

New compounds with small rings in essential oils

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Despite the continuing discovery of new synthetic fragrance raw materials, essential oils still remain the other half of the foundation of perfumery. Consequently, the analysis of essential oils is still very much of interest, as is illustrated by the excellent series of articles by Lawrence in this journal. We now wish to report a number of products containing small (three-, four-, and five-membered) rings, most of which are found for the first time in essential oils. These products were isolated by chemical group separation, liquid and gas chromatography, whereupon the structures were determined by mass, infrared and NMR spectroscopy. All structures were confirmed by synthesis. The essential oils used were obtained from regular commercial sources.

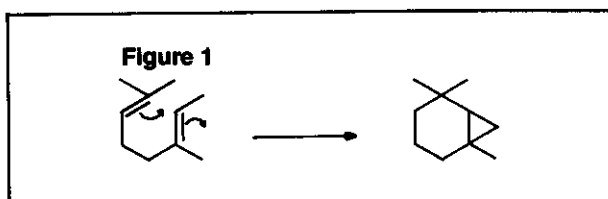
Cyclopropane derivatives

Two homologous acetates were found in ambrette seed oil, which were identified as 1-(2-acetoxyethyl)-2-hexylcyclopropane (I) and 1-(4-acetoxybutyl)-2-hexylcyclopropane (II) (see Table I).

Although three-member ring compounds with a terpenoid skeleton (e.g., chrysanthemum acid, thujane and carane derivatives) are not uncommon in essential oils, only a few cyclopropane derivatives with straight chain substituents were found. One example is cascarillic acid (III), a constituent of cascarilla oil,¹⁻³ another, 2-pentylcyclopropane carboxylic acid (IV), which we recently reported to occur in patchouli oil.⁴ Longer chain cyclopropane carboxylic acids are found in bacteria as a part of phospholipid molecules or as triglycerides.⁵ The biosynthesis of these compounds involves the methylation of unsaturated fatty acids by S-adenosyl-L-methionine,⁵ and probably the ambrette acetates are formed by a similar pathway.

The syntheses of the ambrette acetates (I and II) was performed by a well established method: Simmons-Smith reaction on 3-decenol and 5-dodecenol, respectively, followed by esterification with acetic anhydride.³

Another type of cyclopropanoid compounds are those with a hitherto unknown terpenoid skeleton, 7-acetoxy-1,1,5-trimethylbicyclo[4.1.0]heptane (V, found in cistus oil) and 1,1,5-trimethylbicyclo[4.1.0]heptane-7-carboxylic acid (VI, found in labdanum oil). Formally this skeleton can be derived from the geranyl ion (or its pyrophosphate, the key intermediate in the biosynthesis of monoterpenes) by two cyclizations as shown in figure 1. Possibly these compounds are really formed in this way, although other pathways such as alkylation cannot be excluded.



The route by which we prepared these compounds is shown in figure 2. In this route the key intermediate is the cyclohexene VII, which we prepared from the Naarden fragrance raw material ethyl safranate (ethyl dehydrocyclogeraniate, a mixture of double bond isomers, VIII). Hydrogenation followed by hydrolysis and decarboxylation afforded the desired 1,1,3-trimethylcyclohexene (VII) in an overall yield of 60%.

Reaction of the alkene with ethyl diazoacetate followed by hydrolysis gave the labdanum com-

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pound VI.

Synthesis of the cistus compound V could be effected by reaction of VII with dibromocarbene to the dibromo derivative IX, from which one bromo atom could be removed selectively by reduction with tri-n-butyltinhydride.⁶ Air oxidation of the lithium compound afforded the alcohol, which was esterified with acetylchloride.

A more common cyclopropanoid terpenoid skeleton is found in the thujane derivatives X and XI. 10-Thujanic acid (X) was reported to be a constituent of olibanum oil,⁷ which could be

confirmed. We also found this acid in the oil of juniper berries and in carrot seed oil. 10-Thujanic aldehyde (XI) had up to now only been known as a synthetic material;^{8,9} we could prove its presence in the oil of juniper berries.

Cyclobutane derivatives

In Table I some four membered ring compounds are shown (XII-XIV), which have been known since the beginning of this century as synthetic degradation products of α -pinene. Pinonic acid (XIIa) was described for the first

Table I

No.	Name	Structure	Occurence (lit.)
I	1-(2-acetoxyethyl)-2-hexylcyclopropane		Ambrette seed oil
II	1-(4-acetoxybutyl)-2-hexylcyclopropane		Ambrette seed oil
III	2-hexylcyclopropane acetic acid (cascarilic acid)		Cascarilla oil (1,2,3)
IV	2-pentylcyclopropane carboxylic acid		Patchouli oil (4)
V	7-Acetoxy-1,5,5-trimethyl bicyclo (4.1.0.)heptane		Cistus oil
VI	1,5,5-trimethylbicyclo (4.1.0.)heptane-7-carboxylic acid		Labdanum oil
X	10-thujanic acid		Olibanum oil (7); carrot seed oil; juniper berry
XI	10-thujanic aldehyde		Juniper berry
XIIa	pinonic acid		Hyssop oil (11)
XIIb	methyl pinonate		Hyssop oil (11)
XIIc	ethyl pinonate		Labdanum oil
XIII	pinic acid		Spike lavender oil
XIV	pinonic aldehyde		Spike lavender oil

time by Tiemann.¹⁰ Recently this acid and its methyl ester (XIb) were found to be constituents of hyssop oil.¹¹ We can now prove the presence of the ethyl ester in labdanum oil.

Pinic acid (XIII) was encountered in spike lavender oil; this odourless dicarboxylic acid has been known since 1907.¹² Pinonic aldehyde (XIV) has been mentioned several times as having an agreeable odour¹³⁻¹⁵; we now found this material also in spike lavender oil. All these compounds were synthesized according to well-established methods.^{10,12,13}

Cyclopentane derivatives

In Table I three types of five membered ring compounds are shown. They have a camphonane skeleton (XV-XVII), an α -campholene skeleton (XXI-XXV), or a γ -campholene skeleton (XXVI-XXVIII).

Camphonanic acid (XV) has been known for a long time as a synthetic degradation product of camphor. It is also formed upon ozonolysis of the sesquiterpene cuparene.^{16,17} Although it has been reported to occur in the acidic fraction of a

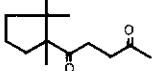
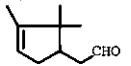
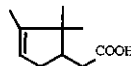
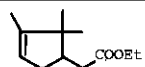
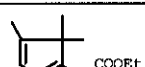
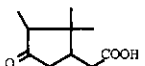
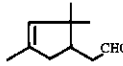
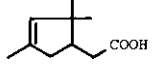
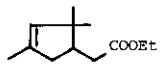
XV	Camphonanic acid		Labdanum oil
XVI	1-acetyl-1,2,2-trimethylcyclopentane		Labdanum oil
XVII	1-(1,2,2-trimethylcyclopentyl)-1,4-pentandione		Labdanum oil
XXI	α -campholenic aldehyde		Juniper berry (22), lavandin oil (23), labdanum oil, spike lavender oil
XXII	α -campholenic acid		Olibanum oil (4,7), cistus oil (24), labdanum oil, spike lavender oil, calamus oil, rosemary oil, coriander seed oil, Juniper berry, carrot seed oil, parsley seed oil, cardamome oil.
XXIII	ethyl α -campholenate		Labdanum oil
XXIV	ethyl dehydro- α -campholenate		Labdanum oil
XXV	2,2,3-trimethyl-4-oxocyclopentane acetic acid		Spike lavender oil
XXVI	γ -campholenic aldehyde		Labdanum oil, juniper berry
XXVII	γ -campholenic acid		Olibanum oil (4,7), cistus oil (24), labdanum oil, spike lavender oil, carrot seed oil, rosemary oil, coriander oil, juniper berry dill oil, parsley seed oil
XXVIII	ethyl γ -campholenate		Labdanum oil

Figure 2

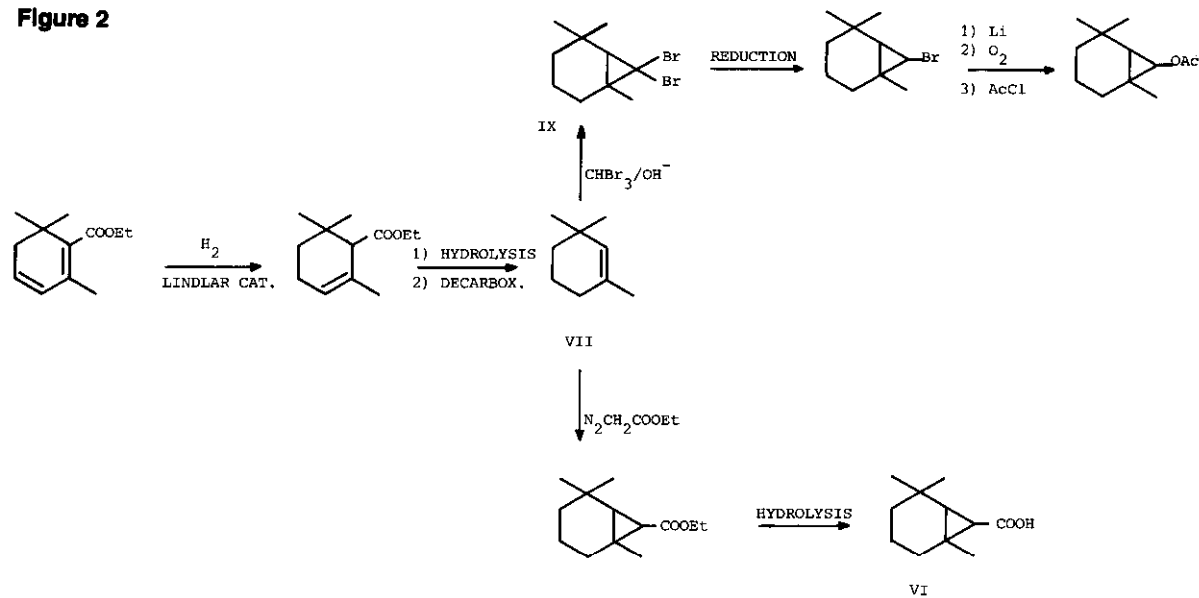


Figure 3

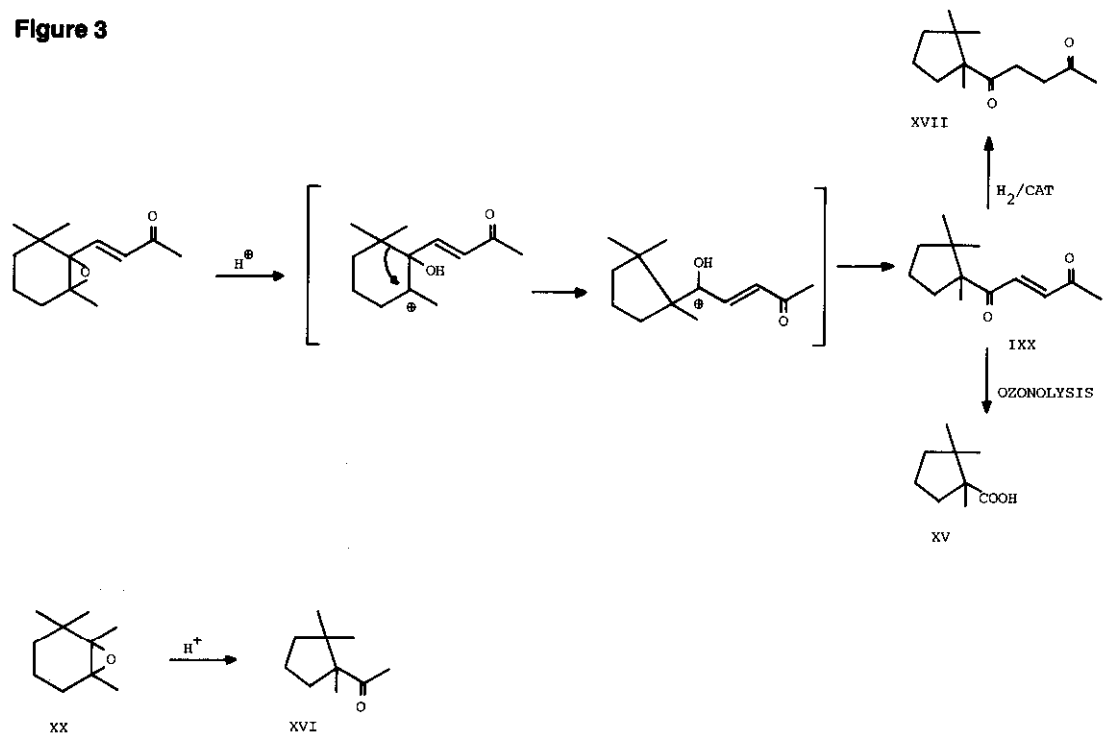
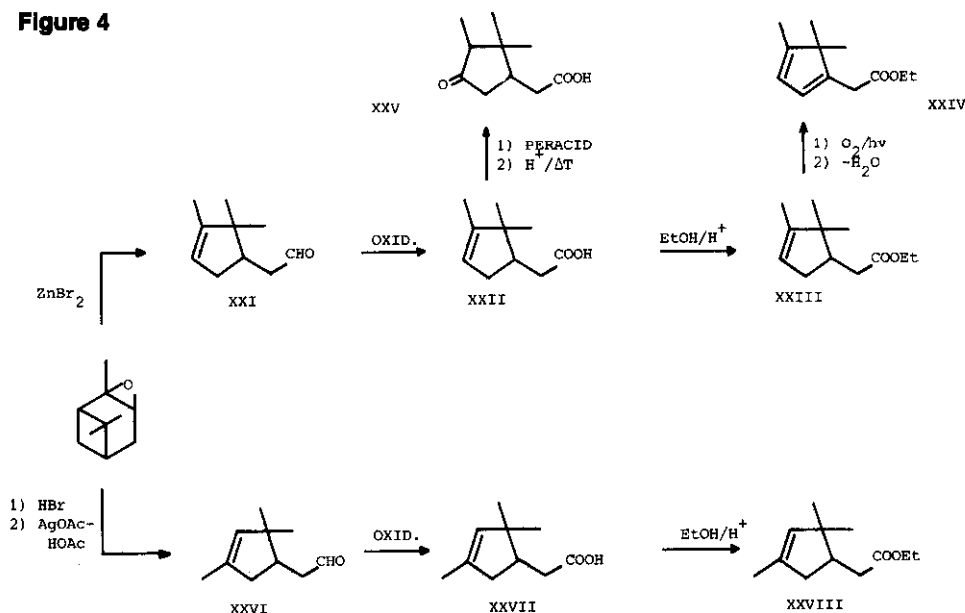


Figure 4



Californian gasoline distillate,¹⁸ this is the first time camphonan acid has been reported as being present in an essential oil—labdanum oil. Apart from camphonan acid we also found in labdanum oil the related compounds XVI (1-acetyl-1,2,2-trimethylcyclopentane) and XVII (1-(1,2,2-trimethylcyclopentyl)-1,4-pentanedione).

The diketone XVII has been described in connection with the acidic rearrangement of β -ionone epoxide.¹⁹ Initially, this rearrangement affords the unsaturated diketone IXX (see fig. 3). However, when protic acids such as p-toluene sulphonic or formic acid are used the selectivity to IXX is very low.^{19,20} We found that when a Lewis acid, for example, boron trifluoride etherate, is used, a yield of 50-60% of IXX could be obtained. Hydrogenation gave the labdanum diketone XVII, whereas camphonan acid could be prepared by ozonolysis of IXX in a moderate yield (50%). This is, nevertheless, an improvement over the methods mentioned in the literature, such as the Hunsdiecker degradation of camphoric acid for which an overall yield of 2% is reported.^{18,21}

The monoketone XVI could be synthesized by rearrangement of the cyclohexane epoxide XX (yield: 50%), so this type of rearrangement of substituted cyclohexane epoxides seems to be rather general.

Some compounds with an α -campholene skeleton are reported to occur in essential oils.

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Table II

No.	Name	Odour
I	1-(2-acetoxyethyl)-2-hexylcyclopropane	Fatty, somewhat musty
II	1-(4-acetoxybutyl)-2-hexylcyclopropane	Rather weak, fatty
V	7-acetoxy-1,5,5-trimethylbicyclo(4.1.0)heptane	Sweet-floral
VI	1,5,5-trimethylbicyclo(4.1.0)heptane-7-carboxylic acid	Rather weak, somewhat hay-like
XI	10-Thujanic aldehyde	Green, resembles Ligustral (Naarden Int.), some cumini notes
XIIc	Ethyl pinonate	Woody, fruity
XV	Camphanic acid	Very weak, somewhat fruity
XVI	1-acetyl-1,2,2-trimethyl cyclopentane	Camphoraceous, borneol-like
XVII	1-(1,2,2-trimethylcyclopentyl)-1,4-pentandione	Woody, dusty with fruity notes
XXIII	Ethyl α -campholenate	Fruity, fresh
XXIV	Ethyl dehydro- α -campholenate	As No. XXIII but also with musty, herbal notes
XXV	2,2,3-trimethyl-4-oxo-cyclopentane acetic acid	Virtually odourless

α -Campholenic aldehyde (XXI) has been reported in juniper berries and lavandin oil^{22,23}; it was now found also in labdanum and spike lavender oil.

α -Campholenic acid (XXII) has been found in olibanum oil and in cistus oil.^{4,7,24} This acid seems to occur in all kinds of natural materials; we found it for instance in labdanum, spike lavender, calamus, rosemary, coriander, and juniper berry oil.

Next to these two compounds we could also prove the presence of ethyl α -campholenate (XXIII) and its dehydro derivative XXIV in labdanum oil, while in spike lavender oil the oxo acid XXV was found.

Of the compounds with a γ -campholene skeleton (XXVI-XXVIII), up to now only γ -campholenic acid (XXVII) has been found in natural materials; in olibanum oil and in cistus oil.^{4,7,24} Like the α -isomer it is now also found in a great number of other essential oils—labdanum, spike lavender, carrot seed, rosemary, coriander and juniper berry oil. γ -Campholenic aldehyde (XXVI) was encountered in the oil of juniper berries and in labdanum oil; ethyl γ -campholenate (XXVIII) in labdanum oil.

The biogenesis of the compounds with campholene skeleton is not yet established. As Thomas has commented, they could very well stem from a pinene or bornane precursor.²² Synthesis of both skeletons is possible starting from α -pinene epoxide. Treatment with a weak Lewis acid like zinc bromide affords α -campholenic aldehyde in high yield,²⁵ while reaction with dry hydrogen bromide followed by heating with silver acetate according to Hartshorn gives γ -campholenic aldehyde (see fig.

4).^{26,27} The other compounds can be prepared from these aldehydes according to well established methods. Oxidation with silver oxide afforded the acids, which were esterified to the ethyl esters. The α -dehydro ester XXIV was prepared by photooxidation of ethyl α -campholenate, followed by dehydration, whereas oxo acid XXV could be synthesized by epoxidation of α -campholenic acid and subsequent rearrangement.

Sensory properties of the new compounds mentioned in this paper are given in Table II.

Acknowledgement

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