Synthetic Sandalwood Aroma Chemicals

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The word "sandalwood" refers, in general, to the essential oils which include East Indian sandalwood oil (oil of *Santalum album* Linn.), West Indian sandalwood oil (oil of *Amyris balsamifera* Linn.), West Australian sandalwood oil (oil of *Eucarya spicata, Santalum lanceolatum, Santalum preissianum* and *Eremophilia mitchelli)* and African sandalwood oil (oil of *Osyris tenuifolia).* Of these, the East Indian sandalwood oil is extensively used in perfumery and commerce because of its non-varying composition, fixative properties and, most important of all, its sweet, warm, spicy and tenacious fragrance.

The East Indian sandalwood oil is obtained by the steam distillation of the heartwood of *Santalum album* which grows mainly in the states of Karnataka and Tamil Nadu in South India (formerly known as Mysore and Madras States). The heartwood obtained from the stem as well as root portions of the tree is used for the distillation of the oil.

The sandalwood oil E.I. has been found to contain greater than 90% α-santalol and β-santalol, 6% hydrocarbons (α-santalene, β-santalene and epi-β-santalene[1]), aldehydes (tricycloekasantalal, exo-norbicycloekasantalal and teresantalal), ketones, phenols, acids (teresantalic acid),[2] and heterocyclic compounds.[3-4]

The major odoriferous components of the sandalwood oil E.I. are the sesquiterpenoid constituents, α-santalol (1), and β-santalol (2), while α-santalene and β-santalene also contribute to a minor extent to the overall odour character of the sandalwood oil E.I.

Apart from its importance as a supremely satisfying source of fragrance, the sandalwood oil E.I. finds use in medicine as an antiseptic, as an antiscabietic, as a diuretic, and for the treatment of gonorrhoea, bronchitis, and bladder infection. However, its use as a base of fragrance has far outweighed its use in medicine.

A general widespread shortage and a steep rise in the price of natural sandalwood oils led research workers in the aroma chemical industry to search for synthetic substitutes for sandalwood E.I. Serious efforts were made to develop synthetically the natural fragrance compounds of sandalwood oil E.I., α-santalol and β-santalol,[5-8] and compounds which possess the fragrance of sandalwood chemicals. Although successfully attained, the manufacture of the synthetic α- and β-santalols did not become a practical possibility. The synthesis involved many steps and required the use of reagents which are difficult to handle in industrial equipment while the overall yields are generally low. As a result, research effort was directed towards obtaining synthetic substitutes possessing the fragrance of sandalwood by economic and commercially feasible processes from easily available and low-cost starting materials.

The important synthetic sandalwood aroma chemicals synthesised so far are mentioned below.

Sandela

Sandela[9] is a mixture of terpenocyclohexanols marketed by Givaudan Corporation. The mixture of terpenocyclohexanols is obtained by the hy-

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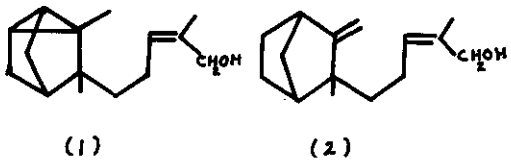
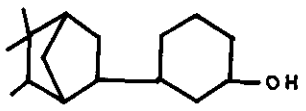


(1) (2)



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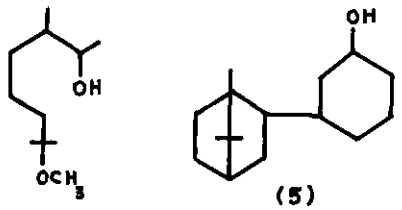


(4) (5)

drogenation of the odorless condensation product of camphene and phenol. The sandalwood odour in the mixture is mainly due to trans-3-isocamphyl cyclohexanol (3).[10-12]

Osyrol

Osyrol (4)[13] is a Bush Boake Allen product. It is an acyclic compound having a methoxyl and a secondary alcohol group.

Santalydol

Santalydol is an alkylation product of camphene and guaicol, followed by hydrogenation. The main note is due to 3-isobornyl cyclohexanol (5).[10]

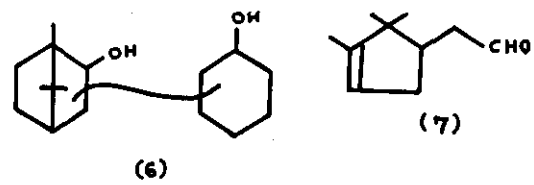
Borneol-Phenol Condensate

Borneol-phenol condensate (6) is prepared by the reaction of borneol with phenol in presence of *p-toluene sulphonic* acid, followed by hydrogenation of the benzene ring. The main note is due to 4-camphanyl cyclohexanol.[14]

Campholenic Aldehyde—Carbonyl Compound Condensate

Campholenic aldehyde (7) has been used as an effective building block for the synthesis of sandalwood aroma chemicals.

Condensation of campholenic aldehyde with methyl ethyl ketone, followed by the hydrogena-



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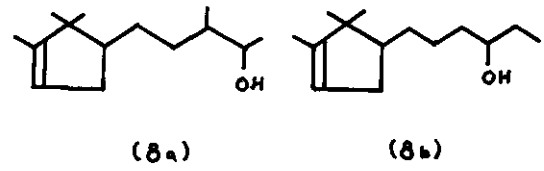
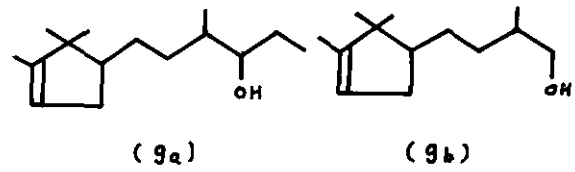
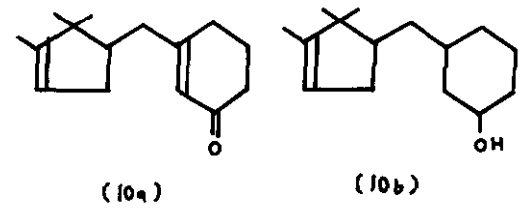


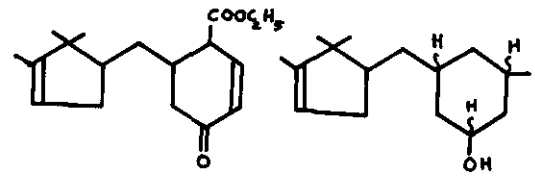
(8a) (8b)



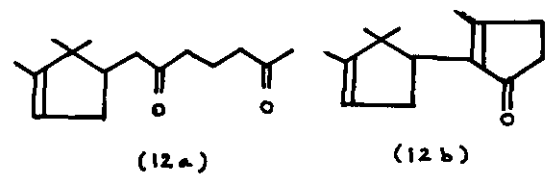
(9a) (9b)



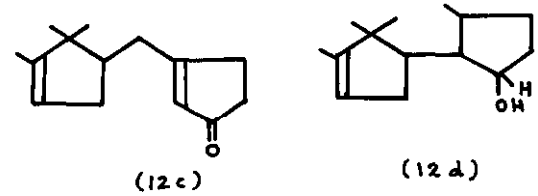
(10a) (10b)



(11a) (11b)



(12a) (12b)



(12c) (12d)

tion of the condensate gives a mixture of the secondary alcohols, (8a) and (8b), of which the isomer (8a) possesses a strong sandalwood note.[15]

Condensation of campholenic aldehyde with diethyl ketone or propionic aldehyde followed by hydrogenation gives rise to the compounds (9a) and (9b) respectively, both of which possess a strong sandalwood scent.[16]

Treatment of campholenic aldehyde in a Grignard reaction with chloroacetal yields a carbinol, the oxidation of which with Jones reagent and subsequent aldol condensation gave the cyclohexenone (10a) which on hydrogenation gave the alcohol (10b) possessing a strong sandalwood odour.[16]

Condensation of campholenic aldehyde with aceto-acetic ester gives a bicyclic ketoester (11a) which on hydrogenation gives a mixture of stereoisomers (11b) possessing a strong and tenacious sandalwood odour.[16,16a]

Compholenic aldehyde on treatment with methyl vinylketone, yields a diketone (12a) which on aldol condensation gives the mixture of isomers (12b) and (12c). Hydrogenation of the isomer (12b) led to formation of the cyclopentanol (12d) possessing a pleasant and long lasting sandalwood odour.[16]

Camphene-Catechol Condensate

Hydrogenation of camphene-catechol condensate forms a mixture of isomers (13) possessing sandalwood odour.[17]

8-Formyl Camphene-Acetone Condensate[18]

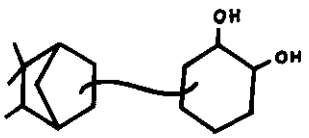
Desmethyl β-santalol (14) and Desmethyl Dihydro β-Santalol (15)[19]

Decahydro β-Naphthyl Formate[20]

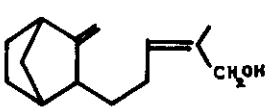
Decahydro β-naphthyl formate (16) is a synthetic sandalwood oil substitute used in India for a long time.

Brunke and Klein[16] and Naipawer et al.[21] made the following general conclusions regarding the structure-odour relationship in synthetic sandalwood aroma compounds: The sandalwood odour appears to be manifested by molecules with 12 to 16 carbon atoms (an ether oxygen atom being considered equivalent to a carbon atom) which possess a hydroxyl group at a certain distance to a voluminous substituent which may be polycyclic or monocyclic or aliphatic system containing an electron donating group which may be an ether oxygen atom or a double bond or a cyclopropyl group.

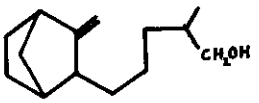
It is of interest to note that decahydro β-



(13)



(14)



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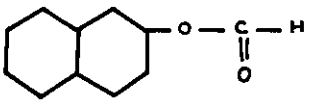

(16)

naphthyl formate forms an exception to the general rule. It is possible that a certain set of structural features, other than those embodied in the above general rule, also satisfy the structure-odour relationship to give sandalwood fragrance to the synthetic substitute.

In conclusion, while a host of considerations led to the development of a multitude of synthetic sandalwood aroma chemicals, none of them is a match to the natural East Indian sandalwood oil in its sweet, fragrant, persistent and woody odour, or possesses its many medicinal properties.

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