Pure & Appl. Chem., Vol. 51, pp. 565-580.
Pergamon Press Ltd. 1979. Printed in Great Britain.

0033-4545/79/0301-0565 $02.00/0

SYNTHESIS OF CAROTENOID GLYCOSYLESTERS AND OTHER CAROTENOIDS

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Abstract:

The naturally occurring crocetin di(β-D-glucosyl)ester can be synthesised from crocetin diimidazolide or crocetin di-(1,2,4-triazolide) and β-D-glucose in pyridine in presence of a base. The application of this new method to other carboxylic acids (8'-apo-β-carotene-8'-oic acid, vitamin A acid, benzoic acid and stearic acid) and carbohydrates (galactose, lactose) shows that this new method, using unprotected carbohydrates and azolides proceeds with a high degree of regioselectivity and stereoselectivity and is of general importance.

The synthesis of the three chiral C_{30}-apocarotenoids β-citraurin, β-citraurol and β-citraurinene, isolated from orange peel, was carried out with (3R)-3-hydroxy-β-ionone as starting material. Furthermore, C_{30}-apocarotenoids with one methyl group shifted by one carbon atom (= diapocarotenoids) were prepared as model compounds.

According to the scheme $C_{10} + C_{20} + C_{10}$, starting with trans-citral via geraniol epoxide, the corresponding C_{15}-epoxy Wittig salt and crocetin dialdehyde 1,2-epoxy-lycopene, 1,2,1',2'-di-epoxy-lycopene and a 1,2-epoxy-C_{30}-apocarotinal were synthesised.

INTRODUCTION

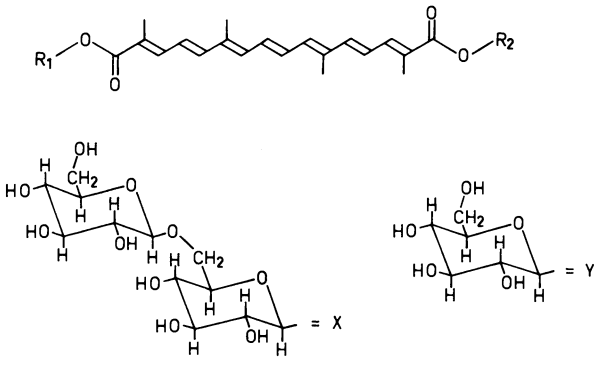
An ever increasing number of carotenoids has been isolated from natural sources in the past few years. Furthermore, the absolute configuration of some chiral carotenoids has been determined. The great importance of these polyenes as provitamin A and the wide variety of natural carotenoids has led to intense efforts towards the synthesis of these pigments especially the chiral compounds.

The following paper is a contribution to the problems in carotenoid synthesis.

SYNTHESIS OF CAROTENOID GLYCOSYLESTERS

On the occasion of the Fourth International Symposium on Carotenoids, we reported the isolation of four new glycosyl-esters of crocetin from saffron (Crocus sativus) (1,2,3). Besides crocin (I) which is the major pigment in saffron, we isolated the diglucosyl ester (II)(di(β-D-glucosyl)8,8'-diapocarotene-8,8'-dioate), the diester in which crocetin is esterified with a molecule each of D-glucose and D-gentiobiose (III) (β-D-gentiobiosyl β-D-glucosyl 8,8'-diapocarotene-8,8'-dioate) and the two monoesters with D-glucose (IV) (β-D-glucosyl hydrogen 8,8'-diapocarotene-8,8'-dioate) and with D-gentiobiose (V) (β-D-gentiobiosyl hydrogen 8,8'-diapocarotene-8,8'-dioate). (Fig. 1). The

PMR-spectra of the different compounds indicated the β-D-configuration of the carbohydrates.



	R_1	R_2
I	X	X
II	Y	Y
III	X	Y
IV	Y	−H
V	X	−H

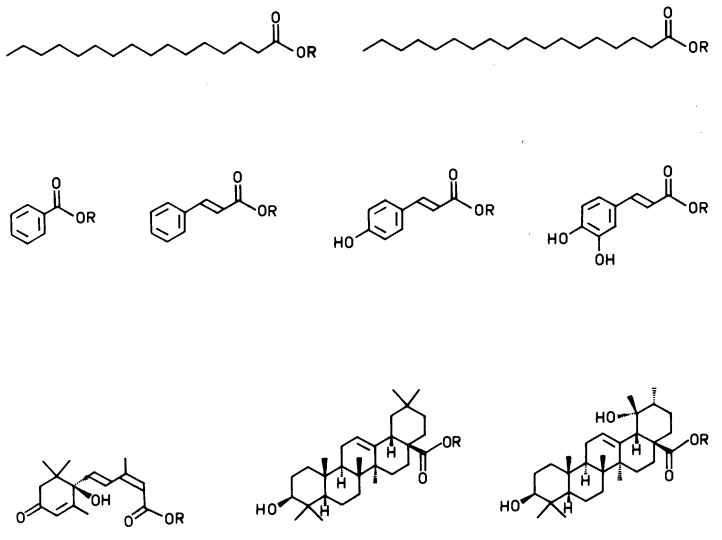
Fig. 1

Recently, Dinghra et al. (4,5) isolated the monogentiobiosyl ester of crocetin (V) as major component from Nycanthes arbortristis, a small tree with rough leaves and sweet-scented flowers. As minor carotenoids, crocin (I) and the diester with D-glucose and D-gentiobiose (III) were observed.

At that time, the question remained open as to whether these minor compounds are formed during the drying process. In the meantime, we have shown through an investigation with fresh saffron that was carried out in Mund (Canton Wallis), the only place where saffron is cultivated in Switzerland, that these minor glycosylesters are natural products (6).

Investigations directed towards the synthesis of crocin and the diglucosylester of crocetin (II) were already carried out by Karrer (7) and Kuhn (8). Through the reaction of α-acetobromoglucose and α-acetobromogentiobiose with crocetin, the peracetylated derivatives of the diglucosylester and of crocin were obtained. Subsequent attempts to remove the acetyl groups without cleaving the bond between the carbohydrate and crocetin were not successful.

The synthesis of compounds in which the carbohydrate is esterified at C(1) with a carboxylic acid is of general interest, as these compounds are numerous and widespread in nature. As aglycone fatty acids (palmitic and stearic acid (9)), benzoic acid and its hydroxylated derivatives (10,11), cinnamic acid (12) and its hydroxylated derivatives such as caffeic and coumaric acid (13), abscisic acid (14) and especially the pentacyclic triterpenoid acids from the oleanane and ursane series (15,16) have to be mentioned. (Fig. 2).



R = Glycosyl

Fig. 2

For the synthesis of these compounds, two different types of reactions are described in the literature. In both methods, the hydroxyl groups at all positions except at the anomeric carbon atom are protected in order to obtain esterification exclusively at C(1).

In one method, a nucleophilic attack of the carboxylate anion at the anomeric carbon atom of the carbohydrate which is activated at C(1) by a suitable leaving group takes place. The Koenigs-Knorr-type reaction (8) belongs to this group, using the aceto-bromocompound of the carbohydrate and the silver salt of the carboxylic acid.

The other type of reaction involves a nucleophilic attack of the oxygen atom of the hemiacetal hydroxyl group at the carboxylic carbon atom of the carboxylic acid or its derivative.

To this group belongs the AAE-method (accelerated active ester) using pentachlorophenyl- or p-nitrophenyl-ester and imidazole and the DCC-method (dicyclohexylcarbo-diimide) where DCC and imidazole are employed. Both methods have been successfully used for the synthesis of glycosylesters of aminoacids (17). Acid chlorides have also been used for the synthesis of glycosylesters.

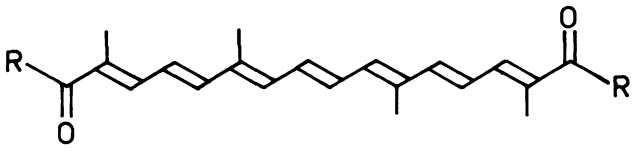
Although the above-mentioned reactions were applied with success to the synthesis of different naturally occurring glycosylesters, they all have one major disadvantage. The introduction and especially the specific removal of the protecting groups of the carbohydrate without cleaving the glycosylester bond very often proves to be difficult and therefore the overall yield of the reaction drops considerably.

With regard to the synthesis of the isolated glycosylesters of crocetin, we prepared different reactive derivatives of the dicarboxylic acid. (Fig. 3).

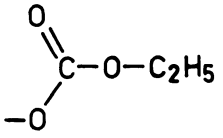
The crocetin dichloride (VI) was prepared by reaction of crocetin with phosphorus trichloride in tetrahydrofurane at a temperature of 50°C. After a reaction time of 2 1/2 hours, the crystalline dichloride was isolated in 85 % yield. The bathochromic shift of the absorption maxima of the dichloride of 25 - 30 nm compared to crocetin is consistent with the values in the vitamin A series (18).

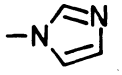
Since carboxylic acid anhydrides are often used in peptide synthesis, an analogous compound of crocetin was prepared. Treatment of crocetin with ethyl chloroformate ($ClCOOC_2H_5$) in tetrahydrofurane and triethylamine gave the mixed dianhydride (VII) of crocetin in crystalline form in 95 % yield.

The crocetin diimidazolide (VIII) and the crocetin di(1,2,4-triazolide) (IX) were prepared in yields between 90 and 95 % by the reaction of crocetin with N,N'-carbonyldiimidazole and N,N'-carbonyldi-(1,2,4-triazole) respectively in dimethylformamide as solvent.



VI R = —Cl

VII R = 

VIII R = 

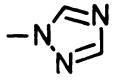
IX R = 

Fig. 3

In order to avoid the difficulties at the introduction and removal of the protecting group of the carbohydrate, the reactivity of the different crocetin derivatives with β-D-glucose was investigated in various solvents. The reaction of the dichloride and the dianhydride were not suitable for the synthesis of the diglucosylester of crocetin. At low temperature (- 16°C) no reaction occurred, whereas at room temperature up to ten different reaction products could be observed.

However, the synthesis of the desired crocetin-diglucosyl-ester was achieved in a very simple and elegant way through the reaction of β-D-glucose with crocetin-diimidazolide or crocetin-di-(1,2,4-triazolide) in pyridine as solvent. As catalyst, sodium hydride, sodium imidazolide or metallic sodium could be used. (Fig. 4).

In a typical experiment (19), the crocetin diazolide, a twofold molar excess of β-D-glucose and the sodium hydride were added to dry pyridine and stirred at room temperature. After three hours, the product was worked up by partitioning between butanol and phosphate buffer pH 7, washing the butanol with water and then

partitioning between 80 % ethanol and petrol ether. The crocetin diglucosylester was crystallized afterwards from 80 % ethanol in 70 % yield.

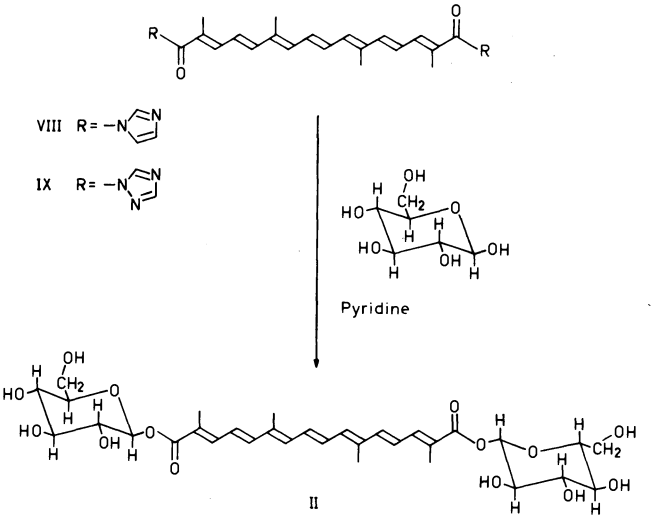


Fig. 4

Comparison of the spectroscopic data of the synthesised product with those of the isolated compound and those of the peracetylated derivative that was prepared by the method of Kuhn shows complete identity.

In the PMR-spectra, the triplet of the hydroxyl proton of the primary hydroxyl group at C(6) can be observed at 4.66 ppm and the doublet at 5.41 ppm with a coupling constant of J≈ 8 Hz indicated the β-D-configuration. (Fig. 5). Thus under the described experimental conditions the esterification took place exclusively at the anomeric carbon atom and furthermore produced only the β-anomer.

The next step was the investigation of the method with other polyene carboxylic acids (20). For these experiments, we chose 8'-apo-β-carotene-8'-oic acid (X) (C_{30}-acid) and vitamin A acid (XI). For both compounds the desired glucosylesters were synthesised with the imidazolides as well as with triazolides. (Fig. 6).

The reaction of the C_{30}-triazolide with β-D-glucose gave exclusively the β-D-glucosylester in 84 % yield, whereas under the same conditions, vitamin A glucosylester was isolated in 62 % yield.

The glycosylation can also be carried out as a one-pot-reaction without isolation of the azolides. The acid and the N,N'-carbonyl diazolide were dissolved in pyridine and stirred at room temperature for one hour. Afterwards, the β-D-glucose was added and after a total reaction time of three hours the product was worked up. Under these conditions, the C_{30}-glucosylester was synthesised via the triazolide in up to 60 % yield.

The application of the reaction to aromatic and saturated carboxylic acids and other carbohydrates showed the general importance of the method. The esterification of D-glucose with benzoic acid as well as with stearic acid furnished the glucosylesters at C(1) of the carbohydrate as mixture of the α- and β-anomers. The

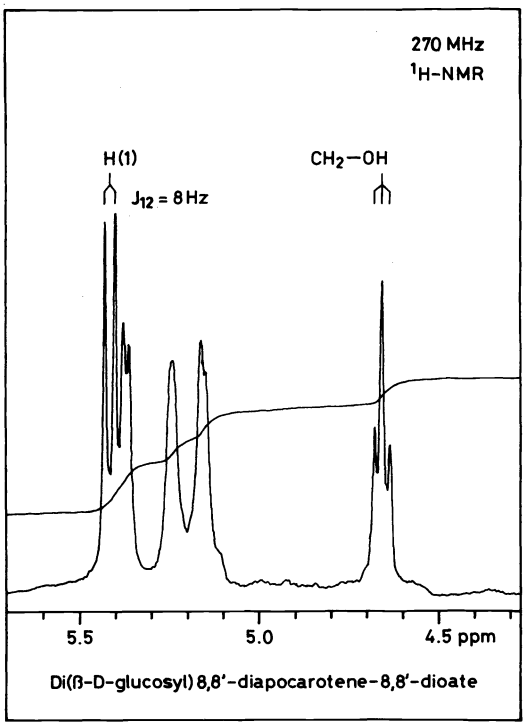


Fig. 5

reactions of the C_{30}-acid with D-galactose and lactose showed that the method proceeds with a high degree of regioselectivity, also in these examples.

Our investigations have shown that through the reactions of azolides with unprotected carbohydrates the glycosylesters at the anomeric carbon atom of the carbohydrate can be synthesised in a very simple way, whereby the high degree of regioselectivity and stereoselectivity are noteworthy.

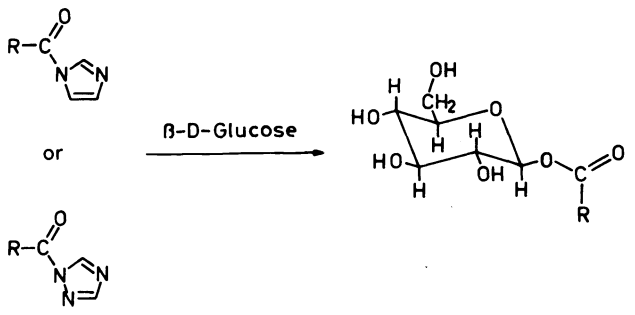
The chemistry of the azolides such as pyrazolides, imidazolides, 1,2,4- and 1,2,3-triazolides and especially their use for the synthesis of peptides and esters have been thoroughly investigated by Staab (21), but so far the method has not been applied to the glycosylation of carboxylic acids.

Furthermore as far as we know this is the first time that unprotected carbohydrates have been used for the selective synthesis of glycosylesters at the anomeric carbon atom. Bearing in mind the difficulties in the introduction and removal of the protecting groups, this represents the major advantage in this method. The expected higher acidity of the anomeric hydroxyl group compared with the other hydroxyl groups of the carbohydrate seems to be responsible for this selectivity.

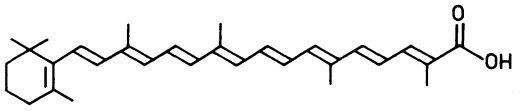
In the AAE- and the DCC-method, which both also use imidazole, the question arises whether the imidazolides are formed as intermediates.

Three further advantages of the method should be mentioned:

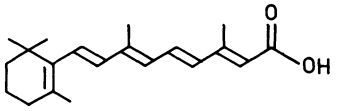
- The azolides which are used in the synthesis can be prepared either from the acid chloride or from the acid in very high yields. In our investigations, the azolides were always formed in yields between 80 to 95 %.



R–COOH:



8'-Apo-ß-carotene-8'-oic acid X (C_{30}-acid)



Vitamin A acid XI

Fig. 6

- The mild conditions during the glycosylation makes the reactions also suitable for relatively labile compounds.
- The possibility of recycling the azolides also permit reactions on a larger scale.

The ratio of the α- to ß-anomer can be influenced by changing the reaction conditions. Preliminary experiments with N,N'-dimethylformamide as a solvent have shown that the α-anomer of the crocetin di(D-glucosylester) is formed in about 70 % yield.

The expected enhanced reactivity of the triazolides compared with the imidazolides gave better yields and fewer by-products. The question arises whether the even more reactive tetrazolides can also be used for this synthesis.

It seems to us that the method is of general importance in carbohydrate chemistry and once again research in the field of carotenoid chemistry leads to methods of general interest.

SYNTHESIS OF CITRUS CAROTENOIDS AND RELATED COMPOUNDS

The bright colours of citrus fruits ranging from yellow to orange and red are due primarily to carotenoids. In the literature, over 100 different carotenoids isolated from citrus fruits are reported. However, the question remains open whether all these compounds are really natural and not formed during isolation. Furthermore, in some cases, the determination of structure raises some doubts because not all of the modern spectroscopic methods were applied.

The occurrence of C_{30}-apocarotenoids as 8'-apocarotinal (8'-apo-β-carotene-8'-al XII), β-citraurin (3-hydroxy-8'-apo-β-carotene-8'-al XIII), β-citraurol (8'-apo-β-carotene-3,8'-diol XIV) (22) and β-citraurinene (8'-apo-β-carotene-3-ol XV) (23) is characteristic for the pigment composition in orange peel. (Fig. 7).

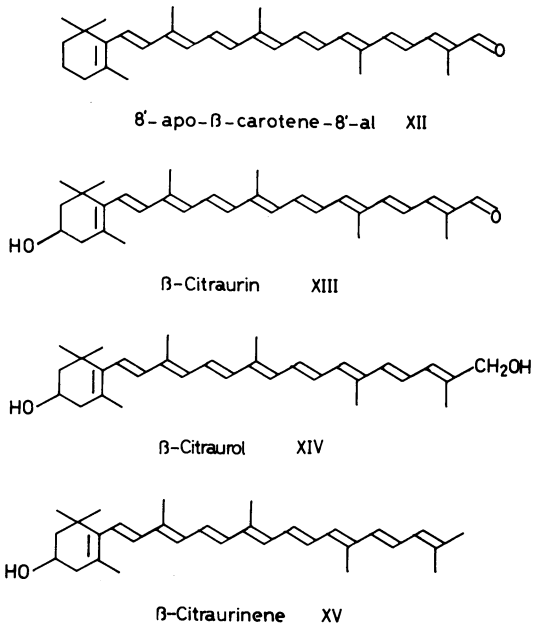


Fig. 7

Investigations of the biosynthesis of these C_{30}-carotenoids were so far not carried out. It has been proposed that these compounds are degradation products of zeaxanthin (β,β-carotene-3,3'-diol) (24).

In principle, two different pathways for the biosynthesis of C_{30}-carotenoids are possible. (Fig. 8).

- The formation of these C_{30}-carotenoids can proceed through degradation of a C_{10}-fragment from one side of a C_{40}-carotenoid or by the reaction of a C_{20}- and a C_{10}-compound, leading in both cases to apo-carotenoids.
- Another possibility is the degradation of two C_5-fragments from both ends of a C_{40}-molecule or the biosynthesis via squalene as was shown for the biosynthesis of the carotenoids in Streptococcus faecium (25), followed by dehydration and cyclization. Both sequences lead to diapocarotenoids.

The two possible pathways - the asymmetric degradation or synthesis on the one hand and the symmetric degradation or

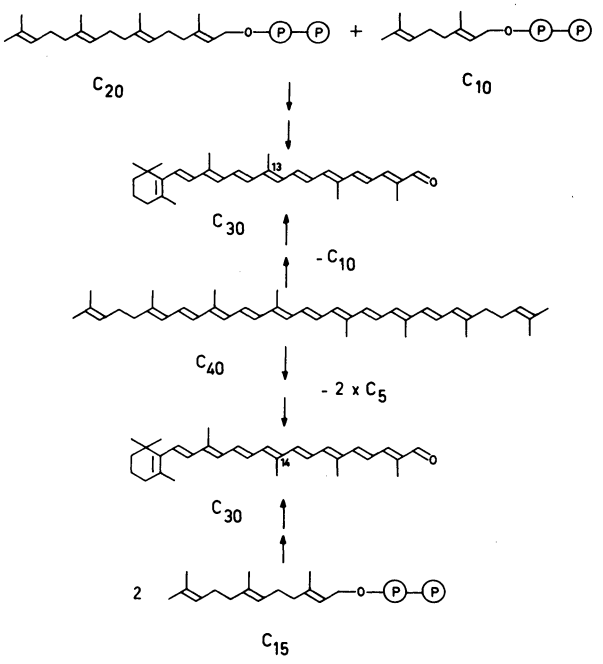


Fig. 8

synthesis lead to two different compounds. They only differ in the position of one methyl group. Whereas in the apo-carotenoid (XII) the methyl group is at the C(13)-position, it is shifted in the diapocarotenoid (XVI) by one carbon atom. * (Fig. 9).

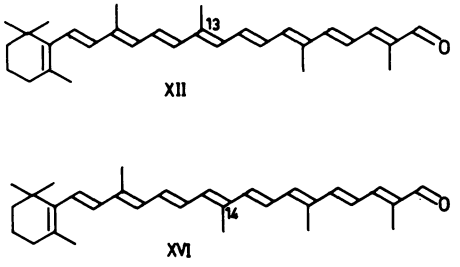


Fig. 9

A literature search shows that the data, especially the NMR-data, do not permit a definite structure elucidation.

In order to get characteristical spectroscopic data, 8'-apo-carotinal with the methyl group in position 14 (XVI) was synthesised and compared with the 8'-apocarotinal (XII) and the natural product.

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* For the sake of clearness, this position will be named as position C(14) in contrast to carotenoid nomenclature.

As starting products for the synthesis, the β-ionylidenacetaldehyde (XVII) as C_{15}-end group and the C_{10}-ester aldehyde (ethyl 3,7-dimethyl-8-oxo-2,4,6 octatrienoate XVIII) were used and the synthesis carried out according to the general scheme C_{15} + (C_{10} + C_2 + C_3) = C_{30}. (Fig. 10).

The C_{10}-ester aldehyde was converted to the ester acetal and through an enol ether condensation transferred to the C_{12}-ester aldehyde (ethyl 3,7-dimethyl-10-oxo-2,4,6,8-decatetraenoate XIX) in 95 % yield.

The enol ether condensation of the C_{12}-ester acetal with ethyl propenyl ether produced the C_{15}-ester aldehyde (ethyl 3,7,11-trimethyl-12-oxo-2,4,6,8,10-dodecapentaeonate XX).

Treatment of the C_{15}-ester acetal with diisobutylaluminium hydride and afterwards with p-toluene sulfonic acid gave the C_{15}-hydroxy-aldehyde (12-hydroxy-2,6,10-trimethyl-2,4,6,8,10-dodecapentaenal XXI).

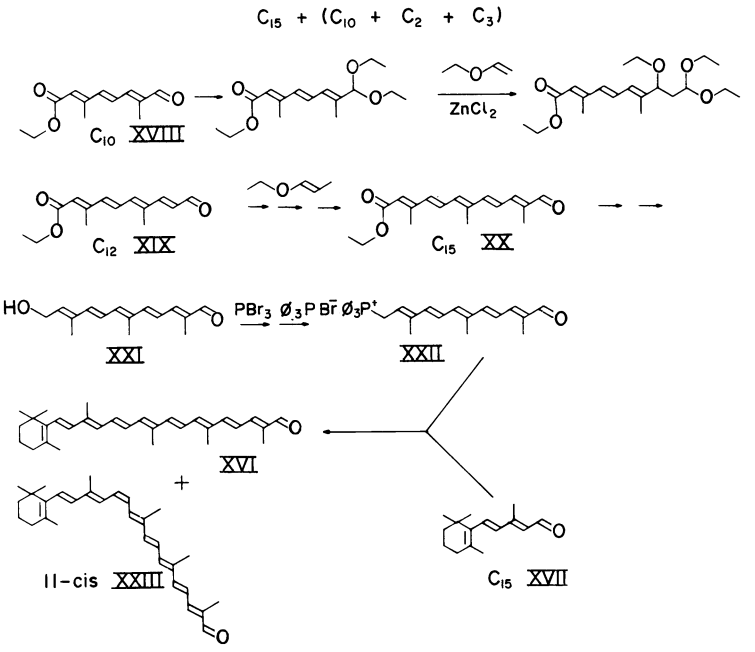

Fig. 10

The preparation of the Wittig salt (XXII) was achieved in 40 % yield by bromination with phosphorus tribromide followed by treatment with triphenylphosphine.

The Wittig salt was transformed to the corresponding acetal and the reaction of the latter with β-ionylidenacetaldehyde (XVII) gave the C_{30}-compound as a mixture of the all-trans- (XVI) and 11-cis-isomers (XIII). Subsequent column chromatography yielded the two isomers in crystalline form.

The comparison of the 8'-apocarotinal (XII) with the synthesized isomer (XVI) gave the following results:

As expected, the separation of the two compounds with TLC proves to be very difficult, but a good separation could readily be obtained by HPLC. No significant differences were observed in the electronic spectrum. The mass spectra, however, showed characteristical differences especially in the ratio of the intensities of the fragments M-92 and M-106. Whereas in the case of the 8'-apo-

carotinal the fragment M-toluene (M-92) was more intense compared to M-xylene (M-106), the situation was the other way around with the synthetic isomer XVI. This is consistent with the results obtained by Schwieter et al. (26) for the synthesis of 13-des-methyl-14-methyl-β-carotene. With β-carotene, the fragment

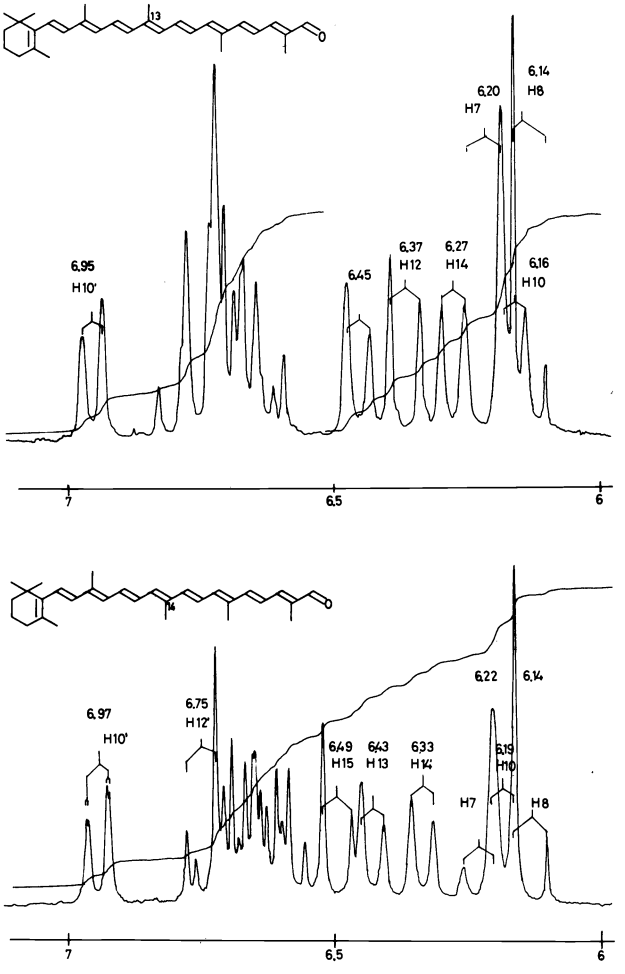

Fig. 11

M-toluene showed a greater intensity than M-xylene, whereas the isomer showed opposite intensities. One possible explanation is that the fragmentation of this molecule is favoured in the middle of the polyene chain and that with shifting one methyl group to the central part of the chain, the loss of xylene becomes favoured.

Part of the 270 MHz-PMR-spectra of the two compounds is shown in Fig. 11.

In the spectra of the 8'-apocarotinal, the doublets at 6.37 ppm and 6.27 ppm can be attributed to H(12) and H(14) respectively, whereas in the spectra of the isomer the doublets at 6.43 ppm and 6.49 ppm for H(13) and H(15) can be observed.

The next step was the comparison of the data obtained with those of the natural pigments. 8'-Apocarotinal and β-citraurin as well as fatty acid esters of β-citraurin were isolated in crystalline form from the peels of Robinson oranges from Florida.

The chromatographic behaviour as well as the spectroscopic data of these isolated apocarotenoids, especially the data of the PMR- and mass spectra clearly prove that in the natural products, the methyl

group is located at the C(13)-position and that they therefore belong to the apocarotenoids.

The synthesis of the three chiral C_{30}-apocarotenoids isolated from orange peels is shown in Fig. 12.

(3R)-3-Hydroxy-β-ionone (XXIV) as starting material was converted with vinylmagnesium bromide using THF as solvent in a Grignard reaction to vinyl-3-hydroxy-β-ionol (XXV). After normal work up the ionol was converted without further purification into the corresponding Wittig salt (XXVI) by treatment with triphenylphosphonium bromide in methanol in 60 % yield related to the 3-hydroxy-β-ionone.

(3R)-3-Hydroxy-12'-apo-β-carotene-12'-al (XXVII) was obtained in 70 % yield by Wittig reaction of the C_{10}-dialdehyde with the C_{15}-Wittig salt in a two-phase reaction using methylene chloride and an aqueous solution of sodium hydroxide with a reaction time of 5 minutes.

β-Citraurin (XIII) was prepared by reaction of the C_{25}-compounds (XXVII) with the acetal of the C_5-Wittig salt using again methylene chloride and an aqueous solution of sodium hydroxide as solvents. Subsequent separation of the reaction mixture and hydrolysis with acetic acid furnished the desired compound in 68 % yield. The reduction of β-citraurin (XIII) with $LiAlH_4$ gave the dihydroxy compound β-citraurol (XIV).

In addition, the reaction of the C_{25}-compound (XXVII) with the C_5-Wittig salt furnished β-citraurinene (XV) in 50 % yield.

The chromatographic as well as the spectroscopic data of the synthesised products were fully identical with those of the isolated compounds, the chiroptical data confirming the 3R-configuration of the C_{30}-apocarotenoids.

Synthesis of β-Citraurin, β-Citraurol and β-Citraurinene

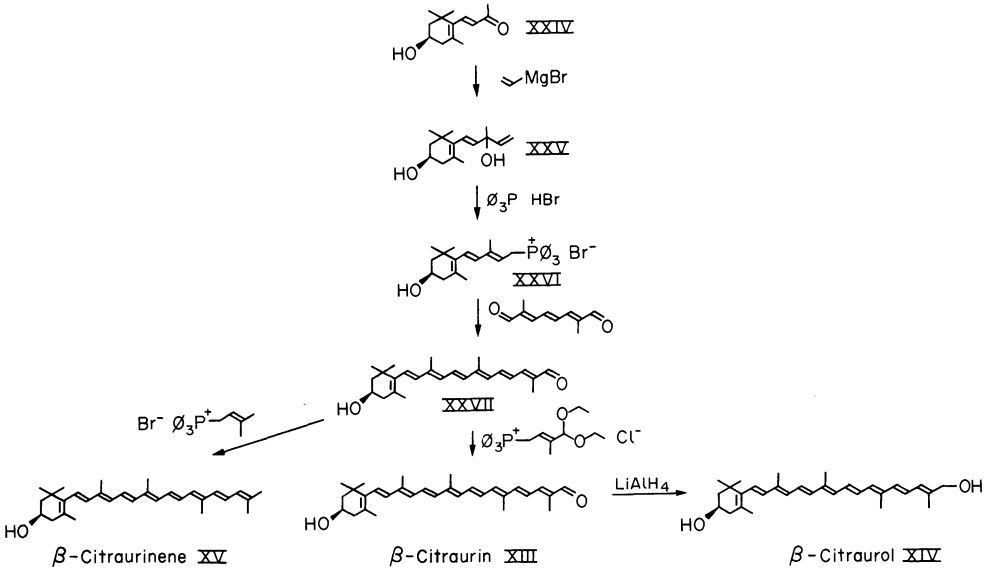

Fig. 12

SYNTHESIS OF 1,2-EPOXY CAROTENOIDS

Carotenoids with epoxy groups are frequently encountered in natural carotenoids. In the list of the natural carotenoids of Straub (27) 59 different epoxy carotenoids are mentioned. For the carotenoids with cyclic end groups, especially the 5,6-epoxides are characteristical as in violaxanthin and neoxanthin.

The isolation of epoxides of carotenoids with the acyclic ψ-end group from tomatoes was reported by Britton, Goodwin and Ben-Aziz (28,29,30).

As shown in Fig. 13, the isolated carotenoids belong to the 1,2-epoxy carotenoids with one exception where the epoxy group is in the 5,6-position. In one respect, the structures of these 1,2-epoxy compounds differ in the degree of saturation of the polyene chain. Furthermore, the second end group may be either acyclic (ψ-end group) or cyclic (β- and ε-end group). The small quantity of the isolated carotenoids permitted the structure elucidation by chromatographical and chemical behaviour and by electronic and mass spectra, but the absolute configuration of these compounds could not be determined.

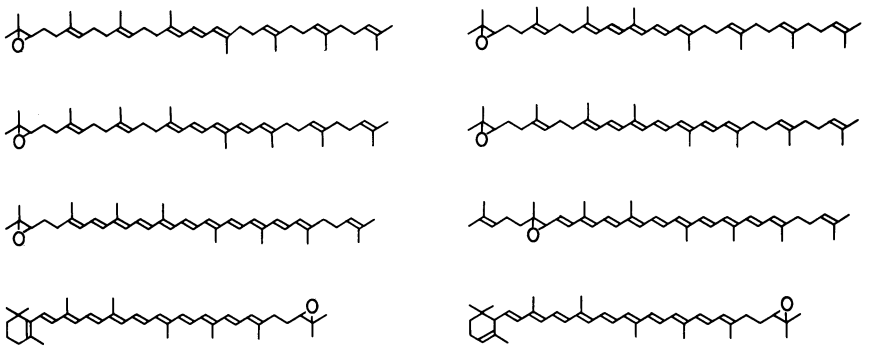

Fig. 13

Partial synthesis of 1,2-epoxy carotenoids by oxidation of the polyenes with m-chloroperbenzoic acid proved to be unsuitable on a preparative scale.

A possible synthesis of lycopene-1,2-epoxide (1,2-epoxy-1,2-dihydro-ψ,ψ-carotene XXVIII) has been proposed by Rønneberg and Liaaen-Jensen (31) starting with acrolein via apo-2'-lycopenal.

As the 1,2-epoxy carotenoids may be important intermediates in the synthesis of C_{45}- and C_{50}-carotenoids or of compounds with the 2-hydroxy-β-end group, an alternative approach to the synthesis of these compounds was investigated in our laboratories. According to the scheme $C_{10} + C_{20} + C_{10}$ which has already been used for the synthesis of lycopene (ψ,ψ-carotene) by Isler (32), the preparation of lycopene-1,2-epoxide (XXVIII) and lycopene-1,2,1',2'-diepoxide (1,2,1',2'-diepoxy-1,2,1',2'-tetrahydro-ψ,ψ-carotene XXIX) was achieved, using crocetindialdehyde (8,8'-diapocarotene-8,8'-dial) as C_{20}-compound. As intermediate also 1,2-epoxy-C_{30}-apocarotinal (1,2-epoxy-1,2-dihydro-8'-apo-ψ-carotene-8'-al XXX) was synthesised.

The reaction scheme for the three compounds is shown in figure 14. Trans-citral (XXXI) was converted with m-chloroperbenzoic acid in a two-phase system of methylene chloride and an aqueous solution of sodium hydrogen carbonate to the corresponding epoxide (XXXII) in 90 % yield. The epoxy aldehyde was subsequently transformed

with $NaBH_4$ in THF to geraniol epoxide (XXXIII), which was used without purification for the further synthesis.

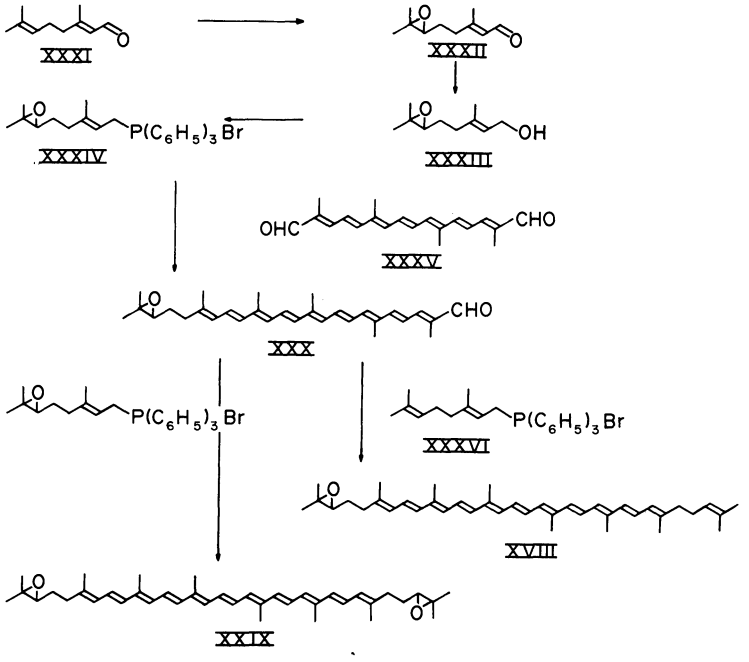

Fig. 14

Experiments to prepare the corresponding epoxy bromide with different methods were unsuccessful, always yielding a complex mixture of reaction products. The direct conversion of the geraniol epoxide to the Wittig salt (XXXIV) was achieved by treatment with triphenylphosphonium bromide in ethanol, yielding the desired compound in a mixture that was used for the following Wittig reaction without further purification.

The suspension of the Wittig salt in ether was converted to the ylide with sodium methoxide and the crocetindialdehyde in methylene chloride was added. Depending on the ratio of the ylide and the C_{20}-dialdehyde either the 1,2-epoxy-C_{30}-apocarotinal (XXX) or the 1,2,1',2'-diepoxy-lycopene (XXIX) was prepared. For the synthesis of the naturally occurring 1,2-epoxy-lycopene (XXVIII), geranyltriphenylphosphonium bromide (XXXVI) was converted into the ylide with sodium methoxide and treated with the 1,2-epoxy-C_{30}-apocarotinal (XXX). After chromatographical separation, the three compounds were crystallized from methylene chloride/methanol.

The spectroscopic data of these three 1,2-epoxy carotenoids are fully consistent with the proposed structures. Important information in view of the structure elucidation of compounds with the 1,2-epoxy-end group can be taken from the PMR-spectra.

For the ψ-end group, especially the two singlets at 1.61 ppm and 1.68 ppm corresponding to the met l groups at C(1) and the signal at 5.10 ppm of the proton at C(2) are characteristic

For the 1,2-epoxy-ψ-end group, the singlets of the two methyl groups at C(1) are shifted towards higher field and appear at 1.27 and 1.31 ppm respectively. The signal for the epoxy proton at C(2) can be observed as triplet at 2.78 ppm.

The main disadvantage of the outlined reaction is the low yield

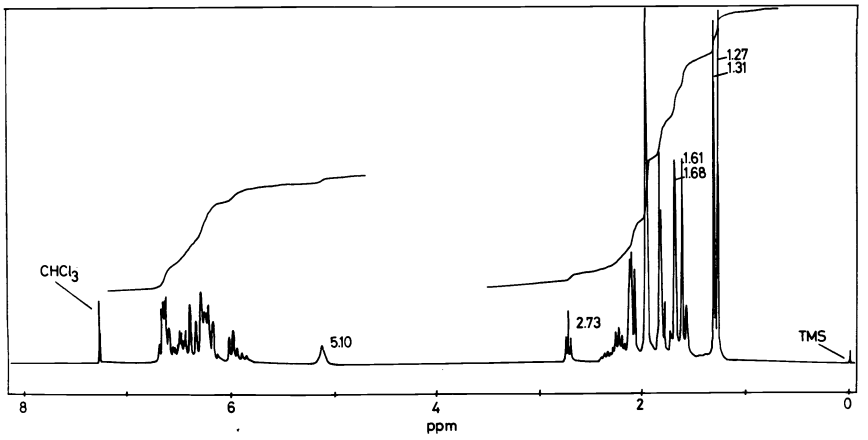

Fig. 15

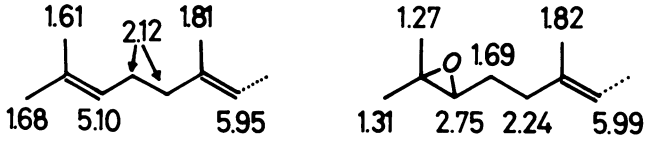

Fig. 16

in the preparation of the Wittig salt from the corresponding alcohol. Experiments for an alternative synthesis of the bromide or the Wittig salt as key intermediates via the triol and the acetonide are currently under investigation. The synthesis of optically active (S)-epoxy geraniol starting from L-glutamic acid and the conversion of the former to the corresponding chloride was recently reported by Yomada et al. (33). This makes it possible to synthesise optically active 1,2-epoxy-carotenoids and thus the absolute configuration of these compounds may be determined.

The reaction scheme opens the possibility of a simple synthesis of the 1,2-epoxy carotenoids isolated by Britton et al. (28,29, 30). Furthermore, these compounds may serve as valuable intermediates for the preparation of C_{40}- and C_{50}-carotenoids and for cyclization reactions.

Acknowledgements:

Part of this work was supported by the Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung (Project Nr. 2.670-0.76).

In conclusion, I should like to express my most sincere appreciation to my collaborators. They are given in alphabetical order: Dr. Yvonne Battegay-Nussbaumer, Dr. Martin Hadorn, Mr. Matthias Kamber, Mr. Andreas Lachenmeier, Mr. Manfred Läderach and Dr. Fritz Wittwer. I am also most grateful to F. Hoffmann-La Roche + Co. Ltd. (Basle), especially to Dr. Gloor and Dr. Mayer, for their kind support which made part of our work possible and to the Institute of Organic Chemistry of the University of Berne.

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