ON TERPENES. CCXVI.*
SESQUITERPENIC LACTONES FROM *Eupatorium cannabinum* L. REVISION OF THE STRUCTURE OF EUPATORIOPICRIN**

B.Drozdz[a], H.Grabarczyk[a] Z.Samek[b], M.Holub[b], V.Herout[b] and F.Šorm[b]

[a]*Biological and Pharmaceutical Institute, Medical Academy, Poznan, Poland,*
[b]*Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6*

Received March 12th, 1971

From the aboveground part of *Eupatorium cannabinum* L. three native sesquiterpenic lactones have been isolated. One of them was identical with eupatoriopicrin (*I*) described earlier[1], the second was identical with the product of hydrolysis of eupatoriopicrin, *i.e.* eupatolide (*II*), and for the third one, called eucannabinolide, the main structural features and partial stereo-structure were proposed on the basis of its PMR spectrum. On the basis of the PMR study the stereo-structures of eupatoriopicrin and eupatolide proposed earlier were revised.

In connection with the study of sesquiterpenic lactones from the species of *Compositae* we resumed the investigation of *Eupatorium cannabinum* L. In addition to eupatoriopicrin[1] (*I*) we isolated from it two additional sesquiterpenic lactones. One of them $C_{15}H_{20}O_3$ had m.p. 186–188°C and $[\alpha]_D^{20}$ +41·3°. Its IR spectrum demonstrated the presence of a free hydroxy group (3400 and 3600 cm^{-1}), a γ-lactone ring with an exocyclic double bond (1750 and 1140 cm^{-1}), and a double bond (1655 cm^{-1}) in its molecule. From the comparison of the mentioned IR spectrum with that of eupatolide[1] (*II*) it followed that the two substances should be identical. The identity of both substances was then proved on the basis of the mixture melting point of the native substances with an authentic eupatolide sample prepared by the procedure[1] described.

In the original paper[1] the constitutions and the stereostructures represented by formulae *IV* or *V* were proposed for eupatoriopicrin and eupatolide on the basis of chemical reactions and the ORD curve of ketone *III*. Now we measured the PMR spectra of both these compounds and carried out their detailed analysis which disclosed some discrepancies with the original views on the stereochemistry of both substances.

The PMR spectra of eupatoriopicrin and eupatolide, as well as their assignment carried out by means of decoupling experiments are represented in Fig. 1 and 2 and

* Part CCXV: This Journal *37*, 1346 (1972).

** Preliminary communication: Dissertation Pharm. Pharmacol. *23*, 537 (1971).

the characteristic parameters obtained are summarised in Table I. In principle the PMR spectra corroborated the original conclusions regarding the constitution and structural interrelation of both substances. From the practically identical topological continuity of the magnitudes of vicinal long-range interactions of protons on fragments $C_{(5)}$ to $C_{(9)}$ and on $C_{(13)}$, and from the chemical shifts of protons $H_{(6)}$ (identical in both substances, *I* and *II*) and protons $H_{(8)}$ (in the PMR spectrum of substance *I* the signal $H_{(8)}$ is shifted downfield with respect to the PMR spectrum of substances *II* by approx. 0·55 p.p.m. which corresponds to the usual acylation shift) it followed unequivocally that the position of the γ-lactone ring is identical in both substances and that eupatoriopicrin must be eupatolide esterified at position $C_{(8)}$. The nature of the acid residue was confirmed by the presence of a triplet of an olefinic proton at 6·88 p.p.m. (J = 6 Hz, β-H), a doublet of the corresponding CH_2-group at 4·36 p.p.m. (2 H, β-CH_2OH, J = 6 Hz), and a two-proton singlet at 4·29 p.p.m. (2 H, α-CH_2OH); the position of the signal β-H indicated its *cis*-orientation with respect to the carbonyl group (on the basis of the analogy with *cis*- and *trans*-α,β-unsaturated esters[2]), hence, the residue was that of α,β-*cis*-(bis-hydroxymethyl)acrylic acid (the same residue was also described in guaianolides from *Bahia pringlei*[3]). However, from the observed values of allylic interactions of protons $H_{(13)}$ and $H_{(13')}$ ($^4J_{7,13}$ = 3·4, and $^4J_{7,13'}$ = 3·0 Hz in eupatoriopicrin (*I*), and $^4J_{7,13}$ = 3·55, and $^4J_{7,13'}$ = 3·1 in eupatolide (*II*), (Table I) it followed, on the basis of the empirical rule for the relationship of these interactions of exomethylene protons

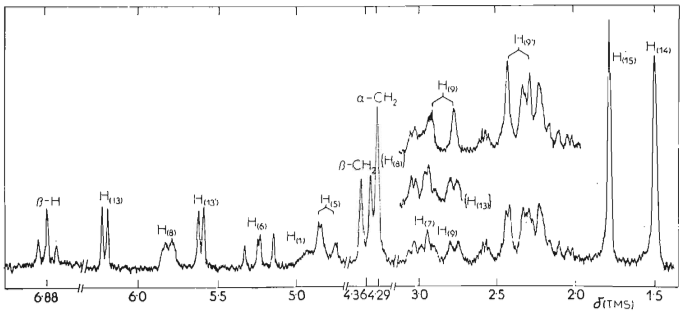


FIG. 1

PMR Spectrum of Eupatoriopicrin (*I*) (100 MHz; deuteriochloroform with the addition of a small amount of hexadeuteriodimethyl sulfoxide) and Some Decoupling Experiments (the position of the irradiated proton is indicated by {H})

TABLE I

Chemical Shifts of PMR Spectra of Eupatoriopicrine (*I*), Eupatolide (*II*) and Costunolide (*VI*); Varian HA-100, First-Order Analysis, Chemical Shifts in δ (TMS) Scale

Compound	Solvent[a]	$H_{(1)}$	$H_{(5)}$	$H_{(6)}$	$H_{(7)}$	$H_{(8)}$	$H_{(9)}$	$H_{(9')}$	$H_{(13)}$	$H_{(13')}$	$H_{(14)}$	$H_{(15)}$
I	A[b]	4·90	4·80	5·25	2·98	5·81	2·84	2·35	6·22	5·61	1·50	1·78
II[c]	A	4·84	4·74	5·24	2·79	4·60	2·74	2·29	6·37	5·57	1·63	1·73
VI[c]	A	4·87	4·75	4·54	2·51	—	—	—	6·25	5·51	1·42	1·70
I[d]	B	4·93	4·87	5·21	3·17	5·74	2·72	2·40	6·12	5·62	1·45	1·74
II	B	4·76	4·79	5·15	2·82	4·47	2·52	—	6·15	5·63	1·59	1·64

with the stereochemistry of the γ-lactone ring ($|^4J|$ (*trans*-fusion) $\geqq$ 3 Hz; $|^4J|$ (*cis*-fusion) $\leqq$ 3 Hz) (ref.[4]), that the annelation of the γ-lactone ring should have been *trans* in both cases, which is in contradiction to the original conclusions[1]. The vicinal interaction of protons $H_{(6)}$ and $H_{(7)}$ (Table I) indicated rather the topology of bonds typical of germacranolides derived from costunolide[5] (*VI*) supposing that the confi-

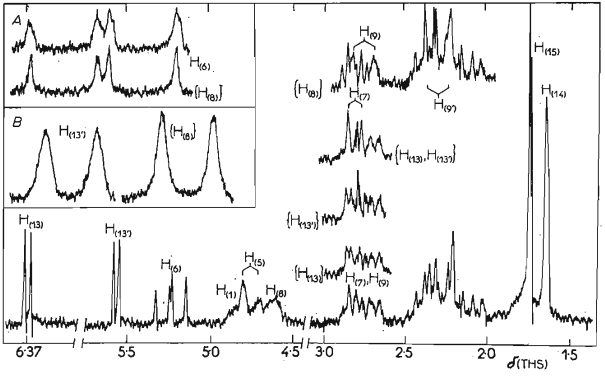


FIG. 2

PMR Spectrum of Eupatolide (*II*) (100 MHz; deuteriochloroform) and Some Double and Triple Resonance Experiments (the position of the irradiated proton is indicated by {H})

A Proof of $^4J_{6,8}$ coupling. *B* Proof of homoallylic coupling $^5J_{8,13'}$.

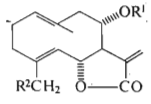
TABLE I
(*Continued*)
Coupling Constants (in Hz)

$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{8,9'}$	$J_{9,9'}$	$J_{13,13'}$[g]	$J_{7,13}$	$J_{7,13'}$	$J_{6,8}$[e]	$J_{8,13}$[e,f]	$J_{8,13'}$[e,f]	$J_{1,14}$[g]	$J_{5,15}$
10·0	8·5	≦1	~5	~2	14	0	3·40	3·00	±0	0	±0	±0	1·1
9·6	8·2	≦1	~5	~2	14	0	3·50	3·10	≦0·6[h]	0	≦0·3[h]	±0	1·4
10·0	8·0	—	—	—	—	0	3·50	3·20	—	—	—	±0	1·3
9·8	8·2	≦1	4·7	2	14	0	3·45	3·10	±0	—	—	±0	1·2
10·0	8·0	≦1	~5	~2	14	0	3·55	3·10	±0	0	±0	1·1	1·3

[a]A deuteriochloroform; internal standard tetramethylsilane; B hexadeuteriodimethyl sulfoxide; internal standard hexamethyldisiloxane (chemical shifts recalculated to TMS-scale using $\delta = 0{\cdot}06$ p.p.m for hexamethyldisiloxane). [b]With small addition of hexadeuteriodimethyl sulfoxide, —OCOC.(CH_2OH)=CH(CH_2OH): β-H: 6·88 t ($J = 6$); α-CH_2: 4·29 s (2 H); β-CH_2: 4·36 d ($J = 6$). [c]Own measurements; less complete data from 60 MHz spectra were presented in ref.[10]. [d]OCOC.(CH_2OH)=CH(CH_2OH): β-H: 6·76 t ($J = 6$): α-CH_2: 4·14 s (2 H); β-CH_2: 4·27 d ($J = 6$). [e]Confirmed by decoupling experiments. [f]Analogous homoallylic coupling with $H_{(6)}$ was not observed. [g]Unresolved splittings in most cases. [h]From half-line width measurement (Fig. 2).

guration of the —O.CO.R group at $C_{(8)}$ is β, *i.e.*, in the sense of absolute stereostructures of *I* and *II* (cf. for example the PMR spectra of salonitenolide[6,7] (*VII*), cnicin[8] (*VIII*) or onopordopicrin[9] (*IX*).

In the course of our work on the elucidation of these discrepancies the paper by Doskotch and El-Feraly[10] on tulipinolide (*X*) and epitulipinolide (*XI*) was published in which the identity of deacetylepitulipinolide with eupatolide (*II*), as well as of derivatives *XII* and *XIII* with similar substances prepared from eupatoriopicrin and described in the original paper[1], was determined on the basis of the correlation of physical constants and IR and UV data. On the basis of this identity it was clear that a revision of the stereostructure of eupatoriopicrin was necessary, *i.e.*, that the originally assumed formula *IV* must be changed to *I*. The correctness of these conclusions[10] is thus corroborated by our own analyses of the PMR spectra. Our data for eupatolide are identical with the data of the 60 MHz spectrum of deacetylepitulipinolide, and the PMR spectrum of eupatoriopicrin also corresponds closely to that of epitulipinolide (Table I and ref.[10]). Hence, the structure *I* for eupatoriopicrin and *II* for eupatolide may be regarded as correct. However, we propose that the name eupatolide should be used for 8β-hydroxycostunolide (*II*) in view of its natural occurrence in *E. cannabinum*.



I; $R^1 = O.CO.C(=CH_2)CH_2OH$ (CH$_2$OH)

$R^2, R^3 = H$

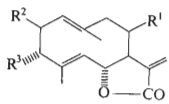
II; $R^1 = OH$; $R^2 = R^3 = H$

VI; $R^1, R^2, R^3 = H$

XVI; $R^1, R^3 = H$; $R^2 = OH$

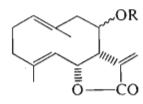
XVII; $R^1, R^3 = H$; $R^2 = O.CO.CH_3$

XVIII; $R^1, R^2 = H$; $R^3 = OH$



IV; $R = CO.C(=CH_2)CH_2OH$ (CH$_2$OH)

V; $R = H$



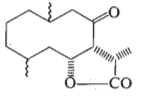
VII; $R^1 = H$; $R^2 = OH$

VIII; $R^1 = CO.C(=CH_2).CHOH.CH_2OH$

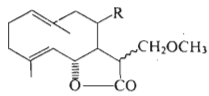
$R^2 = OH$

IX; $R^1 = CO.C(=CH_2).CH_2OH$; $R^2 = OH$

X; $R^1 = CO.CH_3$; $R^2 = H$

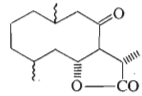


III

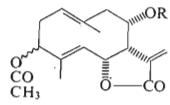


XII; R = OH, H

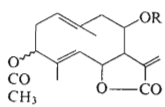
XIII; R = =O



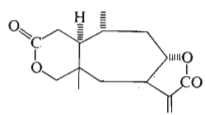
XIX



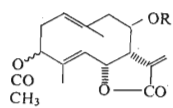
XIV, $R = CO.C(=CH_2)CH_2OH$ (CH$_2$OH)



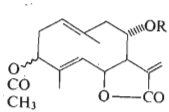
XIVa



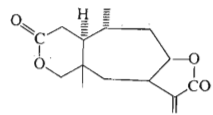
XX



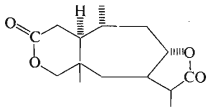
XV, $R = CO.C(=CH_2)CH_2OH$ (CH$_2$OH)



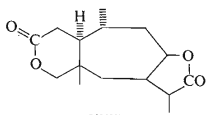
XVa



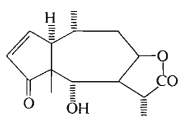
XXI



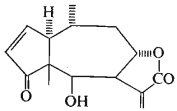
XXII



XXIII



XXIV



XXV

The third of the isolated lactones, which was difficult to separate from eupatoriopicrin and which we obtained, therefore, only in a small quantity and in a non-crystalline state, is in our opinion the casuse of fallacious conclusions on the stere-structure of eupatoriopicrin in the original paper[1]. This newly isolated lactone *XIV* has the composition $C_{22}H_{28}O_8$ and $[\alpha]_D^{25}$ $-121{\cdot}0°$ and we propose the name eucannabinolide for it. Its IR spectrum shows the presence of a γ-lactone ring with a conjugated exocyclic double bond (1755 and 1140 cm^{-1}), an acetyl group (1260 and inflexion at 1735 cm^{-1}), and α,β-unsaturated ester group (1710 cm^{-1}), a double bond (1660 cm^{-1}), and a hydroxyl group (3470 and 3600 cm^{-1}). Its PMR spectrum contained signals characteristic of an acetyl group (singlet at 2·12 p.p.m.), a residue of α,β-*cis*-bis(hydroxymethyl)acrylic acid (β-H as triplet at 6·92 p.p.m., J = 6 Hz, β-CH_2OH as doublet at 4·00 p.p.m., J = 6 Hz, and α-CH_2OH as singlet at 4·34 p.p.m.; compare the PMR spectrum of eupatoriopicrin), two methyl groups on the double bonds (doublet at 1·82 p.p.m., J = 1·3 Hz and a broadened singlet at 1·79 p.p.m.), and typical signals of two protons of the exomethylene group[4] of the CH_2= =C(CO—O—)—CH type (doublet at 6·36 p.p.m., ^4J = 2·1 Hz, and doublet at 5·78 p.p.m., ^4J = 2·1 Hz).

On the basis of these facts it could be supposed that it is also a sesquiterpenic lactone of the germacrane type. This supposition was also supported by a preliminary detailed analysis of its PMR spectrum, carried out by the conventional method, *i.e.* decoupling experiments, beginning with the localisation of the signal of the allylic proton of the lactone ring. The assignment of signals obtained under the supposition of the localisation of the methylene protons on $C_{(13)}$ is the following: $H_{(7)}$ as an unresolved multiplet at 3·00 p.p.m. ($^4J_{7,13} = {}^4J_{7,13'}$ = 2·1 Hz, $J_{7,6}$ = 2·5 Hz, $J_{7,8} \neq 0$, and according to double resonance experiments it is very small), $H_{(6)}$ as a doublet of doublets at 5·96 p.p.m. ($J_{6,7}$ = 2·5 Hz, $J_{6,5}$ = 10·5 Hz), $H_{(5)}$ as a complex doublet at approx. 5·20 p.p.m. ($J_{5,6}$ = 10·5 Hz, $^4J_{5,15}$ = 1·3 Hz) superimposed in the 5·12 – 5·34 p.p.m. region together with the multiplets of protons $H_{(1)}$ ($^4J_{1,14} \neq 0$), and two pro-

tons of the CH—OR type of which one may be assigned to the $H_{(8)}$ proton ($J_{8,7} \neq 0$) and the second to the proton $H_{(2)}$ or $H_{(3)}$. This assignment follows from the presence of the signals of two protons forming a doublet of doublets at 2·78 p.p.m., $J_1 = 14$ Hz and $J_2 = 3$ Hz, and a doublet of doublets at 2·44 p.p.m., $J_1 = 14$ Hz and $J_2 = 2$ Hz, the small coupling constants of which are due to interactions with one of the protons of the 5·12 to 5·34 p.p.m. region. Hence, under the supposition of a germacrane skeleton they can be assigned either to protons $H_{(9)}$ or to protons $H_{(3)}$ if the substituent is at $C_{(2)}$.

From the presented analysis of the PMR spectrum the following conclusion may be drawn regarding the structure of eucannabinolide (*XIV*): From the magnitude of allylic interactions of protons $C_{(13)}$ and on the basis of the above mentioned rule[4] it can be concluded that the lactone ring is *cis*-fused similarly as in the case of nobilin (*XV* or *XVa*) (ref.[11]). This conclusion is also corroborated by the small values of vicinal coupling constants $J_{6,7}$ and $J_{7,8}$ which are in accordance with the *cis*-fusion in both alternative cases of the orientation of the lactone ring at $C_{(6)}$ or $C_{(8)}$. Further a comparison of the multiplet of proton $H_{(6)}$ in the PMR spectrum of eucannabinolide with a multiplet of the proton $H_{(6)}$ in the PMR spectrum of nobilin (*XV* or *XVa*) ($H_{(6)}$ at 5·93 p.p.m., $J_{5,6} = 10$ Hz and $J_{6,7} = 2$ Hz) (ref.[11]) allows the supposition that the lactone ring has the same orientation at $C_{(6)}$ in both substances. Supposing that the lactone ring is closed at $C_{(6)}$ the small value of the vicinal coupling $J_{7,8}$ indicates a relative *cis*-configuration of protons $H_{(7)}$ and $H_{(8)}$, in accordance with the absence of a significant geminal coupling of protons $C_{(13)}$ (compare the analysis of the PMR spectrum of nobilin[11] and ref.[12]). From the comparison of the position of signals of protons $H_{(1)}$ in the PMR spectra, for example, of taumalipin A (*XVI*) (approx. 5·00 p.p.m.)[13] and its acetate *XVII* (5·02 p.p.m.)[13], tamaulipin B (*XVIII*) (approx. 5·25 p.p.m.)[14] and nobilin (*XV* or *XVa*) (5·29 p.p.m.)[11], and in the PMR spectra of germacranolides unsubstituted at $C_{(2)}$ or $C_{(3)}$, which display a signal $H_{(1)}$ at about 4·90 p.p.m. (for example, Table I and refs[6–9]), it followed that the position of signal $H_{(1)}$ in the 5·2–5·3 p.p.m., region is significant to a certain extent for the substitution at $C_{(3)}$. The application of this empirical rule to eucannabinolide also leads to the supposition that one of the ester groups is located in position 3. Another indirect indication of the location of one of the ester groups in this position may consist in the shape of the signal of methyl protons $H_{(14)}$ which is present in the PMR spectrum of eucannabinolide in the form of a broadened singlet, similarly as in other germacranolides with an endocyclic double bond $\Delta^{1(10)}$ of the —CH_2—CH=$C(CH_3)$—CH_2— type (Table I). In the case of the substitution at $C_{(2)}$ it may be expected, in consequence of the reduction of the number of homoallylic interactions $^4J_{2,14}$ and in view of the commonly small values of isopropylidenic couplings $^4J_{9,14}$, that the signal $H_{(14)}$ will be split to a doublet, in analogy with the case[13] of tamaulipin A (*XVI*) and its acetate *XVII*. However, this argument need not be generally utilisable in view of the known stereospecificity of the mentioned long-range interactions.

On the basis of the given conclusions on the structure of eucannabinolide, derived from its PMR spectrum, and on the basis of its biogenetical relationship with eupatoriopicrin, the alternative partial absolute stereostructures *XIV* or *XIVa* may be tentatively proposed for the mentioned substance. The simultaneous occurrence in the same plant species of two sesquiterpenic lactones differing in the *cis* and *trans* arrangement of the lactone ring has already been described, such as vermeerin (*XX*) (ref.[15]) and floribundin (*XXI*) (ref.[15]) from *Hymenoxys richardsonii* (HOOK) CKLL. var. *floribunda* and from *H. anthemoides* (JUSS.) CASS., the above mentioned pair (*XX* and *XXI*) and anthemoidin (*XII*) and themoidin (*XXIII*) (ref.[15]) mexicanin C (*XXIV*) (refs.[16,17]) and mexicanin I (*XXV*) (ref.[18]) from *Helenium mexicanum* H. B. K. In these cases the orientation of the $C_{(7)}-C_{(11)}$ bond is the same and the change is on the $C_{(8)}-O$ bond. The opposite case, when the pair of *cis*- and *trans*-sesquiterpenic lactones differs in orientation of the $C_{(7)}-C_{(11)}$ bond has never been described as yet.

On the basis of the stereostructure *XIV* an explanation can be given of why the determination of the stereostructure of eupatoriopicrin in paper[1] was not correct: In view of the difficult separation of eupatoriopicrin and eucannabinolide, eupatoriopicrin of various degrees of purity was utilised for the study. For the preparation of ketone *III* the authors took a fraction which predominantly contained eucannabinolide, from which they prepared ketone *III* by hydrogenation combined with hydrogenolysis, saponification and oxidation. They suceeded in preparing this substance only once. In repeated experiments they obtained only ketone *XIX*, in spite of the fact that they used the same reaction sequence for preparation.

EXPERIMENTAL

Melting points were determined on a Kofler block and were not corrected. For column chromatography silica gel according to Pitra and Štěrba[19] has been used (30—60 μ, deactivated by addition of 11% of water). For thin-layer chromatography silica gel Merck according to Stahl was employed. The IR spectra were measured in chloroform on Unicam S. P. 200 apparatus. The PMR spectra were measured in deuteriochloroform (unless stated otherwise) on a Varian HA-100 apparatus, using tetramethylsilane as the internal standard. Optical rotation was determined on a Jasco UV-5 spectropolarimeter in methanol.

Isolation of Sesquiterpenic Lactones

Dry, powdered aboveground parts of *Eupatorium cannabinum* L. (*Compositae*) (3 kg), collected near Poznań (Poland) in summer 1969, were mixed with 12 l of methanol and heated in a 70°C warm bath for 1 hour. After cooling the extract was filtered and the filtrate concentrated *in vacuo* to approx. 2 l volume. Water (2 l) was added and the solution was evaporated again under reduced pressure to approx. 2 l volume. The residue was then diluted with 10 l of water and additioned with an excess of lead acetate. After 4 hours standing the mixture was filtered through diatomaceous earth and the filtrate was extracted three times with 3 l of chloroform. The combined chloroform extract was dried over anhydrous sodium sulfate and the solvent was distilled off under reduced pressure. The residue (20 g) which contained according to thin layer chromatography three substances (R_F 0·70, 0·40 and 0·35; chloroform–acetone 3 : 1) was chromatographed on 500 g of silica gel with chloroform and chloroform–acetone mixture (3 : 1). The first fractions contained eupatolide (*II*) (R_F 0·70), m.p. 186—188°C (methanol), $[\alpha]_D^{20}$ +41·3° (*c* 0·13). For $C_{15}H_{20}O_3$ (248·3) calculated: 72·55% C, 8·12% H, 0·41% H act.; found: 72·61% C, 8·09% H,

0·43% H act. Further fractions contained eupatoriopicrin (*I*) the identity of which was proved on the basis of its IR and PMR spectrum and mixture melting point with an authentic sample of eupatoriopicrin[1]. The subsequent fractions which still contained eupatoriopicrin contained predominantly eucannabinolide, R_F 0·35, which was obtained in a pure state by repeated chromatography in the form of a viscous oil, $[\alpha]_D^{25} -121°$ (*c* 1·0). For $C_{22}H_{28}O_8$ (420·4) calculated: 62·85% C, 6·71% H, 0·48% H act.; found: 62·67% C, 6·87% H, 0·51% H act.

Elemental analyses were carried out in the analytical department of our institute (head Dr J. Horáček) by Mrs V. Rusová, Mr V. Štěrba, and Mrs L. Pejchalová. The IR spectra were measured by Mrs S. Holubová and optical rotation by Mrs H. Pilařová. Our thanks are due to all those mentioned, as well as to Mrs M. Snopková for technical assistance.

REFERENCES

1. Dolejš L., Herout V.: This Journal *27*, 2654 (1962).
2. Emsley J. W., Feeney J., Sutcliffe L. H.: *Magnetic Resonance Spectroscopy*, Vol. II., Pergamon Press, London 1965.
3. Romo de Vivar A., Ortega A.: Can. J. Chem. *47*, 2849 (1969).
4. Samek Z.: Tetrahedron Letters *1970*, 671.
5. Šorm F., Suchý M., Holub M., Línek A., Hadinec I., Novák C.: Tetrahedron Letters *1970*, 1893.
6. Suchý M., Samek Z., Herout V., Šorm F.: This Journal *32*, 2016 (1967).
7. Yoshioka H., Renold W., Mabry T. J.: Chem. Commun. *1970*, 148.
8. Samek Z., Holub M., Herout V., Šorm F.: Tetrahedron Letters *1969*, 2931.
9. Drozdz B., Holub M., Herout V., Samek Z., Šorm F.: This Journal *33*, 1730 (1968).
10. Doskotch R. W., El-Feraly F. S.: J. Org. Chem. *35*, 1928 (1970).
11. Benešová V., Samek Z., Herout V., Šorm F.: Tetrahedron Letters *1970*, 5017.
12. Yoshioka H., Mabry T. J., Irwin A. A., Geissman T. A., Samek Z.: Tetrahedron *27*, 3317 (1971).
13. Fisher N. H., Mabry T. J., Kagan H. B.: Tetrahedron *24*, 4091 (1968).
14. Fisher N. H., Mabry T. J.: Chem. Commun. *1967*, 1235.
15. Herz W., Aota K., Holub M., Samek Z.: J. Org. Chem. *35*, 2611 (1970).
16. Romo de Vivar A., Romo J.: Chem. Ind. (London) *1959*, 882.
17. Herz W., Romo de Vivar A., Romo J., Viswanathan N.: Tetrahedron *19*, 1359 (1963).
18. Dominguez E., Romo J.: Tetrahedron *19*, 1415 (1963).
19. Pitra J., Štěrba J.: Chem. listy *56*, 544 (1962).

Translated by Ž. Procházka.