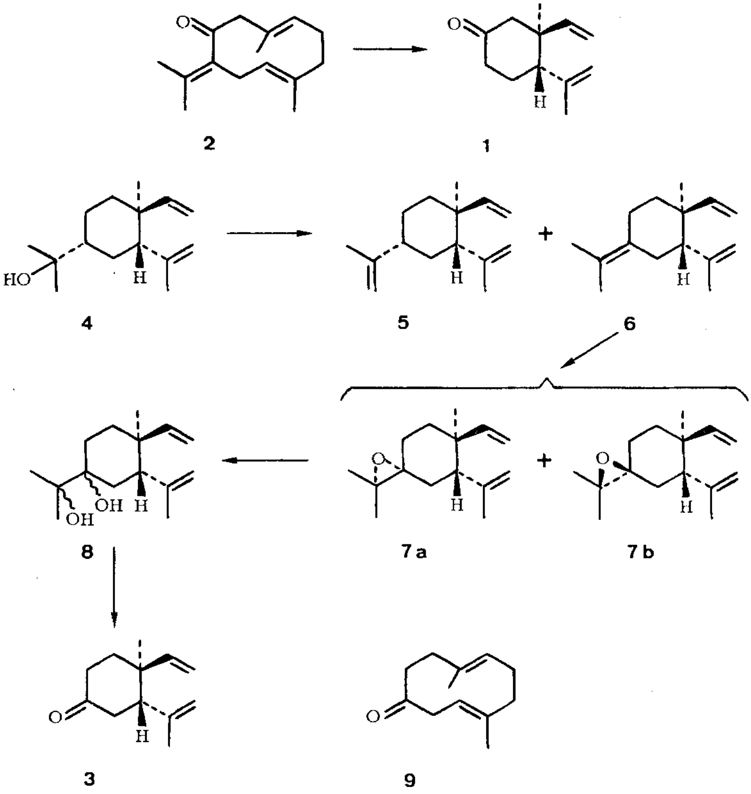
[1]) Other compounds recently isolated from the same sample of oil have been described [1].
[2]) *cf. e.g.* [2].

The product synthesized from elemol (**4**) had $[\alpha]_D^{20} = -26.7°$, while the natural ketone (**3**) had $[\alpha]_D^{20} = -27.8°$. It is often supposed that natural products of the elemol type are artefacts arising from 10-membered ring compounds, elemol from hedycaryol [6], geijerene from pregeijerene [7], δ-elemene from germacrene-C [8], and so on. In the present case, '*pregeijerone*' (**9**) has no asymmetric carbon atom, any chirality it might have being due only to the helicity of the double bonds. It seems unlikely that chirality of this kind would be more resistant to racemization than the cyclodecadiene to a thermal *Cope* reaction[3]), i.e. we would expect the geijerone to be racemic if it is formed during its isolation from a pregeijerone. The fact that it is optically active is evidence that it is either formed enzymically as such, or that it is an artefact formed in a different way from the other elemol-like compounds[4]).



## Experimental part

Conditions for the measurements of spectra and for glpc. are as given previously [1]. Distillations were carried out by following a first, rapid distillation with a careful fractionation on a *Nester-Faust* Auto-annular spinning band column.

*Isolation of* geijerone (**3**) *from* J. communis *oil.* Of the crude material, about 5% had bp. 81–86°/0.1 Torr. Chromatography of 125 g of this fraction on silica gel resulted in the elution of

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[3]) It is significant that germacrone (**2**) is a racemate.

[4]) The formation of $C_{12}$ terpenoids is discussed in a recent paper from these laboratories, describing the isolation of another $C_{12}$ ketone from vetiver oil [9].

110 g of a mixture of hydrocarbons (migrating with the solvent front on thin-layer chromatography (tlc.) in hexane/ether 8:2). Increasing the polarity of the solvent through benzene to ether resulted in elution of a fraction (1.2 g) that was very complex, but in which the major component was identified as geranyl acetate. With a Carbowax column, glpc. allowed the latter to be separated first, followed by the substance subsequently identified as geijerone, then 2-(*p*-methylphenyl)-propyl acetate. The geijerone was purified by a second passage over an Apiezon column at 150°, and then had $[\alpha]_D^{20} = -27.8°$ ($c = 12.5\%$, $CCl_4$). On tlc, geijerone does not give a readily visible colour with either phosphomolybdic acid or with anisaldehyde. The spot can be developed with a spray of 2,4-dinitrophenylhydrazine (1% in dilute hydrochloric acid), followed by a second spray of phosphomolybdic acid, when, on warming, a yellow spot on a blue background is obtained.

NMR.-spectrum: 1.17 (3H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.73 (3H, broad *s*, $CH_3\text{—}\overset{|}{C}{=}$), 4.62, 4.8–4.95, 5.05–5.2 (4H, *m*, $\overset{|}{\underset{|}{C}}{=}CH_2$ and $\text{—}CH{=}CH_2$), 5.87 (1H, $d \times d$, $J = 10$ and 17.5 Hz, $\text{—}CH{=}CH_2$). MS.: *m/e* (% rel. abundance): 68 (100), 67 (48), 41 (19), 69 (14), 82 (21), 39, 53, 101 (18), 27 (14), 97 (12), 55, 81, 122 (11), 178 ($M^{+\cdot}$, 2.5). After base-catalyzed exchange with deuterium oxide [3], the main fragment was at *m/e* 69, and the molecular ion at *m/e* 182.

*Dehydration of elemol.* A solution of 222 g (1 mol) of elemol (distilled, purity about 95% by glpc.) in 185 g of pyridine was treated dropwise with 169 g of distilled phosphorus oxychloride. The temperature was allowed to rise to 40–50°, and after the introduction was complete (40 min), the mixture was stirred for 3 h then poured onto about 1 kg ice. Extraction in ether, acid then sodium carbonate and water washing, gave after concentration, 192 g of crude material. After double distillation, 44 g of β-elemene (bp. 42°/0.01 Torr) and 51 g of γ-elemene (bp. 44°/0.01 Torr) were obtained in purities of over 99%. The spectra corresponded with those of ref. [5].

*Epoxidation of γ-elemene.* A suspension of 45 g of γ-elemene and 20.6 g of anhydrous sodium acetate in 500 ml of dichloromethane was treated dropwise with 1.1 equivalents of peracetic acid in acetic acid at 0°. After the end of the addition (30 min), the mixture was stirred for 3 h at room temperature. Workup as usual yielded 48 g of crude epoxides, bp. 57–59/0.01 Torr. For analysis, a small amount was purified by glpc. Two substances were characterized: *peak 1*, corresponding to **7b**. NMR.-spectrum: 1.07 (3H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.29 (6H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.69 (3H, narrow *m*, $CH_3\text{—}\overset{|}{C}{=}$), 2.00 (1H, *m*, $C{=}C\text{—}\overset{|}{\underset{|}{C}}\text{—}H$). The structure is assigned on the basis of the latter signal, arising from the proton on the carbon carrying the isopropenyl group, being at higher field *i.e.* away from the epoxide oxygen atom than in **7a**. The methyl group on the carbon carrying the vinyl group is, correspondingly, at lower field; *peak 2*, corresponding to **7a**. NMR.-spectrum: 1.01 (3H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.25 (6H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.71 (3H, narrow *m*, $CH_3\text{—}\overset{|}{C}{=}$), 2.13 (1H, *m*, $C{=}C\text{—}\overset{|}{\underset{|}{C}}\text{—}H$). In both compounds the following signals are present: 4.5–4.65, 4.7–4.85, 4.9–5.05 (4H, *m*, $>C{=}CH_2$ and $\text{—}CH{=}CH_2$), 5.75 (1H, $d \times d$, $J = 10$ and 17.5 Hz, $\text{—}CH{=}CH_2$).

The mass spectra of the two isomers were identical: 79 (100), 93 (87), 41 (79), 91 (73), 105 (67), 119 (55), 43, 107 (49), 81 (47), 67, 147 (46), many other fragments, including 205 (6), 220 ($M^{+\cdot}$, <1).

$C_{15}H_{24}O$ Calc. C 81,76 H 10.98% Found C 81.30 H 11.05%

*1-(2-Hydroxypropyl(-2)-3-isopropenyl-4-methyl-4-*trans*-vinylcyclohexanol.* A solution of 0.57 g of the epoxide mixture in 8 ml of tetrahydrofuran and 10 ml of water containing 2.6 g of concentrated sulfuric acid was stirred for one hr. The product was purified by chromatography on silica gel in ether/hexane 6:4.

NMR.-spectrum: 0.93 (3H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.21 (6H, *s*, $CH_3\text{—}\overset{|}{C}\text{—}$), 1.70 (3H, broad *s*, $CH_3\text{—}\overset{|}{C}{=}$), 4.5–4.6, 4.65–4.85, 4.9–5.05 (4H, *m*, $>C{=}CH_2$ and $\text{—}\overset{|}{C}H{=}CH_2$), 5.75 (1H, $d \times d$, $J = 10$ and 17.5 Hz, $\text{—}CH{=}CH_2$). MS.: 43 (100), 41 (47), 55 (38), 29, 69 (29), 70 (24), 27, 93, 179 $(M-59)^+$ (21), 161 (15).

*Geijerone.* A solution of 193 g γ-elemene epoxides in 1000 ml of tetrahydrofuran was added over 20 min to a stirred solution of 200 g of periodic acid in 2400 ml of tetrahydrofuran and 1600 ml of water. After stirring for 5 h, the mixture was extracted with petroleum ether (bp. 30–50°) and the extract washed with a saturated solution of sodium thiosulfate then with water. Concentration gave 124 g of material distilling with bp. 54–60°/0.001 Torr. After shaking this material with a saturated solution of sodium bisulfite, the solid bisulfite derivative of geijerone was removed by filtration; geijerone was recovered by heating the bisulfite compound with 20% sodium carbonate solution. Pure geijerone has bp. 57°/0.01 Torr, $[\alpha]_D^{20} = -26.7°$ ($c = 13.5$, $CCl_4$). NMR. and MS. were identical with those described for the natural product.

$C_{12}H_{18}O$ Calc. C 80.85 H 10.18% Found C 80.41 H 10.22%

Semicarbazone, m.p. 205–207° (dec.).

$C_{13}H_{21}N_3O$ Calc. N 17.86% Found N 18.07%

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# 242. Eine verbesserte Synthese von Chinuclidin-4-carbonsäure

Chinuclidinreihe, 10. Mitteilung

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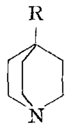
Institut für Organische Chemie der Universität Basel

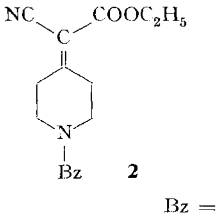
(7. VIII. 72)

*Summary.* An improved synthesis of 4-carbethoxyquinuclidine from 1-benzyl-4-piperidone is described.

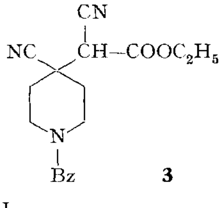
Für eine Untersuchung, über welche gesondert berichtet wird [1], wurde eine grössere Anzahl von 4-substituierten Chinuclidinen **1** benötigt. Für die Herstellung dieser Verbindungen schien Chinuclidin-4-carbonsäure-äthylester (**1a**), dessen Syn-



**1a**) R = $COOC_2H_5$
**b**) R = COOH

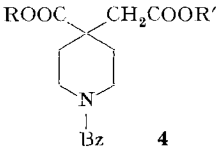


**2**



**3**

Bz = $C_6H_5CH_2$



**4**

**a**) R = R′ = H
**b**) R = R′ = $C_2H_5$
**c**) R = H, R′ = $C_2H_5$
**d**) R = H, R′ = $(CH_3)_2CH$
**e**) R = $(CH_3)_2CH$, R′ = H