Ozonolysis used for synthesis of odor compounds

By Jozef Kula, Jozef Gora, Jerzy Podlejski, and Janusz Kulesza
Institute of General Food Chemistry
Technical University, Lodz ul. Gdanska, Poland

Development of new, more economic techniques of ozone production has created practical advantages for its use in industrial chemical processes based on the reactions of oxidative cleavage of ethylene bond in organic compounds.[1-3] This paper concerns, in particular, new or modified methods for the synthesis of odor compounds, drugs, and pesticides. Intensive studies in this field are still in progress in the USA, Japan, the Soviet Union, France, the German Democratic Republic, and Poland. The oxidation process for organic compounds, called ozonolysis, shows some advantages in comparison to classical oxidation methods: high yield (60-100%), no troublesome waste products, continuous process with relatively simple equipment with possibilities to adapt it for various substrates.

The generally approved mechanism of the ozonolysis of olefins according to Criegee is shown in figure 1.[4,5] In the first stage there is an electrophilic combination of ozone to ethylene bond resulting in an intermediate product whose structure depends on the structure of substrate, type of solvent, and reaction temperature. Mostly, ozonolysis reactions are carried out in polar solvents such as water, methanol, ethanol, and low-molecule carboxylic acids. In these solvent systems appropriate hydroperoxide predominates as an intermediate product.
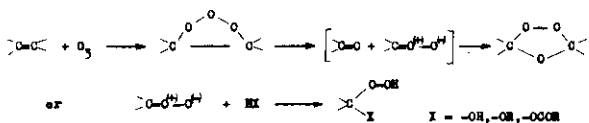

Fig. 1

Primary ozonides and intermediate compounds resulting from their rearrangement are unstable products, susceptible to explosion, polycondensation, and formation of other undesirable products. Therefore, the products obtained in the ozonization process are subjected to further changes as soon as possible to produce more stable and safe compounds such as carboxylic acids, carbonyl compounds, alcohols, or epoxides, depending on the type of substrates and conditions of the given process. Known methods for the decomposition of products of olefins ozonization may be arranged into the types discussed below.

Oxidative decomposition

Oxidative decomposition is usually aimed at converting the intermediate products into carboxylic acids (fig. 2).
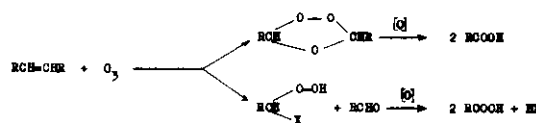

Fig. 2

The necessary condition to produce an acid is the presence of at least one hydrogen atom at carbons combined with a double bond. Hydrogen peroxide and molecular oxygen are mostly used as oxidizing agents.

Bailey recommends carrying out ozonolysis in methanol and the oxidative decomposition of produced methoxyhydroperoxide with perhydrol (30% H_2O_2) in formic acid.[6] In this way adipic acid is produced from cyclohexane, the yield being 85%. The most economic agent to finish oxidation is oxygen (air).[7,8] For example, brassylic acid is prepared by the ozonolysis of erucic acid (fig. 3). The ozonization is carried out in acetic acid at room temperature and the oxidation is finished with oxygen at 100°C. Good results are obtained by a one-step method comprising ozonolysis of olefins or cycloolefins in an aqueous alkaline solution of hydrogen peroxide in the presence of emulsifiers.[9,10]
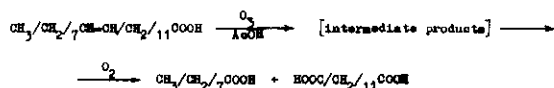
Fig. 3

Reductive decomposition

The reductive decomposition of intermediate products results in the formation of carbonyl compounds or alcohols (fig. 4).
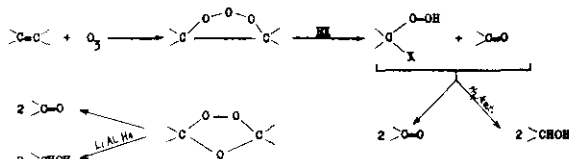

Fig. 4

Many reducing agents have been examined. The most important include metal-acid, hydrogen in presence of catalysts (Pt, Pd, Ni), alkyl sulphides, alkyl phosphates, sulphites and pyrosulphites, and metal hydrides.[11,12]

The reduction of intermediate products with hydrogen under normal pressure in the presence of palladium deposited on carbon deserves particular attention. Extensive studies carried out especially on ozonolysis of fatty acids prove that the reduction of intermediate products under such conditions allows in some cases preparation of carbonyl compounds at a high yield.[13,14] The ozonolysis and reduction are performed in protonic solvents (alcohol, organic acid) at a temperature close to room temperature. The yield of carbonyl compounds depends, among other things, on the type of solvent, which is shown by the example of ozonization of methyl oleate (see Table I).

Table I. Yields of carbonyl compounds prepared by ozonolysis of methyl[13] oleate depending on the type of solvent

Solvent	Carbonyl Yield %	Solvent	Carbonyl Yield %
Methanol	84	Ethanol + 10% pyridine	91
Ethanol	80	1-Propanol + 10% pyridine	93
1-Propanol	85	Methanol + ArOH (1:1)	94
2-Propanol	75	Ethanol + ArOH (1:1)	97
i-Butanol	84	1-Propanol + ArOH (1:1)	97
2-Butanol	79	2-Propanol + propionic acid (1:1)	83
2-Methyl-1-propanol	86	1-Butanol + AcOH (1:1)	97
2-Methyl-2-propanol	66	2-Butanol + propionic acid (1:1)	87
Benzyl alcohol	79	2-Methyl-1-propanol + propionic acid (1:1)	82
Cyclohexanol	81	2-Methyl-2-propanol + propionic acid (1:1)	79
Methoxyethanol	75	Benzyl alcohol + acetic acid (1:1)	97
Acetic acid	62	Cyclohexanol + propionic acid (1:1)	89
Propionic acid	63	2-Methoxyethanol + acetic acid (1:1)	97
Methanol + 10% pyridine	91		
i-Butanol + 10% pyridine	92		
2-Methoxyethanol + 10% pyridine	70		

If these reactions take place in alcohol, very often acetals are formed in addition to carbonyl compounds. Sometimes addition of pyridine increases the yield of the final product considerably.[15,16] In the case of ozonolysis of methylene cycloalkanes in the presence of

pyridine, ketones are produced at a yield of 75-85%.

In 1966 Pappas and coworkers reported on a very convenient method for reduction of alkoxyhydroperoxides (ozonolysis in alcohols) with dimethyl sulphide (fig. 5).[17] The ozonolysis process is carried out in methanol and then dimethyl sulphide is added to decompose the intermediate product. The reduction is completed within several hours at temperatures −10°C and +20°C at a yield of 60-96%. Yields of some aldehydes prepared by this method are shown in Table II. Dimethyl sulphoxide here is a by-product which can be easily separated either by distillation under reduced pressure or by extraction with water. Similarly satisfactory results have been obtained using alkyl phosphates as reducing agents for alkoxyhydroperoxides.[18]
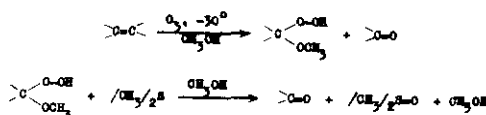

Fig. 5

Table II. Yields of aldehydes prepared by the reduction of the ozonization products with dimethyl sulphide[17]

Olefin	Aldehyde	Yield %
Styrene	Benzaldehyde	89
Isosafrole	Piperonal	96
4-Vinylpyridine	4-Pyridinecarboxaldehyde	80
1-Octene	Heptanal	75
Phenanthrene	2,2'-Diphenyldicarboxaldehyde	91
Naphthalene	Phthalaldehyde	68
Cyclohexene	Adipaldehyde	62

White has given a method for the reduction of alkoxyhydroperoxides with hydrogen in the presence of Raney nickel or platinum, leading directly to alcohols (fig. 6).[19] The ozonization is carried out in methanol, ethanol, or butanol; then the intermediate product is reduced with hydrogen, first under a pressure of several atmospheres at 0.20°C, then raised to 80-100°C, with pressure to about 70 atm. The method obtains good yields of several products which are of interest to both perfumery and cosmetic industries (see Table III). It seems that the method can be used on a commercial scale if the hydrogenation is a continuous process.
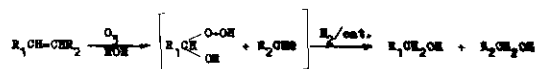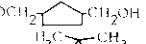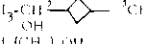

Fig. 6

Hydrolytic decomposition

Intermediate products formed during the action of ozone on olefinic links can be decomposed to carbonyl compounds with water.[20,21] The best results have been obtained in synthesis of aromatic aldehydes. The ozonization was carried out at a temperature of the dry ice and acetone mixture in a methanol solution or in a

solution of methylene chloride and methanol, then the product was immediately steam distilled. Among other things, benzaldehyde was prepared from stilbene at a yield of 93% and from styrene at a yield of 87%; anisic aldehyde from anethole at a yield of 92%; and heliotropin from isosafrole at a yield of 87%.

Table III. Yields of alcohols (diols) in the ozonolysis of olefins[19]

Olefin	Catal.	Products	% Yield
Cyclopentene	Pt	$HO(CH_2)_5OH$	80
Cyclohexene	Pt	$HO(CH_2)_6OH$	95
1-Methylcyclohexene	Ni	$CH_3CH(OH) (CH_2)_5OH$	77
Cyclooctene	Pt	$HO(CH_2)_8OH$	95
Cyclooctene	Ni	$HO(CH_2)_8OH$	92
1,5-Cyclooctadiene	Ni	$HO(CH_2)_4OH$	86
Cyclododecene	Pt	$HO(CH_2)_{12}OH$	85
1,5,9-Cyclododecatriene	Pt	$HO(CH_2)_4OH$	95
Norbornene	Ni	$HOCH_2\!-\!\!\diagup\!\!\diagdown\!\!-CH_2OH$	91
α-Pinene	Ni	$CH_3\text{-}CH\text{-}\diagup\!\!\diagdown\text{-}CH_2CH_2OH$	85
1-Octene	Ni	$CH_3(CH_2)_6OH$	86
Methyl oleate	Ni	$CH_3(CH_2)_8OH$	87
		$HO(CH_2)_8COOCH_3$	91

Pyrolytic and photochemical decomposition

This type of intermediate products decomposition has recently been of wide interest for chemists. Studies are carried out on decomposition of intermediate products both in liquid and in gaseous phases.[22-25] For example, the pyrolysis of n-1-hexene ozonide at a temperature of 100°C gives a product of complex composition, but main components are valeric aldehyde, valeric acid, formic aldehyde, and formic acid (fig. 7).[26]
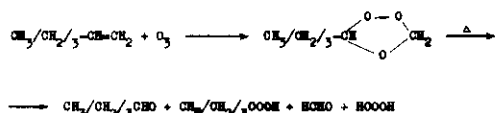
Fig. 7

From the point of view of the ozonized substrate structure the ozonolysis process may be classified into the types discussed below.

Ozonization of alkenes and their functional derivatives

The ozonolysis of alkenes and their functional derivatives has a long-term tradition in the synthesis of mono- and dicarboxylic acids which find their application as intermediates in the cosmetic and perfume industries.

As mentioned above, brassylic acid is prepared by the ozonolysis of erucic acid. Cyclic ethylene ester of this acid is one of the inexpensive, generally used synthetic musks.[27] Similarly, the ozonolysis of oleic acid and oxidative decomposition of intermediate products gives pelargonic and azelaic acids.[28] On the other

hand, the reductive decomposition of intermediate products provides pelargonic and azelaic aldehydes at a good yield (fig. 8).[29]
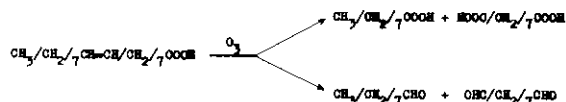
Fig. 8

Oleic acid and its esters are ozonized in methanol, water, or in aqueous methanol solution; and the intermediate products formed are reduced with hydrogen in the presence of palladium catalyst or by a hydrolytic process.[30,31] The yield of carbonyl compounds is about 80%. It is good to perform the ozonolysis process in a continuous manner, as was shown by Pryde in a pilot plant scale.[32]

A high yield of carboxylic compounds is obtained when the ozonolysis of unsaturated fatty acids is carried out in the presence of BF_3CH_3OH.[33,34] Several aliphatic aldehydes $C_6\text{-}C_{12}$ of interest to perfumery can be produced at a good yield by the ozonization of suitable alpha olefins manufactured by the petrochemical industry.[35]

Ozonization of aryloalkenes and their derivatives

A benzene ring can be attacked by ozone under some conditions, but the rate constant of the process is relatively low due to the stability of the aromatic system.[36] Aryloalkenes can be, then, oxidized with ozone to produce corresponding oxy-derivatives without disturbing the aromatic system to a higher extent (the rate constant for vinyl group in styrene is at least $2\cdot10^7$ times as much as the rate constant for the reaction between benzene and ozone). It is, therefore, possible to prepare by ozonolysis such popular odor synthetics as vanillin from isoeugenol or heliotropin from isosafrole (fig. 9).[37,38]
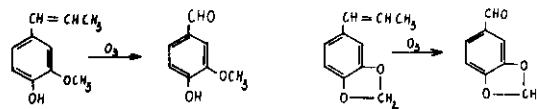
Fig. 9

Naphthalene and its alkyl derivatives are easily substituted with two ozone molecules, after which the reaction rate violently drops. This property has been utilized for the methods of manufacturing phthalic dialdehyde and o-diacetylbenzene (fig. 10).[39,40]
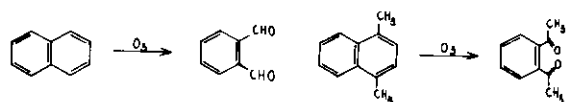
Fig. 10

The ozonolysis of dihydronaphthalene gives formylindene (yield 70%) which can be used as

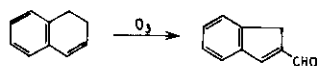intermediate to synthesize compounds of musk odor-indane derivatives (fig. 11).[41]

Fig. 11

The ozonolysis of some easily available, existing-in-nature alkenylcycloparaffins or their derivatives provides several oxy-compounds which are or could be a potential source of intermediates for the synthesis of odor substances. By this method napinone is prepared from β-pinene, and so-called sabina-ketone from sabinene.[16,42] Sabina-ketone, after alkylation, condensation with methylpropenylketone, addition and splitting off of hydrogen chloride, gives a mixture of nootkatone and α-vetivone (fig. 12).
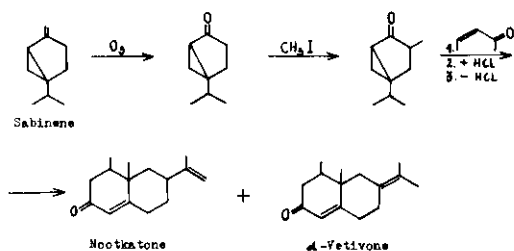

Sabinene

Nootkatone   α-Vetivone

Fig. 12

Nootkatone exists in the stones of the chamaecyparis nootkatensis tree and in lemon oils. It has an extremely strong and sweet lemon odor. α-Vetivone is a component of oil of vetiver and shares the responsibility of its odor.

An important stock to prepare compounds with amber odor is diterpenic unsaturated alcohol—sclareol and manool. Sclareol is isolated from salvia salarea. Manool can be found in some forms of dacrydium, cupressus, and abies plants. Sclareol is modified into compounds of amber or musk odor according to figure 13.
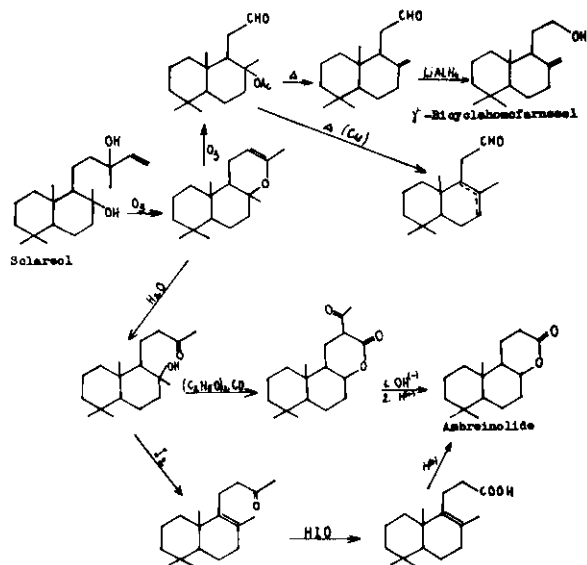

γ-Bicyclohomofarnesol

Sclareol

Ambreinolide

Fig. 13

The ozonolysis of sclareol gives sclareol oxide, while the reozonolysis results in acetoxyaldehyde which is changed into bicyclohomofarnesal by pyrolysis.[43-47] The strongest and most distinct amber odor is exhibited by γ-bicyclohomofarnesal and γ-bicyclohomofarnesol.

Ambreinolide, a product of the ambreine oxidation, is another compound which can be prepared from sclareol. This lactone has been produced from scalareol oxide by two methods.[48-51]

Practical application of manool was not possible before working out its synthesis from easily available sclareol (fig. 14).[52] The ozonolysis of manool and its derivatives is used in the process of transforming manool into compounds with amber odor (fig. 15). Manool is subjected to epoxidation which results in a mixture of stereoisomeric epoxides. Further oxidation of these compounds with ozone gives a mixture of epoxyketones which in the presence of p-toluensulphonic acid undergoes cyclization to give stereoisomeric ketals of amber odor.[53] Ketals are prepared at a yield of 24%. Other changes of manool accomplished by ozonolysis have been reported by Hosking and Grant.[54,55]
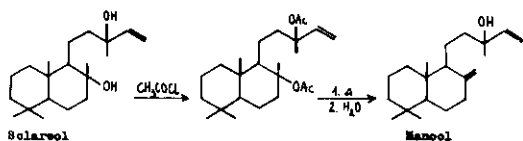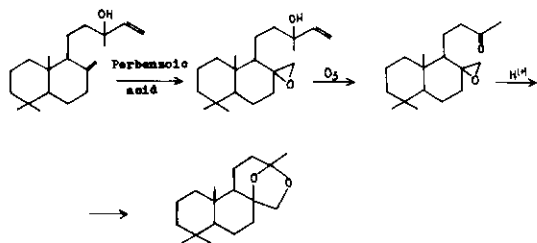

Fig. 14

Fig. 15

According to Ohloff, γ-cyclohomogeraniol is prepared at a good yield in accordance with figure 16.[56] The ozonization of vinyl ether is car-
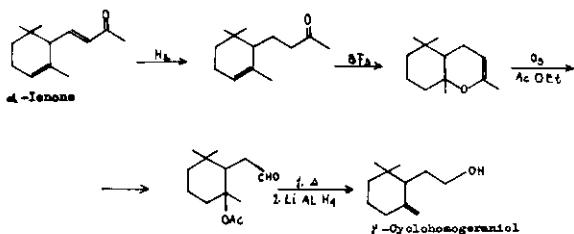

Fig. 16

ried out in a solution of ethyl acetate at 0°C. Then water is added to decompose ozonide and the whole is heated to a boil. Acetoxyaldehyde is produced at a yield of 75%, which is changed by pyrolysis into γ-cyclohomocitral at a yield of 61%. The latter is then reduced with lithium aluminum hydride to give γ-cyclohomogeraniol of amber odor at a yield of 92%. It is worth notice that a method of patchoulione synthesis has recently been patented.[57] The compound has a strong, striking odor with a note of gray amber. It is prepared by the ozonolysis of α- and β-patchoulenes (fig. 17).

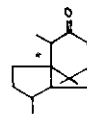
Fig. 17

Ozonization of oligoenes

Chemical affinity of ozone to double bond of the molecule which contains several such bonds depends, first of all, on the type, number, and configuration of substituents; on location of double bonds, reaction temperature, type of solvent, and concentration of substrates. The effect of some of these parameters has been studied by Odinakov.[58]

Isolated bonds C=C react with ozone as units kinetically independent, and addition of ozone to one of them influences the reactivity of remaining bonds to a smaller extent. An example can be the same value of the rate constant for the reaction between cyclododecatriene and ozone in all three stages.[59]

The more the bond is alkylated the more easily it reacts with ozone in 1,3-electrophilic addition. It seems that isopropylidene bond easily undergoes ozonolysis.[58] Taking advantage of this property, methods for the synthesis of several valuable odor sesquiterpene compounds have been recently developed based on acyclic oligoenes.

One of the methods for the synthesis of β-sinesal consists in the selective ozonolysis of myrcene which leads to corresponding diene aldehyde.[60-62] The latter is an important intermediate product in further three-stage synthesis of β-sinesal according to figure 18. Myrcene is ozonized in methanol at −78°C and the reduction of metoxyhydroperoxide is carried out with dimethyl sulphide. 4-Methylidene-5-hexene-1-al is thus obtained at a yield of 74%. After the Wittig process with suitable derivative of triphenylphosphine, hydrolysis, and repeated Wittig process, it gives a mixture of cis and trans β-sinesals.

Fig. 18
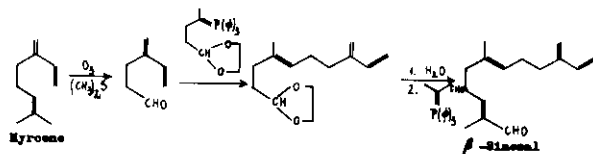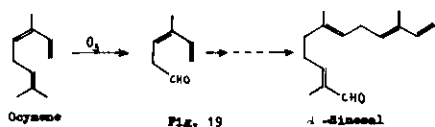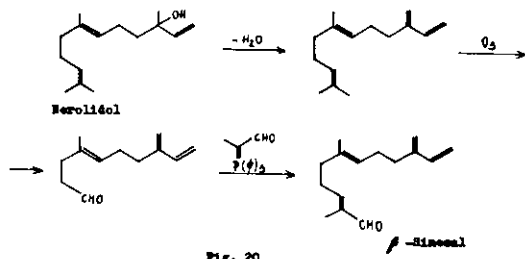
Similarly, α-sinesal is prepared starting from ocymene. (fig. 19)[60,61]

Fig. 19

β-Sinesal can also be prepared at a good yield in the synthesis illustrated in figure 20.[60]

Fig. 20

β-Farnesene prepared by the dehydration of nerolidol is subjected to selective ozonization; then the aldehyde thus produced reacts in the Wittig process with suitable triphenylphosphine, giving β-sinesal at a yield of 80%. α- and β-sinesals are components of Chinese orange oil where they exist in the trans configuration. They have strong orange odor and can be widely used in the perfumery and food industries.

Similar to sinesal in structure is 2,6,10-trimethyl-10-hydroxy-2,6,11-dodecatriene-1-al, a compound of strong flower odor (fig. 21).[63] This hydroxyaldehyde is prepared from nerolidol which gives a derivative of tetrahydrofurane with N-bromoimide of succinic acid at a quantitative yield. The action of ozone on this derivative splits off the isopropylidene bond resulting in the formation of corresponding aldehyde, which, according to figure 21, is used for the synthesis of the mentioned hydroxyaldehyde.

Fig. 21
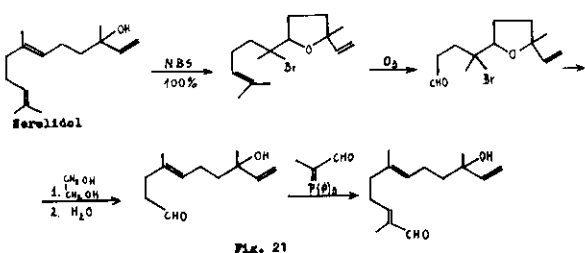
To prepare β-cyclocitral of high purity Muller and Hoffmann used the reaction of selective ozonization of β-ionone.[64,65] Cyclocitrals are important odor substances and intermediates in the synthesis of natural odor substances and other products (damaskone, vitamin A, carotenoides). According to these authors, the numerous known methods of synthesis of cyclocitrals are multi-stage of a low yield and are not useful for technical applications. Therefore, one more method for the synthesis of β-cyclocitral has

been proposed, starting from easily available β-ionone (fig. 22). The ozonization is performed in methanol at a temperature below 0°C, and the decomposition of intermediate products is carried out with steam or a mixture of Zn/AcOH. The yield of β-cyclocitral of 98% purity is within 67-90%. Starting from β-irone one can prepare methyl-β-cyclocitral by the same method.
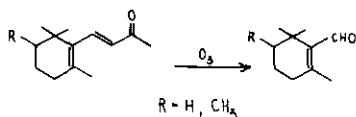

R = H, CH₃

Fig. 22

Ozonization of cycloalkenes and their derivatives

The ozonolysis of cycloalkenes gives difunctional compounds which are difficult to prepare by other methods.[7] Many of them can be used as intermediates in the synthesis of odor substances.

Ohloff and coworkers have reported a method for the synthesis of macrocyclic ketones based on the ozonolysis of dicyclic olefins (fig. 23).[66] Bicyclo [10,3,0]-1-pentadecene is prepared from easily available cyclododecanone which is also used for similar preparation of racemic muscone. The synthesis of macrocyclic ketones is at the same time an excellent example of utilization of ozonolysis for the expansion of alifatic ring.
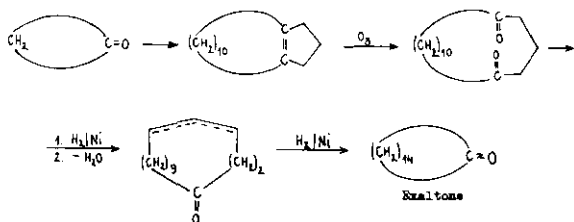

Fig. 23

The ozonolysis process is also used in the reaction of ring contraction. An example may be the synthesis of a very interesting odor compound called margeritone.[67] It is prepared by ozonolysis of carotol, the main oxy component of oil from carrot seeds (Daucus carota L) (fig. 24).
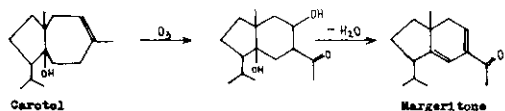

Carotol   Margeritone

Fig. 24

Carotol is ozonized in a solution of acetic acid at 0°C, +10°C. After decomposition of the intermediate product with zinc powder in acetic acid, ketodiol is obtained at a yield of 70%, which due to dehydration changes into margeritone at a yield of 60%. The odor of margeritone is described as one of musk with a note of gray amber. This kind of reaction, connected with ring contraction, which is actually a secondary transformation, was also used in the multi-stage

synthesis of hydroazulene alcohol, the main component of guaiacwood oil from Bulnesia sarmienti Lor guaiole (fig. 25).[68]
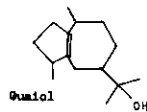

Guaiol

Fig. 25

Some interesting intermediates for the synthesis of odor compounds can be prepared by the ozonolysis of cyclic terpene hydrocarbons such as α-pinene, limonene (dipentane), 3-carene. These hydrocarbons are inexpensive raw materials plentifully existing in turpentines and some lemon oils. They have olefin bonds asymmetrically substituted, and therefore they are useful for the preparation of corresponding difunctional compounds by ozonolysis (fig. 26). The ketoaldehydes or ketoacids obtained in this way, due to the presence of two reactive groups and small rings (pinene and carene derivatives), are basis for further multi-direction changes leading to synthesis of many new odor substances. According to a U.S. patent, pinonic aldehyde can be selectively reduced with hydrogen in the presence of Raney nickel to give corresponding hydroxyketone which finds its application as a component for perfumery compositions.[69]
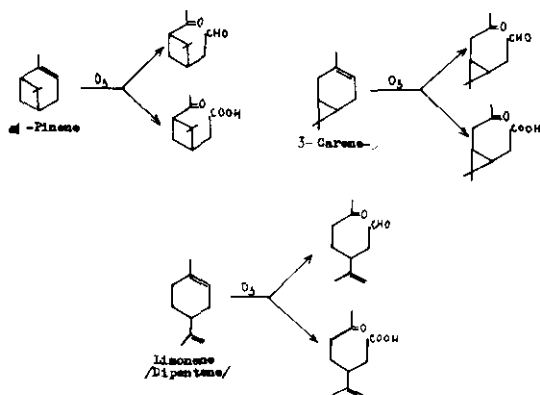

α-Pinene   3-Carene

Limonene
/Dipentene/

Fig. 26

In 1959 Eschinazi proposed a method for the synthesis of irones based on pinonic aldehyde prepared by the ozonolysis of α-pinene.[70] This process is relatively short and proceeds only in five stages, illustrated in figure 27. It should be
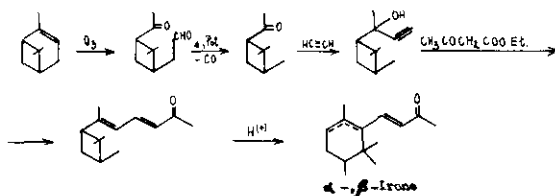

α-,β-Irone

Fig. 27

mentioned, however, that during further studies

the decarbonylation of pinonic aldehyde is accompanied by many by-products and the process yield is considerably lower.[71]

Some pinonic acid esters available by esterification of commercial cis-pinonic acid have a pleasant odor (fig. 28).[72] They can be used as odor or flavor substances.
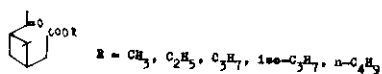

R = CH₃, C₂H₅, C₃H₇, iso-C₃H₇, n-C₄H₉

Fig. 28

Also, pinanic acid esters are interesting as odor compounds (fig. 29). For their preparation pinonic acid is reduced by the Wolff-Kishner method to give a mixture of stereoisomeric pinanic acids at a yield of 90%, which are then esterified.[73]

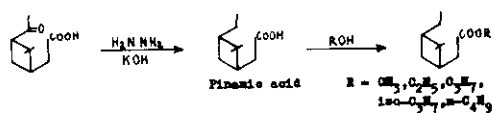Pinanic acid   R = CH₃,C₂H₅,C₃H₇,
iso-C₃H₇,n-C₄H₉

Fig. 29

Isomeric, in relation to pinonic acid, ketoacid, prepared by ozonolysis of 3-carene, is used for the synthesis of (+)transchrizantemic and cis-homochrizantemic acids (fig. 30).[74-77] On the other hand, the ketoaldehyde available by the ozonolysis of 3-carene is used for the synthesis of new dicyclic compounds (fig. 31).[78,79] Depending on the conditions of intramolecular aldol condensation of ketoaldehyde, either ketone or aldehyde is obtained.

trans-Chrysantemic acid
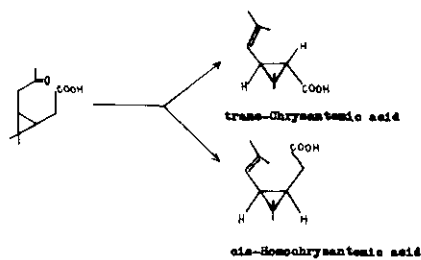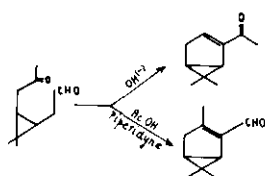
cis-Homochrysantemic acid

Fig. 30

Fig. 31

The selective ozonolysis of limonene gives 3-isopropenyl-6-heptanone-1-al in a more economic and simple way than that described in the literature.[80-83] This ketoaldehyde is often used as substrate for the preparation of natural products from the group of terpenes and sesquiterpenes.

Wolinsky has carried out the cyclization of 3-isopropenyl-6-heptanone-1-al in two directions (fig. 32).[83,84] Depending on the reaction conditions, either cyclic ketone or aldehyde is obtained. The presence of 1-isopropenyl-3-acetyl-3-cyclopentene was confirmed, among other things, in Eucalyptus globulus.
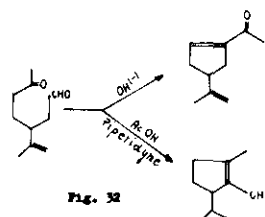

Fig. 32

Kaiser has prepared ketoaldehyde from limonene and used it for the synthesis of photocitrals (fig. 33).[85] These aldehydes in their cis, trans, and trans cis configurations are components of Lippia citriodora oil from the Verbenaceae family.

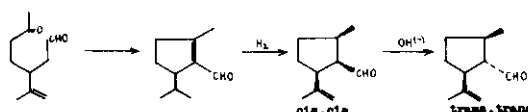

cis,cis   trans,trans

Fig. 33

Another aldehyde, namely 3-isopropyl-6-heptanone-1-al prepared by the ozonolysis of p-1-menthene, was used to synthesize sesquiterpene ketones of the spiro [4,5] decane-acorenone and aceronone B back bones.[86] These ketones are components of sweet-ylang oil Acorus calamus L. Their synthesis is illustrated in figure 34.
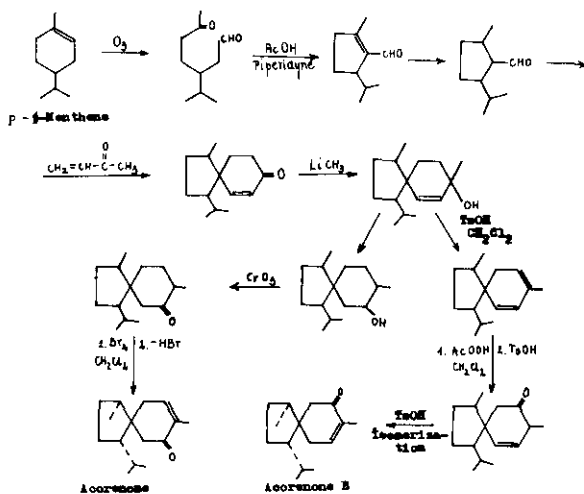

p - 1-Menthene

Acorenone   Acorenone B

Fig. 34

A competitive method for the acorenone synthesis, using the same ketoaldehyde, has been proposed by Lange.[87,88]

Siemion reported on the synthesis of citronellol based on ketoaldehyde prepared by the ozonolysis of p-3-menthene (fig. 35)[89] Citronellol is produced at a yield of 36% calculated as p-3-menthene. The ketoaldehyde used here can be reduced to a corresponding diol also with hydrogen in the presence of Raney nickel, which is described by Eschinazi in his patent.[90]
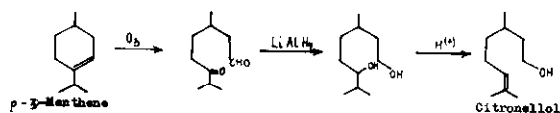
Fig. 35

Several interesting odor compounds have been prepared at our institute, based on the ozonolysis of α-pinene, 3-carene, limonene, and p-1-menthene. Hydrogenalysis of the prepared ketoaldehydes gives corresponding secondary alcohols containing one carbon atom less in a molecule than the original ketoaldehydes (fig. 36).[91] Taking advantage of the different reactivity of aldehyde and ketone groups in ketoaldehydes, it was possible to prepare several interesting new odor terpene compounds (fig. 37).[81,82,91,92]
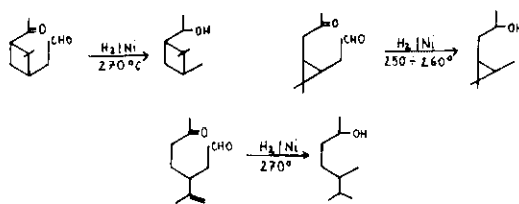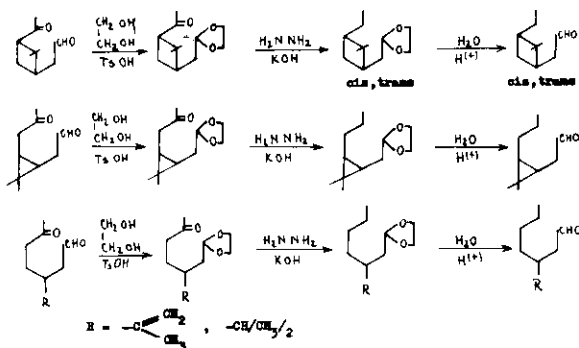

Fig. 36

Fig. 37

Condensation of the prepared terpene aldehydes with acetone gives corresponding α,β-unsaturated ketones (fig. 38).[81] The odors of α,β-unsaturated ketones are very attractive as animal, wood, and flower types.
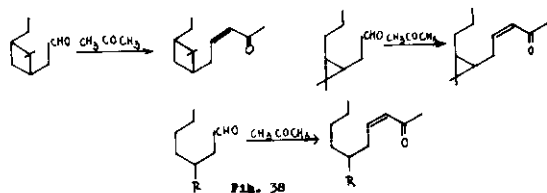

Fig. 38

In recent years numerous studies have been performed on the selective ozonolysis of cyclopolienes. Splitting off only one double bond in a molecule while maintaining the rest of them gives a simple possibility for the synthesis of difunctional mono- and poly-unsaturated compounds. Thus, for example, the selective ozonolysis of 1,5,9-cyclododecatriene gives twofold unsaturated dialdehyde or dicarboxylic

acid (fig. 39).[93-95] These compounds were then changed into corresponding esters, lactones, and acetals.
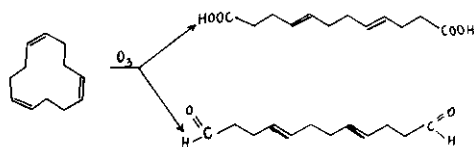

Fig. 39

Finally, we should like to pay attention to some less-known trends in the ozonolysis utilization for organic synthesis.

The ozonolysis of deprotonated (aci form) nitroparaffines gives in some cases carbonyl compounds with a good yield (fig. 40).[96] This reaction has been used by Dubs and Schenk for the total synthesis of trans 6,10-dimethyl-9-methylidene-5-undecene-2-one[97] which was isolated by Ohloff from costus root oil.[98] He also found out its structure (fig. 41).
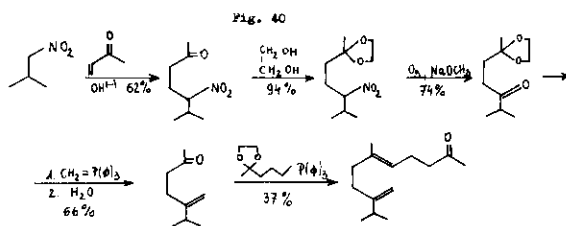

Fig. 40
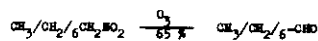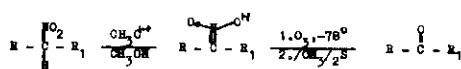
Fig. 41

The authors consider the ozonolysis of deprotonated nitroacetal to be short and the best way to prepare one of the intermediates required for further modification. The ozonolysis is carried out in methanol in the presence of sodium methoxide.

If the double bond of substrate contains volume substitutes, often during the ozonolysis so-called abnormal products are obtained. The abnormal direction of the ozonide decomposition was used in the total synthesis of grandisol, sexual attractant of the pheromone group (fig. 42).[99] It should be stated that if the ozonization proceeds at room temperature, mainly a normal product, ketone, is prepared.

Also we must note the use of ozone for the oxidation of compounds without multi-bonds. The ozonolysis of acetals may be an example.[100,101] The process proceeds generally at a good yield. It makes it possible to change acetals into esters in an oxidative way. It has been observed that the process has a stereospecific course.

Fig. 42

Esters also can be prepared directly from olefins if the ozonization takes place in methanol solution of chlorine or hydrogen chloride.[102,103]

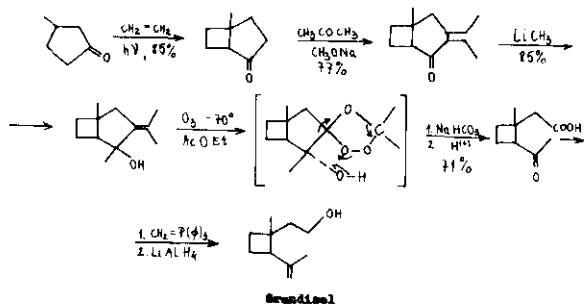Also possible is the oxidation of alcohols with ozone to carboxylic acids and to carbonyl compounds as well as cycloparaffins to alcohols.[104-106]

References

1. M. Emelyanow, Jr., and M. E. Emelyanow, Belg. 832 112 (1975); C.A. **86**, 19080y (1977)
2. J. D. von Bargen and K. U. Siddiqui, Germ. West 2620540 (1976); C.A. **86**, 31581y (1977)
3. G. Schwan, Germ. West 2610809 (1976); C.A. **86**, 57511
4. R. Criegee, A. Banciu, Chem. Ztg. **98**, 261 (1974)
5. R. Criegee, Angew. Chem. **87**, 765 (1975)
6. P. S. Bailey, Ind. Eng. Chem. **50**, 993 (1958)
7. A. T. Mieniajlo, I. E. Pokrovskaja, and A. K. Jakovleva, Neftokhimija **7**, 70 (1967)
8. K. D. Carlson and V. E. Sohnes, Ind. Eng. Chem. Prod. Res. Dev. **16**, 95 (1977)
9. M. I. Fremery and E. K. Fields, J. Org. Chem. **28**, 2537 (1963)
10. D. G. M. Diaper, Can. J. Chem. **44**, 2819 (1966)
11. P. S. Bailey, Chem. Rews. **58**, 925 (1958)
12. R. H. Callighan and M. H. Wilt, J. Org. Chem. **26**, 4912 (1961)
13. D. J. Moore, E. H. Pryde, and J. C. Cowan, J. Am. Oil Chemist's Soc. **42**, 894 (1965)
14. V. E. Sohns, ibid. **48**, 362A (1971)
15. E. H. Pryde, D. E. Anders, H. M. Teeter, and J. C. Cowan, J. Org. Chem. **27**, 3055 (1962)
16. J. M. Conia and P. Leriverend, Compt. rend. **250**, 1078 (1960)
17. J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, Tetrahedron Lett. 4273 (1966)
18. W. S. Knowles and Q. E. Thompson, J. Org. Chem. **25**, 1031 (1960)
19. R. W. White, S. W. King, J. L. O'Brien, Tetrahedron Lett. 3587 (1971)
20. L. A. Subluskey et al., Advan. Chem. **21**, 149 (1959)
21. M. G. Sturrock, E. L. Cline, and K. R. Robinson, J. Org. Chem. **28**, 2340 (1963)
22. P. R. Story et al., Tetrahedron Lett. 3291 (1968)
23. S. D. Razumovskij, J. N. Juriev, and B. K. Cyskovskij, Zhur. Org. Khim. **6**, 254 (1970)
24. N. J. Boldenkov and S. D. Razumovskij, Khim. Prom. 100 (1977)
25. L. A. Hull, I. C. Hisatsune, and J. Heicklen, J. Phys. Chem. **76**, 2659 (1972)
26. S. D. Razumovskij and J. N. Juriev, Zhur. Org. Khim. **3**, 251 (1967)
27. Emery Industries, Chem. Eng. News **43** (41), 101 (1965)
28. Organic Ozone Reaction and Techniques, The Welsbach Corporation, Philadelphia, PA, 1961
29. P. E. Throckmorton, L. J. Hansen, R. C. Christenson, J. Am. Oil Chemist's Soc. **45**, 59 (1968)
30. E. H. Pryde, J. Moore, and J. C. Cowan, ibid. **45**, 888 (1968)
31. R. A. Awl, E. H. Pryde, D. Weisleder, W. K. Rohwedder, and J. C. Cowan, ibid. **48**, 232 (1971)
32. P. E. Throckmorton and E. H. Pryde, ibid. **49**, 643 (1972)
33. R. G. Ackman, Lipids **12**, 293 (1977)
34. J. L. Sebedio and R. G. Ackman, Can. J. Chem. **56**, 2480

(1978)

35. J. Kulesza and B. Knobloch, Riechstoffe, Aromen, Kör-perpflegemittel **21**, 84 (1971)
36. S. D. Razumovskij and G. E. Zajkov, Izv. Acad. Nauk SSSR ser.khim. 2657 (1971)
37. Kirk-Othmer, Encyclopedia of Chemical Technology, Vol. 21, New York, 1970, p. 184
38. M. Indo, Nippon Kagaku, Zasshi **81**, 1106 (1960); C.A. **56**, 373 (1962); Japan 4771 (1954); C. A. **49**, 10682 (1955)
39. M. G. Sturrock, B. J. Cravy, and V. A. Wing, Can. J. Chem. **50**, 3047 (1971)
40. J. Góra and K. Smigielski, Polish J. Chem. **52**, 2069 (1978)
41. O. W. Topalova and L. A. Shabrova, Zhar. Org. Khim. XI, 2444
42. N. V. Naarden, Germ. West 2130184 (1971)
43. L. Ruzicka and M. M. Janot, Helv. Chim. Acta **14**, 645 (1931)
44. M. M. Janot, Ann. Chem. **17**, 5 (1932)
45. M. Stoll and M. Hinder, Helv. Chim. Acta **33**, 1251 (1950)
46. M. Hinder and M. Stoll, ibid. **33**, 1308 (1950)
47. M. Stoll and M. Hinder, ibid. **36**, 1984 (1952)
48. E. Lederer and M. Stoll, ibid. **33**, 1345 (1950)
49. E. Lederer and M. Stoll, ibid. **34**, 789 (1951)
50. D. B. Bigley, N. A. J. Rogers, and J. A. Barltrop, Chem. Ind. 558 (1958)
51. D. B. Bigley, N. A. J. Rogers, and J. A. Barltrop, J. Chem. Soc. 4613 (1960)
52. G. Ohloff, Helv. Chim. Acta **41**, 845 (1958)
53. E. Demole, Experimenta **20**, 609 (1964)
54. J. R. Hosking, Ber. **69**, 780 (1936)
55. P. K. Grant and H. T. L. Liau, Aust. J. Chem. **31**, 1791 (1978)
56. G. Ohloff and G. Schade, Ber. **91**, 2017 (1958)
57. G. H. Buchi, U.S.A. 2942029 (1960)
58. W. N. Odinakov, W. R. Achunova, G. A. Tolstikov, A. W. Siemienowskij, and W. L. Mizjuk, Zhur. Org. Khim., XIV, 1851 (1978)

59. S. D. Razumovskij and G. E. Zajkov, Ozone and its reactions with organic compounds, Moscow 1974, p. 86
60. E. Bertele and P. Schudel, Helv. Chim. Acta **50**, 2445 (1967)
61. E. Bertele and P. Schudel, Germ. West 1 768 793 (1972)
62. E. Bertele and P. Schudel, Swiss 493 451 (1970)
63. E. Demole and P. Enggist, Helv. Chim. Acta **56**, 2053 (1973)
64. W. Hoffmann and N. Muller, Germ. West 2432231 (1976); C.A. **84**, 180433j (1976)
65. W. Hoffmann and N. Muller, Synthesis 781 (1975)
66. G. Ohloff, J. Becker, and K. H. Schulte-Elte, Helv. Chim. Acta **50**, 705 (1967)
67. J. Kulesza, J. Kula, and J. Kwiatkowski, Riechstoffe, Aromen, Körperpflegemittel **22**, 39 (1973)
68. J. A. Marshall and A. E. Greene, J. Org. Chem. **37**, 982 (1972)
69. R. W. White and S. W. King, U.S.A. 3361820 (1968)
70. H. E. Eschinazi, J. Am. Chem. Soc. **81**, 2905 (1959)
71. J. M. Conia and G. Faget, Bull. Soc. Chim. France 1963 (1964)
72. P. Wirth, G. E. M. Dannenberg, V. Schmied-Kowarzik, P. Weinhold, and D. Gudel, Germ. West 2624654 (1976); C.A. **86**, 95881 (1977)
73. F. M. Avotnisz and Z. F. Bore, Izv. Acad. Nauk Lotv, SSR 449 (1971)
74. Y. R. Naves and A. V. Grampoloff, Helv. Chim. Acta **44**, 637 (1961)
75. M. Matsui, H. Yoshioka, Y. Yamada, H. Sakamoto, and T. Kitahara, Agr. Biol. Chem. **29**, 789 (1965)
76. R. Sobti, S. Dev, Tetrahedron **30**, 2927 (1974)
77. T. Sasaki, S. Eguchi, M. Ohmo, and T. Oyobe, Bull. Chem. Soc. Japan **42**, 3582 (1969)
78. P. H. Boyle, W. Cocker, and R. L. Gordon, J. Chem. Soc. C 2127 (1971)
79. M. Matsui, Y. Yamada, and H. Sakamoto, Japan 6913500 (1969); C.A. **71**, 123728s (1969)
80. J. Kulesza and J. Kula, Riechstoffe, Aromen, Körperpflegemittel **25**, 317 (1975)
81. J. Kula, Doctoral Thesis, Technical University, Lódź, Poland, 1979
82. J. Kula and J. Podlejski, Polish J. Chem., in press
83. J. Wolinsky and W. Barker, J. Am. Chem. Soc. **82**, 636 (1960)
84. J. Wolinsky and M. R. Slabaugh, J. Org. Chem. **29**, 3740 (1964)
85. R. Kaiser and D. Lamparsky, Helv. Chim. Acta **59**, 1797 (1976)
86. M. Pesaro and J. P. Bachmann, J. Chem. Soc. Comm. 203 (1978)
87. G. L. Lange, W. J. Orrom, and D. J. Wallace, Tetrahedron Lett. 4479 (1977)
88. G. L. Lange, E. E. Neidert, W. J. Orron, and D. J. Wallace, Can. J. Chem. **56**, 1628 (1978)
89. I. Z. Siemion, Roczniki Chem. **33**, 1183 (1959)
90. E. H. Eschinazi, U.S.A. 3052730 (1962); C.A. **58**, 5516c (1963)
91. J. J. Kulesza and J. Kula, Pollena-Tluszcze, Srodki Piorace, Kosmetyki **XIX**, 501 (1975)
92. J. Kulesza and J. Kula, Roczniki Chem. **49**, 1911 (1975)
93. W. N. Odinokov et al., Zhur. Org. Khim. **XIII**, 532 (1977)
94. G. Ohloff, H. Roger, and G. Wolfgang, Swiss 577274 (1976); C.A. **85**, 130383 (1976)
95. A. Dossena and V. L'Acqua, J. Chrom. **157**, 432 (1978)
96. I. E. McMurray, J. Org. Chem. **39**, 259 (1974)
97. P. Dubs and H. P. Schenk, Helv. Chim Acta **61**, 984 (1978)
98. B. Maurer and G. Ohloff, J. Chem. Soc. Chem. Comm. 353 (1977)
99. R. L. Cargill and B. W. Wright, J. Org. Chem. **40**, 120 (1975)
100. P. Deslongchamps, C. Moreau, D. Frehel, and P. Atlani, Can. J. Chem. **50**, 3402, 3405 (1972)
101. P. Deslongchamps, P. Atlani, D. Frehel, A. Malaval, and C. Moreau, ibid. **52**, 3651 (1974)
102. W. D. Lloyd and G. W. Hedrick, Ind. Eng. Chem. Prod. Res. **2**, 143 (1963)
103. J. Neumeister, H. Keul, M. Saxena, and K. Griesbaum, Angew, Chem. **90**, 999 (1978)
104. S. Miyazaki and Y. Suhara, J. Am. Oil Chemist's Soc. **55**, 536 (1978)
105. W. Waters, A. Rollin, C. Bardwell, J. Schneider, and T. Aanerud, J. Org. Chem. **41**, 889 (1976)
106. Z. Cohen, E. Keinan, Y. Mazur, and T. H. Varkony, ibid., **40**, 2141 (1975)