RUSSIAN CHEMICAL REVIEWS
Uspekhi Khimii

July 1964

U. D. C. 547.518:668.54

PROCESS IN THE SYNTHESIS OF MACROCYCLIC AND OTHER PERFUMERY MATERIALS

V. N. Belov and N. I. Skvortsova

CONTENTS

I. Macrocyclic perfumery materials 351

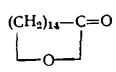
II. Musk preparations of the aromatic series — polyalkylindanes, etc. 354

III. Other perfumary materials 357

I. MACROCYCLIC PERFUMERY MATERIALS

Perfumery materials of macrocyclic structure are highly esteemed in the industry, and it is natural that the development of preparative methods for these compounds and the study of their properties should continue to attract the attention of chemists. In addition to papers describing new syntheses of macrocyclic compounds, an increasing number of papers and patents are being published which describe successful solutions of practical problems. It is with these reports, which greatly extend the opportunities for large-scale production, that we shall begin a review of recent achievements in the chemistry of macrocyclic perfumery materials.

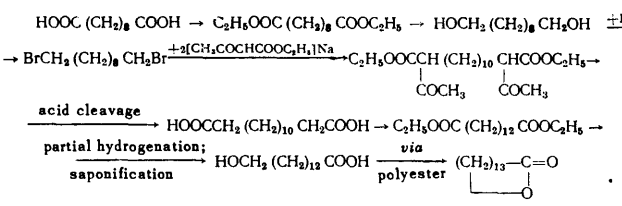
The compound which has acquired the greatest practical importance among macrocyclic compounds is pentadecanolactone,



It is marketed under the trade names Exaltolide and Thibetolide, among others, and has exceptional perfuming properties, imparting fragrance and persistence and tending to "ennoble" a whole composition. Moreover, the methods that have been developed for preparing macrocyclic lactones are very convenient compared with those used for other macrocyclic compounds.

Papers describing very simple and convenient methods for converting ω-hydroxy-acids into macrocyclic lactones have already been noted[1]. The main problem in the development of an industrial method of preparing pentadecanolactone and similar macrocyclic lactones has been reduced to a search for the most efficient route to the ω-hydroxy-acids required. In recent years several papers have been devoted to a solution of this problem. Several methods of synthesising hydroxyalkanoic acids have been developed at the All-Union Research Institute for Synthetic and Natural Perfumery Materials (VNIISNDV). In one of these the carbon skeleton of the hydroxy-acid is built up by condensing an αω-dihalogeno-derivative with two molecules of ethyl acetoacetate. Acid cleavage of the condensation products leads to an αω-dicarboxylic acid containing four carbon atoms more than the initial dihalogeno-derivative.

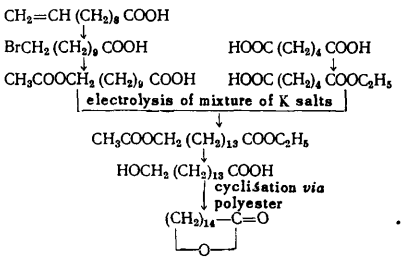
When a convenient method had been developed for the preparation of alkylacetoacetic esters by direct alkylation of sodium acetoacetic ester (prepared by ester condensation of ethyl acetate [and (?)] sodium [ethoxide (?)], which is obtained from alcohol and alkali[2]), this production stage presented no fundamental difficulties. This route was used for the preparation of tetradecanolactone, the next lower homologue of Thibetolide:



The tetradecanolactone obtained in this way has the persistent odour of musk and sandalwood[3].

In other methods for extending the carbon chain developed at VNIISNDV, salts of monoesters of dicarboxylic acids are electrolysed, when the acid radicals combine. Work in which two like acid residues were condensed electrolytically has been considered in a previous review[1]; this route was used for the preparation of hexadecanolactones, the next higher homologue of Thibetolide. Hexadecanolactone has a musk odour somewhat weaker but "softer" than that of Thibetolide[3].

Another electrochemical method of lengthening the carbon chain consists in the "cross" condensation of radicals of two different acids. This procedure is the basis of a method worked out at VNIISNDV[3-5] for the synthesis of pentadecanolactone; the general scheme may be represented



If electrochemical condensation is accomplished in one of the later stages of the synthesis (compared, for example, with the possible method of condensing undecenoic acid with ethyl hydrogen adipate), the amount of material to be electrolysed is greatly reduced. The development of a successful design of electrolyser[6] has made this method acceptable in production. All stages of the synthesis have been thoroughly worked out and tested in the production of Thibetolide in commercial undertakings[7-9].

However, although these schemes include a simple and elegant method of cyclisation, the starting ω-hydroxy-acids can be prepared only with difficulty and in relatively low yields; in the preparation of Thibetolide, the main difficulty arises from the combination of like as well as of unlike acid residues in the electrochemical cross-condensation.

The composition of the mixture of products formed together with ω-hydroxypentadecanoic ester in the electrolytic cross-condensation of ω-acetoxyundecanoic acid and monoethyl adipate has been thoroughly studied[10].

In the VNIISNDV laboratories several routes from αω-dicarboxylic acids to ω-hydroxyalkanoic acids (*via* the diesters or polyanhydrides) have been tried. Partial catalytic hydrogenation of the diesters of αω-dicarboxylic acids gives the ω-hydroxy-carboxylic ester and the corresponding diol[11] in about equal amounts. The conditions for the formation of glycols and hydroxy-acids in the hydrogenation of aliphatic dicarboxylic acids and their esters have been studied by other workers[12]. An investigation into the catalytic dehydrogenation of αω-diols in the presence of copper–nickel and copper–chromate catalysts has been described[13].

The use of tetrachloroalkanes, formed by the telomerisation of ethylene and carbon tetrachloride

$$n\,CH_2{=}CH_2 + CCl_4 \xrightarrow{\text{initiator}} Cl(CH_2CH_2)_nCCl_3,$$

presents entirely new opportunities for the synthesis of ω-hydroxy-acids and many other products required for the preparation of macrocyclic compounds.

In recent years this process, and also the varied chemical reactions of the tetrachloroalkanes, have been studied in detail in the Laboratory of Organoelementary Synthesis of the USSR Academy of Sciences. This work has led to the development of convenient methods for the preparation of various bifunctional compounds, including ω-hydroxy--acids.

To develop a method of preparing macrocyclic lactones based on tetrachloroalkanes, conditions for the formation of higher tetrachloroalkanes, containing 13–17 carbon atoms, in the telomerisation reaction had to be studied. It has been established[14] that increases in pressure and in the relative concentration of ethylene promote the formation of higher telomerisation products; conditions were so chosen that the telomerisate contained up to 20% of the C_{13}–C_{17} tetrachloroalkane fraction. A flow-type plant has been described for the continuous production of higher tetrachloroalkanes that consistently reproduces the synthetic process under a pressure of less than 150 atm with increased concentrations of ethylene and initiator[15].

The conversion of ααaω-tetrachloroalkanes into ω-hydroxy-acids is achieved by the following simple scheme

$$Cl(CH_2CH_2)_nCCl_3 \xrightarrow{\text{acid hydrolysis}} Cl(CH_2CH_2)_nCOOH \xrightarrow{\text{alkaline hydrolysis}} \rightarrow HO(CH_2CH_2)_nCOOH.$$

These reactions have been studied with various telomers[16].

The following sequence of operations has proved most useful in the development of a method for the production of macrocyclic lactones from tetrachloroalkanes. A broad C_{13}–C_{17} telomer fraction is separated and converted *via* the corresponding chloro- and hydroxy-acids into a mixture of lactones, which can then be easily fractionated to give individual macrocyclic lactones[17,18]. Because ααaω-tetrachloroalkanes are unstable at high temperatures in the presence of even slight traces of heavy-metal salts, the separation from the telomerisate of the higher tetrachloroalkane fraction for use in large-scale production is difficult. Under these conditions dehydrochlorination occurs, leading to the formation of trichloroalkenes, which readily form resins:

$$Cl(CH_2CH_2)_nCCl_3 \xrightarrow{-HCl} Cl(CH_2CH_2)_{n-1}CH_2CH{=}CCl_2.$$

This problem has been solved in several ways. For example, good results have been obtained by first separating the tetrachloroalkane mixture by extraction with polar solvents, and also by distilling off lighter fractions on an ordinary column apparatus, with subsequent separation of higher fractions by hydrovacuum distillation or by fractional distillation with glycerol or ethylene glycol vapour under reduced pressure.

ααaω-Tetrachloroalkanes may also be converted into ω-chloro-acids by the action of concentrated sulphuric[19], nitric[20,21], or perchloric[22] acid. The C_{13}–C_{17} telomers are most conveniently hydrolysed by heating with nitric acid, first to 40–45°, and then at 70°. The yield of chloro--acid mixture is about 89%, calculated on the C_{15} acid[17]. The ω-chloro-acids are converted into ω-hydroxy-acids in 83% yield by the action of aqueous alkali at 6–7 atm.[17] Hydroxy-acids are successfully lactonised *via* the intermediate polyester, which is then subjected to thermal depolymerisation in the presence of an alkaline catalyst[23]:

$$x\,HO(CH_2CH_2)_nCOOH \xrightarrow{-(x-1)H_2O} H[O(CH_2CH_2)_nCO]_xOH \rightarrow x\,(CH_2CH_2)_n{-}CO.$$

The polyester is readily obtained in quantitative yield by heating the hydroxy-acid (or mixture of hydroxy-acids) to 200–220° under slightly reduced pressure; this is lactonised without purification by heating with glycerol. The lactone formed is distilled off in glycerol vapour.

The formation of lactone from polyester may be considered as an unusual intramolecular transesterification

$$H\{-O(CH_2CH_2)_nCO\ldots[-O(CH_2CH_2)_nCO-]_x\ldots O(CH_2CH_2)_nCO-\}OH \rightarrow$$
$$\rightarrow H\{-O(CH_2CH_2)_nCO\ldots[-O(CH_2CH_2)_nCO-]_{x-1}\ldots O(CH_2CH_2)_nCO-\}OH + \text{cyclic } (CH_2CH_2)_nCO$$

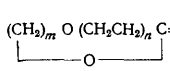
Glycerol in the reaction mixture facilitates removal of the lactone formed and promotes lactonisation. The intramolecular transesterification appears to be coupled with transesterification of the polyester by glycerol, which leads to the formation of glycerides of differing molecular weight; in turn these undergo cleavage to form the lactone. The addition of an alkaline reagent evidently promotes transesterification[23]. The yield of lactones is 70–75%, based on the initial mixture of hydroxy-acids.

ω-Chloroalkanoic acids may also be converted into lactones without the hydroxy-acid stage: treatment with alkali yields directly a polyester of the structure $Cl(CH_2CH_2)_nCO[O(CH_2CH_2)_nCO]_xOK$,[24,25] which is then converted into a lactone (or mixture of lactones if a mixture of chloro-acids has been used) by the method described above for the lactonisation of polyesters obtained from hydroxy-acids.

The rational use of telomers derived from ethylene and carbon tetrachloride, other than the C_{13}–C_{17} compounds, makes the production of macrocyclic lactones still more useful. One of the most promising ways of using tetrachloroalkanes as starting materials is the production of oxa-lactones with multiple links. Some of the macrocyclic oxa-lactones, which differ from the macrocyclic lactones by having one $-CH_2-$ link replaced by an $-O-$ link, are of undoubted interest in perfumery as musk preparations with a characteristic variation in odour.

Virtually no macrocyclic oxa-lactones have hitherto been synthesised on the industrial scale, because of the inaccessibility of the ω-halogeno-acids. There are references to the use in perfumery practice only of those oxa-lactones that can be obtained from a halogen derivative of undecenoic acid, for example 12-oxatetradecanolactone, synthesised by the reaction of 11-bromoundecanoic acid with ethylene glycol, and 12-oxahexadecanolactone, obtained from bromoundecanoic acid and tetramethylene glycol.

Now that various ω-halogeno-acids have become readily available, the production of perfumery materials from oxa-lactones of general formula



presents many possibilities.

A number of oxa-lactones have been synthesised by the reaction of C_5, C_7, C_9, and C_{11} chloro-acids with ethylene glycol[17], butanediol[26], pentanediol[26], hexanediol[17], nonanediol[17] and decanediol[17], the oxa-hydroxy-acid formed being subsequently coverted into the oxa-lactone *via* the polyester:

$$HO(CH_2)_mONa + Cl(CH_2CH_2)_nCOOH \rightarrow$$
$$\rightarrow HO(CH_2)_mO(CH_2CH_2)_nCOOH \xrightarrow{\text{lactonisation}} \text{cyclic } (CH_2)_mO(CH_2CH_2)_nC{=}O.$$

Preliminary conclusions have been reached about the dependence of odour on structure in this group of perfumery materials[17,26]. The odour of oxa-lactones containing 15 carbon atoms in the ring is close to that of pentadecanolactone, while C_{16} oxa-lactones have an odour similar to that of hexadecanolactone. The introduction of an oxa-link into the molecule of a macrocyclic lactone leads to some loss of odour, and when two oxa-links are introduced the odour disappears almost completely. The odour of oxa-lactones in which the oxa-link is close to the alkoxycarbonyl group is less intense than the odour of those in which the link is more remote.

A number of oxa-lactones have been tested for persistence with respect to rate of evaporation. 10- and 12-Oxahexadecanolactone are highly valued for their properties; they have a musk odour to that of Thibetolide, but are more persistent[26,27]. References to the good properties of 12-oxahexadecanolactone have also appeared in foreign [non-Russian] papers[28,29]. An American patent[30] gives a method for the preparation of 12-oxatetradecanolactone from undecenoic acid and ethylene glycol.

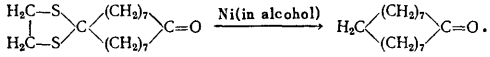
A method recently proposed[31] for the preparation of higher αω-diols by degradative hydrogenation of the polyesters of the corresponding ω-hydroxy-acids:

$$x\,HO(CH_2)_nCOOH \rightarrow H[O(CH_2)_nCO]_xOH \xrightarrow{+2x\,H_2} x\,HO(CH_2)_{n+1}OH + H_2O,$$

greatly extends the possibilities for the production of various oxa-lactones.

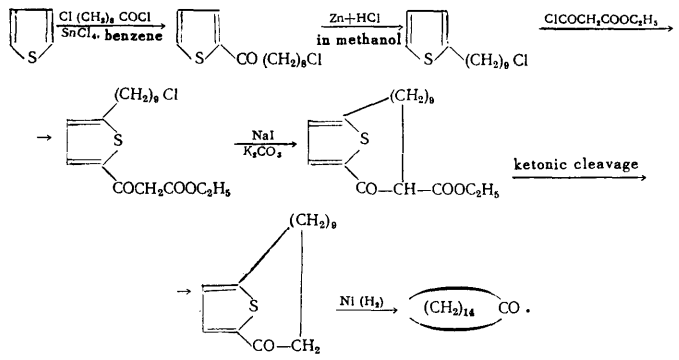
Some papers on the synthesis of macrocyclic compounds are exploratory and have not found practical application.

Blomquist *et al.*[32] have synthesised the musk preparations cyclohexadecanone and cyclooctadecanone by heating the monoethylene dithioketals of the corresponding diketones with Raney nickel in alcohol, for example

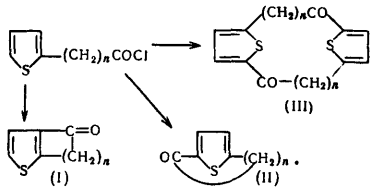


A similar reaction has been described by Cram[33].

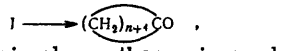
An interesting method has been described[34,35] for the preparation of cyclopentadecanone, which is the main carrier of the musk odour in the product known as Exaltone, isolated from the glands of the musk-rat. It was synthesised by the scheme



In very interesting work, Gol'dfarb *et al.*[36-40] have studied conditions for the formation of intramolecular acylation products (I) and (II) and intermolecular cyclisation products (III) from ω-thien-2'-ylalkanoyl chlorides according to the schemes



Detailed development of methods for the preparation of new ketones of type (I) containing the thiophen ring[37-39,41,42] and also methods for their reductive desulphurisation[37]

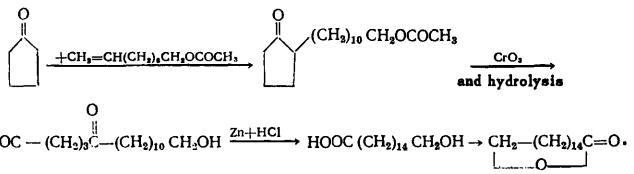


has led to relatively simple syntheses in good yield of a number of useful macrocyclic ketones with a musk odour, including cyclopentadecanone (exaltone), cyclohexadecanone, and cycloheptadecanone (dihydrocivetone). The desulphurisation of thiophen systems for the preparation of intermediates in the synthesis of macrocyclic compounds has been described in other papers[43-47].

Attention has been directed[48] to wastes from cork oak and Amur cork woods as possible additional sources for the preparation of perfumery materials. These contain phloionic acid $HOOC(CH_2)_7(CHOH)_2(CH_2)_7COOH$, which can be converted into macrocyclic compounds.

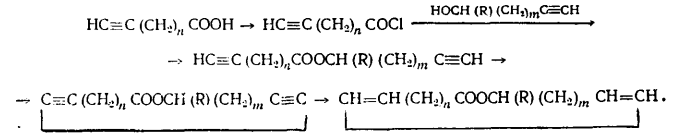
Preobrazhenskii and his coworkers[49] have achieved a multistage synthesis of 3-methylhexadecane-1,16-dioic acid, an intermediate in the preparation of muscone. Some new schemes have been proposed for the synthesis of Exaltolide (Thibetolide)[50,51], ambrettolide[52], exaltone[50,51,53], civetone[54], and dihydrocivetone[51,53,54].

New methods of synthesising dicarboxylic acids[55] and hydroxy-acids[56] which may be converted into macrocyclic compounds are based on the addition of cyclopentanone and cyclohexanone to undecenoic acid[55] or undecenyl acetate[56] in the presence of t-butyl peroxide. Thus, dihydroambrettolide has been obtained[56] in the following way

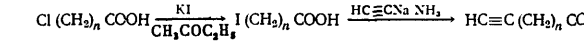


The importance of studying compounds with large and medium rings has been emphasised in a review by Gol'dfarb and Belen'kii[57]. Very interesting work has recently been reported on the preparation and properties of macrocyclic compounds containing aromatic rings[58] and conjugated double[59], or double and triple[60,61], bonds; a review has been published[62] on polymethylene rings containing an acetylenic bond.

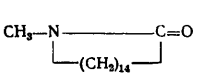
A method has been developed for the preparation of diyne and diene macrocyclic lactones according to the scheme[63-65]



Hydrogenation of the unsaturated macrocyclic lactones, which are practically odourless, gave the corresponding saturated cyclic compounds. In a similar way, saturated macrocyclic ketones were obtained *via* diacetylenic ketones[66]. The ω-acetylenic acids used as starting materials in these new syntheses were prepared from the readily accessible ω-chloro-carboxylic acids[64]:

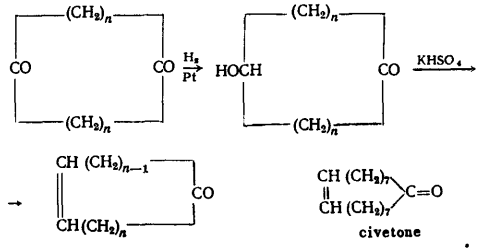


The synthesis of homologues and analogues of previously known musk preparations are dealt with in a number of papers. The recently synthesised 2-methyl-2-azacyclohexadecanone



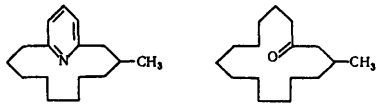
[other] macrocyclic *N*-methylamides, and macrocyclic *N*-methylurethanes, in which nitrogen is a component of the many-membered ring, have been described as compounds with a musklike odour[67,68]. These examples again emphasise that the odour of a compound is determined not only by the presence of certain groups of atoms, but also by the structure of the molecule as a whole.

Cyclohexadec-8-en-1-one (IV) and cyclooctadec-9-en-1-one (V), homologues of civetone with an intense musk odour, have been synthesised[69,70] by partial hydrogenation of cyclohexadecane-1,9-dione and cyclooctadecane-1,10-dione respectively, followed by dehydration of the hydroxy-ketones obtained:



(IV) $n=7$
(V) $n=8$

Ruzicka[71] isolated a compound $C_{16}H_{25}N$ from the glands of the musk-deer (*Moschus moschiferus*), which he termed "muscopyridine". Recently its structure has been determined and confirmed by synthesis[72]. This compound shows some structural similarity to the known macrocyclic ketone muscone, which also occurs in the glands of some musk animals.



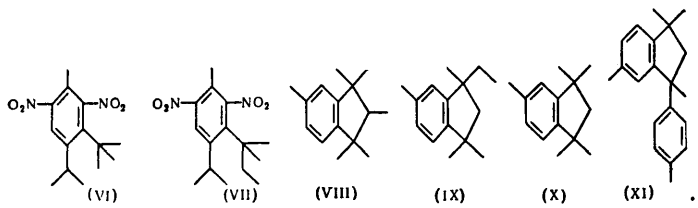
muscopyridine ($C_{16}H_{25}N$) muscone ($C_{16}H_{30}O$)

II. MUSK PREPARATIONS OF THE AROMATIC SERIES — POLYALKYLINDANES, ETC.

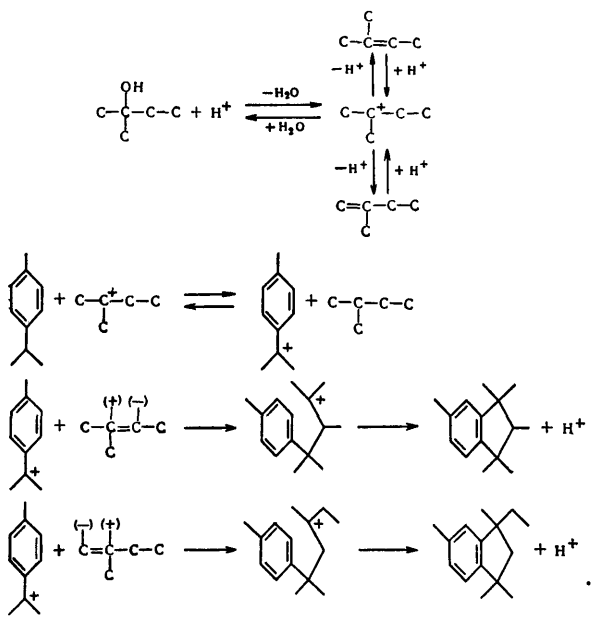
A study of the alkylation of *p*-cymene led to the discovery of an essentially new class of perfumery compounds with a musk odour. Until recently it was thought that the action of a tertiary alcohol or a branched olefin on *p*-cymene in the presence of a catalyst[73-77] resulted in nuclear alkylation. Thus, the fragrant compound prepared by reaction of t-butyl alcohol with *p*-cymene followed by

nitration of the alkylated product was described as dinitro--t-butyl-*p*-cymene (VI)[76,77]. The structure (VII) was assigned to the homologue synthesised some time later by alkylating *p*-cymene with 2-methylbutan-2-ol.[74]

It has been established that in these reactions *p*-cymene behaves in a different way from other aromatic hydrocarbons. The reaction in the presence of concentrated sulphuric acid of tertiary or secondary alcohols having a tertiary carbon atom gives a mixture of indane hydrocarbons as the main product, not products alkylated in the aromatic nucleus[78-82]. Thus, alkylation of *p*-cymene with 2-methylbutan-2-ol gives 1,1,2,3,3,5-hexamethylindane (VIII) (41%), 1-ethyl-1,3,3,6-tetramethylindane (IX) (23%), 1,1,3,3,5-pentamethylindane (X) (12%), a substituted indane $C_{16}H_{24}$ (structure not established), and 1,1,3,5-tetramethyl--3-*p*-tolylindane (XI)[78]. The stoichiometric equation for the main reaction may be expressed: 1 mole of *p*-cymene + + 2 moles of 2-methylbutan-2-ol = 1 mole of C_{15} indanes + + 1 mole of isopentane + 2 moles of H_2O.



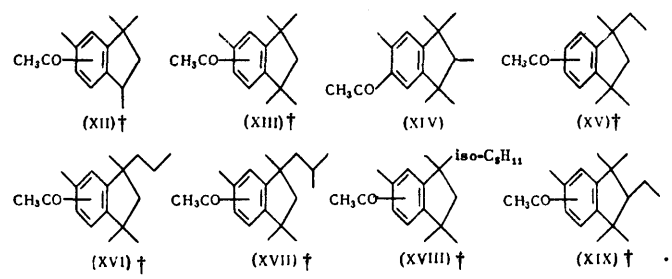
The following mechanism has been proposed to explain the formation of the main products of this reaction[78,79]



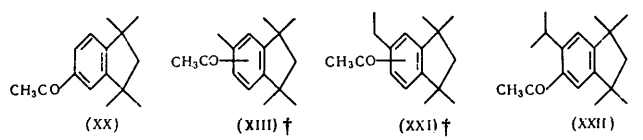
Side-reactions with elimination and migration of the methyl group give C_{14} and C_{16} indanes. *p*-Ethylcumene and *p*-t-butylcumene also tend to form indane derivatives in similar alkylations[79].

A large number of derivatives of different kinds have been synthesised from the polyalkylindanes obtained, and some relationships between structure and odour have been established. Weber *et al.*[78,79,83] found that acetylpolyalkylindanes have a musk odour when there are two pairs of *geminal* methyl groups on the carbon atoms adjacent to the benzene ring. Most of these indanes have 1–3 alkyl groups in the benzene nucleus; an additional 6-methyl group weakens the musk odour. According to Beets *et al.*[84], the presence of an acyl group and two tertiary or quaternary carbon atoms attached to the benzene nucleus is the minimum condition for the presence of a musk odour in indane derivatives. These tertiary or quaternary carbon atoms may be present in the non-aromatic ring, or one of them may be introduced as an independent alkyl group. Compounds with an acyl and two quaternary groups have a strong musk odour.

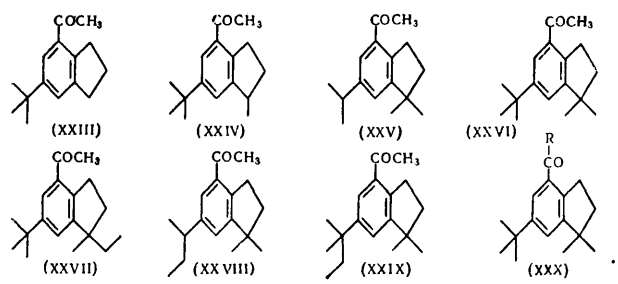
Some special odour–structure relationships of polyalkylindane derivatives may be traced in the following compounds



Compound (XII) is odourless[78]; according to one report[80], compound (XIII) has a weak musk odour, but according to other workers[78,82] it has a musk-wood odour weaker than that of (XIV); (XIV) has a strong musk odour[78-82], and the odour of (XV) does not differ in character but is much weaker[78,82]. Compounds (XVI)–(XVIII) are completely odourless[59], and (XIX) has a musk odour[79].



In the series (XX), (XIII), (XXI), (XXII), which contain the same non-aromatic ring, the first two members have a weak musk odour[78-80,82,84]; (XXI) has been described as a compound with a musk odour; and its homologue (XXII), with an isopropyl group in the benzene ring, is odourless[79].



Of the compounds (XXIII)–(XXIX) with an acetyl group on the same carbon atom of the benzene ring, (XXIII)[84] is

† Later work indicates that in all these compounds the acetyl group is in the same position as in compound (XIV), the structure of which has been established[85].

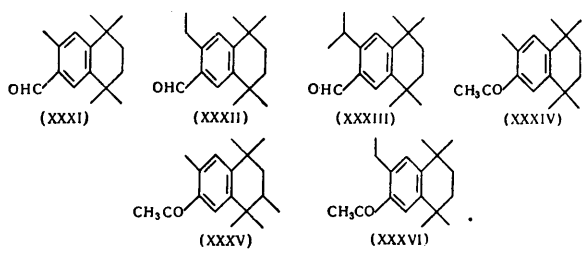
odourless, its homologue (XXIV) has a very weak musk-type odour[84], the ketones (XXV)–(XXVII) have been described as compounds with a strong musk odour[84,86-88], and compounds (XXVIII) and (XXIX)[84] have a weak musk odour.

Among compounds of general formula (XXX) that have been synthesised, the aldehyde (R = H) has a very strong musk odour[84], and the acetyl derivative (R = CH_3) has a strong musk odour (see above), which gradually becomes weaker as the molecular weight of the ketone increases (R = C_2H_5; R = C_3H_7).[84,86]

It will be noted that, both in the example given above and in the other cases described, the aldehydes of the polyalkylindane series have a stronger musk odour than the corresponding methyl ketones[83,84]

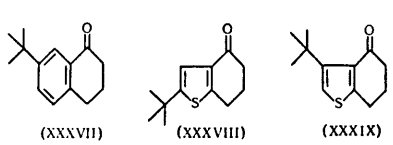
Some of the new polyalkylindane derivatives have found applications in the perfumery industry. Thus, 5-acetyl-1,1,2,3,3,6-hexamethylindane (XIV), provisionally termed Phantolid[82,89,90], has become known as a perfumery material with a persistent musk odour. Special mention has been made in the perfumery journals of the high odoriferous qualities of the indane derivatives (XXVI), (XXIX), and (XXX) with R = C_2H_5,[86,87,91,92] and they have been recommended for use in compositions for perfumes, eau de Cologne, scented soap, powders, etc.

Polyalkyltetralin derivatives with a musk odour, and similar in structure to the above compounds of the indane series, are described in a number of reports, mainly from the patent literature. 1,2,3,4-Tetrahydro-1,1,4,4-tetramethylnaphth-6-aldehydes containing an extra methyl or an ethyl group at position 7 — (XXXI) and (XXXII) — have a strong musk odour; the corresponding 7-isoproyl derivative (XXXIII)[93,94] has a weaker musk-type odour.

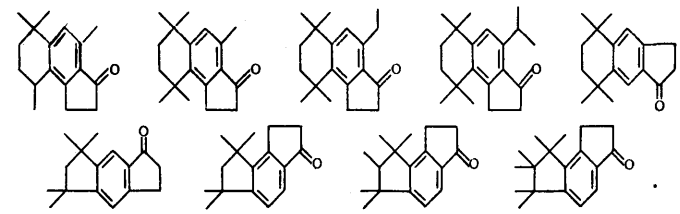


Ketones of the substituted alkyltetralin group that have been described as compounds with a musk odour include the homologues of 6-acetyl-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene containing 7-methyl (XXXIV)[95], 3,7-dimethyl (XXXV)[96], and 7-ethyl (XXXVI) groups, the last of these compounds being used in perfumery under the name Versalide[97,98].

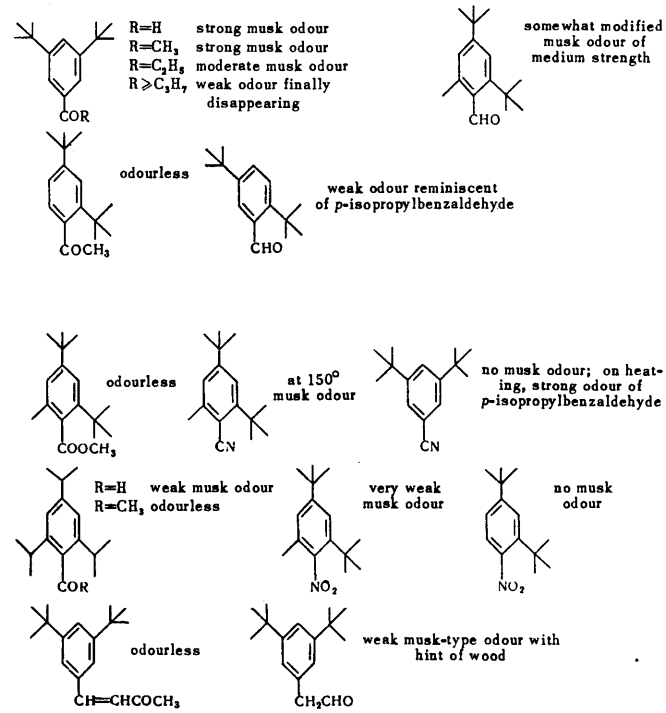
Buu-Hoi and other chemists have described 7-t-butyltetral-1-one (XXXVII) as a compound with the odour of burning sandalwood[99,100]. For comparison, its isologues 2- and 3-t-butyl-4,5,6,7-tetrahydro-4-oxobenzo[*b*]thiophen (XXXVIII) and (XXXIX)[101] have been synthesised; (XXXVIII) is found to have the characteristic odour of burning sandalwood, but the odour of (XXXIX) is less interesting.



In recent years compounds with a musk odour belonging to more complex fused systems have become known. Patents have been obtained for a number of polyalkylhexahydrocyclopentanaphthalenes[102] and for polyalkylhydroindacene derivatives[103], the formulae of which are given below. It is noteworthy that compounds of such high molecular weight (18–20 carbon atoms per molecule) should have an odour; these products are perhaps the "heaviest" known perfumery materials.



In an investigation[104] to elucidate the relationship between the non-aromatic indane ring and the presence of a musk odour, various benzene derivatives were synthesised, and some correlations were found between structure and the character and strength of odour. These products included benzene derivatives without a nitro-group that had a musk odour. Up to now only a few representatives of this group of musk preparation[1,105] have been known. The following are the formulae and characteristic odours of the compounds prepared in this work



From a comparison of the odour of these benzene derivatives with compounds of the indane series, Beets concluded that the non-aromatic indane ring is not essential for the presence of odour. He considered that the benzene nucleus, with bulky groups (*e.g.* t-butyl) and also aldehyde or ketone substituents, preferably in a sterically unhindered position, is the carrier of the musk odour. Beets observed that compounds in which the carbonyl group is

sterically hindered to such a degree that it does not react with carbonyl-group reagents have no musk odour, unlike their isomers with a more "accessible" carbonyl group.

Work on the chemistry of the "nitro-musks" that deserves mention included an investigation into the separate stages of the preparation of musk xylene[106] and a new synthesis of 4-bromo-5-t-butyl-2,6-dinitro-*m*-xylene[107] previously described by Carpenter.

III. OTHER PERFUMERY MATERIALS

Improvements in the preparation of benzyl and phenethyl alcohols and their derivatives continue to attract attention. An industrial method has been described for obtaining benzyl alcohol by hydrolysing benzyl chloride with sodium carbonate solution, and also a method for esterifying benzyl alcohol with acetic acid in the presence of sulphuric acid to give an ester of high perfumery quality[108]. Another paper recommends that benzyl alcohol should be esterified by carboxylic acids (formic, acetic, and some others) in chloroform with chlorosulphuric acid as catalyst[109]. A good yield (86%) of ester was obtained from benzyl alcohol and acetic acid, the water formed being distilled off with toluene vapour[110]. New work has also been described on the preparation of benzyl acetate from benzyl chloride and sodium acetate[111].

A considerable part of the work done to develop industrial methods for the preparation of phenethyl alcohol has been devoted to the study of separate stages in its synthesis from styrene *via* the halogenohydrin and the oxide

$$C_6H_5CH{=}CH_2 \rightarrow C_6H_5CH(OH)CH_2Hal \rightarrow C_6H_5{-}\underset{\diagdown O \diagup}{CH{-}CH_2} \rightarrow C_6H_5CH_2CH_2OH.$$

Apart from a number of patents obtained in different countries that deal mainly with the catalytic hydrogenation of styrene oxide[112–115], the process as a whole has been thoroughly examined by Beets[116], who points out that this method, which gives phenethyl alcohol of high purity, appears to have been adopted on an industrial scale in the U. S. A. The high quality of the 2-phenylethanol obtained from styrene has recently been confirmed by Soviet workers[117]. The reduction of a number of oxides, including styrene oxide, with lithium tetrahydroaluminate has been described[118].

The preparation of 2-phenylethanol from phenylacetic ester has been described in two recent papers: Daniewski[119] somewhat modified the well-known Bouveault–Blanc‡ reduction of phenylacetic ester, and Bag and Bliznyak[121] obtained good results in the catalytic hydrogenation of this ester with a copper–calcium catalyst§ (at 165–170° and an initial pressure of 200 atm); alcohol of high purity was obtained in 60% yield, based on the ester consumed.

Phenethyl alcohol has been prepared from benzene and ethylene oxide by the Friedel–Crafts reaction[123]. The results have been reported of an investigation into the purification of phenylethanol by vaporised solvents in an injector column[124]. Shutikova and Cherkaev[125] have described the 2-methylation of 2-phenylethanol and 2-cyclohexylethanol, and have reported on the perfumery properties of the products (2-phenylpropanol and 2-cyclohexylpropanol) and also of the corresponding aldehydes.

3-Phenylpropanol has been prepared by two methods, by the reaction of benzylmagnesium chloride with ethylene oxide in ether, and by the reduction of ethyl cinnamate with sodium and pentanol in toluene[126]. These methods are, however, less suitable for industrial use than the method worked out a few years ago at VNIISNDV for its preparation from styrene[127].

Several papers describe the preparation of cinnamyl alcohol by the reduction of cinnamaldehyde. Two variants of the reduction with aluminium isopropoxide[128] have been developed, and the effect of adding aluminium halide alkoxides in this reaction has been studied[129]. Several carbonyl compounds, including cinnamaldehyde, were reduced with a mixture of aluminium isopropoxide and $ClAl[OCH(CH_3)_2]_2$, cinnamyl alcohol being obtained in 92% yield. The alcohol has also been obtained in the same yield (90–92%) by a method in which less the usual amount of aluminium benzyloxide was used[130].

Gorshkov and Freidlin have made a comprehensive study of the reduction of a number of unsaturated carbonyl compounds, including cinnamaldehyde, on zinc catalysts obtained by leaching out Zn–Al and Zn–Cu–Al alloys. They find that selective reduction of the ethylenic bond or of the carbonyl group depends on their relative positions[131]. Polish workers have proposed a new method for the preparation of cinnamyl alcohol from styrene *via* pentylzinc chloride and the corresponding acetate[132].

Several papers deal with the preparation of alcohols of interest in the perfumery industry. Japanese workers have described[133] the hydrogenation of aliphatic acids, isolated from coconut oil, to the corresponding alcohols in the presence of a mixed $CuSO_4$–$Na_2Cr_2O_7$ catalyst and aqueous ammonia. They consider that hydrogenation of the acid itself occurs only in the initial stage; the alcohol formed then esterifies the acid, and the ester is now hydrogenated to the alcohol. Indian workers have suggested reducing esters to the corresponding alcohols by the action of aluminium amalgam in alcohol; the method is said to have advantages in work with small quantities[134]. Sladkov *et al.*[135], using 2-methylpent-1-ene and 2-ethylhex-1-ene, have made an interesting study of the Ziegler reaction for the conversion of olefins into alcohols *via* organoaluminium compounds

$$6RCH{:}CH_2 + 2Al + 3H_2 \rightarrow 2(RCH_2CH_2)_3Al,$$

$$2(RCH_2CH_2)_3Al + 3O_2 \rightarrow 2(RCH_2CH_2O)_3Al,$$

$$(RCH_2CH_2O)_3Al + 3H_2O \rightarrow 3RCH_2CH_2OH + Al(OH)_3.$$

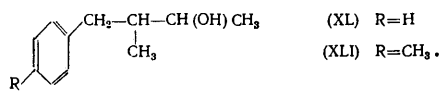
They point out the relative simplicity of this method and the good yield of alcohols obtained (60–65% of theoretical). This reaction was also used for the preparation of 2-phenylpropanol in 55% yield, based on the initial methylstyrene[136]. A group of Soviet workers[137] have described the preparation of 2-phenylpropanol by the reaction of *α*-methylstyrene with isobutylaluminium followed by oxidation with air of the 2-phenylpropylaluminium formed.

According to Weissenborn[138], 3-methyl-4-phenylbutan-2-ol (XL) and 3-methyl-4-*p*-tolylbutan-2-ol (XLI), prepared by the condensation of benzaldehyde and *p*-tolualdehyde with ethyl methyl ketone in acid medium, followed

‡ Filipescu and Manisor[120] recommend that the Bouveault–Blanc reduction of esters should be carried out in aromatic hydrocarbons with sodium and such alcohols as cyclohexanol, methylcyclohexanol, pentanols, etc.

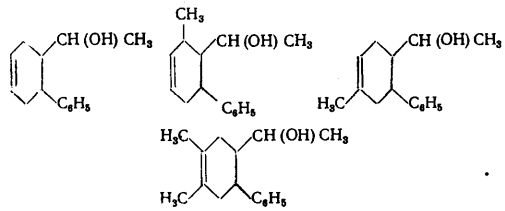
§ According to a patent[122], high yields of aromatic alcohols (up to 95% and above) are obtained in the hydrogenation of esters under pressure in the presence of copper chromite.

by reduction of the unsaturated ketone, have an odour similar to that of linalool.



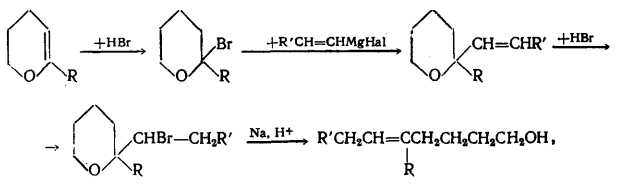
(XL) R=H
(XLI) R=CH$_3$.

A floral odour has been noted[139] in secondary alcohols obtained by the reaction of methylmagnesium iodide with 2-formyl-1,2,3,6-tetrahydrobiphenyl and its homologues, which in turn are obtained by diene synthesis from cinnamaldehyde and the corresponding diene hydrocarbons



An odour close to that of methyl oct-2-ynoate (Folione) has been noted in oct-2-yn-1-ol, obtained by condensing hept-1-yne with formaldehyde[140].

The method developed by Normant for carrying out Grignard syntheses with organomagnesium compounds containing a vinyl-type radical[142] has presented more opportunities for the synthesis of various unsaturated alcohols. Thus, various ethylenic aliphatic secondary and tertiary alcohols[142,143] have been obtained by the reaction of vinylmagnesium bromide, and also its alkyl-substituted derivatives, with saturated aliphatic aldehydes and ketones; analogous reactions with unsaturated carbonyl compounds and esters have led to diethylenic and polyethylenic alcohols[144,145]. Condensation of vinylmagnesium halides and their substituted derivatives with dihydropyran and dihydrofuran hydrobromides gives 2-alkenyltetrahydropyrans and 2-alkenyltetrahydrofurans respectively, which are then converted into δ- and γ-unsaturated primary alcohols[146]

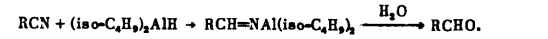


Heptenols and octenols have been synthesised from isohexene and isoheptene hydrocarbons (obtained by the polymerisation of simple olefins), by condensing the latter with formaldehyde (Prins reaction). Under certain conditions the yield of unsaturated primary alcohols reaches 80 wt. %.[147]

Much work has recently been done in the search for new and improved methods for preparing phenylacetaldehyde, cinnamaldehyde, α-p-isopropylbenzylpropionaldehyde, and their homologues and analogues.

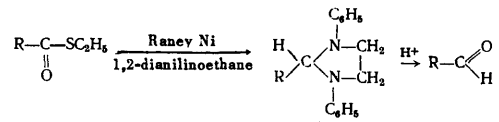
The use of aluminium or iron oxide[148] and of activated aluminium oxide[149] has been proposed for the conversion of styrene oxide into phenylacetaldehyde; when the isomerisation is conducted in an inert gas at 170°, an almost quantitative yield is obtained[149]. Styrene[150] has been used as starting material in the synthesis of cinnamaldehyde: the styrene is chloromethylated to give cinnamyl chloride, which is then subjected to the Sommelet reaction; however, the yield is low. The Sommelet reaction has recently been used[151] for converting 2,4,5-triisopropylbenzyl chloride into the corresponding aldehyde, which had previously been described as a compound with a musk-type odour[105]. Cinnamaldehyde[152] and triisopropylbenzaldehyde[153] have recently been obtained from the corresponding halogeno--derivatives by Kröhnke's method.

Phenylacetaldehyde can be prepared in yields up to 90%[154,155] by the electrolytic oxidation of cyclooctatetraene[156-159]. Zakharkin and Khorlina[160] have prepared phenylacetaldehyde, anisaldehyde, and some other aldehydes by reducing the nitriles with diisobutylaluminium hydride:



The yield of phenylacetaldehyde reaches 86%, that of aubépine (anisaldehyde) 88%.

A new method of preparing phenylacetaldehyde, β-phenylpropionaldehyde, and other aromatic and aliphatic aldehydes by the reduction of carbothiolic esters with Raney nickel has been described[161]. To prevent further reduction of the aldehyde, it is combined with 1,2-dianilinoethane; the compound thus formed is easily decomposed by mineral acids:



This method gives yields of 79%, 84%, and 80% respectively of phenylacetaldehyde, β-phenylpropionaldehyde, and benzaldehyde, calculated on the initial carbothiolates.

New patents have been obtained for a method of stabilising phenylacetaldehyde as its trimer[162,163], which can be decomposed to give the free aldehyde[164].

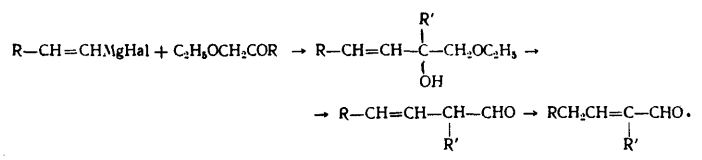
The preparation of aliphatic ketones by pyrolysis of manganese salts of the acids has been studied, as well as the preparation of aldehydes by pyrolysis of manganese formate and a manganese salt of the carboxylic acid. In the synthesis of ketones this method has advantages over the classical Piria reaction (pyrolysis of calcium salts); the yield of aldehydes is generally low, however, but C_7 and C_8 aldehydes can be prepared with good results[165].

A method has been described for the preparation of normal C_{10}, C_{12}, and C_{14} aldehydes by oxidation of the alcohols with selenium dioxide[166]. Dodecanal has been obtained by dehydrating dodecyl alcohol on a copper chromite catalyst[167]; and undecanal and dodecanal have been synthesised from the corresponding bromides and 2-nitropropane in the presence of alcoholic alkali[168].

Conditions for increasing the yield of heptanal and undecenoic acid in the pyrolysis of castor oil have been described in a patent[169].

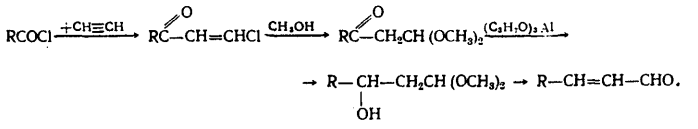
Normant[170] has proposed a method for the preparation of $\alpha\beta$-unsaturated aliphatic aldehydes in which ethoxy--ketones of the type $RCOCH_2OC_2H_5$ react with 1-substituted

vinylmagnesium halides, and the resulting 1-ethoxybut-3--en-2-ols are decomposed with formic acid:



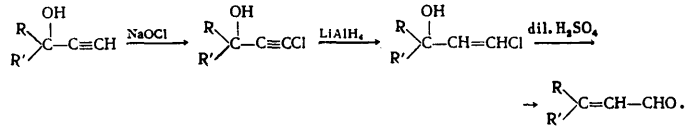
Aldehydes obtained by this scheme include 2-propylidenenonanal (R = CH_3, R′ = C_7H_{15}) with a floral odour, and 2-ethylidenenonanal (R = H, R′ = C_7H_{15}) with a lemon odour.

Two new methods of synthesising $\alpha\beta$-unsaturated aldehydes have been reported. Dec-2-enal, octadec-2-enal, and some other aldehydes of similar structure are prepared by the scheme[171]



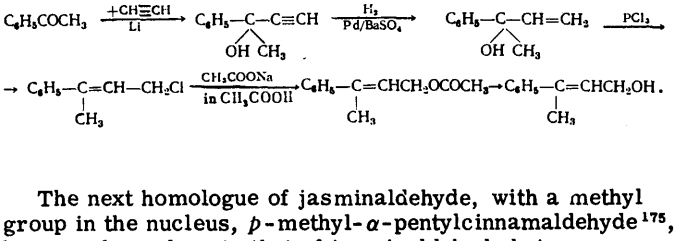
The odour characteristics of these compounds are not mentioned.

Substituted ethylcarbinols are used as starting materials in another method[172]:



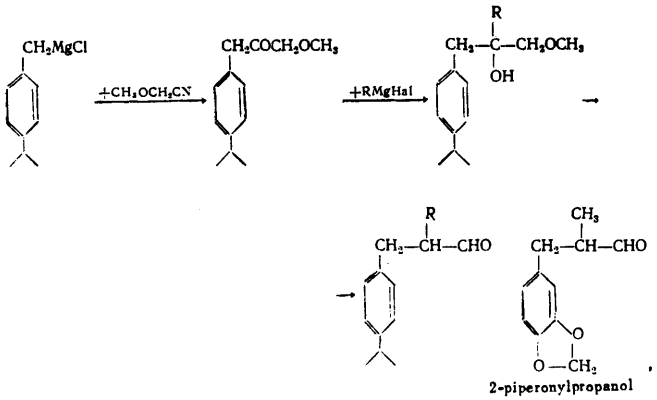
The aldehydes were not separated in the pure state but were characterised as their semicarbazones.

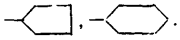
Homologues and analogues of well-known perfumery materials are described in a number of other papers. Thus, β-methylcinnamaldehyde, which has an odour similar to that of cinnamaldehyde, has been obtained[173] by reduction of ethyl β-methylcinnamate to the corresponding alcohol, which is then oxidised to the aldehyde. A year later, γ-methylcinnamyl alcohol, from which this aldehyde can readily be obtained, was synthesised from acetophenone according to the scheme[174]



The next homologue of jasminaldehyde, with a methyl group in the nucleus, p-methyl-α-pentylcinnamaldehyde[175], has an odour close to that of jasminaldehyde but coarser.

Cyclamenaldehyde (α-p-isopropylbenzylpropionaldehyde) and several of its homologues and analogues with different alkyl groups in the α position to the carbonyl group have been synthesised by the new scheme[176,177]



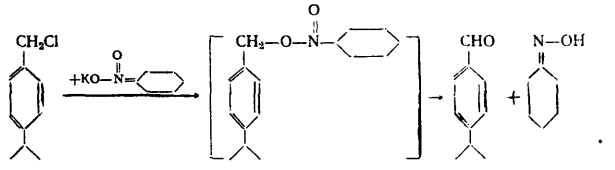
where R = CH_3 (cyclamenaldehyde), C_2H_5, n-C_3H_7, iso-C_3H_7, iso-C_4H_9, iso-C_5H_{11}, .

The odour of these compounds is inferior in strength and quality to that of cyclamenaldehyde itself; 2-p-isopropylbenzyl-5-methylhexanal (R = iso-C_5H_{11}) is the only one that has been described as a compound of distinctive odour with a musk trend.

A method of synthesis of the new perfumery material 2-piperonylpropanal [α-(3,4-methylenedioxybenzyl)propionaldehyde], an analogue of cyclamenaldehyde, was patented in 1960 [178] and then developed in detail by Laskina and Devitskaya[179]. Its excellent perfumery properties have been noted.

Among other isomers and homologues of cyclamenaldehyde that have been synthesised recently, β-(p-t-butylphenyl)propionaldehyde[180] has a strong odour of lilies, β-p-cumenylbutyraldehyde[181], an agreeable odour, and α-p-methylbenzylbutyraldehyde[182] an odour reminiscent of cyclamenaldehyde. Japanese workers have patented[183] a series of homologues of cyclamenaldehyde that differ from it in having alkyl groups in the α position to the aldehyde group, and also in the *para* position to the propyl chain. In a United States patent[184] the dimethylacetal of 2-benzylpropanal, a lower homologue of cyclamenaldehyde, is recommended for use in perfumery.

Some research was done on the preparation of cyclamenaldehyde itself. A synthesis *via* the substituted acetoacetic ester p-iso-C_3H_7.C_6H_4.CH_2.$C(CH_3)(COCH_3).COOC_2H_5$ has been published: acid cleavage gives α-p-isopropylbenzylpropionic acid, which is then reduced to the aldehyde[185,186]. p-Isopropylbenzyl chloride has been converted[187] into the aldehyde by the action of an alkaline aqueous-alcoholic solution of nitrocyclohexane:



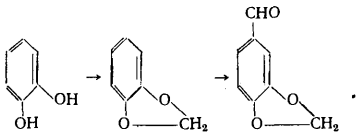
Oxidation of p-isopropylbenzyl chloride followed by condensation with propionaldehyde of the p-isopropylbenz-

aldehyde formed gives *p*-isopropyl-α-methylcinnamaldehyde in 58% yield, calculated on the initial *p*-isopropylbenzyl chloride.

The reduction of *p*-isopropyl-α-methylcinnamaldehyde to cyclamenaldehyde in the presence of Raney Ni–W-5 (from an Ni–Al alloy) in methanol[188] has been studied by infrared spectroscopy and gas chromatography. It has been shown that the mixture obtained under these conditions contains ~ 53% of cyclamenaldehyde; *p*-isopropyl-β--methylcinnamyl alcohol and 2-*p*-isopropylbenzylpropanol are formed as by-products. The latter can be converted into cyclamenaldehyde in 60% yield by dehydrogenation at 230–240° and a residual pressure of 28–30 mm in the presence of copper–chromic oxide catalyst with the addition of barium oxide[189].

It has been suggested that in the preparation of cyclamenaldehyde it is useful to hydrogenate *p*-isopropyl-α-methylcinnamaldehyde to 2-*p*-isopropylbenzylpropanol and then convert this to the aldehyde[190].

Workers at VNIISNDV have continued to develop a method for the synthesis of heliotropin (3,4-methylenedioxybenzaldehyde) from catechol. Simplifications have been introduced into separate stages of the synthesis, which was first proposed in 1938 [191]



Until recently the methylenation stage was effected by heating catechol with methylene chloride in alkaline medium under pressure; this was accompanied by the formation of much resin. It has been shown that methylenation can be successfully carried out at ordinary pressures in the presence of sodium iodide in benzyl alcohol[192,193]. To introduce the aldehyde group into the molecule of catechol methylene ether, several variants have been employed of a method for preparing hydroxy-aldehydes containing a free phenolic group which has been widely used, for example in the synthesis of vanillin[194–196].

In another scheme the aldehyde group is introduced directly into the catechol molecule, and the resulting aldehyde converted into the methylene ether[197].

In the production of heliotropin from the essential oil of sassafras, isosafrole, obtained by isomerisation of the safrole contained in the oil, has been oxidised electrolytically[198].

It is natural that new synthetic methods for preparing vanillin and the improvement of existing industrial methods should attract attention. The synthesis of vanillin from salicylic acid in two stages has recently been reported[199]. However, until the results are confirmed it is difficult to evaluate the method.

The so-called chloral method for the preparation of vanillin and vanillal has been improved[200]. When dichloroethane is used as solvent in the formation of 4-hydroxy-3--methoxyphenylglycollic acid (and also the 3-ethoxy-compound), a yield of 80–85% is obtained, based on the initial guaiacol (or guethol); technical chloral hydrate was used in the condensation. It has been proposed that oxidation of the condensation product in the last stage of the synthesis should be carried out with an air spray in the presence of a permanganate catalyst. The total yield of vanillin was 50–55%, calculated on the guaiacol taken.

Comparative results on the preparation of vanillin from guaiacol and formaldehyde with the use of nitrosodimethylaniline (the so-called nitroso-method) or *m*-nitrobenzenesulphonic acid are given in a paper published in 1963 [201].

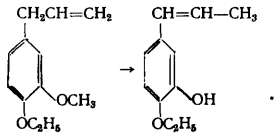
The products of the condensation of guaiacol with formaldehyde have been investigated[202] with the object of preparing 4-hydroxy-3-methoxybenzyl alcohol, a supposed intermediate in the synthesis of vanillin from guaiacol, but the pure alcohol could not be isolated from the reaction mixture

The development of convenient methods for the preparation of guaiacol and guethol from catechol and its mixtures[203–205] extends the range of raw materials available for the synthesis of vanillin and vanillal.

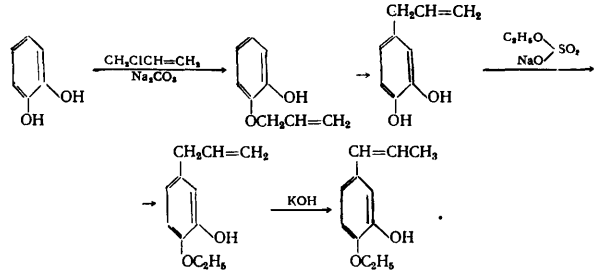
The search has continued for improved conditions for the preparation of vanillin from lignin, its derivatives, or lignin-containing materials; most of these investigations have been reported in the patent literature (reviewed in Ref. 206).

Good results have been obtained in work on the preparation of vanillin by alkaline oxidation of lignosulphonates contained in post-alcohol residues, a waste product of the sulphite–alcohol industry[207–209].

The odour of a series of recently synthesised aromatic aldehydes — analogues of vanillin, vanillal, and heliotropin — has been described[210]. Patents have been obtained[211,212] for the preparation of 2-ethoxy-5-propenylphenol, an interesting perfumery material with the odour of vanilla¶, from the ethyl ether of eugenol, which is subjected to demethylation accompanied by isomerisation of the allyl group to propenyl:

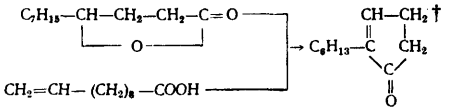


Laskina *et al.* [214] have recently developed the following synthesis of Vanitrope



¶ Marketed by the American firm Shulton Inc. as Vanitrope.[213]

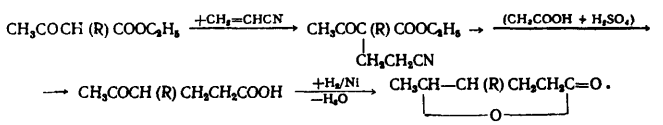
Some new work has been devoted to the preparation of substituted cyclopentenones, a group that includes the interesting perfumery material jasmone (3-methyl-2-pent-2'-enyl-cyclopent-2-enone), a constituent of the essential oil of jasmin. 2-Hexylcyclopentenone, the so-called dihydrojasmone, has been used in the industry; it is obtained by cyclodehydration of γ-undecanolactone or of undecenoic acid.



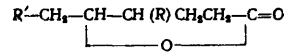
Polyphosphoric acid has recently been proposed for converting γ-lactones [215,216], δ-lactones [217], and unsaturated acids [218,219] into alkylcyclopentenones. High yields have been obtained and new interpretations of the mechanism of reactions of this kind have been put forward.

According to some reports [220], the use of polyphosphoric acid for the preparation of dihydrojasmone itself from undecenoic acid gives the required product in good yield; according to other reports [219], a mixture of isomeric ketones is formed and the yield of dihydrojasmone is low. Comparative results on the preparation of dihydrojasmone from undecanolactone and from undecenoic acid by the action of polyphosphoric acid have been reported [221]. A new synthesis of dihydrojasmone has also been described [222].

Work in recent years on the development of new methods for the preparation of alkyl-substituted γ- and δ-lactones includes the promising synthesis suggested by Belov and Dil'man [223] of γδ-dialkylated δ: lactones; this has been further developed by Belov and Voitsekhovskaya [224,225]:



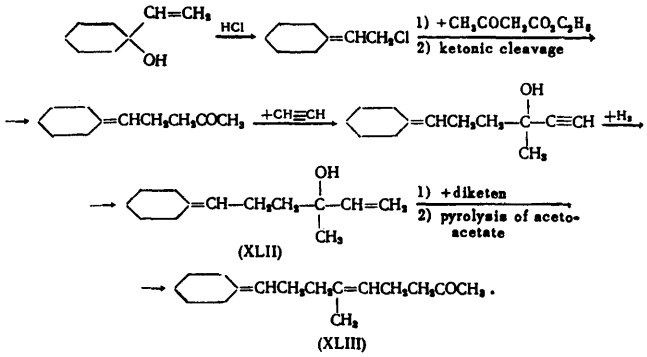
The use in this synthesis of esters of keto-acids $R'CH_2COCH(R)COOC_2H_5$, obtained by ester condensation of esters of aliphatic acids, enables δ-lactones of general formula



to be synthesised relatively easily; new substituted cycloalkenones, analogues of dihydrojasmone, may be obtained from these by cyclodehydration.

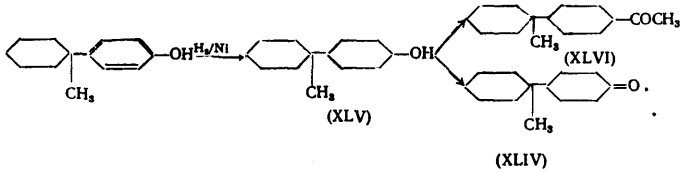
Petrov, Nikishin, and their coworkers [226-228] have recently published detailed papers on the preparation of various alkylated γ- and δ-lactones, several of which may be of interest in perfumery.

Surmatis [229,230] and Kimel [231] have described the preparation of 6-cyclohexylidene-3-methylhex-1-en-3-ol (XLII), which has a musty odour (recommended for conferring an earthy odour on floral compositions), and 9-cyclohexylidene-6-methylnon-5-en-2-one (XLIII), which has been described as a compound of rose fragrance with a fruity shade. These compounds were synthesised from 1-vinylcyclohexanol by the scheme

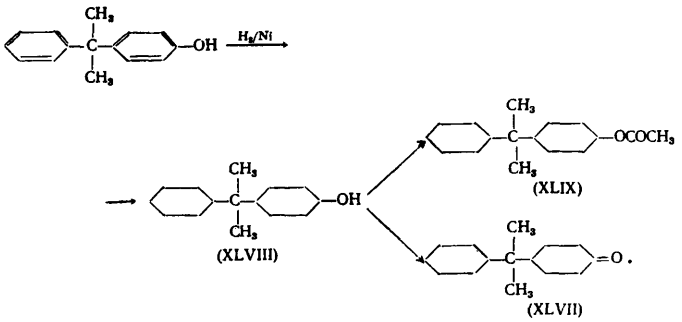


The acetates, propionates, butyrates, and isobutyrates of *cis*- and *trans*-isomers of 4-t-butylcyclohexanol have been found to differ greatly: the odour of the *cis*-isomers is 2–5 times as strong as that of the corresponding *trans*-isomers, and it is also more delicate [232].

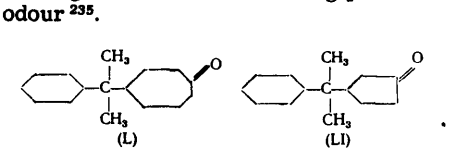
Belov and his coworkers [233] have observed an interesting odour, resembling that of vetiver oil, in the ketone (XLIV); the corresponding alcohol (XLV) has a strong characteristic odour, and its acetate (XLVI) an odour close to that of musterone. These compounds are easily prepared from *p*-1-methylcyclohexylphenol:



The ketone (XLVII), the alcohol (XLVIII), and its acetate (XLIX) have only a weak, uncharacteristic odour, that of the ketone being somewhat stronger. These compounds are prepared by the scheme [234]



Change from a five- to a seven-membered ketonic ring has no material effect on the odour. The ketones (L) and (LI) have the same kind of odour as the ketone (XLVII); the ketone having a five-membered ring possesses the strongest odour [235].



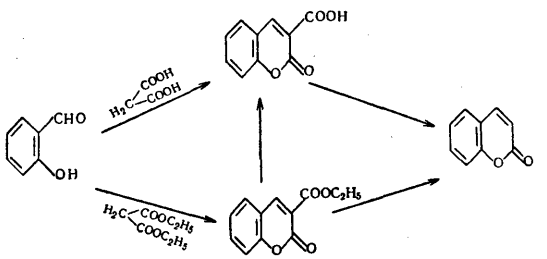
Improvements in the synthesis of isoeugenol from guaiacol *via* its propionate are reported in several publications. The propionate is converted by Fries' rearrangement into

† One of the isomers, which differ in the position of the double bond in the ring, is shown.

4-hydroxy-3-methoxypropiophenone, which is hydrogenated to the corresponding alcohol; the alcohol is then dehydrated to give isoeugenol[236-241]. In work on the direct *C*-allylation of guaiacol *para* to the hydroxy-group, Tsukervanik and Mel'kanovitskaya[242-244] developed a method of preparing eugenol by the interaction of guaiacol and allyl chloride in the presence of a copper catalyst. The yield of the resulting mixture of allylguaiacols is ~29%, based on the allyl chloride taken, or 39% on the guaiacol consumed; the eugenol content of this mixture, determined by infrared spectroscopy[245], is 59%[244].

Allylation in the presence of a copper catalyst has also been used for the preparation of safrole from methylenedioxybenzene[246].

Bratus and Voronin[247-249] have studied the separate stages of the synthesis of coumarin [2-oxochromen] by the Knoevenagel reaction, in which salicylaldehyde is condensed with malonic acid or its ester, and the 2-oxochromen-3-carboxylic acid obtained is decarboxylated:

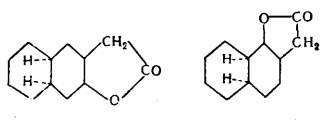


In the search for a more convenient method of synthesising coumarin, the preparation of the 3-carboxylic acid by interaction of salicylaldehyde and sodium cyanoacetate has been studied; sodium cyanoacetate is an intermediate in the production of malonic ester[250].

A method proposed[251] in 1958 for the conversion of 2-oxochromen-3-carboxylic acid into coumarin, based on the addition of bisulphite to the double bond of the pyran ring with simultaneous elimination of carbon dioxide, has been successfully extended to the ester. High yields of coumarin indicate that the method is suitable for industrial use[252].

Some problems in the preparation of coumarin by the interaction of salicylaldehyde and acetic anhydride[253,254] have been examined. Belov *et al.*[255] report an improvement in the synthesis of salicylaldehyde by the Reimer–Tiemann reaction.

In work on the relation between odour and structure in organic compounds[256,257], a lactone of the octalin series, with the proposed structure (LII) or (LIII), has been synthesised; an analogue (LIV), with a t-butyl group instead of one of the cylcohexane rings, has also been synthesised. Both lactones have an agreeable sandalwood odour, that of the first being the stronger.



(LII) (LIII) (LIV)

1. V.N.Belov, N.A.Daev, N.I.Skvortsova, and E.K.Smol'yaninova, Uspekhi Khim., 26, 96 (1957).
2. V.M.Rodionov, V.N.Belov, E.A.Ogorodnikova, and N.N.Shevyakova, Trudy Vses.Nauch.-Issled.Inst.Sintet. Nat.Dush.Veshch., No.1, 5 (1952).
3. V.N.Belov, E.K.Smol'yaninova, E.A.Ogorodnikova, V.M.Rodionov, N.P.Solov'eva, G.E.Svadkovskaya, and N.N.Shevyakova, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat. Dush.Veshch., No.4, 3 (1958).
4. G.E.Svadkovskaya, S.A.Voitkevich, E.K.Smol'yaninova, and V.N.Belov, Zhur.Obshch.Khim., 27, 2146 (1957).
5. V.M.Rodionov, V.N.Belov, E.K.Smol'yaninova, E.A.Ogorodnikova, N.P.Solov'eva, N.N.Shevyakova, and G.E.Svadkovskaya, USSR P. 93 680 (1952).
6. S.A.Voitkevich, G.E.Svadkovskaya, and O.K.Sladkova, USSR P. 101 078 (1955).
7. V.N.Belov, N.A.Daev, and N.I.Skvortsova, Zhur.Vses. Khim.Obshch.Mendeleeva, 5, 362 (1960).
8. I.M.Lebedev and S.Z.Gankin, USSR P. 149 401 (1962); Ref. Zhur.Khim., 10N49 (1963).
9. M.Ya.Fioshin, I.M.Lebedev, L.I.Kazakova, S.Z.Gankin, O.M.Khol'mer, G.I.Gurevich, and E.Ya.Neiman, Khim. Prom., No.1, 41 (1962).
10. G.E.Svadkovskaya, E.K.Smol'yaninova, and V.N.Belov, Zhur.Obshch.Khim., 28, 2268 (1958).
11. V.M.Rodionov, N.P.Solov'eva, E.K.Smol'yaninova, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat. Dush.Veshch., No.2, 29 (1954).
12. A.Guyer, A.Breler, and M.Sommaraga, Helv.Chim.Acta, 38, 976 (1955).
13. N.P.Solov'eva, E.K.Smol'yaninova, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.4, 22 (1958).
14. A.N.Nesmeyanov, Sh.A.Karapetyan, and R.Kh.Freidlina, Dokl.Akad.Nauk SSSR, 109, 791 (1956).
15. Sh.A.Karapetyan and L.A.Pichugin, Dokl.Akad.Nauk SSSR, 114, 549 (1957).
16. A.N.Nesmeyanov, L.I.Zakharkin, T.A.Kost, and R.Kh.Freidlina, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 211 (1960).
17. A.N.Nesmeyanov, R.Kh.Freidlina, V.N.Belov, Sh.A.Karapetyan, E.K.Smol'yaninova, N.P.Solov'eva, E.A.Ogorodnikova, E.I.Vasil'eva, L.I.Zakharkin, and N.N.Shevyakova, Zhur.Vses.Khim.Obshch.Mendeleeva, 5, 371 (1960).
18. Z.N.Bychkova, Z.I.Agarysheva, N.M.Shvarev, and V.P.Semenov, Masl.-Zhirov.Prom., No.9, 27 (1961).
19. R.Joyce, W.Hanford, and I.Harmon, J.Amer.Chem.Soc., 70, 2529 (1948).
20. R.Kh.Freidlina and E.I.Vasil'eva, Dokl.Akad.Nauk SSSR, 100, 85 (1955).
21. R.Kh.Freidlina and E.I.Vasil'eva, Izv.Akad.Nauk SSSR, Otd. Khim.Nauk, 35 (1958).
22. R.Kh.Freidlina and E.I.Vasil'eva, USSR P. 105 135 (1957).
23. E.K.Smol'yaninova and V.N.Belov, USSR P. 94 159 (1952).
24. V.N.Belov and S.G.Polyakova, USSR P. 135 483 (1960).
25. V.N.Belov and S.G.Polyakova, Masl.-Zhirov.Prom., No.8, 18 (1963).
26. N.P.Solov'eva, V.P.Osipova, S.A.Voitkevich, and V.N.Belov, Masl.-Zhirov.Prom., No.5, 34 (1961).
27. E.S.Kaboshina, A.G.Lifshits, V.P.Osipova, P.V.Ivanov, and K.I.Agafonova, Trudy Vses.Nauch.-Issled.Inst.Sintet. Nat.Dush.Veshch., No.6, 85 (1963).
28. Soap, Perfumery, and Cosmetics, 32, 911 (1959).
29. Amer.Perfumer Aromatics, 73, No.3, 40 (1959).
30. E.Spanagel, U.S.P. 2 163 109; Perfumery Essent.Oil Record, 48, 28 (1957).
31. S.G.Polyakova and V.N.Belov, Zhur.Vses.Khim.Obshch.

Mendeleeva, 7, 578 (1962); Zhur.Obshch.Khim., 34, 565 (1964).
32. A.T.Blomquist, J.Prager, and J.Wolinsky, J.Amer.Chem. Soc., 77, 1804 (1955).
33. D.J.Cram and M.Cordon, J.Amer.Chem.Soc., 77, 1810 (1955).
34. S.Z.Taits and Ya.L.Gol'dfarb, USSR P. 132 221 (1960); Ref.Zhur.Khim., 16N482 (1961).
35. S.Z.Taits and Ya.L.Gol'dfarb, Izv.Akad.Nauk SSSR, Otd. Khim.Nauk, 1698 (1960).
36. Ya.L.Gol'dfarb, S.Z.Taits, and L.I.Belen'kii, Izv.Akad. Nauk SSSR, Otd.Khim.Nauk, 1262 (1957).
37. Ya.L.Gol'dfarb, S.Z.Taits, and L.I.Belen'kii, Zhur.Obshch. Khim., 29, 3564 (1959).
38. Ya.L.Gol'dfarb, S.Z.Taits, and L.I.Belen'kii, USSR P. 120 841 (1958).
39. L.I.Belen'kii, S.Z.Taits, and Ya.L.Gol'dfarb, Dokl.Akad. Nauk SSSR, 139, 1356 (1961).
40. Ya.L.Gol'dfarb, S.Z.Taits, and L.I.Belen'kii, Izv.Akad. Nauk SSSR, Otd.Khim.Nauk, 1451 (1963).
41. S.Z.Taits, L.I.Belen'kii, and Ya.L.Gol'dfarb, Izv.Akad. Nauk SSSR, Otd.Khim.Nauk, 1460 (1963).
42. Ya.L.Gol'dfarb, S.Z.Taits, and L.I.Belen'kii, USSR P. 140 432 (1961); Ref.Zhur.Khim., 4N88 (1963).
43. M.Sy, N.Buu-Hoi, and N.Xuong, J.Chem.Soc., 21 (1955).
44. N.Buu-Hoi, M.Sy, and N.Xuong, Bull.Soc.chim.France, 1583 (1955).
45. N.Buu-Hoi, M.Sy, and N.Xuong, Compt.rend., 240, 785 (1955).
46. Ya.L.Gol'dfarb and M.L.Kirmalova, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 570 (1955).
47. G.Badger, H.Rodda, and W.Sasse, J.Chem.Soc., 4162 (1954).
48. V.M.Sautin, Masl.-Zhirov.Prom., No.1, 32 (1957).
49. I.K.Sarycheva, G.A.Shatenshtein, M.G.Pleshakov, and N.A.Preobrazhenskii, Zhur.Obshch.Khim., 30, 2539 (1960).
50. B.Ghatge, U.Nayak, K.Chakravarti, and S.Bhattacharyya, Chem.and Ind., 1334 (1960).
51. V.Dhekne, B.Ghatge, U.Nayak, K.Chakravarti, and S.Bhattacharyya, J.Chem.Soc., 2348 (1962).
52. S.Sabnis, H.Mathur, and S.Bhattacharyya, J.Chem.Soc., 2477 (1963).
53. S.Bhattacharyya, K.Chakravarti, and U.Nayak, Chem.and Ind., 588 (1960).
54. S.Bhattacharyya and H.Mathur, Chem.and Ind., 1087 (1960).
55. G.I.Nikishin, G.V.Somov, and A.D.Petrov, Dokl.Akad. Nauk SSSR, 136, 1099 (1961).
56. G.I.Nikishin, G.V.Somov, and A.D.Petrov, Dokl.Akad. Nauk SSSR, 144, 579 (1962).
57. Ya.L.Gol'dfarb and L.I.Belen'kii, Uspekhi Khim., 26, 362 (1957).
58. G.Eglinton and A.Galbraith, Proc.Chem.Soc., 350 (1957).
59. F.Sondheimer and R.Wolovsky, Tetrahedron Letters, No.3, 3 (1959).
60. F.Sondheimer and R.Wolovsky, J.Amer.Chem.Soc., 81, 1771 (1959).
61. F.Sondheimer, Y.Amiel, and Y.Gaoni, J.Amer.Chem. Soc., 81, 1771 (1959).
62. R.Kolinskii, Uspekhi Khim., 30, 701 (1961) [Russ.Chem. Rev., 309 (1961)].
63. L.D.Bergel'son, Yu.G.Molotkovskii, and M.M.Shemyakin, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 1139 (1960).
64. L.D.Bergel'son, Yu.G.Molotkovskii, and M.M.Shemyakin, Zhur.Obshch.Khim., 32, 58 (1962).
65. L.D.Bergelson, Jul.G.Molotkovsky, and M.M.Shemyakin, Chem.and Ind., 558 (1960).
66. L.D.Bergel'son, Yu.G.Molotkovskii, and L.I.Ilyukhina, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 2099 (1961).
67. Y.Iwakura and K.Uno, J.Org.Chem., 25, 1227 (1960).
68. Y.Iwakura and K.Uno, Bull.Tokyo Inst.Technol., No.42, 89 (1961).
69. A.Blomquist and J.Wolinsky, J.Amer.Chem.Soc., 77, 5423 (1955).
70. A.Blomquist and J.Wolinsky, U.S.P. 2 790 005 (1957).
71. H.Schinz, L.Ruzicka, U.Geyer, and V.Prelog, Helv.Chim. Acta, 29, 1524 (1946).
72. K.Biemann, G.Büchi, and B.Walker, J.Amer.Chem.Soc., 79, 5558 (1957).
73. V.N.Ipatieff, H.Pines, and R.Olberg, J.Amer.Chem.Soc., 70, 2123 (1948).
74. M.Carpenter and W.Easter, J.Org.Chem., 16, 618 (1951).
75. German P. 918 747 (1954).
76. H.Barbier, Helv.Chim.Acta, 15, 592 (1932).
77. H.Barbier, Helv.Chim.Acta, 19, 1345 (1936).
78. S.Weber, D.Spoelstra, and E.Polak, Rec.Trav.chim., 74, 1179 (1955).
79. S.Weber, J.Stofberg, D.Spoelstra, and R.Kleipool, Rec. Trav.chim., 75, 1433 (1956).
80. A.Grampoloff, Parfümerie u.Kosmetik, 178 (1956).
81. A.Grampoloff, Helv.Chim.Acta, 38, 1263 (1955).
82. A.Post, Amer.Perfumer Aromatics, 71, No.3, 46 (1958).
83. D.Spoelstra, S.Weber, and R.Kleipool, Rec.Trav.chim., 76, 205 (1957).
84. M.Beets, H.Essen, and W.Meerburg, Rec.Trav.chim., 77, 854 (1958).
85. S.Weber, R.Kleipool, and D.Spoelstra, Rec.Trav.chim., 76, 193 (1957).
86. J.Pickthall, Soap, Perfumery, and Cosmetics, 32, 889 (1959).
87. Soap, Perfumery, and Cosmetics, 33, 416 (1960).
88. C.Ferrero and R.Helg, Helv.Chim.Acta, 42, 2111 (1959).
89. Parfümerie u.Kosmetik, 37, 36 (1956).
90. A.Post, Amer.Perfumer Aromatics, 71, No.3, 46 (1958).
91. Amer.Perfumer Aromatics, 73, No.6, 55 (1959).
92. Parfümerie u.Kosmetik, 40, 521 (1959).
93. M.Carpenter and W.Easter, U.S.P. 2 800 511 (1957).
94. M.Carpenter, W.Easter, and T.Wood, German P. 951 267 (1956).
95. M.Carpenter, B.P. 760 667 (1956).
96. M.Carpenter, W.Easter, and T.Wood, U.S.P. 2 997 503 (1961).
97. Ind.Parfumerie, 514 (1956).
98. R.Classen, Parfümerie u.Kosmetik, 39, 270 (1958).
99. N.Buu-Hoi and P.Cagniant, Compt.rend., 214, 115 (1942).
100. P.Cagniant and N.Buu-Hoi, Bull.Soc.chim.France, [v], 9, 111 (1942).
101. M.Sy, N.Buu-Hoi, and N.Xuong, J.Chem.Soc., 21 (1955).
102. M.Carpenter, W.Easter, and T.Wood, U.S.P. 2 815 382 (1957).
103. M.Carpenter, U.S.P. 2 815 381 (1957).
104. M.Beets, W.Meerburg, and H.van Essen, Rec.Trav.chim., 78, 570 (1959).
105. V.M.Rodionov, V.N.Belov, and S.A.Kore, Trudy Vses. Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.1, 27 (1952).
106. H.Horiguch, Koryo, No.34, 24 (1955).
107. E.Burgoyne, T.Klose, and D.Watson, J.Org.Chem., 20, 1508 (1955).
108. F.Schmitt, Parfümerie u.Kosmetik, 36, 312 (1955).
109. J.Erdos and M.Salazar, Ciencia, 12, 228 (1953).
110. K.A.Bogdanov, E.F.Yakusheva, V.P.Agaryshev, and L.M.Gol'denshtein, Masl.-Zhirov.Prom., No.11, 38 (1959).
111. D.Joshi and J.Merchant, J.Sci.Ind.Res., India, 14B, 482 (1955).
112. B.P. 699 062 (1953).

113. H.Frisch, Canad.P. 512236 (1955).
114. B.P. 760768 (1956).
115. French P. 1116792 (1956).
116. M.Beets, Soap, Perfumery, and Cosmetics, 29, 665 (1956).
117. G.V.Vorob'eva, Yu.A.Kireev, I.N.Bratus, and V.G.Voronin, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush. Veshch., No.6, 48 (1963).
118. E.Eliel and D.Delmonte, J.Amer.Chem.Soc., 78, 3226 (1956).
119. W.Daniewski, Przemysl spozywczy, 10, 348 (1956).
120. M.Filipescu and E.Manisor, Rev.Chim.(Roumania), 4, 9 (1953); Ref.Zhur.Khim., 44363 (1956).
121. A.A.Bag and N.V.Bliznyak, Trudy Vses.Nauch.-Issled. Inst.Sintet.Nat.Dush.Veshch., No.4, 63 (1958).
122. M.Takao and M.Kumamoto, Jap.P. 6566 (1954).
123. Beijing Daxue Xuebao-Ziran Kexue, Acta Sci.Natur.Univ. Pekinensis, 5, No.1, 71 (1959); Ref.Zhur.Khim., 42663 (1960).
124. E.N.Kiseleva, N.I.Gel'perin, and V.A.Shestakova, Zhur. Prikl.Khim., 34, 167 (1961).
125. L.A.Shutikova and V.G.Cherkaev, Trudy Vses.Nauch.--Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 37 (1963).
126. M.Miyazaki and T.Terakawa, J.Pharm.Soc.Japan, 74, 310 (1954).
127. A.A.Bag, N.V.Shorygina, and N.V.Bliznyak, Trudy Vses. Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.2, 57 (1954).
128. K.Chakravarti and S.Bhattacharyya, J.Indian Chem.Soc., Ind.News Edn., 18, 31 (1955).
129. G.Gál and I.Krasznai, Magyar Kém.Folyóirat, 62, 155 (1956).
130. Y.Okada, Kagaku Kogyo Siryo (Chem.Engr's Digest), 27, 25 (1959).
131. V.I.Gorshkov and L.Kh.Freidlin, "VIII Mendeleevskii S'ezd, Referat — Sektsiya Organicheskikh Khimii i Tekhnologii" (Eighth Mendeleev Congress, Organic Chemistry and Technology Section), Izd.Akad.Nauk SSSR, Moscow, 1959, p.9.
132. W.Daniewski and T.Strojny, Przemysl Chem., 41, 68 (1962).
133. S.Matsuda and R.Toyoda, J.Japan Oil Chemists' Soc., 4, 10 (1955).
134. J.N.Ray, A.Mukherji, and N.D.Gupta, J.Indian Chem.Soc., 38, 705 (1961).
135. A.M.Sladkov, V.A.Markevich, I.A.Yavich, L.K.Luneva, and V.N.Chernov, Dokl.Akad.Nauk SSSR, 119, 1159 (1958).
136. A.M.Sladkov and L.K.Luneva, Zhur.Obshch.Khim., 28, 2894 (1958).
137. B.I.Golovanenko, A.M.Sladkov, L.L.Ivanov, Z.S.Kalashnikova, and A.T.Menyailo, Zhur.Vses.Khim.Obshch. Mendeleeva, 5, 594 (1960).
138. A.Weissenborn, East German P. 4560 (1955); Ref.Zhur. Khim., 66471 (1956).
139. N.P.Sopov and M.L.Kovner, Zhur.Obshch.Khim., 28, 2145 (1958).
140. V.E.Sibirtseva and V.N.Belov, Trudy Vses.Nauch.-Issled. Inst.Sintet.Nat.Dush.Veshch., No.4, 50 (1958).
141. V.N.Belov and N.I.Skvortsova, Uspekhi Khim., 32, 265 (1963) [Russ.Chem.Rev., 121 (1963)].
142. H.Normant, Compt.rend., 240, 314 (1955).
143. V.Levy and H.Normant, Compt.rend., 244, 202 (1957).
144. H.Normant, Compt.rend., 240, 1435 (1955).
145. H.Normant and P.Maitte, Bull.Soc.chim.France, 951 (1956).
146. J.Ficini, Bull.Soc.chim.France, 119 (1956).
147. P.G.Sergeev and L.A.Ivanova, "Sintez Spirtov i Organicheskikh Produktov iz Neftyanykh Uglevodorodov" (The Synthesis of Alcohols and Organic Products from Petroleum Hydrocarbons), Goskhimizdat, Moscow, 1960, p.239.
148. B.P. 761040 (1956).
149. French P. 1111933 (1956).
150. O.Wichterle and J.Cerný, Chem.Listy, 49, 1038 (1955).
151. S.A.Kore and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst. Sintet.Nat.Dush.Veshch., No.4, 41 (1958).
152. M.Chaco and B.Iyer, J.Indian Inst.Sci., 36A, 160 (1954).
153. S.A.Kore, S.D.Kustova, and V.N.Belov, Trudy Vses. Nauch.Issled.-Inst.Sintet.Nat.Dush.Veshch., No.4, 39 (1958).
154. S.Murahashi, N.Harihara, and Y.Ueno, Osaka Daigaku Sangyo Kagaku Kenkyusyo-me, Jap.P. 4922 (1954); Ref. Zhur.Khim., 20907 (1957).
155. Y.Ueno, T.Kobayashi, J.Furukawa, N.Harihara, and S.Murahashi, J.Soc.Org.Synth.Chem.Japan, 20, 555 (1962); Ref.Zhur.Khim., 13Zh130 (1963).
156. S.N.Ushakov and O.F.Solomon, USSR P. 105651 (1953).
157. W.Reppe, W.Pfab, N.Kutepow, and W.Büche, German P. 1029369 (1958).
158. T.Matsuda, Kagaku To Kogyo (Tokyo) (Chem.and Chem. Ind.), 12, 434 (1959); Ref.Zhur.Khim., 4951 (1960).
159. K.Wintersberger and G.Zirker, German P. 1025870 (1958).
160. L.I.Zakharkin and I.M.Khorlina, Dokl.Akad.Nauk SSSR, 116, 422 (1957).
161. H.Bestmann and H.Schulz, Chem.Ber., 92, 530 (1959).
162. D.C.Young, U.S.P. 2649462 (1953).
163. J.Erickson and G.Grammer, J.Amer.Chem.Soc., 80, 5466 (1958).
164. W.Trapp, U.S.P. 2770654 (1956).
165. P.Mastagli, P.Lambert, and C.Hirigoyen, Compt.rend., 248, 1830 (1959).
166. H.Kaufmann and D.Spannuth, Chem.Ber., 91, 2127 (1958).
167. A.Halasz, Canad.J.Chem., 31, 297 (1953).
168. S.Lieberman, J.Amer.Chem.Soc., 77, 1114 (1955).
169. French P. 1120247 (1956).
170. H.Normant, Compt.rend., 240, 1435 (1955).
171. S.Wakayama, S.Itoh, S.Yui, and H.Maekawa, J.Chem. Soc.Japan, 78, 1525 (1957); Ref.Zhur.Khim., 57345 (1958).
172. M.Julia and J.-M.Surzur, Bull.Soc.chim.France, 1615 (1956).
173. E.Royals and E.Covington, J.Amer.Chem.Soc., 77, 1697 (1955).
174. H.Martin, Compt.rend., 242, 1486 (1956).
175. K.A.Bogdanov and K.A.Antonova, Trudy Vses.Nauch.--Issled.Inst.Sintet.Nat.Dush.Veshch., No.5, 16 (1961).
176. M.Mousseron-Canet, M.Mousseron, L.Benezet, and G.Igolen, France et ses Parfums, 1, 28 (1958).
177. M.Mousseron-Canet, M.Mousseron, L.Benezet, and G.Igolen, Parfümerie u.Kosmetik, 40, No.2, 71 (1959).
178. M.Beets and H.Essen, B.P. 841921 (1960).
179. E.D.Laskina and T.A.Devitskaya, Masl.-Zhirov.Prom., No.5, 23 (1963).
180. J.Dorsky and W.Easter, U.S.P. 2976321 (1961).
181. S.Suzuki, K.Muroshima, and T.Takeshima, Sci.Papers Inst.Phys.Chem.Res., Tokyo, 55, 83 (1961); Ref.Zhur. Khim., 10Zh147 (1962).
182. B.P. 850360 (1960).
183. T.Kuwata, A.Yasukawa, and S.Abe, Jap.P. 13627 (1961); Ref.Zhur.Khim., 9N60 (1963).
184. J.Dorsky and W.Easter, U.S.P. 2976327 (1961).
185. S.Shin'ya, J.Agric.Chem.Soc.Japan, 29, 91 (1955); Ref. Zhur.Khim., 15998 (1960).
186. S.Shin'ya, J.Agric.Chem.Soc.Japan, 29, 94 (1955); Ref. Zhur.Khim., 15999 (1956).
187. I.M.Lebedev, I.A.Gorker, and V.B.Mochalin, Masl.-

-Zhirov.Prom., No.2, 33 (1961).
188. S.Shin'ya, J.Agric.Chem.Soc.Japan, 33, 261 (1959); Ref. Zhur.Khim., 73546 (1960).
189. V.N.Kraseva, A.A.Bag, L.L.Malkina, and O.M.Khol'mer, Masl.-Zhirov.Prom., No.12, 23 (1958).
190. T.Kumata, A.Yoshikoshi, and B.Okazaki, Annual Rept. Engng.Res.Inst.Fac.Engng.Univ.Tokyo, 18, No.2, 50 (1960).
191. P.P.Shorygin, A.A.Simanovskaya, and A.V.Bogdanova, Zhur.Obshch.Khim., 8, 975 (1938).
192. E.D.Laskina, USSR.P. 106564 (1957).
193. E.D.Laskina, Zhur.Prikl.Khim., 32, 878 (1959).
194. V.N.Eliseeva and T.A.Devitskaya, Zhur.Prikl.Khim., 29, 1894 (1956).
195. E.D.Laskina, T.A.Devitskaya, Z.N.Bychkova, R.F.Shilina, and T.V.Sukhorukova, Trudy Vses.Nauch.-Issled. Inst.Sintet.Nat.Dush.Veshch., No.5, 21 (1961).
196. E.D.Laskina, T.A.Devitskaya, R.F.Shilina, T.V.Sukhorukova, and Z.N.Bychkova, USSR P. 142302 (1961).
197. V.N.Eliseeva and T.A.Devitskaya, Trudy Vses.Nauch.--Issled.Inst.Sintet.Nat.Dush.Veshch., No.4, 31 (1958).
198. A.Arend, Perfumery Essent.Oil Record, 49, No.1, 21 (1958).
199. P.Stefanescu, Rev.Chim.(Roumania), 7, 726 (1956).
200. R.Yu.Shagalova, N.A.Daev, N.I.Gel'perin, and M.P.Kuznetsova, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush. Veshch., No.4, 34 (1958).
201. K.I.Bogacheva, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat. Dush.Veshch., No.6, 59 (1963).
202. M.Rubel, Uch.Zap.Tartusk.Univ., No.55, 51 (1958); Ref. Zhur.Khim., 53377 (1959).
203. E.D.Laskina and V.N.Belov, Trudy Vses.Nauch.-Issled. Inst.Sintet.Nat.Dush.Veshch., No.4, 27 (1958).
204. L.Kh.Freidlin, V.Z.Sharf, O.M.Khol'mer, L.L.Malkina, and I.M.Lebedev, Masl.-Zhirov.Prom., No.10, 24 (1960).
205. E.D.Laskina, E.A.Simanovskaya, V.N.Belov, Z.N.Bychkova, R.F.Shilina, Z.T.Emel'yanenko, and Z.V.Mikhailova, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush. Veshch., No.5, 25 (1961).
206. N.N.Shorygina and T.V.Izumrudova, Khim.Nauka i Prom., 4, 754 (1959).
207. A.I.Kozlov and I.I.Gorshkov, Med.Prom., No.2, 31 (1958).
208. S.A.Sapotnitskii, O.D.Kamaldina, and Ya.A.Massov, Gidroliznaya i Lesokhim.Prom., No.7, 14 (1956).
209. O.D.Kamaldina, Khim.Nauka i Prom., 2, 462 (1957).
210. V.N.Eliseeva, T.A.Devitskaya, and E.D.Laskina, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.5, 18 (1961).
211. S.Joffre, U.S.P. 2663741 (1953); Ref.Zhur.Khim., 22473 (1955).
212. S.Joffre, Canad.P. 517423 (1955); Ref.Zhur.Khim., 72789 (1957).
213. "The Condensed Chemical Dictionary", 5th Edn., New York, 1956, p.1146.
214. E.D.Laskina, T.A.Devitskaya, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 31 (1963).
215. C.Rai and S.Dev, Experientia, 11, 114 (1953).
216. C.Rai and S.Dev, J.Indian Chem.Soc., 34, 178 (1957).
217. C.Rai and S.Dev, J.Indian Chem.Soc., 34, 266 (1957).
218. O.Riobé, Compt.rend., 247, 1016 (1958).
219. M.Ansell and S.Brown, J.Chem.Soc., 2955 (1958).
220. J.Dominguez, G.Diaz, and J.Slim, Ciencia, 16, No.7–8, 151 (1956–1957).
221. I.V.Machinskaya and A.S.Podberezina, Masl.-Zhirov.Prom., No.12, 29 (1961).
222. J.Amin, R.Razden, and S.Bhattacharyya, Perfumery Essent.Oil Record, 49, 502 (1958).
223. V.N.Belov and T.A.Dil'man, Khim.Nauka i Prom., 2, 135 (1957).
224. A.L.Voitsekhovskaya and V.N.Belov, Trudy Vses.Nauch.--Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 62 (1963).
225. A.L.Voitsekhovskaya and V.N.Belov, Trudy Vses.Nauch.--Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 66 (1963).
226. G.I.Nikishin, V.D.Vorob'ev, and A.D.Petrov, Dokl.Akad. Nauk SSSR, 136, 360 (1961).
227. G.I.Nikishin and V.D.Vorob'ev, USSR P. 137911 (1961); Ref.Zhur.Khim., 20N273 (1962).
228. G.I.Nikishin, Yu.N.Ogibin, and A.D.Petrov, Dokl.Akad. Nauk SSSR, 138, 393 (1961).
229. J.D.Surmatis, U.S.P. 2812361 (1957).
230. J.D.Surmatis, U.S.P. 2847479 (1958).
231. W.Kimel, U.S.P. 2789130 (1957).
232. W.Somerville and E.Theimer, U.S.P. 2840599 (1958).
233. L.A.Kheifits, G.I.Moldovanskaya, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.5, 6 (1961).
234. L.A.Kheifits, G.I.Moldovanskaya, V.N.Belov, and L.N.Nikolenko, Khim.Nauka i Prom., 2, 658 (1957).
235. L.A.Kheifits, G.I.Moldovanskaya, and V.N.Belov, Zhur. Obshch.Khim., 30, 1367 (1960).
236. I.M.Lebedev, V.D.Gorchakov, O.M.Khol'mer, and S.G.Polyakova, USSR P. 103727 (1955).
237. S.G.Polyakova, N.A.Daev, O.M.Khol'mer, and I.M.Lebedev, USSR P. 126879 (1958).
238. S.G.Polyakova, L.L.Malkina, O.M.Khol'mer, I.M.Lebedev, V.D.Gorchakov, and E.D.Laskina, USSR P. 114197 (1958).
239. O.M.Khol'mer, S.G.Polyakova, and E.D.Laskina, Masl.--Zhirov.Prom., No.9, 31 (1958).
240. S.G.Polyakova, O.M.Khol'mer, and I.M.Lebedev, Masl.--Zhirov.Prom., No.8, 23 (1959).
241. O.M.Khol'mer and S.G.Polyakova, Masl.-Zhirov.Prom., No.4, 26 (1959).
242. I.P.Tsukervanik and S.G.Mel'kanovitskaya, USSR P. 117492 (1958).
243. S.G.Mel'kanovitskaya and I.P.Tsukervanik, Dokl.Akad. Nauk Uzbek.SSR, No.11, 40 (1959).
244. S.G.Mel'kanovitskaya and Ya.V.Rashkes, Zhur.Obshch. Khim., 32, 2232 (1962).
245. Ya.V.Rashkes and S.G.Mel'kanovitskaya, Zhur.Anal.Khim., 17, 751 (1962).
246. S.G.Mel'kanovitskaya and I.P.Tsukervanik, Dokl.Akad. Nauk Uzbek.SSR, No.8, 50 (1961).
247. I.N.Bratus and V.G.Voronin, USSR P. 130518 (1959).
248. I.N.Bratus and V.G.Voronin, USSR P. 132235 (1960).
249. I.N.Bratus and V.G.Voronin, Trudy Vses.Nauch.-Issled. Inst.Sintet.Nat.Dush.Veshch., No.5, 34 (1961).
250. I.N.Bratus, V.G.Voronin, and V.N.Belov, Trudy Vses. Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 81 (1963).
251. W.Daniewski, Roczniki Chem., 32, 667 (1958).
252. I.N.Bratus, Zhur.Vses.Khim.Obshch.Mendeleeva, 5, 410 (1960).
253. K.A.Bogdanov, USSR P. 101027 (1954).
254. V.G.Voronin, I.N.Bratus, E.I.Kraevskaya, I.A.Filatova, A.V.Sobolevskaya, and V.N.Belov, Masl.-Zhirov.Prom., No.4, 37 (1963).
255. I.N.Bratus, I.A.Filatova, V.G.Voronin, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.6, 45 (1963).
256. E.V.Shevlyagina, E.I.Gushchina, and V.N.Belov, Trudy Vses.Nauch.-Issled.Inst.Sintet.Nat.Dush.Veshch., No.4, 44 (1958).
257. E.V.Shevlyagina, E.I.Gushchina, and V.N.Belov, Trudy

Vses. Nauch.-Issled. Inst. Sintet. Nat. Dush. Veshch., No. 4, 47 (1958).

All-Union Research Institute
for Synthetic and Natural
Perfumery Materials

U. D. C. 612.39 : 543.5

THE CHEMISTRY OF THE ODOUR OF FOODSTUFFS

R. V. Golovnya, G. A. Mironov, and S. D. Sokolov

CONTENTS

I.	Introduction	366
II.	Methods of isolation and identification	366
	Methods of isolation	366
	Methods of identification	367
III.	The odour of milk and milk products	367
	1. Milk, cream, butter	367
	2. Cheese	371
IV.	The odour of bread	375
V.	The odour of cocoa and coffee	377
VI.	The odour of meat and fish products	379
	The aroma of meat	379
	The aroma of fish	380
	The odour of smoked products	381

I. INTRODUCTION

The last few years have seen the introduction and vigorous development of a new field of chemistry — the chemistry of the odour of foodstuffs. This review considers the main lines of investigation from 1956 to 1961 on the chemistry of the odour of meat, fish†, bread, milk and milk products, cocoa, and coffee.

At present the primary task of the chemistry of odour is to investigate the connection between odour and the physicochemical nature of the material, and on this basis to construct a theory to explain the mechanism of the interaction of substances with the olfactory organs. A theory of odour will enable a directed "synthesis" of the aroma of food products to be achieved and an objective odour analyser to be created; such an analyser will find wide application not only in the food and perfumery industries, but also in chemistry as an improved method for the analysis of volatile compounds. In medicine it may be used as a sensitive diagnostic apparatus for various diseases associated with the disturbance of metabolism.

Investigations of the chemistry of odour should also help in solving many of the most important problems of the food industry, in the first place retention of the original odour of commercial food products, avoidance of undesired flavours, shortening of ripening periods, and prevention of aging processes. Of particular significance for the food industry is the creation of aromatic mixtures to reproduce the odours of foodstuffs. In the future, synthetic compositions of food aromas will have particular value in connection with the production of artificial food. Solution of the above problems requires the combined efforts of chemists, physiologists, microbiologists, and food technologists.

The rapid development of the chemistry of odour has been held back by the absence of proper methods of analysis. Our olfactory organs are unsurpassed as analytical devices, and the best methods of analysis cannot as yet compete with them. A man can, for example, distinguish vanillin at a concentration of 10^{-14}. Additional difficulties in studying the odour of food products arise because the odour and the taste of food are extremely closely related, and can be separated only with difficulty, especially in the case of products having little taste and aroma, the latter being perceived only during actual consumption. Analysis of the odour of food products is also made difficult by the fact that odour is associated with the presence of minute quantities of a mixture of volatile substances: for example, 1 kg of cheese contains 1–2 mg of the material responsible for its aroma. Moreover, the aromatic mixture which provides the odour of food products is a multicomponent composition, containing sometimes up to 70 volatile substances. It is not surprising therefore, that the main advances in the chemistry of odour have been made in the last five years, and are principally associated with the use of various types of chromatography, particularly gas chromatography. Investigation of the odour of food products has required specific methods for the isolation and identification of the volatile substances responsible for the odour.

II. METHODS OF ISOLATION AND IDENTIFICATION

Methods of Isolation

Steam distillation in a current of nitrogen at 1–2 mmHg and 35–40° is generally used to separate the odoriferous principles from the mass of foodstuff [1-5]. The aromatic substances are sometimes distilled under a high vacuum (10^{-5}–10^{-6} mmHg) in a film evaporator over the same temperature range; the distillate is collected in a series of traps cooled to temperatures of -10° to -180°. [6-10] When these methods of concentration are used, there is the possibility of a change in the composition of the aromatic material when the foodstuff is heated.

The aromatic substances are sometimes separated by centrifuging [11] or by repeated extraction with solvents [12]; with the latter method, possible losses of readily volatile substances must be borne in mind, as well as the danger of contamination by trace impurities present in the solvent.

† Section VI has been written by S. D. Sokolov.