Phytochemistry, Vol. 22, No. 11, pp. 2335–2348, 1983.
Printed in Great Britain.

0031–9422/83 \$3.00+0.00

REVIEW

CHROMENES AND BENZOFURANS OF THE ASTERACEAE, THEIR CHEMISTRY AND BIOLOGICAL SIGNIFICANCE*

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(*Received* 9 *March* 1983)

Key Word Index—Asteraceae; chromenes; benzofurans; biosynthesis; distribution; biological activities; chemotaxonomy.

Abstract—Chromenes (benzopyrans) and benzofurans are characteristic natural products of certain tribes of the Asteraceae. This review highlights recent findings on their distribution, biosynthesis, isolation and biological activities. The structures of 167 chromenes and benzofurans reported from close to 170 taxa of the Asteraceae are examined and their utility as taxonomic characters discussed.

INTRODUCTION

In the last 30 years close to 200 chromenes (benzopyrans) and benzofurans have been isolated from many species of higher plants, such as the Rutaceae [1–4], Liliaceae [5, 6], or Cyperaceae [7–9]. The vast majority, however, are known to occur in the Asteraceae.

Chromenes and benzofurans of the Asteraceae have only been reviewed once before, in 1977 [10]. Since then, a plethora of publications on the chemistry as well as on the biological importance of these natural products has necessitated an update on what is known in terms of their biosynthesis, general distribution, isolation techniques, biological activities and chemotaxonomic utilization.

BIOGENESIS

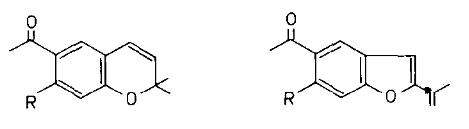
Chromenes (benzopyrans) and benzofurans are biogenetically formed by combining one isoprene unit and a phenolic system. It has been speculated in the past that the phenolic ring is derived from *p*-hydroxyacetophenone via the shikimic acid pathway. However, more recent radioactive tracer and subsequent degradative studies have shown the origin of the phenolic ring as derived from acetate, whereas the heterocyclic ring is formed by a C_5 unit from terpenoid metabolism [11, 12]. The heterocyclic ring formation can take place in two different ways giving rise to 2,2-dimethylchromenes (**6**; Fig. 3) or 2-isopropylenebenzofurans (**55**; Fig. 3). The majority of the known chromenes and benzofurans exhibit a methyl ketone moiety, usually but not always, in a position *para* to the oxygen function of the heterocyclic ring. Compounds which lack the methyl ketone (e.g. **49**; Fig. 3) are much rarer in nature.

*The data presented in this review have been reported partly at the XIIIth International Workshop on Essential Oils held at Würzburg, West Germany, in September 1982.

WITHIN PLANT DISTRIBUTION

Chromenes and benzofurans have mostly been reported in the leaves and stems, with occasional reports indicating their presence in roots. During our recent chemical analysis of *Encelia californica* (Asteraceae) we studied the distribution of chromenes and benzofurans on an organ specific basis and detected them in roots, stems, leaves, capitula and achenes [13]. The roots and achenes exhibited relatively simple patterns with one or two compounds missing that were present in all other parts of the plant screened (Fig. 1). Leaves, stems and capitula showed no qualitative chemical differences. The quantities of chromenes and benzofurans were found to be highest in leaves, stems and capitula, comprising *ca* 5% of the dry wt.

A populational phytochemical survey of *Encelia farinosa* noted the occurrence of several putative chemical races which varied in the total amounts of chromenes and benzofurans [14]. Individual plants showed significant quantitative differences of chromenes and benzofurans during ontogenesis.



1 R=H
2 R=OH
3 R=OMe

4 R=OH
5 R=OMe

Roots: **2-4**
Stems: **1-5**
Leaves: **1-5**
Capitula: **1-5**
Achenes: **1-4**

Fig. 1. Organ specific distribution of chromenes and benzofurans in *Encelia californica*.

ISOLATION AND QUANTIFICATION

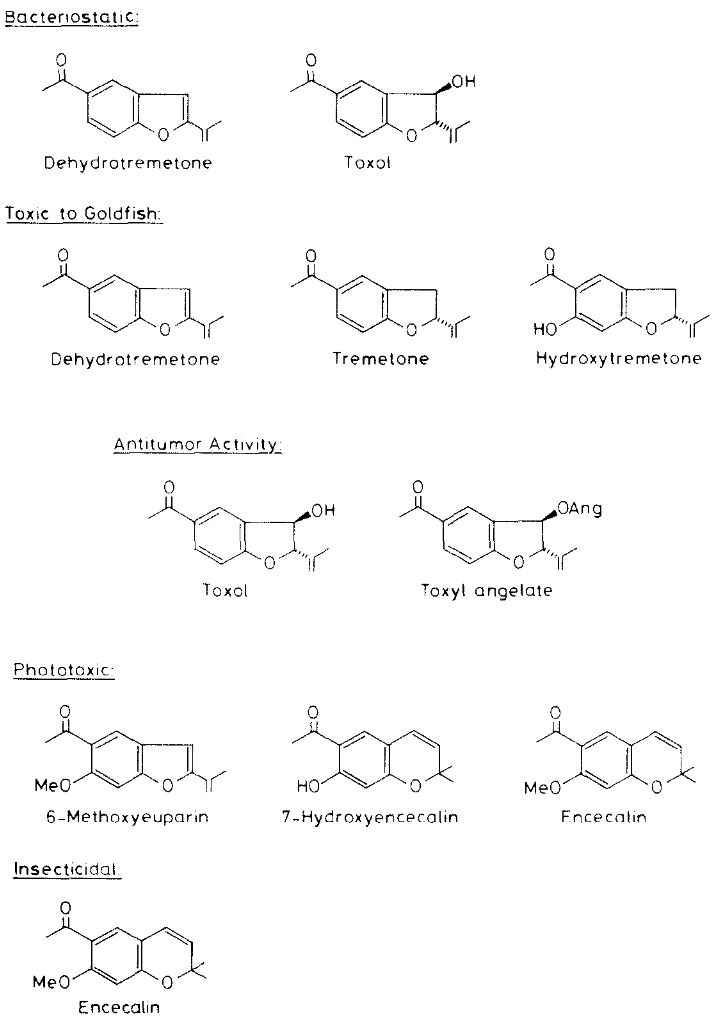
Several chromenes and benzofurans, such as ageratochromene (= precocene II) (**51**; Fig. 3) are volatile and can be extracted from plant material by steam distillation. However, a more effective and milder procedure is the solvent extraction of fresh or dried plants with organic solvents such as methylene chloride or methanol. The crude syrup thus obtained can be fractionated by chromatographic methods. We have successfully applied Sephadex LH-20 CC with methanol as eluent for fractionation and purification. We have also used LH-20 with more simple mixtures of chromenes and benzofurans for the isolation of single components from the crude extract [15]. Si gel CC or prep. TLC with mobile phases such as methylene chloride or diethyl ether–petrol mixtures are the standard chromatographic methods for the isolation of chromenes and benzofurans.

More recently, HPLC on reversed phase stationary phases has been applied successfully for the analysis and quantification of chromenes and benzofurans in crude plant extracts [14, 15]. Our first results suggest prep. HPLC to be a very efficient and rapid method for obtaining large quantities of spectroscopically pure compounds from crude extracts or prepurified fractions.

BIOLOGICAL ACTIVITIES

Several chromenes and benzofurans of the Asteraceae have been shown to be biologically active. Compounds in the toxol and tremetone series, implicated as the causative agents of milk sickness [16], have also shown activity in various bioassays. For example, they inhibit the growth of *Bacillus cereus* [17]. Tremetone, dehydrotremetone and hydroxytremetone proved to be toxic to goldfish [18], and a further study indicated that a benzofuran-containing extract of *Eupatorium urticaefolium* caused ketoacidosis in chicks [19]. In an antitumor screening conducted by the National Institute of Health, toxol and toxyl angelate were reported to exhibit weak antitumor activity against P-388 lymphocytic leukemia tumors (Fig. 2) [16].

In a recent study, we were able to demonstrate that two chromenes, encecalin and 7-hydroxyencecalin and one benzofuran, 6-methoxyeuparin, were phototoxic against several fungi and bacteria [20] (Fig. 2). The compounds, when applied to the micro-organisms, were active at a concentration of 100 μg of each compound per assay after irradiation in long-wave UV light. The chromenes and benzofurans tested did not exhibit any antibiotic properties with dark controls, suggesting that these compounds are a new class of naturally occurring photo-



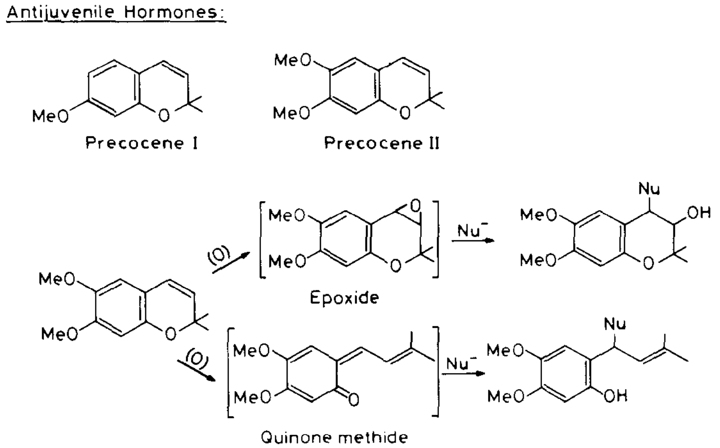


Fig. 2. Bioactive chromenes and benzofurans reported from the Asteraceae.

sensitizers. Experiments on the mode of action of these bioactive chemicals suggest an interaction with nucleic acids or intracellular molecules in light [Proksch, P. and Rodriguez, E., unpublished results].

Precocenes I and II (Fig. 2), chromenes of a rarer structural type lacking the methyl ketone group, have been shown by Bowers and associates to act as anti-juvenile hormones against insects [21]. When the precocenes are topically applied or incorporated into artificial diets, the insects undergo physiological changes that include precocious metamorphosis, sterilization, inhibition of sex attractant production, embryogenetic damage, interrupted circadian feeding rhythms or diapause induction [21–24]. Studies on the mode of action of the precocenes have indicated that these chemicals undergo oxidative activation within the corpora allata to form highly reactive epoxides or quinone methides that are able to alkylate nucleophilic substrates, such as enzymes (Fig. 2) [25–32].

Recently, we have shown that encecalin, a chromene isolated from many taxa of the Asteraceae (Table 1), proved to be lethal, when applied to first instar nymphs of *Oncopeltus fasciatus* at a concentration of 1 mg per 25–30 nymphs treated in one assay [20] (Fig. 2), but showed no effect on the metamorphosis of the insects. Further experiments indicate that encecalin, when applied to artificial diets at concentrations present in natural populations of *Encelia farinosa*, acts as a strong feeding deterrent to the insect *Heliothis zea* [33]. Continued investigations on the physiological action of insecticidal and repellent chromenes and benzofurans should provide useful information in our understanding of the evolution and adaptive role of these natural products in flowering plants.

CHEMOTAXONOMY

The Asteraceae is a well-defined family in both morphological and chemical terms. In a recent chemotaxonomic review of terpenoids in the Asteraceae, it was noted that sesquiterpene lactones are useful in delineating tribes, with many tribes, such as the Astereae, Calenduleae, Liabeae and Tageteae, lacking any appreciable amounts of lactones [151]. A similar situation is found in the distribution of chromenes and benzofurans within the 14 tribes of the Asteraceae [34]. Our literature survey and phytochemical screening revealed the structures of 167 different chromenes (benzopyrans) and benzofurans that have been reported so far from a total of close to 170 various taxa of the Asteraceae (Fig. 3 and Table 1). The number of new compounds is increasing rapidly with the development of new and sensitive analytical tools like HPLC.

In the past several authors have suggested that chromenes and benzofurans may become useful taxonomic markers within the Asteraceae [10, 35, 36] and the data accumulated so far seem to support this suggestion (Table 1, Fig. 3). On a tribal level, chromenes and benzofurans have been almost exclusively isolated from the Astereae, Eupatorieae, Heliantheae, Inuleae and Senecioneae (Table 2). In comparison, few reports exist on the occurrence of these compounds in the Calenduleae, Mutisieae and Tageteae (Table 2). Bearing in mind that new investigations might alter this picture, the present data suggest a biphyletic grouping of the Asteraceae based on the presence or absence of chromenes and benzofurans. Group I, consisting of the Astereae, Eupatorieae, Heliantheae, Inuleae and Senecioneae, accumulate chromenes and benzofurans in detectable amounts and exhibit appreciable structural diversities. Group II, consisting of the rest of the tribes, synthesize very few of these compounds or none at all (Table 2). Without overemphasizing this proposed scheme, it shows interesting parallels to other biphyletic groupings of the Asteraceae, that have been proposed and are based on systematic studies using a variety of morphological characters (Table 3). The proposed chemical grouping is in close agreement with the classification system of Wagenitz [37]. The only difference is in the positioning of the Anthemideae and Calenduleae (Table 3). Wagenitz assigns the Anthemideae only reluctantly to Group I, since the pollen morphology does not seem to support this placement. The grouping, as suggested by Carlquist [38], differs from the system of Wagenitz and from the proposed chemical grouping by the assignment of the Eupatorieae to Group II instead of Group I (Table 3).

In addition, each of the five tribes listed in Table 4 accumulates characteristic structural types that might

Table 1. Chromenes and benzofurans isolated from the Asteraceae

Tribe	Species	Compounds isolated (see Fig. 3)	Ref.
Heliantheae subtribes: Melampodiinae			
	Clibadium armanii	**73, 82, 156, 159**	[46]
	Smallanthus fruticosus	**68, 71**	[47]
	S. riparius	**43**	[48]
Verbesininae			
	Lagascea rigida	**6–9, 21, 22, 29, 47**	[49]
	Oyedaea boliviana	**158**	[50]
	Podachaenium eminens	**68**	[51]
	Verbesina alternifolia	**6, 7, 49**	[52]
	V. helianthoides	**6, 7, 49**	[52]
	V. luetzelburgii	**157**	[53]
	V. tetraptera	**7**	[52]
	V. virginica	**56**	[54]
	Zexmenia brevifolia	**12**	[55]
Helianthinae			
	**Encelia californica*	**6–8, 56, 57, 70**	[13, 56]
	E. farinosa	**8, 27, 30, 34, 36, 53, 56, 67**	[57]
	E. halimifolia	**6–8, 54, 56, 57**	[15, 43]
	E. laciniata	**6–8, 54, 56, 57**	[15, 43]
	E. palmeri	**6–8, 54, 56, 57**	[15, 43]
	E. ventorum	**6–8, 54, 56, 57**	[15, 43]
	**Fluorensia cernua*	**6, 7, 15, 17, 29, 31, 34, 56, 73, 79, 90–93**	[58]
	F. heterolepis	**6, 7, 17, 29, 56, 64, 73, 84, 86**	[59]
	F. oolepis	**56**	[60]
	F. resinosa	**62–64**	[58]
	**Helianthella uniflora*	**6, 7, 59, 73, 75, 78**	[61]
	Viguiera pazensis	**9, 74**	[62]
Fitchiinae			
	Fitchia speciosa	**82, 155**	[63]
Madiinae			
	Hemizonia congesta	**6–8, 73, 82**	[64]
	H. fitchii	**7, 8, 29, 164, 165**	[64]
	Madia sativa	**6, 7, 21, 22, 43, 112**	[65]
Galinsoginae			
	Calea hymenolepis	**168, 172**	[66]
	C. morii	**8, 23, 29, 31**	[67]
	C. oxylepis	**7, 8**	[68]
	C. zacatechichi	**14, 20**	[69]
Ambrosiinae			
	Ambrosia cumanensis	**43**	[70]
Eupatorieae subtribes or groups: Eupatoriinae			
	Austroeupatorium charapense	**56**	[71]
	Eupatoriadelphus fistulosus	**56, 65, 83, 108**	[72]
	Eupatorium aschenbornianum	**15, 16, 49, 161, 166, 167, 171**	[73]
	E. compositifolium	**58**	[74]
	E. fortunei	**56**	[75]
	E. glandulosum	**8**	[76]
	E. lindleyanum	**56**	[75]
	E. purpurem	**56**	[77]
	E. riparium	**7, 10, 11, 13, 24, 25**	[76, 79]
	E. rugosum	**7, 11, 55, 72**	[11]
	E. serotinum	**82**	[74]
	E. sternbergianum	**170**	[80]
	E. urticafolium	**55, 72, 73**	[81, 82]
	Stomatanthes africanus	**56, 84, 102**	[83]
	S. corumbensis	**6, 82, 100**	[84]

Table 1. (*continued*)

Tribe	Species	Compounds isolated (see Fig. 3)	Ref.
Disynaphia group			
	Disynaphia halimifolia	**59, 94, 109, 110**	[85]
Gyptis group			
	Bahianthus viscidus	**97, 102, 105–107**	[86]
	Lasiolaena morii	**43, 76, 100**	[87]
	Trichogonia grazielae	**41, 42**	[88]
	T. salviaefolia	**35, 41**	[88]
	T. scottmorii	**6**	[88]
	T. villosa	**35**	[88]
	Trichogoniopsis morii	**56, 55, 84, 102, 106, 108, 169**	[89]
Acritopappus group			
	Acritopappus morii	**106**	[90]
	A. teixeirae	**100**	[90]
Piqueria group			
	Ageratum houstonianum	**49, 51, 65, 128**	[91]
	A. conyzoides	**49, 51, 52**	[92]
	A. mexicanum	**51**	[93]
	Stevia serrata	**13**	[94]
Ayapana group			
	Ayapana amygdalina	**56, 85, 118, 123, 145**	[95]
	A. ecuadorensis	**56, 85, 102, 105**	[96]
	Condylidium iresinoides	**56, 84, 85, 105**	[97]
	Heterocondylus vitalbae	**59**	[97]
	Isocarpha atriplicifolia	**9, 56**	[42]
	I. oppositifolia	**56, 83, 84, 86, 129**	[41, 42]
	Polyanthina nemorosa	**56, 57, 59, 65, 102, 124, 145**	[98]
Alomiinae			
	Austrobrickellia patens	**7, 59, 73, 94**	[99]
	Brickellia californica	**141**	[100]
	B. veronicaefolia var. *typica*	**72, 75, 142**	[101]
	Goyazianthus tetrastichus	**72, 106**	[102]
	Planaltoa lychnophoroides	**59, 85, 94, 95**	[103]
Liatris group			
	Liatris cylindracea	**56, 57, 65, 81, 84, 85**	[104]
	L. platylepis	**56, 72, 81, 84, 85, 87, 88**	[105]
	L. provincialis	**111**	[106]
	L. scariosa	**56, 66, 104, 105**	[107]
	L. spicata	**56**	[108]
	L. sqarrosa	**56, 105**	[109]
	L. tenuifolia	**56**	[110]
Critonia group			
	Critonia daleoides	**72**	[72]
	Fleischmanniopsis leucocephala	**68, 113**	[72]
Ageratina group			
	Ageratina altissima	**6–8, 10, 15, 24, 72, 118, 119, 132, 161**	[74, 72]
	A. aromatica	**6, 7, 49–51**	[74, 72]
	A. aschenbornia	**6, 49**	[74]
	A. espinosara	**77**	[111]
	A. exertovenosa	**29, 31–33**	[97]
	A. glabrata	**89**	[111]
	A. petiolaris	**6, 7**	[111]
	A. pinchinchensis	**49**	[97]
	A. scorodonoides	**7, 8, 10, 11, 13, 15, 16, 24, 25**	[111]
	Kaunia arbuscularis	**113**	[112]
Hofmeisteria group			
	Hofmeisteria fasciculata	**56, 84, 86, 102**	[113]
Oaxacania group			
	Carterothamnus anomalochaeta	**56, 84, 86, 102**	[113]
subtribal position unclear:			
	Carelia cistifolia	**56, 84, 86**	[114]

Table 1. (*continued*)

Tribe	Species	Compounds isolated (see Fig. 3)	Ref.
	Morithamnus crassua	**56, 73, 96–99, 102, 103, 114**	[115]
Senecioneae subtribes: Senecioninae			
	Bedfordia salicina	**43**	[116]
	Doronicum austriacum	**119, 120, 125, 126**	[117]
	D. hungaricum	**120, 126**	[118]
	D. macrophyllum	**119, 120, 123–126, 131, 143, 145**	[119]
	D. pardalianches	**119, 120, 123–126, 130, 131, 143, 145**	[120]
	Ligularia intermedia	**56, 73, 160, 162**	[121]
	L. przewalskii	**160**	[122]
	L. sibirica	**82, 84, 160**	[122]
	L. speciosa	**56, 73, 99, 102, 160**	[123]
	L. stenocephala	**160,**	[122]
	L. veitchiana	**56, 73, 160**	[122]
	Othonna arborescens	**163**	[124]
	O. novae	**163**	[124]
	Senecio aetnensis	**73, 102**	[125]
	S. amplexicaulis	**73, 160**	[126]
	S. chrysanthemoides	**59**	[125]
	S. echinatus	**56**	[125]
	S. halimifolius	**117, 128**	[127]
	S. joppensis	**56, 102**	[125]
	S. leucanthemifolius	**56, 59, 60, 102**	[125]
	S. longifolius	**51**	[128]
	S. phonolithicus	**99**	[125]
	S. rodriguezii	**56, 59, 101, 102**	[125]
	S. rupestris	**56, 59, 102**	[125]
	S. squalidus	**56, 60, 101, 102**	[125]
	S. tussilaginis	**56, 105**	[125]
	S. vernalis	**56, 59**	[125]
	S. webbii	**56, 102, 105**	[125]
Blennospermatinae			
	Abrotanella fosteroides	**56, 73**	[129]
	A. nivigena	**56**	[129]
Inuleae subtribes: Inulinae			
	Inula salicina	**6**	[130]
Gnaphaliinae			
	Helichrysum cephaloideum	**152, 153**	[131]
	H. italicum	**133, 151**	[131]
	H. monticola	**38**	[132]
	H. plicatum	**39**	[131]
	H. stoechas	**37, 116, 154**	[131]
	H. umbraculigerum	**73**	[133]
	Leontonyx spatulatus	**40**	[134]
	L. squarrosus	**40**	[134]
Athrixiinae			
	Leyssera gnaphaloides	**146**	[135]
	L. tenella	**146**	[135]
	Macowania corymbosa	**147–149**	[136]
	Stoebe alopecuroides	**46**	[134]
	S. cinerea	**19, 102**	[134]
	S. incana	**17, 18**	[134]
	S. plumosa	**46**	[137]
	S. sphaerocephala	**17**	[134]
	S. vulgaris	**46**	[134]

Table 1. (*continued*)

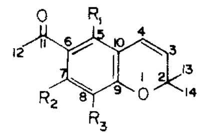
Tribe	Species	Compounds isolated (see Fig. 3)	Ref.
Subtribal position unclear:			
	Relhania pungens var. *angustifolius*	**150**	[134]
Astereae			
	Baccharis alaternoides	**136, 139**	[138]
	B. calvescens	**6, 72, 134, 139, 140**	[139]
	B. cassinaefolia	**6, 28, 72, 139, 143**	[139]
	B. conferta	**72, 136, 139**	[140]
	B. intermixta	**136, 139**	[139]
	B. juncea	**144**	[141]
	B. ramosissima	**6, 139**	[139]
	B. salzmanii	**139**	[139]
	B. tricuneata var. *ruiziana*	**6, 72, 73, 144**	[141]
	Chrysothamnus parryi	**139**	[142]
	C. viscidiflorus	**44, 45, 48, 116, 144,**	[143]
	Grindelia paludosa	**72**	[144]
	Haplopappus tenuisectus	**55, 61, 72, 97**	[145]
	Haplopappus heterophyllus (syn *Isocoma wrightii*)	**55, 69, 72, 96, 97, 115**	[16]
	Parastrephia lepidophylla	**72, 75, 122**	[146]
Calenduleae			
	Chrysanthemoides monilifera var. *canescens*	**143, 145**	[147]
(Helenieae)			
	Lasthenia glabrata	**56, 160**	[148]
correct tribal position probably in Heliantheae			
Mutisieae subtribes: Mutisiinae			
	Gerbera krausii	**18**	[149]
	Leibnitzia anandria	**137, 138**	[149]
Tageteae subtribes: Tagetinae			
	Tagetes patula	**6, 73**	[150]

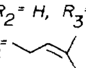
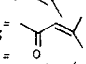
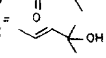
*According to a recent treatment on the tribal and subtribal limits of the Heliantheae [153] the genera *Encelia, Fluorensia* and *Helianthella* are grouped in the subtribe Ecliptinae.

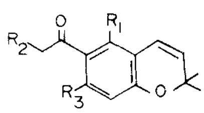
serve as tribal markers. The Heliantheae yields almost as many different chromenes as benzofurans. The benzofurans show no substitution at the isopropylene group, whereas this is a common feature in the Astereae, Eupatorieae, Inuleae and Senecioneae (Table 4). The Inuleae produces the same ratio of structural types of chromenes (benzopyrans) and benzofurans. A phloroglucinol type substitution seems to be found more frequently in this tribe than in the others. The Astereae and Eupatorieae show a marked increase of benzofurans resulting in 1:2 or even 1:3 ratios of chromenes–benzofurans. The Astereae produces several benzofurans with an unusual *m*-hydroxyacetophenone substitution pattern. In the Senecioneae the trend towards the production of benzofurans rather than chromenes is even more distinct. In comparison to 25 benzofurans, only two chromene derivatives have been isolated so far from this tribe.

These chemical characters have been used to help clarify the correct tribal placement of the genus *Isocarpha*, traditionally placed in the Heliantheae [39], to the Eupatorieae. This revision is supported both by morphological [40], and by reasons based on the type of benzofurans present [41, 42]. Our data on the chromenes and benzofurans present in the genus *Encelia* [15, 43] show an interesting correlation with the phylogenetic relationships proposed for the genus. The chromene and benzofuran chemistry agrees well with the division of the genus into three distinct phylogenetic groupings [44, 45]. The chemistry seems remarkably uniform within each section and no obvious qualitative infraspecific differences, based on chromenes and benzofurans, have been found as yet.

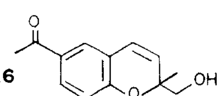
It is apparent from our survey that chromenes and benzofurans represent useful taxonomic characters at the tribal and generic level of the Asteraceae. It is also

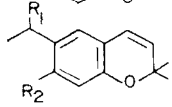


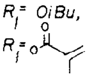
6 $R_{1,2,3}$ = H
7 R_1 = H, R_2 = OH, R_3 = H
8 R_1 = H, R_2 = OMe, R_3 = H
9 $R_{1,2}$ = H, R_3 = OH
10 $R_{1,2}$ = H, R_3 = OMe
11 R_1 = H, R_2 = OH, R_3 = OMe
12 R_1 = H, R_2 = OMe, R_3 = OH
13 R_1 = H, $R_{2,3}$ = OMe
14 R_1 = OH, $R_{2,3}$ = H
15 R_1 = OH, R_2 = H, R_3 = OMe
16 R_1 = OMe, R_2 = H, R_3 = OMe
17 $R_{1,2}$ = H, R_3 = 
18 $R_{1,2}$ = H, R_3 = 
19 $R_{1,2}$ = H, R_3 = 

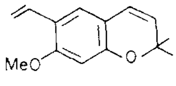


20 R_1 = OH, R_2 = OAc, R_3 = H
21 R_1 = H, $R_{2,3}$ = OH
22 R_1 = H, R_2 = OH, R_3 = OMe
23 R_1 = H, R_2 = OAc, R_3 = OMe
24 R_1 = H, R_2 = OAc, R_3 = OH
25 R_1 = H, R_2 = OiBu, R_3 = OH

26




27 R_1 = H, R_2 = OMe
28 R_1 = OH, R_2 = H
29 R_1 = OH, R_2 = OMe
30 $R_{1,2}$ = OMe
31 R_1 = OAng, R_2 = OMe
32 R_1 = OiBu, R_2 = OMe
33 R_1 = , R_2 = OMe

34


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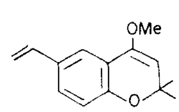

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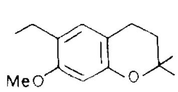

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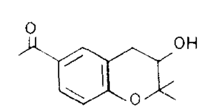

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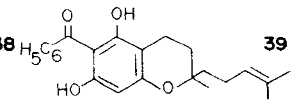

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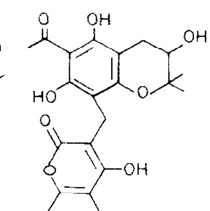

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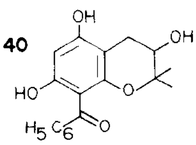

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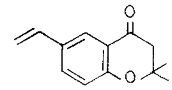

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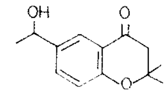

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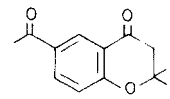
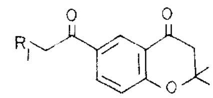
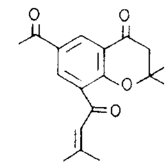




44 R_1 = OH
45 R_1 = OAc

46


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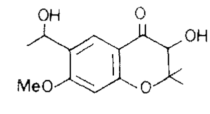

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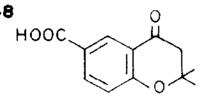
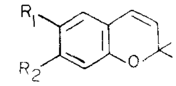
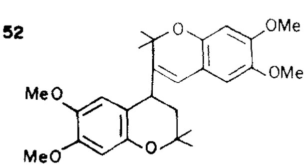




49 R_1 = H, R_2 = OMe
50 R_1 = OMe, R_2 = H
51 $R_{1,2}$ = OMe

52


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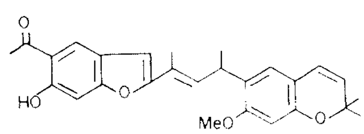

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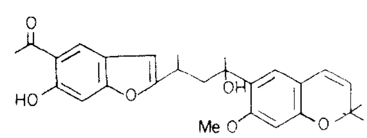
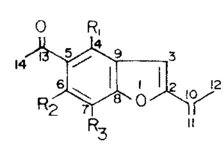
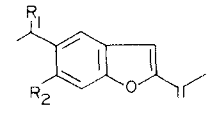
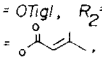
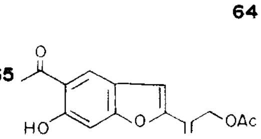




55 $R_{1,2,3}$ = H
56 R_1 = H, R_2 = OH, R_3 = H
57 R_1 = H, R_2 = OMe, R_3 = H
58 R_1 = H, $R_{2,3}$ = OH
59 R_1 = H, R_2 = OH, R_3 = OMe
60 R_1 = H, $R_{2,3}$ = OMe



61 R_1 = OH, R_2 = H
62 R_1 = OTigl, R_2 = OMe
63 R_1 = , R_2 = OMe
64 R_1 = OAng, R_2 = OMe

65


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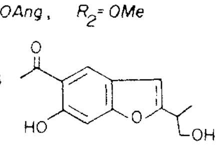
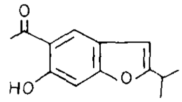
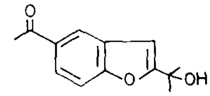
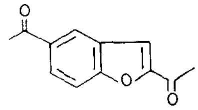
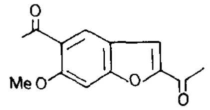
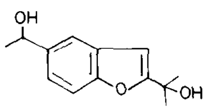


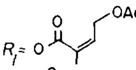
67 

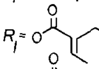
68 

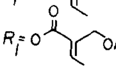
69 

70 

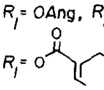
71 

103 R_1 =  , R_2= OH, R_3= H

104 R_1 =  , R_2= OH, R_3= H

105 R_1 =  , R_2= OH, R_3= H

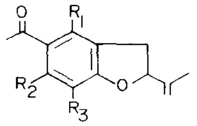
106 R_1 = OAng, R_2= OMe, R_3= H

107 R_1 =  , R_2= OMe, R_3= H

108 R_1 = OTigl, R_2= OMe, R_3= H

109 R_1 = OMe , R_2= OH , R_3= OMe

110 R_1 = OAng, R_2= OH, R_3= OMe



72 $R_{1,2,3}$ = H

73 R_1 = H, R_2= OH, R_3= H

74 $R_{1,2}$ = H, R_3= OH

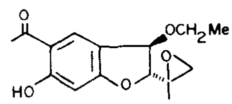
75 $R_{1,2}$ = H, R_3= OMe

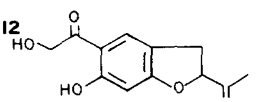
76 R_1 = OH, $R_{2,3}$= H

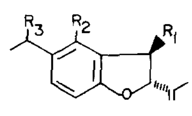
77 R_1 = H, $R_{2,3}$= OH

78 R_1 = H, R_2= OH, R_3= OMe

79 R_1 = OMe, R_2= OH, R_3= H

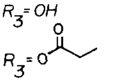
111 

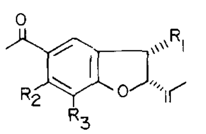
112 



113 R_1 = H, R_2= OMe, R_3= OH

114 R_1 = OH, R_2= H, R_3= OH

115 R_1 = OH, R_2= H, R_3= 



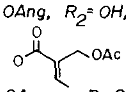
80 R_1 = OH, $R_{2,3}$= H

81 R_1 = OAng, $R_{2,3}$= H

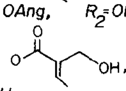
82 $R_{1,2}$ = OH, R_3= H

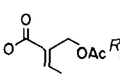
83 R_1 = OTigl, R_2= OH, R_3= H

84 R_1 = OAng, R_2= OH, R_3= H

85 R_1 =  , R_2= OH, R_3= H

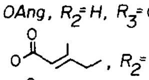
86 R_1 = OAng, R_2= OMe, R_3= H

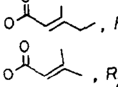
87 R_1 =  , R_2= OMe, R_3= H

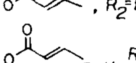
88 R_1 =  R_2= OMe, R_3= H

89 R_1 = OH, R_2= H, R_3= OH

90 R_1 = OAng, R_2= H, R_3= OMe

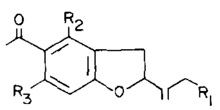
91 R_1 =  , R_2= H, R_3= OMe

92 R_1 =  , R_2= H , R_3= OMe

93 R_1 =  R_2= H, R_3= OMe

94 R_1 = OAng, R_2= OH, R_3= OMe

95 R_1 = OAng, $R_{2,3}$= OMe



116 R_1 = OH, $R_{2,3}$= H

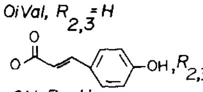
117 R_1 = OH, R_2= H, R_3= OH

118 R_1 = OAng, $R_{2,3}$= H

119 R_1 = OiBu, $R_{2,3}$= H

120 R_1 = OMeBu, $R_{2,3}$= H

121 R_1 = OiVal, $R_{2,3}$= H

122 R_1 =  , $R_{2,3}$= H

123 $R_{1,2}$ = OH, R_3= H

124 R_1 = OAc, R_2= OH, R_3= H

125 R_1 = OiBu, R_2= OH, R_3= H

126 R_1 = OMeBu, R_2= OH, R_3= H

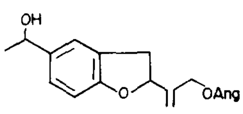
127 $R_{1,2}$ = H, R_3= OH

128 R_1 = OAc, R_2= H, R_3= OH

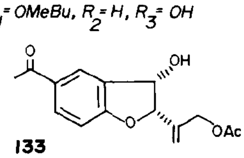
129 R_1 = OAc, R_2= H , R_3= OMe

130 R_1 = OiBu, R_2= H, R_3= OH

131 R_1 = OMeBu, R_2= H, R_3= OH



132



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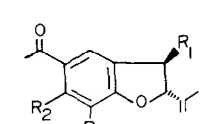
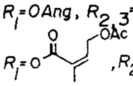


96 R_1 = OH, $R_{2,3}$= H

97 R_1 = OAng, $R_{2,3}$= H

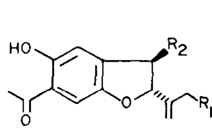
98 R_1 =  , $R_{2,3}$= H

99 $R_{1,2}$ = OH, R_3= H

100 R_1 = OMe, R_2= OH, R_3= H

101 R_1 = OMe Bu , R_2= OH, R_3= H

102 R_1 = OAng, R_2= OH, R_3= H



134 $R_{1,2}$ = H

135 R_1 = OH, R_2= H

136 R_1 = OAc, R_2= H

137 R_1 = OMe Bu, R_2= H

138 R_1 = OiVal, R_2= H

139 R_1 = HO, R_2= H

140 R_1 = H, R_2= OAc

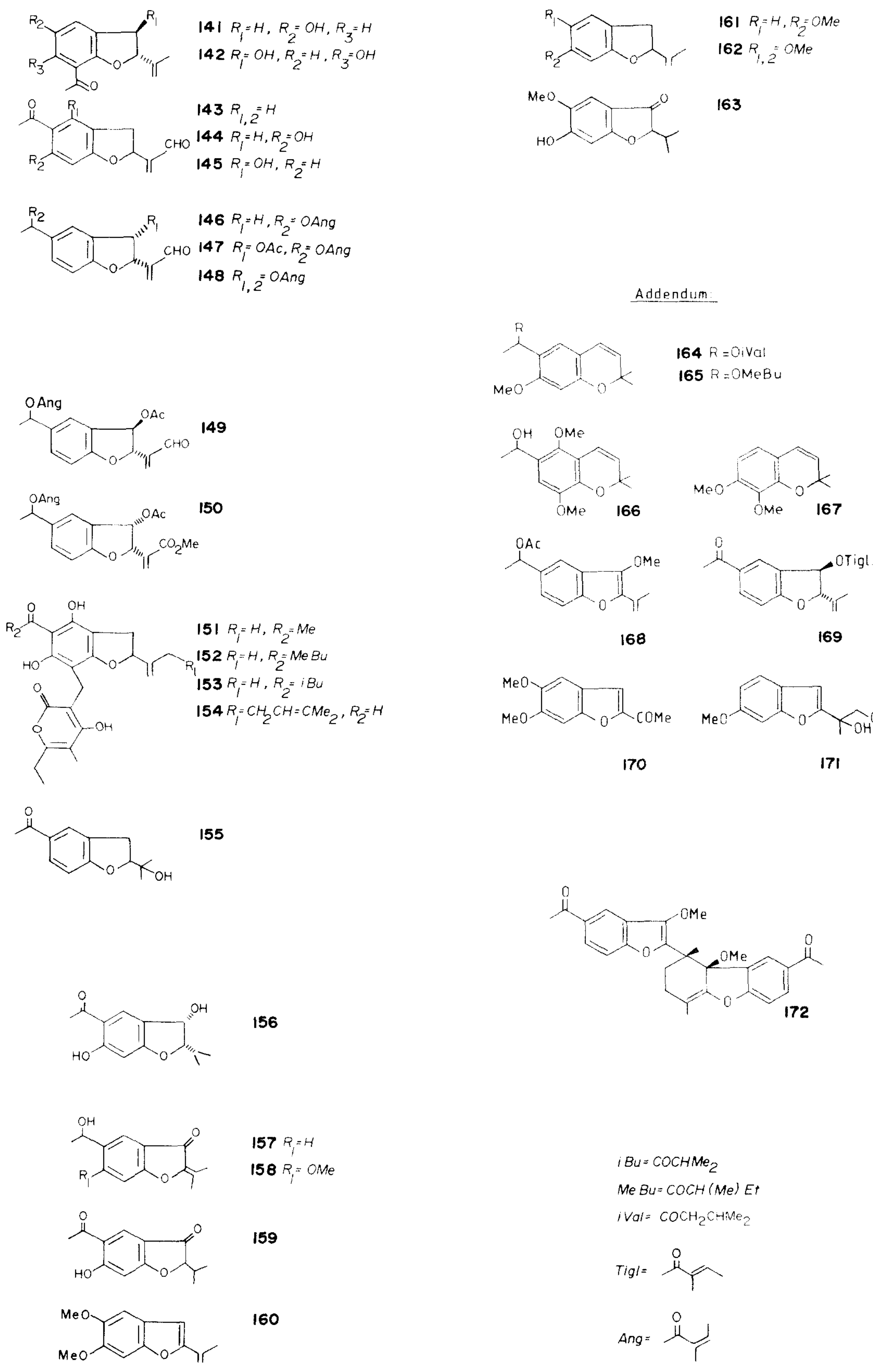


Fig. 3. Chromenes and benzofurans isolated from the Asteraceae.

Table 2. Distribution of chromenes and benzofurans in the Asteraceae

Tribes (No. of genera)*	No. of genera reported to produce chromenes and benzofurans	No. of species reported to produce chromenes and benzofurans
Astereae (135)	6	15
Eupatorieae (160)	30	65
Heliantheae (211)	17	33
Inuleae (180)	7	19
Senecioneae (100)	6	30
Calenduleae (8)	1	1
Mutisieae (89)	2	2
Tageteae (18)	1	1
Anthemideae (102)	—	—
Arctotideae (15)	—	—
Cardueae (79)	—	—
Lactuceae (70)	—	—
Liabeae (15)	—	—
Vernonieae (70)	—	—

*According to ref. [34].

Table 3. Tribal groupings of the Asteraceae

Group	Morphological characters*	Chromenes and benzofurans present (+) or not present (−)	Morphological characters†
I	Astereae	Astereae (+)	Astereae
	Eupatorieae	Eupatorieae (+)	
	Heliantheae (including Helenieae, Tageteae)	Heliantheae (+) (including Helenieae)	Heliantheae (including Helenieae, Tageteae)
	Inuleae	Inuleae (+)	Inuleae
	Senecioneae	Senecioneae (+)	Senecioneae
	Calenduleae		Calenduleae
	Anthemideae		Anthemideae
		Anthemideae (−)	
II	Arctotideae	Arctotideae (−)	Arctotideae
		Calenduleae (−) (+)	
	Cardueae	Cardueae (−) (= Cynareae)	Cardueae
	Echinopeae		Eupatorieae
	Lactuceae	Lactuceae (−)	Lactuceae
	Liabeae	Liabeae (−)	
	Mutisieae	Mutisieae (−) (+)	Mutisieae
		Tageteae (−) (+)	
	Vernonieae	Vernonieae (−)	Vernonieae

*[37].
†[38].

Table 4. Tribal characterization based on chromene and benzofuran chemistry

Tribes	Structural types of chromenes vs benzofurans	Substitution at isopropylene group	Structural speciality
Heliantheae	1:1	—	—
Inuleae	1:1	+	Phloroglucinol type substitution common
Eupatorieae	1:3	+	—
Astereae	1:3	+	*m*-hydroxyacetophenone type substitution common
Senecioneae	1:10	+	—

interesting to note that those compounds exhibiting insecticidal activity and feeding deterrency are more widespread than previously thought and probably represent a major adaptive advantage of many Asteraceae plants to insect herbivory and microbial attack [152].

Acknowledgements—We thank NSF (8209100) and NIH (AI 18398) for financial support. We are also indebted to Professor G. Wagenitz (University of Göttingen, West Germany) for his suggestions on the manuscript and to Professor G. H. N. Towers (UBC), M. Aregullin (UCI) and Professor C. Clark (Pomona College) for information on the distribution of chromenes and benzofurans in the Asteraceae.

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