947. *C-Glycosyl Compounds. Part IV.*[1] *The Structure of Homonataloin and the Synthesis of Nataloe-emodin.*

By L. J. Haynes, J. I. Henderson, and (in part) Jean M. Tyler.

Homonataloin is shown to have the structure (II) from its ultraviolet and infrared spectra, by periodate oxidation, and oxidation to D-glucose, D-arabinose, and nataloe-emodin monomethyl ether; the ether is shown to have structure (I; R = Me) by spectral studies and by synthesis of nataloe-emodin.[1]

Homonataloin, isolated from Natal aloes, is similar to barbaloin [2] isolated from Cape and Curaçao aloes. Early work [3] had shown the presence in Natal aloes of a pale yellow crystalline material which was called nataloin. Léger [4] claimed to have separated this material into two components which he termed nataloin and homonataloin and to which he assigned the molecular formulæ $C_{22}H_{22}O_{10}$ and $C_{23}H_{24}O_{10}$ respectively. He showed that both these compounds contained one *O*-methyl group: on prolonged (one year) treatment with acid they gave D-arabinose and with sodium peroxide they gave an anthraquinone derivative, methylnataloe-emodin (nataloe-emodin monomethyl ether) $C_{16}H_{12}O_5$, which formed a diacetate and on demethylation with hydrochloric acid at 170° gave nataloe-emodin, $C_{15}H_{10}O_5$; this in turn formed a triacetate. Structures, now known to be incorrect, were advanced for all those compounds. Tschirch and Klaveness [5] were only able to isolate homonataloin from Natal aloes but Rosenthaler [6] obtained both nataloin and homonataloin.

Through the kindness of Dr. J. W. Fairbairn, we obtained a sample of Natal aloes (which is no longer a commercial product) from the Museum of the London School of Pharmacy. Treatment of this by Léger's procedure gave homonataloin, but no nataloin was found.

Analysis of a rigorously dried sample of homonataloin showed the molecular formula to be $C_{22}H_{24}O_9$, although as normally prepared homonataloin forms a stable monohydrate. Re-examination of Léger's analytical figures shows that they correspond to $C_{22}H_{26}O_{10}$ rather than to $C_{22}H_{22}O_{10}$. Homonataloin contains one methoxyl and one *C*-methyl group and six active hydrogen atoms. The molecular weight determined by a mass-spectrophotometric method by Drs. Reed and Wilson of the University of Glasgow, whom we thank, is 432 ($C_{22}H_{24}O_9$ requires *M*, 432).

The ultraviolet spectrum of homonataloin [$\lambda_{max.}$ 222, 250 (infl.), 273 (infl.), 294, 347 mμ (log ε 4·38, 3·85, 3·85, 4·12, 3·85)] shows maxima similar in position to, although differing slightly in intensity from, those shown by barbaloin [$\lambda_{max.}$ 208, 255 (infl.), 270, 297, 363 mμ

[1] Part III, *J.*, 1959, 1033; cf. Haynes and Henderson, *Chem. and Ind.*, 1960, 50.
[2] Hay and Haynes, *J.*, 1956, 3141 and references therein.
[3] Fluckiger and Hanbury, *Arch. Pharm.*, 1871, **4**, 11.
[4] Léger, *Ann. Chim.* (*France*), 1917, **8**, 265.
[5] Tschirch and Klaveness, *Arch. Pharm.*, 1901, **239**, 231.
[6] Rosenthaler, *Pharm. Acta Helv.*, 1931, **6**, 115.

(log ε 4·41, 3·77, 3·91, 3·96, 4·05)], proving that, like barbaloin, homonataloin is a derivative of an anthrone [7] rather than of an anthraquinone. This conclusion is confirmed by the presence of only one band in the carbonyl stretching frequency region of the infrared spectrum: the position of this band, at 1638 cm.$^{-1}$, shows that the carbonyl group is hydrogen-bonded to a neighbouring α-hydroxyl group, but less strongly than that in barbaloin ($\nu_{C=O}$ 1630 cm.$^{-1}$).

Oxidation of homonataloin by ferric chloride gives D-arabinose and Léger's nataloe-emodin monomethyl ether $C_{16}H_{12}O_5$. This ether contains one methoxyl and one *C*-methyl group, is demethylated by concentrated hydrochloric acid to nataloe-emodin $C_{15}H_{10}O_5$, and is methylated by diazomethane in methanol–ether to nataloe-emodin dimethyl ether $C_{17}H_{14}O_5$. The ultraviolet spectrum of these compounds (Table 1) suggests, on the

TABLE 1.

Nataloe-emodin Me ether		Nataloe-emodin			Nataloe-emodin Me_2 ether	
		$\lambda_{max.}$ (mμ)	log ε			
$\lambda_{max.}$ (mμ)	log ε		Nat.	Synth.	$\lambda_{max.}$ (mμ)	log ε
228	4·36	232	4·30	4·42	228	4·34
275	4·22	260	4·30	4·36	272	4·20
295	4·02	290	4·00	4·10	293	3·95
400	3·80	434	3·89	4·01	396	3·76

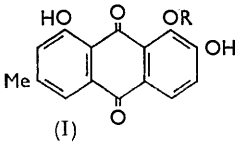
lassification of spectra of polyhydroxyanthraquinones developed by Briggs, Nicholls, and Paterson,[8] that nataloe-emodin is an anthraquinone with two α-hydroxyl groups and that the two methyl ethers each contain only one α-hydroxyl group. In the infrared spectra (Table 2) the absorption of the mono- and the di-methyl ether at 1638 and 1636 cm.$^{-1}$

TABLE 2.

	C=O stretching frequencies (cm.$^{-1}$)	
Nataloe-emodin Me ether	1658	1638
Nataloe-emodin Me_2 ether	1667	1636
Nataloe-emodin	1660	1626
Anthraquinone	1676	

respectively corresponds to the presence of the hydrogen-bonded carbonyl group [9] which is observed in homonataloin. In nataloe-emodin, the absorption is displaced to a lower frequency, showing that the carbonyl group is more strongly hydrogen-bonded. All three compounds also show bands corresponding to the presence of unassociated carbonyl groups. These spectra strongly suggest therefore that nataloe-emodin and its mono- and its di-methyl ether are respectively 1,8,β-trihydroxy-, 1,β-dihydroxy-8-methoxy-, and 1-hydroxy-8,β-dimethoxy-*x*-methylanthraquinone.

Evidence that nataloe-emodin is a 1,2,8-trihydroxy-*x*-methylanthraquinone first came from colour reactions, since with magnesium acetate [10] it gives the deep purple colour shown by 1,2-dihydroxyanthraquinones. Methylation, by diazomethane in methanol, of the phenolic hydroxyl groups of homonataloin gives a homonataloin dimethyl ether which has $\nu_{C=O}$ 1666 cm.$^{-1}$, showing that the carbonyl group is no longer hydrogen-bonded and that both α-hydroxyl groups are methylated. Permanganate oxidises this ether to 3,4-dimethoxyphthalic anhydride, confirming the presence of a 1,2-dihydroxy-system in nataloe-emodin and showing that the *C*-methyl group is not on the ring carrying these groups. It follows then that if anthraquinones from higher plants are formed from acetate units then nataloe-emodin probably has structure (I; R = H). That this is correct was shown by synthesis: condensation of



(I)

[7] Birch and Donovan, *Austral. J. Chem.*, 1955, **8**, 523; Barnes and Holfeld, *Chem. and Ind.*, 1956, 873.

[8] Briggs, Nicholls, and Paterson, *J.*, 1952, 1718.

[9] Flett, *J.*, 1948, 1441.

[10] Shibata, Takito, and Tanaka, *J. Amer. Chem. Soc.*, 1950, **72**, 2789.

m-cresol with hemipinic anhydride in the presence of aluminium chloride gives 2-(2-hydroxy-*p*-toluoyl)-3,4-dimethoxybenzoic acid [11] which on treatment with sulphuric acid undergoes ring closure with simultaneous demethylation to give 1,2,8-trihydroxy-6-methylanthraquinone identical with nataloe-emodin.

The infrared and ultraviolet spectra had shown that nataloe-emodin monomethyl ether is either the 1- or the 8-methyl ether, and the ready formation of a dimethyl ether also shows the presence of a free β-hydroxyl group. R_F values reported by Shibata, Takito, and Tanaka [10] for the paper chromatography of polyhydroxyanthraquinones in light petroleum saturated with methanol (97%) appear to fall into two groups, anthraquinones with a free β-hydroxyl group having R_F values in the range 0·04—0·52 whereas those without have R_F values in the range 0·89—0·92. The R_F values for nataloe-emodin and its mono- and di-methyl ether in this solvent system are given in Table 3.

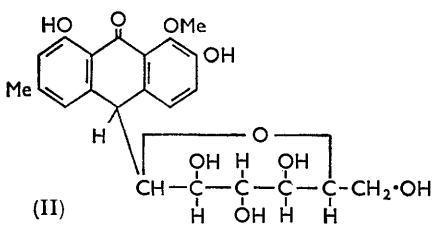
TABLE 3.

Substance	Substituents	R_F	Colour with $Mg(OAc)_2$
Nataloe-emodin	$1,2,8(OH)_3$-6-Me	0·07	Purple
,, Me ether	$2,8\text{-}(OH)_2$-1-OMe-6-Me	0·27	Orange
,, Me_2 ether	8-OH-$1,2\text{-}(OMe)_2$-6-Me	0·89	Yellow

The reactions with magnesium acetate show that the 1,2-dihydroxy-system present in nataloe-emodin is not present in its monomethyl ether. This is confirmed by periodate oxidation studies. As with aloe-emodin,[2] nataloe-emodin monomethyl ether is unaffected by sodium metaperiodate solution at 0°, but nataloe-emodin is very readily oxidised with the consumption of 1·8 mol. of oxidant. (It may be noted that periodate oxidation of catechol, resorcinol and quinol can be satisfactorily performed at 0° on a micro-scale by the usual methods, the observed consumption of oxidant after 18 hr. being 3·1, 2·75, and 1·1 mol. respectively [12].)

The monomethyl ether is thus 2,8-dihydroxy-1-methoxy-6-methylanthraquinone (I; R = Me).

As with barbaloin, homonataloin is not hydrolysed by dilute acid and consumes two mol. of periodate with production of formic acid [13] at 0°. On oxidation with ferric chloride it gives D-arabinose and on ozonolysis it gives both D-arabinose and D-glucose.[14] Neither ethylene glycol nor glycerol is formed when periodate-oxidised homonataloin is reduced with sodium borohydride and then treated with acid.[2,15] Homonataloin does not give the c our reaction with dimethyl-*p*-nitrosoaniline given by anthrones carrying only hydrogen at position 10.[16]



(II)

Homonataloin thus is 10-D-glucopyranosyl-2,8-dihydroxy-1-methoxy-6-methylanthrone (II).

The Botanical Origin of Natal Aloes.—There is some doubt in the literature [17] about the original source of Natal aloes. Paper chromatography of the juice from samples of the leaves of *Aloe candelabrum*, *A. distans*, *A. macracantha*, *A. plicatilis*, *A. ferox*, *A. vera*, *A. eru*, and *A. perryi*, with butan-1-ol saturated with water as solvent, and examination of the chromatograms by ultraviolet light after they had been exposed to ammonia, show that *A. macracantha* and *A. distans* both contain a

[11] Simonsen, *J.*, 1924, 721.
[12] Cf. Freiger, Smith, and Willeford, *J. Org. Chem.*, 1959, **24**, 91.
[13] Buchanan, Dekker, and Long, *J.*, 1950, 3162.
[14] Ali and Haynes, *J.*, 1959, 1033.
[15] Smith and Van Cleve, *J. Amer. Chem. Soc.*, 1955, **77**, 3091; Viscontini, Hoch, and Karrer, *Helv. Chim. Acta*, 1955, **38**, 642.
[16] Kariyone, *J. Pharm. Soc. Japan*, 1954, **74**, 234.
[17] Cf. Marloth, *Pharm. Acta Helv.*, 1928, **3**, 10; Bryant, *Pharm. J.*, 1933, **130**, 174.

substance with the R_F (0·68) and giving the brown fluorescence of homonataloin. Moreover, when kept in air, the spots of those substances slowly become purple, as does that of homonataloin. The appearance of the paper chromatogram of the juice from *A. distans* was virtually identical with that from our sample of Natal aloes.

Experimental

Chromatography was on Whatman No. 1 paper with the upper phase of the following solvent systems (v/v): *A*, butan-1-ol saturated with water; *B*, butan-1-ol–acetic acid–water (4 : 1 : 5); *C*, butan-1-ol–acetic acid–water (2 : 1 : 1); *D*, butan-1-ol–pyridine–water–benzene (5 : 3 : 3 : 1); *E*, ethyl acetate–pyridine–water (10 : 4 : 3); *F*, light petroleum (b. p. 47—70°) saturated with 97% aqueous methanol.[10] Ultraviolet absorption spectra were determined for ethanol solutions, infrared absorption spectra for potassium bromide discs. Aniline oxalate was used for the detection of reducing sugars.

Isolation of Homonataloin (cf. Léger [4]).—Natal aloes (78 g.) was powdered and shaken with acetone (156 ml.) for 24 hr. Undissolved solid (28 g.) was collected and refluxed with 2 : 3 aqueous ethanol (300 ml.), and the resulting solution filtered. The filtrate was left overnight. The first crop to separate crystallised from aqueous ethanol (60%), to yield a product (1A) {2·2 g., $[\alpha]_D^{17}$ −117·3° (*c* 1·108)}; and evaporation of the mother-liquor gave a crop (1B) {1·6 g., $[\alpha]_D^{27}$ −113° (*c* 1·002)}. Further evaporation of the original mother-liquor gave crops 2, 3, and 4 {respectively, 0·7, 0·4, 1·2 g., $[\alpha]_D^{27}$ −116·5°, −109·7°, −29·5° (*c* 0·953, 0·976, 1·082)}, which all crystallised from 2 : 3 aqueous ethanol.

The infrared spectra of samples 1A—3, after two crystallisations from methanol, were identical and showed peaks at 3730w, 3480s, 3220s, 2900m, 2350w; 1638s, 1610s, 1588s, 1487s, 1452m, 1440m, 1378s, 1360m, 1330m, 1294s, 1270s, 1258m, 1215s, 1173w, 1160w, 1147w, 1128m, 1110m, 1087s, 1070s, 1068s, 1040m, 1025s, 984w, 969w, 935m, 908m, 882w, 856w, 842w, 833w, 776m, 757s, 727w, 696s cm.$^{-1}$.

Sample 4, crystallised once from 60% ethanol, had a similar spectrum but showed additional peaks almost certainly due to impurities. Samples of homonataloin of m. p. 202—204°, and $[\alpha]_D$ −111·5° and −112·3° (*c* 1·121 and 1·042 respectively) (lit.,[4] $[\alpha]_D^{20}$ −112·6° in EtOAc and −149·7° in EtOH) were analysed: (*a*) Dried over P_2O_5 under reduced pressure at room temperature, no loss in weight being observed (Found: C, 58·9; H, 5·9; O, 35·4; OMe, 7·4. Calc. for $C_{22}H_{24}O_9,H_2O$: C, 58·7; H, 5·8; O, 35·5; 1OMe, 6·9%). (*b*) Dried over P_2O_5 under reduced pressure at 100° (Found: C, 59·0; H, 5·9; O, 35·6; OMe, 7·2; *C*-Me, 3·7; active H, 1·7; loss in wt., 0·9. Calc. for $C_{22}H_{24}O_9,H_2O$: *C*-Me, 3·3; 8 active H, 1·8; 7 active H, 1·6%). (*c*) Dried over P_2O_5 under reduced pressure at 140° [Found: C, 61·2; H, 5·6; O, 33·2; H_2O, 3·8 (4·0 on a 30 mg. sample). Calc. for $C_{22}H_{24}O_9$: C, 61·1; H, 5·6; O, 33·3; H_2O, 4·0%].

Chromatography of homonataloin in the solvent systems *A*, *B*, and *C* gave discrete spots of R_F 0·68, 0·69, and 0·83 respectively; streaking occurred in the basic solvents *D* and *E*. Ultraviolet absorption maxima were at 222, 250 (infl.), 273 (infl.), 294, 347 mμ (log ε 4·38, 3·85, 3·85, 4·12, 3·85, based on the hydrate).

Action of Various Reagents on Homonataloin.—Spots of a methanol solution of homonatalon were chromatographed with solvent *A*, and, after drying of the paper, were treated with the following sprays: (*a*) diazotised sulphanilic acid, which gave an orange colour showing the presence of phenolic hydroxyl groups; (*b*) periodate–permanganate [18] which gave a yellow-green spot on a red background, showing that periodate oxidation had occurred; (*c*) iodate–iodide spray which produced no iodine, showing that carboxylic acid groups were absent.

In a test with dimethyl-*p*-nitrosoaniline [16] homonataloin gave no colour change (nor did mono-*O*-methylnataloe-emodin or barbaloin), but anthrone and 4,8-dihydroxyanthrone gave respectively dark red and green solutions. With concentrated sulphuric acid (Histedt's reaction) a yellow solution was obtained that became green on exposure to nitric acid fumes. Spots of homonataloin on paper chromatograms changed from pale yellow to purple on aerial oxidation (3—6 months); homonataloin dimethyl ether changed from pale yellow to orange, and barbaloin from pale to bright yellow.

Paper chromatography showed that no reducing sugars were formed on treatment of homonataloin with N-acid at 100° for 2 hr.

[18] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.

Homonataloin decomposed on treatment with aqueous borax and phenylhydrazine hydrochloride (cf. Hauser; [19] Hay and Haynes [2]) but no product could be isolated.

Oxidation of Homonataloin by Periodate.—(a) *Qualitative.* Spots of methanolic solutions of homonataloin and barbaloin were sprayed with the reagents (sodium metaperiodate, followed by ethylene glycol, followed by potassium iodide) for the detection of 1,2,3-triols.[13] The iodine liberated by both aloins, though obscured by red oxidation products, became evident on spraying with 1% starch solution.

(b) *Quantitative.* Samples (4—5 mg.) of homonataloin, dissolved in the minimum of 50% ethanol, were oxidised at 0° with 0·04N-potassium periodate (10 ml.). Saturated aqueous borax (5 ml.), boric acid (1 g.), and 10% potassium iodide solution (5 ml.) were added after 18 hr. and the liberated iodine was titrated with 0·01N-arsenite (1% starch indicator). Periodate consumption was 2·0, 2·0, and 1·9 mols. in three experiments.

(c) *Reduction and attempted hydrolysis of the periodate oxidation product* (cf. Viscontini *et al.*,[15] Hay and Haynes [2]). Homonataloin (10 mg., 25 millimoles) in ethanol (2 ml.) was oxidised at 0° for 4 hr. with sodium metaperiodate (10 mg., 50 millimoles, in 2 ml. of water). Sodium borohydride (15 mg.) in water (2 ml.) was added and the solution left overnight at 0°. A sample (2 ml.) was hydrolysed with 2N-hydrochloric acid (2 ml.) at 100° for 15 min. The hydrolysate, examined (with ethylene glycol and glycerol as standards) by paper chromatography with solvent *E*, gave no spot corresponding to glycerol (R_F 0·43) or ethylene glycol (R_F 0·54) after spraying with the periodate–permanganate reagent.[18]

Oxidation of Homonataloin by Ferric Chloride.—Homonataloin (1·5 g.) was treated with ferric chloride solution [20,2] (7·5 g. in 22·5 ml. of water; the homonataloin was not completely soluble). (i) The dark toluene extract was extracted with sodium hydrogen carbonate solution until the aqueous phase was colourless. Evaporation of the toluene solution to dryness gave a residue (70 mg.) of m. p. 208—228°. Purification by sublimation was unsuccessful. Crystallisation from ethanol (charcoal) yielded orange needles (30 mg.), m. p. 235—236°, of mono-*O*-methylnataloe-emodin (lit.,[4] m. p. 238°) [Found: C, 67·9; H, 4·0; *C*-Me, 3·7. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·3; 1*C*-Me, 5·3%], $\lambda_{max.}$ 228, 275, 295, 400 mμ (log ε 4·36, 4·22, 4·02, 3·80), $\nu_{max.}$ 3680w, 3350s, 2870w, 2340m, 1935w, 1915w, 1860w, 1840w, 1820w, 1800w, 1790w, 1770w, 1755w, 1730w, 1713w, 1700w, 1680w, 1658m, 1638s, 1615m, 1555s, 1535w, 1520w, 1505w, 1495w, 1480s, 1460m, 1447m, 1435w, 1417w, 1365m, 1338w, 1293s, 1274s, 1203m, 1156w, 1133w, 1140m, 995w, 928w, 863m, 852w, 798s, 760w, 749m cm.$^{-1}$. With the solvent system *F*, by the ascending method, the product had R_F 0·27 and gave an orange spot with methanolic magnesium acetate spray.[10]

(ii) The original highly coloured aqueous fraction (after toluene extraction) was extracted with pentyl alcohol (10 × 50 ml.), and the aqueous portion treated with resins [Dowex W 50 (H) and Dowex 2(OH)] to remove ferrous and chloride ions. The resulting neutral solution was evaporated under reduced pressure to small volume, a trace of solid that had separated was removed, and the filtrate was freeze-dried. The resulting syrup, which was strongly lævorotatory, did not crystallise but was identical on chromatography in solvents *C*, *D*, and *E* with arabinose (xylose and glucose were also run as standards). The benzoylhydrazone [21] (28 mg. prepared from 59 mg. of the sugar) had m. p. 203—204° (twice crystallised from methanol) alone or mixed with D-arabinose benzoylhydrazone of m. p. 204—205°. Authentic D- and authentic L-arabinose benzoylhydrazone (m. p. 201—202°) gave, on admixture, a depression of m. p. (196—198°) (cf. Ali and Haynes [14]). Repetition of the ferric chloride oxidation of homonataloin (1·5 g.) in 50% ethanol (30 ml.) gave a further sample (58 mg.) of mono-*O*-methylnataloe-emodin of m. p. 235—236°.

Ozonolysis of Homonataloin.[14]—Ozonised oxygen from a high-tension discharge apparatus (7500 v) was passed through a cooled solution of homonataloin (700 mg.) in 1 : 1 aqueous ethanol (100 ml.) for 2 hr., the colour changing yellow to red to orange-yellow. The solution was steam-distilled until ethanol had been removed and the residue was ozonised for another 3 hr. The dark brown residue present after steam-distillation was extracted with ether (4 × 200 ml.), and saturated lead acetate solution (25 ml.) added to the aqueous layer. The precipitate was filtered off after 1 hr. and excess of lead was removed by three treatments with hydrogen sulphide. The final colourless solution was evaporated to dryness under reduced pressure and

[19] Hauser, *Pharm. Acta Helv.*, 1931, **6**, 79.
[20] Cahn and Simonsen, *J.*, 1932, 2573.
[21] Hirst, Jones, and Woods, *J.*, 1947, 1048.

yielded a pale yellow syrup (approx. 230 mg.). Chromatography of the product with solvents *C*, *D*, and *E* (with glucose, arabinose, and xylose as standards) showed it to contain glucose and arabinose. Separation of the sugars on Whatman 3MM paper with solvent *D* gave pure (by chromatography) specimens of (*a*) D-arabinose (120 mg.) identified by its benzoylhydrazone derivative,[21] m. p. and mixed m. p. 203—204° (from ethanol), and (*b*) D-glucose (90 mg.), which gave a *p*-nitroaniline derivative,[22] m. p. and mixed m. p. 182—183°, $[\alpha]_D^{28}$ −158° (*c* 0·164 in 10% aqueous pyridine) {lit.,[22] $[\alpha]_D^{20}$ −150° ⟶ −215° (*c* 0·24)}.

Methylation of Homonataloin.—Homonataloin (250 mg.) in methanol (50 ml.) was set aside overnight with ethereal diazomethane (50 ml. prepared from 1·0 g. of toluene-*p*-sulphonylmethylnitrosamide [23]). The solvents were removed under reduced pressure. Crystallisation of a portion of the residue from several solvents was attempted, but was unsuccessful. Partial evaporation of an ethyl acetate solution of the product was most successful and gave *homonataloin dimethyl ether* as a light brown solid of m. p. 144—147° [Found: 60·5; H, 5·9; OMe, 18·6. $C_{21}H_{19}O_6(OMe)_3$, H_2O requires C, 60·2; H, 6·3; OMe, 19·4%]. Chromatography with solvent *A* gave a single spot of R_F 0·70 (cf. homonataloin, 0·68). The infrared absorption peaks were at 3400s, 2900s, 2850m, 2330w, 1666s, 1610s, 1580m, 1535w, 1487s, 1454s, 1413m, 1361w, 1320w, 1306w, 1270s, 1155m, 1087s, 1053s, 1011m, 970s, 893w, 838m, 780m, 742w, 723w, 696m cm.$^{-1}$.

Permanganate Oxidation of Methylated Homonatalion.—2·5% Potassium permanganate solution (100 ml.) was added during 0·5 hr. to the methylated homonataloin suspended in a little water. The mixture was heated at 100° for 3 hr. After cooling, precipitated manganese dioxide was removed and the filtrate was acidified and continuously extracted with ether. Evaporation of the extract under reduced pressure gave a yellow solid which on sublimation in a high vacuum at 150° gave a cream-coloured product (23 mg.) of m. p. 148—160°. Two further sublimations gave a white solid (10 mg.), m. p. 161—166°, that gave a positive resorcinol test.[24] The product did not depress the m. p. (165—167°) of authentic hemipinic anhydride, and the infrared spectra were identical [Found: C, 56·3; H, 4·05; OMe, 29·1. Calc. for $C_8H_2O_3(OMe)_2$: C, 57·7; H, 3·9; OMe, 29·8%].

Di-O-methylnataloe-emodin.—A solution of ethereal diazomethane (10 ml., prepared from 0·2 g. of toluene-*p*-sulphonylmethylnitrosamide [23]) was added to a solution of the monomethyl ether (47 mg.) in 1 : 1 methanol–ether (10 ml.), and the mixture left overnight. The solution was evaporated to small volume and, on cooling, orange needles separated. After crystallisation from methanol di-*O*-methylnataloe-emodin (25 mg.) had m. p. 204—206° [Found: C, 69·7; H, 4·8; OMe, 20·3. Calc. for $C_{15}H_8O_3(OMe)_2$: C, 68·5; H, 4·7; OMe, 20·8%], $\lambda_{max.}$ 228, 272, 293, 396 mμ (log ε 4·34, 4·20, 3·95, 3·76), $\nu_{max.}$ 3480w, 2870m, 2820w, 2310w, 1667m, 1636s, 1563s, 1537w, 1513w, 1483s, 1450m, 1415m, 1385w, 1365s, 1332s, 1280s, 1265s, 1206s, 1162w, 1140w, 1070s, 1033m, 995m, 962s, 938m, 906w, 863m, 843w, 833w, 817m, 802m, 786m, 764w, 750s, 706w, 695w, 666w cm.$^{-1}$. On paper chromatography with solvent *B* the compound ran at the solvent front, but in solvent *F* (ascending technique) had R_F 0·85, and gave a yellow spot with the methanolic magnesium acetate spray.[10]

Demethylation of Mono-O-methylnataloe-emodin (*cf.* Léger [4]).—Mono-*O*-methylnataloe-emodin (10 mg.) was heated with concentrated hydrochloric acid (0·5 ml.) at 170—180° for 12 hr. No reaction appeared to have occurred. The crystalline product was collected and washed with water. Crystallisation from methanol afforded orange needles of m. p. 205—225°. Sublimation in a high vacuum gave a product (4 mg.) consisting of scarlet needles, m. p. 212—213°. The product (0·5 mg.) in glacial acetic acid showed no fluorescence in ultraviolet light [25] and was thus not a 1,4-dihydroxyanthraquinone. After chromatography with solvent *F* the product, R_F 0·07, gave a purple spot with the magnesium acetate spray [10] (a 1,2-dihydroxyanthraquinone system was indicated). The ultraviolet absorption spectrum had $\lambda_{max.}$ 232, 260, 290 (infl.), 432 (log ε 4·30, 4·30, 4·00, 3·89). The infrared absorption peaks were at 3550m, 3200m, 2930w, 2320w, 1660m, 1626s, 1555w, 1537w, 1455s, 1435m, 1423m, 1335s, 1212w, 1200w, 1135w, 1075w, 1033m, 866m, 822m, 746s, 695w cm.$^{-1}$.

Synthesis of 1,2,8-*Trihydroxy*-6-*methylanthraquinone* (*Nataloe-emodin*).—2-(2-Hydroxy-*p*-toluoyl)-3,4-dimethoxybenzoic acid [11] was crystallised to constant m. p. (237—238°) from

[22] Weygand, Perkow, and Kuhner, *Ber.*, 1951, **84**, 594.
[23] DeBoer and Backer, *Rec. Trav. chim.*, 1954, **73**, 229.
[24] Feigl, "Spot Tests," Elsevier Publ. Co., Inc., New York, 1946, p. 360.
[25] Raistrick, Robinson, and Todd, *Biochem. J.*, 1934, **28**, 559.

diluted acetic acid (lit., m. p. 229—230°). After cyclisation of the acid (1·2 g.) in concentrated sulphuric acid (6 ml.) at 150—160° for 0·5 hr., the mixture was poured on ice (50 g.), and the precipitated solid was filtered off. Rigorous drying over P_2O_5 *in vacuo* gave a black solid (127 mg.) which in a high vacuum at 80—185° gave a scarlet sublimate (64 mg.), m. p. 205—206°. Re-sublimation in a high vacuum at 175—185° gave scarlet needles (55 mg.), m. p. 216—217°, of 1,2,8-*trihydroxy*-6-*methylanthraquinone* (Found: C, 67·0; H, 4·0; OMe, 0. $C_{15}H_{10}O_5$ requires C, 66·6; H, 3·7%). On chromatography in solvent *F* the compound was identical with nataloe-emodin and had R_F 0·07 and gave a purple colour with the magnesium acetate spray.[10] The m. p. of the synthetic product was not depressed on admixture with nataloe-emodin (m. p. 212—213°) obtained from homonataloin. The ultraviolet absorption spectrum [$\lambda_{max.}$ 232, 260, 291 (infl.), 434 mμ; log ε 4·42, 4·36, 4·10, 4·01] was identical (though the log ε values are slightly higher) with that of nataloe-emodin, as was the infrared absorption.

Synthetic nataloe-emodin (3·27 mg.) in ethanol (10 ml.) was oxidised with 0·01M-potassium periodate (10 ml.) at 0°. Aliquot parts (3 × 5 ml.) were withdrawn after 18 hr. and saturated borax solution (2·5 ml.), boric acid (0·5 g.), and potassium iodide (0·5 g.) were added to each sample. The liberated iodine was titrated with 0·01N-arsenite (1% starch indicator). Periodate consumption was 1·77 mols.

We thank the Tropical Products Institute for a Research Studentship (to J. I. H.) and the Royal Society and Nuffield Foundation for a Bursary (to J. M. T.).

CHEMISTRY DEPARTMENT, UNIVERSITY COLLEGE OF THE WEST INDIES,
KINGSTON 7, JAMAICA, W.I. [*Received, February 19th*, 1960.]