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SESQUITERPENE LACTONES OF *CALEA ZACATECHICHI* AND *C. URTICIFOLIA**

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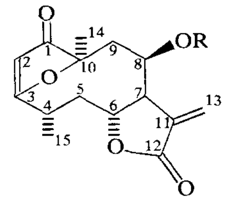
Key Word Index—*Calea zacatechichi*; *C. urticifolia*; Compositae; Heliantheae; Galinsoginae; sesquiterpene lactones; heliangolides; flavones.

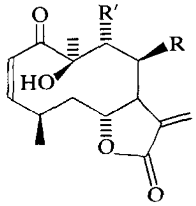
Abstract—*Calea zacatechichi* yielded the sesquiterpene lactone zexbrevin and a new analog, several analogs of neurolenin B including calein A, two analogs of budlein A and the flavones acacetin and *O*-methylacacetin. *Calea urticifolia* contained additional analogs of neurolenin B as well as a series of epoxidation products. Structures were established by spectrometric techniques. The results are contrasted with previous findings.

INTRODUCTION

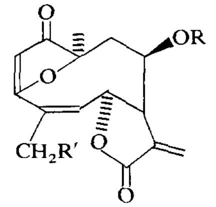
Two recent articles [1, 2] dealing with the constituents of *Calea zacatechichi* reported isolation of different sesquiterpene lactones. Moreover, the spectroscopic data reported for the caleins from *C. zacatechichi* [2] and for several apparently similar lactones isolated from *C. urticifolia* [3] seemed more in keeping with structures of type **2** analogous to neurolenin A (**2a**) and neurolenin B (**2b**) from *Neurolaena lobata* [4] than with the formulae [2] or the stereochemistry [3] originally assigned to them. We have therefore reinvestigated these two species. Our own work on collections from Honduras has resulted in isolation of the sesquiterpene lactones **1a** (zexbrevin), **1b**, **2c–2e**, **3a** and **3b** from *C. zacatechichi*, whereas *C. urticifolia* gave **2f–2h** as well as **4a–4e**. Substance **2e** was identical with calein A [2] whose structure must be revised.† Compounds **2c**, **2f** and **2g** have been found previously in *C. urticifolia* but were assigned different stereochemistry [3].



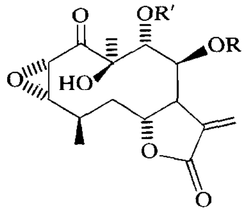
1a R = MeAcr
1b R = Tigl



2a R = O-*i*Val, R′ = H
2b R = O-*i*Val, R′ = OAc
2c R = OMeAcr, R′ = OAc or reverse
2d R = OTigl, R″ = OAc or reverse
2e R = OAng, R′ = OAc or reverse
2f R = OAng, R′ = OMeAcr or reverse
2g R, R′ = OMeAcr
2h R = O*i*Bu, R′ = OMeAcr or reverse



3a R = Tigl, R′ = OH
3b R = MeAcr, R′ = OH
3c R = Ang, R′ = OH



4a R = MeAcr, R′ = Ang or reverse
4b R = MeAcr, R′ = *i*Val or reverse
4c R, R′ = MeAcr
4d R = MeAcr, R′ = *i*Bu or reverse
4e R = MeAcr, R′ = Ac or reverse

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* Work supported in part by a grant from the U.S. Public Health Service (CA-13121) through the National Cancer Institute.

† Dr. A. Romo de Vivar has informed us (March 1979) that he has also come to the conclusion that calein A and calein B possess structure **2e** and its reverse; see also Quijano, L., Romo de Vivar, A. and Rios, T. (1979) *Phytochemistry* **18**, 1745.

RESULTS AND CONCLUSIONS

The pair of lactones **1a** and **1b** could not be separated satisfactorily; analysis of the 270 MHz ^{1}H HMR and 67.09 MHz ^{13}C NMR spectra by spin-decoupling and single frequency off-resonance decoupling when feasible permitted the assignments given in Tables 1 and 2. Lactone **1a** appeared to be identical with zexbrevin [5] to which we have recently [6] assigned H-8α rather than H-8β stereochemistry on the basis of a correlation with tirotundin.

Lactone pairs **2c** and **2d**, on the one hand, and **2g** and **2h** on the other, could not be separated satisfactorily, but analysis of the ^{1}H and ^{13}C NMR spectra and solvent shift studies permitted identification of the various constituents. Extensive spin decoupling in different solvents and comparison (see Tables 1 and 2) with the ^{1}H and ^{13}C NMR spectra of neurolenin B (**2b**) whose structure was established by X-ray crystallography [4] clearly showed that lactones **2c**–**2h** had structures and stereochemistries entirely analogous to those of the neurolenins. The remaining uncertainty as to the distribution of ester side chains between C-8 and C-9 could not be resolved since selective hydrolysis of one of the ester functions was not successful.

Lactone **2e** was identical with calein A from Mexican *C. zacatechichi* [2] by direct comparison; the structures of this substance and of calein B therefore require revision. Lactones **2c**, **2f** and **2g**, on the other hand, appeared to be identical with those lactones which were reported earlier [3] from a Guatemalan collection of *C. urticifolia*, but were assigned enantiomeric stereochemistry at C-4 on the basis of paramagnetic shifts of H-4 and H-7 during NaBH$_4$

Table 1. ^{1}H NMR spectra of *Calea* constituents*

Compound	H-2	H-3	H-4	H-5	H-6	H-7	H-8	H-9	H-13	H-14†	H-15†	Misc.
1a,b	5.54*br* (1)	—	3.03*quibr* (7, 1)	2.59*ddd* (15, 9, 7) 2.05*ddbr*	4.48*ddbr* (9, 5, 0.*d*)	3.30*m* (5, 2.3, 1)	5.13*ddd* (5, 2.5, 1)	2.70*dd* (15.5, 5) 2.23*dd* (15.5, 2.5)	6.34*d* (3.5) 5.68*d* (3)	1.4	1.39*d* (7)	‡, §
2a	6.58*d* (12)	5.88*t* (12)	3.08*tqui* (12, 6)	1.81*td* (12, 5.5) 1.42*td* (12, 6)	4.50*dd* (12, 5.5)	2.61*br* (3, 1.5, 1)	5.29*ddd* (11, 6, 3,)	2.25*dd* (14.5, 11) 2.03*dd* (14.5, 6)	6.27*br* (1) 5.73*d* (1.5)	1.44	1.13*d* (6)	‖
2b	6.58*d* (12)	6.00*t* (12)	3.10*tqui*	1.83*td* 1.43*td*	4.54*dd*	2.5*qm*	5.5*m*	5.5*m*	6.32*br* 5.8*br*	1.34	1.14*d*	2.05 (Ac) ‖
2b††	5.99*d*	4.93*t*	2.79*tqui*	1.24*td* 0.95*td*	4.34*dd*	2.43*m*	5.91*dd* (10, 1.5)	5.64*d* (10)	6.18*d* 5.20*d*	1.09	0.58*d*	
2c,d	6.60*d*	6.01*t*	3.10*tqui*	1.81*td* 1.42*td*	4.60*dd*	2.63*br*	5.60*br*	5.60*br*	6.31*br* 5.82*br*	1.34	1.13*d*	2.03 (Ac) 1.97 (Ac)
2c††	6.02	5.00*t*	2.80*tqui*	1.26*td* 0.99*td*	4.40*dd*	2.48*br*	5.98*dd*	5.69*d*	6.17*br* 5.27*br*	1.11	0.61*d*	1.64 (Ac)
2d	6.06*d*	5.08*d*	2.80*tqui*	1.26*td* 1.00*td*	4.48*dd*	2.48*br*	5.98*dd*	5.73*d*	6.17*br* 5.31*br*	1.15	0.56*d*	1.64 (Ac) §
2e	6.60*d*	6.02*t*	3.12*tqui*	1.84*td* 1.44	4.58*dd*	2.64*br*	5.68*dd*	5.59*d*	6.33*br* 5.84*br*	1.37	1.14	2.00 (Ac) ¶
2f	6.61*d*	6.00*t*	3.10*tqui*	1.82*td* 1.46*td*	4.62*dd*	2.63*br*	5.61*dd*	5.74*d*	6.29*br* 5.81*br*	1.33	1.14*d*	‡, ¶
2g	6.63*d*	6.01*t*	3.10*tqui*	1.85*td* 1.45*td*	4.61*dd*	2.64*dd*	5.67*br*	5.67*br*	6.32*br* 5.82*br*	1.34	1.14*d*	¶ (double)
2h	6.61*d*	6.00*t*	3.10*tqui*	1.85*td* 1.45*td*	4.61*dd*	2.63*br*	5.64*br*	5.64*br*	6.31*br* 5.82*br*	1.33	1.13*d*	‡, **
3a	5.68	—	—	6.23*dt* (4, 1.5)	5.31*dt* (4, 1)	3.75*m* (4, 3.3, 3, 1.5)	5.19*ddd* (5.5, 3.5, 1.5)	2.54*dd* (14.5, 5.5) 2.31*dd* (14.5, 3.5)	6.34*d* (3.3) 5.68*d* (3)	1.49	4.41*br*** (1.5, 1)	§
3b	5.70	—	—	6.22*dt*	5.30*dt*	3.77	5.20	2.60*dd* 2.32*dd*	6.35*d* 5.69*d*	1.49	4.42*br***	‡
4a,b	4.29*d* (4.5)	3.33*dd* (9, 4.5)	1.47*m*	1.90*m* 1.48	4.84*dd* (12, 5.5)	2.37*br* (1.5, 1, 1)	5.72*dd* (10, 1.5)	5.89*d* (10)	6.32*br* (1) 5.82*br* (1)	1.45	1.22*d* (6)	‡, ¶ and ‡, ‖ 3.90 (OH)
4c	4.29*d*	3.33*dd*	1.46*m*	1.90*m* 1.48	4.82*dd*	2.83*br*	5.83*br*	5.83*br*	6.32*br* 5.82*br*	1.46	1.23*d*	‡ (double) 3.91 (OH)
4d	4.25*d*	3.32*dd*	1.46*m*	1.94*m* 1.48	4.82*dd*	2.36*br*	5.70*dd*	5.78*dd*	6.32*br*	1.45	1.24*d*	‡, ** 3.89 (OH)
4e	4.23*d*	3.33*dd*	1.47*m*	1.97*m* 1.47	4.80*dd*	2.35*br*	5.66*dd*	5.76*d*	6.32*br* 5.82*br*	1.47	1.22*d*	2.04 (Ac) 3.94 (OH)

* Run at 270 MHz in $CDCl_3$ unless indicated otherwise with TMS as internal standard. Values are in ppm. Unmarked signals are singlets. Figures in parentheses are coupling constants in hertz and are not repeated in the same column for similar compounds.

† Intensity three protons.

‡ MeAcr—1.87*dd* (1.5, 1, H-3′)†, 5.97*dq* (2, 1, H-4′), 5.59*dq* (2, 1.5, H-4′).

§ Tigl—6.72*qbr* (7, 1, H-3′), 1.79 (7, H-4′),† 1.75*br* (1, H-5′).†

‖ *i*-Val—2.25*m*, 2.03*m* (H-2′), 1.99*m* (H-3′)‡‡, 0.88*d*(6H, H-4′).

¶ Ang—6.10*qq* (7.5, 1.5, H-3′), 1.94*dd* (7.5, 1.5, H-4′),† 1.76*q* (1.5, H-5′).†

** *i*-Bu—2.55*sept* (7.5, H-2′), 1.07*d* (6H, H-3′).

†† In C_6D_6.

‡‡ Intensity two protons.

Table 2. ^{13}C NMR spectra of *Calea* constituents*

Carbon	**1a** **(1b)**	**2a**†	**2b**†	**2c** **(2d)**	**2e**	**2f**	**2g** **(2h)**	**3a**	**3b**	**4a** **(4b)**	**4c** **(4d)**	**4e**
1	205.18	205.7	204.3	204.41	204.60	204.85	204.71	205.12	205.42	206.07 (206.75)	205.98	205.72
2	102.95	125.3*d*	125.3*d*	125.58*d*	125.39*d*	125.58*d*	125.48*d*	104.94*d*	104.94*b*	55.88*d*	55.94*d*	55.70*d*
3	192.13	146.6*d*	147.9*d*	147.92*d*	148.07*d*	147.86*d*	147.92*d*	182.76	182.76	62.81*d*	62.83*d*	62.88*d*
4	31.37*d*	28.3*d*	28.2*d*	28.21*d*	28.29*d*	28.29*d*	28.29*d*	138.88	138.88	26.08*d*	25.14*d*	25.96*d*
5	40.96*t*	40.2*t*	40.2*t*	40.17*t*	40.36*t*	40.30*t*	40.28*t*	133.85*d*	133.85*d*	38.92*t*	38.99*t*	38.72*d*
6	74.73*d*	75.9*d*	76.3*d*	76.35*d*	76.31*d*	76.37*d*	76.35*d*	75.25*d*	75.28*d*	74.79*d* (74.16*d*)	74.81*d*	74.73*d*
7	51.61*d*	42.4*d*	41.2*d*	41.18*d*	41.25	41.29*d*	41.23*d* (41.34*d*)	48.25*d*	48.23*d*	41.12*d*	41.12*d* (41.23*d*)	40.83*b*
8	74.25*d* (74.41*d*)	73.9*d*	73.9*d*	74.52*d*‡ (74.11*d*)‡	73.37*d*‡	74.46*d*‡	74.30*d*‡	75.55*d*	74.87*d*	74.16*d*	74.11*d*	74.05*d*
9	43.06*t* (43.10*t*)	40.4*d*	73.8*d*	74.00*d*‡	74.05*d*‡	73.07*d*‡	74.05*d*‡ (73.23*d*)	42.63*t*	42.63*t*	70.89*d* (71.33*d*)	72.01*d* (71.20*d*)	71.68*d*
10	88.29	76.5	79.3	79.28	79.28	79.34	79.40	88.00	87.99	79.93	80.04	79.74
11	139.53 (139.64)	136.1‖	134.8	134.77§	134.82	134.87§	134.85§	136.00	135.99	134.98‡	134.76‡	134.33‡
12	168.46 (168.54)	169.0	170.0	170.15	170.14	168.70	168.67	168.95	168.95	168.34	168.29	170.34
13	123.05*t* (122.91*t*)	124.5*t*	126.2*t*	126.25*t*	126.26*t*	126.33*t*	126.33*t* (126.49*t*)	123.38*t*	123.36*t*	126.35*t*	126.35*t* (126.48*t*)	126.67*t*
14	22.74*q*	28.1*q*‖	23.6*q*	23.50*q*	23.67*q*	23.83*q*	23.63*q*	21.30*q*	21.38*q*	24.75*q*	24.55*q*	24.43*q*
15	16.04	19.9*q*	19.6*q*	19.64*q*	19.71*q*	19.72*q*	19.72*q*	62.30*t*	62.26*t*	18.57*q*	18.57*q*	18.52*q*
1′	165.44 (166.12)	171.3	170.8	165.19*d* (165.78)	165.21	165.19	165.32 (165.19)	165.40	166.44	165.24	165.10 (165.05)	165.21
2′	135.12 (127.50)	43.0*t*	42.5*t*	134.90§ (127.25)	126.51	134.71§	134.63§	134.51	127.33	134.63‡	134.71‡	134.79‡
3′	18.05*q* (138.83*d*)	25.4*d*	24.9*d*	17.98*q* (138.83*d*)	140.79*d*	17.98*q*	18.06*q* (17.98*q*)	18.24*q*	139.76*d*	17.92*q*	17.97*q* (17.98*q*)	18.03*q*
4′	126.70*t* (14.54*q*)	22.2*q*	22.3*q*	126.85*t* (14.46*q*)	20.12*q*	126.59*t*	127.60*t* (127.19*t*)	127.35*t*	14.62*q*	126.62*t* (127.01*t*)	127.84*t* (127.13*t*)	127.84*t*
5′	(11.90*q*)	22.2*q*	22.3*q*	(11.76*q*)	15.71*q*				11.84*q*			
1″			168.6	168.66 (168.73)	168.72	166.58	166.50 (176.50)			166.77 (173.00)	166.74 (176.50)	168.37
2″			20.5*q*	20.31*q* (20.31*q*)	20.31	126.46	134.69 (33.96*d*)			126.43 (42.45*t*)	126.35 (34.07)	20.26*q*
3″						141.14*d*	18.00*q* (18.65*q*)			141.65*d* (24.56*d*)	17.97*q* (16.57*q*)	
4″						20.12*q*	126.73*t* (19.01*q*)			20.00*q* (15.15*q*)	126.70*t* (18.95*q*)	
5″						15.85*q*				15.80*q* (10.14*q*)		

* Run at 67.09 MHz in $CDCl_3$ on a Bruker HX-270 Instrument with TMS as internal standard. Values are in ppm. Unmarked signals are singlets. Values in parentheses correspond to those signals of pair which differ in shift.

† Taken from ref. [4]. Assignments of C-4 and C-3′, and C-12 and C-1′, have been interchanged.

‡, § Assignments interchangeable.

‖ Probably misprints.

reduction of **2c**. However, the coincidence of chemical shifts, coupling constants and other physical properties leaves no doubt that the stereochemistry of these compounds is as shown in formulae **2c**–**2h**.* The observed coupling constants adduced in support of the earlier stereochemistry [3] are equally compatible with the conformation of the neurolenins established by X-ray crystallography [4]. Inspection of the models and of Fig. 2 of ref. [4] shows that the ketone carbonyl is not in the plane of the 2,3-double bond; this accounts not only for the frequency of the C-1 signal in the ^{13}C NMR spectra of **2a**–**2h** (~205 ppm) which is characteristic of a saturated, not an α,β-unsaturated cyclohexenone carbonyl, but also, in the ^1H NMR spectra, for an interesting inversion in the frequencies of the α- and β-protons. The signal of H-2 appeared as a doublet near δ 6.6 and that of H-3 as a triplet near 6 ppm (not a doublet as reported in ref. [4]). The unusual paramagnetic shift of H-2 which lies fairly close to the x-axis at the 'carbon end' of the carbonyl group is difficult to explain in terms of the usual model, but may be related to similar observations discussed elsewhere [7]. On the other hand, the IR band near 1690 cm^{-1} which is that of the ketone carbonyl (not that near 1735 cm^{-1} as claimed earlier [3] which is that of the saturated ester function of

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* In the case of our **2c** from *C. urticifolia*, a difference in the distribution of the acetate and methacrylate esters between C-8 and C-9 cannot be excluded with certainty.

2a–2f and **2h**) indicates a certain degree of conjugation (or possibly hydrogen bonding) as is evident by comparison with the IR spectra of **4a–4e** (*vide infra*).

Lactones **4a–4e** from *C. urticifolia* were clearly α-ketoepoxides and biological oxidation products of lactones of type **2**. This was evidenced by the shift of the ketone IR frequency to longer wavelengths (near 1705 cm^{-1}), and by the diamagnetic shift of the signals of H-2 and H-3 to near δ 4.4 and 3.3, respectively. Corresponding upfield shifts of C-2 and C-3 were noted in the ^{13}C NMR spectra, while the frequency of C-1, out of the plane of the former double bond, remained invariant. Spin decoupling established the complete sequence of protons on C-2 through C-10. The stereochemistry assigned to the new asymmetric centres was based on coupling constants involving H-2, H-3 and H-4 and, in the rest of the molecule, on the correspondence between the NMR spectra of lactones of type **2** and type **4**. Lactones **4a,b** and **4c,d** could not be separated satisfactorily and, as in the case of the lactones of type **2**, the allocation of the two ester functions to C-8 and C-9 of **4a,b,d** and **e** remains uncertain for the time being.

The gross structure of lactones **3a,b** from our collection of *C. zacatechichi* was established by the IR and UV spectra, double resonance experiments and the ^{13}C NMR spectrum (Tables 1 and 2). That they were analogs of budlein A (**3c**) [8] from *Viguiera buddleiaeformis* rather than goyazensolide (**3b** with a *trans*-lactone ring closed to C-8) [9] was clear from the chemical shifts of H-8 (near δ 5.3 instead of 4.5) and the coupling constants which defined the stereochemistry at C-8. Derivatives of **3** carrying an additional hydroxyl group on C-10 and 15-desoxy analogs with the same stereochemistry have been isolated from *C. urticifolia* [3] and *C. axillaris* [10, 11] and from *Isocarpha atriplicifolia* [12], *Helianthus ciliaris* [10] and *H. lehmannii* [13].

There are obvious similarities in the sesquiterpene lactone chemistry of *Calea* (Heliantheae subtribe Galinsoginae) and several representatives of subtribe Helianthinae. The very limited results based on examination of a mere handful of species also suggest similarities in the sesquiterpene lactone chemistry of *Calea* and *Neurolaena*, a genus recently transferred from Senecioneae to Heliantheae and placed in a newly erected subtribe Neurolaeninae which is close to Galinsoginae [14]. Additional chemical studies may shed further light on these relationships.

EXPERIMENTAL

Extraction of C. zacatechichi. Aerial parts of *C. zacatechichi* Schlecht. (12 kg), collected by Mr. Gustavo Cruz in the fall of 1975 in the vicinity of Tegucigalcapa, Honduras (voucher on deposit in herbarium of Universidad Nacional Autonoma de Honduras, coll. No. 4116 and accession No. PR-80864 of Medicinal Plant Resources Laboratory, U.S.D.A.), were extracted with $CHCl_3$ and worked up in the usual manner [15]. The crude gum (75 g) was adsorbed on 500 g of Si gel (Mallinckrodt 100 mesh) and chromatographed over 1 kg of Si gel (toluene-$CHCl_3$, 4:1), 500 ml fractions being eluted in the following order: 1–5 (toluene-$CHCl_3$, 4:1), 6–11 (toluene-$CHCl_3$, 1:1), 12–26 ($CHCl_3$–MeOH, 99:1), 27–35 ($CHCl_3$-MeOH, 97:3), 36–45 ($CHCl_3$-MeOH, 19:1). TLC of fractions 6–11 showed a major spot; PLC (EtOAc–hexane, 3:7) and crystallization from hexane gave material, mp 189–200°, which was homogeneous on TLC in several solvent systems but was a 5:1 mixture of **1a** and **1b** (^{1}H and ^{13}C NMR and MS analysis, $[\alpha]_D + 60°$ (c 0.03, $CHCl_3$); CD curve (MeOH) $[\theta]_{304} + 1390$, $[\theta]_{281} - 630$, $[\theta]_{250} + 26\,700$, $[\theta]_{218} - 2770$ (last reading); IR ν_{max}^{KBr} cm^{-1}: 1763, 1720, 1690, 1655, 1630 and 1592. (Calc. for **1a**, $C_{19}H_{22}O_6$: MW, 346.1415. Found: MW(MS), 346.1427 (6.2%). Calc. for **1b**, $C_{20}H_{24}O_6$: MW, 360.1571. Found: MW(MS), 360.1579 (10.8%)). Other significant peaks in the high resolution MS were at m/e (rel. int.): 316 ($C_{18}H_{20}O_5$, 2.4), 302 ($C_{17}H_{18}O_5$, 3.0), 261 ($C_{15}H_{17}O_4$, 12.2), 260 ($C_{15}H_{16}O_4$, 40), 233 ($C_{12}H_{17}O_3$, 3.7), 232 ($C_{14}H_{16}O_3$, 1,1.2), 217 ($C_{13}H_{13}O_3$, 7.4), 204 ($C_{12}H_{12}O_3$, 7.1), 125 ($C_7H_9O_2$, 100), 124 ($C_7H_8O_2$, 66.5), 83 (C_5H_7O, 83.7), 82 (C_5H_8O, 52.9), 69 (C_4H_5O, low resoln.). Fractions 12–20 gave a yellow solid which was recrystallized from $CHCl_3$–MeOH to give 7-*O*-methylacacetin, mp 158°. UV and NMR spectra as reported. This flavone has been isolated previously from *C. zacatechichi* [16]. Fractions 21–26 were combined and purified by PLC (EtOAc–hexane, 1:1 3 developments). The slightly more mobile component was recrystallized from $CHCl_3$–hexane, mp 180–182°, yield 0.10 g, but was a 4:1 mixture of **2c** and **2d** (^{1}H and ^{13}C NMR spectra, MS, lit. [3] mp of **2c** 168°; $[\alpha]_D - 290°$ (c 0.05, $CHCl_3$); CD curve (MeOH) $[\theta]_{302} - 350$, $[\theta]_{256} + 3000$, $[\theta]_{214} - 100\,500$ (last reading); IR ν_{max}^{KBr} cm^{-1}: 3420, 1770, 1745, 1730, 695, 1665, 1650, 1630 and 1230. (Calc. for **2a**, $C_{22}H_{28}O_8$: MW, 420.1725. Found: MW(MS), 420.1757 (4.4%). Calc. for **2b**, $C_{21}H_{26}O_8$: MW, 406.1626. Found: MW(MS), 406.1635 (0.6%)). Other significant peaks in the high resolution MS were at m/e (rel. int.): 378 ($C_{20}H_{26}O_7$, 1.5), 364 ($C_{19}H_{24}O_7$, 9.4), 346 ($C_{19}H_{22}O_6$, 9.4), 321 ($C_{17}H_{21}O_6$, 1.1), 320 ($C_{17}H_{20}O_6$, 1.3), 279 ($C_{15}H_{19}O_5$, 5), 278 ($C_{15}H_{18}O_5$, 209), 277 ($C_{15}H_{17}O_5$, 13.9), 261 ($C_{15}H_{17}O_4$, 9.9), 260 ($C_{15}H_{16}O_4$, 12.8), 83 (C_5H_7O, 100), C_5H_6O (96.8), 69 (C_4H_5O, low resoln.). The slower moving component **2e** was recrystallized from $CHCl_3$-hexane, mp 178°, yield 0.15 g, $[\alpha]_D - 344°$ (c 0.04, $CHCl_3$); CD curve (MeOH) $[\theta]_{302} - 2100$, $[\theta]_{255} + 2000$, $[\theta]_{210} - 6300$ (last reading); MS m/e: 420 (M^+), 400, 378, 360, 335, 278, 261, 83 and 60. Fractions 27–35 contained two very similar substances which were separated by PLC (Si gel, EtOAc–hexane, 1:1, 4 developments). The more mobile component **3a** was a gum, yield 70 mg, $[\alpha] - 80°$ (c 0.03, $CHCl_3$), CD curve $[\theta]_{320} + 28\,000$, $[\theta]_{286} - 2800$, $[\theta]_{250} + 5700$; IR ν_{max}^{KBr} cm^{-1}: 3500, 1720.1690,1660,1640 and 1592. (Calc. for $C_{20}H_{22}O_7$: MW, 374.1365. Found: MW(MS), 374.1353 (12.9%)). Other prominent peaks in the high resolution MS were at m/e (rel. int.): 356 ($C_{20}H_{20}O_6$, 0.9), 330 ($C_{18}H_{18}O_6$, 1.2), 291 ($C_{15}H_{15}O_6$, 1.6), 275 ($C_{15}H_{15}O_5$, 2.4), 274 ($C_{15}H_{14}O_5$, 5.6), 256 ($C_{15}H_{12}O_4$, 1.2), 248 ($C_{13}H_{12}O_5$, 12.3), 138 ($C_7H_8O_3$, 10.5), 83 (C_5H_7O, low resoln.). The less mobile component **3b** was also non-crystalline, yield 60 mg, $[\alpha]_D - 87°$ (c 0.023, $CHCl_3$); CD curve (MeOH) $[\theta]_{318} + 1080$, $[\theta]_{288} - 1050$, $[\theta]_{250} + 2160$; IR ν_{max}^{KBr} cm^{-1}: 3500, 1765, 1720, 1680, 1640 and 1590. (Calc. for $C_{19}H_{20}O_7$: MW, 360.1208. Found: MW(MS), 360.1198 (16.4%)). Other significant peaks in the high resolution MS were at m/e (rel. int.): 342 ($C_{19}H_{18}O_6$, 1.4), 316 ($C_{17}H_{16}O_6$, 3.7), 291 ($C_{15}H_{15}O_6$, 2.9), 275 ($C_{15}H_{15}O_5$, 3.5), 274 ($C_{15}H_{14}O_5$, 9.6), 248 ($C_{13}H_{12}O_5$, 37.4), 138 ($C_7H_8O_3$, 31), 69 (C_4H_5O, low resoln.). Fractions 36–42 gave a yellow solid which after recrystallization from MeOH–$CHCl_3$ melted at 262°, yield 0.12 g, and was identified as acacetin.

Extraction of C. urtificolia. Aerial parts of *C. urtificolia* (Mill.) DC (3.4 kg), collected by Mr. Gustavo Cruz in the fall of 1974 in the vicinity of Tegucigalpa, Honduras (voucher on deposit in herbarium of U.N.A.H., accession No. PR-43871 of Medicinal Plant Resources Laboratory, U.S.D.A.), were extracted and worked up as usual. The crude gum (25 g) was adsorbed on 30 g Si gel and chromatographed over 300 g of the same adsorbent (toluene–$CHCl_3$, 1 : 1), 250 ml fractions being eluted in the following order: 1–5 (toluene–$CHCl_3$, 1 : 1), 6–13 ($CHCl_3$), 14–20 ($CHCl_3$–MeOH, 99 : 1), 21–26 ($CHCl_3$–MeOH, 97 : 3), 27–34 ($CHCl_3$–MeOH, 19 : 1), 35–45 ($CHCl_3$–MeOH, 9 : 1). Fractions 6–13 contained a major component which was recrystallized ($CHCl_3$–hexane) to give **2f**, mp 161–162°, lit. [3] mp 158.5°, yield 0.10 g, $[\alpha]_D - 400°$ (*c* 0.013, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3420, 1770, 1735, 1730, 1692, 1660, 1640 and 1625. Fractions 14–20 were further purified by PLC (hexane–EtOAc, 1 : 1). The upper band, though homogeneous on TLC in several solvent systems, was a 3 : 1 mixture of **2g** and **2h** by NMR spectrometry, mp 155–157° (hexane–$CHCl_3$), yield 0.10 g, $[\alpha]_D - 375°$ (*c* 0.016, $CHCl_3$), IR ν_{max}^{KBr} cm^{-1}: 3415, 1770, 1730, 1720, 1695, 1662, 1630, 1625 and 1615. (Calc. for **2g**, $C_{23}H_{28}O_8$: MW, 432.1783. Found: MW(MS), 432.1803, 0.6%). M^+ of **2h** was not observed. Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 414 ($C_{23}H_{26}O_7$, 1.1), 347 ($C_{19}H_{23}O_6$, 1.9), 346 ($C_{19}H_{22}O_6$, 4.6), 278 ($C_{15}H_{18}O_5$, 4.8), 261 ($C_{15}H_{17}O_4$, 260 ($C_{15}H_{16}O_4$, 11), 233 ($C_{14}H_{17}O_3$, 4.3), 232 ($C_{14}H_{16}O_3$, 6.8), 217 ($C_{13}H_{13}O_3$, 11.7), 125 ($C_7H_9O_2$, 10.2), 85 ($C_6H_{13}O$, 51), 83 ($C_6H_{11}O$, 47.2), 82 (C_5H_6O, 100), 71 (C_4H_7O) and 69 (C_4H_5O, low resoln.). The lower band gave a 5 : 1 mixture of **4a** and **4b**, mp 105–108° ($CHCl_3$–hexane, yield 0.15 g, $[\alpha]_D - 192°$ (*c* 0.089, $CHCl_3$); CD curve $[\theta]_{290} - 4600$, $[\theta]_{250} + 4550$, $[\theta]_{214} - 14\,700$ (last reading); IR ν_{max}^{KBr} cm^{-1}: 3410, 1775, 1730, 1720, 1708, 1660, 1630, 1620, 910 and 820. (Calc. for **4a**, $C_{24}H_{30}O_9$; MW, 462.1939: Found: MW(MS), 462.1905, 9.1%). M^+ of **4b** was not observed. Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 444 ($C_{24}H_{28}O_8$, 3.4), 376 ($C_{20}H_{24}O_7$, 4.8), 224 ($C_{12}H_{16}O_4$, 9.2, 206 ($C_{12}H_{14}O_3$, 8.8), 168 ($C_9H_{12}O_3$, 4.4), 164 ($C_{10}H_{12}O_2$, 6.9), $C_{10}H_{11}O_2$, 4.7), 153 ($C_8H_9O_3$, 3.2), 151 ($C_9H_{11}O_2$, 4.4), 125 ($C_7H_9O_2$, 4.0). 85 (C_5H_9O, 57.5), 83 (C_5H_7O, 100), 82 (C_5H_6O, 74.5), 69 (C_4H_5O, low resoln.). Fractions 21–26 were further purified by PLC (hexane–EtOAc 1 : 1, 3 developments). The more mobile fraction was a 2 : 1 mixture of **4c** and **4d**, mp 120–122°, wt 0.32 g, $[\alpha]_D - 169°$ (*c* 0.098, $CHCl_3$); CD curve (MeOH), $[\theta]_{295} - 4500$, $[\theta]_{248} + 4450$, $[\theta]_{214} - 33\,750$ (last reading); IR ν_{max}^{KBr} cm^{-1}: 3420, 1770, 1730, 1720, 1660, 1630, 920 and 820. (Calc. for **4c**, $C_{23}H_{28}O_9$: MW, 448.1782. Found: MW(MS), 448.1752, 2.5%). M^+ of **4d** was not observed. Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 420 ($C_{22}H_{28}O_8$, 3.3), 363 ($C_{19}H_{23}O_7$, 2.2), 362 ($C_{19}H_{22}O_7$, 2.0), 319 ($C_{17}H_{19}O_6$, 2.4), 292 ($C_{16}H_{20}O_5$, 21.0), 277 ($C_{15}H_{17}O_5$, 2.4), 276 ($C_{15}H_{16}O_5$, 6.8), 249 ($C_{14}H_{17}O_4$, 3.6), 248 ($C_{14}H_{16}O_8$, 2.9), 224 ($C_{12}H_{16}O_4$, 21.2), 206 ($C_{12}H_{14}O_3$, 49.5), 205 ($C_{12}H_{13}O_3$, 11.2), 193 ($C_{11}H_{13}O_3$, 8.2), 178 ($C_{11}H_{14}O_2$, 21.8), 164 ($C_{10}H_{12}O_2$, 23.3), 149 ($C_8H_5O_3$, 23.7), 83 (C_5H_7O, 76.6), 82 (C_5H_6O, 28.7), 71 (C_4H_7O) and 69 (C_4H_5O, low resoln.). The less mobile fraction was non-crystalline **4e**, yield 0.18 g $[\alpha]_D -$ 106° (*c* 0.044, $CHCl_3$); CD curve (MeOH) $[\theta]_{292} - 4200$, $[\theta]_{245} + 4200$, $[\theta]_{217} - 42\,200$ (last reading); IR ν_{max}^{KBr} cm^{-1}: 3420, 1780, 1750, 1725, 1708, 1650 and 1235. (Calc. for $C_{21}H_{26}O_9$: MW, 422.1575. Found: MW(MS) 422.1575). Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 295 ($C_{15}H_{19}O_6$, 1.0), 294 ($C_{15}H_{18}O_6$, 3.8), 276 ($C_{15}H_{16}O_5$, 8.1), 266 ($C_{14}H_{18}O_5$, 8.2), 250 ($C_{13}H_{14}O_5$, 9.3), 224 ($C_{12}H_{16}O_4$, 62.6), 206 ($C_{12}H_{14}O_3$, 31.8), 164 ($C_{10}H_{12}O_2$, 27.3). 153 ($C_8H_9O_3$, 14.3), 151 ($C_9H_{11}O_2$, 16.4), 136 ($C_8H_8O_2$, 12.0), 125 ($C_7H_9O_2$, 18.2), 97 (C_6H_9O, 27.6), 83 (C_5H_7O, 23), 82 (C_5H_6O, 23.5) and 69 (C_4H_5O, low resoln.).

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