Phytochemistry, 1978, Vol. 17, pp. 845–864 © Pergamon Press Ltd Printed in England. 0031-9422/78/0501-0845 $05.00/0

REVIEW

COUMARINS IN THE RUTACEAE*

ALEXANDER I. GRAY† and PETER G. WATERMAN
Department of Pharmaceutical Chemistry, University of Strathclyde, Glasgow G1 1XW, Scotland

(*Received* 24 *October* 1977)

Key Word Index—Rutaceae; coumarins; distribution; chemotaxonomy; function; review.

Abstract—The biogenesis, structural diversity and distribution of simple, furano- and pyranocoumarins in the Rutaceae is reviewed. The potential value of these compounds as taxonomic markers and their possible functions are discussed. The distribution of simple cinnamic acid precursors of coumarins in the family is also reviewed.

INTRODUCTION

The term coumarin is applied, collectively, to a large group of naturally occurring compounds possessing a 2*H*-1-benzopyran-2-one nucleus (**1**). At present the total number of coumarins reported from natural sources is well in excess of six hundred [1] and is still rising steadily. Included within this assemblage are compounds of varying biogenetic origin. Most coumarins probably derive their benzopyran nucleus from the cyclisation of a C-2-oxygenated *cis*-cinnamic acid but significant numbers appear to be formed from a mixed cinnamic acid/acetate pathway (4-phenylcoumarins) or totally from acetate (4-*n*-propylcoumarins) [1, 2].

Simple structures likely to be derived from cinnamic acids, such as coumarin (**1**), umbelliferone (**2a**) and herniarin (**2b**) are known to occur in many plant families [2–4]. On the other hand, coumarins that have undergone elaboration of the basic structure by the addition of C_5 units originating from mevalonic acid have been noted in relatively few families. The resulting simple prenyl coumarins and derived furano- and pyranocoumarins have been reported sporadically in, among others, the Leguminosae, Moraceae and Meliaceae [3]. It is now apparent, however, that these compounds are of common occurrence only in the Umbelliferae and Rutaceae [3–6].

Whilst the chemistry of coumarins has recently been reviewed [1], there have been no recent compilations on the distribution of these compounds in either family other than the incomplete coverage achieved in *Chemotaxonomie der Pflanzen* [3]. For the Umbelliferae the last exhaustive reviews were those of Neilsen [7, 8] published seven years ago. The Rutaceae has been even less well served, except for inclusion in discussions on individual taxa or other groups of compounds [9–12], and no comprehensive listings have appeared since that of Chakraborty [13].

The purpose of this paper is to give an up-to-data listing of the distribution of coumarins in the Rutaceae within the framework of their probable mode of biogenesis.

BIOGENESIS OF RUTACEOUS COUMARINS

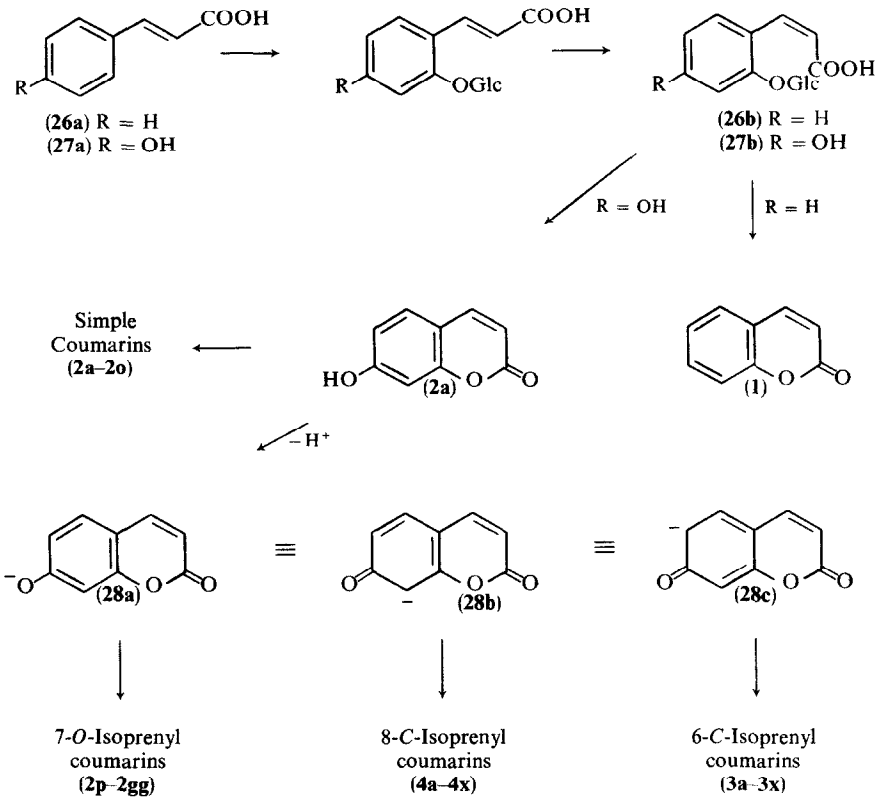
Almost two hundred coumarins (**1–25b**) have been reported to occur in members of the Rutaceae. All, with the possible exception of the 2*H*-naphtho-[2,3b]-pyran-2-ones (**25a, 25b**), appear to be cinnamic acid derived coumarins and to share the same biogenetic pathways observed in other families producing them.

Thus *trans*-cinnamic acid (**26a**) (Scheme 1), formed from the enzyme mediated deamination of phenylalanine [14], undergoes *ortho* oxidation [15], glucosylation and isomerization to the corresponding *cis* acid (**26b**). These processes may include both enzyme catalysed steps and photochemical phenomena [16, 17]. With the exception of coumarin (**1**) and compounds (**25a**) and (**25b**), all known rutaceous coumarins are oxygenated at C-7 indicating that the *trans* and *cis* *p*-coumaric acids (**27a, 27b**) are the usual precursors. The central role of *p*-coumaric acid has been substantiated by numerous feeding experiments (see for example [18]) that indicate, contrary to an earlier hypothesis [19], that further substitution to yield simple substituted coumarins (**2b–8i**) occurs only after cyclisation.

The major feature in the diversification of simple coumarins in both Rutaceae and Umbelliferae is the widespread incorporation of prenyl units. Prenylation has been demonstrated to occur at the umbelliferone stage [20]. In *Ruta graveolens* the addition of the dimethylallyl unit at C-6 appears to be specifically controlled by the enzyme dimethylallylphosphate:umbelliferone transferase [21, 22]; *O* and *C*-8 prenylation presumably being mediated by other, similar, enzyme systems that have still to be resolved. It is possible that one or more of these enzymes could also be responsible for the build up of longer geranyl and farnesyl side-chains in a sequential manner thereby explaining the observation [23] that the majority of labelled mevalonic acid was incorporated into the terminal third of the umbelliprenin (**2gg**) side-chain in *Thamnosma montana*. The

* Part IX in the series 'Chemosystematics in the Rutaceae'. For Part VIII see *Biochem. System. Ecol.* **4**, 259 (1976).

† Present Address: Department of Pharmacognosy, The School of Pharmacy, 29/39 Brunswick Square, London WCIN 1AX, England.



Scheme 1. Origins of simple coumarins

mechanism of prenylation of umbelliferone is visualized as involving the formation of the stable anion (**28a–28c**) which will permit the electrophilic attack of a prenyl carbonium ion at either C-6 or C-8 to yield *C-prenyl* coumarins (**3a–4x**) or on the phenoxide to give *O*-prenyl compounds (**2p–2hh**, Scheme 1). Perhaps the role of the prenylating enzyme(s) is to localize the charge on the anion and thereby direct the attack of the prenyl unit.

A most significant contribution to the proliferation of coumarins is made by the large number of secondary modifications that may then take place on the prenyl side-chain, usually via the initial epoxidation of the olefinic double bond (Table 1). Grundon and McColl [24] have studied the stereochemical aspects of epoxidation of both *O* and *C* prenyl units and suggest that the process may be controlled by two distinct mono-oxygenases, probably because of differing stereoelectronic requirements for the two prenyl types. In addition to the range of simple modifications illustrated in Scheme 1 and Table 1, these side-chains occasionally exhibit more complex elaborations. These may involve intramolecular condensations such as those seen in micromelumin (**3i**) and obtusifol (**6**) or intermolecular reactions between similar *C*-prenyl-7-methoxy coumarins yielding complex pentacyclic *bis*-coumarins such as thamnosin (**7d**).

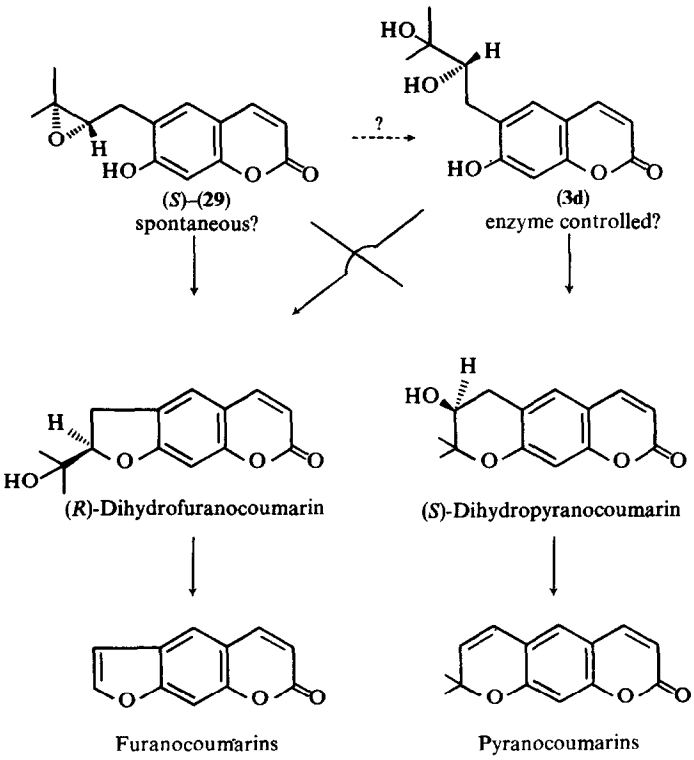
The literature on the formation of furanocoumarins has been reviewed by Floss [25]. The direct involvement of demethylsuberosin (**3a**) and osthenol (**4a**) as precursors of linear (**9a–15f**) and angular (**16a–17c**) furanocoumarins respectively has been established by feeding experiments in both Rutaceae and Umbelliferae [see e.g. 20, 21, 26]. The intermediate would appear to be either the prenyl epoxide (**29**) or the diol (**3d**) for the linear type or their *C*-8-prenyl equivalents for the angular type. During the process of cyclization to the 2′,3′-dihydro-2′-isopropylfuranocoumarin (Scheme 2) inversion of configuration from the prenyl epoxide occurs [24].

One of the problems still to be resolved concerns the mechanism by which the normal furanocoumarins (**13–15, 17**) are formed from their 2′,3′-dihydro-2′-isopropyl counterparts (**9–12, 16**). It seems certain that marmesin (**9a**) is directly involved [20] and tracer experiments indicate the (+)-(*S*)-form, rather than the (−)-(*R*) (nodakenetin). is preferentially incorporated [27]. The sequence of further substitution of furanocoumarins has been studied by Caporale *et al.* [28, 29]. Their findings have been contradictory, the most recent supporting the suggestion [20] that further substitution, in the form of hydroxylation followed by methylation or *O*-prenylation (**13a–13z**), occurs after furan ring formation. The timetable of events leading to the rarer *C*-prenyl furanocoumarins (**14a–14h**) has not yet been studied.

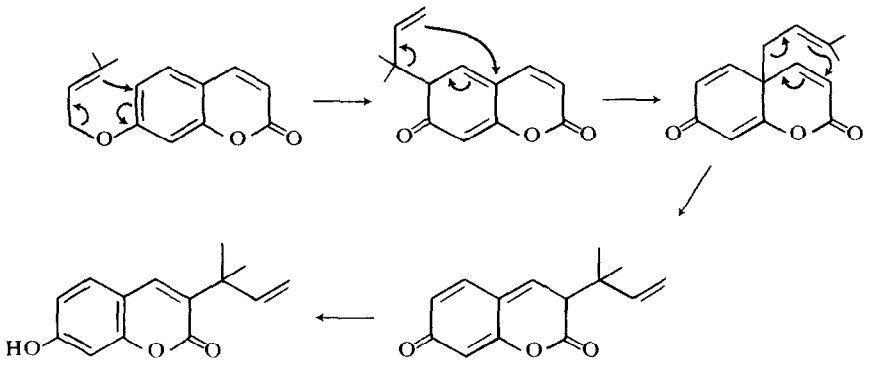
Although no detailed investigations into the formation of pyranocoumarins (**18–24**) have yet been reported the observation [26] that demethylsuberosin (**3a**) is heavily incorporated into 3′,4′-dihydroxanthyletin suggests a pathway analagous to that for furanocoumarins is in operation. It has been noted [30] that, as anticipated [24], the configuration of the *C*-prenyl epoxide intermediate is retained during the formation of pyrano-

Table 1. Mevalonate derived side chains reported from rutaceous coumarins

(i) *3,3-Dimethylallyl*		(ii) *3-Methyl-buta-1,3-dienyl*	
DMA[a]	$CH_2CH{:}C(Me)_2$	IPT[a]	$CH^{1}{:}CHC(Me){:}CH_2$
DMA[b]	$CH_2CH{-}C(Me)_2$ (O)	IPT[b]	$CH{-}CHC(Me){:}CH_2$ (O)
DMA[c]	$CH_2CH(OH)C(OH)Me_2$	IPT[c]	$CH(OH)CH(OH)C(Me){:}CH_2$
DMA[d]	$CH_2CH{:}C(COOH)Me$	IPT[d]	$CH^{1}{:}CHC(OH)Me_2$
DMA[e]	$CH_2CH_2CH(COOH)Me$	IPT[e]	$CH^{c}{:}CHC(OH)Me_2$
DMA[f]	$CH_2COCH(Me)_2$	IPT[f]	$CH^{1}{:}CHCOMe$
DMA[g]	$COCH{-}C(Me)_2$ (O)	IPT[g]	$CH_2CH(OH)C(Me){:}CH_2$
DMA[h]	$COCH_2CH(Me)_2$	IPT[h]	$CH_2COC(Me){:}CH_2$
DMA[i]	$COCH{:}C(Me)_2$	IPT[i]	$COCH_2C(Me){:}CH_2$
DMA[j]	$CHCH{-}C(Me)CO$ (O, O)	(iii) *Abnormal C-5 Units*	
		1,1DMA	$C(Me)_2CH{:}CH_2$
DMA[k]	$CH_2CH{:}C(CH_2OH)Me$	2,2DMA	$CH_2C(Me)_2CHO$
DMA[l]	$CHCOCH(Me)_2$ | $OCOCH_2CH(Me)_2$	1,2DMA	$CH(Me)CH(Me)CHO$
		2,2CP	$CH{-}C(Me)_2$ (CH_2)
DMA[m]	$CH(OH)CH(OH)C(OH)Me_2$		
DMA[n]	$CH_2CH(OH)C(OMe)Me_2$		
DMA[o]	$CH_2CH_2C(OH)Me_2$		
(iv) *Geranyl*			
GER[a]	$CH_2CH{:}C(Me)CH_2CH_2CH{:}C(Me)_2$	GER[b]	$CH_2CH{:}C(Me)CH_2CH_2CH(OH)CH(OH)Me_2$
GER[c]	$CH_2CH{:}C(Me)C{:}CHCOC(Me_2)$ (O)	GER[d]	$CH_2CH_2CH(Me)C{:}CHCOC(Me)_2$ (O)
GER[e]	$CH_2CH{:}C(Me)CH_2CH_2COC(OH)Me_2$	GER[f]	$CH_2CH{:}C(Me)CH_2CH_2C(Me)_2CHO$
(v) *Farnesyl*			
FRN	$CH_2CH{:}C(Me)CH_2CH_2CH{:}C(Me)CH_2CH_2CH{:}C(Me)_2$		



Scheme 2. Formation of linear furanocoumarins and pyranocoumarins from 6-*C*-isoprenyl coumarin precursor (after Grundon and McColl [24]). An analagous pathway involving 8-*C*-isoprenyl coumarin precursors must also exist.



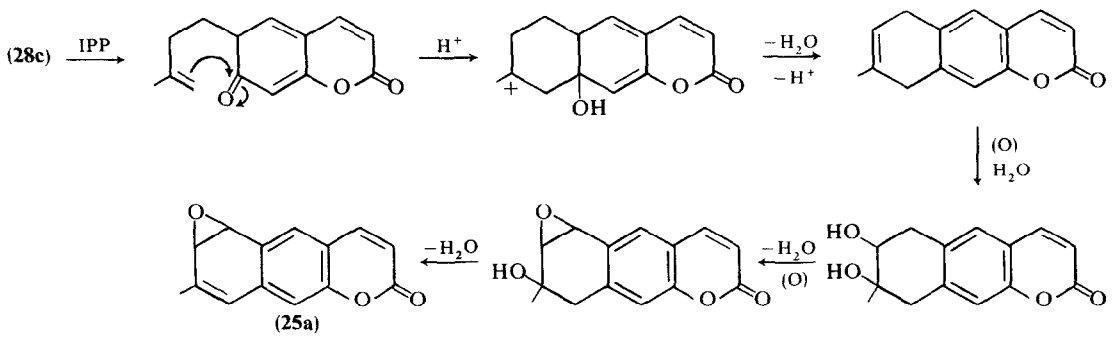
Scheme 3. Possible mechanism for the formation of 3-(1,1-dimethylallyl)-coumarins from 7-(3,3-dimethylallyloxy)-coumarins.

coumarins (Scheme 2). The unusual 2,3-*f* angular pyranocoumarins (**23a–f, 24**) are probably the product of cyclization of a C-6 prenyl unit and a free C-5 hydroxy substituent.

Whilst the general mechanism of the cyclization of furan and pyran rings is now understood much of the detail remains unresolved. One of the foremost questions to be answered concerns the likely intermediate, the epoxide or the diol (Scheme 2). *In vitro* experiments [31] have shown cyclization to occur spontaneously upon epoxidation of a prenyl group to which there is a free *ortho* hydroxy substituent and suggest the epoxide to be the more likely intermediate. The relative paucity of prenyl coumarins isolated with free *ortho* hydroxy functions from the Rutaceae would seem to agree with this contention. A second unanswered question concerns the mechanism governing the choice of formation of either furano- or pyrano coumarin rings. No enzyme system has yet been found to govern either and, in the light of the acknowledged spontaneity of cyclization, it seems feasible that none need exist. In this context the observation [31] that, *in vitro*, the furan ring was formed under neutral or basic conditions and the pyran ring under acidic conditions may well be significant If this situation is paralleled *in vivo* then external factors affecting the pH at the site of synthesis will obviously play a primary role in deciding the structures of the coumarins produced.

In addition to the above the Rutaceae have yielded a number of coumarins referred to by Steck and Mazurek [32] as *'abnormal'* because of the presence of *O* or *C* substituents in the lactone ring (**7f–8i, 11, 12, 15, 19**). Those with *O* substitution are relatively rare and consist of either *bis*-coumarins linked between C-7 of one unit and C-3 of the other by an ether bridge (**7f–7h**) or simple C-3/C-4 *O*-alkyl ethers (**15a–15d**). With one exception, (**8d**), *C*-substitution takes the form of *C*-prenylation at C-3, the isoprene unit usually taking the form of the 1,1-dimethylallyl group rather than the 3,3-dimethylallyl group normally found in other situations. The observation [33] that the C-3 position in umbelliferone is more electronegative than C-6 or C-8, although relevant, does not explain the prevalence of the 1,1-DMA unit. A seemingly attractive hypothesis is the suggestion that the 3-(1,1-DMA)-coumarin arises via a triple Claisen type rearrangement from a 7-(3,3-DMAoxy)-coumarin precursor (Scheme 3). Although such rearrangements are normally performed at elevated temperatures [34] it has long been established [35] that they can take place at low temperatures under catalysis.

Recently two novel coumarins, designated I and II, with proposed structures (**25a**) and (**25b**) have been reported from *Zanthoxylum arnottianum* [36]. At present their structures, which rest solely upon spectral studies, remain to be substantiated by synthesis. If proven correct it would seem unlikely that such a nucleus would have arisen from coumarin itself, a more likely intermediate being a C-6 prenyl umbelliferone which then undergoes an unusual series of oxidation and dehydration steps (Scheme 4) to yield the naphthopyranone nucleus.



Scheme 4. Putative biogenetic pathway to the naphthopyranones of *Zanthoxylum arnottianum*.

DISTRIBUTION OF COUMARINS

The known sources of coumarins within the Rutaceae are listed in Table 2. Where known the plant parts examined are given. It should be noted that not all coumarins reported from a species are necessarily present in all parts examined. In addition a much smaller number of, obviously closely allied, simple cinnamic acids have been found to occur. The commonest of these, substituted *trans* acids and methyl cinnamate, have been recorded in numerous species [263–270], the remainder are listed in Table 3.

An examination of Table 2 shows that coumarins have been recorded from a wide variety of plant parts. The impression gained that the leaf and bark (stem or root) are the predominant sources may not necessarily be true but may simply reflect the greater frequency of studies on these parts. In *Citrus* and its allies where fruit and seed have been widely studied, they also have yielded many coumarins.

Structurally the greatest number of compounds (about 60%) can be described as simple coumarins but the greatest number of isolations would appear to be of furanocoumarins. In both structural diversity and in number of isolations the pyranocoumarins fall well behind the other two types. The commonest individual compound is the furanocoumarin bergapten (**13e**) followed closely by the pyranocoumarin xanthyletin (**19a**). The next four most common are all furanocoumarins, xanthotoxin (**13c**), isopimpinellin (**13g**), psoralen (**13a**) and imperatorin (**13h**). The commonest simple coumarins appear to be scoparon (**2f**) and aurapten (**2s**). About half of the coumarins reported are, to date, known only from single sources.

It is notable that none of the many C-6 or C-8 prenyl coumarins seems to be particularly common, osthol

Table 2. Distribution of coumarins in the Rutaceae (classification after Engler [261])

Species	Plant part(s)	Compounds	References
Rutoideae/Zanthoxyleae			
Zanthoxylum L.[a]			
Z. ailanthoides Sieb. & Zucc.[b]	L, W, R	**2d, 2f, 2k, 13c. 13g, 19a**	[37–43]
Z. americanum Mill.	R	**19a, 19b, 23a, 23b**	[44, 45]
Z. arnottianum Maxim.	R, W, B	**3a, 3b, 3e, 3w, 4a, 4c, 9a, 9g, 9h, 13a, 16a, 18b, 19a, 25a, 25b**	[36, 46, 47]
Z. avicennae Lam.	R	**23c, 23d**	[48]
Z. belizense Lundell	S, L	**2j, 9a, 13g**	[49]
Z. decaryi H. Perr.	B, R, L, F	**2e, 2f**	[50, 50a]
Z. dipetalum H. Mann	R	**19b, 23b, 23d, 24**	[51, 52]
Z. elephantiasis Macfad.	R, B	**19b, 23c, 23d, 23e, 24**	[53–55]
Z. faurei Ohwi	R	**19a**	[56]
Z. flavum Vahl.	R, B, W	**3b, 13a, ?13c, 13h**	[57, 58]
Z. gilletii Waterm.[c]	W	**2f, 2k**	[57]
Z. leprieurii Guill. & Perr.	W	**2k**	[59]
Z. mayu Bertol. *ex* Hook. & Arn.	L	**13a, 13c, 13e, 13g**	[60]
Z. monophyllum P. Wilson	S	**16a**	[61]
Z. ovalifolium Wight[d]	B	**2s, 3b, 3n, 3p, 7d, 13g**	[62–64]
Z. piperitum DC.	R	**2f**	[65]
Z. piperitum v. *inerme* Makino	B	**13h**	[66]
Z. pluviatile Hartley	L	**19a**	[67]
Z. rhetsa DC.	W	**3b**	[68]
Z. schinifolium Sieb. & Zucc.	W, F	**2e, 2f, 13e**	[41, 69, 70]
Z. setosum Hemsl.	L	**2f, ?2k**	[57, 71]
Z. xanthoxyloides Waterm.	F	**13c**	[72]
Geijera Schott.			
G. parviflora Lindl.	L, F	**2s, 2t, 2u, 2v, 2w, 3h**	[73, 74]
G. salicifolia Schott.	L, B	**2a, 2u, 3g, 3h**	[75, 76]
Euodia Forst.			
E. alata F. Muell.		**2a**	[77]
E. beleha Baill.	B	**3d, 9a**	[78]
E. hupehensis Dode	F	**13b, 13c, 13e, 13g, 13l**	[79]
E. viteflora F. Muell.[e]	Resin	**2p, 2q, 2r**	[80]
Orixa Thunb.			
O. japonica Thunb.	L, S	**13c, 13e, 13h**	[81, 82]
Melicope Forst.			
M. mantellii Buch.	B	**19b**	[83]
M. melanophloia C. T. White		**13g**	[84]
M. ternata Forst.	B	**19b**	[85]
Pelea A. Gray			
P. barbigera Hillebr.		**2e, 9a, 10, 13a**	[86]
Choisya HBK			
C. arizonica Standl.	S	**4h, 19a**	[87]
C. mollis Standl.	S	**4h, 19a**	[87]
C. ternata HBK[f]		**4h, 19a**	[87]

Table 2—*continued*

Species	Plant part(s)	Compounds	References
Rutoideae/Zanthoxyleae (contd.)			
Pitavia Mol.			
P. punctata Mol.	L, S	**22c**	[88]
Rutoideae/Ruteae			
Boenninghausenia Reichb.			
B. albiflora Reichb.[g]	L. S. R	**2a, 2h, 3j, 3k, 3o, 3p, 4p, 7c, 7f, 9c, 12, 13c, 13e, 13g, 15e, 16b, 19a, 19h**	[89–98]
Ruta L.			
R. bracteosa DC.[h]	S	**13a, 13c, 13e**	[99]
R. chalepensis L.	S	**11, 12, 13a, 13c, 13e, 13g, 13w, 15e, 19a**	[100–102]
R. graveolens L.[i]	L, S, R	**1, 2a, 2b. 2e, 2g, 3o, 7f, 7g, 7h, 8a, 8b, 8c, 8e, 8f, 8g, 8i, 9a, 9b, 9d, 9e, 9f, 11, 12, 13a, 13c, 13e, 13g, 13l, 13q, 13w, 15e, 19a, 19i**	[101, 103–108]
R. microcarpa Svent.[j]	L	**13e, 13w, 19a, 19c**	[109, 110]
R. montana L.	S, L	**2b, 11, 13a, 13c, 13e, 15e, 15f**	[111–113]
R. oreojasme Webb	L, S, R	**1, 2a, 2b, 2d, 2j, 2k, 2n, 7a, 7b, 8g, 13a, 13c, 13e, 13g, 13h, 13w, 14f, 19a, 19c, 22a**	[110, 114–117]
R. pinnata L f.	L, S, R, F	**1, 2a, 2b, 2d, 2e, 2j, 2n, 2o, 2ee, 2ff, 3e, 4x, 5, 7d, 8g, 8h, 9a, 13a, 13c, 13e, 13g, 13h, 13i, 13j, 13l, 13m, 13n, 13o, 13q, 13u, 13w, 14f, 14g, 17a, 17b, 19a, 19c, 22a**	[110, 114, 118–120]
R sp. Tene 29,62	S	**2l, 2m, 2o, 8d, 9a, 13e, 13l, 14f, 14g**	[110, 121, 122]
Haplophyllum Juss.			
H. dzhungaricum N. Rubtz.	S, R	**19a, 22a**	[123]
H. hispanicum Spach.	S	**2a, 2e, 2n** (artefact), **2s, 2x, 2dd**	[124]
H. multicaule Vved.	S, R	**19a, 22a**	[123]
H. obtusifolium Ledeb.	S	**6**	[125]
H. pedicillatum Juss.	S	**2e, 2x, 2y, 2z**	[126]
Thamnosma Torr.			
T montana Torr. & Frem.	S, R	**2gg, 3l, 3m, 7d, 13a, 13c, 13e, 13g, 13l, 13v, 13w, 14b, 14c, 14d, 14e**	[127–129]
Cneoridium Hook. f			
C. dumosum Hook. f.	S	**4b, 9a, 13c, 13e, 13g, 13h, 13l**	[130]
Dictamnus L.			
D. albus L.	S, F	**2s, 13a, 13c, 13e**	[131–133]
D. dasycarpus Turcz.	S	**13a, 13c**	[134]
D. gymnostylis Stev.	S, F	**13a, 13c**	[134]
D. hispanicus Webb	S	**13c, 13e**	[102]
Rutoideae/Boronieae			
Myrtopsis O. Hoffm.			
M. macrocarpa Schltr.	S	**4b, 22a**	[135]
M. myrtoidea Guillaum.	S	**13e, 22a**	[135]
M. novae-caledonica Engl.	S	**4b, 13e, 13v, 22a**	[135]
M. sellingii Guillaum.	S	**4i, 4l, 13e, 13v**	[135, 136]
Eriostemon Sm.			
E. brucei F. Muell.	S	**20a, 20b, 21a, 21b**	[137, 138]
E. coccineus C. A. Gard.	S	**23c**	[48, 139]
E. obovalis A. Cunn.		**2j, 13e, 19b**	[140]
E. tomentellus Diels	L, S	**3r**	[141]
E. trachyphyllus F. Muell.	L, R	**13e, 19b, 19d**	[142]
Phebalium A. Juss.			
P. argenteum Sm.	L	**13a, 13c, 13e, 22a**	[143]
P. dentatum Sm.	L	**4m**	[144]
P. drummondii Benth.	L	**4m, 13i**	[139]
P. filiforme Turcz.	L	**13c**	[139]
P. nudum Hook.	B	**7e, 13f, ?13v**	[13, 145, 146]
P. tuberculosum F. Muell.	L	**4m**	[139]
Rutoideae/Diosmeae			
Agathosma Willd.			
A. puberula Fourc.	L	**2cc**	[147]
Coleonema Bartl. & Wendl.			
C. album Bartl. & Wendl.	F	**3e**	[87]

Table 2—*continued*

Species	Plant part(s)	Compounds	References
Flindersioideae			
Flindersia R. Br.			
F. bennetiana F. Muell.	L, B, W	**4b, 13g, 22a**	[148]
F. brayleyana F. Muell.	B	**4t, 22c**	[148]
F. collina Baill.	B	**2aa**	[148]
F. dissosperma Domin.	B	**2aa**	[148]
F. iffliana F Muell.	B	**22a**	[148]
F. maculosa Lindl.	L, B	**2aa**	[148]
F. pimenteliana F. Muell.	B	**19a, 22a**	[149]
F. pubescens Baill.	B	**4b**	[148]
F. schottiana F. Muell.	L, B, W	**4b**	[148]
Chloroxylon DC.			
C. swietenia DC.	L, W	**2f, 3a, 3x, 9a, 11, 13e, 13g, 14h, 15e, 19a, 19b, 19c, 23a**	[57, 150–152]
Toddalioideae			
Helietta Tul.			
H. longifoliata Britt.		**11**	[153]
Ptelea L.			
P. aptera Parry	L, S	**13a, 13v**	[154]
P. baldwinii Torr. & Gray	S	**13i**	[155]
P. crenulata Green	L, S, F	**2s, 9a, 13a, 13e, 13h, 13i**	[154]
P. trifoliata L.	L, S	**2e, 2g, 2s, 9a, 13e, 13g, 13h, 13v, 13w**	[154, 156–159]
P. trifoliata ssp. *pallida* v. *confinis* Bailey	L	**9a, 9b, 13v, 13w, 13x**	[160, 161]
Casimiroa Llave & Lex.			
C. edulis Llave & Lex.	B, R, Sd	**2e, 13e, 13f, 13g, 13v, 13y**	[162–164]
Toddalia Juss.			
T. aculeata Pers.	S, R, B	**2m, 3s, 3t, 3u, 13e, 13g, 17c, 19c, 22b**	[165–167]
Halfordia F. Muell.			
H. kendack F. Muell.	B	**15a, 15b, ?15c, 15d**	[168–170]
H. scleroxyla F. Muell.	B	**15b, 15c, 19b**	[168, 171]
Hortia Vand.			
H. arborea Engl.	R	**15e, 16c, 19a, 19h, 24**	[172]
H. badinii M. A. Lisboa	W	**4u**	[173]
H. longifolia Benth. *ex* Engl.	W	**2f, 4u**	[174]
Skimmia Thunb.			
S. formanii Knight		**13l, 13m**	[175]
S. fortunii Mast.	L	**2c**	[176]
S. japonica Thunb.	L	**2a, 2c, 2e, ?4d, 4e, 4f, 13e, 13l, 13m, 13n, 13p, 22a**	[13, 176, 177]
S. laureola Sieb. & Zucc.	L, B	**2a, 2c, 2e, 13e, 13g**	[176, 178, 179]
S. repens Nakai	S	**22a**	[180]
Amyris P. Br.			
A. madrensis Watt	L, S	**3f, 3h**	[181]
A. simplicifolia Karst.	L	**19g**	[182]
Aurantioideae/Clauseneae[k]			
Micromelum Blume			
M. minutum Seem.[l]	L, S	**3i, 4b**	[183]
M. pubescens Blume[l]	L, S	**3e, 3i, 4p**	[184, 185]
Glycosmis Correa			
G. cyanocarpa Spreng.	L, S, R	**2j, 3p, 19a**	[186]
Clausena Burm.			
C. anisata Willd.	R	**4b, 4u, 11, 13h, 19b. 19h**	[187–189]
C. dentata R. & S.	R	**13h, 19e, 19f**	[190—191]
C. excavata Burm. f.	R, S	**18c, 23f**	[192]
C. heptaphylla Wight & Arn.	R, S	**18c, 19f, 23f**	[191, 193–194]
C. indica Oliv.	R	**11, 13h, 13v, 15e, 15f**	[195, 196]
C. pentaphylla DC.		**19f, 19j, 23f**	[197]
Murraya L.			
M. elongata A. DC.	L, B.	**4n, 4s**	[198, 199]
M. koenigii Spreng.	L	**2g**	[200]
M. paniculata Jack.[m]	L, B, F, Fl	**2e, 2g, 4b, 4d, 4e, 4g, 4j, 4m, 4n, 4s, 4u, 4v**	[201–209]

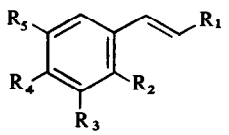
Table 2—*continued*

Species	Plant part(s)	Compounds	References
Aurantioideae/Citreae			
Triphasia Lour.			
T. trifolia P. Wils.	Sd	**13g**	[87]
Luvunga Buch. Ham.			
L. eleutherandra Dalz.	S	**3r, 19a**	[210]
L. scandens Buch. Ham	F	**13c, 13g, 19a, 19c**	[211]
Severinia Ten			
S buxifolia Ten.	L, F	**4w, 13e, 13g, 13h, 22a**	[212]
Hesperathusa Roem.			
H. crenulata Roem.[n]	L	**3b, 3c, 3n, 3p, 9a, 19c**	[213–215]
Atalantia Correa			
A. missiones Oliv.[o]	L	**3r, 13g**	[216]
A. monophylla Correa	R	**2s, 9a, 19a**	[217–218]
A. wightii Tan.	R	**2s**	[219]
Eremocitrus Swingle			
E. glauca Lindl.	F	**2a, 3e**	[220]
Poncirus Raf.			
P. trifoliata Raf.[p]	W, R, F, Sd	**2s, 2x, 4j, 4k, 9a, 13b, 13e, 13g, 13h, 13i, 13j, 14a, 19f, 22a**	[155, 221–228]
Citrus L.[q]			
C. acida Roxb.	L, B	**2j, 13e, 13g, 19a**	[229–230]
C. aurantifolia Swingle	F	**2e, 2j, 2bb, 13d, 13e, 13g, 13h, 13k, 13l, 13n, 13r, 13v, 13w, ?13z**	[11, 231–234]
C. aurantium L.	B, R, W, F	**2a, 2f, 2s, 4b, 4o, 13e, 19a, 22a**	[233, 235, 236]
C. aurantium v. *amara* L.	R, F	**4o, 22a**	[235, 237]
C aurantium v. *natsudaidai*	F	**2a, 2b, 2s, 4o, 13d, 19f**	[13, 238–240]
C. bergamia Risso	F	**2j, 2bb, 13d, 13e, 13r**	[11, 13, 233]
C limetta Risso	R, F	**2j, 2bb, 13g, 13r, 13w, 22a**	[241]
C. limettoides Tan.	B, R, W, F	**19a**	[236]
C. limon Burm. f.	B, W. R. F	**2f, 2j, 2bb, 2hh, 13e, 13g, 13h, 13k, 13l, 13n, 13r, 13v, 13w, ?13z, 19a**	[11, 233, 235, 236, 242, 243]
C. macroptera Montr.	F	**13r, 13s**	[244]
C. medicus v. *sarcodactylis* Sw.	R	**2j, 19a, 19e**	[245, 246]
C. medicus v. vulgaris Risso		**19a**	[13]
C. meyeri	S	**13h**	[247]
C. mitis Blanco		**2f**	[234]
C. nobilis v. *sunkii* Lour.	R	**19a**	[248]
C. paradisii Macfad.[r]	B, W, R, F	**2a, 2j, 2s, 2t, 4b, 4r, 13d, 13e, 13r, 13t, 13w, 19a, 22a**	[11, 233, 235, 236, 242, 249]
C. sinensis Osbeck.	B, W, R	**2f, 4o, 19a**	[234, 236, 250]
C tankan Sieb?		**19a**	[251]
Aegle Correa			
A. marmelos Correa	B, R, F	**2a, 2c, 2e, 2f, 2s, 2t, 9a, 13a, 13c, 13h, 14a, 18a**	[252–256]
Afraegle Engl.			
A. paniculata Schumm. & Thonn.	S	**2f, 2s, 9a, 13c, 13h, 13i, 19a, 19b**	[257]
Aegleopsis Swingle			
A. chevalieri Swingle	F, Sd	**2f, 13g, 13h**	[221, 222, 258]
Feronia Correa			
F. elephantum Correa	L, B, R	**2s, 2x, 9a, 13e, 13g**	[259, 260]

Plant part(s): B – stem bark; F – whole fruit; Fl – flower; L = leaf; R – whole root or root bark; S = whole stems or branches; Sd = seed; W = wood. [a] Including *Fagara* L. [b] Including *Z. inerme* Koidz and *F. ailanthoides* v. *yakumontana* Sagumoto. [c] = *Fagara macrophylla* Engl. [d] Including *Z. dominianum* Merr. & Perr. and *Z. suberosum* C. T. White. [e] = *E. littoralis* Endl. [f] Implied presence of coumarins from ref. [87]. [g] Including *B. albiflora* v. *japonica* Suzuki. [h] Conspecific with *R. chalepensis* L.? [i] Some of the coumarins reported from *R. graveolens* have been isolated only from tissue cultures. [j] = *R.* sp. 46,782. [k] Aurantioideae classified according to Swingle [262]. [l] Conspecific? [m] Including *M. exotica* L. [n] Including *Limonia crenulata* Roxb. [o] = *Pamburus missiones* Swingle. [p] Includes *Citrus trifoliata* L. [q] *Citrus* nomenclature remains confused, only references and isolations that seem assignable to a recognized taxa are included. [r] Includes *C. decumana* L. and *C. grandis* Hassk.

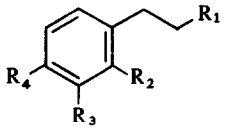
Table 3. Simple cinnamic acid derivatives of the Rutaceae

(a) *Cinnamic acids*



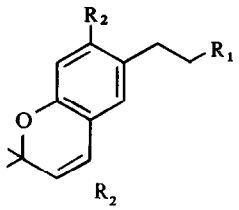
		R_1	R_2	R_3	R_4	R_5	
	(30a)	COOMe	H	H	OH	H	*Boenninghausenia albiflora* [97]
	(30b)	COOMe	H	H	OMe	H	*Eriostemon obovalis* [271]
	(30c)	COOMe	H	H	OGER[a]	H	*Acronychia baueri* Schott. [272]
	(30d)	COOMe	H	H	OGER[a]	OMe	*Acronychia baueri* [272]
	(30e)	COOMe	OMe	H	OH	OMe	*Zanthoxylum piperitum* [65]
Parvifloral	**(30f)**	CHO	H	OMe	OH	DMA[a]	*Zanth. parviflorum* Benth. [273]
	(30g)	COOH	OH	H	OH	DMA[a]	*Chloroxylon swietenia* [152]

(b) *Dihydrocinnamic acids*



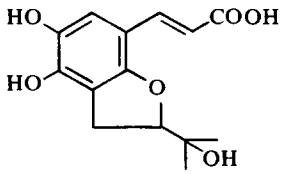
		R_1	R_2	R_3	R_4	
	(31a)	COOMe	OMe	DMA[a]	OMe	*Hortia badinii* [173]
	(31b)	CH_2OH	H	H	OH	*Zanthoxylum cuspidatum* Benth. [274]
Cuspidiol	**(31c)**	CH_2OH	H	H	ODMA[a]	*Zanthoxylum cuspidatum* [274]
Xanthoxylol	**(31d)**	CH_2OH	H	DMA[a]	OH	*Zanthoxylum xanthoxyloides* [59]

(c) *Pyranodihydrocinnamic acids*



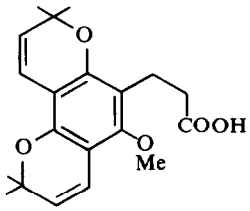
	R_1	R_2	
(32a)	COOH	H	*Hortia badinii* [173]
(32b)	COOMe	H	*Hortia badinii* [173]
(32c)	COOMe	OMe	*Hortia badinii* [173]

(d) *Furanocinnamic acids*

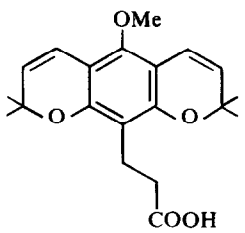


gravolenic acid (**33**) — *Ruta graveolens* [275]

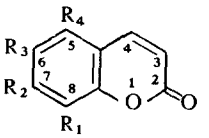
(e) *Dipyranodihydrocinnamic acids*



eriostemoic acid (**34a**) — *Eriostemon thryptomenoides* Moore [141] (L); *Eriostemon tomentellum* Diels [141] (L); *Geleznowia verrucosa* Turcz. [141] (L)



eriostoic acid (**34b**) — *Eriostemon coccineus* [276] (L, S); *Eriostemon dessertii* Pritz. [276] (L, S); *Eriostemon diformis* A. Cunn. [276] (L, S); *Eriostemon hispidulis* Sieb. *ex* Spreng. [277] (L); *Philotheca hassellii* F. Muell. [276]

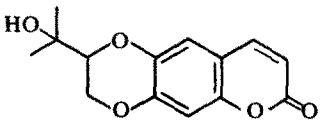


	R_1	R_2	R_3	R_4
Coumarin (**1**)	H	H	H	H
Umbelliferone (**2a**)	H	OH	H	H
Herniarin (**2b**)	H	OMe	H	H
Skimmin (**2c**)	H	Ogl	H	H
Aesculetin (**2d**)	H	OH	OH	H
Scopoletin (**2e**)	H	OH	OMe	H
Scoparon (**2f**)	H	OMe	OMe	H
Scopolin (**2g**)	H	Ogl	OMe	H
— (**2h**)*	OH	OMe	H	H
— (**2i**)*	OMe	OMe	H	H
Limettin (citropten) (**2j**)	H	OMe	H	OMe
— (**2k**)	OMe	OMe	OMe	H
— (**2l**)	OH	OMe	H	OMe
— (**2m**)	OMe	OMe	H	OMe
Sabandinin (**2n**)		O—CH_2—O	H	OMe
Sabandin (**2o**)	OMe		O—CH_2—O	OMe
— (**2p**)	H	ODMA[a]	H	H
— (**2q**)	H	ODMA[d]	H	H
— (**2r**)	H	ODMA[e]	H	H
Aurapten (**2s**)	H	OGER[a]	H	H
Marmin (**2t**)	H	OGER[b]	H	H
Geiparvarin (**2u**)	H	OGER[c]	H	H
— (**2v**)	H	OGER[d]	H	H
— (**2w**)	H	OGER[e]	H	H
— (**2x**)	H	OGER[a]	OMe	H
— (**2y**)	H	OGER[b]	OMe	H
Pedicellone (**2z**)	H	OGER[e]	OMe	H
Collinin (**2aa**)	OMe	OGER[a]	H	H
— (**2bb**)	H	OMe	H	OGER[a]
Puberulin (**2cc**)	OMe	ODMA[a]	OMe	H
— (**2dd**)	H	OGER[d]	OMe	OMe
Sabandinol (**2ee**)		O—CH_2—O	H	ODMA[c]
Sabandinone (**2ff**)		O—CH_2—O	H	ODMA[f]

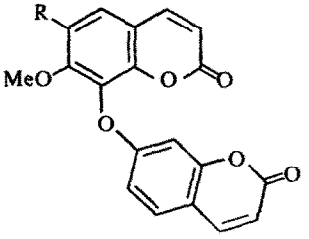
	R_1	R_2	R_3	R_4
Umbelliprenin (**2gg**)	H	OFRN	H	H
— (**2hh**)	H	OMe	H	ODMA[a]
Demethylsuberosin (**3a**)	H	OH	DMA[a]	H
Suberosin (**3b**)	H	OMe	DMA[d]	H
— (**3c**)	H	OMe	DMA[b]	H
Peucedanol (**3d**)	H	OH	DMA[c]	H
— (**3e**)	H	OMe	DMA[c]	H
Hopeyhopine (**3f**)	H	OMe	DMA[g]	H
Geijerin (**3g**)	H	OMe	DMA[h]	H
— (**3h**)	H	OMe	DMA[i]	H
Micromelumin (micromelin) (**3i**)	H	OMe	DMA[j]	H
— (**3j**)	H	OH	IPT[j]	H
— (**3k**)	H	OH	IPT[e]	H
Thamnosmin (**3l**)	H	OMe	IPT[b]	H
Thamnosmonin (**3m**)	H	OMe	IPT[c]	H
Suberenol (**3n**)	H	OMe	IPT[d]	H
Suberenone (**3o**)	H	OMe	IPT[f]	H
Crenulatin (**3p**)*	H	OMe	CHO	H
— (**3q**)†	H	OMe	CH_2OH	H
Ostruthin (**3r**)	H	OH	GER[a]	H
Toddaculine (**3s**)	H	OMe	DMA[a]	OMe
Aculeatin (**3t**)	H	OMe	DMA[b]	OMe
Toddalolactone (**3u**)	H	OMe	DMA[c]	OMe
— (**3v**)*	OMe	OH	DMA[a]	H
Arnottianol (**3w** tent)	OH	OMe	DMA[a]	H
Swietenol (**3x**)	H	OH	DMA[o]	H

	R_1	R_2	R_3	R_4
Osthenol (**4a**)	DMA[a]	OH	H	H
Osthol (**4b**)	DMA[a]	OMe	H	H
Arnottinin (**4c** tent)	DMA[k]	OH	H	H
Meranzin (**4d**)	DMA[b]	OMe	H	H
— (**4e**)	DMA[c]	OMe	H	H
Isomeranzin (**4f**)	DMA[f]	OMe	H	H
Paniculation (**4g**)	DMA[l]	OMe	H	H
— (**4h**)	DMA[a]	ODMA[a]	H	H
Myrselline (**4i**)	DMA[a]	ODMA[b]	H	H
Poncimarin (**4j**)	DMA[b]	ODMA[b]	H	H
Isoponcimarin (**4k**)	DMA[f]	ODMA[b]	H	H
Myrsellinol (**4l**)	DMA[a]	ODMA[c]	H	H
Phebalosin (**4m**)	IPT[b]	OMe	H	H
Murrangetin (**4n**)	IPT[c]	OMe	H	H
Auraptenol (**4o**)	IPT[g]	OMe	H	H
Micropubescin (**4p**)‡	IPT[h]	OMe	H	H
Murrayone (**4q**)‡	IPT[i]	OMe	H	H
Citrusal (**4r**)	22DMA	OMe	H	H
Murralongin (**4s**)	12DMA	OMe	H	H
Brayleyanin (**4t**)	DMA[a]	ODMA[a]	OMe	H
Coumurrayin (**4u**)	DMA[a]	OMe	H	OMe
Mexoticin (**4v**)	DMA[c]	OMe	H	OMe
— (**4w**)	DMA[f]	OMe	H	OMe
Pinnarin (**4x**)	11DMA	OMe	H	OMe
Ulopterol (**5**)§	H	OMe	H	DMA[c]

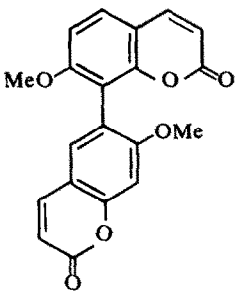
* Not, as described in ref. [186], angelical which is the C-8 aldehyde isomer.
† Coumarins not actually isolated but occur as 3-(11DMA) substituted compounds.
‡ The situation of murrayone (**4q**) is confused. It may well be identical to micropubescin.
§ Ref. [120] states ulopterol is present in *Ruta pinnata* but gives structure (**3e**).



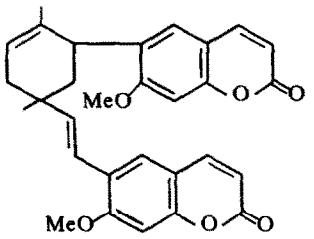
Obtusifol (**6**)



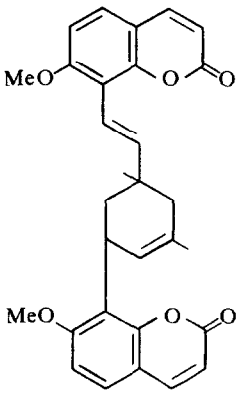
Fatagenin (**7a**) R = H
Oreojasmin (**7b**) R = OMe



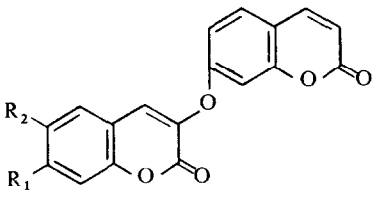
Masukaze lactone (**7c**)



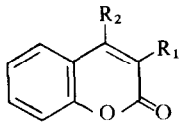
Thamnosin (cyclobisuberodiene) (**7d**)



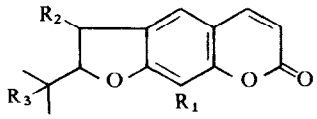
Phebalin (**7e**)



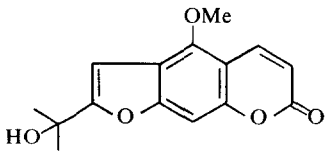
	R_1	R_2
Daphnoretin (**7f**)	OH	OMe
— (**7g**)	OMe	OMe
Daphnorin (**7h**)	Ogl	OMe



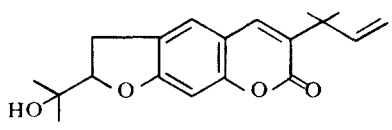
	Basic Type	R_1	R_2
— (**8a**)	**2b**	11DMA	H
— (**8b**)	**2e**	11DMA	H
Rutacultin (**8c**)	**2f**	11DMA	H
— (**8d**)	**2h**	H	11DMA
Gravelliferon (**8e**)	**3a**	11DMA	H
— (**8f**)	**3b**	11DMA	H
Pinnaterin (**8g**)	**3q**	11DMA	H
— (**8h**)	**3v**	11DMA	H



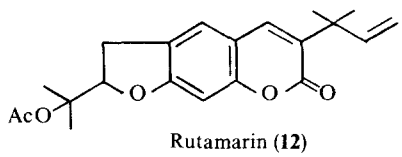
	R_1	R_2	R_3
(+)Marmesin (**9a**)	H	H	OH
(−)Nodakenetin			
Marmesinin (**9b**)	H	H	Ogl
— (**9c**).	H	H	OAc
Rutaretin (**9d**)	OH	H	OH
Rutarin (**9e**)	Ogl	H	OH
Isorutarin (**9f**)	OH	H	Ogl
— (**9g**)	OMe	H	OH
Xanthoarnol (**9h**)	H	OH	OH



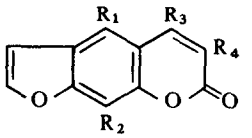
(**10**)



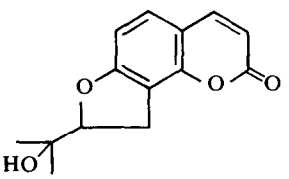
Chalepin (**11**)
(heliettin)



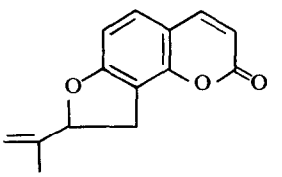
Rutamarin (**12**)



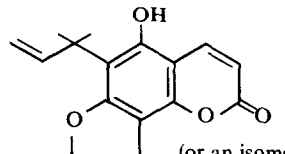
	R_1	R_2	R_3	R_4
Psoralen (**13a**)	H	H	H	H
Xanthotoxol (**13b**)	H	OH	H	H
Xanthotoxin (**13c**)	H	OMe	H	H
Bergaptol (**13d**)	OH	H	H	H
Bergapten (**13e**)	OMe	H	H	H
— (**13f**)	OMe	OH	H	H
Isopimpinellin (**13g**)	OMe	OMe	H	H
Imperatorin (**13h**)	H	ODMA[a]	H	H
Heraclenin (**13i**)	H	ODMA[b]	H	H
Heraclenol (**13j**)	H	ODMA[c]	H	H
(**13k**)	H	OGER[a]	H	H
Isoimperatorin (**13l**)	ODMA[a]	H	H	H
Oxypeucedanin (**13m**)	ODMA[b]	H	H	H
Prangol (**13n**)	ODMA[c]	H	H	H
Isooxypeucedanin (**13o**)	ODMA[f]	H	H	H
— (**13p**)	ODMA[n]	H	H	H
Pangeline (**13q**)	OIPT[g]	H	H	H
Bergamottin (**13r**)	OGER[a]	H	H	H
— (**13s**)	OGER[b]	H	H	H
— (**13t**)	OGER[f]	H	H	H
Tederin (**13u**)	$OCHMe_2$	OMe	H	H
Phellopterin (**13v**)	OMe	ODMA[a]	H	H
Byakangelicin (**13w**)	OMe	ODMA[c]	H	H
— (**13x**)	OMe	OIPT[g]	H	H
— (**13y**)	OMe	OGER[a]	H	H
— (**13z**)	OGER[a]	OMe	H	H
Alloimperatorin (**14a**)	DMA[a]	OH	H	H
— (**14b**)	DMA[a]	OMe	H	H
— (**14c**)	DMA[b]	OMe	H	H
— (**14d**)	DMA[c]	OMe	H	H
Thamontanin (**14e**)	DMA[m]	OMe	H	H
Benahorin (**14f**)	11DMA	OMe	H	H
Furopinnarin (**14g**)	OMe	11DMA	H	H
Swietenone (**14h**)	H	$COCMe_3$	H	H
Halkendin (**15a**)	H	H	OMe	OMe
Halfordin (**15b**)	OMe	H	OMe	OMe
Isohalfordin (**15c**)	H	OMe	OMe	OMe
Halfordinin (**15d**)	OMe	H	O11DMA	OMe
Chalepensin (**15e**) (Xylotenin)	H	H	H	11DMA
Rutolide (**15f**) (Clausindine)	H	H	H	22CP



Columbianetin (**16a**)

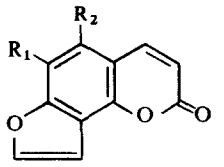


Angenomilin (**16b**)

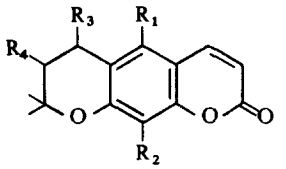


(or an isomer thereof)

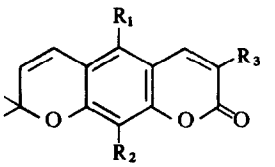
Hortiolone (**16c**)



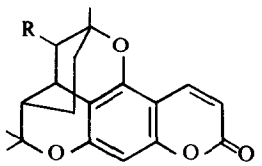
	R_1	R_2
Sphondin (**17a**)	OMe	H
Isobergapten (**17b**)	H	OMe
Pimpinellin (**17c**)	OMe	OMe



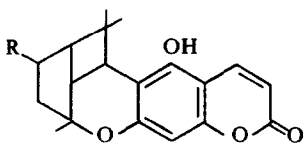
	R_1	R_2	R_3	R_4
Decursinol (**18a**)	H	H	H	OH
Arnottianin (**18b**)	H	OMe	H	OH
Clausenin (**18c**)	OH	H	=O	H



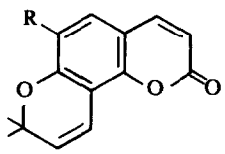
	R_1	R_2	R_3
Xanthyletin (**19a**)	H	H	H
Xanthoxyletin (**19b**)	OMe	H	H
Luvangetin (**19c**)	H	OMe	H
Trachyphyllin (**19d**)	OH	DMA[a]	H
Nordentatin (**19e**)	OH	11DMA	H
Poncitrin (**19f**) (Dentatin)	OMe	11DMA	H
— (**19g**)	H	H	DMA[a]
— (**19h**)	H	H	11DMA
— (**19i**)	H	DMA[a]	11DMA
Clausarin (**19j**)	OH	11DMA	11DMA



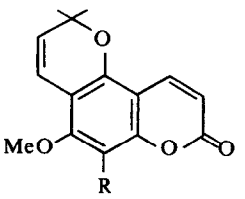
Bruceol (**20a**) R = OH
— (**20b**) R = H



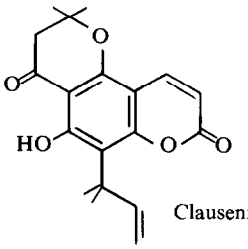
Eriobrucinol (**21a**) R = H
Hydroxyeriobrucinol (**21b**) R = OH



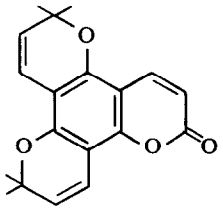
Seselin (**22a**) R = H
Norbraylin (**22b**) R = OH
Braylin (**22c**) R = OMe



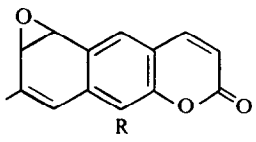
Alloxanthoxyletin (**23a**) R = H
Dipetaline (**23b**) R = DMA[a]
Avicennin (**23c**) R = IPT[a]
Avicennol (**23d**) R = IPT[d]
c-Avicennol (**23e**) R = IPT[c]



Clausenidin (**23f**)



Dipetalolactone(**24**)
(Hortiline)



— (**25a**) R = H
— (**25b**) R = OMe

(**4b**) being the most frequent. The great range of side-chain structures found among these two groups can, without doubt, be attributed to prior methylation of the *ortho* hydroxyl function before epoxidation blocking any chance of cyclization and permitting the secondary modifications to occur.

CHEMOTAXONOMIC SIGNIFICANCE

Above the family level, two observations of a positive nature can be made. Firstly, among those families usually considered to make up the natural order Rutales (Rutaceae, Simaroubaceae, Meliaceae, Burseraceae, Cneoraceae and, perhaps, Anacardiaceae) coumarins have been found only in the Rutaceae and Meliaceae [278]. In the latter, coumarins appear largely restricted in distribution to genera of the subfamily Cedreloideae which Hartley has suggested [279] may have significant morphological similarities to the Flindersioideae. Whilst the co-occurrence of coumarins in these subfamilies may well be pertinent to an understanding of the phylogeny of Rutaceae and Meliaceae, it must be observed that the secondary metabolism of the Flindersioideae is typically rutaceous [9, 148] and does not support the proposal [280] that it be raised to the level of a family *inter cedis* Rutaceae and Meliaceae.

The second point of note concerns the high degree of similarity between the coumarins of the Rutaceae and Umbelliferae which has already led to the suggestion [281] that these families, not normally regarded as closely allied, are phylogenetically adjacent. The co-identity of many of their coumarins is indeed striking, a comparison of Neilsen's list of umbelliferous coumarins [7] with that given here shows no major area where they are distinct, and if a direct phylogenetic link were to prove untenable would represent a major case of chemical convergence. A comparison of the secondary modifications to the prenyl side-chains that abound in both families does however show some interesting distinctions. In the Umbelliferae the widespread occurrence of senecioyl (DMA[i]), isovaleryl (DMA[h]), 2-methylbutyryl (—COCH(Me)CH_2CH_3) and angeloyl (—COC:(Me)$CHCH_3$) side-chains, often esterifying 3′,4′-dihydroxydihydropyranocoumarins, shows a distinct difference in coumarin ornamentation between the two families. Similarly in its use of the isopentenyl moiety and the formation of C-3 prenyl coumarins the Rutaceae also demonstrates distinct pathways. These distinctions are probably even more marked than they at first appear as there is strong evidence [7] that the prenyl-like compounds of the Umbelliferae are actually degradation products of amino acids, a route not yet reported to occur in the Rutaceae.

Within the Rutaceae it would appear that there is no significant variation in the overall distribution of coumarin types between the three major subfamilies. The total number of isolations of all coumarins have been made in the approximate ratio of 6:1:3 between Rutoideae, Toddalioideae and Aurantioideae. A breakdown of the isolations of linear, angular and dihydro furano- and pyranocoumarins shows little deviation from this ratio. Similarly among simple coumarins the overall ratio remains about the same although it should be noted that if the C-8 prenyl and C-3 prenyl subgroups are considered separately it swings more toward the Aurantioideae and Rutoideae (tribe Ruteae) respectively.

The seemingly random distribution among furano- and pyranocoumarin types both within the Rutaceae and between Rutaceae and Umbilliferae appears to suggest that these structures *per se* have little taxonomic value. Such a state of affairs complies with that anticipated if they are the result of spontaneous uncontrolled cyclization. Until such time as this hypothesis is disproved by the discovery of the controlling system, it would seem prudent to consider only those processes known to be

enzyme controlled (coumarin formation, prenylation, and further ornamentation) as potentially useful taxonomic markers.

Few rutaceous genera that have been thoroughly investigated have been found to lack coumarins. One group which may be atypical in this respect are the African Toddalioideae, other than *Toddalia* itself, which, despite considerable investigation [50a, 282, 283], have yet to yield coumarins. The chemically atypical *Phellodendron* Rupr. (Toddalioideae) also appears to be devoid of coumarins.

Some trends do appear to exist in the substitution patterns of coumarins. Oxygenation at more than two positions in the coumarin nucleus is relatively rare, the 5,7,8 pattern being found in *Ruta* and the 6,7,8 mainly in *Zanthoxylum*. The unusual IPT type side-chain is found at C-6 mainly in the closely allied genera *Ruta* and *Thamnosma* and at C-8 in the apparently unrelated *Murraya* and *Phebalium*. A further possible trend occurs among monosubstituted furanocoumarins going from relatively little prenylation in the Rutoideae (Zanthoxyleae) to regular prenylation in the Aurantioideae, with the Toddalioideae and Rutoideae (Ruteae) in an intermediate position. With the exception of the ubiquitous aurapten (**2s**) *O*-geranyl substituents occur mainly in *Geijera* (Zanthoxyleae) and in the Aurantioideae. Substitution at C-3, usually with a 1,1-DMA group, occurs in only a small number of genera and appears to be particularly significant in *Ruta* (with simple coumarins) and *Clausena* (with pyranocoumarins). Prenyl substitution at C-8 would appear to occur much less frequently than at C-6 and may reflect a relative rarity of the C-8 enzyme which could be taxonomically valuable.

A few taxa are characterized by their own highly individual coumarins. Among these the most striking are the genus *Halfordia* (3,4-oxygenated coumarins), *Eriostemon brucei* (compounds **20a–21b**), and *Toddalia aculeata* (5,7-dimethoxy-6-prenyl coumarins).

Finally, the taxonomic potential of coumarins at the subspecific and population levels has still to be explored. The only study to date, relating to varieties of *Ptelea trifoliata* [284], suggests that they may have some value.

POSSIBLE ROLES FOR COUMARINS

Recently increasing attention has been paid to the possible protective role of secondary compounds [285, 286]. A wide range of toxic effects on animals have been attributed to coumarins [287, 288] including antibacterial activity, vasodilatory and diuretic effects, anticoagulent properties, hepatoxicity and respiratory stimulation. Not surprisingly many species of Rutaceae and Umbelliferae have been used in ethnic medicine [289] and it would seem certain that coumarins are implicated in many of their activities. Some furanocoumarins have been observed to cause skin photosensitization on contact, a phenomenon that has been attributed to combination between the coumarin and the pyrimidine moieties of DNA on irradiation with sunlight or long wave UV [290, 291]. A well defined structure–activity relationship is exhibited among furanocoumarins, psoralen being the most active followed by xanthotoxin and bergapten. Phenolic furanocoumarins and more highly substituted compounds have found to be inactive. It has recently been observed that the dihydrofurano-coumarin rutamin (**12**) possesses cytotoxic activity of the same order as 6-mercaptopurine [292] and the heliettin (**11**) and xantyletin (**19a**) also appreciable activity. Fifteen other coumarins tested proved to be inactive.

In light of the wide range of toxic effects noted above it would seem certain that the ingestion of, or even prolonged external contact with, plants containing significant quantities of coumarins would have a detrimental effect on an organism not adapted to their detoxification. Some coumarins can therefore be regarded, whether as their *raison d'être* or as a valuable side-effect is uncertain, as performing a protective function against generalist herbivores.

Other studies [293, 294] have demonstrated that furanocoumarins are active against many fungi and suggest that they may be employed by *Citrus* species to combat fungal withertip disease. In the umbelliferous plants celery [295] and parsnip [296] it has been shown that the synthesis of furanocoumarins may be induced by inoculation with fungi. No studies have yet been carried out to ascertain if this phytoalexin-like response can be induced in the Rutaceae. Furanocoumarins have also been demonstrated to inhibit seed germination, psoralen once more proving to be the most active [297, 298]. Baskin *et al.* [299] have suggested that in the legume genus *Psoralea* psoralen acts as an allelochemic capable of serious impairment in the growth of competing species. Whilst self-inhibition has sometimes been observed to occur, it has recently been shown [300] that in the umbelliferous genus *Heracleum* detoxification of furanocoumarins can take place.

Unfortunately few studies have been made of the antifungal activity of coumarins in the Rutaceae and none at all on possible allelochemic activity. It is noteworthy however that the concentrations of coumarins known to exist in parts of these plants is often well in excess of the minimum required concentrations for these actions to occur so it would seem probable that in some cases they will fulfill both of these roles.

Many of the observed activities of coumarins appear attributable to the benzofuran system, but simple coumarins are also toxic and are reported to deter some generalist herbivores [285]. In low concentrations simple coumarins and *cis*-cinnamic acids appear to stimulate plant growth [288] whilst the *cis* acids have also been found to be much greater feeding deterrents to certain insects than the *trans* isomers [301].

Acknowledgements—The authors wish to thank the following for supplying them with unpublished data: Prof. F. R Stermitz, University of Colorado, Dr R. D. H. Murray, University of Glasgow, Dr J. Vaquette, Université de Paris Sud, and Dr I. Mester, Universistät Munster.

REFERENCES

1. Murray, R. D. H. (1977) *Fortschr. Chem.* in press.
2. Dean, F. M. (1963) *Naturally Occurring Oxygen Ring Compounds* p. 176. Butterworths, London.
3. Hegnauer, R. (1963–1973) *Chemotaxonomie der Pflanzen* Vols 2–6. Birkhauser Verlag, Basle.
4. Chakraborty, D. P., Chatterjee, D. and Bhattacharyya, P. (1973) *Trans. Bose Res. Inst., Calcutta* **38**, 23.
5. Games, D. E. (1973) *Aromatic and Heteroaromatic Chemistry* Vol. 1, p. 378; (1974) *loc. cit.*, Vol. 2, p. 455. Chemical Society Specialist Periodical Report.

6. Murray, R. D. H. (1975) *Aromatic and Heteroaromatic Chemistry* Vol. 3, p. 436; (1976) *loc. cit.*, Vol. 4, p 422. Chemical Society Specialist Periodical Report.
7. Neilsen, B. E. (1970) *Dansk. Tidsskr. Farm.* **44**, 111.
8. Neilsen, B. E. (1971) *Biology and Chemistry of the Umbelliferae* (Heywood, V. H. ed.) p. 325. Academic Press, London.
9. Waterman, P. G. (1975) *Biochem. Syst. Ecol.* **3**, 149.
10. Fish, F. and Waterman, P. G. (1973) *Taxon* **22**, 177.
11. Stanley, W. L. and Jurd, L. (1971) *J. Agric. Food. Chem.* **19**, 1106.
12. Dreyer, D. L. (1977) *Rev. Latinoamer. Quim.* **8**, 11.
13. Chakraborty, D. P. (1964) *Bull. Bot. Soc. Bengal.* **18**, 103.
14. Camm, E. L. and Towers, G. H. N. (1973) *Phytochemistry* **12**, 961.
15. Gestetner, B. and Conn, E. E. (1974) *Arch. Biochem. Biophys.* **163**, 617.
16. Steck, W. (1967) *Can. J. Biochem.* **45**, 889.
17. Edwards, K. G. and Stoker, J. R. (1967) *Phytochemistry* **6**, 655; (1968) *Phytochemistry* **7**, 73.
18. Sato, M. and Hasegawa, M. (1972) *Phytochemistry* **11**, 657.
19. Frittig, B., Hirth, L. and Ourisson, G. (1970) *Phytochemistry* **9**, 1963.
20. Brown, S. A., El-Dakhakhny, M. and Steck, W. (1970) *Can. J. Biochem.* **48**, 863.
21. Ellis, B. E. and Brown, S. A. (1974) *Can. J. Biochem.* **52**, 734.
22. Dhillon, D. S. and Brown, S. A. (1976) *Arch. Biochem. Biophys.* **177**, 74.
23. Kutney, J. P., Verma, A. K. and Young, R. N. (1973) *Tetrahedron* **29**, 2645.
24. Grundon, M. F. and McColl, I. S. (1975) *Phytochemistry* **14**, 143.
25. Floss, H. G. (1972) *Rec. Adv. Phytochem.* **4**, 143.
26. Brown, S. A. and Steck, W. (1973) *Phytochemistry* **12**, 1315.
27. Steck, W. and Brown, S. A. (1971) *Can. J. Biochem.* **49**, 1213.
28. Caporale, G., Dall'Acqua, F., Capozzi, A., Marciani, S. and Crocco, R. (1971) *Z. Naturforsch.* **26B**, 1256.
29. Dall'Acqua, F., Innocenti, G. and Caporale, G. (1975) *Planta Med.* **27**, 343.
30. Bowman, R. M., Collins, J. F. and Grundon, M. F. (1973) *J. Chem. Soc. Perkin Trans. I* 626.
31. Murray, R. D. H., Sutcliffe, M. and McCabe, P. H. (1971) *Tetrahedron* **27**, 4901.
32. Steck, W. and Mazurek, M. (1972) *Lloydia* **35**, 418.
33. Wald, R. W. and Feuer, G. (1971) *J. Med. Chem.* **14**, 1081.
34. Murray, R. D. H., Ballantyne, M. M., Hogg, T. C. and McCabe, P. H. (1975) *Tetrahedron* **31**, 2960.
35. Gerrard, W., Lappert, M. F. and Silver, H. B. (1957) *Proc. Chem. Soc.* 19.
36. Ishii, H., Hosoya, K., Ishikawa, T., Ueda, E. and Haginawa, J. (1974) *Yakugaku Zasshi* **94**, 322.
37. Nakaoki, T. and Morita, N. (1953) *Yakugaku Zasshi* **73**, 770.
38. Hasegawa, M. and Miyoshi, T. (1960) *J. Jap. For. Soc.* **42**, 222.
39. Ishii, H. and Komaki, T. (1966) *Yakugaku Zasshi* **86**, 631.
40. Morita, N. and Shimizu, M. (1966) *Yakugaku Zasshi* **86**, 732.
41. Morita, N. and Fukata, M. (1967) *Yakugaku Zasshi* **87**, 319.
42. Morita, N., Shimazu, M. and Arisawa, M. (1968) *Yakugaku Zasshi* **88**, 1214.
43. Ishii, H., Okida, H. and Haginawa, J. (1972) *Yakugaku Zasshi* **92**, 118.
44. Robertson, A. and Subramaniam, T. S. (1937) *J. Chem. Soc.* 1545 and references cited therein.
45. Sun, G. C. (1975) *Diss. Abs.* **35B**, 5826.
46. Ishii, H. and Hosoya, K. (1972) *Chem. Pharm. Bull.* **20**, 860.
47. Ishii, H., Hosoya, K., Ishikawa, T. and Haginawa, J. (1974) *Yakugaku Zasshi* **94**, 309.
48. Gray, A. I., Waigh, R. D. and Waterman, P. G. (1975) *J. Chem. Soc., Perkin Trans I* 488.
49. Najjar, S., Cordell, G. A. and Farnsworth, N. R. (1975) *Phytochemistry* **14**, 2309.
50. Vaquette, J., Pousset, J. L., Delaveau, P. and Paris, R. R. (1973) *Ann. Pharm. France* **31**, 49.
50a. Vaquette, J. (1974) PhD Thesis, University of Paris.
51. Fish, F., Gray, A. I. and Waterman, P. G. (1975) *Phytochemistry* **14**, 2073.
52. Fish, F., Gray, A. I., Waigh, R. D. and Waterman, P. G. (1976) *Phytochemistry* **15**, 313.
53. Tomko, J., Awad, A. T., Beal, J. L. and Doskotch, R. W. (1968) *J. Pharm. Sci.* **57**, 329.
54. Fish, F., Gray, A. I. and Waterman, P. G. (1976) *J. Pharm. Pharmacol.* **28**, 69P.
55. Gray, A. I., Waigh, R. D. and Waterman, P. G. (1977) *Phytochemistry* **16**, 1017.
56. Morita, N., Arisawa, M. and Takezaki, T. (1968) *Yakugaku Zasshi* **87**, 1017.
57. King, F. E., Housley, J. R. and King, T. J. (1954) *J. Chem. Soc.* 1392.
58. Waterman, P. G. (1976) *Phytochemistry* **15**, 578.
59. Eshiett, I. T. and Taylor, D. A. H. (1968) *J. Chem. Soc. C* 481.
60. Torres, R. and Cassels, B. K. (1975) *Anal. Ass. Quim. Argentina* **63**, 187.
61. Stermitz, F. R. (1977) *Phytochemistry* **16**, 2003.
62. Ewing, J., Hughes, G. K. and Ritchie, E. (1950) *Australian J. Sci. Res.* **3A**, 342.
63. Guise, G. B., Ritchie, E., Senior, R. G. and Taylor, W. C. (1967) *Australian J. Chem.* **20**, 2429.
64. Talapatra, S. K., Dutta, S. and Talapatra, B. (1973) *Phytochemistry* **12**, 729.
65. Abe, F., Furukawa, M., Nonaka, G., Okabe, H. and Nishioka, I. (1973) *Yakugaku Zasshi* **93**, 624.
66. Komasaki, H., Kasumoto, H., Ohsuka, A. and Kotake, M. (1968) *J. Chem. Soc. Japan* **89**, 717.
67 Corrie, J. E. T., Green, G. H., Ritchie, E. and Taylor, W C. (1970) *Australian, J. Chem.* **23**, 133.
68. Gupta, V. N. and Seshadri, T. R. (1957) *J. Sci. Ind. Res. India* **16C**, 71.
69. Sakuno, N. (1940) *J. Orient. Med.* **33**, 793.
70. Ishii, H. (1961) *Yakugaku Zasshi* **81**, 1633.
71. Araki, T. and Miyashita, Y. (1928) *Yakugaku Zasshi* **48**, 437.
72. Thoms, H. (1911) *Chem. Ber.* **44**, 3325.
73. Lahey, F. N. and Macleod, J. K. (1967) *Australian J. Chem.* **20**, 1943.
74. Dreyer, D. L. and Lee, A. M. (1972) *Phytochemistry* **11**, 763.
75. Lahey, F. N. and Wluka, D. J. (1955) *Australian J. Chem.* **8**, 125.
76. Ritchie, E., Taylor, W. C. and Young, L. M. (1968) *Australian J. Chem.* **21**, 1381.
77. Lauterer, J. (1897) *Proc. Roy. Soc. Queensland* **12**, 72.
78. Rondest, J., Das, B. C., Ricroch, M. N., Kan-Fan, C., Poitier, P. and Polonsky, J. (1968) *Phytochemistry* **7**, 1019.
79. Gellert, M., Szendrei, K., Novak, I. Csedo, K. and Reisch, J. (1972) *Phytochemistry* **11**, 2894.
80. Lassak, E. V. and Southwell, I. A. (1972) *Australian J. Chem.* **25**, 2491.
81. Abe, H., Kawashima, T., Maruta, I., Kodama, M. and Ito, S. (1971) *Phytochemistry* **10**, 3330.
82. Donnelly, W. J. and Grundon, M. F. (1972) *J. Chem. Soc. C* 2116.
83. Cambie, R. C. (1960) *J. Chem. Soc.* 2376.
84. Johns, S. R., Lamberton, J. A., Price, J. R. and Sioumis, A. A. (1968) *Australian J. Chem.*, **21**, 3079.
85. Briggs, L. H. and Locker, R. H. (1951) *J. Chem. Soc.* 3131.
86. Higa, T. and Scheuer, P. J. (1974) *J. Chem. Soc. Perkin Trans. I* 1350.
87. Dreyer, D. L., Pickering, M. V. and Cohan, P. (1972) *Phytochemistry* **11**, 705.
88. Silva, M., Cruz, M. A. and Sammers, P. G. (1971) *Phytochemistry* **10**, 3255.
89. Ohta, T. and Miyazaki, T. (1958) *Yakugaku Zasshi* **78**, 1067.
90. Miyazaki, T. and Mihashi, S. (1964) *Chem. Pharm. Bull.* **12**, 1232.

91. Miyazaki, T., Mihashi, S. and Okabayashi, K. (1964) *Chem. Pharm. Bull.* **12**, 1236.
92. Najar, M. N. S., Bhan, M. K. and George, V. (1973) *Phytochemistry* **12**, 2073.
93. Talapatra, S. K., Mukhopadhyay, S. K. and Talapatra, B (1973) *Phytochemistry* **12**, 2312.
94. Bhan, M. K., Raj, S., Najar, M. N. S. and Handa, K. L. (1973) *Phytochemistry* **12**, 3010.
95. Kozawa, M., Baba, K., Minami, M., Nitta, H. and Hata, K (1974) *Chem. Pharm. Bull.* **22**, 2746.
96. Rozsa, Zs., Szendrei, K., Novak, I., Reisch, J. and Minker, E. (1975) *Pharmazie* **30**, 753.
97 Talapatra, S. K., Mukhopadhyay, S. K. and Talapatra, B. (1975) *Phytochemistry* **14**, 836.
98. Shibata, S. and Noguchi, M. (1977) *Phytochemistry* **16**, 291.
99. Gonzalez, A. G., Estevez, R. R. and Diaz, C. E (1974) *Ann Quim.* **70**, 281.
100. Brooker, R. M., Eble, J. N. and Starkovsky, N. A. (1967) *Lloydia* **30**, 73.
101. Gonzalez, A. G., Lopez, D. H., Rodriguez, M. M. and Rodriguez, L. F. (1974) *Ann. Quim.* **70**, 60.
102. Gonzalez, A. G., Diaz, C. E., Lopez, D. H., Luis, J. R. and Rodriguez, L F (1977) *Ann. Quim.* **73**, 430.
103. Reinhard, E., Corduan, G. and von Brocke, W. (1971) *Herb. Hungarica* **10**, 9.
104. von Brocke, W., Reinhard, E., Nicholson, G. and Konig, W. A. (1971) *Z. Naturforsch.* **26B**, 1252.
105. Reisch, J., Szendrei, K., Novak, I. and Minker, E. (1972) *Magy. Kem. Folyoirat.* **78**, 6.
106. Varga, E., Szendrei, K., Novak, I., Reisch, J. and Mirhom, Y. M. (1974) *Herb. Hungarica* **13**, 39.
107. Varga, E., Szendrei, K., Novak, I. and Minker, E. (1974) *Acta Pharm. Hungarica* **44**, 36.
108. Varga, E., Szendrei, K., Novak, I., Sohar, P. and Horvath, Gy. (1976) *Fitoterapia* **47**, 107.
109 Aguillo Martinez, E., Estevez, R. R., Gonzalez, A. G and Rodriguez, L. F. (1967) *Ann. Quim.* **63**, 197.
110. Gonzalez, A. G. and Rodriguez, L. F. (1971) *Herb. Hungarica* **10**, 95.
111. St. Pfau, A. (1939) *Helv. Chim. Acta* **22**, 382
112. Kuffner, F., Nikiforov, A. and Schulz, G. (1973) *Monatsch. Chem.* **104**, 911.
113. Sepulvida, Arques, A., Viguera Lobo, J and Sanchez Pararedo, J. (1973) *Ann. Quim.* **69**, 365; *Ann. Quim.* (1974) **70**, 1020.
114. Estevez, R. R. and Gonzalez, A. G. (1966) *Ann. Quim.* **62B**, 981.
115. Gonzales, A. G., Estevez, R. R. and Jaraiz, I. (1972) *Ann. Quim.* **68**, 415.
116. Estevez, R R. and Gonzalez, A. G. (1972) *Farm. Nueva* **37**, 903.
117. Gonzalez, A. G., Estevez, R. R. and Baez Arencibia, J. (1975) *Ann. Quim.* **71**, 842.
118 Gonzalez, A. G., Aguillo Martinez, E., Iniguaz, M. A. M. and Rodriguez, L. F. (1971) *Ann. Quim.* **67**, 441.
119. Gonzalez, A. G., Estevez, R. R. and Jaraiz, I. (1972) *Ann. Quim.* **68**, 425.
120. Gonzalez, A. G., Estevez, R. R., Baez Arencibia, J. and Ruano Perez, T. (1973) *Ann. Quim.* **69**, 1141.
121. Gonzalez, A. G., Lopez, D. H., Iniguaz, M. A. M., Melian, R. M. and Rodriguez, L. F. (1972) *Ann. Quim.* **68**, 1139.
122. Gonzalez, A. G., Diaz, C. E., Lopez, D. H. Medina, J. M. and Rodriguez, L. F. (1976) *Ann. Quim.* **72**, 191.
123. Tikhomirova, L. I., Pimenov, M. G. and Kuznetsova, G. A. (1974) *Khim. Prirod. Soedin.* 401.
124. Gonzalez, A. G., Cardona, R. J. Moreno Ordenez, R. and Rodriguez, L. F. (1973) *Ann. Quim.* **69**, 781.
125. Gashimov, N. F. and Kuznetsova, G. A. (1974) *Khim. Prirod, Soedin.* **303**.
126. Kuznetsova, G. A. and Gashimov, N. F. (1973) *Khim. Prirod. Soedin.* 113.
127. Dreyer, D. L. (1966) *Tetrahedron* **22**, 2923.
128. Kutney, J. P., Verma, A. K. and Young, R. N. (1972) *Tetrahedron* **28**, 5091.
129. Chang, P. T. O., Cordell, G. A., Aynilian, G. H., Fong, H. H. S. and Farnsworth, N. R. (1976) *Lloydia* **39**, 134
130. Dreyer, D. L and Lee, A (1969) *Phytochemistry* **8**, 1499.
131. Berrens, L. and van Dijk, E. (1964) *Experientia* **20**, 615.
132. Reisch, J., Szendrei, K., Minker, E. and Novak, I. (1967) *Planta Med.* **15**, 320.
133. Gellert, M., Novak, I. Szendrei, K., Reisch, J. and Minker, E. (1971) *Herb. Hungarica* **10**, 123.
134. Komissarenko, N. E. (1968) *Khim Prirod. Soedin.* 377.
135. Hifnawy, M. S., Vaquette, J., Sevenet, T., Pousset, J. L. and Cave, A. (1977) *Phytochemistry* **16**, 1035
136. Hifnawy, M. S., Vaquette, J. Pousset, J. L and Cave, A. (1977) *Planta Med.* **31**, 156.
137. Duffield, A. M., Jefferies, P. R., Maslen, E. N. and Rae, A. I. M. (1963) *Tetrahedron* **19**, 593.
138. Jefferies, P. R. and Worth, G. K. (1973) *Tetrahedron* **29**, 903
139. Chow, P. W., Duffield, A. M. and Jefferies, P. R. (1966) *Australian J. Chem.* **19**, 483.
140. Southwell, I. A. (1973) *Phytochemistry* **12**, 235.
141. Duffield, A. M. and Jefferies, P. R. (1963) *Australian J. Chem.* **16**, 123.
142. Lassak, E. V. and Pinhey, J. T. (1969) *Australian J. Chem.* **22**, 2175.
143. Jarvis, M. W. (1968) *Australian J. Chem.* **21**, 537.
144. Pinhey, J. T. and Southwell, I A. (1973) *Australian J. Chem.* **26**, 409.
145 Briggs, L. H. and Cambie, R. C (1958) *Tetrahedron* **2**, 256.
146. Brown, K. L., Burfitt, A. I R., Cambie, R. C., Hall, D., and Mathai, K. P. (1975) *Australian J. Chem.* **28**, 1327.
147. Finkelstein, N. and Rivett, D. E. A. (1976) *Phytochemistry* **15**, 1080.
148. Ritchie, E. (1964) *Rev. Pure Appl. Chem.* **14**, 47.
149. Bowden, B. F., Cleaver, L., Ndalut, P. K., Ritchie, E. and Taylor, W. C. (1975) *Australian J. Chem.* **28**, 1393.
150. Talapatra, S K., Bhattacharya, M., Talapatra, B and Das, B. C (1968) *J. Indian Chem. Soc.* **45**, 861.
151. Vrkoc, J. and Sedmera, P. (1972) *Phytochemistry* **11**, 2647.
152. Mujumdar, R. B., Rama Rao, A. V., Rathi, S. S and Venkataraman, K. (1975) *Tetrahedron Letters* 867, Mujumdar, R. B., Rathi, S. S. and Rama Rao, A. V (1977) *Indian J. Chem.* **15B**, 200.
153. Pozzi, H., Sanchez, E. and Comin, J. (1967) *Tetrahedron* **23**, 1129.
154. Dreyer, D. L. (1969) *Phytochemistry* **8**, 1013.
155. Weinstein, B., Craig, A. R., Fuller, L. W., Kang, J.-B and McBreen, S. A. (1972) *Phytochemistry* **11**, 1530.
156. Reisch, J., Mirhom, Y. W., Korosi, J., Szendrei, K. and Novak, I. (1973) *Phytochemistry* **12**, 2552.
157. Korosi, J., Papp, E., Szendrei, K., Novak, I., Reisch, J and Minker, E. (1974) *Herb. Hungarica* **13**, 23.
158. Mitscher, L. A., Bathala, M. S., Clark, G. W. and Beal, J. L. (1975) *Lloydia* **38**, 117
159. Reisch, J., Korosi, J., Szendrei, K., Novak, I. and Minker, E. (1975) *Phytochemistry* **14**, 1678.
160. Szendrei, K., Novak, I., Petz, M., Reisch, J., Bailey, H. E. and Bailey, V. L. (1973) *Lloydia* **36**, 333.
161. Szendrei, K., Petz, M., Novak, I., Reisch, J Bailey, H. E. and Bailey, V. L. (1974) *Herb. Hungarica* **13**, 49.
162. Kincl, F. A., Romo, J., Rosenktanz, G. and Sondheimer, F. (1956) *J. Chem. Soc.* 4163.
163 Iriarte, J., Kincl. F. A., Rosenkranz, G and Sondheimer, F. (1956) *J. Chem. Soc.* 4170.
164. Dreyer, D. L. (1968) *J Org. Chem.* **33**, 3577
165 Combes, G., Pernet, R. and Pierre, R. (1961) *Bull Soc. Chim, France* 1609.
166. Desai, P. D., Govindachari, T. R., Nararajan, K. and Viswanathan, N. (1967 *Indian J. Chem.* **5**, 41.
167. Deshmukh, M. N., Deshpande, V. N and Rama Rao, A. V. (1976) *Phytochemistry* **15**, 1419

168. Hegarty, M. P. and Lahey, F. N. (1956) *Australian J. Chem.* **9**, 120.
169. MacLeod, J. K. (1970) *Tetrahedron Letters* 1319, 3611.
170. Nakayama, M., Fujimoto, S., Fukui, K. and MacLeod, J. K. (1971) *Australian J. Chem.* **24**, 209.
171. Lahey, F. N. and MacLeod (1968) *Tetrahedron Letters* 447.
172. Monache, F. D., Marletti, F., Marini-Bettolo, G. B., Francisco de Mello, J. and Goncalves de Lima, O. (1976) *Gazz. Chim. Ital.* **106**, 681.
173. Correa, D. de B., Gottlieb, O. R. and De Padua, A. P. (1975) *Phytochemistry* **14**, 2059.
174. Correa, D. de B., Gottlieb, O. R., De Padua, A. P. and Da Rocha, A. I. (1976) *Rev. Latinoamer. Quim.* **7**, 43.
175 Weinstein, B. and Craig, A. R. (1971) *Phytochemistry* **10**, 2556.
176. Plouvier, V. (1966) *Compt. Rend.* **263D**, 439.
177. Atkinson, E., Boyd, D. R. and Grundon, M. F. (1974) *Phytochemistry* **13**, 853.
178. Bhattacharjee, S. R. and Mullick, D. K. (1960) *J. Indian Chem. Soc.* **37**, 420.
179. Bhargava, K. K. and Seshadri, S. K. (1973) *Current Sci. (India)* **42**, 59.
180. Bose, P. K., Matzke, J. and Guha, N. C. (1939) *Chem. Ber.* **72**, 821.
181. Dominguez, X. A., Cano, G., Luna, I. and Dieck, A. (1977) *Phytochemistry* **16**, 1096.
182. Cordova, H. E. and Garelli, L. N. (1974) *Phytochemistry* **13**, 758.
183. Lamberton, J. A., Price, J. R. and Redcliffe, A. H. (1967) *Australian J. Chem.* **20**, 973.
184. Chatterjee, A., Dutta, C. P. and Bhattacharyya, S. (1967) *Sci. Cult. (Calcutta)* **33**, 371.
185. Joshi, P. P., Shukla, Y. N., Bhakuni, D. S. and Dhar, M. M. (1975) *Indian J. Chem.* **13**, 772.
186. Talapatra, B., Chaudhuri, M. K. and Talapatra, S. K. (1975) *Indian J. Chem.* **13**, 835.
187. Abe, M. O. and Taylor, D. A. H. (1971) *Phytochemistry* **10**, 1167.
188. Okorie, D. A. (1975) *Phytochemistry* **14**, 2720.
189. Mester, I., Szendrei, K. and Reisch, J. (1977) *Planta Med.* **32**, 81.
190. Govindachari, T. R., Pai, B. R., Subramaniam, P. S. and Muthukamaraswamy, N. (1967) *Tetrahedron* **24**, 753.
191. Fuhrer, H., Govindachari, T. R., Joshi, B. S. and Pai, B. R. (1970) *Indian J. Chem.* **8**, 198.
192. Bose, P. K., Chakravarti, S. and Barua, A. K. (1973) *J. Indian Chem. Soc.* **50**, 753.
193. Joshi, B. S., Kamat, V. N. and Saksena, A. (1967) *Tetrahedron* **23**, 4785.
194. Bhattacharyya, P. and Chakraborty, D. P. (1973) *Phytochemistry* **12**, 1831.
195. Joshi, B. S. and Gawad, D. H. (1971) *Phytochemistry* **10**, 480.
196. Joshi, B. S., Kamat, V. N. and Gawad, D. H. (1974) *Experientia* **30**, 223.
197. Anwer, F., Shoeb, A., Kapil, R. S. and Popli, S. A. (1977) *Experientia* **33**, 412.
198. Talapatra, S. K., Dutta, L. N. and Talapatra, B. (1973) *Tetrahedron* **29**, 2811.
199. Talapatra, S. K., Lakshmi, L. D. and Talapatra, B. (1973) *Tetrahedron Letters* 5005.
200. Gupta, G. L. and Nigam, S. S. (1970) *Planta Med.* **19**, 83.
201. Chakraborty, D. P. and Chowdhury, B. K. (1967) *Tetrahedron Letters* 3471.
202. Ramstad, E., Lin, W.-N. C., Lin, T.-J. and Koo, W.-Y. (1968) *Tetrahedron Letters* 811.
203. Khosa, R. L. (1972) *Indian J. Pharm.* **34**, 72.
204. Sanyal, P. K. and Bose, P. K. (1972) *Sci. Cult. (Calcutta)* **35**, 332.
205. Steck, W. (1972) *Can. J. Chem.* **50**, 443.
206. Lakshmi, M. V., Ratnam, C. V. and Subba Row, N. V. (1972) *Indian J. Chem.* **10**, 564.
207 Wu, T.-S., Lin, C.-N., Yang, L.-K. and Lin, S.-T. (1975) *J. Chinese Chem. Soc.* **22**, 167.
208. Sanyal, P. K., Bosak, A., Barua, A. K. and Bose, P. K. (1975) *J. Indian Chem. Soc.* **52**, 1213.
209. Raj, K., Misra, S. C., Kapil, R. S. and Popli, S. P. (1976) *Phytochemistry* **15**, 1787.
210. Ganguly, A. K., Govindachari, T. R., Manmade, A. and Mohamed, P. A. (1966) *Indian J. Chem.* **4**, 293.
211. Bose, P. K. and Mookerjee, A. (1944) *J. Indian Chem. Soc.* **21**, 181.
212. Dreyer, D. L. (1967) *Tetrahedron* **23**, 4613.
213. Shabbir, M. and Zaman, A. (1968) *J. Indian Chem. Soc.* **45**, 279.
214. Najar, M. N. S. and Bhan, M. K. (1972) *Phytochemistry* **11**, 3331.
215. Basa, S. C. (1975) *Australian J. Chem.* **28**, 1159.
216. Barua, A. K., Banerjee, S. K., Basak, A., Chakravarti, S., Ghosh, S., Sethi, K. and Bose, P. K. (1974) *Phytochemistry* **13**, 2017.
217. Desai, H. K., Gawad, D. H., Govindachari, T. R., Joshi, B. S., Kamat, V. N., Modi, J. D., Mohamed, P. A., Parthasarathy, P. C., Patankar, S. J., Sidhaye, A. R. and Viswanathan, N. (1970) *Indian J. Chem.* **8**, 851.
218. Talapatra, S. K., Bhattacharyya, S. and Talapatra, B. (1970) *J. Indian Chem. Soc.* **47**, 600.
219. Desai, P. D., Ganguly, A. K., Govindachari, T. R., Joshi, B. S., Kamat, V. N., Manmade, A. H., Mohamed, P. A., Nagle, S. K., Nayak, S. K., Saksena, A. K., Sothe, S. S. and Viswanathan, N. (1966) *Indian J. Chem.* **4**, 457.
220. Dreyer, D. L. and Huey, P. F. (1974) *Phytochemistry* **13**, 1237.
221. Dreyer, D. L. (1965) *J. Org. Chem.* **30**, 749.
222. Dreyer, D. L. (1966) *Phytochemistry* **5**, 367.
223. Tomimatsu, T. and Hashimoto, M. (1968) *Yakugaku Zasshi* **88**, 643, 1357.
224. Tomimatsu, T., Hashimoto, M., Shingu, T. and Tori, K. (1972) *Tetrahedon* **28**, 2003.
225. Guiotto, A., Rodighiero, P. and Fornasiero, U (1973) *Z. Naturforsch.* **28C**, 260; *Z. Naturforsch.* (1974) **29C**, 201.
226. Guiotto, A. Rodighiero, P. and Quintily, U. (1975) *Z. Naturforsch.* **30C**, 420.
227. Guiotto, A., Rodighiero, P., Quintily, U. and Pastorini, G. (1976) *Phytochemistry* **15**, 348.
228. Guiotto, A., Rodighiero, P., Pastorini, G. and Celon, E. (1977) *Phytochemistry* **16**, 1257.
229. Mookerjee, A. (1946) *J. Indian Chem. Soc.* **23**, 41.
230. Khastagir, H. (1947) *J. Indian Chem. Soc.* **24**, 421.
231. Caldwell, A. G. and Jones, E. R. H. (1945) *J. Chem. Soc.* 540.
232. Horowitz, R. M. and Gentili, B. (1960) *J. Org. Chem.* **25**, 2183.
233. Stanley, W. L. and Vannier, S. H. (1967) *Phytochemistry* **6**, 585.
234. Tatum, J. H. and Berry, R. E. (1977) *Phytochemistry* **16**, 1091.
235. Tomer, E., Goren, R. and Monselise, S. P. (1969) *Phytochemistry* **8**, 1315.
236. Goren, R. and Stanley, W. L. (1970) *Phytochemistry* **9**, 2069.
237. Stanley, W. L., Waiss, A. C., Lundin, R. E., and Vannier, S. H. (1965) *Tetrahedron* **21**, 89.
238. Komatsu, S., Tanaka, S., Ozawa, S., Kubo, R., One, Y. and Matsuda, Z. (1930) *J. Chem. Soc. Japan* **51**, 478.
239. Nomura, D. (1950) *Kagaku No Ryoiki* **4**, 561.
240. Tomimatsu, T. (1971) *Shoyakugaku Zasshi* **25**, 55.
241. Di Giacomo, A. and Rispoli, G. (1969) *Essenze Deriv. Agrumari* **39**, 115.
242. Stanley, W. L. and Vannier, S. H. (1957) *J. Am. Chem. Soc.* **79**, 3488.
243. Bernhard, A. A. (1958) *Nature* **182**, 1171.
244. Dreyer, D. L. and Huey, P. F. (1973) *Phytochemistry* **12**, 3011.
245. Matsumo, T. (1958) *Yakugaku Zasshi* **79**, 540.
246. Yen, K.-Y. (1970) *T'ai Wan Yao Hsueh Tsa Chih* **22**, 21.

247. Nikonev, G. K. and Molodzhnikov, M. M. (1964) *Med. Prom. S.S S.R.* **18**, 26.
248. Yen, K.-Y., Yang, L.-L. and Huang, T.-Y. (1970) *T'ai Wan Yao Hsueh Tsa Chih* **22**, 29.
249. Fisher, F and Nordby, H. E. (1966) *Tetrahedron* **22**, 1489.
250 Bohme, H and Pietsch, G. (1938) *Chem. Ber.* **72**, 773.
251. Yen, K.-Y. and Yang, L.-L. (1970) *T'ai Wan Yao Hsueh Tsa Chih* **22**, 26.
252. Saha, S. K. and Chatterjee, A. (1957) *J. Indian Chem. Soc.* **34**, 228.
253. Chatterjee, A. and Chaudhury, B. (1960) *J. Indian Chem. Soc.* **37**, 334.
254. Chatterjee, A., Dutta, C. P., Bhattacharyya, S., Audier, H. E. and Das, B. C (1967) *Tetrahedron Letters* 471.
255. Shoeb, A, Kapil, R S and Popil, S. P. (1973) *Phytochemistry* **12**, 2071
256. Basu, D. and Sen, R. (1974) *Phytochemistry* **13**, 2329.
257. Adesogan, E. K. (1973) *Phytochemistry* **12**, 2310.
258. Dreyer, D L. (1968) *J. Org. Chem.* **33**, 3658.
259. Chakraborty, D. P. (1959) *J. Sci. Ind. Res. India* **18B**, 90.
260. Talapatra, S. K., Chaudhuri, M. K. and Talapatra, B. (1973) *Phytochemistry* **12**, 236.
261. Engler, A (1931) *Die Naturlichen Pflanzenfamilien* (Engler, A. and Prantl, K. eds) 2nd edn, Vol. 19a, p. 187. Engelmann, Leipzig.
262. Swingle, W T. and Reece, P. C. (1967) *The Citrus Industry* (Reuther, W., Webber, H. J. and Batchelor, L. D. eds) 2nd edn, Vol. 1, p. 195. University of California Press, Berkley.
263 Bate-Smith, E. C. (1962) *J. Linn. Soc. Botany* **58**, 371
264. Feldman, A W. and Hanks, R. W (1965) *Nature* **207**, 985.
265. Dubey, P and Purohit, R. M. (1970) *Indian Perfumer* **14**, 11.
266. Kumar, S., Rohatgi, H. L. and Banerjee, B. C. (1957) *Indian Perfumer* **1**, 50.
267. Sharma, M. L., Vashist, V. N. and Handa, K. L. (1964) *Perf. Essential Oil Rec.* **55**, 720.
268. Goutam, M. P and Purohit, R. M. (1975) *Riv. Ital. Essenze-Profumi, Piante Offic. Vegetali-Saponi* **57**, 9.
269. Sakai, T., Yoshihara, K. and Hirose, Y. (1970) *Bull. Chem. Soc. Japan* **43**, 484.
270. Baslas, K. K. and Deshapande, S. S. (1950) *J. Indian Chem. Soc.* **27**, 379.
271. Lassak, E. V. and Southwell, I. A. (1974) *Australian J. Chem.* **27**, 2703.
272. Prager, R. H. and Threadgold, H. M. (1966) *Australian J. Chem.* **19**, 451.
273. Dimcnt, J. A., Ritchie, E. and Taylor, W. C. (1967) *Australian J. Chem.* **20**, 565.
274 Ishii, H., Ishikawa, T., Lu, S.-T. and Chen, I.-S. (1976) *Yakugaku Zasshi* **96**, 1458.
275. Reisch, J., Novak, I., Szendrei, K. and Minker, E. (1966) *Acta Pharm. Suecica* **3**, 423.
276. Duffield, A M, Jefferies, P R. and Lucich, P. H (1962) *Australian J. Chem.* **15**, 812.
277. Lassak, E. V and Southwell, I. A. (1972) *Australian J. Chem.* **25**, 2517.
278. Hegnauer, R. (1969) *Chemotaxonomie der Pflanzen* Vol. **5**, p. 54. Birkhauser Verlag, Basle.
279. Hartley, T. G. (1969) *J. Arnold Arbor.* **50**, 481.
280. Airy-Shaw, H. K. (1965) *Kew. Bull.* 249.
281. Meeuse, A. D J. (1970) *Acta Botan. Neerl.* **19**, 61, 133.
282. Waterman, P. G. (1973) *Biochem. Syst. Ecol.* **1**, 153.
283. Hall, J. B., Meshal, I. A., Swaine, M. D. and Waterman. P. G (1978) *Biochem. System Ecol.* submitted for publication.
284. Bailey, H. E. and Bailey, V. L. (1965) *Lloydia* **28**, 27.
285. Levin, D. A. (1976) *Ann. Rev. Ecol. Syst.* **7**, 121.
286. Rhoades, D. E. and Cates, R. G. (1976) *Recent Advances in Phytochemistry* Vol. 10, p. 168. Academic Press, New York.
287. Soine, T. O. (1964) *J Pharm. Sci.* **53**, 231
288. Feuer, G. (1974) *Prog. Med Chem.* **10**, 85.
289. Usher, G. (1971) *A Dictionary of Plants Used by Man.* Constable, London and references cited therein.
290. Musajo, L. and Rodighiero, G. (1970) *Photochem. Photobiol* **11**, 27.
291. Musajo, L. and Rodighiero, G. (1971) *Herb Hungarica* **10**, 79
292. Gonzalez, A. G., Darias, V., Alonso, G., Boada, J. N and Rodriguez, L. F. (1977) *Planta Med.* **31**, 351.
293. Martin, J. T, Baker, E A. and Byrde, R. J. W (1966) *Ann. Appl Biol.* **57**, 491
294. Martin, J. T., Baker, E. A. and Byrde, R. J W. (1966) *Ann. Appl. Biol.* **46**, 501.
295. Wu, C. M., Koehler, P E. and Ayres, J C. (1972) *Appl. Microbiol* **23**, 852.
296. Johnson, C., Brannon, D. R. and Kuc, J. (1973) *Phytochemistry* **12**, 2961
297. Van Sumere, C. F., Cottenie, J., De Greef, J. and Kint, J. (1972) *Recent Advances in Phytochemistry* Vol. **4**, p 165. Academic Press, New York.
298. Sinha-Raj, S. P. and Chakraborty, D. P. (1976) *Phytochemistry* **15**, 2005.
299. Baskin, J. M., Ludlow, C. J., Harris, T. M and Wolf, F. T. (1967) *Phytochemistry* **6**, 1209
300. Camm, E. L., Wat, C.-K. and Towers, G H N. (1976) *Can. J. Botany* **54**, 2562.
301. Todd, G W., Getchum, A and Cress, D. C. (1971) *Ann. Entomol Soc Am.* **64**, 718

ADDENDA

Hortiolone (**16c**) has now been confirmed as the linear furanocaumarin isomer and four additional coumarins, **11**, **15f**, isoangenomilin (linear **16b**), and hortinone (linear 5-OMe-**16b**) have been isolated from *Hortia arborea* root [Monache *et al.* (1977) *Gazz. Chim. Ital.* **107**, 399]. The leaves of *Dictamnus hispanicus* have yielded **13a**, **13c** and **13e** [Parareda *et al.* (1977) *Ann. Quim.* **73**, 914] and from the same part of *Ruta pinnata* two novel 6-prenyl-7-methoxy coumarins, tamarin with a 6-IPT[g] substituent and a second compound with a 6-DMA[f] substituent, have been isolated [Gonzalez *et al.* (1977) *Phytochemistry* **16**, 2033]. A large number of new coumarins are reported by Bhide *et al.* [(1977) *Chem. Abs.*, **87**, 180653t)] from the bark of *Chloroxylon swietenia* including **14h**, 8-DMA[a]-**9a**, demethyl-**19c** and five other compounds of coumarin type. Isopimpinellin (**13g**) has been found, together with **13c** and **13e**, in the leaf of *Orixa japonica* [Yojima *et al.* (1977) *Agric. Biol. Chem.* **4**, 1263] and all three have been established as feeding inhibitors to *Spodoptera lituna*. Isopimpinellin was found to be the most effective Another furanocoumarin, heraclenol (**13j**) has been shown to inhibit the germination of parsley seed [Kato *et al.* (1978) *Phytochemistry* **17**, 158]. The biogenesis of isopimpinellin has been investigated by Brown and Sampathkumar [(1977) *Can. J. Biochem.* **55**, 686] who found that xanthotoxin (**13c**) was a better precursor than bergapten (**13e**) in both *Ruta* and *Heracleum*. Aegelinol, the (−)-(R)-epimer of decursinol (**18a**), has been reported from the root and stem barks of *Aegle marmelos* [Chatterjee *et al.* (1978) *Phytochemistry* **17**, 328].