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GRINDELANE DITERPENOIDS FROM *GRINDELIA CAMPORUM* AND *CHRYSOTHAMNUS PANICULATUS*

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Key Word Index—*Grindelia camporum*; *Chrysothamnus paniculatus*; Compositae; Soladiginae; diterpenes; labdanes; grindelic acid derivatives.

Abstract—The structures of nine grindelic acid related diterpenes isolated as methyl esters from *Grindelia camporum* and *Chrysothamnus paniculatus*, were elucidated based on their spectral properties.

INTRODUCTION

We have previously reported the isolation and identification of three diterpenes (**1a, 2a, 12a**) from *Chrysothamnus paniculatus* (Gray) Hall [1]. We now report the isolation and structure elucidation of nine additional diterpenes isolated as methyl esters (**3b–11b**) from the same plant as well as from *Grindelia camporum* Greene, both members of the tribe Astereae of the Compositae.

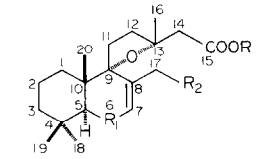
RESULTS AND DISCUSSION

The isolation of the diterpene methyl esters **3b–11b** was accomplished by methylating the acid fraction of the ethyl acetate extracts of the aerial parts of *Grindelia camporum* and *Chrysothamnus paniculatus*, followed by HPLC and TLC.

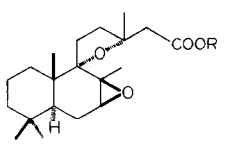
Quantitative GC analyses of the methyl ester mixtures of both plants displayed very similar chromatograms except for the proportions of the components. Qualitative GC analyses were performed in order to check the purity of the isolated TLC pure components and to identify the components present in any mixture. Based on the quantitative analysis, five 17-substituted diterpene homologs (**4b–8b**) were isolated from the methyl ester mixture of *G. camporum*, while the methyl ester mixture of *C. paniculatus* was used to isolate three additional diterpenes (**9b–11b**). The presence of methyl 6β-hydroxygrindelate (**3b**) in the methyl ester mixtures of both plants was established by direct GC retention time comparison with an authentic sample.

Guerreiro *et al.* [2] reported the isolation of **1a** and **9a–11a** from *G. pulchella* and *G. chiloensis*, and Bohlmann *et al.* [3] reported all compounds except **4b** and **11b** from *G. stricta*, and **4b–8b** and **11b** from *G. camporum*. The spectral data (IR and ^{1}H NMR) of our compounds are in good agreement with those reported by these workers. We present herein hitherto unreported ^{13}C NMR spectral data for **10b** and **11b** (Table 1) and mass spectral data for **4b–8b** (Scheme 1), **10b** and **11b** (Scheme 2).

The nature and size of the side chain at C-17 in **4b–8b** were established from ^{1}H NMR and mass spectral data. The latter displayed very similar fragmentation modes after initial retro-Diels–Alder breakdown as shown in



	R_1	R_2
1	CH_2	H
2	C=O	H
3	CHOH	H
4	CH_2	OMe
5	CH_2	OCOMe
6	CH_2	$OCOCH_2$ Me
7	CH_2	$OCOCH(Me)_2$
8	CH_2	$OCOCH_2CH(Me)_2$



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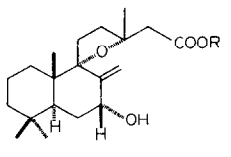

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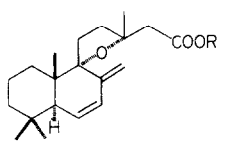

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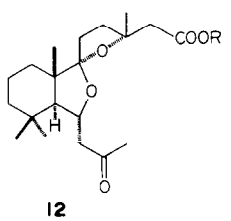

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1a – 12a R = H, **1b – 12b** R = Me

Table 1. ^{13}C NMR shifts (δ) in $CDCl_3$ for **10b** and **11b**

C	10b	11b
1	37.6	37.9
2	19.1	19.0
3	42.0	41.1
4	33.3	33.1
5	40.6	48.1
6	32.2*	129.1†
7	75.2	130.2†
8	148.1	147.2
9	93.5	89.1
10	42.1	41.5
11	25.9	25.8
12	32.0*	31.2
13	82.5	82.0
14	46.7	46.8
15	171.4	171.9
16	26.5	27.5
17	111.1	110.9
18	33.4	32.8
19	22.0	22.4
20	16.8	17.4
MeO	51.4	51.2

*†The shift values with the same sign may be interchanged.

Scheme 1. Similarly, **10b** and **11b** exhibited very similar fragmentation patterns (the former showing peaks displayed by the latter in addition to the peaks with appropriate shifts to mass numbers higher by 18) verified by high resolution data and, where indicated by *m*, substantiated by metastable peaks (Scheme 2).

EXPERIMENTAL

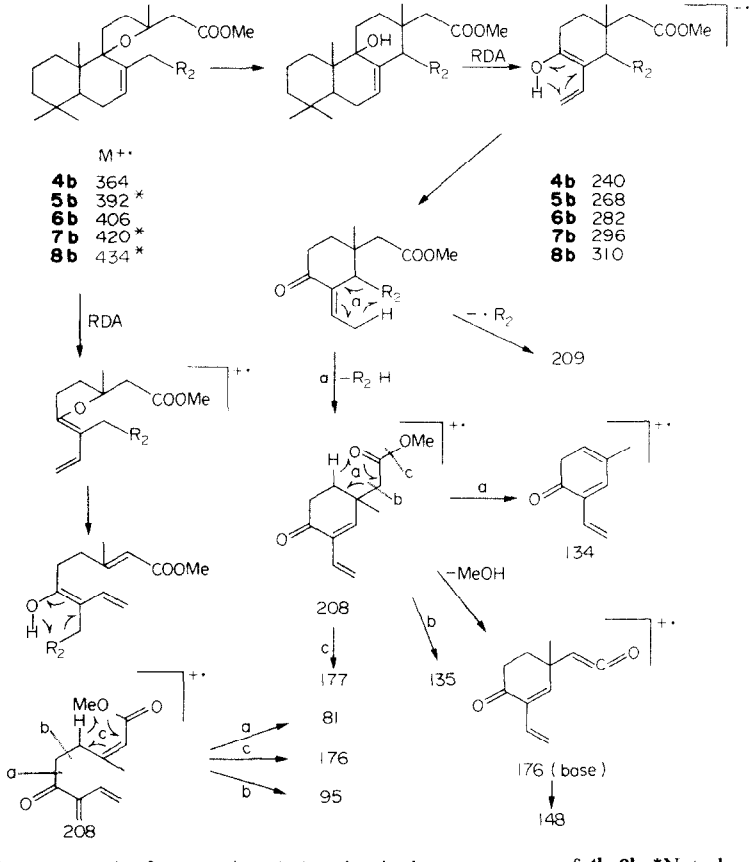
See ref. [4] for the description of the analytical procedures used here. Aerial plant material and vouchers of *G. camporum* and *C. paniculatus* were collected in the Mojave Desert of California. Voucher specimens are deposited in the Herbarium at the University of Arizona. All plant material was air-dried and ground to 3 mm particle size prior to extraction.

Isolation of acid fraction. The ground *G. camporum* (2 kg) was extracted exhaustively with EtOAc, solvent freed and the resulting residue was extracted with MeOH, left in the freezer overnight and filtered. The filtrate, after being freed from solvent, was dissolved in Et_2O and ppted with light petrol. From the supernatant, after decantation from the resinous residue, the acid fraction was separated following the usual work-up, decolorized, solvent freed under vacuum and subjected to methylation.

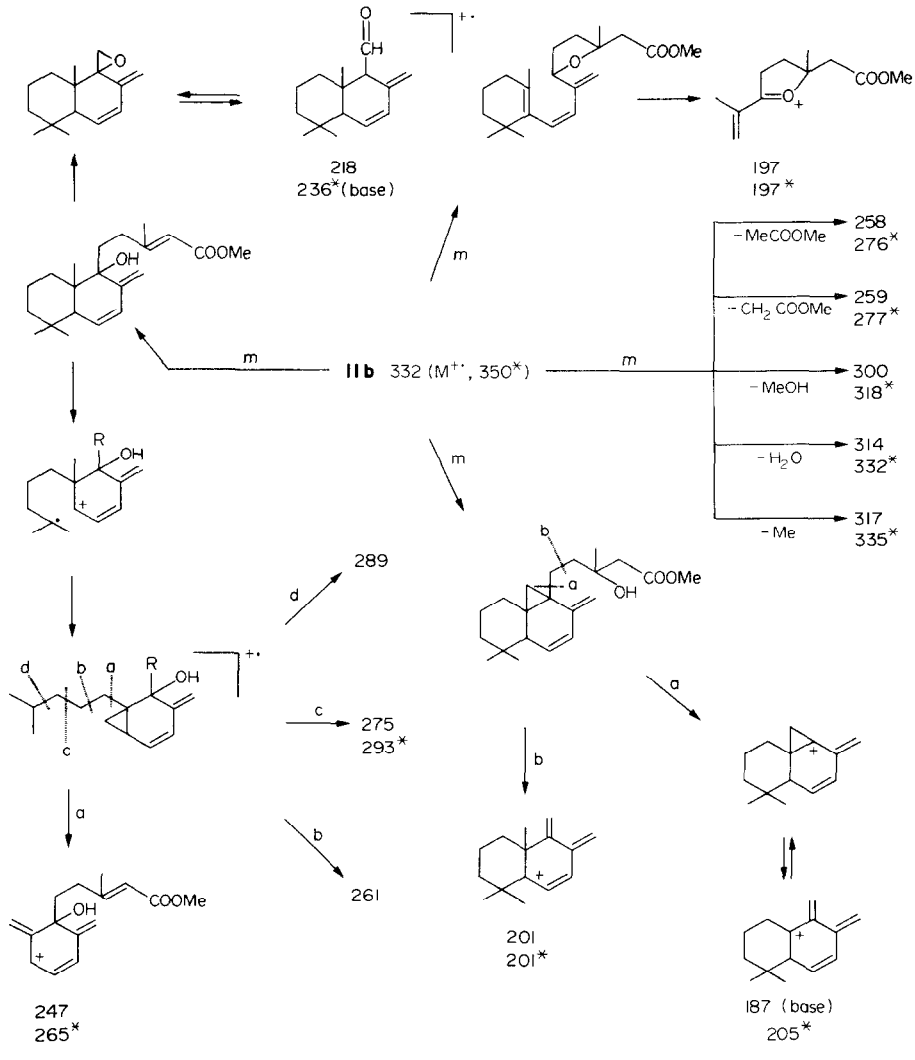
In the case of *C. paniculatus*, the acid fraction was separated from the Et_2O-soluble fraction of the EtOAc extract of the plant followed by pptn with light petrol as above. Repetition of the pptn procedure followed by decolorization and work-up gave an oil which was subjected to methylation.

Methylation of acid fraction. In dry Me_2CO with K_2CO_3 and MeI for 6 hr under reflux. Removal of the solvent after work-up gave a nearly colorless heavy oil (IR showing no C=O).

Separation of methyl ester mixture by HPLC. The methyl ester mixture in 4% EtOAc in *n*-hexane was separated on a Waters PrepPAK-500/Silica cartridge column with a refractive index



Scheme 1. Major fragment ions (*m/z* ratios) in the mass spectra of **4b–8b**. *Not observed.



Scheme 2. Major fragment ions (*m/z* ratios) in the mass spectrum of **11b**. *In **10b**; *m*, metastable peak.

detector. The column was eluted with various EtOAc–hexane mixtures: from 4:96 to 3:7 to give fractions I–IV. TLC and GC analyses showed that fraction I contained **1b** and **11b**, while fraction II was essentially **1b**. Fraction III, which was complex, contained **4b–9b**, while fraction IV contained **3b**, **10b**, and **12b**.

Isolation of individual diterpene methyl esters. Final separation and purification of each diterpene methyl ester from the above fractions was carried out by repeated TLC (SiO_2 60 PF-254) and, where necessary, by EM SiO_2 60 CC followed by TLC. All the isolated diterpene esters were pure colorless oils (as judged from TLC and GC) except **7b** and **8b** which could not be separated from each other. GC was performed on a Varian Model 3700 gas chromatograph (FID) and Model 8070 Interface. The glass capillary column (10 m × 0.25 mm) was WCOT OV-101 with He at 3.6 ml/min. The temp. program was 148° 15 min, 3°/min to 215°, hold 4 min. The GC data was analysed with a Varian VISTA 401 chromatography data system.

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