Chemistry of the Annonaceae, Part 18. Benzylated Indoles and Dihydrochalcones in Uvaria angolensis from Tanzania

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CHEMISTRY OF THE ANNONACEAE, PART 18.[1] BENZYLATED INDOLES AND DIHYDROCHALCONES IN *UVARIA ANGOLENSIS* FROM TANZANIA

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ABSTRACT.—Full details[2] on the isolation and structure elucidation of three dihydrochalcones and four indoles with 2-hydroxybenzyl or related substituents, from the stem bark of *Uvaria angolensis*, are reported, with particular emphasis being placed on high-field [1]H-nmr and ^{13}C-nmr data. The indoles represent a novel class of natural product and have been given the trivial names uvarindole-A [4, 1,2,3-tri-(2-hydroxybenzyl)indole], uvarindole-B [6, 1,2,3,5-tetra(2-hydroxybenzyl)indole], uvarindole-C [7, 2-(2-hydroxybenzoyl)-3-(2-hydroxybenzyl) indole], and uvarindole-D [11, 1,2,2-tri(2-hydroxybenzyl)dihydroindole-3-one].

Uvaria angolensis Oliv. (Annonaceae) is a liane, scandent shrub or small tree occurring widely throughout tropical Africa, from Sierre Leone to Tanzania and Zambia (1). From material collected in Nigeria, Hufford and Oguntimein (2,3) have reported a number of dihydrochalcones (DHCs) and flavanones substituted at C-3' and/or C-5' (C-6 and/or C-8 in the case of flavanones) with either methyl or 2-hydroxybenzyl groups. Two of the DHCs, uvaretin (1) and isouvaretin (2), were considered to be responsible for the antimicrobial and cytotoxic activities of root extracts of this species (3). We have recently examined a sample of stem bark of *U. angolensis* from East Africa belonging to what Verdcourt (1) considers to be the discrete variety "A." This material has yielded a wide range of 2-hydroxybenzylated derivatives including DHCs, indoles, and sesquiterpenes, the latter two groups representing novel types of natural products. In this paper, we report on the DHCs and give a more detailed account of the indoles, on which a preliminary report has already been published (4).

RESULTS AND DISCUSSION

By initial column chromatography and subsequent circular preparative tlc, three DHCs and four indoles were isolated. The most abundant DHC (yield 0.18%) was identified as uvaretin (1) which has previously been isolated from this species (2,3). A second DHC (0.09%) analyzed for $C_{30}H_{28}O_6$, which is equivalent to 1 plus an additional 2-hydroxybenzyl unit. A comparison of spectral data with that published confirmed its identity as the 3',5'-disubstituted diuvaretin (2) which has previously been recorded only from *Uvaria chamae* (5).

The third, minor, DHC (0.006%) analyzed as $C_{29}H_{24}O_5$. It lacked the methoxyl substituent of both 1 and 2 and, in addition, had lost the elements of H_2O through linkage of one of the benzyl hydroxy groups to the B-ring of the chalcone to form a xanthene nucleus. Cyclization could not involve C-2' of the DHC as ^{1}H nmr indicated a chelated hydroxy function so requiring the involvement of either the hydroxy at C-4' or C-6' in the xanthene. The known DHC, chamuvaritin (3), also previously isolated from *U. chamae* (6), was indicated by comparison of chemical and spectral data for the isolated DHC with that published. This was supported by the ^{13}C nmr (Table 1) which revealed almost identical resonances for the two benzyl methylenes suggesting that they

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[1]For Part 17, see I. Muhammad, P.G. Waterman, and D.W. Thomas, *J. Nat. Prod.*, **48**, 328 (1985).

[2]For a preliminary report, see Waterman and Muhammad (4).

1   R=H
2   R= -C-
        H₂

3
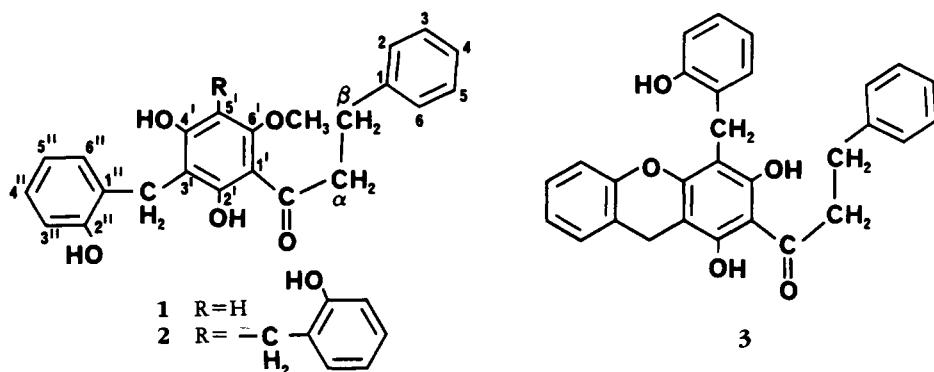
were in similar environments, e.g., with one adjacent hydroxyl. Resonances for C-1″ and C-2″ in **3** were in good agreement with published data for xanthenes (7).

In the course of this work, ^{13}C-nmr spectra were obtained for all three DHCs (Table 1). Chemical shifts for **1** and **2** had been reported previously (2), but only at low field where not all signals were distinguished.

TABLE 1. ^{13}C-NMR Spectra of Benzylated Dihydrochalcones

Carbon	Compound		
	1[a]	**2**[b]	**3**[a]
1	142.65	141.05	142.06
2,6	127.27	128.34[c]	128.65[d]
3,5	129.12	128.32[c]	128.59[d]
4	126.60	126.34	126.11
β-CH₂	31.40	31.05	30.80
α-CH₂	46.36	43.83	45.94
C=O	205.40	206.17	206[s]
1′	107.81[d]	109.08[e]	109.52[f]
2′	163.12[g]	159.09[h]	159.61[i]
3′	109.07[d]	113.47[e]	104.85[f]
4′	165.50[g]	161.15[h]	153.14[j]
5′	91.88	111.85[e]	100.38[f]
6′	162.62[g]	158.63[h]	162.80[i]
3′-CH₂	22.74	23.07	22.13[k]
1″	126.60	126.06[l]	120.70
2″	154.39	152.51[m]	150.98
3″	115.91	115.68[h]	116.24
4″	129.18	127.92[o]	127.91[p]
5″	120.68	121.27[q]	124.24
6″	131.26	132.10[r]	129.55
5′-CH₂	—	23.63	22.23[k]
1‴	—	125.94[l]	127.24
2‴	—	152.49[m]	152.47[j]
3‴	—	115.54[n]	115.16
4‴	—	127.74[o]	127.65[p]
5‴	—	121.21[q]	121.08
6‴	—	131.46[r]	131.38
OMe	56.02	63.53	—

[a]Run in $(CD_3)_2CO$, **1** at 62.6 MHz and **3** at 90.56 MHz.
[b]Run in $CDCl_3$ at 90.56 MHz.
[c-r]Signals with the same superscript are interchangeable.
[s]Signal not visible under that for solvent,

TABLE 2.   ¹H-NMR Spectra of Benzylated Indoles

| Compound	N-CH$_2$	C-CH$_2$	NH	OH	H-4(3')	H-5(4')	H-6(5')	H-7(6')	4-5	4-6	5-6	5-7	6-7
											J-values		
4	5.22s	4.14s	—	5.50s	7.42dd	7.04ddd	7.11ddd	7.20dd	7.5	2.0	8.0	2.0	7.6 indole
		4.21s			6.36dd	6.64ddd	6.84ddd	6.59dd	7.6	1.5	8.0	1.5	7.5
					6.59dd	6.69ddd	6.85ddd	6.72dd	8.0	1.5	7.5	1.5	7.8
					6.78dd	7.02ddd	6.95ddd	7.19dd	7.5	1.6	7.5	1.6	7.7
6	5.17	3.99s	—	5.20-5.80	7.29d	—	6.95dd	7.10d	—	1.0	—	—	7.5 indole
		4.10s											
		4.13s											
					not separable (12H) 6.33-7.15								
7		4.33s	11.35	8.44-8.48	7.77dd	6.94ddd	7.10ddd	7.53dd	8.0	2.0	8.2	2.0	8.0 indole
					7.11dd	7.20ddd	7.04ddd	7.71dd	8.0	2.0	7.5	2.0	8.0
					6.81dd	7.15ddd	6.91ddd	7.48dd	8.0	2.0	8.0	2.0	7.5
11	4.89	3.24ᵃ	—	8.24-8.66	7.42dd	7.03ddd	7.19ddd	6.89dd	8.0	1.5	8.4	1.5	8.4 indole
		3.36ᵃ											
					not separable (12H) 6.34-6.95								

ᵃAB quartet J = 14.2 Hz.
Spectra of **4**, **6**, and **7** run in CDCl$_3$; **11** in (CD$_3$)$_2$CO.
All spectra run at 360 MHz.

Four further compounds isolated from *U. angolensis* were found to be nitrogenous. The major of these (yield 0.11%), which has been assigned the trivial name uvarindole-A, analyzed for $C_{29}H_{25}NO_3$ and on tlc gave an orange spot with vanillin (1%) in H_2SO_4 spray but no reaction with Dragendorff's reagent. The uv spectrum gave maxima typical of indole and 2-hydroxybenzyl units and showed a bathochromic shift on addition of alkali. The mass spectrum confirmed the presence of indole by significant ions at m/z 130 $[C_9H_8N]^+$ and 117 $[C_8H_7N]^+$ and of 2-hydroxybenzyl substituents by an ion at m/z 107 $[C_7H_7O]^+$. From the above, it appeared probable that uvarindole-A consisted of an indole nucleus substituted with three 2-hydroxybenzyl units.

This was confirmed by the ^{1}H-nmr spectrum (Table 2), which revealed three methylene singlets at δ 5.22 (N-CH$_2$) and at δ 4.14 and 4.21 (2×C-CH$_2$), together with a 3H broad singlet at δ 5.50 for replaceable phenolic hydroxyls. The remaining 16 protons all appeared in the aromatic region of the spectrum, and by careful decoupling experiments, these were resolved into four ABCD systems. The indole aromatics were distinguished from the deshielded resonance (δ 7.42) for H-4 (8). Given the presence of an unsubstituted indole aromatic nucleus and the absence of signals assignable to N-1, H-2, and H-3 of indole, uvarindole-A was assigned structure **4**.

The ^{13}C nmr (Table 3) was in agreement with the proposed structure. Signals for the indole nucleus were assigned by comparison with published data for corynantheine (**5**) and other 2,3-disubstituted indoles (9, 10). The N-CH$_2$ resonance at 42.12 ppm showed the anticipated deshielding (11), and C-1' and C-6' of the N-benzyl unit were distinguishable from corresponding positions in the two C-benzyl units. The C-CH$_2$ groups resonated at 24.79 and 25.78 ppm, a deshielding of about 2 ppm when compared with the C-CH$_2$ groups in the benzylated DHC's (Table 1).

The mass spectrum of uvarindole-A revealed a relatively simple fragmentation pattern based on loss of hydroxybenzyl units from the indole nucleus. Major pairs of ions at m/z 329/328 and 223/222 can be interpreted as depicted in Scheme 1, m/z 222 (usually the base peak) representing a stable 3-benzylindole ion.
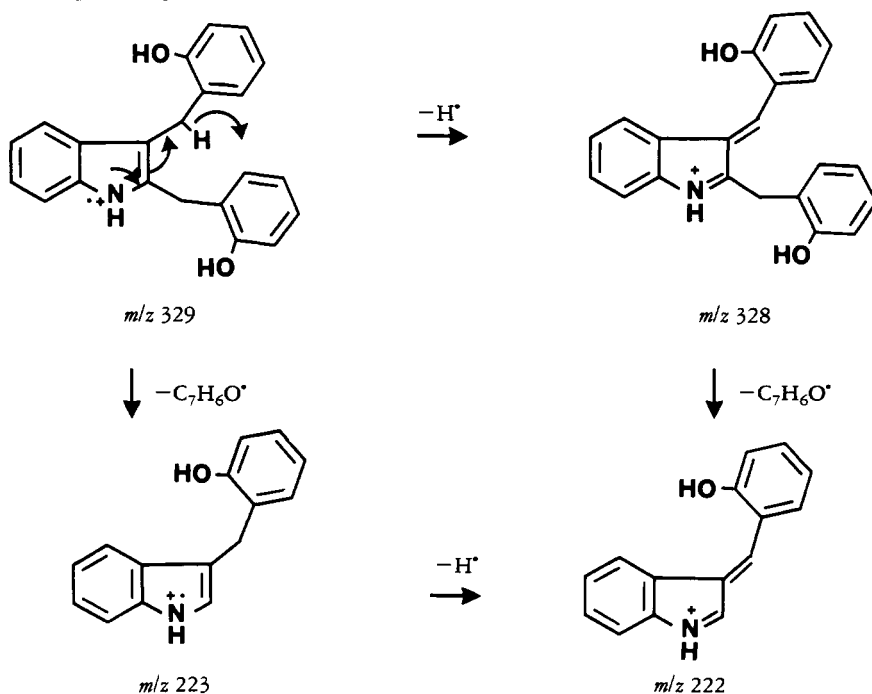
SCHEME 1

A minor compound, uvarindole-B (yield 0.019%), showed the same general characteristics as uvarindole-A but analyzed for $C_{36}H_{31}NO_4$, which is equivalent to uvarindole-A plus an additional hydroxybenzyl substituent. This was confirmed by nmr studies which showed four benzyl methylenes, one attached to nitrogen and the others to carbon. In the ^{13}C-nmr spectrum, the new CH_2 was highly deshielded (36.75 ppm), indicating its attachment to an aromatic nucleus and without adjacent oxygen substituents (12). On this basis, uvarindole-B could be considered as identical to uvarindole-A except for the addition of a further hydroxybenzyl unit, which must be placed either on the indole aromatic nucleus or *para* to the hydroxy substituent on one of the other benzyl groups [cf. the DHC uvarinol (12)].

As required from the above assumption, the ^1H-nmr spectrum showed resonances for 19 aromatic protons with the most important feature being the deshielded doublet at δ 7.29 ($J=1$ Hz). This must be attributed to H-4 of the indole and, as only *meta*-coupling occurs, requires that C-5 be substituted and that uvarindole-B must be **6**. Placement of the additional substituent at C-5 was supported by the ^{13}C nmr (Table 3), which gave an additional quaternary resonance at 130.24 ppm and a series of resonances in good agreement with published data (13) for the aromatic nucleus of 5-methyl-indole.

4   R=H
6   R= —C-H₂-
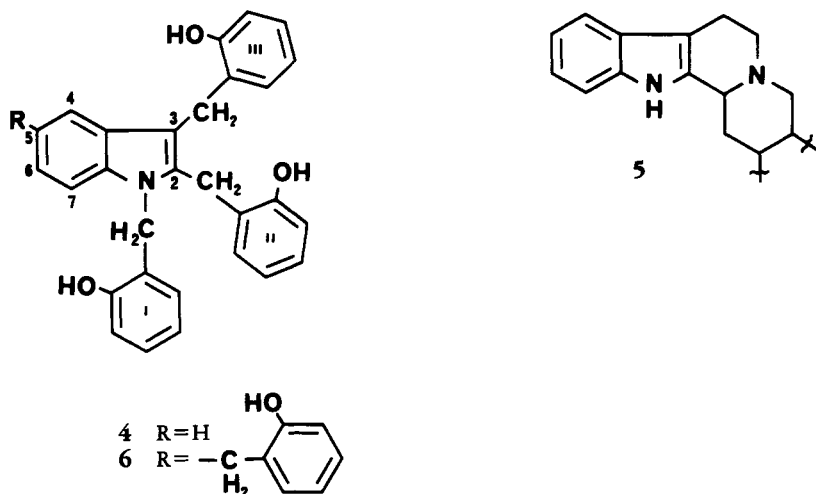
Uvarindole-C (yield 0.08%) exhibited the same tlc characteristics as **4** and **6**, but analyzed for $C_{22}H_{17}NO_3$, indicating a structure that was appreciably different. The ir spectrum revealed a band at 1625 cm^{-1} for a carbonyl, and the uv spectrum showed maxima at 263 and 338 nmr comparable to a 2-acylindole (14) rather than a 2-alkyl-indole (cf. 277, 292 nm for **4**). A bathochromic shift in the uv spectrum on addition of alkali confirmed the phenolic nature of uvarindole-C. The mass spectrum partly resolved the problem by exhibiting, in addition to the fragments for indole and 2-hydroxybenzyl, an ion at m/z 121 $[C_7H_5O_2]^+$, which can be attributed to an hydroxybenzoyl residue.

The ^1H-nmr spectrum (Table 2) revealed 12 aromatic protons as three ABCD systems, a single C-CH₂ singlet, and three replaceable protons, one of which was at δ 11.25, which is typical of NH in a 2-acylindole (14). A significant feature of the aromatic region was the deshielding of one of the nonindolic aromatic protons to δ 7.71. This must be attributed to H-6' of the benzoyl ring which is *ortho* to the deshielding carbonyl substituent. From these data, uvarindole-C was clearly an indole substituted at C-2 and C-3 with 2-hydroxybenzoyl and 2-hydroxybenzyl units, leaving the two possible structures **7** and **8**, with circumstantial evidence favoring the former.

TABLE 3. ^{13}C-nmr Spectra of Uvarindoles

Carbon	Compound						
	4	5	6	5-methyl-indole	7	9	11
2	135.42	135.2	136.06	—	129.80	134.4	76.24
3	109.81	107.4	109.75	—	119.79	120.4	204.24
3a	126.72	127.4	127.67	128.7	127.79	128.1	124.31
4	118.84	117.9	122.44	123.3	118.73	121.1	136.87
5	120.86	120.9	130.24	128.4	121.75	120.2	116.85
6	119.41	119.0	120.91	120.4	126.75	126.5	123.88
7	109.62	110.8	109.98	110.9	111.94	112.1	110.26
7a	137.16	136.2	135.77	134.8	137.12	136.3	154.69
N-CH$_2$	42.12		42.16		—		42.13
C-CH$_2$	24.79		24.89		27.99		34.41
	25.78		25.73		(192.45)^c		34.41
	—		36.75		—		—
1'	120.86^a		120.70^a		124.00		120.97^a
1"	124.24		124.20		124.58		127.80
1'''	124.57		124.50		—		127.80
1''''	—		126.73^b		—		—
2'	152.36^a		152.36^a		155.17		161.16^a
2"	153.05		153.12		(162.80)^c		155.70
2'''	153.86		153.86		—		155.70
2''''	—		153.90		—		—
3'	114.98		115.04		116.50		115.04^a
3"	115.26		115.35		(119.33)^c		115.85
3'''	115.50		115.58		—		115.85
3''''	—		115.92		—		—
4'	127.30		127.27		128.20		127.65^a
4"	127.51		127.52		(131.12)^c		127.85
4'''	127.96		127.52		—		127.85
4''''	—		127.96		—		—
5'	120.66		118.43		120.98		119.40^a
5"	120.86		120.66		119.87		119.25
5'''	121.57		120.70		—		119.25
5''''	—		120.86		—		—
6'	127.96^a		128.00^a		132.30		128.58^a
6"	129.53		129.53		(136.61)^c		131.97
6'''	130.15		130.16		—		131.97
6''''	—		130.79^b		—		—

Spectra of uvarindoles run at 90.56 MHz, **4, 6,** and **7** in CDCl$_3$ and **11** in (CD$_3$)$_2$CO.
^{a}Signals in any one column assignable to the N-hydroxybenzyl group.
^{b}Signals assignable to the hydroxybenzyl group at C-5 of the indole.
^{c}In **7** signals in brackets are for the benzoyl substituent.

Confirmation of structure **7** for uvarindole-C came primarily from the ^{13}C-nmr spectrum. Placement of the carbonyl at C-2 or C-3 will lead to shielding of the indole carbon at the point of attachment and deshielding at the β-position. Comparison of shifts for C-2 and C-3 with those reported for 2,3-dimethylindole (**13**) showed a deshielding of C-2 from 106.5 to 119.79 ppm and a shielding of C-3 from 131.2 to 129.80 ppm. These data also show close agreement with that published (10, 15, 16) for other 2-acylindoles, such as 16-epiaffinine (**9**) (Table 3). The carbonyl resonance for **7** occurred at 192.45 ppm and that for the remaining C-CH$_2$ was deshielded by about 2 ppm in comparison with **4** and **6**. Resonances for C-2', C-3', C-4', and C-6' of the benzoyl substituent were readily distinguishable from those of the benzyl unit (Table 3). Further support for **7** came from the mass spectrum, which exhibited a base peak m/z
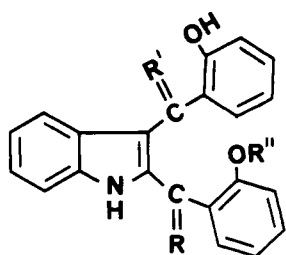
|			
7	R=O	R'=H$_2$	R''=H
8	R=H$_2$	R'=O	R''=H
10	R=O	R'=H$_2$	R''=CH$_3$
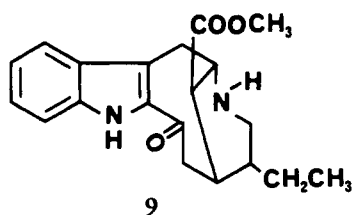
222, identical to that from **4**, suggesting the presence of the ion depicted in Scheme 1, which arises from a 3-(2-hydroxybenzyl)-indole.

Attempts to reduce the carbonyl group of **7** with sodium borohydride and with lithium aluminium hydride led, in each case, to numerous products, presumably due to facile rearrangements on the indole nucleus. Methylation using CH_2N_2 produced a monomethyl ether, which can be attributed to **10** as the mass spectrum revealed that m/z 222 was still the base peak and that the $[C_7H_5O_2]^+$ ion had been replaced to a large extent by the ion $[C_8H_7O_2]^+$, which can be assigned to a 2-methoxybenzoyl fragment. The selective methylation of the benzoyl hydroxy substituent was somewhat surprising in view of the presence of a *peri*-carbonyl, with which it would normally be expected to form a hydrogen-bond and thereby become resistant to methylation. However, it is clear from the ^{1}H-nmr spectrum (Table 2) that, in this case, there is no hydrogen-bonding between the benzoyl carbonyl and *peri*-hydroxy group, presumably because of interaction between carbonyl and the NH proton, thereby accounting for the deshielding of the latter to δ 11.35.

The final indolic compound, uvarindole-D (yield 0.075%), differed in being yellow and in giving a green color with vanillin-H_2SO_4 but still did not react to Dragendorff's reagent. It analyzed for $C_{29}H_{25}NO_4$, suggesting indole plus three hydroxy benzyl units. The uv spectrum was strikingly different from other uvarindoles exhibiting maxima at 233, 272, and 419 nm which complies well with published data for the indoxyl (dihydroindole-3-one) nucleus (17). This was also suggested by the ir spectrum which exhibited a carbonyl band at 1670 cm^{-1}, again similar to the indoxyl carbonyl (18). The occurrence of the indoxyl system received further support from the mass spectrum which showed major fragments at m/z 145 $[C_9H_7NO]^+$ and 133 $[C_8H_7NO]^+$ attributable to this nucleus [for structures of ions see Waterman and Muhammad (4)]. In addition, the mass spectrum revealed fragmentation typical of repeated loss of 2-hydroxybenzyl units from an indoxyl nucleus, suggesting that uvarindole-D was a tri-(2-hydroxybenzyl)indoxyl.

The ^{1}H-nmr spectrum (Table 2) showed four ABCD aromatic systems for the indole and benzyl groups and three methylenes, one as a singlet at δ 4.89 for N-CH$_2$ and the other two in the form of an AB quartet (J = 14.2 Hz) at δ 3.36 and 3.24. These data, with the C-CH$_2$ resonances equivalent and shielded in comparison with the other indoles, suggested that uvarindole-D was **11**. The ^{13}C-nmr spectrum (Table 3) was in agreement with this. The carbonyl resonance at 204.24 ppm showed close agreement with that reported (19) for the C-3 carbonyl of the indoxyl alkaloid iboluteine but not with that for the dihydroindol-2-one tasmanine which resonates (20) at 186.6 ppm. The resonances for two of the 2-hydroxybenzyl substituents were equivalent, as would be anticipated for *gem*-substituted groups at C-2 of indoxyl with the methylene resonances appreciably deshielded at 34.41 ppm. The carbon resonances for the aromatic in-

doxyl ring were assigned by comparison to those in iboluteine (19). In an analogous fragmentation to that observed in the mass spectra of the benzylated indoles, the base peak for **11** was observed at m/z 238/237 for the stable ions (**12, 13**) formed from uvarindole-D after loss of the N-benzyl and one of the 2-benzyl units. The structure of uvarindole-D has subsequently been confirmed by X-ray analysis (21).
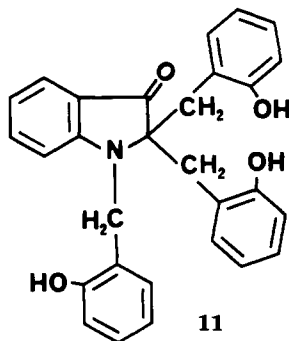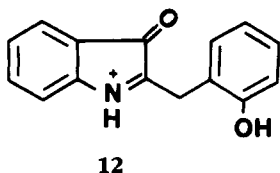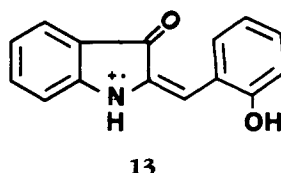
The uvarindoles represent a novel class of alkaloids and further illustrate the capability of *Uvaria* species to form *C*-benzyl derivatives (22). Whilst rare compared with the typical 1-benzyltetrahydroisoquinoline-derived alkaloids of the family (22), there are now several reports of the incorporation of indole in alkaloids in the Annonaceae. In addition to the uvarindoles, these include simple prenylated indoles in *Uvaria* and *Monodora* (22) and a range of indolosesquiterpenes in *Greenwayodendron (Polyalthia)* (23).

EXPERIMENTAL

GENERAL.—Melting points were measured on a Kofler hot plate and are uncorrected. Uv spectra were run in MeOH on a Unicam SP 800A instrument and ir spectra as KCl discs using a Perkin-Elmer 157 spectrophotometer. Optical rotations were measured on a Varian Model-60 polarimeter. ^{1}H nmr were recorded on Perkin-Elmer R23B (90 MHz), Brucker WH-250 (250 MHz) or Brucker WH-360 (360 MHz) instruments using TMS as internal standard and CDCl$_3$ as solvent unless otherwise stated. ^{13}C-nmr spectra were recorded on either the WH-250 (62.6 MHz) or WH-360 (90.56 MHz) instruments using the same internal standard and solvents. High resolution mass spectra were obtained on an AEI MS 902 spectrometer at 70 eV using a probe temperature between 120 and 150°. Petroleum ether refers specifically to the bp 60-80° fraction.

PLANT MATERIAL.—The stem bark material of *U. angolensis* used in this work was collected in the Gombe National Park, Tanzania. A voucher is deposited at the East African Herbarium, Nairobi.

EXTRACTION OF DIHYDROCHALCONES AND INDOLES.—The powdered stem bark (500 g) was extracted separately and successively with petroleum ether followed by EtOAc. The concentrated petroleum ether fraction was subjected to column chromatography over silica gel to give seven pure compounds and three mixtures (Table 4). Each of the mixtures was subsequently separated by circular preparative tlc (Chromatotron, silica gel, 1 mm disc) to give further pure compounds.

UVARETIN (**1**).—Needles from petroleum ether-EtOAc, mp 169-170° [lit. (24) 164-165°]; ms m/z (rel. int.) 378.1459 (M$^+$, 88) (calcd. for C$_{23}$H$_{22}$O$_5$ 378.1467), 347 (2), 273 (84), 246 (47), 179 (100), 167 (70), 107 (24), 91 (51); uv 217, 290, 320sh, (+NaOH) 217, 308, 325 nm; ir 3300, 1630 cm^{-1}; ^{1}H nmr [90 MHz, (CD$_3$)$_2$CO] δ 2.95 (2H, t, J=8.5, H-α), 3.35 (2H, t, J=8.5, H-β), 3.61 (3H, s, 6'-

TABLE 4.   Column Chromatography (cc) and Preparative tlc (ptlc) of the Petroleum Ether Extract

	Solvent					Weight (mg)	R_f^a	Identity
	toluene	EtOAc	HOAc	CHCl₃	MeOH			
cc	100	—	—	—	—	600	0.90	benzyl benzoate
	98	2	0.1	—	—	300	0.78	sesquiterpene mixture
	96	4	0.1	—	—	400	0.75	uvarindole-C
						30	0.82	chamuvaritin mixture-A
	93	7	0.1	—	—	550	0.50	uvarindole-A mixture-B mixture-C
ptlc . . . . . (mixture A)	98	2	0.1	—	—	350	0.68	diuvaretin
						600	0.63	uvaretin
						350	0.58	uvarisesquiterpene-1ᵇ
						50	0.48	uvarisesquiterpene-2ᵇ
ptlc . . . . . (mixture B)	—	—	—	49	1	375	0.38	uvarindole-D
						75	0.42	uvarindole-B
ptlc . . . . . (mixture C)	90	10	0.1	—	—	20	0.42	uvarindole-D
						15	0.31	uvarisesquiterpene-3ᵇ

ᵃRf values for silica gel G plates with solvent toluene-EtOAc-HOAc, 40:9:1.
ᵇThe uvarisesquiterpenes will be reported separately.

OMe), 3.89 (2H, s, CH₂-Ar), 5.73 (1H, s, H-5′), 7.21 (5H, br.s, H-2-H-6), 6.75-7.60 (4H, m, H-3″-H-6″), 14.80 (1H, s, OH-2′); ¹³C nmr see Table 1.

DIUVARETIN (**2**).—Amorphous solid; ms *m/z* (rel. int.) 484.1844 (M⁺, 100) (calcd. for $C_{30}H_{28}O_6$ 484.1886), 453 (10), 378 (84), 347 (12), 273 (67), 253 (14), 246 (48), 167 (21), 107 (80), 91 (75); uv 217, 280, 335, (+NaOH) 217, 285, 338 nm; ir 3350, 1610 cm⁻¹; ¹H nmr (90 MHz) δ 2.95 (2H, t, *J*=8, H-α), 3.39 (2H, t, *J*=8, H-β), 3.68 (3H, s, 6′-OMe), 3.82, 3.90 (2×2H, 2×s, CH₂-Ar), 6.70-7.60 (13H, m, H-Ar), 14.00 (1H, s, OH-2′); ¹³C nmr see Table 1.

CHAMUVARITIN (**3**).—Plates from petroleum ether-EtOAc, mp 155-156° [lit. (6) 152-155°]; ms *m/z* (rel. int.) 452.1621 (M⁺, 91) (calcd. for $C_{29}H_{24}O_5$ 452.1624), 346 (15), 320 (25), 253 (100), 241 (51), 214 (24), 107 (56), 91 (79); uv (log ε) 217 (3.98), 290 (3.85), 338 (3.40), (+NaOH) 217, 295, 340 nm; ir 3400, 1625 cm⁻¹; ¹H nmr [90 MHz, (CD₃)₂CO] δ 3.05 (2H, t, *J*=9, H-α), 3.62 (2H, t, *J*=9, H-β), 3.81, 3.91, (2×2H, 2×s, CH₂-Ar), 6.70-7.20 (8H, m, H-Ar), 7.30 (5H, br.s, H-2-H-6), 14.25 (1H, s, OH-2′); ¹³C nmr see Table 1.

UVARINDOLE-A (**4**).—Amorphous solid ppt. from CHCl₃ with cyclohexane, mp 66-68°; [α]D =0°; ms *m/z* (rel. int.) 435.1789 (M⁺, 78) (calcd. for $C_{29}H_{25}NO_3$ 435.1834), 328 (65), 328 (38), 223 (77), 222 (100), 130 (10), 117 (30), 107 (55); uv (log ε) 225 (4.27), 277 (3.89), 292 (3.78), (+NaOH) 230 (4.36), 288 (3.95) nm; ir 3400, 1600, 1460, 1270, 1100, 760 cm⁻¹; ¹H nmr see Table 2; ¹³C nmr see Table 3.

Uvarindole-A monomethylether.—Compound **4** (50 mg) on treatment with ethereal CH₂N₂ gave a monoethyl ether, in quantitative yield, mp 60-61°; uv 223, 276, 293 nm; ir 3400, 1600 cm⁻¹; ¹H nmr (90 MHz) δ 3.81 (3H, s, OMe), 4.10, 4.20 (2×2H, 2×s, 2×CH₂-Ar), 5.20 (2H, s, N-CH₂), 6.30-7.20 (15H, m, H-Ar, 7.45 (1H, dd, *J*=8, 1, H-4).

UVARINDOLE-B (**6**).—Amorphous solid ppt from CHCl₃ with cyclohexane, mp 61-62°; ms *m/z* (rel. int.) 541.2184 (M⁺, 20) (calcd. for $C_{36}H_{31}NO_4$ 541.2253), 435 (100), 329 (56), 328 (55), 223 (25), 222 (18), 130 (1), 117 (14), 107 (31); uv (log ε) 225 (4.65), 278 (4.10), 300 (4.19) nm; ir 3425, 1600, 1460, 1260, 1210, 1095, 760 cm⁻¹; ¹H nmr see Table 2; ¹³ C nmr see Table 3.

UVARINDOLE-C (**7**).—Yellow needles from CHCl₃, mp 151-153°; [α]D 0°; ms *m/z* (rel. int.) 343.1212 (M⁺, 86) (calcd. for $C_{22}H_{17}NO_3$ 343.1208), 236 (84), 222 (100), 220 (38), 130 (4), 121 (27), 117 (37), 107 (2); uv (log ε) 217 (4.22), 263 (3.81), 338 (3.91), (+NaOH) 217 (4.25), 232 (4.05), 323 (3.80), 380 (3.94) nm; ir 3300, 1625, 1600, 1540, 1495, 1470, 1380, 1350, 1250, 750 cm⁻¹; ¹H nmr see Table 2; ¹³C nmr see Table 3.

Uvarindole-C 2′-monomethylether.—Compound **7** (60 mg) was allowed to react with ethereal CH₂N₂

for 20 min at room temperature. Workup of the reaction mixture yielded the 2'-monomethylether as needles from $CHCl_3$, mp 146-148°; ms m/z (rel. int.) 357.1353 (M^+, 94) calcd. for $C_{23}H_{19}NO_3$ 357.1365), 326 (12), 250 (3), 222 (100), 220 (21), 135 (89), 130 (4), 117 (4), 107 (1), 91 (2); uv 215, 240, 322 nm; ^1H nmr (90 MHz) δ 3.69 (3H, s, 2'-OMe), 4.30 (2H, s, CH_2-Ar), 6.70-7.60 (11H, m, H-Ar), 7.76 (1H, dd, J=8, 2, H-4).

UVARINDOLE-D (**11**).—Yellow plates from $CHCl_3$, mp 170-175°; ms m/z (rel. int.) 451.1758 (M^+, 26) (calcd. for $C_{29}H_{25}NO_4$ 451.1783), 345 (61), 344 (32), 239 (99), 238 (100), 145 (49), 133 (68), 130 (13), 107 (88), 91 (20); uv (log ϵ) 223 (4.16), 272 (3.80), 419 (3.68), (+NaOH) 233, 285, 422 nm; ir 3500-3200, 1670, 1620, 1460, 1380, 1340, 1260, 760 cm^{-1}; ^1H nmr see Table 2; ^{13}C nmr see Table 3.

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LITERATURE CITED

1.   B. Verdcourt, "Annonaceae," in: *Flora of Tropical East Africa*, Crown Agents, London 1971, pp. 15-17.
2.   C.D. Hufford and B.O. Oguntimein, *Phytochemistry*, **19**, 2036 (1980).
3.   C.D. Hufford and B.O. Oguntimein, *J. Nat. Prod.*, **45**, 337 (1982).
4.   P.G. Waterman and I. Muhammad, *Chem. Commun.*, 1280 (1984).
5.   C.D. Hufford and W.L. Lasswell Jr., *J. Org. Chem.*, **41**, 1297 (1976).
6.   D.A. Okorie, *Phytochemistry*, **16**, 1591 (1977).
7.   J.F. Castelao, O.R. Gottlieb, R.A. De Lima, A.A.L. Mesquita, H.E. Gottlieb, and E. Wenkert, *Phytochemistry*, **16**, 735 (1977).
8.   W.A. Remers, "Indoles, Part 1," in: *Heterocyclic Compounds* (W.J. Houlihan ed.), Wiley Interscience, New York, 1972, pp. 33-34.
9.   E. Wenkert, J.S. Bindra, C.J. Chang, D.W. Cochran, and F.M. Schell, *Acc. Chem. Res.*, **7**, 46 (1974).
10.   F.W. Wehrli and T. Nishida, *Fortschr. Chem. Org. Naturst.*, **36**, 24 (1979).
11.   P. Rasoanaivo and G. Lukacs, *J. Org. Chem.*, **41**, 376 (1976).
12.   C.D. Hufford and W.L. Lasswell Jr., *Lloydia*, **41**, 151 (1978).
13.   R.G. Parker and J.D. Roberts, *J. Org. Chem.*, **35**, 996 (1970).
14.   D.G.I. Kingston and O. Ekundaya, *J. Nat. Prod.*, **44**, 511 (1981).
15.   A. Ahond, A.M. Bui, P. Potier, E.W. Hagaman, and E. Wenkert, *J. Org. Chem.*, **41**, 1878 (1976).
16.   R.M. Braga, H.F.L. Filho, and F.A.M. Reis, *Phytochemistry*, **23**, 175 (1984).
17.   P.S. Steyn, *Tetrahedron*, **29**, 107 (1973).
18.   D.S. Bhakuni, M. Silva, S.A. Matlin, and P.G. Sammes, *Phytochemistry*, **15**, 574 (1976).
19.   E. Wenkert and H.E. Gottlieb, *Heterocycles*, **7**, 753 (1977).
20.   R. Kyburz, E. Schopp, I.R.C. Bick, and M. Hesse, *Helv. Chim. Acta*, **64**, 2555 (1981).
21.   M.A. Meek, C.H. Schwalbe, P.G. Waterman, and I. Muhammad, *Acta Cryst.* (Ser. B) (in press).
22.   M. Leboeuf, A. Cave, P. Bhaumik, B. Mukherjee, and R. Mukherjee, *Phytochemistry*, **21**, 2783 (1982).
23.   P.G. Waterman, "Indolosesquiterpene Alkaloids," in: *Alkaloids: Chemical and Biological Perspectives*. Ed. by S.W. Pelletier. John Wiley and Sons, New York, 1985, Vol. 3, pp. 91-112.
24.   W.L. Lasswell Jr. and C.D. Hufford, *J. Org. Chem.*, **42**, 1295 (1977).

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