Table 2. Observed and calculated relative Bijvoet difference

(h, k, l)	Equivalent pairs in set	% ratio observed*	% ratio calculated†
1, 4, 3	4	−6.6	−5.0
1, 1, 3	6	19.5	16.6
2, 3, 5	6	2.1	2.3
2, 4, 2	6	3.1	2.8
4, 4, 4	6	−3.5	−3.9
−11, 7, 8	2	−12.2	−13.7
3, 7, 5	6	−13.8	−9.2
2, 9, 3	6	5.0	5.5
6, 6, 3	2	−4.5	−3.6

* $100[2\Sigma F^2(h, k, l)-\Sigma F^2(\bar{h}, \bar{k}, \bar{l})]/[\Sigma F^2(h, k, l)+\Sigma F^2(\bar{h}, \bar{k}, \bar{l})]$

† $100(2)[(F_{\text{correct}})^2-(F_{\text{mirror}})^2]/[(F_{\text{correct}})^2+(F_{\text{mirror}})^2]$

ment using anisotropic thermal parameters gave final discrepancy indices of $R=0.034$ and $R_w=0.039$. Reflections with optimal Bijvoet differences for CuKα radiation were found with the program ABSCON [4] based on f″ for carbon and oxygen. Bijvoet differences for 9 Friedel pairs, including all 6 intensity equivalent pairs for 6 of the 9 sets,—in all, 88 reflections-were measured. The intensity equivalents were summed, and each sum was treated as an individual reflection and compared with values calculated for the structure shown in Fig. 1 and its mirror image. The data for all sets, which are summarized in Table 2, are in accord with the absolute configuration shown.

Tables of positional and thermal parameters and structure factors are available from the Directory of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K. The request should be accompanied by the full literature citation for this report.

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(+)-α-COPAEN-8-ONE AND OTHER CONSTITUENTS FROM *NEOMIRANDEA* SPECIES

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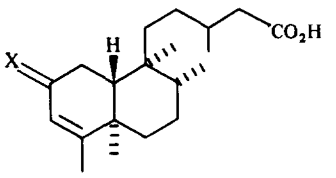
Key Word Index—*Neomirandea angularis*, *N. arthodes*, *N. exima*, *N. guevarii*, *N. parasitica*; Compositae; Eupatorieae; diterpenes; *ent*-clerodanes; sesquiterpenes; copaene derivative; sesquiterpene lactone; heliangolide.

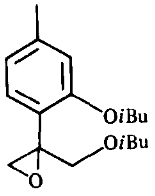
Abstract—The investigation of five *Neomirandea* species gave two known *ent*-clerodanes, a heliangolide, a cadinene and a new copaene derivative as well as some widespread compounds.

The genus *Neomirandea* with 27 species is distributed over Central America from Mexico up to Ecuador. It has been placed in the monogeneric subtribe Neomirandiinae [1]. Nothing was known on the chemistry of this genus. We therefore have studied the constituents of five species from Costa Rica. The results are summarized in Table 1.

The aerial parts of *N. angularis* (B. L. Robins.) K. et R. contain in high concentration the *ent*-clerodanes (−) **1** [2] and (−) **2** [3], while those of *N. parasitica* (Klatt.) K. et R. gave the heliangolide (−) **7** [4]. The aerial parts of



1 X = H_2
2 X = O



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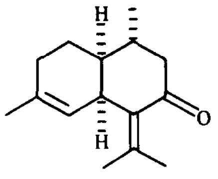

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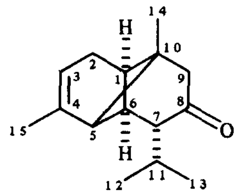

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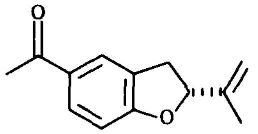

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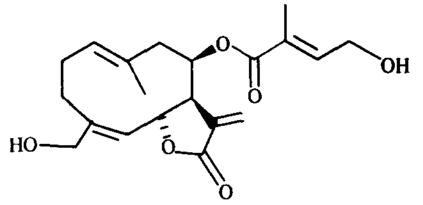

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N. guevarii K. et R. gave the cadinene derivative (+) **4** [5] and (+)-α-copaen-8-one (**5**). The structure of the latter was elucidated by its ^1H and ^{13}C NMR spectra which were similar to those of α-copaene. However, some signals were shifted and spin decoupling indicated that a keto group had to be placed at C-8. The stereochemistry was examined by NOE difference spectroscopy. Clear effects were observed between H-12 and H-6 (4%), between H-14 and H-9 (4%) as well as between H-13, H-6 (5%) and H-1 (5%). From the optical rotation and the observed Cotton-effect the absolute configuration was proposed. The roots gave isoeugenol and **6** while two further species afforded no characteristic compounds.

The results on the chemistry of *Neomirandea* do not indicate clear taxonomic relevances. The occurrence of *ent*-clerodanes may be of some importance, as such diterpenes are also reported from *Fleischmannia* which is placed in a subtribe next to Critoniinae from which *Neomirandea* has been separated [1]. However, as only one species shows a high accumulation of these compounds, this fact is of limited importance. Proposed relationships to *Mikania* are not indicated, as for this genus germacra-12,8-olides are characteristic.

EXPERIMENTAL

The air-dried plant material was extracted with Et_2O–MeOH–petrol (1:1:1). The extracts were worked-up and

Table 1. Investigated species and isolated constituents

Species (vouchers, collection places)	aerial parts	
Neomirandea angularis (B. L. Robins.) K. et R. (voucher 82–4, Empalme, Costa Rica, January 1982)	470 g	25 mg germacrene D, 100 mg squalene, 1.4 g **1**, 3.0 g **2**
N. arthodes (B. L. Robins.) K. et R. (voucher 89108, Empalme, Costa Rica, October 1983)	500 g	germacrene D, **3**
N. exima (B. L. Robins.) K. et R. (voucher 124284, Tapanti, Costa Rica, April 1987)	600 g	lupeol
N. guevarii K. et R. (voucher 124282, Tapanti, Costa Rica, April 1987)	875 g	43 mg **4**, 12 mg **5** (roots 660 g: 80 mg **6**, 80 mg isoeugenol)
N. parasitica (Klatt) K. et R. (voucher RMK 9670, Tapanti, Costa Rica, April 1987)	75 g	130 mg **7**, 250 mg ferulic acid, 20 mg methylferulate

separated as reported previously [6]. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

(+)-*Copaen-8-one* (**5**). Colourless oil (TLC: Et_2O–petrol, 1:4, R_f 0.69); IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1715 (C=O); MS m/z (rel. int.): 218.167 $[M]^+$ (22) (calc. for $C_{15}H_{22}O$: 218.167), 203 $[M - Me]^+$ (9), 175 $[M - C_3H_7]^+$ (21), 134 $[M - C_5H_8O]^+$ (54), 119 $[134 - Me]^+$ (100); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.06 (*m*, H-1), 2.33 and 2.25 (*m*, H-2), 5.32 (*dddq*, H-3), 1.85 (*dd*, H-5), 1.99 (*d*, H-6), 2.33 (*m*, H-7), 2.49 and 2.44 (*d*, H-9), 2.28 (*m*, H-11), 0.81 (*d*, H-12), 0.97 (*d*, H-13), 0.85 (*s*, H-14), 1.71 (*dt*, H-15); *J* [Hz]: 1,5 = 6.5; 2,3 = 2′,3 = 3,5 = 3, 15 ~ 1.5; 6,7 = 2; 11,12 = 6.5; 11,13 = 6; ^{13}C NMR ($CDCl_3$, C-1–C-15): δ 41.7, 30.0, 116.7, 142.0, 50.9, 40.7, 59.3, 213.1, 52.5, 38.5, 28.0, 19.3, 18.5, 21.3, 22.9; $[\alpha]_D^{24} = +14$ ($CHCl_3$; *c* 0.53); CD (MeCN): $\Delta\varepsilon_{305} + 0.12$.

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REVISED STRUCTURES FOR GUAIANOLIDE α-METHYLENEBUTYROLACTONES FROM FEVERFEW

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Key Word Index—*Tanacetum parthenium*; Compositae; feverfew; sesquiterpene lactones; parthenolide; guaianolides; migraine.

Abstract—The structures of two series of guaianolides present in feverfew, *Tanacetum parthenium*, are established as tanaparthin-α-peroxide, canin and *seco*-tanapartholide-A [major group] and the corresponding 'β'-series [β-peroxide, artecanin and the *seco*-B derivative] using a combination of spectroscopic and X-ray crystallographic analyses and chemical transformations.

Feverfew, *Tanacetum parthenium*, has been used since ancient times for a variety of medicinal purposes, and has gained considerable prominence recently due to its ability to alleviate the symptoms of migraine [1–3], arthritis and psoriasis [4], and to inhibit blood platelet aggregation [5]. During the latter studies [5], a clear link was established between the anti-aggregatory properties of feverfew extracts and the presence therein of a series of sesquiterpene lactones containing α-methylenebutyrolactone units (**1**). This function is known to be a potent Michael acceptor of sulphydryl groups [(**1**)→(**2**)] [5, 6], and it appears [5] that such reactions are a key feature of the ability of feverfew extracts to suppress blood platelet aggregation *in vitro*, and are also possibly linked with the anti-inflammatory and migraine prophylactic properties of the plant. During our studies of feverfew extracts [5], some spectroscopic inconsistencies taken with the considerable confusion existing in the literature over the structures of two bis-epoxides, canin and artecanin, found in the plant led us to re-investigate the nature of these and related sesquiterpene lactones.

The major sesquiterpene lactone present in feverfew is parthenolide (**3**) [7], a germacranolide found in a variety of other plants [8]. Our extraction of feverfew also gave parthenolide (**3**) as the major component, accompanied by six other α-methylenebutyrolactones: epoxy-artemorin (**4**) [7], and a closely related series consisting of two bis-epoxides, an endoperoxide and two cyclopentenones [7]. Our starting point was the major bis-epoxide which appeared to be identical with canin, a material which has been the subject of a highly confusing series of structural assignments during the past two decades [9]. Originally designated as the bis-α-epoxide (**5**) [10], the compound was later given the bis-β-stereochemistry (**6**) and also confused with isomeric chrysartemin structures (**7**). X-Ray analysis [9] has established that canin (identical with chrysartemin A) from various *Artemisia* species is indeed the bis-α-epoxide (**5**) or its enantiomer. However, Bohlmann and Zdero [7] have used the bis-β-epoxide structure (**6**) for 'canin', the major bis-epoxide of feverfew. A divergence of spectroscopic data [7, 9] together with closely similar physical properties led us to carry out our own X-ray analysis of feverfew canin, which was shown to be identical with *Artemisia* canin [9], and to have the bis-