Tetrahedron, 1965, Vol. 21, pp. 3687 to 3695. Pergamon Press Ltd. Printed in Northern Ireland

GENTIAN PIGMENTS—III

PENTA-OXYGENATED XANTHONES FROM *GENTIANA BELLIDIFOLIA*

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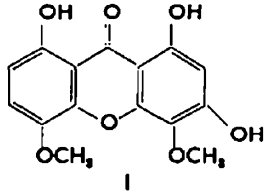
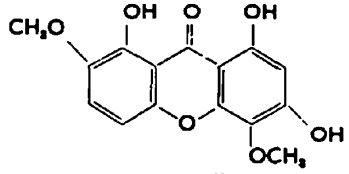
(*Received* 26 *May* 1965)

Abstract—4,5-Di-O-methylcorymbin (corymbiferin) has been isolated along with 4,7-di-O-methylbellidin from the roots of *Gentiana bellidifolia*. These are the only known naturally occurring penta-oxygenated xanthones and the structures are shown to be 1,3,8-trihydroxy-4,5-dimethoxyxanthone and 1,3,8-trihydroxy-4,7-dimethoxyxanthone respectively.

CORYMBIFERIN $C_{15}H_{12}O_7$, the only known naturally occurring penta-oxygenated xanthone, was first isolated[1] in 1950 from the roots of *Gentiana corymbifera* T. Kirk and was correctly thought to be a trihydroxy-dimethoxyxanthone containing a hydroxyl group in the 1-position. This conclusion was supported by the preparation of di- and tri-methyl ethers as well as a triacetate. Ten years later, on the basis of the one published UV spectrum, Dreyer suggested[2] that corymbiferin was 3,4,8-trihydroxy-1,6-dimethoxyxanthone. The present paper describes the isolation and structure elucidation of corymbiferin (I), now renamed 4,5-di-O-methylcorymbin, together with a co-occurring isomer 4,7-di-O-methylbellidin (II).



I



II

Nomenclature. The naming of xanthone natural products has in the past been rather arbitrary and there is no systematic procedure. The new natural products reported here have been named as derivatives of the corresponding pentahydroxyxanthones, corymbin (1,3,4,5,8-pentahydroxyxanthone) and bellidin (1,3,4,7,8-pentahydroxyxanthone). Thus corymbiferin (I) becomes 4,5-di-O-methylcorymbin and 1,3,8-trihydroxy-4,7-dimethoxyxanthone (II) becomes 4,7-di-O-methybellidin. In the case of polyhydroxy-methoxyxanthones of known structure, established names are retained to avoid confusion although more systematic nomenclature could also be applied to these.

4,5-*Di-O-methylcorymbin.* 4,5-Di-O-methylcorymbin was isolated in 0·3% yield from the roots of *Gentiana bellidifolia*, along with four 1,3,5,8-oxygenated xanthones of

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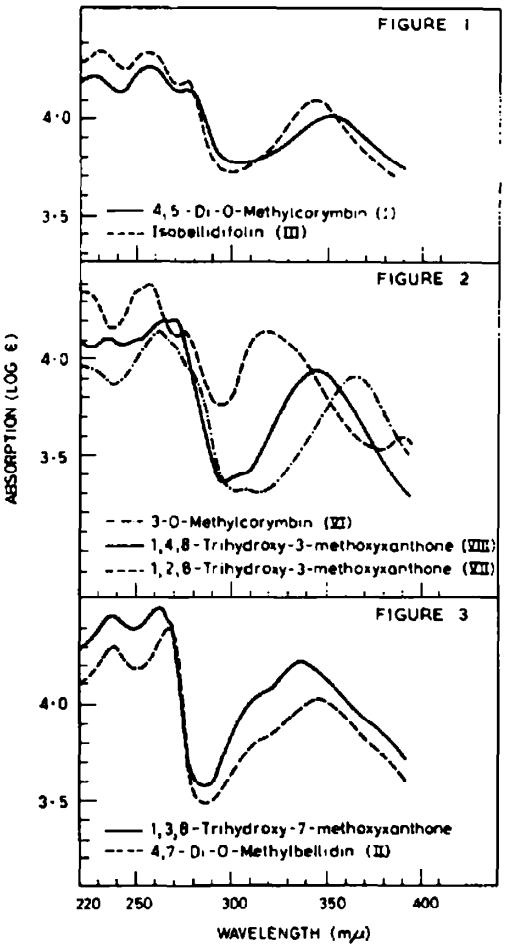
[1] D. J. Ross, *N. Z. J. Sci. and Tech.* **32**, No. 3, 39 (1950); *Chem. Abstr.* **46**, 4539 (1952).

[2] D. L. Dreyer, PhD Thesis, University of Washington (1960); (*Diss. Abstr.* **21**, 1373 (1960); L. C. Card No. Mic 60-4282).

ULTRAVIOLET ABSORPTION SPECTRA OF XANTHONES



the bellidifolin series,[3,4] and was identified by direct comparison with the sample isolated by Ross.[1]

A close similarity between 4,5-di-O-methylcorymbin and xanthones of the bellidifolin series is indicated by both the UV (Fig. 1) and the NMR (Table 1) spectra. The UV absorption spectrum, apart from the long wavelength band, is almost identical with that of isobellidifolin (III) suggesting that the same 1,3,5,8-oxygenation pattern is present in both. The NMR spectrum (60 Mc), shows peaks at 697 and 678 c/s due to two hydrogen bonded hydroxyl groups at C-1 and C-8, and the absence of any other well defined hydroxyl peak clear of the aromatic protons suggests[3,4] that the third hydroxyl group is at C-3. The presence of this acidic hydroxyl group is confirmed by the solubility of 4,5-di-O-methylcorymbin in sodium carbonate and by the 19 mμ bathochromic shift of the long wavelength UV absorption with sodium acetate.[5] Of the

[3] K. R. Markham, *Tetrahedron* **20**, 991 (1964).

[4] K. R. Markham, *Tetrahedron* **21**, 1449 (1965).

[5] The long wavelength absorptions of isobellidifolin and desmethylbellidifolin, but not of bellidifolin shifted bathochromically by about 20 mμ under the same conditions.

TABLE 1. NMR SPECTRA OF XANTHONES*

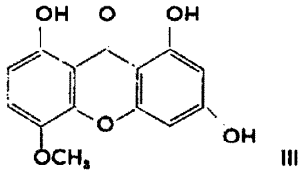
	Hydroxyl protons	Methoxyl groups	Aromatic protons				
			H-7	H-6	H-5	H-4	H-2
4, 5-Di-O-methylcorymbin (I)	697, 678 (2)	236, 232	409, 399	453, 444			380 (3)
† 4,5-Di-O-methylcorymbin triacetate	144, 141, 140 (three-OAc)	238	418, 409	436, 427			405 (3)
Corymbin (V)	677, 669, 653, 559, 537 (5)		398, 389	435, 427			375 (3)
3-O-Methylcorymbin (VI)	676 658 559	234	399, 390	436, 427			390 (3)
3-O-Methylcorymbin tetra-acetate	146 (four-OAc)	237	420, 411	451, 442			400 (3)
Isobellidifolin (III)	709, 674, 435 (3)	231	406 396	450 441		384, 382	374 372 (4)
1,3,8-Trihydroxy-7-methoxyxanthone	713, 707 (2)	233		458, 449	425, 415	387, 384	379, 377 (4)
‡ 4,7-Di-O-methylbellidin (II)	731, 704 (2)	238, 236		451, 444	428, 419		385 (3)
† Bellidifolin dimethylether	758 (1)	242 239 237	405, 395	435, 426		398, 395	383 380 (4)
† Bellidifolin dimethylether acetate	148 (one-OAc)	241 238 235	415, 405	434, 425		395, 393	380, 378 (4)
1,4,8-Trihydroxy-3-methoxyxanthone (VIII)	713, 686, 546 (3)	234	466		397		389 (4)
1,2,8-Trihydroxy-3-methoxyxanthone (VII)	708, 681, 523 (3)	235	468		400	405	(4)
1,3-Dihydroxyxanthone	768 (1)		499	448 (H-5, 6, 7, 8)		386, 383	376, 373 (6)
† 1,3-Diacetoxyxanthone	146, 137 (two-OAc)		499	442 (H-5, 6, 7, 8)		441 439	411 408 (6)
† 1-Hydroxy-3,8-dimethoxyxanthone	798 (1)	238, 229	461		399	376	376 (5)
† 1-Acetoxy-3,8-dimethoxyxanthone	149 (one-OAc)	239, 233	460		401	406, 403	393, 390 (5)

* NMR spectra were measured in deutero-dimethylsulphoxide on a Varian D.P.60 spectrometer and chemical shifts are expressed in cps from TMS. The number of protons in each region is in brackets.

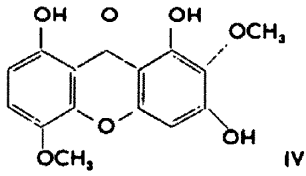
† Deuterochloroform solvent.

‡ Deuterochloroform: deutero-dimethylsulphoxide, 1:1.

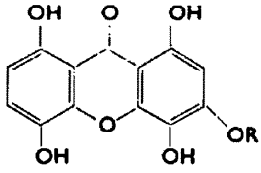
two methoxyl groups shown by peaks at 232 and 236 c/s, one is at C-5 since the NMR spectrum still contains the same *ortho*-proton patterns as is present in the spectrum of isobellidifolin. The other must therefore be at C_2 or C_4, *meta* to the remaining aromatic proton which shows as a singlet at 380 c/s. This evidence leaves only two possible structures for 4,5-di-O-methylcorymbin, I and IV.



III



IV



V, R = H
VI, R = CH_3

Insufficient 4,5-di-O-methylcorymbin was available for degradative work, but physical data on derivatives such as the triacetate, corymbin (V) and 3-O-methylcorymbin (VI) exclusively favours structure I. Corymbin, hitherto unknown, was prepared by demethylation of 4,5-di-O-methylcorymbin and selective methylation of this gave 3-O-methylcorymbin. The relative structures were confirmed by NMR spectroscopy (Table 1), and methylation of 3-O-methylcorymbin to 4,5-di-O-methylcorymbin dimethyl ether excluded the possibility of rearrangement. Corymbin is assigned the 1,3,4,5,8-oxygenation pattern rather than a 1,2,3,5,8-pattern because it appears to lose the *ortho*-dihydroxy system on methylation to 3-O-methylcorymbin. In contrast to 3-O-methylcorymbin it gave a red precipitate with lead acetate; a positive sodium molybdate test and the long wavelength absorption in its UV spectrum shifted 21 mμ bathochromically on the addition of boric acid–sodium acetate. This evidence strongly suggests (cf. Refs 6, 7, 8) that the *ortho*-dihydroxy system has been lost from corymbin on methylation of the 3-hydroxyl group, and this is only possible if the 1,3,4,5,8-oxidation pattern is present, i.e. if 4,5-di-O-methylcorymbin has structure I. Further support for structure I is gained from the NMR spectrum of 4,5-di-O-methylcorymbin triacetate. The acetylation produces a 25 c/s downfield shift of the aromatic proton singlet, and comparison of this shift with those observed for protons in 1,3-dihydroxyxanthone on acetylation (C-2,35 c/s; C-4,55 c/s) indicates that position C-2 is unsubstituted in 4,5-di-O-methylcorymbin.

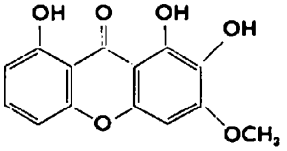
In order to show that the UV and NMR spectra were consistent with the above conclusion, 1,2,8-trihydroxy-3-methoxyxanthone (VII) and 1,4,8-trihydroxy-3-methoxyxanthone (VIII) were synthesized as reference compounds by reaction of γ-resorcylic acid with 2,6-dimethoxyquinol. The structures were defined by NMR

[6] B. Smith, *Investigation of Reagents for the Qualitative Analysis of Phenols, Chalmers Tek. Högskol. Hand.* No. 263; **35**, (1963)—Molybdate test.

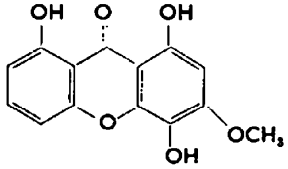
[7] M. J. Saxby, *Analyt. Chem.* **36**, 1145 (1964)—UV shifts.

[8] M. L. Wolfrom, F. Komitsky, G. Fraenkel, J. H. Looker, E. E. Dickey, P. McWain, A. Thompson, P. M. Mundell and O. M. Windrath, *J. Org. Chem.* **29**, 692 (1964)—Lead Acetate test.

spectroscopy (Table 1) and xanthone VII, containing an *ortho*-dihydroxy system, could be distinguished from VIII in the following ways. (a) It gave a red precipitate with lead acetate. (b) On TLC it showed marked acidity relative to VIII (cf. pK_a catechol 9·85 and pK_a hydroquinone 10·35). (c) The long wavelength absorption in

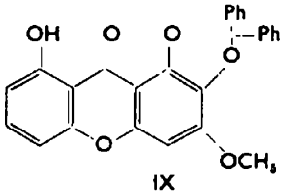


VII



VIII

the UV shifted bathochromically by 25 mμ in boric acid–sodium acetate whilst no change was observed in the spectrum of VIII. (d) With dichlorodiphenylmethane it formed the crystalline derivative IX, the structure of which was established by NMR and elemental analysis.



IX

The NMR spectra of the two isomers VII and VIII (Table 1) indicate that an isolated aromatic proton occurs at 389 c/s when at position C-2 and at 405 cps when at C-4.[9] The isolated aromatic proton in 3-O-methylcorymbin occurs as a singlet at 390 c/s and is therefore probably at C-2. This evidence is strongly suggestive of a 1,3,4,5,8-oxygenation pattern for 3-O-methylcorymbin and is supported by the UV spectral data. The UV absorption spectrum of 1,4,8-trihydroxy-3-methoxyxanthone is very similar to that of 3-O-methylcorymbin while the spectrum of 1,2,8-trihydroxy-3-methoxyxanthone is significantly different (Fig. 2), and since xanthones with similar oxygenation patterns possess similar UV spectra, the 1,3,4,5,8-oxygenation pattern is again favoured. The structure suggested for 4,5-di-O-methylcorymbin is therefore 1,3,8-trihydroxy-4,5-dimethoxyxanthone (I).

4,7-*Di*-O-*methylbellidin* (II) The crude desmethylbellidifolin fraction from *G. bellidifolia*[3] contains small amounts of a further xanthone, 4,7-di-O-methylbellidin ($C_{15}H_{12}O_7$). This compound gives an NMR spectrum which shows the presence of two hydrogen-bonded hydroxyl groups (731, 704 c/s), two methoxyl groups (238, 236 c/s) and three aromatic protons, two of which are adjacent (454/444, 428/419 c/s) and one isolated (385 c/s). The dimethyl ether ($C_{17}H_{16}O_7$) possesses one hydrogen-bonded hydroxyl group (789 c/s) and four methoxyl groups (236, 238(2), 241 c/s) thus confirming that 4,7-di-O-methylbellidin is a trihydroxy-dimethoxyxanthone. Two of the hydroxyl groups are at C-1 and C-8 and the third is at C-3, as is evidenced by the solubility of 4,7-di-O-methylbellidin in sodium carbonate and by the 22 mμ batho-

[9] This is consistent with observations in the flavonoid field in which H-6 is found to occur about 13 c/s upfield from H-8. (J. Massicot, J. P. Marthe and S. Heitz, *Bull. Soc. Chim. Fr.* 1962 (1962); 2712 (1963).)

chromic shift of the long wavelength UV absorption in sodium acetate. This leaves only the two methoxyl groups to be placed.

One methoxyl group is probably at position 4. Chemical shift values for the isolated aromatic proton in 4,7-di-O-methylbellidin (385 c/s) and its dimethyl ether (383 c/s) approximate closely to those observed for 4,5-di-O-methylcorymbin (380, 385 c/s) and strongly suggest that a C-2 proton is present. (A proton at C-4 would be expected to appear 16 c/s downfield from this, cf. VII and VIII.) The second methoxyl group appears to be at C-7 since while the proton at C-6 in 4,7-di-O-methylbellidin has the expected chemical shift, the proton adjacent to it appears at 425 c/s. This value is significantly different from the 400 c/s previously observed for C-7 protons (Table 1), but is very close to that expected for a proton at C-5 (e.g. 422 c/s in 1,3,8-trihydroxy-7-methoxyxanthone). The above evidence positions the methoxyl groups at C-4 and C-7 and therefore strongly favours structure II for 4,7-di-O-methylbellidin. In accord with this formulation 4,7-di-O-methylbellidin is found to be more acidic (R_f 0·14) than its 5,8-isomer, 4,5-di-O-methylcorymbin (R_f 0·52). This is as expected in view of the relative acidities of 1,3,8-trihydroxy-7-methoxyxanthone (R_f 0·22) and 1,3,8-trihydroxy-5-methoxyxanthone (R_f 0·6), and monomethylcatechol (pK_a 9.98) and monomethylhydroquinone (pK_a 10·3).

The UV absorption spectrum also supports structure II since it is found to bear the same relationship to the spectrum of 1,3,8-trihydroxy-7-methoxy-xanthone (Fig. 3) as does that of 4,5-di-O-methylcorymbin to the spectrum of 1,3,8-trihydroxy-5-methoxy-xanthone (Fig. 1). The dominant change on the introduction of the additional 4-methoxyl group is in both cases, a bathochromic shift of the long wavelength band.

Dimethyl ethers of I, II *and* III. In all three dimethyl ethers the free hydroxyl group is strongly hydrogen bonded and preliminary examination indicates that it is at C-8 in each case. In dimethylbellidifolin the chemical shift of the proton at C-7 is moved downfield by 10 c/s on acetylation of the free hydroxyl group while the other protons are relatively unaffected. This is in accord with shifts in the position of aromatic protons adjacent to free hydroxyl groups in 1-hydroxy-3-methoxyxanthone and 1-hydroxy-3,8-dimethoxyxanthone on acetylation (Table 1), and suggests that dimethylbellidifolin is 8-hydroxy-1,3,5-trimethoxyxanthone. Spectral similarities between dimethylbellidifolin and 4,5-di-O-methylcorymbin dimethyl ether indicate that the latter also has a free 8-hydroxyl group. Just as methylation of isobellidifolin (III) to dimethylbellidifolin produces a 15 c/s upfield displacement of the C-6 proton and a hypsochromic shift of the long wavelength UV absorption, so also does methylation of 4,5-di-O-methylcorymbin to its dimethyl ether (Table 2).

Methylation of 4,7-di-O-methylbellidin is thought to produce a dimethyl ether containing an 8-hydroxyl group by analogy with 1,3,8-trihydroxy-7-methoxyxanthone which is known[3] to form 8-hydroxy-1,3,7-trimethoxyxanthone (decussatin) on methylation. In support of this, comparable changes in the UV absorption spectra on methylation are observed in both cases (Table 2).

Biogenetic relationships. The oxidation patterns proposed for the two new xanthones are biogenetically consistent with the patterns previously reported for xanthones from the family *Gentianaceae* (Tables 3 and 4). Oxygen substituents at C-1 and C-3 are in accord with the proposed[10] acetate origin of this ring and substituents at C-5, C-7 and C-8 have all been previously observed.

[10] S. Neelakantan and T. R. Seshadri, *Current Sci. India* **30**, 90 (1961).

TABLE 2. SPECTRA OF XANTHONES AND THEIR DIMETHYL ETHERS

	UV Absorption peaks (mμ)				Chemical shift values (c/s)	
					C-6	C-7
Isobellidifolin (III)	231	251	276	342	445	401
Dimethylbellidifolin	236	251	276	322	430	401
4,5-Di-O-methylcorymbin (I)	231	250	274	352	450	405
4,5-Di-O-methylcorymbin dimethylether	231	254	277	338	435	404
1,3,8-Trihydroxy-7-methoxyxanthone	236	262	314	337		
8-Hydroxy-1,3,7-trimethoxy-xanthone	240	260	315	377		
4,7-Di-O-methylbellidin (II)	237	269	314	347		
4,7-Di-O-methylbellidin dimethylether	238	264	323	388		

TABLE 3. XANTHONES FROM *G. BELLIDIFOLIA*

	Position of substituent							
	1	2	3	4	5	6	7	8
Desmethylbellidifolin	OH		OH		OH			OH
Bellidifolin	OH		OMe		OH			OH
Isobellidifolin	OH		OH		OMe			OH
5-O-Methybellidifolin	OH		OMe		OMe			OH
* Bellidifolin dimethylether	OMe		OMe		OMe			OH
* *Corymbin*	OH		OH	OH	OH			OH
* 3-O-Methylcorymbin	OH		OMe	OH	OH			OH
4,5-Di-O-methylcorymbin (Ccrymbiferin)	OH		OH	OMe	OMe			OH
* 4,5-Di-O-methylcorymbin dimethylether	OMe		OMe	OMe	OMe			OH
* *Bellidin* (Unknown)	OH		OH	OH			OH	OH
4,7-Di-O-methylbellidin	OH		OH	OMe			OMe	OH
* 4,7-Di-O-methylbellidin dimethylether	OMe		OMe	OMe			OMe	OH

Only two oxygenation patterns are known for tetra-oxygenated xanthones from the *Gentianaceae*, namely 1,3,5,8 and 1,3,7,8 and since members of both groups have been isolated from the same genus it is probable that the two patterns represent alternative forms of ring closure of the same intermediate or intermediates e.g. a benzophenone[11] or phloroglucinol/C_7-acid.[10] The present isolation of both a 1,3,4,5,8- and a 1,3,4,7,8-oxygenated xanthone from *G. bellidifolia* gives further support to this hypothesis and constitutes the first isolation of 1,3,5,8- and 1,3,7,8-oxygenated xanthones from the same plant.

The penta-oxygenated xanthones I and II may be formed in the plant either by the oxidation of existing tetra-oxygenated xanthones or by the cyclization of a pre-oxidized intermediate. The cyclization mechanism appears to be excluded on the grounds that it would be expected to produce 1,2,3-oxygenated xanthones as well as 1,3,4- (unless

[11] J. R. Lewis and B. H. Warrington, *J. Chem. Soc.* 5074 (1964).

TABLE 4. OTHER XANTHONES FROM *GENTIANACEAE*[18]

	Position of substituent							
Genus Gentiana	1	2	3	4	5	6	7	8
Gentisin	OH		OMe				OH	
Isogentisin	OH		OH				OMe	
Genus Swertia								
Decussatin	OMe		OMe				OMe	OH
Swertinin	OMe		OMe				OH	OH
† Swerchirin	OH		OMe		OMe			OH
‡ Swertianol	OH		OH		OMe ?			OH ?

* Derivatives of natural products.

† A sample of swerchirin generously supplied by Professor G. H. Stout, University of Washington, Seattle, was shown to be identical with 5-O-methylbellidifolin by m.p., m m.p., and TLC in several solvents.

‡ Structure indefinite (see Ref. 4)

the latter is energetically preferred), and it seems therefore that the 4-methoxyl group in 4,5-di-O-methylcorymbin and 4,7-di-O-methylbellidin is a result of oxidation following γ-pyrone ring closure. A similar oxidation has been suggested to account for the co-occurrence of the flavonol glycosides quercimeritrin (3,5,7,3′,4′-oxygenation) and gossypitrin 3,5,7,8,3′,4′-oxygenation) in the same plant.[12]

EXPERIMENTAL

R_f values are quoted for TLC on silica-gel HF in a solvent mixture of benzene–ethyl acetate–EtOH 50:43:7. IR absorption spectra were determined on KBr discs using a Perkin–Elmer model 21 recording spectrophotometer. NMR spectra were measured on a Varian D.P.60 spectrometer and chemical shifts are expressed in c/s from TMS. Spectra listed in Table 1 are not repeated in this section.

4,5-Di-O-methylcorymbin (I) Chromatograph fraction C of the root extract from *Gentiana bellidifolia*,[8] on recrystallization from EtOH or acetone, gave 4,5-di-O-methylcorymbin as fine yellow needles m.p. 268°. The m.p., m m.p., R_f value (0·52) and the IR absorption spectrum were identical with those of authentic corymbiferin, ν_{max} 3330 br, 2950, 2845, 1670, 1640, 1617, 1580, 1525, 1500 br, 1445, 1360, 1315, 1287, 1240, 1195, 1170, 1110, 1075, 1056, 1000, 958, 932, 831, 819, 805, 757, 741, 697, 685, 663 cm^{-1}, λ_{max} (EtOH) 227, 255, 278, 352 mμ (log ε, 4·22, 4·27, 4·16, 4·03), λ_{max} (0·2% ethanolic NaAc) 225, 247, 281, 371 mμ, λ_{max} (0·2% NaAc, 2% H_3BO_3 in EtOH) 225 sh, 250, 279, 358 mμ. It did not reduce Fehlings solution (cf. Ref. 1).

Pyridine–acetic anhydride treatment of 4,5-di-O-methylcorymbin yielded the triacetate, m.p. 202° (Lit[1] 202–205°). The dimethyl ether m.p. 187° (Lit[1] 187·5) was prepared by overnight treatment of 4,5-di-O-methylcorymbin with diazomethane at 20°. NMR spectrum ($CDCl_3$): hydroxyl 750 (1H) aromatic 436/427 (1H) 405/396 (1H) 385 (1H), methoxyl 241 240 239 238 (12H).

Corymbin (V) 4,5-Di-O-methylcorymbin (0·017 g) in benzene (8·5 ml) was refluxed with $AlCl_3$ (0.1 g) under N_2 for 2 hr, HCl (20%, 7 ml) was then added and the mixture was heated for a further 5 min. The bright yellow precipitate (0·015 g) was removed by filtration and chromatographed in ether on cellulose to give *corymbin* which crystallized as yellow needles m.p. 320° (dec) from acetone, λ_{max} (EtOH) 224, 256, 271 sh, 281, 367, 426 sh, mμ (log ε, 4·27, 4·3, 4·29, 4·31, 4·1, ca. 3·5), λ_{max} (0·2% ethanolic NaAc) 251, 286, 378, 442 sh, mμ, λ_{max} (0·2% NaAc, 2% H_3BO_3 in EtOH) 255, 286, 375, 447 sh, mμ. Corymbin dissolved readily in cold Na_2CO_3 solution and had an R_f of 0·18. A solution in EtOH gave a red precipitate when treated with a saturated alcoholic lead acetate solution and an orange spot when treated on filter-paper with a 2% sodium molybdate solution (cf. Refs 6 and 8).

[18] T. A. Geissman, *Biogenesis of Natural Compounds* (Edited by P. Bernfeld) p. 595. Pergamon Press, Oxford (1963).

[19] J. C. Roberts, *Chem. Revs.* **61**, 592 (1961).

3-O-*Methylcorymbin* (VI). Corymbin (0·013 g) in acetone (10 ml) was refluxed over $NaHCO_3$ (0·2 g) with dry dimethyl sulphate (0·008 ml) for 9 hr in a H_2 atm. The resultant solution was evaporated to dryness and treated with dil. HCl to give a yellow precipitate (0·011 g). Chromatography of this on cellulose in benzene gave 3-O-*methylcorymbin* which crystallized from acetone, m.p. 310–314° with dec, λ_{max} (EtOH) 228, 260, 270 sh, 280 sh, 365 mμ (log ε, 3·9, 4·12, 4·06, 3·94, 3·8), λ_{max} (0·2% ethanolic NaAc) 228, 260, 291 sh, 341 sh, 369 mμ, λ_{max} (0·2% NaAc, 2% H_3BO_3 in EtOH) 228, 260, 270 sh, 280 sh, 365 mμ.

3-O-Methylcorymbin (R_f 0·48) was insoluble in Na_2CO_3 solution, gave no red precipitate with lead acetate in EtOH and gave a negative molybdate test. Overnight treatment with diazomethane at 20° gave 4,5-di-O-methylcorymbin dimethyl ether which was identified by m.p. and TLC in two different solvents. Pyridine–acetic anhydride treatment of 3-O-methylcorymbin produced a tetra-acetate which crystallized as fine white needles m.p. 250–253° from EtOH–acetone.

1,2,8-*Trihydroxy*-3-*methoxyxanthone* (VII) and 1,4,8-*trihydroxy*-3-*methoxyxanthone* (VIII). γ-Resorcylic acid (1·5 g), 2,6-dimethoxyquinol (1·7 g), $POCl_3$ (10 ml) and fused $ZnCl_2$ (3·5 g) were heated together at 75° for 1·75 hr. The red liquid produced was poured onto crushed ice and the resultant precipitate removed by ether extraction. After washing with $NaHCO_3$ aq the ether layer yielded a yellow oil which solidified on the addition of acetone to give a yellow powder (0·2 g). A further 0·15 g was isolated by ether extraction of the $NaHCO_3$ solubles. Recrystallization of this from acetone gave two compounds in approximately equal amounts.

The least soluble product, 1,2,8-*trihydroxy*-3-*methoxyxanthone* m.p. 276–280° has an R_f of 0·25 and gave a red precipitate with ethanolic lead acetate, λ_{max} (EtOH) 223, 249 sh, 254, 275, 317, 388 mμ (log ε, 4·35, 4·35, 4·38, 4·15, 4·14, 3·6), λ_{max} (0·2% ethanolic NaAc) 224, 248 sh, 253, 275, 319, 390 mμ, λ_{max} (0·2% NaAc, 2% H_3BO_3 in EtOH) 253 sh, 259, 282, 323, 413 mμ. When heated with diphenyldichloromethane[14] for 2 min at 200° it gave a pale yellow derivative which crystallized from acetone m.p. 272–273°. (Found: C, 73·7; H, 4·7, Calc. for $C_{26}H_{18}O_6$: C, 73·2; H, 4·3%) NMR spectrum ($CDCl_3$): hydroxyl 762 (1H), aromatic 470–400 (13H) 394 (1H), methoxyl 242 (3H).

The more soluble product 1,4,8-trihydroxy-3-methoxyxanthone (R_f 0·62) crystallized as pale yellow needles m.p. 269–271°. It formed no recognizable derivative with diphenyldichloromethane and no red precipitate with ethanolic lead acetate. λ_{max} (EtOH) 216, 234, 250, 264 sh, 269, 345 mμ (log ε, 4·1, 4·1, 4·1, 4·18, 4·19, 3·94). No changes were observed when the spectrum was determined in NaAc or NaAc–H_3BO_3.

4,7-*Di*-O-*methylbellidin* (II). Column chromatography of fraction D from the root extract from *Gentiana bellidifolia* gave largely desmethylbellidifolin[8], but 4,7-*di*-O-*methylbellidin* (0·011 g from 64 g roots) was isolated as a trailing band which was eluted with 30–40% ethyl acetate in benzene. This was rechromatographed in benzene on cellulose and then crystallized from hot benzene to give yellow needles m.p. 220–221°, λ_{max} (EtOH) 238, 269, 315, 346, 378 sh mμ (log ε, 4·27, 4·38, 3·75, 4·02, ca. 3·8), λ_{max} (0·2% ethanolic NaAc) 236, 272, 277 sh, 368 mμ. No change was observed in NaAc–H_3BO_3. ν_{max} 3500, 3450, 3050, 2930, 2850, 1655, 1625, 1602, 1578, 1513, 1483, 1464, 1453, 1353, 1328, 1303, 1268, 1223, 1178, 1093, 1076, 1050, 998, 978, 893, 860, 811, 763, 736, 722, 702, 663 cm^{-1}. 4,7-Di-O-methylbellidin (R_f 0·13) was readily soluble in Na_2CO_3-solution. Treatment with diazomethane overnight at 20° produced a dimethyl ether which crystallized from $CHCl_3$–acetone m.p. 192–193°. (Found: C, 61·0; H, 5·2. Calc. for $C_{17}H_{16}O_7$: C, 61·4; H, 4·9%), NMR spectrum ($CDCl_3$): hydroxyl 789 (1H), aromatic 440 (2H) 383 (1H), methoxyl 241, 238, 236 (12H).

1-*Acetoxy*-3,8-*dimethoxyxanthone*. 1,3-Dihydroxy-8-methoxyxanthone[4] was treated overnight with diazomethane to produce quantitatively, 1-*hydroxy*-3,8-*dimethoxyxanthone* m.p. 160–164°. When refluxed with pyridine–acetic anhydride for 2·5 hr this material gave 1-*acetoxy*-3,8-*dimethoxyxanthone* which crystallized from ether as colourless needles m.p. 167°.

1,3,8-*Trihydroxy*-7-*methoxyxanthone*. The sample earlier prepared[8] was further purified by chromatography on silica in benzene–10% ethyl acetate and by recrystallization from acetone to give yellow crystals m.p. 296–299° (lit[15] 300°), R_f 0·22, λ_{max} (EtOH) 237, 262, 268 sh, 314 sh, 336, 374 sh, mμ (log ε, 4·46, 4·49, 4·46, 4·05, 4·21, 3·9).

Acknowledgments—The author is indebted to Dr B. R. Thomas of this laboratory for the determination of NMR spectra and for valuable criticism of the manuscript.

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