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NEW CHROMENOCHALCONES FROM *FLEMINGIA*

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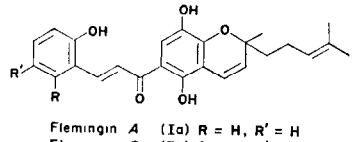
Key Word Index—*Flemingia grahamiana*, *Flemingia congesta*, *Flemingia bracteata*, Leguminosae, chromenes, chalcones, photooxidation

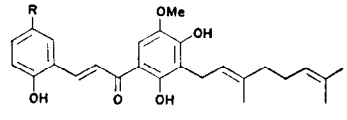
Abstract—2-Methyl-2-(4′-methylpent-3′-enyl)-5,8-dihydroxy-6-(4-hydroxycinnamoyl)-chromene (flemingin-*D*) has been isolated from inflorescences of *Flemingia congesta*, together with the known flemingin-*C* and two other chalcones These (flemingin-*E* and -*F*) are allylic alcohols which differ from flemingin-*D* by an additional OH group in the side chain Photooxidation of model 2-methyl-2-(4′-methylpent-3′-enyl)-chromenes gave pairs of allylic alcohols with the same structural feature The known flemingin-*A*, -*B*, -*C* and homoflemingins have been isolated from *F grahamiana*, and another new chalcone from *F bracteata*

INTRODUCTION

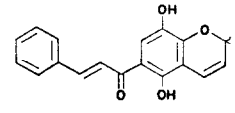
WE BECAME interested in the tropical genus *Flemingia* (syn *Moghania*, Leguminosae) when we investigated the constituents of Wars, an African drug which is stated to consist of powdered seed pods of F *rhodocarpa* [1] From this drug we isolated[2] three chromenochalcones, the flemingins-*A*, -*B*, -*C* (I), and the corresponding open-chain chalcones, desoxyhomoflemingin (IIa)[3] and homoflemingin (IIb) [2] Later we[4] and Adityachaudhury[5] isolated flemichapparin-*A* (III), together with 2,4,4′-trihydroxychalcone, from the aerial parts of *F chappar* It seemed thus possible that the unusual hydroxylation pattern in both rings of the chalcones, i e the presence of hydroxyl groups *para* to those coming from the usual biosynthesis via acetate could be a characteristics of chalcones from *Flemingia* We report here on the investigation of three *Flemingia* species, namely *F. grahamiana*, *F congesta* and *F. bracteata*, in which similar compounds have been found



Flemingin *A* (Ia) R = H, R′ = H
Flemingin *B* (Ib) R = OH, R′ = H
Flemingin *C* (Ic) R = H, R′ = OH



(IIa) R = H
(IIb) R = OH



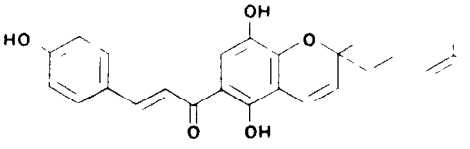
(III)

RESULTS

Inflorescences of *F grahamiana* from Uganda were extracted with ether The extract appeared completely identical to that of Wars therefore this species contains flemingins-*A*, -*B*, -*C*, desoxy- and homo-flemingin It is interesting that the 2 species *F rhodocarpa* and *F grahamiana* are reported to be identical [6]

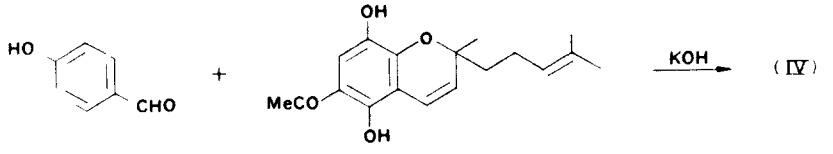
[1] PAVOLINI, T and GAMBARIN, F (1957) *Agrochimica* **2**, 88
[2] CARDILLO, G , MERLINI, L and MONDELLI, R (1968) *Tetrahedron* **24**, 497
[3] CARDILLO, G , MERLINI, L , MONDELLI, R and SELVA, A (1967) *Ric Sci* **37**, 826
[4] CARDILLO, B , GENNARO, A , MERLINI, L , NASINI, G and SERVI, S (1970) *Tetrahedron Letters* 4367
[5] ADITYACHAUDHURY, N and KIRTANIYA, C L (1970) *J Indian Chem Soc* **47**, 1013
[6] KAKOOKO, A B , personal communication

The material of *F congesta* collected in India was a mixture of leaves and flowers, that was extracted as such Four yellow compounds were separated by chromatography of the ether extract, besides carotenoids The first (IV) has a UV spectrum typical of a chalcone The MS shows a molecular peak at 406 *m/e*, and fragments at 391 (M-15), 363 (M-43), 323 (M-83), 286 (M-120), 203 (M-120-83) The NMR spectrum (acetone-d_6) shows the presence of one methyl group linked to a carbon carrying an oxygen (*s*, 1 44 δ), two methyl groups on a sp^2 carbon with no hydrogen (1 54 and 1 62), four protons at high field (1 5–2 2), one vinylic hydrogen adjacent to a CH_2 (5 10, large triplet), the *AB* system of a chromene ring (5 72, 6 76, *J* 10), four protons on a *para*-substituted aromatic ring (A_2B_2, 6 97 and 7 76), one aromatic proton (*s*, 7 53), the *AB* system of a chalcone (7 65 and 7 86, *J* 16) and one chelated OH (15 35 δ) All these data, compared with those obtained already for flemingins,[2] unequivocally establish the structure (IV) for this compound, that we propose to call flemingin-*D*



Flemingin *D* (IV)

Particularly, the M-15 and M-83 peaks in the MS correspond to the formation of a stable pyrylium ion by loss of one or the other of the alkyl groups in 2, and the M-120 peak to the loss of a hydroxystyrene fragment from IV, probably via the flavanone Confirmation for this structure came from its synthesis although in low yield, by condensation of *p*-hydroxybenzaldehyde with the chromene V

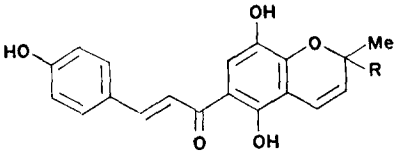


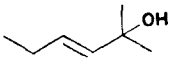
(V)

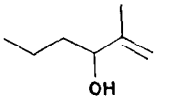
The second isolated chalcone has TLC behaviour, m p , UV, IR, MS and NMR spectra identical to those of flemingin-*C* (Ic) The identification was confirmed by direct comparison

The two other chalcones (VI and VII), that we propose to call flemingin-*E* and -*F*, were very difficult to separate from each other They have the same UV spectrum, which is also identical to that of IV The MS of both show the presence (M = 422) of one oxygen atom more than in IV, and this oxygen must be in the side chain The most important fragmentation is indeed M-99, i e M-$C_6H_{11}O$, corresponding to the formation of the stable pyrylium ion, which on turn breaks down to the M-99-120 ion The NMR spectra of VI and VII confirm this assumption and account for the correct formulae of both flemingin-*E* and -*F*

The pattern of aromatic and heterocyclic protons in both compounds is identical to that in IV The structure of the side chain in position 2 of VI is demonstrated by the presence of three singlets of methyl groups on a carbon carrying an oxygen, of the complex multiplet of a CH=CH (5·48–5·60) adjacent to a methylene, which appears as a multiplet at 2 45 δ On the other hand, in the spectrum of VII there are only two methyl groups, one at the usual position for a 2-methylchromene (1·46), and the other on a vinylic carbon (1·70, with small allylic coupling), the triplet of a $-CH_2-C\underline{H}O-$ hydrogen (4·10), and a $=CH_2$ group (4 46 and 4·54)

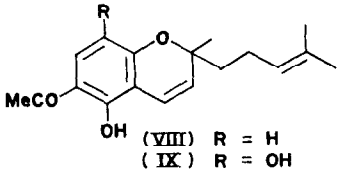


Flemingin *E* (VI) R = 

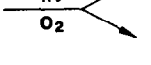
Flemingin *F* (VII) R = 

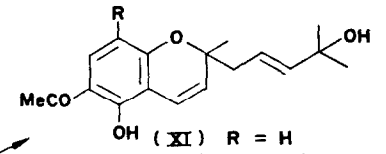
The structures thus established for VI and VII strongly suggest that they could be oxidation products of a common substrate, such as IV or a precursor of it Although VI and VII are the first chromenes with such a side chain to be found in a natural source, these structural features have been observed in the plastochromanols,[7] and in a few isoprenylphenols [8] The possibility of oxidation of terpenes by chlorophyll-sensitized photooxidation has been emphasized[9] and examples of generation of such allylic alcohols by this process are known [10] It is also worth mentioning that photooxidation of an isoprenyl side chain has been proposed by Polonsky[11] as a possible biosynthetic step in the cyclization of isoprenylphenols to chromenes.

In order to check the chemical feasibility of this reaction, we subjected VIII and IX to photooxidation sensitized by hematoporphyrin.

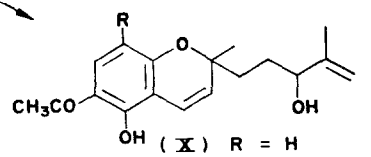


(VIII) R = H
(IX) R = OH





(XI) R = H
(XIII) R = OH

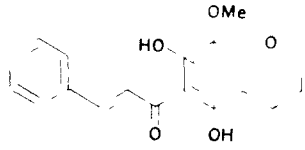


(X) R = H
(XII) R = OH

[7] Peake, I R , Dunphy, P J and Pennock, J F (1970) *Phytochemistry* **9**, 1345
[8] Chan, W R , Taylor, D R and Willis, C R (1967) *J Chem Soc* C, 2540
[9] Dunphy, P J (1971) *Chem Ind (London)* 731
[10] Foote, C S (1968) *Accounts Chem Res* **1**, 104, Schulte-Elte, K H , Gadola, M and Muller, B L (1971) *Helv Chim Acta* **54**, 1870, Cavill, G W K and Coggiola, I M (1971) *Australian J Chem* **24**, 135
[11] Fourrey, J L , Rondest, J and Polonsky, J (1970) *Tetrahedron* **26**, 3839

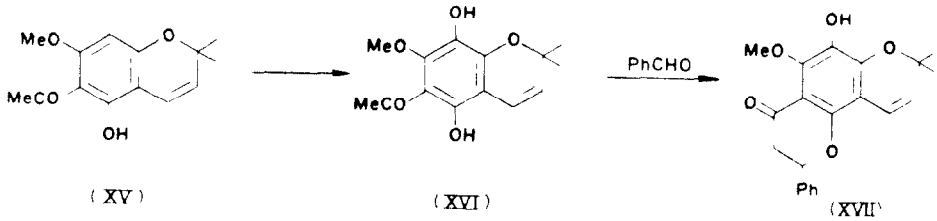
After reduction of the hydroperoxides with triphenylphosphine, we obtained the two allylic alcohols from VIII in 50% yield after purification The yield was lower for the hydroquinones XII and XIII, probably due to their sensitivity to oxidation The MS and NMR spectra of X–XIII are completely consistent with the structures given and support also the structures of VI and VII

The last species examined was *F bracteata*, from the leaf extract a small amount of a chalcone (XIV) was obtained Its MS has a molecular peak at 352 *m e*, and fragments at 337 and 233 (M-104), clearly indicating that ring 4 is not substituted The presence of a 2,2-dimethylchromene ring, of a methoxyl and of a chelated OH is apparent from the NMR spectrum No other information being available, due to the small amount of the substance, we can only formulate a partial structure (XIV)



(XIV)

Attempts to synthesize one of the isomers according to the following scheme



(XV) (XVI) (XVII)

afforded only a cyclized product, the flavanone XVII

EXPERIMENTAL

UV spectra (λ_{max} in nm) were measured in 95% EtOH NMR spectra (values in δ, J in Hz, TMS as internal standard) were measured with Varian A60 or XL100 spectrometers MS with a Hitachi RMU6D instrument, at 70 eV (80 μA), samples being directly introduced in the ion source at 250 Column chromatography was performed with silicagel Merck 0 05–0 20 mm, TLC with Merck HF_{254} Most of the compounds described appeared as low-melting or glassy solids, and they were in too low amount to be crystallized Their purity was checked by TLC

Flemingia grahamiana Inflorescences of *F grahamiana* collected in Uganda were extracted with ether on a steam bath TLC of the ext with $CHCl_3$–Et_2O, 2 1 and hexane–AcOEt, 4 1 show that the constituents were identical to those present in a sample of Wars [2]

F congesta 400 g of dried leaves and flowers of *F congesta* collected in India were extd with hexane, then with ether in a Soxhlet, and the Et_2O ext chromatographed through silicagel with hexane–AcOEt The main fraction, eluted with hexane–AcOEt, 17 3 was purified by prep TLC with hexane AcOEt, 2 1, to give, in the order, 70 mg of *flemingin D* (IV), yellow solid, UV 278, 286, 375 (ϵ 11 100, 11 100, 24 200), MS and NMR see text *flemingin-E* (VI), UV 278, 286, 375 (ϵ 12 150, 12 100, 26 800), MS 422, 404, 361, 351, 323, 241, 231, 203, 165, 147, 120, NMR (acetone-d_6) 3 Me–O (1 16, 1 18, 1 44), R–CH_2–CH (*m* 2 45), CH=CH (5 78, 6 78, *J* 10), 4 arom H (A_2B_2, 6 94, 7 82), 1 H (*s*, 7 56), Aryl–CH=CH–CO (7 70, 7 86, *J* 16), 1 OH (15 7), tetraacetate (with NaOAc and Ac_2O) MS 590, 548 506, 464 449, 422, 407, 365, 323, 203, *flemingin F* (VII), UV 278, 287, 375 (ϵ 12 950, 12 900, 26 000) MS 422, 404, 389, 361, 351, 323, 284, 203, 165, 147, 120, NMR ($CDCL_3$) Me–C–O (1 46), CH_3–C=CH (1 70), CH_2–CHO– (*m*, 4 10), $-CH_2$ (4 26 and 4 54), CH=CH

(5 52, 6 80, *J* 10), 1 H (*s*, 7 63), 4 arom H (A_2B_2, 6 84, 7 85), Aryl-CH=CH-CO (7 95, 8 60, *J* 16), 1 OH chel, tetraacetate (with NaOAc and Ac_2O), MS 590, 575, 548, 533, 506, 488, 473, 449, 407, 365, 245, 203

The following fraction, also eluting with hexane–AcOEt, 17 3, was purified by prep TLC with hexane–AcOEt, 2 1 to give 100 mg of *flemingin C* (Ic), m p 185° (toluene), identical in any respect to an authentic sample [2]

F bracteata The hexane extract of leaves of the plant, collected in India, was chromatographed through silicagel with hexane–AcOEt (19 1) A small fraction containing a sterol and a yellow compound was purified by TLC with hexane–C_6H_6, 1 1 to give the chalcone XIV, MS 352, 337, 233, NMR (acetone-d_6) 2 Me–C–O (1 46, 1 47), 1 OMe (3 82), CH=CH (5 65, 6 60 *J* 10), 5 arom (7 4–7 7), Aryl-CH=CH-CO (7 92, 8 30, *J* 15), 1 OH (14 08)

Synthesis of Flemingin-D 90 mg of 2-methyl-2-(4′-methylpent-3′-enyl)-5,8-dihydroxy-6-acetylchrom-3-ene (V)[12] were treated with 40 mg benzaldehyde and 2 ml 50% KOH in 5 ml MeOH under N_2, and the mixt stirred 6 hr at room temp After TLC with $CHCl_3$–Et_2O (2 1), the product (IV) was found to be identical to the natural product

Photooxidation of VIII *and* IX O_2 was bubbled for 4 hr into 200 mg VIII[12] and 30 mg hematoporphyrin in 80 ml MeOH under irradiation with Wood light Evapn, extn into Et_2O, boiling with excess Ph_3P (200 mg), evapn and prep TLC with C_6H_6–Et_2O (9 1) gave 30 mg of X, viscous oil, MS 302, 287, 284, 203, 185, NMR ($CDCl_3$) Me–C–O (1 41), CH_3–C=CH (1 70), 4 H (1 65–1 80), MeCO (2 51), CH_2–CHO– (*m*, 4 05), =CH_2 (4 43, 4 53), CH=CH (5 50, 6 76, *J* 10), 2 arom (*AB*, 6 30, 7 49, *J* 8 5), 1 OH (12 8) and 50 mg of XI, MS 302, 284, 269, 203, 185, NMR ($CDCl_3$) 3 Me–C–O (1 21, 1 21, 1 42), CH_2–CH= (*m*, 2 40), MeCO (2 50), CH=CH (5 50, 6 75, *J* 10), 2 arom (6 30, 7 48, *J* 8 5), CH=CH–CH_2 (*m*, 5 6–5 7), 1 OH (12 9) A similar reaction on IX (300 mg)[12] gave a small amount of XII (MS 318, 300, 285, 249, 219, 201) and XIII (MS 318)

Synthesis of XVII 0 5 g of 2,2-dimethyl-5-hydroxy-6-acetyl-7-methoxychromene (XV)[13] were dissolved in 10 ml 6% NaOH and slowly added with 1 g $K_2S_2O_8$ dissolved in 25 ml H_2O HCl treatment after 1 night, extn with Et_2O, addn of 10 ml conc HCl, 50 ml $CHCl_3$, boiling 1 hr, extn with $CHCl_3$ and TLC with C_6H_6–Et_2O, 9 1 gave 50 mg of 2,2-dimethyl-5,8-dihydroxy-6-acetyl-7-methoxychromene (XVI), NMR (CCl_4) 2 Me–C–O (1 46), MeCO (2 58), OMe (4 33), CH=CH (5 40, 6 62, *J* 10) MS 264, 249 Condensation of 20 mg XVI with benzaldehyde in MeOH with conc KOH gave, after working up and prep TLC, some mg of XVII, MS 352, 337, 248, 233, 191, NMR (CCl_4) 2 Me–C–O (1 52), Ph–CHO–CH_2– (*ABX*, δ_A = 2 35, δ_B = 2 45, δ_X = 5 26, $J_{AX} \simeq 12$, $J_{BX} \simeq 3\,5$, $J_{AB} \simeq 17$), OMe (3 90), CH=CH (5 45, 6 58, *J* 10), 5 arom. H (7 2–7 4)

Acknowledgements—We are indebted to Mr A G Kenyon (Tropical Products Institute, London) for help in providing the material

[12] BANDARANAYAKE, W M, CROMBIE, L and WHITING, D A (1971) *J Chem Soc* C, 804
[13] BANDARANAYAKE, W M, CROMBIE, L and WHITING, D A (1971) *J Chem Soc* C, 811