GRIGNARD ADDITIONS OF METHYLMAGNESIUM IODIDE TO FENCHONE AND DEHYDROFENCHONE. CONFIGURATIONS OF 1,2,3,3-TETRAMETHYLNORBORNAN-2-OLS AND 1,2,3,3-TETRAMETHYL-5-NORBORNEN-2-OLS

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JYVÄSKYLÄ 1972

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PREFACE

The experimental work of the present investigation was carried out in the Department of Chemistry, University of Jyväskylä, in 1969—1972.

The subject of this investigation was suggested by my teacher Associate Professor Pentti Mälkönen, Ph. D. I wish to express my sincere gratitude to him for valuable advice and encouragement during the work.

I am indebted to Professor Jaakko Paasivirta, Ph. D. and Professor Pekka Hirsjärvi, Ph. D., for their valuable advice and comments. I also wish to thank Miss Kaija Pasanen, M. Sc., for her assistance in the recording of UV spectra.

I wish to express my sincere thanks to Mr Sauli Takala, M. A., and Mr Eero Wuolijoki, M. Sc., for translating the manuscript into English.

This investigation was supported by grants from the Foundation of Neste Oy and the University of Jyväskylä. This aid is gratefully acknowledged.

To my wife and children I owe a great debt of gratitude for their support and understanding.

Jyväskylä, May, 1972

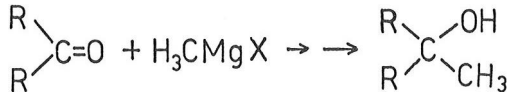
Jorma Korvola

CONTENTS

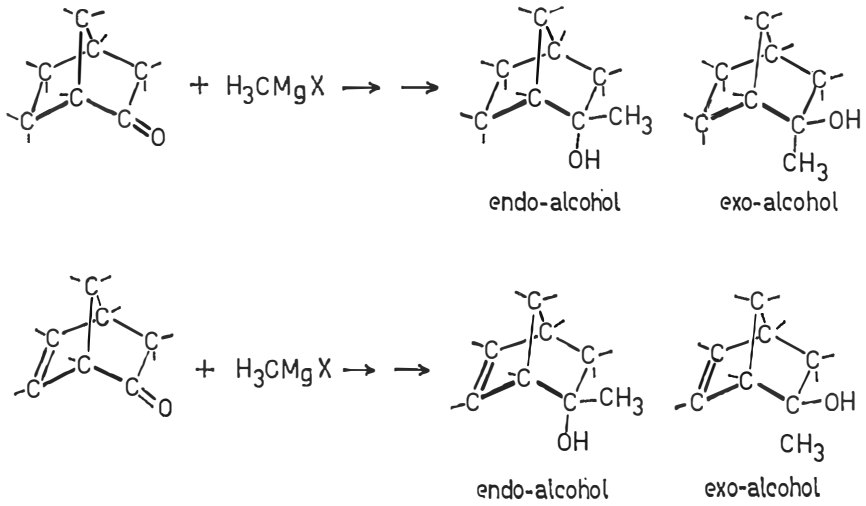
INTRODUCTION

Several researchers, among them also Finnish, have for some time been interested in the branch of stereochemistry which deals with the addition reactions of the ketones of various bicyclo[2.2.1]heptane or norbornane series and bicyclo[2.2.1]heptene or norbornene series and Grignard reagents. Special attention has been given to the addition reactions of methylmagnesium halogenides and to some extent also to the reductions of the ketones produced by the Grignard reagent.

When the ketone and methylmagnesium halogenide react with each other the reaction gives tertiary alcohol according to the following scheme:

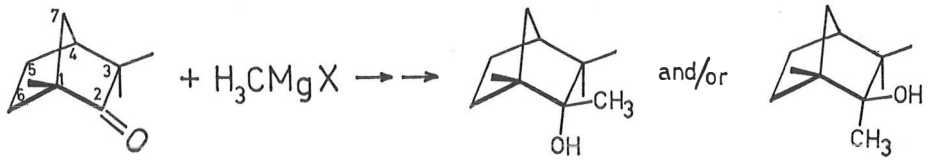


Reaction with a ketone of the bicyclo[2.2.1]heptane or heptene series may, in theory, produce two different kinds of tertiary alcohol which are mutually *endo-exo*-isomers.



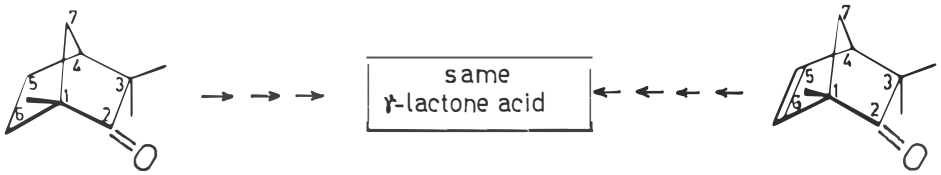
The reaction, however, is very sensitive to the effects of the substituents of the ketone molecule which as spatial hindrances may strongly guide the reaction to a certain direction. Many addition reactions produce only one of the two alcohol epimers irrespective of the reaction conditions.

When 1,3,3-trimethylbicyclo[2.2.1]heptan-2-one or fenchone, as it will be called henceforth, reacts with methylmagnesium halogenides, we may obtain 1,2,3,3-tetramethylnorbornan-2-*endo*-ol (hereafter called 2-*exo*-methyl-2-*endo*-fenchol) and/or 1,2,3,3-tetramethylnorbornan-2-*exo*-ol (hereafter called 2-*endo*-methyl-2-*exo*-fenchol):



Fenchone — 2-*exo*-methyl-2-*endo*-fenchol — 2-*endo*-methyl-2-*exo*-fenchol

The purpose of the present study has been to clarify the stereochemical configurations of the alcohol epimer or epimers formed in the said reaction of fenchone. Two different ways have been used which at the final stages of the reaction series lead to the same compound. In the one reaction series the end product has been reached directly from the fenchone, and in the other through the 1,3,3-trimethyl-5-norbornen-2-on or dehydrofenchone which is synthesized from fenchone.



Fenchone — Dehydrofenchone

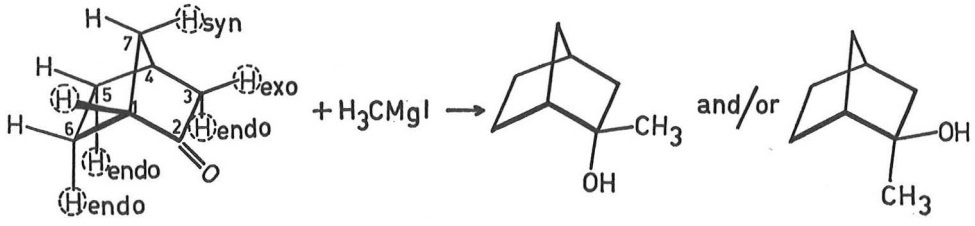
Various spectrometric methods and a method based on the formation of lactone developed by N. J. Toivonen have been used in the determination of the structural formulae of the alcohols.

GENERAL CONSIDERATIONS

ON THE GRIGNARD ADDITIONS OF SOME KETONES OF BICYCLO-[2.2.1]HEPTANE AND HEPTENE SERIES WITH METHYLMAGNESIUM HALOGENIDES. STERIC HINDRANCES AND THEIR EFFECTS ON THE REACTION.

Rather certain assumptions about the stereochemical configurations of the tertiary alcohols formed in the Grignard reaction of methylmagnesium halogenide with fenchone can be made by comparing it with the corresponding reactions of the other ketones of the norbornane and norbornene series.

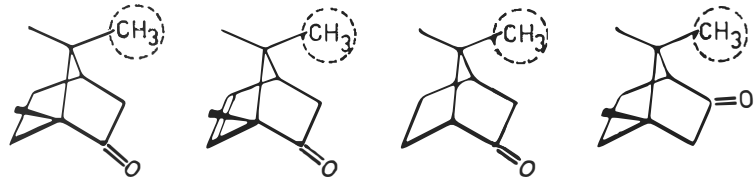
When the most simple of the norbornane ketones, norcamphor (1), reacts with methylmagnesium halogenide, the product is either 2-*exo*-methyl-2-*endo*-norborneol (2) or 2-*endo*-methyl-2-*exo*-norborneol (3).



1 2 3

The spatial structure of the product is determined by the direction from which the nucleophilic Grignard reagent approaches carbonyl carbon. When the methyl group adds to the carbonyl carbon from *exo*-direction the product is *exo*-methyl compound (2) and *endo*-methyl compound (3) if it comes from the *endo*-direction. The structural determination of the tertiary alcohol formed in the reaction of norcamphor with methylmagnesium iodide has shown that the reaction product is nearly 100 per cent 2-*exo*-methyl-2-*endo*-norborneol (2).[1,2] This can be considered to be due to the spatial structure of the

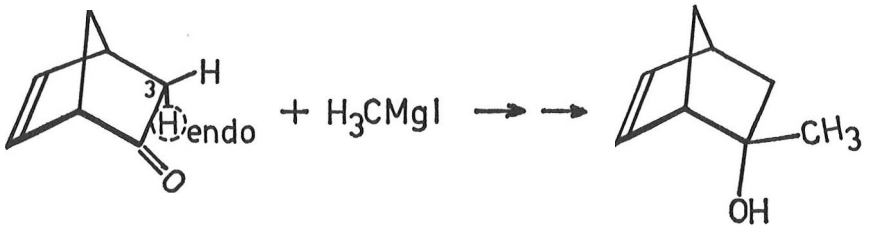
norcamphor molecule, in which the *exo*-side of the molecule is less hindered than the *endo*-side in regard of the approach of a bulky reagent.[cf.21] The attack of the reagent from the *exo*-direction could be hindered mainly by the hydrogen atom in the bridgehead carbon atom C_1 and the H_{3exo} hydrogen in the carbon atom C_3 as well as the H_{7syn} hydrogen which in the bridging carbon C_7 is in *syn*-position as regards the carbonyl group. The reaction product shows, however, that their effects are smaller than the effects of H_{3endo}, H_{5endo} and H_{6endo} hydrogens which are potential hindrances of the *endo*-direction. The steric effect of H_{5endo} and H_{6endo} hydrogens on reaction has not, until now, been directly proved. Mälkönen, however, has found in studying the Grignard additions of camphor (4) and dehydrocamphor (5) that dehydrocamphor reacts more easily.[3] In these cases, however, it is not possible to detect the addition-guiding effects of H_{5endo} and H_{6endo} hydrogens, because both reactions take place almost completely as *endo*-additions owing to the strong steric hindrance caused by the methyl groups (*syn*-methyl) at the bridging C_7 carbon atom. (A similar *endo*-addition occurs also with apocamphor (6)[4] and probably with epicamphor (7)[5], through the latter has not been shown chemically.)



4 5 6 7

However, the differences in reactivity can at least partly be due to the fact that dehydrocamphor lacks the atoms corresponding to H_{5endo} and H_{6endo} hydrogens of camphor (the olefinic hydrogens are directed outward from the molecule); thus the *endo*-side of the dehydrocamphor molecule is more open than that of camphor and the attack of the reagent from that direction is less hindered, which leads to increased reactivity. On the other hand, the differences in reactivity can also, at least in part, be due to different electronic effects in the camphor and dehydrocamphor molecules.[cf.6]

The reaction of dehydronorcamphor (8) with methylmagnesium iodide provides a clearer indication of the guiding effect of the H_{5endo} and H_{6endo} hydrogens of the norbornanones on Grignard additions. The main product in this reaction is 2-*exo*-methyl-2-*endo*-dehydronorborneol (9)[2,7] formed through *exo*-addition which also occurs in the reaction of norcamphor. The reaction, however, is not so stereospecific as the reaction of norcamphor since



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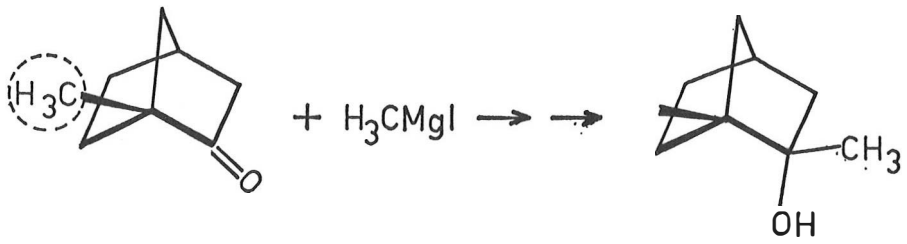
the addition product contains 8—10 per cent 2-*endo*-methyl-2-*exo*-dehydronorborneol formed through *endo*-addition.[8] It must be taken into account that besides the lack of $H_{5\,endo}$ and $H_{6\,endo}$ hydrogens norcamphor is a saturated and dehydronorcamphor an unsaturated compound; thus the carbon skeleton structures of the molecules and their electronic effects are different and can contribute to causing the addition reaction to occur from *endo*-direction.

The $H_{3\,endo}$ hydrogen of the dehydronorcamphor molecule, on the other hand, is not significant as a reaction-guiding hindrance. This is clearly shown by the Grignard addition of dehydrofenchone (carried out in the present study) in which the place of $H_{3\,endo}$ hydrogen is taken by a methyl group with a considerably larger effective radius.

The Grignard addition of the ketones of the norbornane series from the *exo*-direction cannot be hindered, either, by the methyl group in the bridgehead carbon atom C_1, as is shown by the reaction of 1-methylnorcamphor (10), since the reaction product is mainly 2-*exo*-methyl compound (11).[9] Neither has the *exo*-methyl group in the carbon atom C_3 adjacent to the carbonyl group an appreciable effect on guiding the reaction towards the *endo*-direction. This can be seen from the Grignard additions of 3-methylnorcamphor (12)[10] and comphenilone (14).[11] In both cases, the reaction products are *exo*-methyl compounds formed through *exo*-addition.



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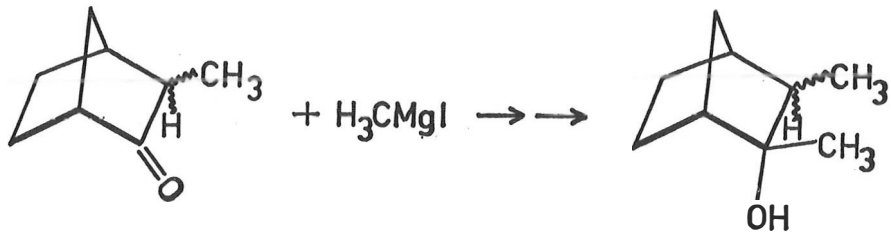

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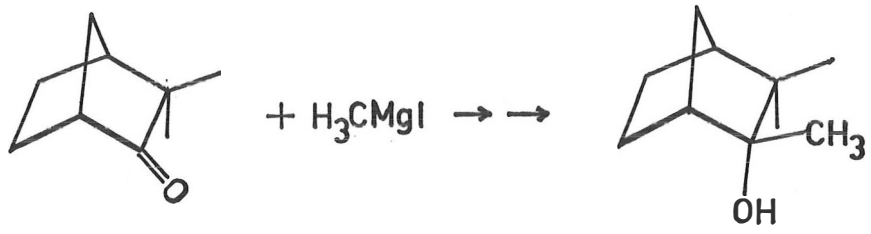
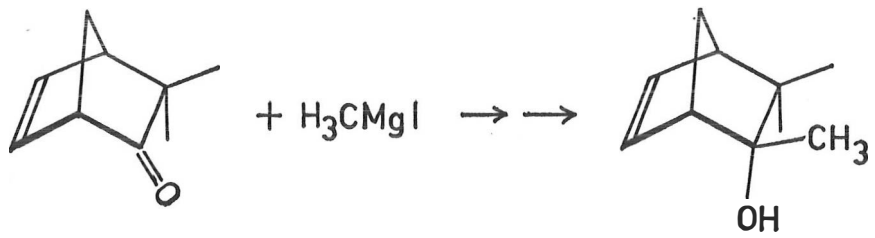


14 15

In view of the present study it is somewhat surprising to note that also the Grignard addition of dehydrocamphenilone (16) with methylmagnesium iodide is reported to be highly stereospecific.[12] The main product is 2-*exo*-methyl-2-*endo*-dehydrocamphenilol (17).

It is true that the melting point of 2-*exo*-methyl-2-*endo*-camphenilol obtained from it by hydrogenation deviated more than 20° from the corresponding compound (15) obtained from camphenilone (14). The determination of the purity of the product could not be carried out by determination of the specific rotation, as the studied compounds were mixtures of enantiomers.

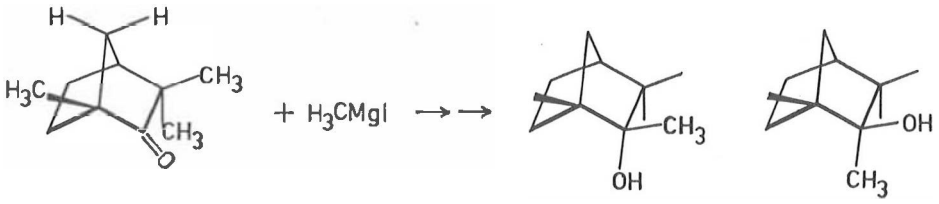
When we, on the basis of the above-mentioned research results, examine the *endo* and *exo*-addition possibilities of the methyl group of the Grignard



16 17

reagent to the fenchone molecule, we find that there is no substituent in the fenchone molecule which *alone* could effectively prevent *exo*-addition. The methyl groups in the bridgehead carbon atom C_1 and the carbon atom C_3 as well as the H_{7syn} hydrogen at the bridge carbon C_7 are all rather ineffective hindrances in guiding the reaction.

It can thus be assumed, as has been shown in the present study, that in the Grignard addition of fenchone with methylmagnesium iodide the methyl group of the reagent attacks the carbonyl carbon mainly from *exo*-direction the main product of the reaction being 2-*exo*-methyl-2-*endo*-fenchol(19) and the potential by-product 2-*endo*-methyl-2-*exo*-fenchol (20).



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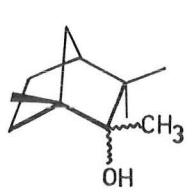
Some indications about the stereochemistry of the Grignard addition of fenchone are provided by the metal hydride reductions of the ketones of the bicyclo[2.2.1]heptane serie.[cf.13–15] Stereochemically they are similarly guided as the Grignard addition, even though not equally specifically.[cf.16–20] Norcamphor[21–23,27,29], 1-methylnorcamphor[21,23], camphenilone[21,23,30] and fenchone[21,23,24,30] yield by $LiAlH_4$ reduction *endo*-alcohol as the main product. Even this result shows that in these compounds the *exo*-side of the molecule is more open and more susceptible to the approach of the hydride-ion $MH_4^{\ominus}$ than the *endo*-side. The case is, however, the reverse if the bridge carbon C_7 contains a methyl group in *syn*-position to the carbonyl group, as is shown by the reductions of camphor,[23,25,26] dehydrocamphor,[31] epicamphor[32] and santenones.[33]

The hydrogenation of fenchone by a surface catalyst (e.g. Raney nickel) also shows that the *exo*-side of the molecule is more open than the *endo*-side, since the hydrogenation product contains 71 per cent α-fenchol (*endo*-OH) and 29 per cent β-fenchol (*exo*-OH).[30]

THE GRIGNARD REACTION OF FENCHONE WITH METHYL IODIDE AND MAGNESIUM

Zclinsky[34] carried out the reaction of fenchone (18) with methylmagnesium halogenide already in 1901 immediately after the Grignard reagent had been discovered (in 1900). He prepared 2-methylfenchol (21) which was not closer specified.[cf.35–38] Its stereochemical structure has never been determined even if it has been used as the basic substance in many studies. Hydrocarbons have been produced from it by eliminating water by various reagents such as sodium[39] and potassium[40–44] bisulphate and acetic anhydride,[45] and the products have been e.g. 1-methylcamphene (22), 1-methyl-α-fenchene (23) and 4-methylcamphene (24). The latter two are formed by rearrangement. Also the formation of two methyltricyclenes has been noted.[41]



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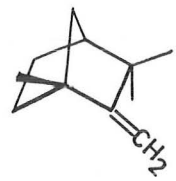

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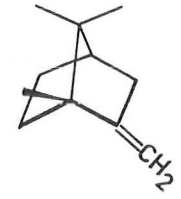

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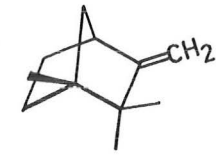

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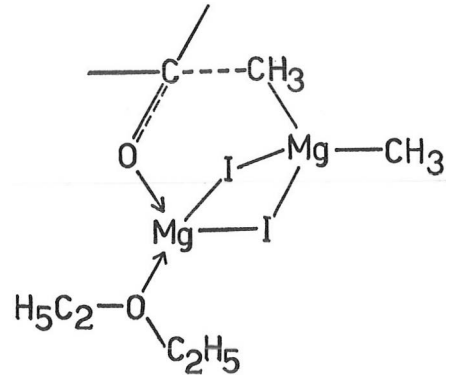
Since the exact structure of the Grignard reagent is still not known,[46–48] we cannot be certain about the mechanism of the addition reaction.[cf.49] Swain[50] has presented one accepted mechanism according to which the reaction occurs through a cyclic intermediate:

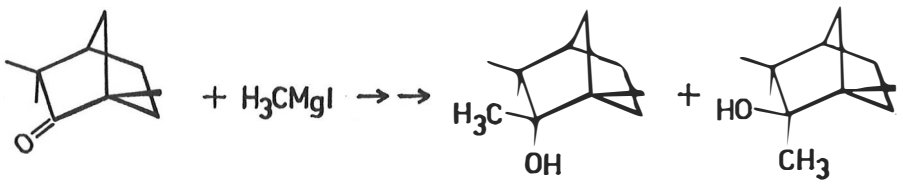


The addition of fenchone to methylmagnesium iodide produces 2-methylfenchol in good yield. The results vary to some extent depending on the molar ratios of fenchone, methyl iodide and magnesium. To the writer's knowledge, no studies have been carried out to determine the optimal molar ratio. According to Toivonen, the Grignard reaction of norcamphor gives the best result when the molar ratios between the ketone, methyl iodide and magnesium are 1:3:3.[1]

In the Grignard reaction of fenchone Nametkin[54] used fenchone, methyl iodide and magnesium in molar ratios 1.0:1.3:1.3 and reported the yield to be nearly quantitative. Zeiss and Pease[55] used a molar ratio of about 1:1.3:1.2 and obtained methyl fenchol with 70 per cent yield (with fenchone as impurity). In the study of Tamminen[40] the yields varied from 71 to 76 per cent when a molar ratio 1:1.3:1.3 was used.

In the present study 1.5 moles of magnesium and 2.0 moles of methyl iodide were used to one mole of fenchone in the Grignard reaction of (+)-fenchone. The ethereal solution of the Grignard reagent was first prepared and the fenchone dissolved in ether was added to it. By this method approximately 96 per cent of fenchone reacted with methylmagnesium iodide which could be verified by means of gas chromatography and determination of the specific rotation. Both methods showed the amount of remaining fenchone to be appr. only 4 per cent.

The gas chromatographic analysis of the Grignard reaction product of fenchone (50 m polypropyleneglycol capillary column, 1 ml N_2/min, 90°) proved that the product consisted of two compounds having almost the same retention times (retention times 37 minutes and 43 minutes). The compounds must have been *endo-exo*-epimeric alcohols, i.e. 2-*endo*-methyl-2-*exo*-fenchol (20) and 2-*exo*-methyl-2-*endo*-fenchol (19). Since these two compounds have the same molecule formula and almost the same retention times it was possible



18* 19 20

*The absolute configuration of (+)-fenchone was determined by the ORD method; J. Korvola and P. J. Mälkönen, unpublished work.

to compute from the chromatogram the relative amounts of isomers on the basis of retention times and peak heights. The relative amounts were found to be 5:95. As shown in the present study, the main product of the reaction was 2-*exo*-methyl-2-*endo*-fenchol (19).

By means of repeated preparative gas chromatography pure isomers were separated in sufficient quantity to permit the run of infrared spectra and the measurement of specific rotations. The rotation of 2-*exo*-methyl-2-*endo*-fenchol was found to be $[\alpha]_D^{20}+4.06°$ (c=2.5, abs. ethanol) and that of 2-*endo*-methyl-2-*exo*-fenchol $[\alpha]_D^{20}$—30.3 (c=2.0 abs. ethanol).

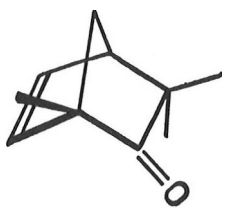
Since it proved difficult to separate the 2-methylfenchol isomers from each other in larger quantities, it was necessary to use the obtained mixture of isomers in the determination of the structures. This, however, is not to be regarded as a marked defect, since the starting product, in point of fact, was almost entirely composed of one isomer only.

THE SYNTHESIS OF DEHYDROFENCHONE

Optically active or even racemic dehydrofenchone (25) has not been produced before, but it is a new trimethyl ketone of the bicyclo[2.2.1]heptene series. A few other unsaturated ketones of this group have been synthesized earlier, for example dehydrocamphor (5)[3,31,56] and dehydroepicamphor (26).[57] There is no mention, either, in the literature of the unsaturated *endo* and *exo* alcohols obtained from dehydrofenchone by the reduction of the carbonyl group, that is, α-dehydrofenchol (27) (*endo*-OH) and β-dehydrofenchol (28) (*exo*-OH). Bays, Cookson and MacKenzie[57] have prepared 5-p-anisyl-α-dehydrofenchol, which is a derivative of α-dehydrofenchol.

The synthesis of dehydrofenchone (p. 21) was started with (+)-fenchone ($[\alpha]_D^{20}+57.58°$, without solvent, 10 cm) which was reduced with sodium and ethanol to a mixture of α- and β-fenchols (30 and 31).[58,59] Since a considerable part of fenchone remained after the first reduction, the reaction product was subjected to another sodium-ethanol treatment. After this the gas chromatograph showed that the amount of fenchone was very small (appr. 3 per cent).

According to Hirsjärvi's infrared spectrometric analysis[23] the sodium-ethanol reduction of fenchone yields 90.8 per cent of α-fenchol (*endo*-OH)[60–66] and 9.2 per cent of β-fenchol (*exo*-OH).[60–66] On the basis of the gas chromatographic analysis Cameron[30] reports the relative amounts of α-and β-fenchols to be 93 per cent and 7 per cent, respectively. The composition of the alcohol mixture obtained in the present study was gas chromatographically determined to be 92 per cent of α- and 8 per cent of β-fenchol. The isomers were not



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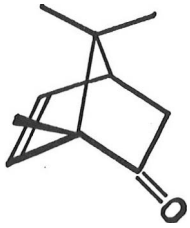

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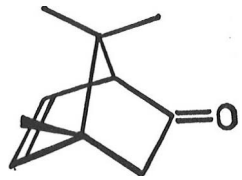

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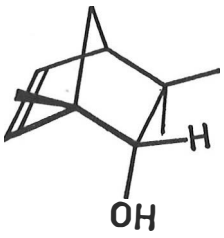

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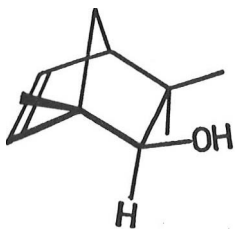

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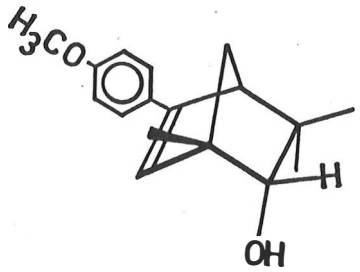

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separated but the mixture was used later on, because from the point of view of the total reaction it did not create any problems. (According to Toivonen[67] α- and β-fenchols can be separated by phosphoric acid treatment).

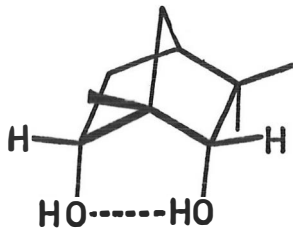
In order to protect the hydroxyl groups of the alcohols they were esterified to acetates (32) in a solution of acetic anhydride and pyridine (molar ratio 1:5:2) by keeping the reaction mixture for 71 hours at the temperature of 90°. When the process was followed by gas chromatography, it was found that the reaction reached equilibrium in 24 hours which did not change much during the following 47 hours.

The obtained fenchyl acetates were oxidized with chromiumtrioxide in glacial acetic acid - acetic anhydride solution to ketofenchyl acetates. According to earlier studies[69] the main product of oxidation is 5-ketofenchyl acetate (33), but the formation of 6-ketofenchyl acetate has also been proved.[cf.70] The oxidation usually gives a poor yield. In the present study it varied from 40 to 50 per cent. The unchanged fenchyl acetate can, however, be recovered in the distillation of the product and the reaction may be repeated.

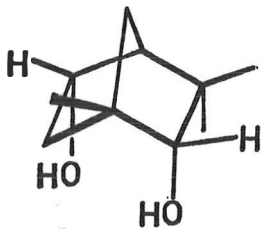
In view of the later stages of reaction the acetate protection of the hydroxyl group of 5-ketofenchol was replaced by the pyranylether protection which is fairly commonly used today.[71–75] For this purpose the ketofenchyl acetate was hydrolyzed (10 per cent K_2CO_3-solution, nitrogen atmosphere) to 5-ketofenchol (34) which was allowed to react with dihydropyran.

The carbonyl group of the pyranyl ether of 5-ketofenchol was reduced with $LiAlH_4$ to a secondary alcohol group (36). Since there are no groups giving cause to steric hindrance at the bridgehead carbon C_4 and particularly at the bridge carbon C_7 (cf. norcamphor (1)), it is most likely that the hydrid ion $AlH_4^{\ominus}$ approaches the carbonyl group from the *exo*-direction and thus the hydroxyl group of the produced alcohol is in *endo*-position.

Hirsjärvi[69] has studied the $LiAlH_4$-reductions of 5-keto-α-fenchyl acetate and other similar ketones and determined by infrared spectrometry the structures of the formed diols. His analysis was based on the existence or non-existence of absorption in the spectrum caused by the intramolecularly bonded OH-group. For instance, in the spectrum of 6-*endo*-hydroxy-α-fenchol the absorption of the intramolecularly bonded hydroxyl group occurs at the wavenumber 3516 cm^{-1}, showing that both hydroxyl groups are on the *endo*-side of the bicyclo[2.2.1]heptane skeleton. However, absorption does not occur in the spectrum of the diol obtained from 5-keto-α-fenchyl acetate. This does not have to mean that the hydroxyl group on carbon atom C_5 would not be on the *endo*-side, because the distance between the hydroxyl groups is already too great to make their intramolecular coupling possible.[cf.76–78]



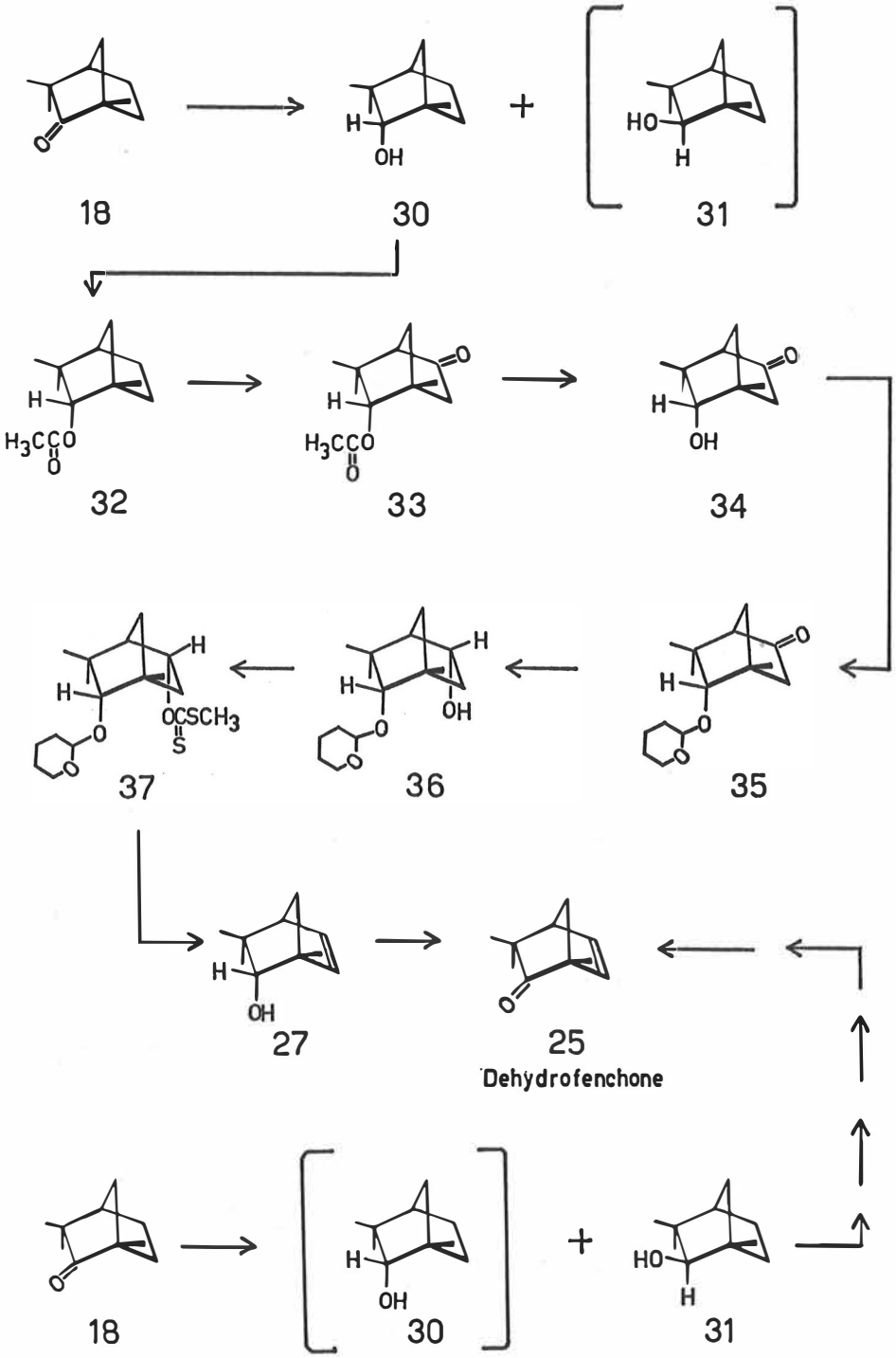
6-*endo*-hydroxy-α-fenchol



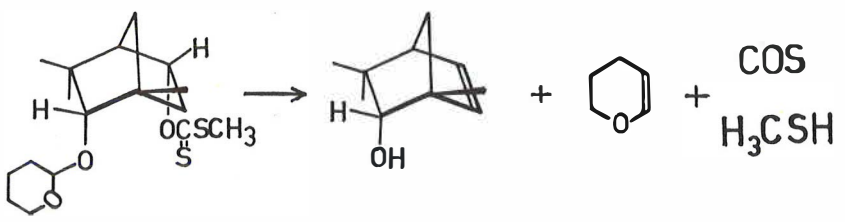
5-*endo*-hydroxy-α-fenchol

The alcohol obtained in the $LiAlH_4$ reduction of the pyranyl ether of 5-ketofenchol was transformed—without studying closer its stereochemical structure—into methylxanthogenate (37) which was decomposed pyrolytically.[79,80] Since the pyrolytic decomposition of the xanthogenate occurs as *cis*-elimination,[81] the cleavage of the xanthogenate group without molecular rearrangement can owing to the structure of the molecule occur only in the

Reaction scheme of the preparation of dehydrofenchone.



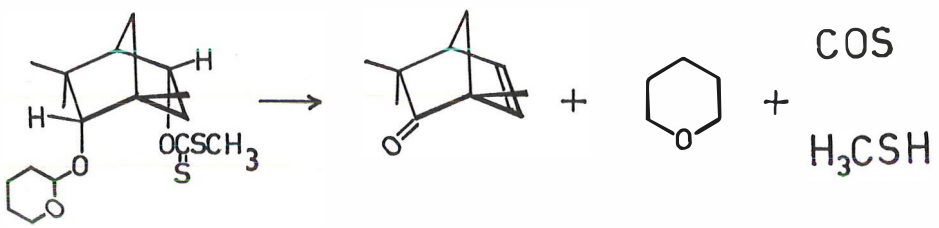
direction of the carbon atom C_6. At the same time occurs also the rupture of the pyranyl ether bond:



37 27

An analogous simultaneous decomposition has been earlier presented by Mälkönen in connection with his synthesis of dehydroborneol.[3,31]

The viscous oily liquid obtained as the pyrolytic product of xanthogenate was divided into three parts by fractional distillation. The middle fraction (bp. 100—130°, 12.8 per cent of the total amount of pyrolytic product) contained dehydrofenchol, which on account of the structure of α-fenchol used in the synthesis was α-dehydrofenchol (27, *endo*-OH). The gas chromatograph revealed clearly about 30 other components in the fraction. In reality, the number is undoubtedly greater, because in the chromatographic conditions used in this connection all compounds were not differentiated into separate peaks, and, furthermore, it is possible that part of the components remained in the column. The retention times suggest that the mixture might also include dehydrofenchone (25) although this could not be ascertained. This assumption is supported by the fact that in the pyrolyses of the pyranylethers of α- and β-fenchols fenchol is oxidized to fenchone.[82,cf.83,84]



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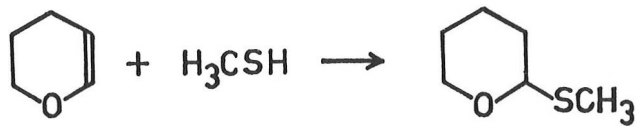
An attempt was made to separate pure dehydrofenchol from the above mentioned middle fraction by preparative gas chromatography but this proved impossible. As comparison substances needed for the determination of the retention times of dehydrofenchol or dehydrofenchone were not available,

it was necessary to search for the correct components as the first step in the separation of the products. In this connection was separated e.g. methyl-2-tetrahydropyranylsulphide which was formed from dihydropyran and methanethiol. Its structure was verified by infrared and nmr spectrometry.



The separation, however, gave a mixture enriched on dehydrofenchol, which was oxidized by the Oppenauer method.[3,85] By means of repeated gas chromatography, pure liquid dehydrofenchone (25) was separated from this oxidized mixture and its structure was determined by infrared, mass and nmr spectroscopy and hydrogenation.

The infrared spectrum of dehydrofenchone had a typical -HC=CH-group absorption at wavenumber 3067 cm^{-1} and the absorption of the carbonyl group at wavenumber 1739 cm^{-1}. The nmr spectrum of the compound shows that it contains e.g. two different double bond protons with signals at δ-values 5.7 and 6.5 ppm (doublet and quartet).

When dehydrofenchone was hydrogenated at room temperature using activated palladium as a catalyst the consumption of hydrogen corresponded to one double bond per molecule. The infrared and mass spectra[cf.86–89] of the hydrogenation product were identical with those of the initial substance (fenchone (18)) and as the specific rotation of the hydrogenation product ($[\alpha]_D^{20}+57.3$, c=5, abs. ethanol) was almost the same as that of the initial substance ($[\alpha]_D^{20}+57{,}58°$), it was certain that there had been no rearrangements during the reaction course which would have changed the configuration.

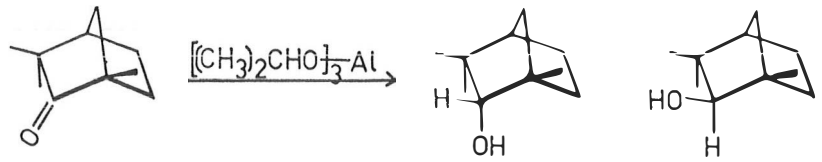
The structure of synthesized dehydrofenchone was also ascertained by the specific rotation and ultraviolet spectrum of the compound. In the determination of the specific rotation the value $[\alpha]_D^{20}+623°$ (c=11.29, abs. ethanol) was obtained. Specific rotations of this order have been found for expressly β,γ-unsaturated bicyclic ketones. For instance, the specific rotations of dehydrocamphor (5), dehydroepicamphor (26) and dehydronorcamphor (8) have been found to be -735°, +864° and +592°, respectively.[56,57,90]

The ultraviolet spectrum of fenchone shows a weak absorption (ε=20) typical of aliphatic ketones at wavelength 288 mμ. If the carbonyl group is conjugated with a double bond, the absorption is usually shifted to a greater wavelength. Even though there is no conjugated double bond system in dehydrofenchone, the absorption shifts to wavelength 304 mμ and at the same time is considerably strengthened (ε=252). This is caused by the spatial

interaction between the carbonyl group and the double bond. This can be either transfer of charge from the double bond to the carbonyl group or more likely n→π^* transition in the carbonyl group caused by the π-electrons of the double bond. A similar long range effect of the double bond can be found in dehydrocamphor[3] and dehydronorcamphor.[91,cf.57]

In the above-mentioned reaction sequence the yield of dehydrofenchone was unexpectedly low, which is mainly caused by the side reactions in the pyrolysis of xanthogenate. As the result of these reactions the main part of the obtained pyrolysis product was a high-boiling viscous oil.

The synthesis of dehydrofenchone was also carried out using an alcohol mixture obtained by the Meerwein-Ponndorf-Verley reduction of fenchone and containing mainly β-fenchol.[23,24,30,92–94] According to various studies the amount of β-fenchol in the reduction product of fenchone varies from about 70 per cent to 80 per cent.



~ 20 % ~ 80 %

18 30 31

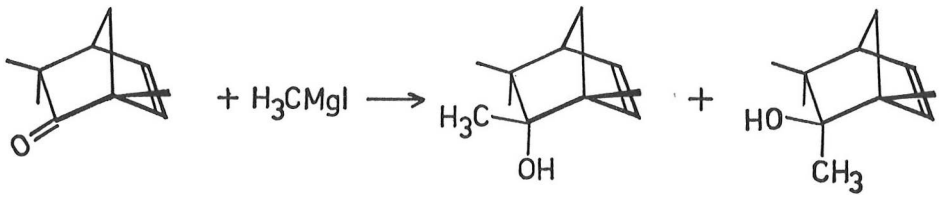
From this alcohol mixture the methylxanthogenate of 5-hydroxy-β-fenchol-2-tetrahydropyranyl ether was prepared in accordance with the above reaction scheme (p. 21). The pyrolytic decomposition of this substance did not yield much dehydrofenchol, either, but the main part of the product was a highboiling viscous oil.

THE GRIGNARD REACTION OF DEHYDROFENCHONE WITH METHYL IODIDE AND MAGNESIUM

In the Grignard reaction of dehydrofenchone ketone, methyl iodide, and magnesium were used in a molar ratio 1:2:1.5. Dehydrofenchone dissolved in ether was added slowly to the ethereal solution of the Grignard reagent. After hydrolysis the very pure product was analysed by gas chromatography and no peak of unchanged dehydrofenchone was found; thus the reaction was quantitative. Since the reaction conditions and the procedure were similar to those in the Grignard reaction of fenchone, we can deduce that dehydro-

fenchone reacts with methylmagnesium iodide better than fenchone. The difference in reactivity is probably caused by the activating effect of the double bond on the carbonyl group. For that reason the carbon atom of the carbonyl group reacts more easily with a nucleophilic reagent. A similar result has been obtained in the reactions of camphor and dehydrocamphor.[3]

The gas chromatograms of the reaction product revealed only two peaks which represented the obtained tertiary alcohol epimers i.e. 2-*exo*-methyl-2-*endo*-dehydrofenchol (1,2,3,3-tetramethyl-5-norbornen-2-*endo*-ol) (38) and 2-*endo*-methyl-2-*exo*-dehydrofenchol (1,2,3,3-tetramethyl-5-norbornen-2-*exo*-ol) (39). Their retention times were 25 minutes and 27 minutes, respectively (50 m polypropyleneglycol capillary column, 1 ml N_2/min, 90°). The relative amounts of the compounds were found to be 57:43 based on the retention times and the peak heights. When the pure isomers were later separated, the result could further be verified by determination of the specific rotations (p. 48).



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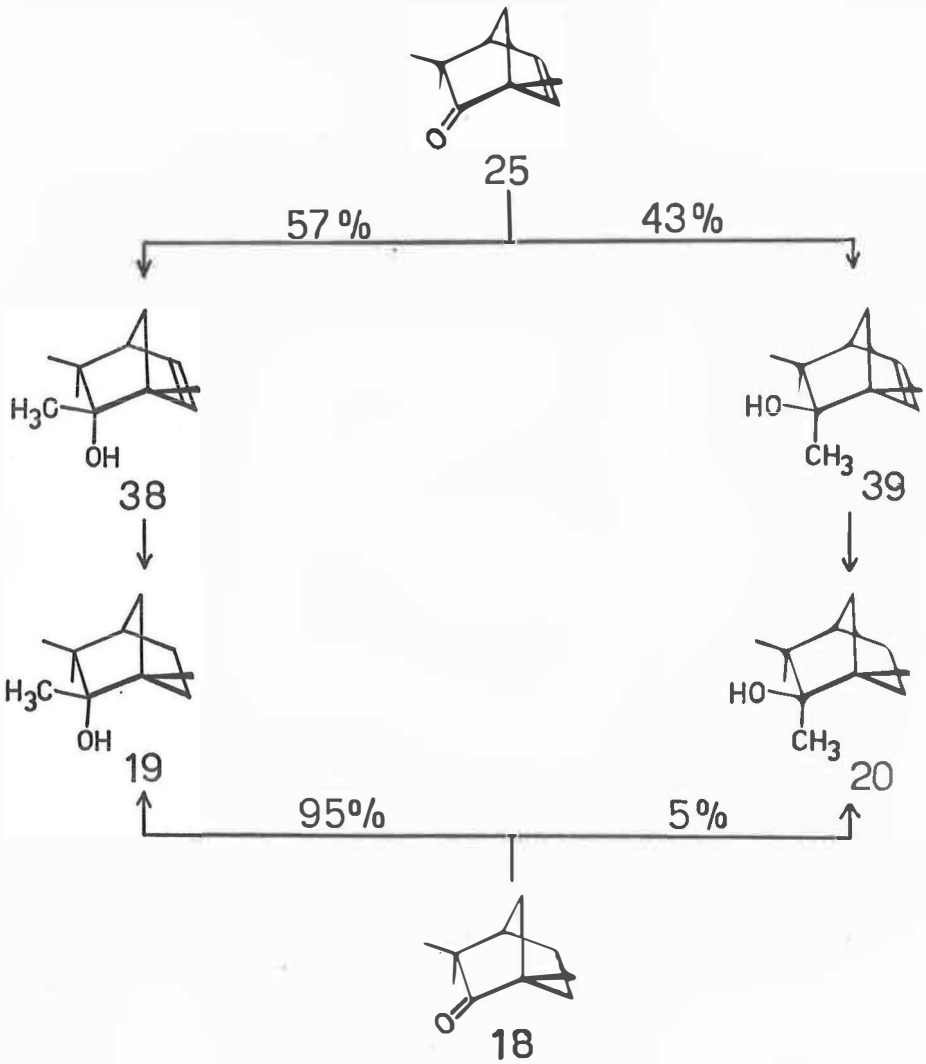
The liquid alcohol epimers formed in the Grignard reaction were separated by means of preparative gas chromatography. On account of their difficult separation it was necessary to carry out the chromatography several times. Infrared and mass spectra were obtained for the pure components, refractive indices and specific rotations were measured, and the components were hydrogenated.

Compound amounting to 57 per cent: The specific rotation of the compound was $[\alpha]_D^{20}+52{,}15°$ (c=5, abs. ethanol) and the refractive index $n_D^{20}=1.4832$. In the infrared spectrum was a strong absorption of alcohol hydroxyl at wavenumber 3500 cm^{-1} and an absorption typical of unsaturated compound at wavenumbers 3062 cm^{-1} and 738 cm^{-1}. When the compound was hydrogenated with palladium-activated hydrogen, the consumption of hydrogen corresponded to one olefinic double bond per molecule. The infrared spectrum of the hydrogenation product was identical with the spectrum of 2-*exo*-methyl-2-*endo*-fenchol (19) which was the main product (95 per cent) of the Grignard reaction of fenchone. The specific rotation and the melting point were also identical with the said reaction product of fenchone.

Compound amounting to 43 per cent: The specific rotation of the compound was $[\alpha]_D^{20}$-24.49° (c=5, abs. ethanol) and the refractive index $n_D^{22}=1.4845$. The infrared spectrum of the compound had the absorption of the alcoholic hydroxyl group at wavenumber 3500 cm^{-1} and absorptions due to an olefinic group at wavenumbers 3060 cm^{-1} and 731 cm^{-1}. The hydrogen consumption of the compound corresponded to one carbon-carbon double bond per molecule. The infrared spectrum of the hydrogenation product was identical with that of 2-*endo*-methyl-2-*exo*-fenchol (20) which is obtained as a by-product (5 per cent) in the Grignard reaction of fenchone. The specific rotation and melting point were also identical with those of the product obtained in the Grignard reaction of fenchone.

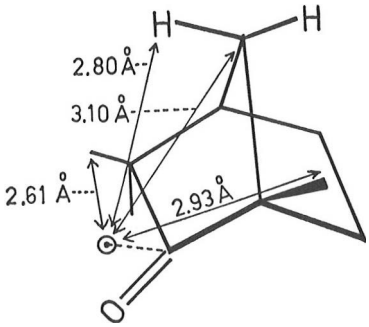


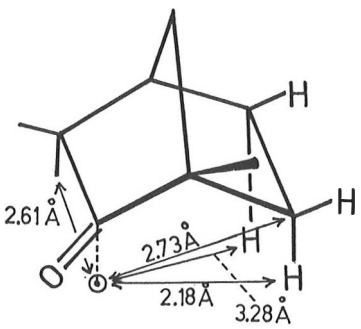
The results indicate that the stereochemical course of the additions of fenchone and dehydrofenchone is different. In the former case *exo*-addition is dominant, in the latter *endo*- and *exo*-additions are almost equally dominant.

COMPARISON OF THE GRIGNARD ADDITIONS OF FENCHONE AND DEHYDROFENCHONE

The significant difference in the *endo-exo* product ratio in the Grignard addition of fenchone and dehydrofenchone can probably be considered to be mostly due to two factors: 1) the different spatial structures of the molecules with ensuing different reaction-guiding steric hindrances and 2) the different electronic effects of the molecules.

A notion about the steric factors directing the course of the Grignard addition of fenchone can be obtained, when we calculate by means of the Wilcox[95] coordinates the distances of the methyl group adding to the carbonyl carbon atom C_2 from certain other carbon and hydrogen atoms of the molecule. The distance of the methyl group entering into *exo*-position (in the *exo*-addition) from the bridge carbon C_7 is 3.10 Å. The distance to the methyl group at the bridgehead carbon C_1 is 2,93 Å, and to the *exo*-methyl group at C_3, 2,61 Å. The distance of the H_{7syn} -hydrogen from the methyl group is 2.80 Å. The distance of the methyl group going into *endo*-position (*endo*-addition) from carbon atom C_6 is 2.73 Å and from the *endo*-methyl group at C_3, 2.61 Å. The H_{6endo} -hydrogen gets very close to the methyl group, the distance being only 2.18 Å.



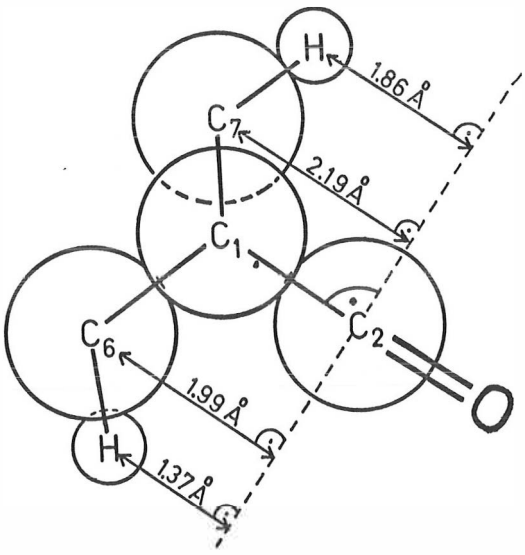


The calculated distances denote clearly that the *exo*-side of the fenchone molecule is more open and more favourable for the approach of the Grignard reagent than the *endo*-side.

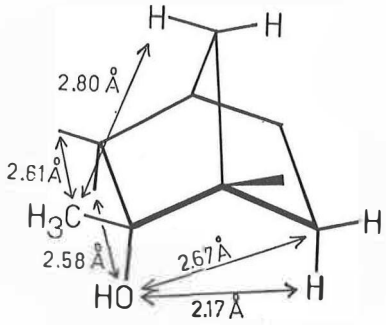
The possibility of *endo*-addition is further considerably reduced if it is assumed that in the reaction the methyl group of the Grignard reagent must

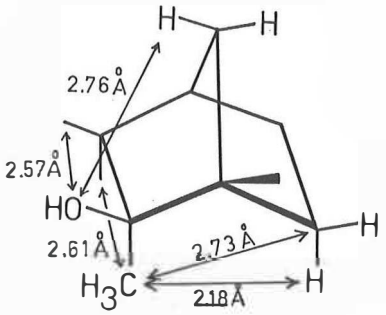
approach the carbonyl carbon of fenchone at a definite angle. It appears most natural that the methyl group must approach from a direction which is vertical to the plane going through the carbon atoms C_1, C_2, C_3 and C_4. The shortest distance of the normal of the plane drawn through carbon atom C_2 from carbon atom C_7 is 2.19 Å and from carbon atom H_{7syn} 1.86 Å. The shortest distance of carbon atom C_6 from the normal is 1.99 Å. Particularly close to the assumed approaching direction of the reagent comes hydrogen atom H_{6endo} whose distance from the normal is only 1.37 Å. When we take into account the fact that the van der Waals radius of the methyl group is about 2.0 Å, we can understand the great steric hindrance effect of H_{6endo}-hydrogen on the addition reaction from the *endo*-direction of the molecule. Also carbon atom C_6 comes partly within the van der Waals radius of the approaching methyl group and contributes to making *endo*-addition difficult. The effects of carbon atom C_5 and hydrogen atom H_{5endo} are slight on account of their long distances.

On the *exo*-side of the fenchone molecule only H_{7syn}-hydrogen atom comes within the effective radius of the methyl group which approaches from the *exo*-direction. However, it cannot be considered to be the only cause of the 5 per cent *endo*-addition found in the Grignard reaction of fenchone, because in that case there should occur partial *endo*-addition in the corresponding reaction of norcamphor, which has not been positively proved. It is to be assumed that hydrogen atom H_{7syn} together with the *exo*-methyl group on the bridgehead atom C_1 and carbon atom C_3 forms a steric hindrance and guides the reaction also towards the *endo*-direction.



When we examine the stereochemical structures of the alcohols 2-*exo*-methyl-2-*endo*-fenchol and 2-*endo*-methyl-2-*exo*-fenchol which are formed in the Grignard addition of fenchone with methylmagnesium iodide, we observe that the structure of both compounds is stereochemically stable, since their methyl groups and hydroxyl groups do not come too close to other atoms or atom groups. The distances computed by means of Wilcox coordinates are shown in the figures below.

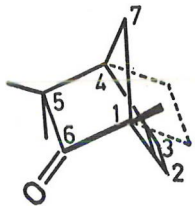




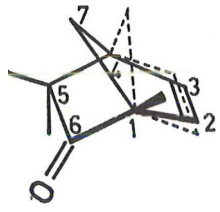
The Grignard addition of methylmagnesium iodide to the dehydrofenchone molecule from the *endo*-direction is less hindered than the corresponding *endo*-addition of fenchone. Dehydrofenchone lacks an atom that corresponds to $H_{6\,endo}$-hydrogen, which is the greatest hindrance in fenchone (as well as an atom corresponding to the $H_{5\,endo}$-hydrogen of fenchone). The hydrogen atoms bonded to carbon atoms C_5 and C_6 are located on the plane going through carbon atoms C_1, C_6, C_5 and C_4 and their bonding direction is outward from the molecule.

On account of the double bond of the dehydrofenchone molecule its carbon skeleton is not identical with that of the saturated bicyclo[2.2.1]heptane compounds. The double bond has the effect that the cyclopentene-ring which is formed from carbon atoms C_1, C_6, C_5, C_4 and C_7 is more planar than the corresponding saturated cyclopentane-ring of fenchone. The formation of the cyclopentene ring as more planar can occur so that either the plane formed by carbon atoms C_1, C_6, C_5 and C_4 turns towards the *endo*-direction of the molecule (A), or the plane formed by carbon atoms C_1, C_7 and C_4 turns towards the carbonyl group of the molecule (B).

The turning of the plane as shown in Figure A is to be regarded as unlikely, because the bulky *endo*-methyl group in carbon atom C_3 with a large effective radius acts as a strong hindrance to the turning of carbon atom C_5. Besides, if the turning occurs as shown in Figure A, carbon atom C_6 comes closer to the carbonyl group, and we would not expect a great difference between the



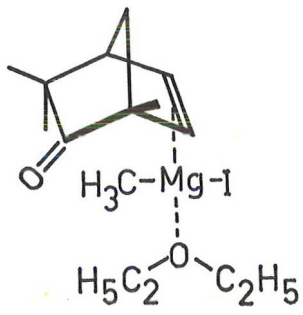
A

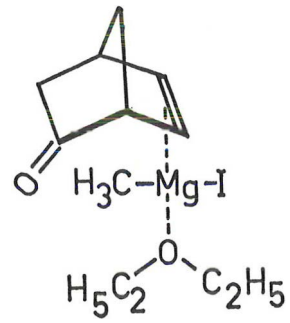


B

endo-exo-addition ratios of fenchone and dehydrofenchone. No atom or atom group is a noteworthy hindrance to the turning of the plane as shown in Figure B. As a result of it, the *exo*-side of the molecule becomes less favourable for the approach of the reagent, because H_{7syn} -hydrogen atom, which is the greatest hindrance on the *exo*-side, comes closer to the carbonyl group and the *exo*-methyl group on carbon atom C_3. Because of the openness of the *endo*-side of the dehydrofenchone molecule and the increased degree of hindrance on the *exo*-side compared with fenchone, the *endo-exo*-addition ratio of the Grignard reaction should be considerably different from that of fenchone, which is supported by empirical results. If the differences in the Grignard additions of fenchone and dehydrofenchone are considered to be due entirely to steric factors, the results indicate that the *exo*-side of the dehydrofenchone molecule is only slightly more open than its *endo*-side.

Besides the above-mentioned different spatial structures of the fenchone and dehydrofenchone molecules, the different electronic effects of the molecules can contribute to the *endo-exo* product ratio in addition reactions. The results obtained in the present study as well as those obtained in the Grignard additions of norcamphor and dehydronorcamphor indicate that the unsaturated compound yields more *endo*-addition product than the corresponding saturated compound. One hypothetical explanation for this phenomenon would be the coordination tendency of the magnesium atom of the Grignard reagent, which is indicated e.g. by the fact that in these reactions the most commonly used solvent diethyl ether is strongly bonded to the reagent.[46] On





the basis of this one might think that the magnesium atom of the reagent possibly tends to coordinate in the π-complex manner with the double bonds of the dehydrofenchone and dehydronorcamphor molecules.

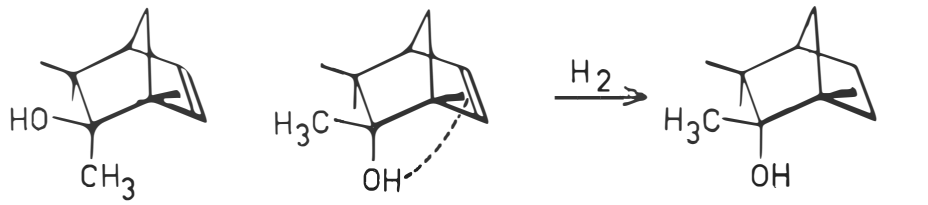
When the coupling of the reagent occurs on the *endo*-side of the molecule, the small—compared with the halogen atom—nucleophilic methyl group for steric reasons comes close to the electrophilic carbon atom of the carbonyl group and the reaction is guided in the *endo*-direction. However, on account of the spatial structures of the molecules (the openness of the *exo*-side) the competing *exo*-addition is dominant in these cases.

THE STRUCTURAL PROOF OF THE TERTIARY ALCOHOLS FORMED IN THE GRIGNARD ADDITIONS OF FENCHONE AND DEHYDROFENCHONE

The structures of the tertiary alcohols formed in the addition of fenchone and dehydrofenchone to methylmagnesium iodide were preliminarily determined by means of gas chromatograms by comparing their retention times with those of some other *endo-exo*-alcohol isomers. With the monoalcohols of the saturated bicyclo[2.2.1]heptane series the retention time of *exo*-alcohol in the polypropyleneglycol column is usually shorter than that of the corresponding *endo* isomer. As examples may be cited α- and β-fenchols, α- and β-nornorneols, and borneol and isoborneol, the rates of elution of all of which are greater than those of the first-mentioned *endo*-isomers. The retention time of the alcohol obtained with 5 per cent yield in the Grignard reaction of fenchone was shorter, and according to what has been said in the above its hydroxyl group should be in *exo*-position. With the unsaturated monoalcohols of the bicyclo[2.2.1]heptene series the retention times are reversed, that is, the *endo*-hydroxyl compound moves faster than the *exo*-isomer. As examples may be cited α- and β-dehydronorborneols, dehydroborneol and dehydroisoborneol.[31] The retention time of the alcohol obtained with a smaller yield (43 per cent) in the Grignard reaction of dehydrofenchone was longer, thus its hydroxyl group should be in *exo*-position. These structural assumptions based on gas chromatograms were subsequently verified.

The structures of the alcohols obtained in the Grignard reaction of dehydrofenchone can be determined with certainty on the basis of infrared spectra run in diluted solutions. In such solutions the absorption caused by intermolecular bonding of hydroxyl groups becomes weaker and that of a free hydroxyl group becomes stronger. The spectrum of the alcohol epimer that constituted 43 per cent of the product formed from dehydrofenchone shows the absorption of the free hydroxyl group at wavenumber 3627 cm^{-1} (0.01-m solution, solvent CCl_4). In the spectrum of the other isomer that constituted 57 per cent the

absorption maximum with the smaller wavenumber is 3604 cm^{-1} (0.01-m solution, solvent CCl_4), which shows that the hydroxyl group is not free but intramolecularly bonded to the double bond. This is possible only in the case that the hydroxyl group of the molecule is in *endo*-position, i.e. the epimer must be 2-*exo*-methyl-2-*endo*-dehydrofenchol.



free OH, abs. 3627 cm^{-1} | bonded OH, abs. 3604 cm^{-1} | free OH, abs. 3622 cm^{-1}

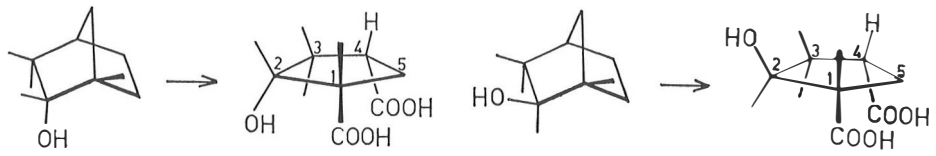
A corresponding shift in the absorption of the hydroxyl group to a smaller wavenumber as a result of the interaction between a double bond and the hydroxyl group is observed, for instance, in the spectra of 2-methyl-dehydronorborneols.[2,cf.12a] The spectrum of 2-*exo*-methyl-2-*endo*-dehydronorborneol shows the absorption of bonded hydroxyl at wavenumber 3591 cm^{-1} and the spectrum of 2-*endo*-methyl-2-*exo*-dehydronorborneol shows the absorption of free hydroxyl at wavenumber 3611 cm^{-1}.

When 2-*exo*-methyl-2-*endo*-dehydrofenchol was hydrogenated the absorption of bonded hydroxyl disappeared and was replaced by the absorption of free hydroxyl at wavenumber 3622 cm^{-1} (0.01 solution, solvent CCl_4). Since the infrared spectra, specific rotations and melting points of the hydrogenation product and the main product obtained in the Grignard reaction of fenchone were identical, the stereochemical configurations of the reaction products can be considered to be proved. The results were further verified by nmr spectroscopy and by the N. J. Toivonen method based on the formation of lactone.

On the basis of the nmr spectra of the products of the Grignard reaction of dehydrofenchone it was possible to deduce the stereochemical structure of the compounds with great certainty. The position of the signal of the H_7-proton which is in *syn*-position to the hydroxyl group is of special interest. In *exo*-alcohol the H_{7syn}-hydrogen becomes subject to the influence of the hydroxyl group and thus its signal must be in a higher field than that of *endo*-alcohol.[96–100] The H_7 proton signal of the compound which the infrared spectrum showed to be 2-*endo*-methyl-2-*exo*-dehydrofenchol was indeed in the higher field the δ-value being 1.87 ppm, and the signal of 2-*exo*-methyl-2-*endo*-dehydrofenchol was in the lower field the δ-value being 1.52 ppm. The

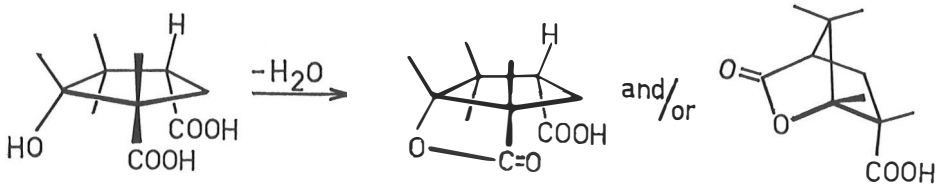
result is in complete accord with the structural interpretation based on infrared spectroscopy.

N. J. Toivonen's structural proof based on the formation of lactone has been used in the structural determination of several *endo-exo*-alcohol isomers of the bicyclo[2.2.1]heptane and -heptene series. The structures of the following compounds have been proved by this method: borneol and isoborneol,[60,68] α- and β-fenchols,[60] 4-methylborneol and 4-methylisoborneol,[40] 2-methylnorborneols,[2,7] 2-methyldehydronorborneols,[2,7] epiborneol and epiisoborneol[101,102] and 2-methylborneols.[3] Applied to the Grignard products of fenchone the method is as follows: when the bond between the carbon atoms C_5 and C_6 of 2-*exo*-methyl-2-*endo*-fenchol (19) is ruptured by oxidation, we obtain 1,2,3,3-tetramethyl-*c*-2-hydroxycyclopentane-*r*-1,*c*-4-dicarboxylic acid (40). 2-*endo*-Methyl-2-*exo*-fenchol gives by similar oxidation 1,2,3,3-tetramethyl-*t*-2-hydroxycyclopentane-*r*-1,*c*-4-dicarboxylic acid. (41).



19 40 20 41

Since in the former compound the hydroxyl group and the carboxyl groups are on the same side of the cyclopentane ring, the compound may give β- and/or γ-lactone acid (42 and 43). The latter compound cannot give lactone acid because the hydroxyl group is *trans* to the carboxyl groups.



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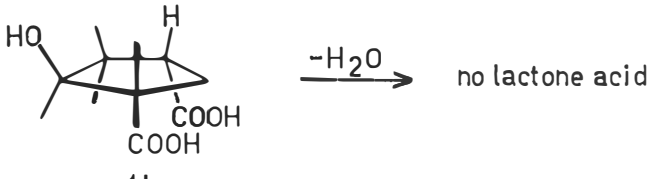

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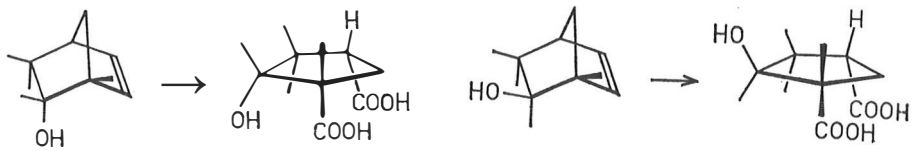
The same hydroxy carboxylic acid can be obtained from the Grignard products of dehydrofenchone by means of rupturing by oxidation with potassium permanganate the double bonds of the molecules.

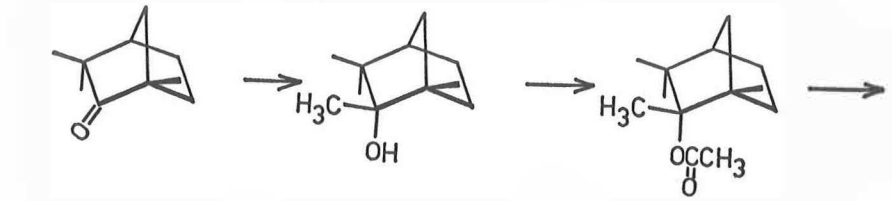


38 40 39 41

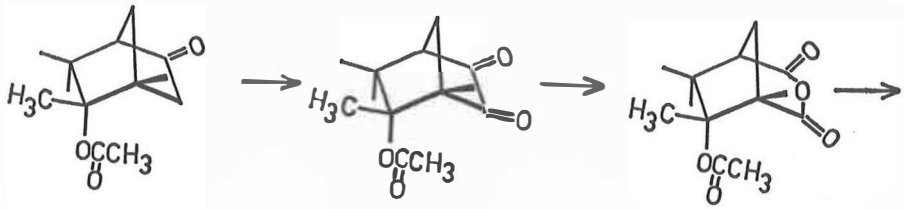
The latter method of producing hydroxy carboxylic acid is in practice much easier than the former, provided that Grignard products of dehydrofenchone are available. As was shown earlier, the synthesis of dehydrofenchone and its purification proved very difficult. For this reason only a very limited amount of dehydrofenchone and its Grignard products were available, and thus it was necessary to perform the synthesis of the other hydroxy carboxylic acid by the former method, as shown in the figure on page 35.

The work was started with (+)-fenchone from which a mixture of 2-*exo*-methyl-2-*endo*-fenchol and 2-*endo*-methyl-2-*exo*-fenchol was produced by Grignard addition. Since on the basis of the presented structural proof it was known that the reaction is up to 95 per cent *exo*-addition, it was not considered necessary to separate the alcohol isomers from one another. In order to protect the hydroxyl group of 2-*exo*-methyl-2-*endo*-fenchol it was esterified in acetic anhydride-pyridine solution to 2-*exo*-methyl-2-*endo*-fenchyl acetate (44). Alcohol, acetic anhydride and pyridine were used in the molar ratio 1:5:2. Since the reaction was slow (the reaction was observed by gas chromatography) the mixture was kept at the temperature of 110° for 108 hours. During this time the reaction mixture turned dark green and fine sediment settled on the walls and bottom of the reaction vessel. Since it was possible that there occurred some rearrangements during the reaction, the structure of the formed acetate was ascertained by hydrolyzing part of it back to the starting material. The use of acetyl chloride was also tried in esterification. When the molar ratio of alcohol and acetyl chloride was 1:1.1 (solvent ether, N, N-dimethylaniline as bounding agent of hydrochloric acid) the alcohol was esterificated at room temperature as fast as in about 24 hours and almost quantitatively. Besides, the reaction mixture remained almost colourless and no sedimentation was observed in contrast to what happened in the esterification with acetic anhydride.

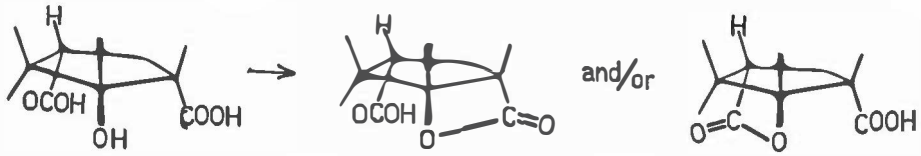
2-*exo*-Methyl-2-*endo*-fenchyl acetate was oxidized with chromium trioxide in glacial acetic acid - acetic anhydride solution to a keto compound. About



18 19 44



45 46 47



40 42 43

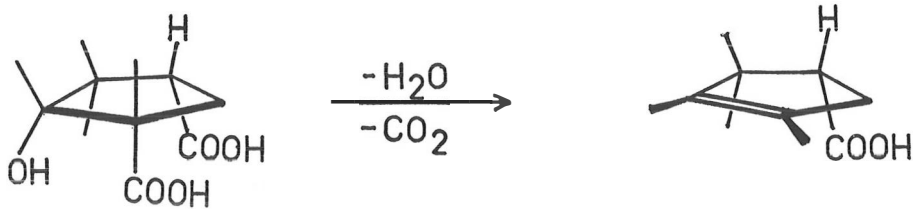
60 per cent of the starting material remained unchanged in the reaction. It was separated by distillation and re-oxidized. The structure of the produced ketoacetate was not studied closer, but if the oxidation reaction took place according to the scheme generally found with the bicyclo[2.2.1]heptane compounds, the main product was 5-keto-2-*exo*-methyl-2-*endo*-fenchyl acetate (45) and the possible by-product 6-keto-2-*exo*-methyl-2-*endo*-fenchyl acetate.

The ketoacetate was oxidized in acetic anhydride solution with selenium dioxide to 5,6-diketo-2-*exo*-methyl-2-*endo*-fenchyl acetate (46). The yield of diketone, which was obtained as long yellow crystallized needles, was about 30 per cent of the theoretical amount, because crystallization had to be repeated in order to remove the formed selenium.

The carbon-carbon bond between the carbonyl carbons of the diketone (46) was ruptured by oxidation in acetic anhydride solution with 30 per cent hydrogen peroxide and as the reaction product was obtained acetoxy carboxylic acid anhydride (41). If it holds true that the Grignard addition of fenchone mainly occurs from the *exo*-direction, the stereochemical structure of the hydroxy acid (40) formed from acetoxy carboxylic acid anhydride by

hydrolysis should be such that either β- or γ-lactone acid (42 or 43) is obtained from it.

The hydrolysis of synthesized acetoxy carboxylic acid anhydride in alcaline solution did not lead to the expected hydroxy carboxylic acid, for when the anhydride was boiled in a 1-n potassium or sodium hydroxide solution and the product was separated after neutralization an oily liquid was obtained. Titrations showed, however, that the consumption of alkali in the reaction corresponded to the calculated amount, i.e. three moles of base per one mole of acetoxy acid anhydride. Part of the oil was purified by vacuum distillation. The product proved to be an unsaturated compound, because on contact with potassium permanganate it immediately decolorized the permanganate and at the same time manganese dioxide was formed. The infrared spectrum of the oil revealed that it was a carboxylic acid. The same result was given by the nmr spectrum, which further showed that the substance was a monocarboxylic acid with no double bond protons. One of the compounds which might come into question is 1,2,3,3-tetramethylcyclopentene-4-carboxylic acid (48), which would be formed from hydroxy carboxylic acid (40) through the elimination of water and carbon dioxide.* In titration the equivalent weight of the compound was found to be 170.0, which is slightly higher than the value computed for the assumed compound (168.2). The closer structural analysis was left to be done in the future.



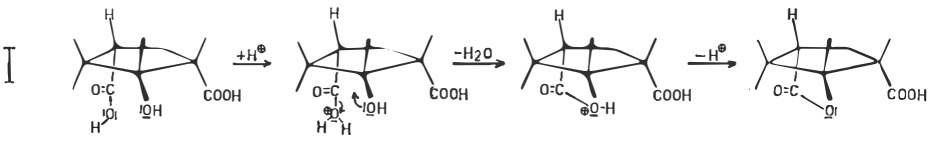
40 48

The hydrolysis of acetoxy carboxylic acid in a diluted hydrochloride acid solution differed considerably from that carried out in alcaline solution. When water was evaporated in a vacuum after boiling, a solid substance remained and was purified by sublimation. The infrared spectrum and titration of the compound showed that the obtained substance was a carboxylic acid. The strongest absorption was, however, at wavenumber 1785 cm^{-1}, which indicates that the compound was also a γ-lactone (43).[40,101,103,104] No hydroxy carboxylic acid (40) could be separated from the product. It may be an intermediate which in the used conditions easily loses water and forms γ-lactone

*An elimination of this kind is noted at least in the pyrolyses of corresponding hydroxy acids prepared from norborneol.[103]

acid, as, e.g., Tamminen[40] and Heinänen[101] have observed in studying some hydroxy carboxylic acids. No β-lactone acid (42), either, is formed in the hydrolysis, which is shown by the fact that the infrared spectrum did not have absorption in the region of 1840 cm^{-1} typical for them.

The lactone formation from hydroxy carboxylic acid in the presence of acid catalyst can in principle be considered to occur in two different ways, either through the splitting off of the acyl hydroxyl group (I)or of the alcohol hydroxyl group (II).



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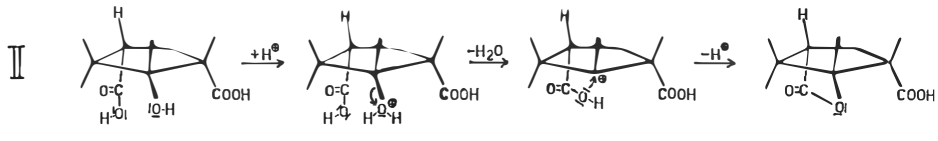
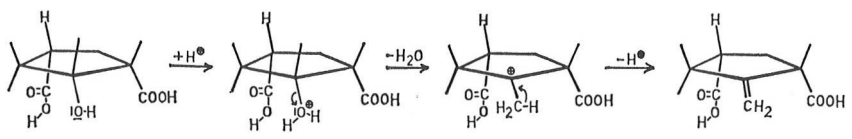


40 43

When the reaction occurs according to the former mechanism, lactone can be formed only from *cis*-hydroxycarboxylic acid. The proposed intermediate (cyclopentane cation) in the latter mechanism can, however, be formed both from *cis*- and *trans*-hydroxy carboxylic acid, and thus lactone formation does not prove the stereochemical structure of the starting material. In the case of the above-mentioned hydroxy carboxylic acids with a secondary hydroxyl group lactone formation takes place according to mechanism I, since it has been found that no lactone is formed when the hydroxyl group is *trans* to the carboxyl group.[40,101] The lactone formation of dicarboxylic acid with a tertiary hydroxyl group examined in the present study also occurs according to mechanism I, since if the intermediate were a cyclopentane cation in accordance with mechanism II, we would expect at least part of the reaction product to be unsaturated dicarboxylic acid (49).



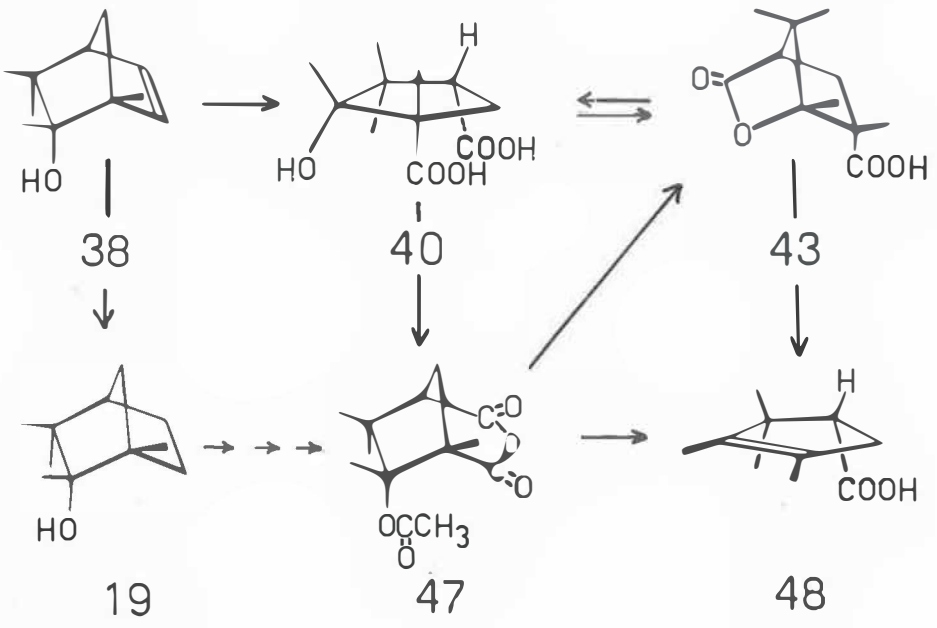
40 49

However, even the unpurified crude product of hydrolysis did not decolorize potassium permanganate with a speed characteristic of alkenes.

The slow alcaline hydrolysis of γ-lactone acid (43) yielded a viscous product. It was purified in a sublimation device and an unsaturated oily liquid was distilled from it, the infrared spectrum of which was identical with that of the liquid compound (48) formed in the alcaline hydrolysis of acetoxy carboxylic acid anhydride. When the dry substance left on the bottom of the sublimation device was purified by crystallization and an infrared spectrum was run on it, it proved identical with hydroxy carboxylic acid (40) produced from the Grignard product of dehydrofenchone (38).

The preparation of hydroxy dicarboxylic acid (40) from the Grignard product of dehydrofenchone (38) was carried out with $KMnO_4$-oxidation in a water-acetone solution buffered with $MgSO_4$. When the synthesized hydroxy dicarboxylic acid was heated in nitrogen atmosphere to about 2° above the melting point, water was split off. The obtained product was identical with γ-lactone acid (43) formed in the acid hydrolysis of acetoxy carboxylic acid anhydride, which was confirmed by infrared spectroscopy. The reaction of acetic anhydride with the hydroxy dicarboxylic acid produced two different compounds, an acid and a neutral compound. The former proved to be γ-lactone acid (43) and the latter the same acetoxy carboxylic acid anhydride (47) that had been produced from the Grignard product of fenchone.

As the same acetoxy dicarboxylic acid anhydride (47), hydroxy dicarboxylic acid (40), and γ-lactone acid (43) were obtained from 2-*exo*-methyl-2-*endo*-



dehydrofenchol (38) and from 2-*exo*-methyl-2-*endo*-fenchol (19) by different methods of preparation, it can be concluded that in carrying out the reaction sequence presented on page 35, no rearrangements changing the structure of the main component had occurred. In additiont, he formation of a γ-lactone acid gives support to the above-mentioned stereochemical structures determined by physico-chemical methods.

In this connection was also produced hydroxy dicarboxylic acid (41) by the potassium permanganate oxidation of the Grignard product (39) of dehydrofenchone. Owing to the limited amount of starting material it was not possible to obtain pure acid. However, the lactonization experiments proved unsuccessful, as expected.

EXPERIMENTAL

SYNTHESIS OF DEHYDROFENCHONE

A. SYNTHESIS OF DEHYDROFENCHONE BY WAY OF α-FENCHOL

Sodium-ethanol reduction of D(+)-fenchone: α-fenchol (30) and β-fenchol (31). 120 g of D(+)-fenchone (Fluka, purum, $[\alpha]_D^{20}+57{,}58°$ (without solvent, 10 cm), $n_D^{20}=1{,}4621$) was dissolved in a three-neck flask in 1200 ml of abs. ethanol. The flask was equipped with a stirrer and a reflux condenser. 120 g of sodium in small pieces was added during ca. 2 hours to the mixture. When all the sodium had been added, the reaction vessel was warmed to 60° until all sodium had reacted. The mixture was then poured into 2,5 litres of water, which brought about the separation of the fenchol to the surface. The fenchol layer was separated and the aqueous solution was extracted with three 350 ml portions of ether. The ethereal extracts were combined with the fenchol and the solution was washed with a concentrated calcium chloride solution and several times with water, and dried thereafter with anhydrous sodium sulphate. The solvent was distilled off, finally under vacuum. Yield 114,2 g.

The gas chromatographic analysis (50 m polypropylene glycol capillary column, 1 ml N_2/min, 115°) showed that ca. 28 % of fenchol remained in the product. According to g c analysis the ratio of α- and α-fenchols was 92:8.

In order to diminish the amount of fenchone the product was anew reduced using the same quantities of sodium and ethanol as above. The obtained crude product (107,1 g) was purified by distillation. Bp. 192—202°, mp. 32—36°, $[\alpha]_D^{20}-11{,}7°$ (c=10, abs. ethanol), $n_D^{36}=1{,}5013$, yield 97,5 g of a colourless compound crystallizing at room temperature.

After a renewed reduction the amount of fenchone was only ca. 3 % and the ratio α- : β-fenchol was the same as after the first reduction (92:8).

Esterification of α-fenchol: α-fenchyl acetate (32). 157 g of α- (and β-) fenchol, 520 g of redistilled acetic anhydride and 161 g of pyridine (distilled over potassium hydroxide) (molar ratios 1:5:2) were mixed. The reaction vessel equipped with a reflux condenser was placed in a 90° water bath. After ca. an hour from the beginning of the reaction the mixture had become dark green. The proceeding of the reaction was observed by gas chromatography. After 24 hours the greater part of the alcohol was esterified, but nevertheless the reaction was left to proceed for 71 hours in all. Between 24—71 hours the reaction did not markedly proceed from the 24 hours state.

The pyridine, acetic acid and acetic anhydride were for the greatest part distilled off from the reaction mixture at slightly reduced pressure. After this 300 ml of n-pentane was added. The pentane solution was washed with 2-n sulphuric acid, diluted sodium hydrogen carbonate solution, finally water, and dried with sodium sulphate. When the pentane had been distilled off, the acetate was distilled in vacuo. Bp. 82—86°/8 torr, $[\alpha]_D^{22}-53{,}2°$

(without solvent, 10 cm), n_D^{22}=1,4572. Yield 162,2 g (82 % of theor.) of colourless liquid. IR spectrum n:o 1.

According to the gas chromatogram the product contained a small amount of unesterified alcohol.

Chromium trioxide oxidation of α-fenchyl acetate: 5-keto-α-fenchyl acetate (*33*). 150 g (0,765 moles) of α- (and β-)fenchyl acetate, 375 g (6,25 moles) of glacial acetic acid, and 300 g (2,94 moles) of redistilled acetic anhydride were mixed in a three-neck flask equipped with a stirrer, a thermometer, and a dropping funnel. 1,5 g of sodium acetate was added, and the mixture was heated to 60°. During a period of 3 hours 185 g (1,85 moles) of chromium trioxide dissolved in 500 g (4,9 moles) of redistilled acetic anhydride was added with vigorous stirring. At the beginning of the addition the temperature of the reaction mixture rose strongly. By regulating the rate of addition of the CrO_3 solution the temperature of the mixture was held between 75—80°. When all of the CrO_3 solution had been added to the mixture, the reaction vessel was kept for one hour in a 80° water bath, and then left to cool. The cooled solution was filtered through a sintered glass funnel. The chromium compound precipitate remaining in the funnel was suspended in a beaker in 300 ml of ether and refiltered. The suspending in ether and filtration were repeated three more times. The ethereal extracts were combined with the mother liquor and the solution was concentrated by distillation at a slightly reduced pressure to ca. 300 ml. To the concentrated solution 400 ml of water and 300 ml of ether were added, whereupon it was neutralized with sodium carbonate. The ether layer was separated from the aqueous solution, which latter was extracted with two 200 ml portions of ether. The ethereal solutions were combined, washed with water, dried with sodium sulphate, and the solvent was distilled off. The residue was distilled under vacuum, unoxidized fenchyl acetate (85 g) distilling firstly and thereupon 5-keto-α-fenchyl acetate at 116—118°/5 torr. Yield 66 g (41 % of theor.) of colourless liquid, $[\alpha]_D^{22}$—34,0° (without solvent), n_D^{22}=1,4683. IR spectrum n:o 3.

The unreacted fenchyl acetate was anew submitted to oxidation using same molar ratios of starting compounds as above. The second time the quantity of oxidized product was 45 %, and the third time 48 % of the theoretical amount.

Hydrolysis of 5-keto-α-fenchyl acetate: 5-keto-α-fenchol (*34*). To 120 g of 5-keto-α-fenchyl acetate was added 2 l of a 10 % potassium carbonate solution. The vigorously stirred mixture was kept under nitrogen atmosphere in a flask equipped with a reflux condenser in a boiling water bath for 22 hours. After that time the ketofenchol which had separated to the surface was extracted with ether, washed with water, dried with sodium sulphate, and the solvent was distilled off. The ketofenchol was distilled in vacuo. Yield 75,4 g (78,5 % of theor.) of a crystalline, almost colourless compound. Bp. 165—167°/9 torr, mp. 74—76°, $[\alpha]_D^{20}$+33,2° (c=10, abs. ethanol). IR spectrum n:o 5.

Reaction between 5-keto-α-fenchol and dihydropyran: 5-keto-α-fenchol-2-tetrahydropyranyl ether (*35*). 70,0 g of 5-keto-α-fenchol and 59,5 g of 2,3-dihydro-4H-pyran (molar ratio 1:1,7) were mixed. Four drops of conc. hydrochloric acid were added, which effectuated a slow rising of the temperature. The reaction was allowed to proceed at room temperature for 13 hours, whereupon a performed gas chromatographic analysis showed that the reaction had proceeded very slowly. In order to increase the reaction rate the vessel was placed for 10 hours into a water bath of 80°. According to a new gas chromatographic analysis there was only a very small amount (< 1 %) of unreacted 5-ketofenchol left. The reaction mixture was allowed to cool, 200 ml of ether was added, the mixture was washed with 100 ml of 1-n sodium hydroxide solution and finally with water. The ethereal solution was dried

and the solvent and excess dihydropyran were distilled off. The residue (100,3 g) was distilled under vacuum. The keto-α-fenchol-2-tetrahydropyranyl ether distilled at 166—171°/4 torr. Yield 87,8 g (83,6 % of theor.) of colourless, oily liquid. $[\alpha]_D^{20}+5,8°$ (c=10, abs. ethanol), $n_D^{22}=1,4840$. IR spectrum n:o 7.

Lithium aluminium hydride reduction of 5-keto-α-fenchol-2-tetrahydropyranyl ether: 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether (*36*). 16,0 g of lithium aluminium hydride was mixed in a flask equipped with a reflux condenser and a mechanical stirrer with 200 ml of diethyl ether previously dried with sodium. To the suspension was gradually added during one and a half hours 85,0 g of 5-keto-α-fenchol-2-tetrahydropyranyl ether dissolved in 150 ml of abs. ether. (Molar ratio of 5-ketofenchol-2-tetrahydropyranyl ether and $LiAlH_4$ 1:1,25). After end of the addition the reaction mixture was boiled for 2 hours, whereupon it was kept for 18 hours at room temperature. Excess $LiAlH_4$ was destroyed by adding plenty of ether saturated with water and finally water. The hydroxide precipitate was removed from the solution by filtration and the ether layer was separated. The aqueous solution was extracted several times with ether, the ethereal extracts were combined with the mother liquor, washed with water, and dried. The solvent was distilled off. The 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether was distilled in vacuo. Yield 75,5 g (88,0 % of theor.) of colourless, viscous oil. Bp. 153-156°/3 torr, $[\alpha]_D^{20}$—10,5° (c=10, abs.ethanol), $n_D^{22}=1,4938$. IR spectrum n:o 9.

According to the IR spectrum the ketone had been completely reduced, as no carbonyl absorption at the wave number 1746 cm^{-1} due to 5-keto-α-fenchol-2-tetrahydropyranyl ether was perceivable.

Preparation of the methyl xanthogenate of 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether (*37*). 72,0 g of 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether was dissolved in 100 ml of toluene dried with sodium. When 14,3 g of finely powdered sodium amide (30 % excess) was added, evolution of gaseous ammonia began immediately. The reaction vessel equipped with a reflux condenser was kept in a water bath of 60° for 2 hours. In that time the evolution of ammonia had almost ceased. A small amount of unreacted sodium amide remained on the bottom of the flask. To the cooled solution 50 ml of abs. diethyl ether was added. The solution was decanted into a three-neck flask equipped with a reflux condenser, a stirrer and a dropping funnel. From the latter 24,7 g (15 % excess) of carbon disulphide, which had been purified with calcium chloride and potassium permanganate and distilled, was slowly added to the vigorously stirred solution. Immediately at the beginning of the adding of the carbon disulphide the solution became turbid and a precipitate was gradually formed with simultaneous elevation of the temperature of the mixture. When all carbon disulphide had been added, the mixture was boiled for 2 hours. During this time the amount of the red-brown precipitate increased considerably and the latter formed a waxy mass, which sank to the bottom of the vessel. The clear solution above the mass (toluene, ether, excess CS_2 and possibly unreacted starting alcohol) was removed from the reaction vessel and instead 150 ml of abs. diethyl ether was poured into the flask. From the dropping funnel 50,2 g (25 % excess) of methyl iodide was very slowly added to the vigorously stirred mixture, the temperature of which rose, and the precipitate began to whiten owing to the formation of sodium iodide. When the adding was ended, the mixture was boiled on a water bath for 1,5 hours, whereupon it was allowed to stand for 35 hours at room temperature. The product was washed several times with water and dried with sodium sulphate. When the solvent had been distilled off, finally at slightly reduced pressure, 91,0 g (93,3 % of theor.) of yellow, viscous oil was obtained as a residue. $[\alpha]_D^{20}$—11,6° (c=10, abs. ethanol), $n_D^{22}=1,5338$. IR spectrum n:o 11.

Pyrolysis of the methyl xanthogenate of 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether: α-dehydrofenchol (27). 86,0 g of methyl xanthogenate was pyrolyzed in an ordinary distillation assembly equipped with a 20 cm Vigreux column (nitrogen flow). The receiver was placed in an ice-salt mixture. The decomposition began, when the temperature of the employed oil bath was ca. 180°. At that time a colourless liquid distilled from the flask (bp. 78—82°). As the distillation was but very slow after 30 minutes, the temperature was raised in 20 minutes to ca. 230°, and held there for 40 minutes. As the distilling was slow even now, the pressure was reduced to 50—60 torr, whereat a viscous yellow oil began to distil from the reaction vessel (bp. 105—132°). When the receiver was removed from the chilling bath at the end of the pyrolysis, the collected liquid began to bubble strongly (boiling of methyl mercaptan?). The amount of distilled liquid was 69,7 g; this was divided by fractional distillation into three parts:

fraction I, bp. ≤ 100°, 24,5 g	(35,2 % of the	product of pyrolysis)
fraction II, bp. = 100—130°, 8,9 g	(12,8 %	»)
residue, bp. ≥ 130°, 36,8 g,	(52 %	»)

Fraction II gave on preparative gas chromatography (10 % Carbowax 20 M on Chromosorb W (80/100 mesh), 5 m, Ø 1/4″ + 10 % FFAP on Chrom W, 80/100 mesh, 5 m, Ø 1/4″, 130°, 35 ml N_2/min) 3,6 g of a mixture enriched on dehydrofenchol (27), which mixture was oxidized by the Oppenauer method. The attempts of isolation of pure dehydrofenchol were not successful under these chromatography conditions.

Oxidation of dehydrofenchol by the Oppenauer method: dehydrofenchone (25). 3,5 g of the mixture containing dehydrofenchol obtained above and 2,0 g of aluminium isopropoxide were heated together in a distillation assembly for 50 min. in a 130° oil bath. In order to remove any possible undistilled isopropanol 20 ml of n-pentane was added to the cooled reaction product. The solvent was distilled off, finally in vacuo, and 5,0 g of benzophenone was added to the residue. The mixture was heated to 140° for an hour in a flask equipped with a reflux condenser, whereupon the formed dehydrofenchone was separated from the mixture by steam distillation. The yellow liquid distilled with the steam was extracted with ether, the ethereal solution dried with sodium sulphate, and the solvent distilled off. The oily residue (2,4 g) contained according to the gas chromatogram still ca. thirty different components. As a result of three preparative gas chromatographic runs on the same sample 0,72 g of pure dehydrofenchone was isolated. $[\alpha]_D^{22}$ +623° (c = 11,29, abs. ethanol), λ_{max} 304 mμ (ε = 251). IR spectrum n:o 13, nmr spectrum n:o 1, mass spectrum n:o 1.

$C_{10}H_{14}O$ (150,21)	Calculated	C = 80,03 %	H = 9,39 %
	Found	C = 80,13 %	H = 9,22 %

In the chromatography a 10 m column (Ø 1/4″) was used, which was filled with 10 % Carbowax 20 M on Chromosorb W (80/100 mesh). In the first run the temperature of the column was 160° (70 ml N_2/min), in the second 140° (50 ml N_2/min), and in the third 130° (35 ml N_2/min).

Hydrogenation of (+)-dehydrofenchone: (+)-fenchone (18). 100 mg of dehydrofenchone was dissolved in 5,0 ml of n-pentane and hydrogenated with hydrogen activated with palladium. The hydrogenation went to completion within a few minutes. The consumption of hydrogen was 98,1 % of the theoretical. The catalyst was removed by filtration. When the solvent was distilled off, (+)-fenchone remained. $[\alpha]_D^{20}$ +57,3° (c = 5, abs. ethanol). The IR spectrum of the compound (n:o 15) was identical with that of the fenchone used as starting compound (n:o 14).

B. SYNTHESIS OF DEHYDROFENCHONE BY WAY OF β-FENCHOL

Reduction of fenchone by the Meerwein-Ponndorf-Verley method: β-fenchol (31) (and α-fenchol, 30). A mixture composed of 26,0 g of aluminium wire, 1,2 g of mercuric chloride, 4,5 ml of carbon tetrachloride and 525 ml of isopropanol, was boiled for 4 hours in a flask equipped wit a reflux condenser, whereupon 150 g of (+)-fenchone was added. In order to remove the acetone formed in the reaction the flask was equipped with a 1,5 m long effective column, which could be heated. The mixture was refluxed for ca. 10 days and nights, then the excess isopropanol was distilled off. Water was added to the residue and the fenchol was extracted with ether. The ethereal solution was washed with 2-n hydrochloric acid, sodium hydrogen carbonate solution, and finally water, and dried with sodium sulphate. When the solvent was distilled off, 126 g of colourless oil remained. $[\alpha]_D^{20}$—26,32° (c=10, abs. ethanol), n_D^{18}=1,4783.

Since the product was according to the gas chromatogram very pure β-fenchol (and α-fenchol) (a small amount of fenchone remained), it was used as such without distillation to the preparation of β-fenchyl acetate.

β-Fenchyl acetate. The preparation of β-fenchyl acetate was carried out as described in the preparation of α-fenchyl acetate. The only significant difference was that the reaction mixture was held at 90° only for 28 hours. 123 g of the above obtained β-fenchol was used to the preparation. The acetate was purified by distillation. Bp. 73—75,5°/2 torr, $[\alpha]_D^{20}$+13,6° (c=10, abs. ethanol), n_D^{21}=1,4572. Yield 134 g (85 % of theor.). IR spectrum n:o 2.

5-Keto-β-fenchyl acetate. The oxidation of β-fenchyl acetate was carried out with chromium trioxide as described for 5-keto-α-fenchyl acetate. 120 g of acetate was used in the oxidation. The yield in the first oxidation round was 43 %, in the second 46 %, and in the third 47 %. Bp. of the ketoacetate : 123—125°/5 torr, $[\alpha]_D^{20}$+37,43° (c=10, abs. ethanol), n_D^{22}=1,4685. IR spectrum n:o 4.

5-Keto-β-fenchol. 100 g of 5-keto-β-fenchyl acetate was saponified in potassium carbonate solution (1,7 l) like the α-isomer. Yield 72 g (90 % of theor.). $[\alpha]_D^{20}$+14,1°, (c=10, abs. ethanol), n_D^{20}=1,4860. The product was not distilled after its isolation, but was used as such for the preparation of the pyranyl ether. IR spectrum n:o 6.

5-Keto-β-fenchol-2-tetrahydropyranyl ether. 70,0 g of 5-keto-β-fenchol and 53,0 g of 2,3-dihydro-4H-pyran (molar ratio 1:1,5) were mixed and four drops of conc. hydrochloric acid were added. Since the reaction between dihydropyran and 5-keto-α-fenchol had proved slow the reaction vessel equipped with a reflux condenser was directly placed into a 80° water bath. A small sample taken from the reaction mixture after 22 hours contained according to a gas chromatogram only a very small quantity (by estimation <1 %) of alcohol. The product was collected as described in the case of the α-isomer. Yield 92,2 g (87,8 % of theor.), bp. 150—160°/5 torr, $[\alpha]_D^{20}$+33,0° (c=10, abs. ethanol), n_D^{20}=1,4828. IR spectrum n:o 8.

5-Hydroxy-β-fenchol-2-tetrahydropyranyl ether. 85,0 g of 5-keto-β-fenchol-2-tetrahydropyranyl ether was reduced in ethereal solution with 16,0 g of $LiAlH_4$. The reduction was carried out in the same way as for the α-isomer. Yield 77,3 g (90,0 % of theor.). The product was not distilled but used as such for the preparation of the methyl xanthogenate. $[\alpha]_D^{20}$—0,70° (c=10, abs. ethanol). IR spectrum n:o 10.

Methyl xanthogenate of 5-hydroxy-β-fenchol-2-tetrahydropyranyl ether. The xanthogenate was prepared from 75,0 g of the above prepared pyranyl ether, 14,0 g of sodium amide, 24,0 g of carbon disulphide, and 50,0 g of methyl iodide. The preparation was performed as for the α-isomer. Yield 93,2 g (92 % of theor.) of a brown oil. IR spectrum n:o 12.

Pyrolysis of the methyl xanthogenate. In the pyrolysis of the methyl xanthogenate different temperatures and heating times were tested on small quantities of substance. The decomposition began usually at ca. 180°, a colourless liquid distilling at this temperature from the reaction flask. The temperature and heating time seemed not to have any marked influence on the final reaction product. This was always a mixture of scores of different compounds, in which the amount of dehydrofenchol was according to gas chromatography very small. In the decomposition tests kaolin was also tried by adding plenty of it to the reaction mixture. It had, however, no essential effect upon the course of the reaction.

As the isolation of dehydrofenchol from the pyrolysis product was difficult on the basis of earlier experience, the procedure in this connection was such that a small quantity of very impure dehydrofenchol was isolated by preparative gas chromatography. The mixture was oxidized by the Oppenauer method and from the product a quantity of dehydrofenchone (not completely pure) necessary for determination of the specific rotation and for the infrared spectrum was isolated. For the specific rotation the value $[\alpha]_D^{20}+592°$ (c=4,932 abs. ethanol) was obtained, which owing to impurities is somewhat smaller than the earlier obtained value ($[\alpha]_D^{20}+623°$). In the earlier and now run infrared spectra no differences could on the other hand be observed.

THE GRIGNARD REACTION OF FENCHONE WITH METHYL IODIDE AND MAGNESIUM. SYNTHESIS OF γ-LACTONE ACID (43).

Grignard reaction of fenchone with methyl iodide and magnesium: 2-exo-methyl-2-endo-fenchol (19) and 2-endo-methyl-2-exo-fenchol (20). 36,45 g (1,5 moles) of magnesium turnings and 250 ml of abs. ether were placed into a flask equipped with a stirrer and a reflux condenser. During 45 minutes 284 g (2,0 moles) of methyl iodide was added from a dropping funnel. In the ensuing reaction all magnesium turnings disappeared. Within a time of 30 minutes 152 g (1 mole) of (+)-fenchone dissolved in 250 ml of abs. ether was added to the reaction mixture. After the end of the addition the mixture was boiled for 3,5 hours, and then poured into an ammonium chloride-ice mixture. The separation of the product was performed by ether extraction and subsequent distillation under vacuum. The yield was 161,0 g (96 % of theor.) of a colourless liquid crystallizing at room temperature. Bp. 83—87°/4 torr, melting range 56—61°, $[\alpha]_D^{22}+4,92°$ (c=10, abs. ethanol). The amount of unreacted fenchone was according to analysis by gas chromatography 4 %. A part of the product was used for the isolation of the formed alcohols by preparative gas chromatography. Owing to the difficulties in the separation of the components the chromatographic process had to be performed in three runs. (Column: 10 m, Ø 1/4″, 10 % Carbowax 20 M on Chromosorb W, 80/100 mesh, 130°, 45 ml N_2/min). The following physical data were obtained for the separated compounds:

2-*exo*-methyl-2-*endo*-fenchol (19): mp. 65—66°, $[\alpha]_D^{20}+4,07°$ (c=2,5, abs. ethanol), IR spectrum n:o 18, mass spectrum n:o 4.

2-*endo*-methyl-2-*exo*-fenchol (20): mp. 75,5°, $[\alpha]_D^{20}$—30,6° (c=2, abs. ethanol), IR spectrum n:o 20, mass spectrum n:o 5.

Esterification of 2-exo-methyl-2-endo-fenchol: 2-exo-methyl-2-endo-fenchyl acetate (44). 150 g of the above obtained, mainly (95 %) 2-*exo*-methyl-2-*endo*-fenchol containing alcohol, 465 g of acetic anhydride, and 114 g of pyridine (molar ratios 1:5:2) were mixed. The reaction vessel equipped with a reflux condenser was kept for 108 hours in a 110° oil bath. The solution became dark green during the reaction, and a finely divided sediment settled on the bottom of the flask. The sediment was filtered off after end of the reaction. The excess acetic anhydride, acetic acid and pyridine were distilled off in vacuo, and 400 ml of pentane was added to the residue. The solution was washed several times with diluted sulphuric acid, sodium hydrogen carbonate solution, and finally water. When the solution had been dried with sodium sulphate, the solvent was distilled off. The crude product (162 g) was distilled under vacuum. The yield of ester was 154 g (81,5 % of theor.). Bp. 97—103°/9 torr, $[\alpha]_D^{20}$—34,62° (without solvent, 10 cm), n_D^{21}=1,4705. IR spectrum n:o 22.

The esterification of 2-*exo*-methyl-2-*endo*-fenchol was carried out also with acetyl chloride. 15,0 g of alcohol, 7,7 g of acetyl chloride, and 14,0 g of N,N-dimethylaniline (molar ratios 1:1,1:1,3) were mixed. The reaction was allowed to proceed at room temperature for 24 hours. The alcohol was esterified almost quantitatively within this time. The reaction mixture remained colourless and no formation of sediment like that in the esterification with acetic anhydride occurred. After end of the reaction 50 ml of water was added and the ester was extracted with ether. The ethereal solution was washed several times with diluted H_2SO_4, $NaHCO_3$ solution, and water. The obtained crude product (17,5 g, 93 % of theor.) was according to a gas chromatogram very pure ester. ($[\alpha]_D^{20}$—35,01°, without solvent, 10 cm).

Chromium trioxide oxidation of 2-exo-methyl-2-endo-fenchyl acetate: 5-keto-2-exo-methyl-2-endo-fenchyl acetate (45). 135 g of 2-*exo*-methyl-2-*endo*-fenchyl acetate, 295 ml of acetic anhydride, and 240 ml of acetic acid were mixed. 1,0 g of sodium acetate was dissolved in the mixture and the latter heated to 70°. 145 g of CrO_3 dissolved in 390 ml of acetic anhydride was added during 1,5 hours to the mixture. By regulating the rate of addition the temperature of the mixture was held at 75—80°. When the CrO_3 solution had been added, the reaction vessel was kept for 2 hours in a water bath of 75°. The precipitate of chromium compounds was filtered from the cooled solution and extracted with ether. The extracts were combined with the mother liquor, which was concentrated by vacuum distillation. After addition of ether to the residue the latter was neutralized with sodium carbonate. The product was collected by ether extraction and distilled in vacuo, unoxidized 2-*exo*-methyl-2-*endo*-fenchyl acetate distilling first (79 g, 58,5 % of the amount of starting substance), and then at 128—134°/3 torr, 5-keto-2-*exo*-methyl-2-endo-fenchyl acetate. Yield 57 g (39,5 % of theor.). $[\alpha]_D^{20}$—8,24° (c=5, abs. ethanol), n_D^{20}=1,4774. IR spectrum n:o 23.

Selenium dioxide oxidation of 5-keto-2-exo-methyl-2-endo-fenchyl acetate: 5,6-diketo-2-exo-methyl-2-endo-fenchyl acetate (46). 85 g of 5-keto-2-*exo*-methyl-2-*endo*-fenchyl acetate was dissolved in 100 ml of acetic anhydride and 35 g of selenium dioxide was added to the mixture. The reaction vessel equipped with a reflux condenser was placed into an oil bath of 110°. The oxidation began when the temperature was raised to ca. 130°. After one hour 35 g of SeO_2 was further added to the mixture, whereupon the latter was held for 6 hours at 130—135°. The selenium and excess selenium dioxide were removed by filtration and the solvent was distilled off in vacuo. The remaining red-brown oily product was dissolved in 500 ml of ether.The solution was washed several times with diluted sodium hydroxide solution, diluted sulphuric acid, and finally water. When the ether had been distilled off after drying with calcium chloride, impure diketone crystallized in long needles remained (69,7 g). This was purified by recrystallizing it several times from ethanol. Yield 28 g (31

% of theor.) of yellow compound crystallizing in needles. Mp. 167—169°. IR spectrum n:o 24.

1,5 g of diketoacetate was hydrolyzed to 5,6-diketo-2-*exo*-methyl-2-*endo*-fenchol by boiling it for 4 hours in 1-n potassium hydroxide solution (10 ml). The consumption of alkali was 97,7 % of the calculated amount. Yield 1,05 g (85 % of theor.).

$C_{11}H_{16}O_3$ (196,25)	Calculated	C=67,32 %	H=8,22 %
	Found	C=67,11 %	H=8,32 %

IR spectrum n:o 25.

Hydrogen peroxide oxidation of 5,6-diketo-2-exo-methyl-2-endo-fenchyl acetate: acetoxy-dicarboxylic acid anhydride (47). 25 g of diketoacetate (46) was dissolved in 150 ml of glacial acetic acid. 100 g of 30 % hydrogen peroxide was gradually added to the solution at room temperature. In the beginning the yellow colour of the solution faded gradually and after 14 hours it had completely disappeared. During this time big colourless crystals of anhydride had formed on the bottom of the vessel, which were separated by filtration. The solution was concentrated in vacuo, whereupon further anhydride crystallized. The recrystallization was carried out from glacial acetic acid. Yield 21,3 g (80 % of theor.). Mp. 170—171,5°.

$C_{13}H_{18}O_5$ (254,28)	Calculated	C=61,41 %	H=7,14 %
	Found	C=61,63 %	H=7,27 %

IR spectrum n:o 26.

Hydrolysis of acetoxy-dicarboxylic acid anhydride (47) in alkaline solution. 10,0 g of acetoxy-dicarboxylic acid anhydride was added to 150 ml of 1-n KOH solution and this was kept for 8 hours in a boiling water bath. After washing with ether the solution was acidified with diluted hydrochloric acid, which caused the separation of an oily liquid. The mixture was extracted several times with small quantities of ether. The ethereal extracts were combined, washed once with water, and dried with sodium sulphate. When the solvent had been distilled off, 5,3 g of a brown oil remained, which was very rapidly oxidized by potassium permanganate (unsaturated compound). A small quantity of the product was purified in a vacuum device equipped with a cold finger condenser. On the basis of the infrared spectrum, nmr spectrum, equivalent weight, elementary analysis, and strong consumption of permanganate of the colourless oil, the structural formula representing 1,2,3,3-tetramethyl-cyclohexene-4-carboxylic acid (48), given on page 37, is considered probable for the compound. A closer structural analysis will be performed subsequently.

$C_{10}H_{16}O_2$ (168,24)	Calculated	C=71,39 %	H=9,59 %	E=168,2
	Found	C=71,94 %	H=9,45 %	E=170,0

IR spectrum n:o 28, nmr spectrum n:o 4.

When the hydrolysis of the acetoxy-dicarboxylic acid anhydride was carried out in 1-n sodium hydroxide solution, the product was a similar oil as above. In the titration 1,0 g of anhydride consumed 510 mg of NaOH, which is 98 % of the theoretical amount calculated on the basis that one mole of acetoxy-dicarboxylic acid consumes three moles of alkali.

Hydrolysis of acetoxy-dicarboxylic acid anhydride (47) in acid solution: γ-lactone acid (43). To 15 ml of 2-n hydrochloric acid was added 1,0 g of acetoxy-dicarboxylic acid anhydride and the mixture was boiled for 3 hours, whereupon it was distilled to dryness under vacuum. The brownish residue was purified by sublimation in vacuo, whereby 520 mg of colourless crystalline γ-lactone acid was obtained. Mp. 192—194,5°.

$C_{11}H_{16}O_4$ (212,24)	Calculated	C=62,25 %	H=7,60 %	E=212,2
	Found	C=62,54 %	H=7,79 %	E=209,7

IR spectrum n:o 31.

Hydrolysis of γ-lactone acid (43): hydroxy-dicarboxylic acid (40). To a mixture of 200 mg of γ-lactone acid and 50 ml of abs. ethanol was added 9,4 ml of 0,1-n sodium hydroxide solution (50 % of the calculated amount). The reaction vessel equipped with a reflux condenser was placed into a 100° oil bath. During 13 hours 9,42 ml of 0,1-n NaOH solution (18,82 ml in all, i.e., the calculated amount) was dropwise added to the mixture. After end of the addition the reaction vessel was kept for further 19 hours in the warming bath, whereupon the ethanol was distilled off. When the aqueous solution had been once extracted with a small quantity of ether, it was acidified with diluted hydrochloric acid. The solution which had become turbid was distilled to dryness under vacuum and the residue was extracted with small amounts of acetone. The acetone extracts were combined and the solvent was distilled off. The remaining brownish sticky mass was transferred into the vacuum sublimation device, where a colourless oil distilled apart from it. The infrared spectrum of the oil was identical with that of the oily product obtained in the alkaline hydrolysis of acetoxy-dicarboxylic acid anhydride. The brown solid remaining on the bottom of the sublimation device was purified by crystallization from a n-hexane-acetone mixture. Yield 28 mg of hydroxy-dicarboxylic acid. Mp. 165—166°. The infrared spectra (IR spectra n:o 29 and n:o 30) of the obtained compound and of the acid which was prepared from the Grignard reaction product (38) of dehydrofenchone were identical.

GRIGNARD REACTION OF DEHYDROFENCHONE WITH MAGNESIUM AND METHYL IODIDE. SYNTHESIS OF γ-LACTONE ACID.

Grignard reaction of dehydrofenchone with magnesium and methyl iodide: 2-exo-methyl-2-endo-dehydrofenchol (38) and 2-endo-methyl-2-exo-dehydrofenchol (39). In a flask equipped with a stirrer and a reflux condenser were placed 97,2 mg of magnesium turnings and 7,0 ml of abs. ether. 740 mg of methyl iodide was gradually added from a dropping funnel. When all magnesium had reacted, 400 mg of dehydrofenchone (25) dissolved in 5 ml of abs. ether was added. (The molar ratios of dehydrofenchone, magnesium and methyl iodide were 1:1,5:2). The mixture was boiled for 2 hours, whereupon a small sample of it was taken for the gas chromatography. The chromatogram showed that no dehydrofenchone was left. To the reaction mixture ca. 5 ml of ice-water saturated with ammonium chloride was added. The ether layer was separated and the aqueous solution was extracted twice with ether. The ethereal extracts were combined with the mother liquor, which was washed with water and dried with sodium sulphate. When the solvent was distilled off, 413 mg (94 % of theor.) of colourless oily liquid remained. $[\alpha]_D^{20}+18,72°$ (c=5, abs. ethanol). The formed alcohols were separated by preparative gas chromatography. This had to be performed three times in succession, on account of the difficulties in the separation of the isomers. In the chromatographic work a 10 m long (Ø 1/4″) column was used, which was

packed with 10 % Carbowax 20 M on Chromosorb W (80/100 mesh). The temperature was 130° and the carrier gas flow rate 35 ml N_2/min. The chromatography yielded colourless liquid compounds.

2-*exo*-methyl-2-*endo*-dehydrofenchol (38): yield 174 mg, $[\alpha]_D^{20}$+52,15° (c=5, abs. ethanol), n_D^{20}=1,4832. IR spectrum n:o 16, nmr spectrum n:o 2, mass spectrum n:o 2.

2-*endo*-methyl-2-*exo*-dehydrofenchol (39): yield 162 mg, $[\alpha]_D^{20}$—24,49° (c=5, abs. ethanol), n_D^{22}=1,4845. IR spectrum n:o 17, nmr spectrum n:o 3, mass spectrum n:o 3.

When on the basis of the specific rotations of the pure alcohols the composition corresponding to the specific rotation of the reaction product $[\alpha]_D^{20}$+18,72° is computed, the value 57:43 is obtained for the ratio of the components, which is the same as that obtained by analytical gas chromatography.

Hydrogenation of 2-exo-methyl-2-endo-dehydrofenchol (38): 2-exo-methyl-2-endo-fenchol (19). 70,0 mg of 2-*exo*-methyl-2-*endo*-dehydrofenchol was hydrogenated with hydrogen activated with palladium. In the hydrogenation abs. ethanol was used as solvent. The reaction was very rapid, as already in ca. two minutes 95 % of the theoretical amount of hydrogen was consumed. The total consumption was 98,8 % of the calculated amount. The obtained hydrogenation product was a solid white substance. $[\alpha]_D^{20}$+4,09° (c=2, abs. ethanol), mp. 65—66°. The values coincide with those for the alcohol obtained as main product (95 %) in the Grignard reaction of fenchone ($[\alpha]_D^{20}$+4,07°, mp. 65—66°), and furthermore the infrared spectra of these two substances prepared by different means were identical (IR spectra n:o 18 and n:o 19).

Hydrogenation of 2-endo-methyl-2-exo-dehydrofenchol (39): 2-endo-methyl-2-exo-fenchol (20). 70,0 mg of 2-*endo*-methyl-2-*exo*-dehydrofenchol was hydrogenated in the way described above. The total consumption of hydrogen was 98,5 % of the calculated amount. The hydrogenation product was a solid white substance. $[\alpha]_D^{20}$—30,3° (c=2, abs. ethanol), mp. 74—75°. The values agree with those of the alcohol obtained as by-product (5 %) in the Grignard reaction of fenchone ($[\alpha]_D^{20}$—30,7°, mp. 75,5—76,5°), and moreover the infrared spectra of these substances prepared by different ways were identical (IR spectra n:o 20 and n:o 21).

Oxidation of 2-exo-methyl-2-endo-dehydrofenchol (38) with potassium permanganate: 1,2,3,3-tetramethyl-c-2-hydroxy-cyclopentane-r-1,c-4-dicarboxylic acid (40). 93,0 mg of 2-*exo*-methyl-2-*endo*-dehydrofenchol, 0,6 ml of acetone, 37,2 mg of magnesium sulphate heptahydrate, and 1,9 ml of water were placed into a flask equipped with a magnetic stirrer and immersed in an ice-water bath. During ca. 3 hours 5,92 ml (100 % of theor.) of an aqueous solution of potassium permanganate (1 g $KMnO_4$/25 ml H_2O) was added to the mixture. In the beginning the permanganate was immediately decolourized as it was added. The reaction became considerably slower when ca. 75 % of the calculated amount of permanganate had been added. The formed manganese dioxide was filtered and washed several times with hot water. The wash solutions were combined with the mother liquor and the obtained solution was concentrated by vacuum distillation to ca. 2 ml. The solution was extracted with small quantities of ether, whereupon it was acidified with diluted hydrochloric acid and evaporated to dryness under vacuum. The solid residue was extracted several times with acetone. When the acetone solutions had been combined and the ɹuǝʌoɹ distilled off, 104,7 mg (81,2 % of theor.) of white crystalline hydroxy-dicarboxylic acid remained. Mp. 165,5—166,5°.

32,3 mg of the acid was dissolved in 10 ml of 0,05-n potassium hydroxide solution and the excess alkali was titrated with 0,05-n hydrochloric acid (phenolphthalein as indicator), 4,35 ml of was being consumed.

$C_{11}H_{18}O_5$ (230,26)	Calculated	C=57,38 %	H=7,88 %	E=115,1
	Found	C=57,22 %	H=7,95 %	E=114,3

IR spectrum n:o 29, mass spectrum n:o 6.

Pyrolysis of 1,2,3,3-tetramethyl-c-2-hydroxy-cyclopentane-r-1,c-4-dicarboxylic acid: γ-lactone acid (43). 50 mg of the above obtained hydroxy-dicarboxylic acid was heated to 168° for 2 hours (nitrogen atmosphere). The brown solid residue was grinded, washed with ether and sublimed in vacuo, whereat 27 mg of white crystalline γ-lactone acid was obtained. Mp. 193—195°. The infrared spectrum (n:o 32) of the compound was identical with that of the γ-lactone acid obtained by the acid hydrolysis of the acetoxy-dicarboxylic acid anhydride (47).

Reaction of 1,2,3,3-tetramethyl-c-2-hydroxy-cyclopentane-r-1,c-4-dicarboxylic acid with acetic anhydride: γ-lactone acid (43) and acetoxy-dicarboxylic acid anhydride (47). 20,2 mg of hydroxy-disarboxylic acid was dissolved in 0,5 ml of acetic anhydride. The reaction was allowed to proceed at room temperature for 50 hours, whereupon the acetic anhydride was distilled off under vacuum. The solid residue was dissolved in 80 ml of ether and the solution was extracted with a saturated sodium hydrogen carbonate solution. The ethereal solution was distilled to dryness and the solid residue (11,2 mg) was recrystallized from glacial acetic acid. The infrared spectrum (n:o 27) of the compound (mp. 169—170,5°) was identical with that of the acetoxy-dicarboxylic acid anhydride (47) (IR spectrum n:o 26) synthesized from 5,6-diketo-2-exo-methylfenchyl acetate (46).

The sodium hydrogen carbonate solution was acidified with diluted hydrochloric acid and distilled to dryness in vacuo. From the residue a small quantity of solid was obtained by extraction with acetone. After sublimation under vacuum this residue was identified on the basis of its infrared spectrum as γ-lactone acid (43).

Oxidation of 2-endo-methyl-2-exo-dehydrofenchol (39) with potassium permanganate: 1,2,3,3-tetramethyl-t-2-hydroxy-cyclopentane-r-1,c-4-dicarboxylic acid (41). Oxidation was performed in the same way as that of 2-*exo*-methyl-2-*endo*-dehydrofenchol (p. 59) using 46,0 mg of 2-*endo*-methyl-2-*exo*-dehydrofenchol, 0,4 ml of acetone, 18,4 mg of $MgSO_4 \cdot 7H_2O$ and 1,0 ml of water. The obtained oxidation product (37,2 mg) was a solid sticky substance. Attempts to purify it by crystallization and vacuum sublimation were unsuccesful. Melting interval 143—152°.

IR-spectrum n:o 33 mass spectrum n:o 8.

Lactonization experiments: (1) Hydroxy-dicarboxylic acid (41) was heated in a capillary tube for 2 hours at the temperature of 150—175°. The infrared spectrum run after heating did not show absorption characteristic of lactones.

(2) Hydroxy-dicarboxylic acid (41) was boiled for two hours with 2-n hydrochloric acid. After boiling the solution was distilled dry in vacuo. The infrared spectrum run on the residue was identical with that of the starting substance.

The infrared spetra

Spectrum n:o	Compound
1	α-Fenchyl acetate (liquid film)
2	β-Fenchyl acetate (liquid film)
3	5-Keto-α-fenchyl acetate (liquid film)
4	5-Keto-β-fenchyl acetate (liquid film)
5	5-Keto-α-fenchol (1,2 mg/150 mg KBr)
6	5-Keto-β-fenchol (liquid film)
7	5-Keto-α-fenchol-2-tetrahydropyranyl ether (liquid film)
8	5-Keto-β-fenchol-2-tetrahydropyranyl ether (liquid film)
9	5-Hydroxy-α-fenchol-2-tetrahydropyranyl ether (liquid film)
10	5-Hydroxy-β-fenchol-2-tetrahydropyranyl ether (liquid film)
11	Methyl xanthogenate of 5-hydroxy-α-fenchol-2-tetrahydropyranyl ether (liquid film)
12	Methyl xanthogenate of 5-hydroxy-β-fenchol-2-tetrahydropyranyl ether (liquid film)
13	Dehydrofenchone (liquid film)
14 and 15	Fenchone (liquid film)
16	2-*exo*-Methyl-2-*endo*-dehydrofenchol (liquid film)
17	2-*endo*-Methyl-2-*exo*-dehydrofenchol (liquid film)
18 and 19	2-*exo*-Methyl-2-*endo*-fenchol (10 % in CCl_4, 0,1 mm cell)
20 and 21	2-*endo*-Methyl-2-*exo*-fenchol (10 % in CCl_4, 0,1 mm cell)
22	2-*exo*-Methyl-2-*endo*-fenchyl acetate (liquid film)
23	5-Keto-2-*exo*-methyl-2-*endo*-fenchyl acetate (liquid film)
24	5,6-Diketo-2-*exo*-methyl-2-*endo*-fenchyl acetate (1,2 mg/150 mg KBr)
25	5,6-Diketo-2-*exo*-methyl-2-*endo*-fenchol (1,2 mg/150 mg KBr)
26 and 27	1,2,3,3-Tetramethyl-*c*-2-acetoxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid anhydride (2 mg/200 mg KBr)
28	1,2,3,3-Tetramethylcyclopentene-4-carboxylic acid (?) (liquid film)
29 and 30	1,2,3,3-Tetramethyl-*c*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid (1,3 mg/150 mg KBr)
31 and 32	γ-Lactone acid of 1,2,3,3-tetramethyl-*c*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid (1,2 mg/130 mg KBr)
33	1,2,3,3-Tetramethyl-*t*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid, crude product (1,2 mg/130 mg KBr)

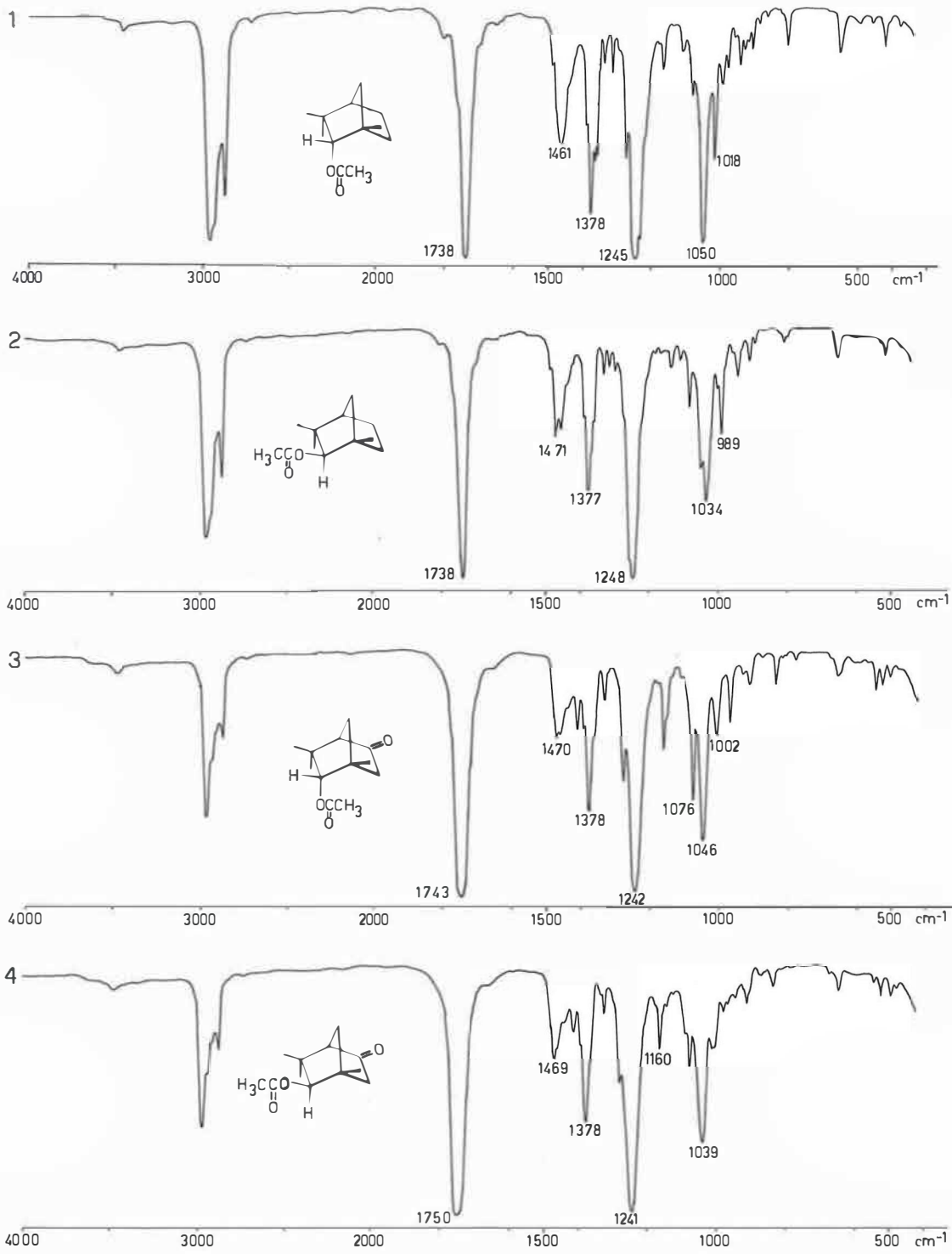
The nmr spectra

Spectrum n:o	Compound
1	Dehydrofenchone
2	2-*exo*-Methyl-2-*endo*-dehydrofenchol
3	2-*endo*-Methyl-2-*exo*-dehydrofenchol
4	1,2,3,3-Tetramethylcyclopentene-4-carboxylic acid (?)

The mass spectra

(electron energy 70 eV)

1	Dehydrofenchone
2	2-*exo*-Methyl-2-*endo*-dehydrofenchol
3	2-*endo*-Methyl-2-*exo*-dehydrofenchol
4	2-*exo*-Methyl-2-*endo*-fenchol
5	2-*endo*-Methyl-2-*exo*-fenchol
6	1,2,3,3-tetramethyl-*c*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid
7	γ-Lactone acid of 1,2,3,3-tetramethyl-*c*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid
8	1,2,3,3-Tetramethyl-*t*-2-hydroxy-cyclopentane-*r*-1,*c*-4-dicarboxylic acid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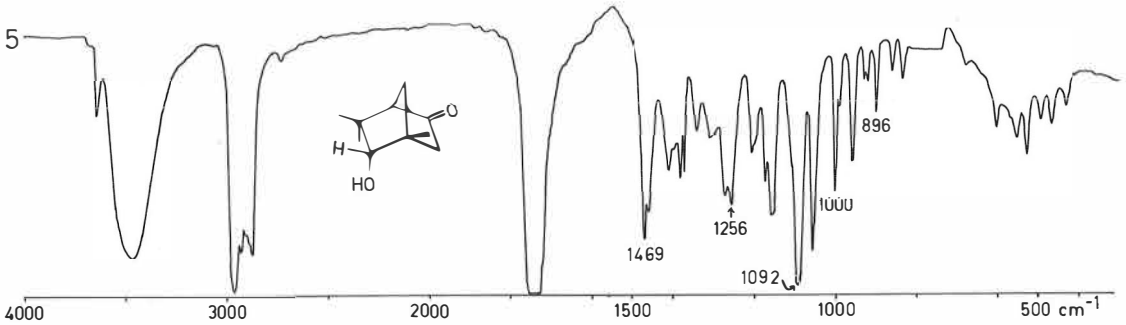
H
OCCH3
O
1738
1461
1378
1245
1050
1018
4000
3000
2000
1500
1000
500
cm-1
2
H3CCO
O
H
1738
1471
1377
1248
1034
989
4000
3000
2000
1500
1000
500
cm-1
3
O
H
OCCH3
O
1743
1470
1378
1242
1076
1046
1002
4000
3000
2000
1500
1000
500
cm-1
4
O
H3CCO
O
H
1750
1469
1378
1241
1160
1039
4000
3000
2000
1500
1000
500
cm-1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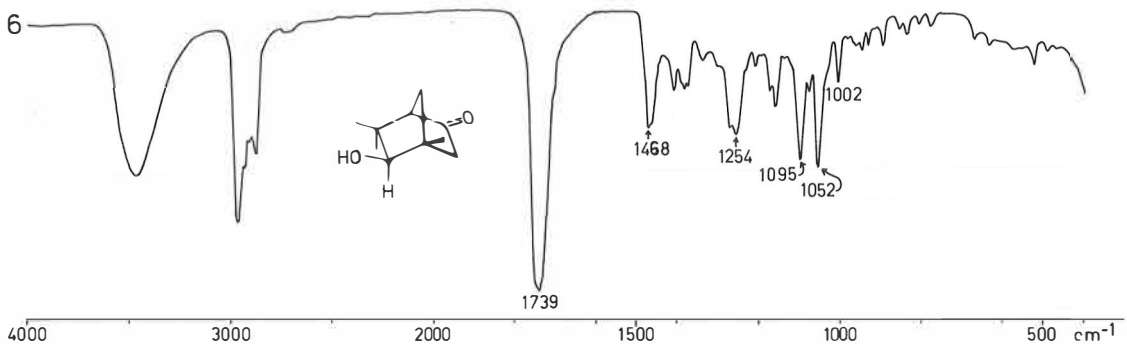
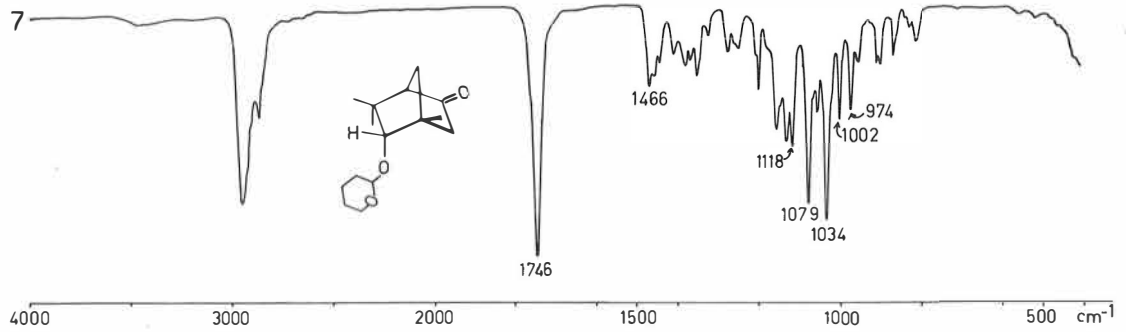
HO
H
O
1469
1256
1092
1000
896
4000
3000
2000
1500
1000
500 cm-1


6
HO
H
O
1739
1468
1254
1095
1052
1002
4000
3000
2000
1500
1000
500 cm-1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1746
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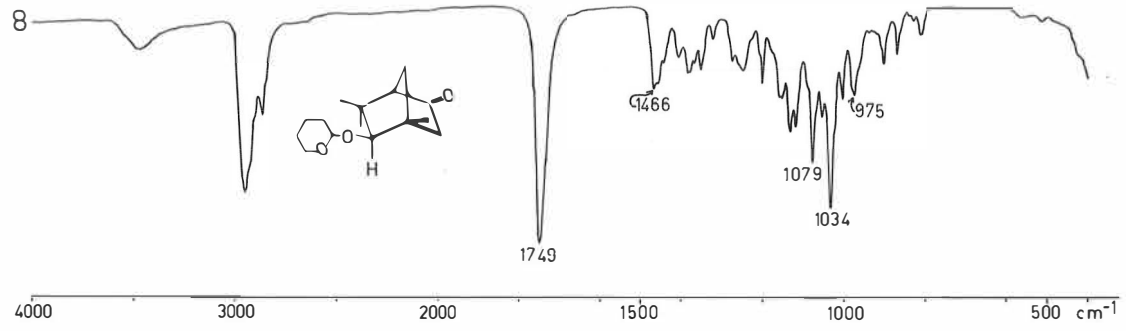
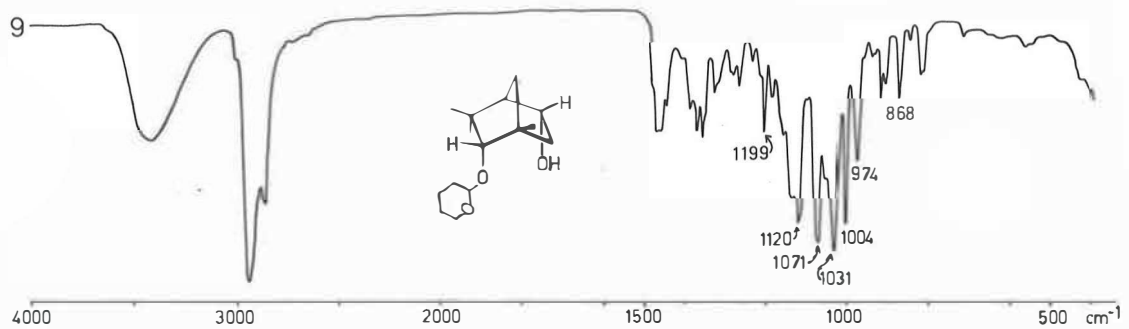
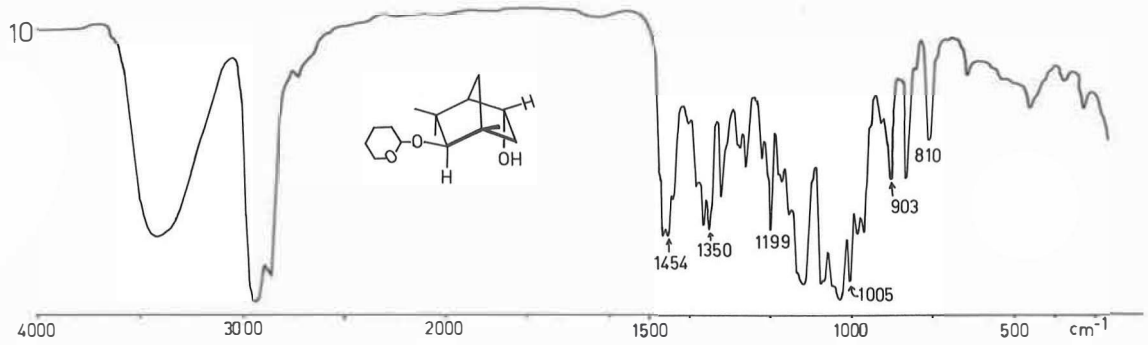
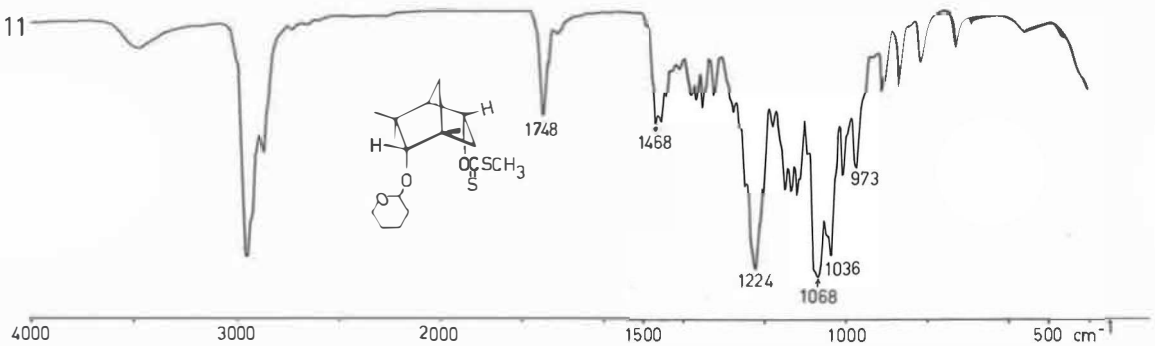
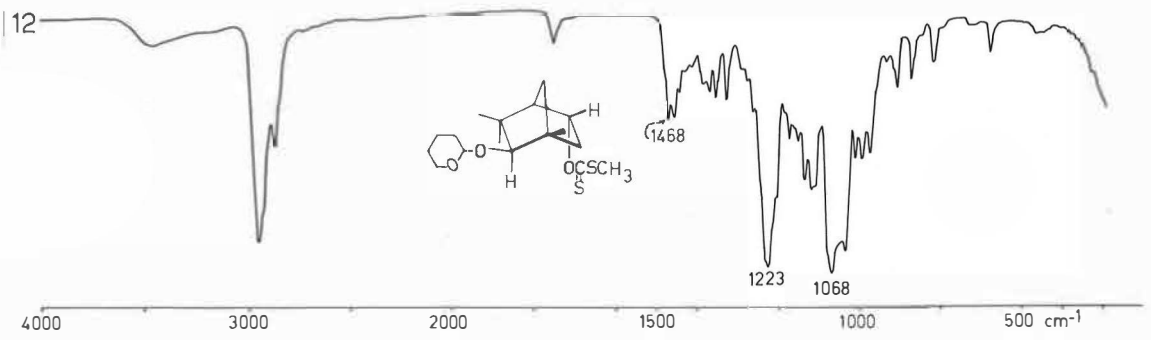
1079
1034
1002
974
4000
3000
2000
1500
1000
500 cm-1

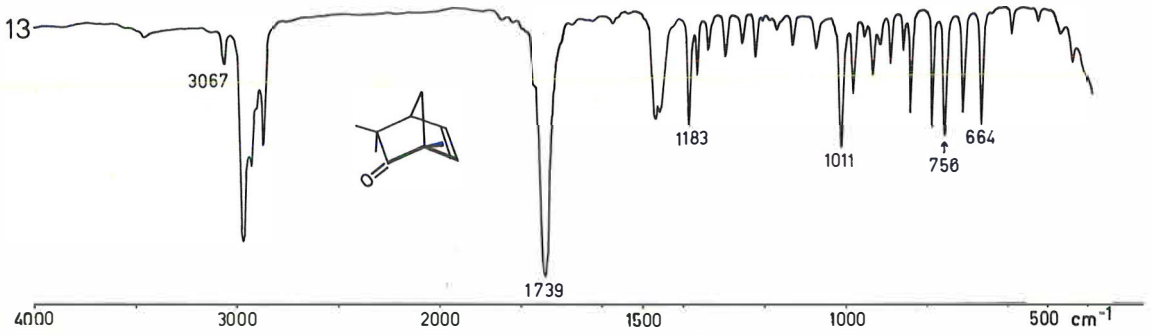

8
O
O
H
1749
1466
1079
1034
975
4000
3000
2000
1500
1000
500 cm-1


9
H
H
O
OH
868
1199
974
1120
1004
1071
1031
4000
3000
2000
1500
1000
500 cm⁻¹


10
O
H
OH
810
903
1454
1350
1199
1005
4000
3000
2000
1500
1000
500 cm⁻¹


11
H
H
O
OCSCH3
S
1748
1468
973
1224
1036
1068
4000
3000
2000
1500
1000
500 cm⁻¹


12
O
H
H
OCSCH3
S
1468
1223
1068
4000
3000
2000
1500
1000
500 cm⁻¹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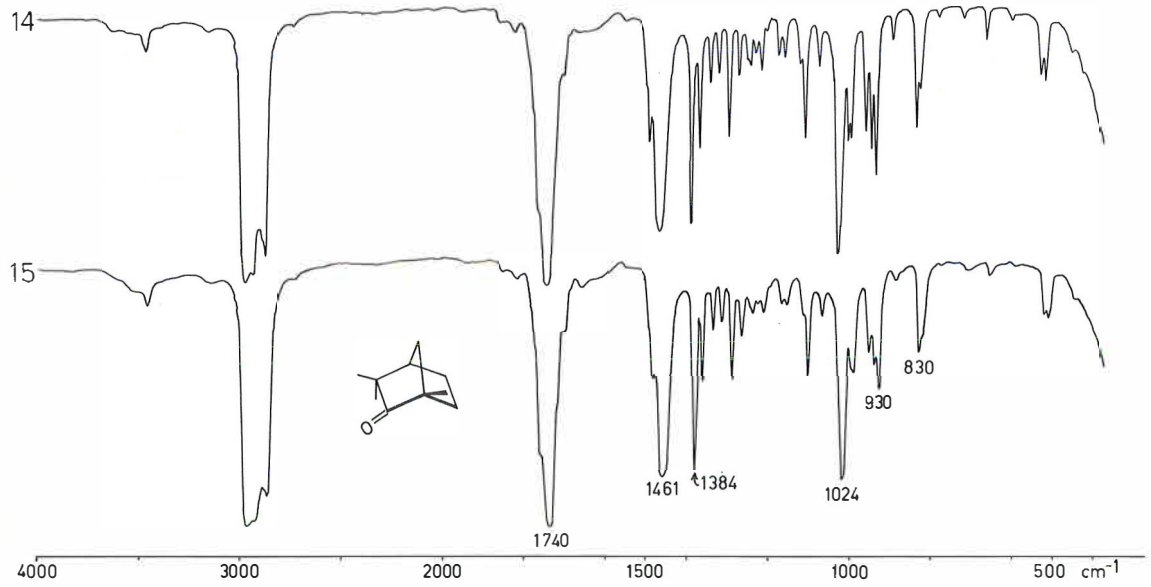
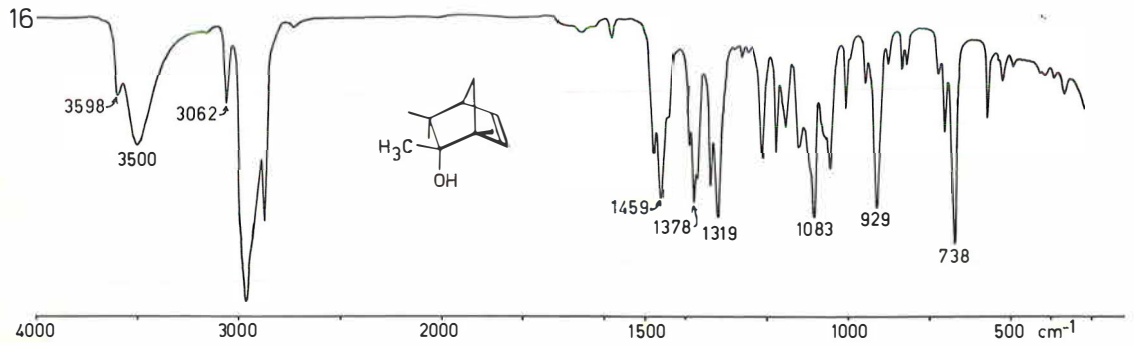
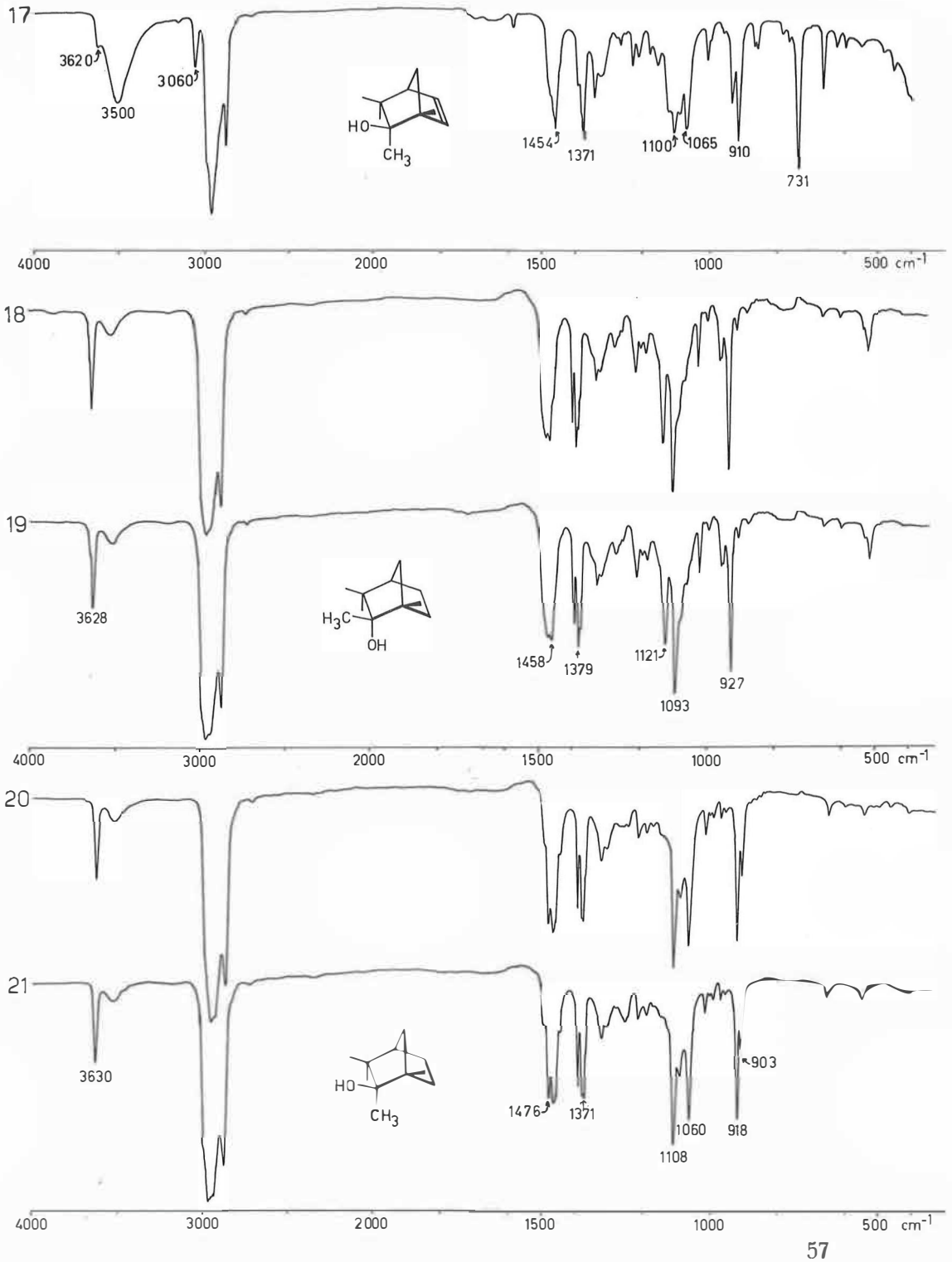
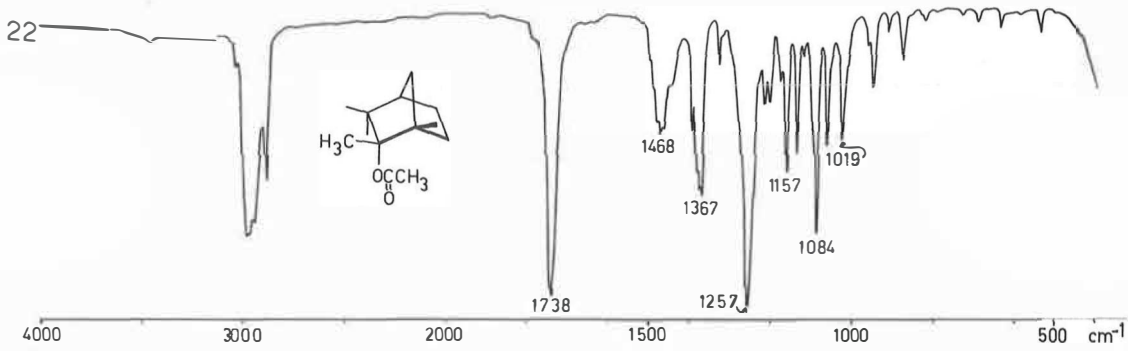
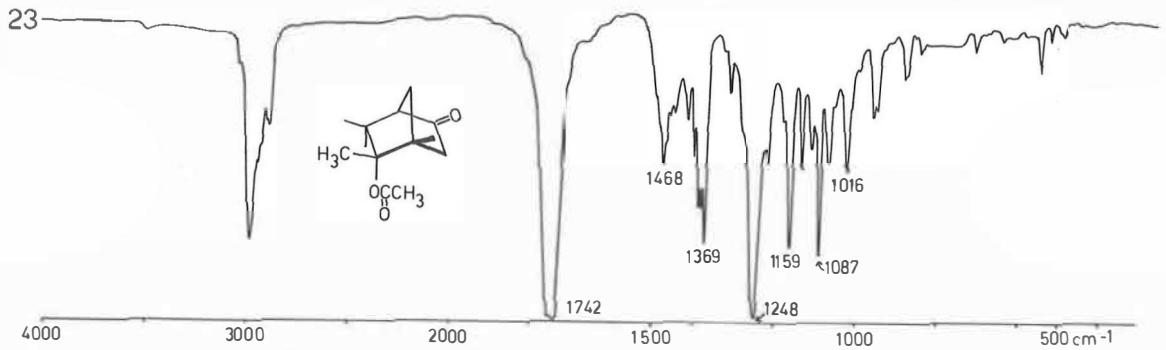
3067
1739
1183
1011
756
664
4000
3000
2000
1500
1000
500 cm-1


14
15
1740
1461
1384
1024
930
830
4000
3000
2000
1500
1000
500 cm-1


16
3598
3500
3062
H3C
OH
1459
1378
1319
1083
929
738
4000
3000
2000
1500
1000
500 cm-1


17
3620
3500
3060
HO
CH3
1454
1371
1100
1065
910
731
4000
3000
2000
1500
1000
500 cm-1
18
19
3628
H3C
OH
1458
1379
1121
1093
927
4000
3000
2000
1500
1000
500 cm-1
20
21
3630
HO
CH3
1476
1371
1108
1060
918
903
4000
3000
2000
1500
1000
500 cm-1


22
H3C
OCCH3
O
1738
1468
1367
1257
1157
1019
1084
4000
3000
2000
1500
1000
500 cm-1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H3C
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O
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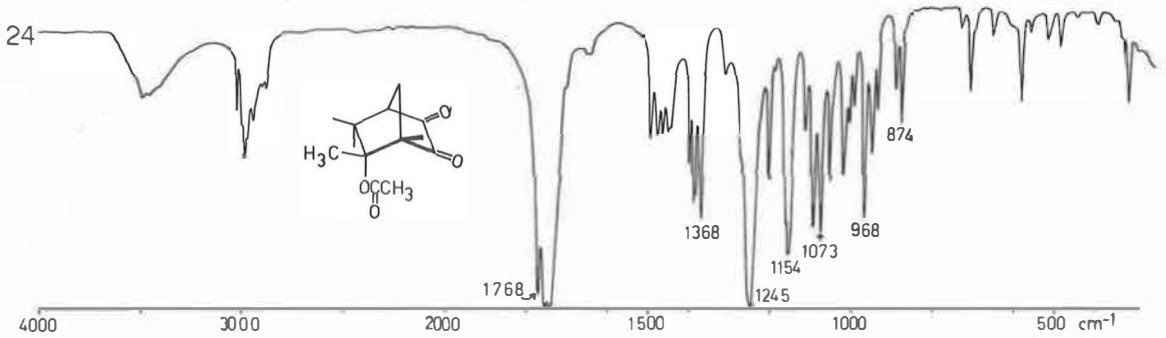
1248
1159
1087
1016
4000
3000
2000
1500
1000
500 cm-1


24
H3C
OCCH3
O
O
O
1768
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1245
1154
1073
968
874
4000
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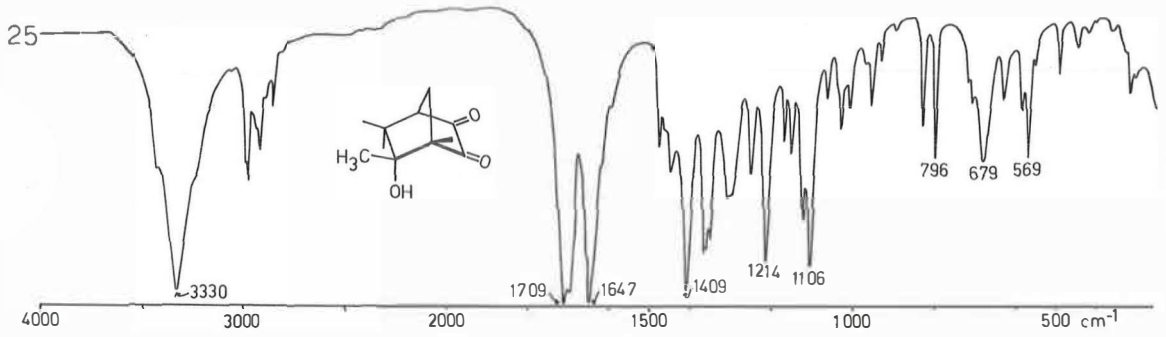
2000
1500
1000
500 cm-1


25
H3C
OH
O
O
3330
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1647
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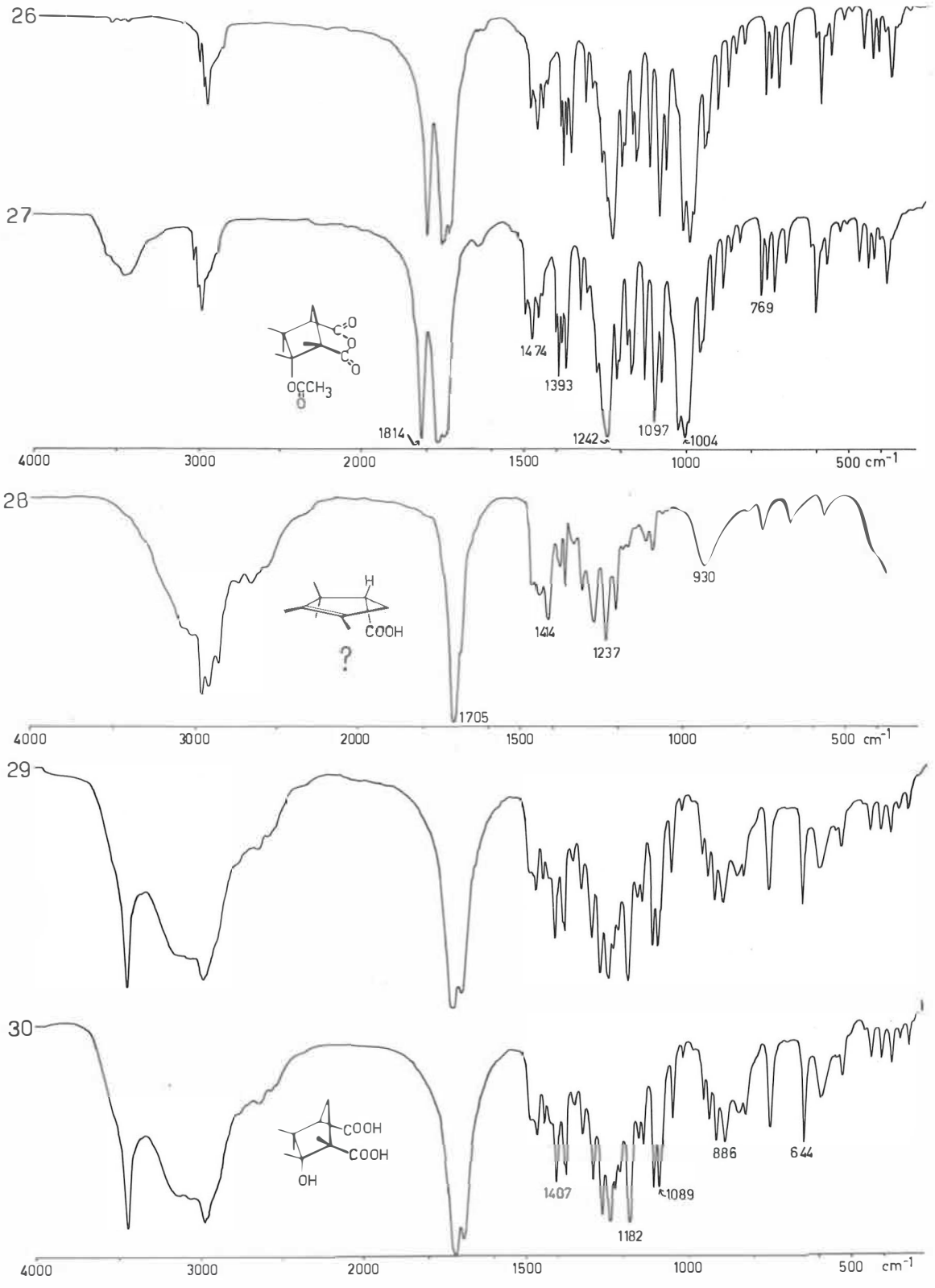
1214
1106
796
679
569
4000
3000
2000
1500
1000
500 cm-1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27
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O
1814
1474
1393
1242
1097
1004
769
4000
3000
2000
1500
1000
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28
H
COOH
?
1705
1414
1237
930
4000
3000
2000
1500
1000
500 cm-1
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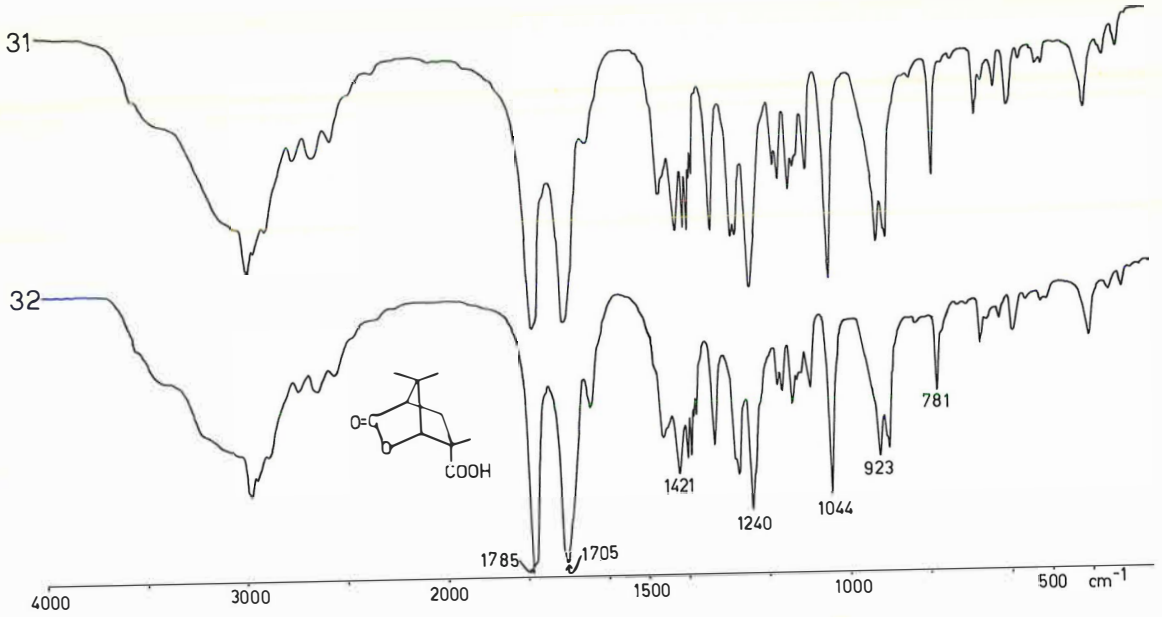
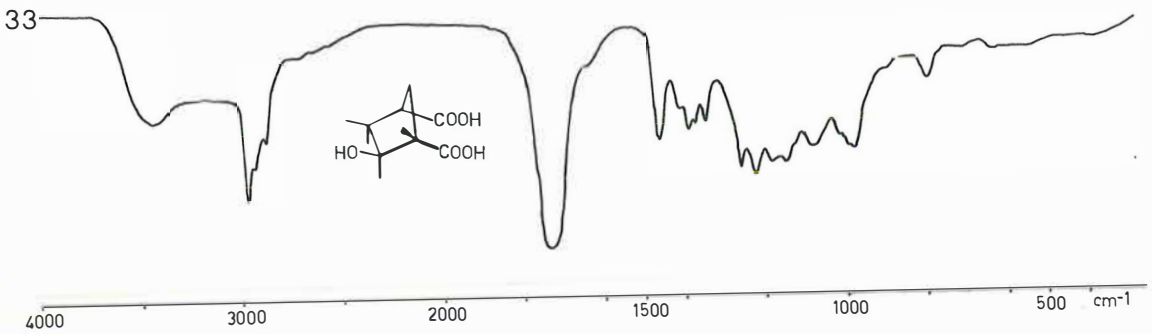
886
644
4000
3000
2000
1500
1000
500 cm-1


31
32
O=C
O
COOH
1785
1705
1421
1240
1044
923
781
4000
3000
2000
1500
1000
500
cm-1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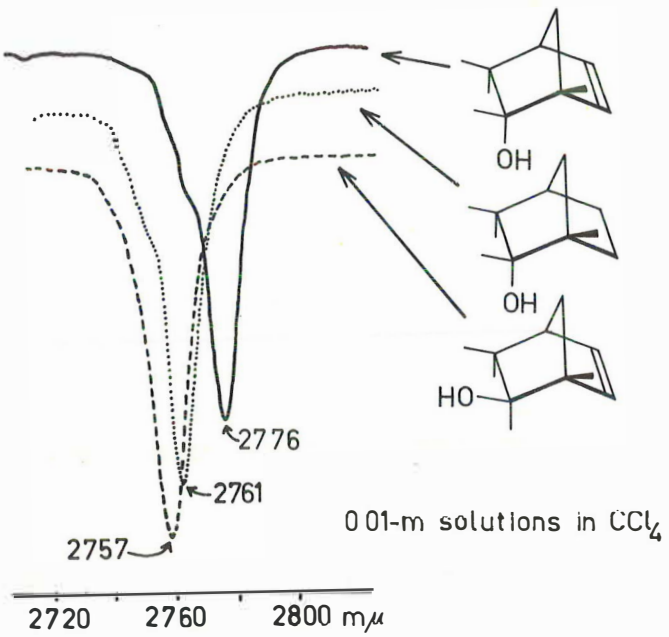
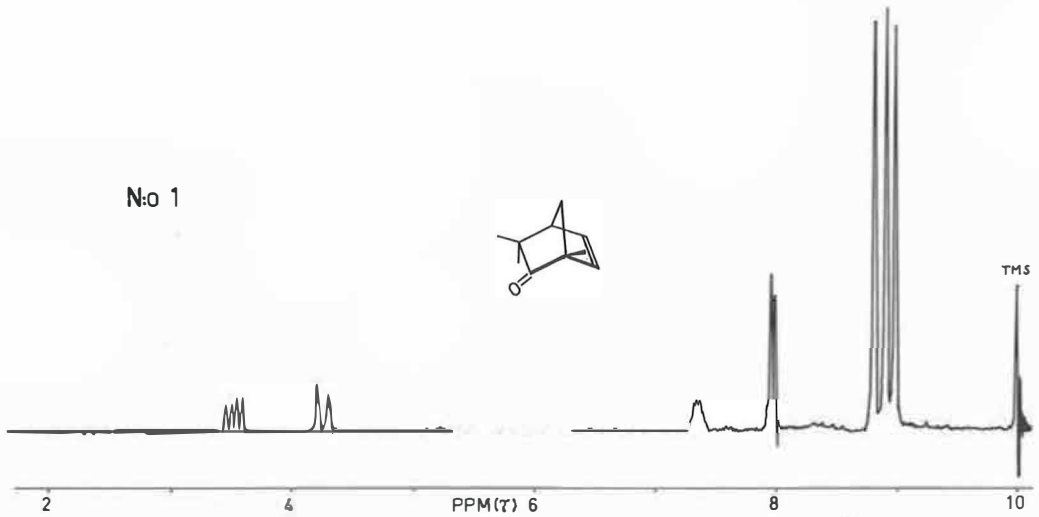
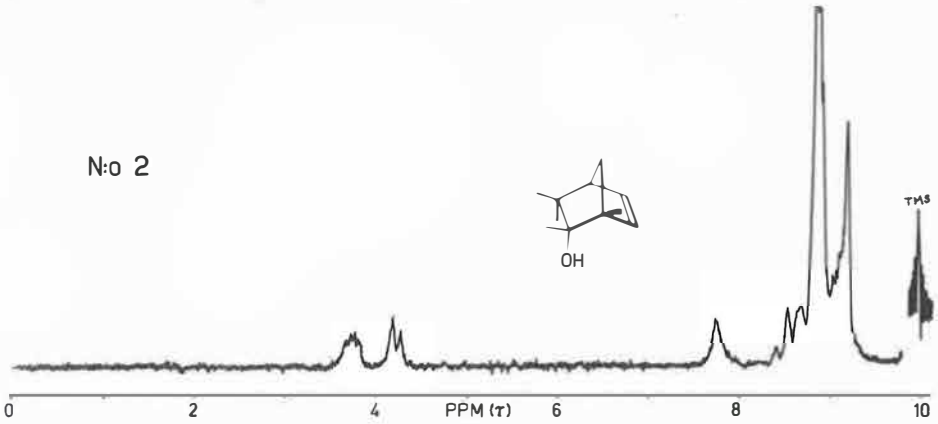
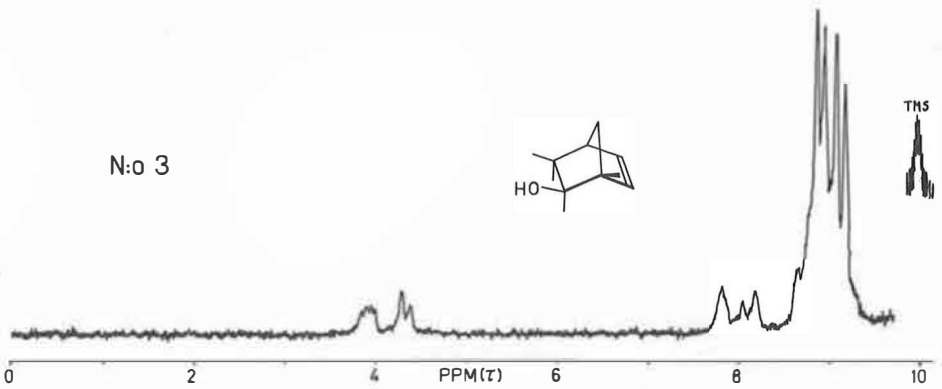
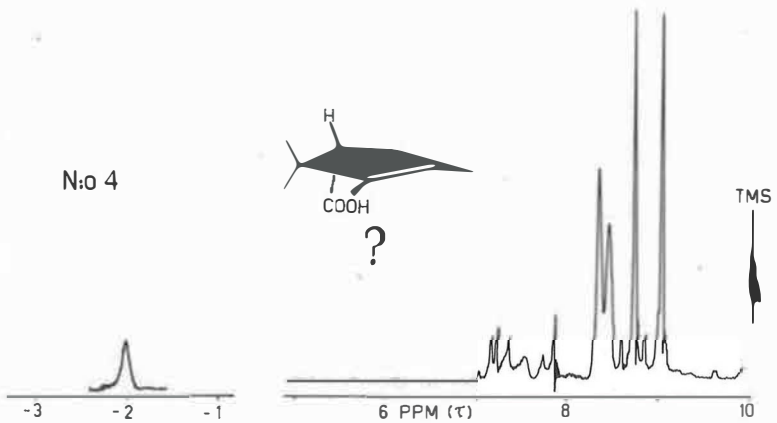
COOH
HO
COOH
4000
3000
2000
1500
1000
500
cm-1

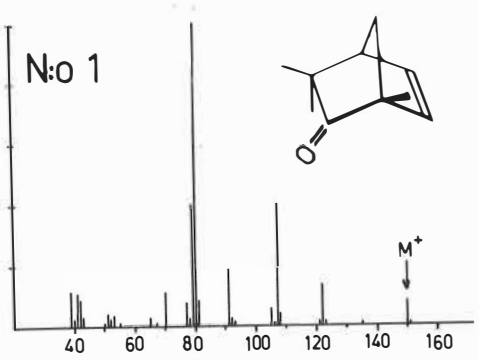

OH
OH
HO
2776
2761
2757
0 01-m solutions in CCl4
2720
2760
2800 mμ

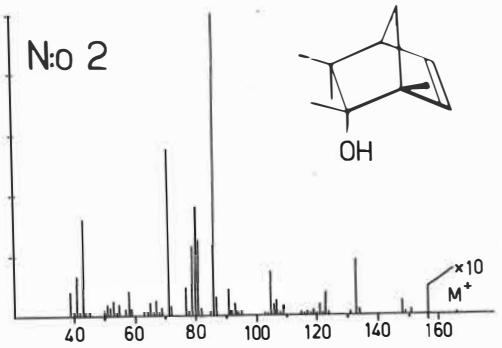

N:o 1
O
TMS
2
4
PPM(τ) 6
8
10

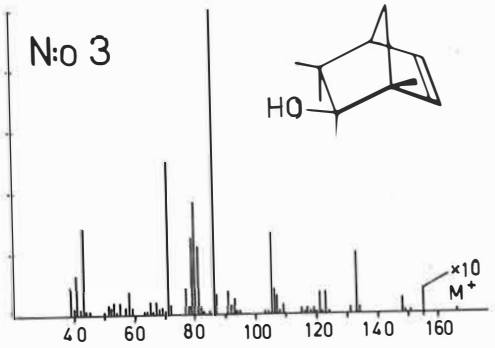

N:o 2
OH
TMS
0
2
4
PPM (τ)
6
8
10

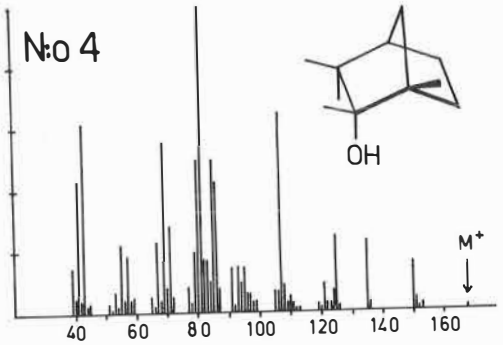

N:o 3
HO
TMS
0
2
4
PPM(τ)
6
8
10

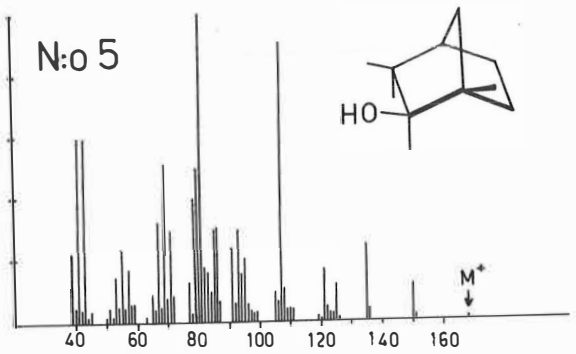

N:o 4
H
COOH
?
TMS
-3
-2
-1
6 PPM (τ)
8
10

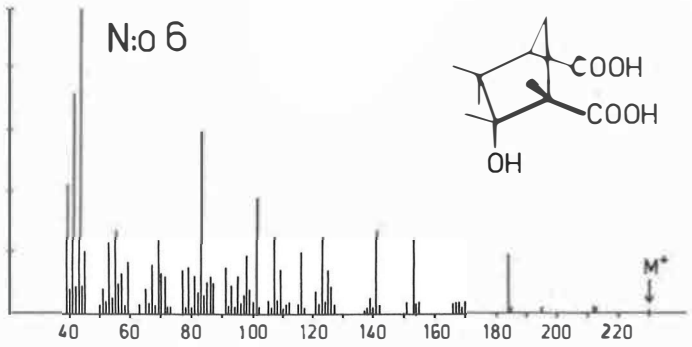

N:o 1
O
M+
40 60 80 100 120 140 160

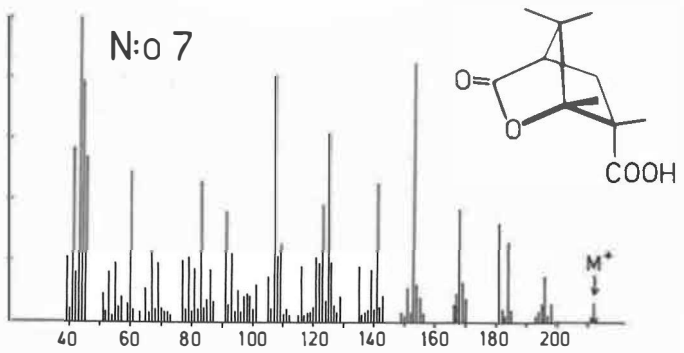

N:o 2
OH
×10
M+
40 60 80 100 120 140 160

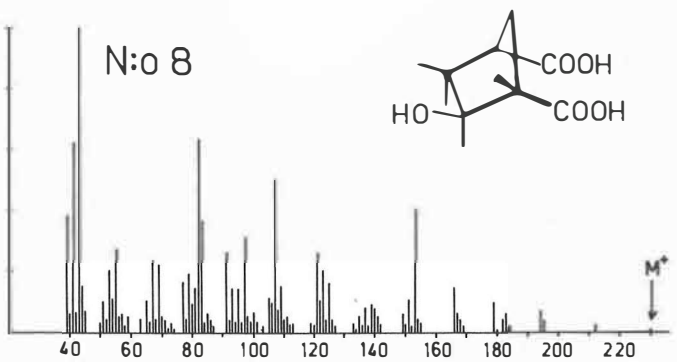

N:o 3
HO
×10
M+
40 60 80 100 120 140 160


N:o 4
OH
M+
40 60 80 100 120 140 160


N:o 5
HO
M+
40 60 80 100 120 140 160


N:o 6
COOH
COOH
OH
M+
40
60
80
100
120
140
160
180
200
220


N:o 7
O=
O
COOH
M+
40
60
80
100
120
140
160
180
200


N:o 8
COOH
HO
COOH
M+
40
60
80
100
120
140
160
180
200
220

SUMMARY

In the performed work the structures of the tertiary alcohols formed in the Grignard additions of fenchone and methylmagnesium iodide as well as of dehydrofenchone and methylmagnesium iodide have been investigated.

It has been shown by structural proof that the alcohol obtained as main product (95 % of the alcohol part) of the Grignard addition of fenchone is 2-*exo*-methyl-2-*endo*-fenchol. The by-product of the reaction (5 % of the alcohol part) is 2-*endo*-methyl-2-*exo*-fenchol. The obtained result is in agreement with the results of analogous investigations performed on other ketones of the bicyclo[2.2.1]heptane series and thus strengthtens the conception of steric factors in these compounds controlling the course of the addition reaction in question.

In the Grignard addition of optically active dehydrofenchone synthesized in connection with this work tertiary alcohol isomers are formed in the ratio 57:43. The main product is 2-*exo*-methyl-2-*endo*-dehydrofenchol and the by-product 2-*endo*-methyl-2-*exo*-dehydrofenchol. The structures of the compounds have been confirmed by spectrometric and chemical methods. Although the result deviates noticeably from the general stereochemical course of the Grignard additions of other ketones of the bicyclo[2.2.1]heptene series, it anyhow gives strong support to the significance of steric factors in this reaction.

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ERRATA

The observed errata are printed below in corrected form.

PAGE 15, line 5 under the figure:
Norcamphor [21–23, 27–29, ...]

PAGE 16, last line:
...a cyclic intermediate: [cf. 51–53]

PAGE 19, line 12:
...to ketofenchyl acetates. [cf. 68]

PAGE 30, Fig. A and B:
The direction of numbering should be reversed, cf. p. 10.

PAGE 31, line 6 from bottom:
...in diluted solutions (spectra on p. 60). In ...

PAGE 35, line 3 from bottom:
...acid anhydride (47). If ...

PAGE 36, line 1 under the figure:
...of acetoxy dicarboxylic acid anhydride in a ...

PAGE 48, line 8:
IR spectrum n:o 31, mass spectrum n:o 7.

PAGE 50, line 12 from bottom:
...of 2-*exo*-methyl-2-*endo*-dehydrofenchol (p. 49) using ...

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94. *delete*
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