181. 1,4-Dimethylcyclohex-3-enyl Methyl Ketone, a Monoterpenoid with a Novel Skeleton

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Dedicated to Professor *Edgar Lederer* on the occasion of his 65th birthday

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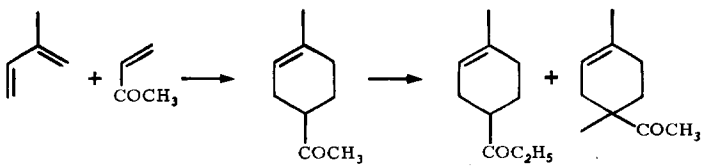
Summary. 1,4-Dimethylcyclohex-3-enyl methyl ketone (**1**) has been isolated from the oil of *Juniperus communis* L. (fruit). This is the first reported occurrence of this skeleton in nature. A curious effect on the NMR.-spectrum of the compound (**1**) by the shift agent, $Eu(fod)_3$, is described.

Earlier publications [1] [2] have described the isolation from the fruit oil of *Juniperus communis* L., of the first reported naturally occurring derivatives of the 2,2,3-trimethyl-1-ethylcyclopentane skeleton (campholenyl), and an unusual C_{12} terpenoid. The present paper describes the isolation of another novel monoterpenoid, derived from the skeleton of 1,4-dimethyl-1-ethylcyclohexane, as yet unreported in nature (*cf.* [3]).

The title substance was isolated from the same distillation fraction of the crude oil as was campholenic aldehyde [1]. After the aldehyde and less polar substances had been removed by chromatography on silica gel, a fraction was obtained that consisted of linalool, camphor, pinocamphone, and the new substance. The latter was purified by gas chromatography (GLPC.) on two columns.

The formula **1**, or the formula of the isomeric 1,2-dimethylcyclohex-2-enyl methyl ketone, was attributed to this new substance on the basis of the NMR.-spectrum. This showed the presence of a quaternary methyl group, a methyl ketone, and a methyl group on a trisubstituted double bond (see experimental part). That the quaternary methyl group was attached to the same carbon atom as the methyl ketone was shown by basecatalyzed exchange with deuterium oxide [4], when only 3 protons were exchanged. Finally, the compound was shown to be **1** by synthesis, when the synthetic substance was identical both spectrally and in retention time with the natural material.



2 **3** **1**

A curious fact of the NMR.-spectrum of ketone **1** was observed when $Eu(fod)_3$ [5] was added to the solution. The spectrum was quite normal before, but there now appeared two signals where there had been only one (this was particularly noticeable

in the case of the methyl groups). At first it was believed that this was due to an impurity, but chromatography on a capillary column failed to reveal any impurity, and the two signals coalesced at higher temperatures, the value depending to some extent on the amount of the shift agent added, but generally being around 30–40°. One explanation is that the barrier to ring inversion is markedly raised in the case of the europium complex, this property having already been described in the case of a tetramethylcyclononanone [6], although this seems unlikely for a simple cyclohexane. Another possibility is that two types of complex with the europium atom are present, although the nature of these cannot yet be stated[1]).

The synthesis of **1** was straightforward; isoprene was allowed to react in a sealed tube with but-3-en-2-one to yield 4-methylcyclohex-3-enyl methyl ketone (**2**) [7], which was methylated with methyl iodide and potassium *t*-butoxide in *t*-butanol. This reaction led to the ethyl ketone **3** as the main product [8], but 18% of the desired ketone **1** was also obtained.

The ketone **1** could arise biogenetically in two ways. Formally, it is a cyclized artemisia skeleton, but it could also be formed by biological methylation of the enol from ketone **2**[3]), a compound also occurring in the oil of *J. communis*, as, indeed, does the fully oxidized *p*-methylacetophenone [10].

Experimental Part

Details of apparatus and techniques have already been described [1].

Isolation of naturally occurring material. The isolation of the fraction having b.p. 82–89°/10 Torr has been described [1]. After the fraction containing campholenic aldehyde had been eluted from a column of silica gel with benzene/chloroform 1:1, the next fraction, in order of increasing polarity, was shown by GLPC. (Carbowax) to be mainly linalool, camphor, pinocamphone, and the new substance. The latter contained a small amount of impurity that was removed by GLPC on OV 17. $[\alpha]_D^{20} = +2.1°$ (c = 1% in CCl_4)[4]). NMR.-spectrum: 1.13 (3H, *s*, CH_3—C<); 1.66 (3H, broad *s*, CH_3—C=); 2.15 (3H, *s*, CH_3CO); 5.37 (1H, broad, —CH=C<). Mass spectrum, *m/e* (% relative abundance): 109 (100), 43 (60), 67 (51), 137 (24), 41 (21), 95 (20), 55, 81, & 152 (M^+) (16). Shaking with dioxan/D_2O/NaOD [4] caused the molecular ion to be displaced to *m/e* 155.

4-Methylcyclohex-3-enyl methyl ketone (**2**) [7]. A mixture of 34 g of isoprene and 35 g of methyl vinyl ketone was heated in a sealed tube at 80° for one h, and the product distilled, b.p. 82°/10 Torr. NMR.-spectrum: 1.63 (3H, broad *s*, CH_3—C(=)—CH—); 2.08 (3H, *s*, CH_3CO—), 5.35 (1H, width ca. 13 Hz, —CH=C<). Mass spectrum: 95 (100), 43 (77), 138 (M^+, 62), 67 (48), 123 (38), 55 (29), 79 (26), 39 & 41 (23).

Methylation of 4-Methylcyclohex-3-enyl methyl ketone. To a solution of 2.4 g of potassium dissolved in 30 ml of dry *t*-butanol were added 5 g of 1-acetyl-4-methyl-cyclohex-3-ene (**2**). After 15 min., the mixture was cooled to 10° while 10.5 g of methyl iodide were added. The mixture was slowly warmed to reflux, and a little more methyl iodide was added until the mixture was neutral. The mixture was filtered, concentrated at reduced pressure, and the residue taken up in ether. Washing, *etc.*, yielded material with b.p. 82–84°/10 Torr, GLPC. (silicone oil) showing that there was nearly 50% of unchanged starting material present, together with two other substances. The mixture was resolved by preparative GLPC. on Carbowax, the substances being eluted as follows:

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[1]) The possibility of another type of complex other than the pseudo-contact model generally considered was discussed privately with Professor *E. Wenkert.*

[2]) *e.g.* [7], although there are certainly many other descriptions of this reaction in the literature.

[3]) Biological C-methylation has been extensively discussed by *Lederer, cf.* [9].

[4]) This determination is not adequate to attribute asymmetry to the natural substance.

1,4-Dimethylcyclohex-3-enyl methyl ketone (**1**), 18%. NMR.- and mass spectra were identical with those of the natural product.

$C_{10}H_{16}O$ Calc. C 78.89 H 10.59% Found C 78.32 H 10.82%

Semicarbazone, m.p. 146–148°.

$C_{11}H_{19}N_3O$ Calc. C 63.12 H 9.15 N 20.08% Found C 63.50 H 9.06 N 20.08%

4-Methylcyclohex-3-enyl methyl ketone (**2**), 50%.

4-Methylcyclohex-3-enyl ethyl ketone (**3**), 32%. NMR.-spectrum: 1.00 (3H, *t*, $J = 7$ Hz, CH_3CH_2—), 1.64 (3H, broad *s*, CH_3—C(I)=CH—), 2.43 (2H, *q*, $J = 7$ Hz, CH_3—CH_2CO—), 5.35 (1H, width ca. 15 Hz, —CH=C<). Mass spectrum: 95 (100), 123 (70), 57 (59), 29 (37), 67 (35), 152 (M^+, 33), 55 (22), 41 & 27 (20), 99 (18).

$C_{10}H_{16}O$ Calc. C 78.89 H 10.59% Found C 78.22 H 10.48%

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182. Utilisation d'ylides du phosphore en chimie des sucres. XVIII[1]) Synthèse de furannoses à insaturation conjuguée.

Communication préliminaire[2])

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Summary. Several sugars with conjugated unsaturation (dienes or α,β-unsaturated carbonyl compounds) have been synthesised by use of *Wittig* reactions. Keto-sugars bearing a carbonyl group α to a furanose ring are prone to undergo an elimination leading to conjugated unsaturated systems. This constitutes a novel kind of side-reaction in the application of *Wittig* reactions to carbonyl sugars. The synthesis of a new kind of acetylenic sugar is also described.

L'introduction d'une insaturation conjuguée dans une molécule de sucre présente un grand intérêt du fait des nombreuses possibilités synthétiques qu'offrent les systèmes ainsi obtenus. Parmi ces motifs structuraux, le plus fréquemment rencontré

[1]) XVII communication, v. [1].

[2]) Une communication plus détaillée paraîtra ultérieurement.