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DITERPENES RELATED TO GRINDELIC ACID AND FURTHER CONSTITUENTS FROM *GRINDELIA* SPECIES*

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Key Word Index—*Grindelia stricta*; *G. paludosa*; *G. camporum*; Compositae; diterpenes; grindelic acid derivatives; tropones; modhephenepoxide.

Abstract—The aerial parts of *Grindelia stricta* afforded in addition to known compounds 21 diterpenes, all closely related to grindelic acid. The aerial parts from *G. paludosa* also contain these diterpenes together with modhephenepoxide, while the roots afforded two tropone derivatives and a tetralin, which is also present in the leaves. Grindelic acid and several derivatives were also isolated from *G. camporum*. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

From the large American genus *Grindelia* (tribe Astereae) the occurrence of C_{10}-acetylenes [1] and several flavones [2–4] has been reported previously. From one species, grindelic acid and its 6-oxo derivative were isolated [5]. We have now investigated *Grindelia stricta*, *G. paludosa* and *G. camporum*. Again, several C_{10}-acetylenes (**1–10**), grindelic acid (**11a**) and **12a** were present together with a large number of other diterpenes, all closely related to **11a**. Two unusual tropones and modhephenepoxides were also isolated.

RESULTS AND DISCUSSION

The aerial parts of *G. stricta* afforded the acetylenic esters **1–5**, the labdanes grindelic acid (**11a**) [5], **12a** [5], **13a** [6], **14a** [7] and **36a** [8] as well as 21 other diterpenic acids, which could be separated only as their methyl esters. ^{1}H NMR investigations led to the structures **15b–35b** (Tables 1 and 2), consequently **15a–35a** were the natural compounds. The structure of **15b** was deduced from the corresponding ^{1}H NMR signals (Table 1) and from decoupling experiments. Irradiation of the broadened doublet at δ 4.00 collapsed the doublet at 1.68 to a singlet, the broadened singlet at 5.50 to a quartet and the signal of the olefinic methyl to a narrow split doublet, indicating that we were dealing with the signals of H-5, H-6, H-7 and H-17. All other signals were close to those of **11b**. The 6a-orientation of the hydroxyl group followed from the coupling $J_{5,6}$. The ^{1}H NMR spectrum of **16b** (Table 1) was very similar to that of **15b**. However, the H-6 signal was shifted downfield to 4.38 and an additional singlet at 7.45 was present. In the mass spectrum fragments at *m/z* 348 and 333 ($C_{21}H_{32}O_4$ and $C_{21}H_{33}O_3$) could be observed, while no molecular ion was present. However, chemical ionization gave a clear M + 1 peak (*m/z* 379), indicating that *m/z* 333 probably was formed by loss of OCHO. Therefore compound **16b** was a formate and consequently, mild hydrolysis afforded **15b**. The molecular formula of **17b** and the IR spectrum of this compound indicated the presence of a further hydroxy derivative of grindelic acid. The ^{1}H NMR spectrum (Table 1) showed that this OH group could only be placed at C-1 or C-3. Comparison of the chemical shifts of H-18, H-19 and H-20 with those in the spectrum of **11b** favoured the C-3 position. The ^{1}H NMR spectrum of **18b** (Table 1) displayed three methyl signals, while the mass spectrum indicated the presence of a norditerpene. The chemical shifts of the methyl signals were in agreement only with the omission of a C-4 methyl group, which was replaced by a hydroxyl. The latter must be α-orientated, as in the corresponding kaurenes the axial hydroxyl group caused a clear downfield shift of the signal of the C-10 methyl group [9]. Compound **19b** was the corresponding formate. All signals (Table 1) were similar to those of **18b**, but again an additional downfield singlet indicated the presence of a formate. Only the H-5 double doublet was shifted downfield due to the deshielding effect of the formate carbonyl. The ^{1}H NMR spectral data of **22b** (Table 1) clearly showed that the acetate of **13b** was present. In **23b**, **24b** and **25b** the acetate group was replaced by isovalerate, 2-methyl butyrate and isobutyrate, respectively, as could be deduced from the corresponding ^{1}H NMR signals (Table 1), though these esters could not be separated completely. The ^{1}H NMR spectrum of **21b** (Table 1) showed that an aldehyde was present. The chemical shifts of the methyl signals indicated that this group was α-orientated at C-4 as the H-20 signal was nearly unchanged. The aldehyde has been prepared previously from **13a** [6]. The molecular formula, as well as the ^{1}H NMR data of **20b**, showed that this diterpene was an isomer of **13b**. Consequently, the ^{1}H NMR signals (Table 1) of H-18 and H-19 showed the characteristic differences if compared with those of **13b** [10]. Compounds **26b–30b** again showed very similar ^{1}H NMR spectra (Table 2). While **26b–28b** could be obtained pure, **29b** and **30b** still

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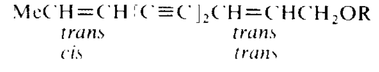
* Part 375 in the series "Naturally Occurring Terpene Derivatives". For Part 374, see Bohlmann, F., Adler, A., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 173.

Table 1. ^1H NMR spectral data of compounds **15b**–**25b** ($CDCl_3$, 400 MHz, TMS as internal standard).

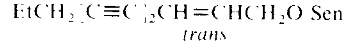
	15b	**16b**	**17b***	**18b**	**19b**	**20b**	**21b**	**22b**	**23b**	**24b**	**25b**
H-5	1.68 *d*	2.08 *d*			2.28 *dd*						
H-6	4.00 *br d*	4.38 *br d*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*		1.85 *m*	1.85 *m*
H-7	5.50 *br s*	5.67 *br s*	5.51 *br s*	5.53 *br d*	5.50 *br s*	5.47 *br d*	5.42 *br s*	5.46 *br s*		5.46 *br s*	5.46 *br s*
H-11	2.05 *ddd*	2.06 *m*	2.05 *m*	2.05 *ddd*	2.05 *ddd*	2.08 *m*	2.08 *ddd*	2.05 *m*		2.05 *ddd*	
H-11′	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*		1.85 *m*	
H-12	2.20 *ddd*	2.19 *ddd*	2.20 *ddd*	2.20 *ddd*	2.20 *ddd*	2.21 *ddd*	2.20 *ddd*	2.20 *ddd*		2.20 *ddd*	
H-12′	1.88 *ddd*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*	1.85 *ddd*	1.85 *ddd*	1.85 *m*		1.85 *m*	
H-14	2.67 *d*	2.66 *d*	2.74 *d*	2.74 *d*	2.70 *d*	2.73 *d*	2.77 *d*	2.70 *d*	2.68 *d*	2.69 *d*	2.68 *d*
H-14′	2.55 *br d*	2.54 *br d*	2.60 *br d*	2.61 *br d*	2.61 *br d*	2.59 *br d*	2.61 *br d*	2.59 *br d*		2.58 *br d*	2.59 *br d*
H-16	1.32 *s*	1.31 *s*	1.32 *s*	1.33 *s*	1.32 *s*	1.32 *s*	1.34 *s*	1.31 *s*		1.31 *s*	1.31 *s*
H-17	1.77 *br s*	1.83 *br s*	1.76 *br s*	1.77 *br s*	1.77 *br s*	1.76 *br s*	1.76 *br s*	1.76 *br s*		1.75 *br s*	1.76 *br s*
H-18	1.12 *s*	1.06 *s*	0.97 *s*	-	—	0.88 *s*	9.26 *s*	2.75 *d*	3.80 *d*	3.82 *d*	3.82 *d*
H-18′								3.73 *d*	3.74 *d*	3.71 *d*	3.71 *d*
H-19	1.00 *s*	0.97 *s*	0.86 *s*	1.18 *s*	1.18 *s*	3.35 *d*	1.10 *s*	0.91 *s*	0.92 *s*	0.91 *s*	0.92 *s*
H-19′						3.17 *br d*					
H-20	0.82 *s*	0.81 *s*	0.80 *s*	0.77 *s*	0.83 *s*	0.84 *s*	0.86 *s*	0.81 *s*	0.83 *s*	0.82 *s*	0.83 *s*
OCOR		7.45 *s*	--		7.05 *s*	-	--	2.04 *s*	2.20 *m* 0.94 *d* 0.93 *d*	2.37 *tq* 1.70 *ddq* 1.48 *ddq* 0.88 *t* 1.13 *d*	2.21 *qq* 1.16 *d* 1.15 *d*
OMe	3.65 *s*	3.64 *s*	3.65 *s*	3.66 *s*	3.66 *s*	3.65 *s*	3.66 *s*	3.64 *s*	3.65 *s*	3.65 *s*	3.65 *s*

*H-3 3.28 *dd* (J = 11 and 4 Hz); J (Hz): 11,12 = 9; 11′,12 = 8;11,12′ = 5; 11′,12′ = 8; 12,12′ = 13; 14,14′ = 14; compounds **15b**/**16b**: 5,6 = 9.5; 6,7 ~ 2; compound **19b**: 5,6 = 12; 5,6′ = 5; compound **20b**: 19,19′ = 11; compounds **22b**–**25b**: 18,18′ = 10.5; OiVal: 3′,4′ = 7; OMeBu: 2′,3′ = 2′,5′ = 3′,4′ = 7; $3'_1,3'_2$ = 14; OiBu: 2′,3′ = 7.



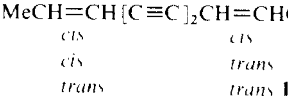
$\underset{\substack{trans\\cis}}{MeCH{=}CH}[C{\equiv}C]_2\underset{\substack{trans\\trans}}{CH{=}CHCH_2OR}$

1 R = Ac **3** R = Sen **5** R = H
2 R = Ac **4** R = Sen **6** R = H



$EtCH_2[C{\equiv}C]_2\underset{trans}{CH{=}CHCH_2O}$ Sen

7



$\underset{\substack{cis\\cis\\trans}}{MeCH{=}CH}[C{\equiv}C]_2\underset{\substack{cis\\trans\\trans}}{CH{=}CHCO_2Me}$ **8** **9** **10**

contained **28b**. The ^1H NMR spectra, however, clearly showed that we were dealing with esters of grindelic acid where an ester function was introduced at C-17, its nature followed from the typical ^1H NMR signals. In all cases the signal of the olefinic methyl was replaced by two doublets around δ 4.5, typical for a CH_2 group of primary allylic esters. The ^1H NMR spectrum of **31b** (Table 2) as well as its mass spectrum showed that this compound had an additional carbomethoxy group. The IR data as well as the ^1H NMR data showed that this ester group was placed equatorially at C-4. Compound **32b** was an oxidation product of **12b**. The ^1H NMR data (Table 2) indicated that again C-18 was oxygenated bearing an *O*-acetate group. Compound **33b** was an isomer of **14b** as was deduced from the corresponding ^1H NMR data (Table 2). The α-orientation of the 7-OH group followed from the hydrogen bond with the ether oxygen (IR: 3500 cm^{-1}). Consequently, the OH-proton signal was a clear doublet. Decoupling allowed the assignments of most signals. Compounds **11b**–**32b** all showed characteristic fragmentations in the mass spectrum. The prominent peak is always the result of a retro-Diels–Alder fragmentation, which may be followed by elimination of oxygen functions. Compounds **34b** and **35b** were also oxidation products of **11b**. The mass spectrum of **34b** indicated the presence of a bisnorditerpene and the ^1H NMR data (Table 2) showed that the olefinic part was missing. While many signals still were similar to those of **11b** new double doublets at δ 2.57 and 2.36, which were coupled with a double doublet at 2.13 indicated the presence of a δ-lactone. As no further downfield signals were visible the only possible arrangement of the oxygens was that shown in **34b**. Though the stereochemistry at C-9 could not be determined, the proposed one was most likely from biogenetic considerations. We have named compound **34a** grindelistrictic acid.

Compound **35b** showed in the ^1H NMR spectrum (Table 2) the presence of a $MeCOCH_2CH(OR)$ group. As the signal of the proton at the carbon bearing the ether oxygen was coupled with only one other proton and as the remaining signals again were close to those of **11b** the structure and stereochemistry shown for **35b** was most

Table 2. ^1H NMR spectral data of compounds **26b**–**35b** ($CDCl_3$, 400 MHz, TMS as internal standard).

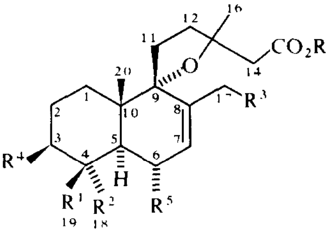
	26b	**27b**	**28b**	**29b**	**30b**	**31b**	**32b**	**33b***	**34b†**	**35b‡**
H-6	1.85 *m*	1.9 *m*	1.9 *m*	1.89 *m*		1.9 *m*	—	1.9 *ddd*	2.57 *dd* 2.36 *dd*	4.3 *ddd*
H-7	5.93 *br s*	5.93 *br s*	5.92 *br s*	5.12 *br s*		5.43 *br s*	5.68 *br s*	4.26 *ddd*	—	2.75 *dd* 2.67 *dd*
H-11	1.85 *m*	1.9 *m*	1.9 *m*	1.89 *m*		2.07 *ddd* 1.9 *m*	2.15 *m* 2.0 *m*		2.06 *m* 1.88 *m*	
H-12	2.1 *m*	2.1 *m*	2.1 *m*	2.10 *m*		2.20 *ddd*	2.3 *m*	2.2–2.0 *m*	2.36 *ddd*	2.2–1.85 *m*
H-12′						1.90 *m*	2.0 *m*		1.88 *m*	
H-14	2.71 *d*	2.72 *d*	2.71 *d*	2.70 *d*		2.75 *d*	2.69 *d*	2.63 *d*	2.72 *s*	2.70 *d*
H-14′	2.65 *br d*	2.65 *br d*	2.63 *br d*	2.60 *br d*		2.65 *br d*	2.55 *br d*	2.59 *br d*		2.65 *br d*
H-16	1.33 *s*	1.35 *s*	1.34 *s*	1.34 *s*		1.33 *s*	1.40 *s*	1.31 *s*	1.30 *s*	1.20 *s*
H-17	4.61 *br d*	4.63 *br d*	4.63 *br s*	4.62 *br d*		1.75 *br s*	1.98 *d*	5.09 *br s*	—	2.22 *s*
H-17′	4.53 *br d*	4.56 *br d*	4.56 *br d*	4.50 *br d*				4.89 *br s*	—	
H-18	0.87 *s*	0.90 *s*	0.89 *s*	0.88 *s*		—	4.30 *d*	0.91 *s*	1.02 *s*	0.99 *s*
H-18′							4.10 *d*			
H-19	0.85 *s*	0.85 *s*	0.86 *s*	0.86 *s*		1.22 *s*	0.97 *s*	0.82 *s*	0.88 *s*	0.98 *s*
H-20	0.77 *s*	0.80 *s*	0.79 *s*	0.79 *s*		0.82 *s*	0.86 *s*	0.74 *s*	0.86 *s*	0.92 *s*
OCOR	2.06 *s*	2.35 *q* 1.14 *t*	2.20 *br d* 2.13 *m* 0.94 *d*	2.55 *tq* 1.68 *ddq* 1.45 *ddq* 0.92 *t* 1.13 *d*	2.36 *qq* 1.16 *d* 1.15 *d*	—	2.03 *s*	—	—	—
OMe	3.62 *s*	3.65 *s*	3.64 *s*	3.64 *s*		3.66 *s* 3.63 *s*	3.65	3.66 *s*	3.65 *s*	3.67 *s*

*OH 4.51 *d*.

†H-5 2.13 *dd*.

‡H-5 1.78 *d*.

J (Hz): 12,12′ = 14,14′ = 14; compounds **26b**–**30b**: 17,17′ = 13.5; compound **32b**: 7,17 = 1.5; 18,18′ = 10.5; compound **33b**: 5,6 = 12; 6,7 = 2.5; 7, OH = 10; compound **34b**: 5,6 = 6.5; 5,6′ = 12.5; 6,6′ = 18.5; compound **35b**: 5,6 = 10; 6,7 = 10; 6,7′ = 2.5.



	11a/b*	**12a/b**	**13a/b**	**14a/b**	**15a/b**	**16a/b**	**17a/b**	**18a/b**	**19a/b**
R^1	Me	Me	Me	Me	Me	Me	Me	Me	Me
R^2	Me	Me	CH_2OH	Me	Me	Me	Me	OH	OCHO
R^3	H	H	H	OH	H	H	H	H	H
R^4	H	H	H	H	H	H	OH	H	H
R^5	H	=O	H	H	OH	OCHO	H	H	H

	20a/b	**21a/b**	**22a/b**	**23a/b**	**24a/b**	**25a/b**
R^1	CH_2OH	Me	Me	Me	Me	Me
R^2	Me	CHO	CH_2OAc	CH_2OiVal	CH_2OMeBu	CH_2OiBu
R^3	H	H	H	H	H	H
R^4	H	H	H	H	H	H
R^5	H	H	H	H	H	H

	26a/b	**27a/b**	**28a/b**	**29a/b**	**30a/b**	**31a/b**
R^1	Me	Me	Me	Me	Me	Me
R^2	Me	Me	Me	Me	Me	CO_2R
R^3	OAc	OProp	OiVal	OMeBu	OiBu	H
R^4	H	H	H	H	H	H
R^5	H	H	H	H	H	H

32a/b R^1 = Me, R^2 = CH_2OAc, R^3 = H, R^4 = H, R^5 = 0

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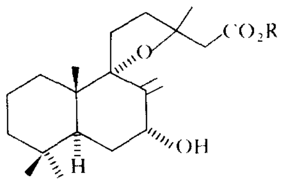
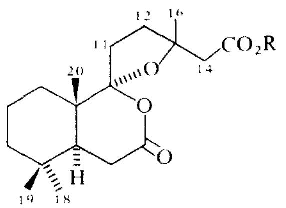
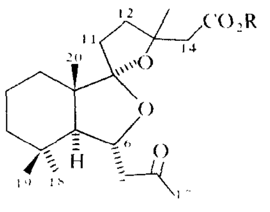
*(a) R = H: (b) R = Me.



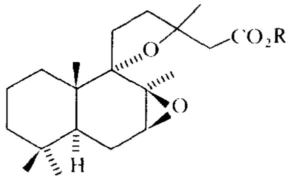
33a R - H
33b R = Me



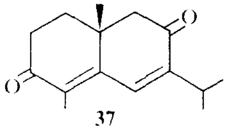
34a R = H
34b R = Me



35a R = H
35b R = Me



36a/b



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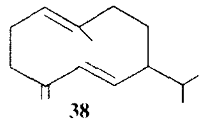

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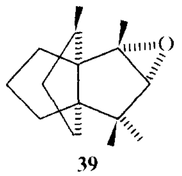

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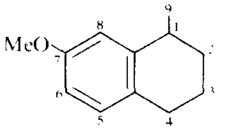

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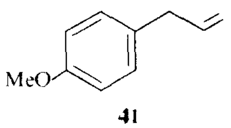

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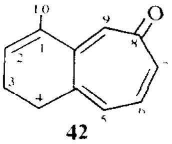

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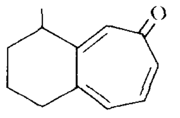

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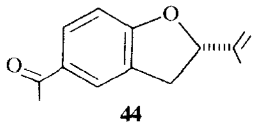

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likely. The 6α-orientation of the acetonyl side-chain was supported by the downfield shift of the H-5 signal. Also, the mass spectrum supported the proposed structure. The loss of an acetone unit from M^+ and $M - {}^{\cdot}CH_2CO_2Me$ is particularly noteworthy. **35a** We have named compound **35a** strictanonic acid.

The aerial parts of *Grindelia paludosa* also afforded grindelic acid (**11a**) and several derivatives (**12a**, **13a**, **15a**, **18a**, **20a**, **22a** and **33a**) and furthermore germacrene D, bornyl and chrysanthemyl acetate, esdragol (**41**), the tetralin derivative **40** and the epoxide **39**. The structure of **40** followed from the molecular formula and the ^1H NMR spectral data. Compound **40** has been prepared previously by cyclization of the corresponding ester [11]. Compound **39** was identical with the epoxide obtained from modhephene. The roots afforded the acetylenic compounds **2**, **5**, **6** and **8**–**10**, the diketone **37** [12], the acetophenone derivative **44** and the two tropone derivatives **42** and **43**, whose ^1H NMR spectral data (Table 3) clearly allowed the assignment of the structures. We have named compound **42** palutropone. While the roots of *Grindelia camporum* afforded **11a**, the aerial parts gave germacrene D, β-farnesene, α-humulene and bisabolene as well as grindelic acid (**11a**) and the derivatives **12a**, **13a**, **15a**, **16a**, **20a**, **22a**, **33a** and **36a**. Again, all diterpenes were isolated as their methyl esters.

The results obtained show again that C_{10}-acetylenes, especially those of types **1**–**6**, may be characteristic for the genus. However, grindelic acid and its derivatives are also typical, though these diterpenes have been isolated from a *Chrysothamnus* [6] and a *Haplopappus* [13] species.

EXPERIMENTAL

The air-dried plant material, collected in California, was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated first by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the IR and ^1H NMR spectra with those of authentic material.

Grindelia stricta DC (voucher RMK 8413, deposited in the U.S. National Herbarium). The aerial parts (320 g) afforded 20 mg **1**, 10 mg **2**, 12 mg **3**, 5 mg **4**, 20 mg **7** and with Et_2O–MeOH (20:1) a complex mixture of acids, which were transformed to the methyl esters by addition of CH_2N_2. TLC using first Et_2O petrol (1:1) and then for the less polar fractions CH_2Cl_2 C_6H_6 (1:1) and CH_2Cl_2–C_6H_6–Et_2O (5:5:1 and 2:2:1) for the more polar ones finally gave 30 mg **11b**, 10 mg **12b**, 10 mg **13b**, 50 mg **14b**, 50 mg **15b**, 40 mg **16b**, 15 mg **17b**, 20 mg **18b**, 10 mg **19b**, 10 mg **20b** (separated from **33b** by HPLC, reversed phase; MeOH–H_2O, 3:2) 30 mg **21b**, 5 mg **22b**, 10 mg **23b**, 40 mg **24b**, 10 mg **25b**, 5 mg **26b**, 20 mg **27b**, 15 mg **28b**, 10 mg **29b**, 20 mg **30b**, 50 mg **31b**, 10 mg **32b**, 10 mg **33b**, 20 mg **34b**, 20 mg **35b**, and 50 mg **36b**.

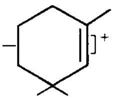
Table 3. ^{1}H NMR spectral data of compounds **42** and **43** ($CDCl_3$, 400 MHz, TMS as internal standard)

	42	**43**
H-1	—	2.75 *m*
H-2	6.29 *dd*	1.9 *m*
H-3	2.3 *m*	2.75 *m*
H-4	2.63 *br t*	2.60 *m*
H-5	6.81 *dd*	6.84 *br d*
H-6	6.98 *dd*	7.02 *dd*
H-7	6.87 *ddd*	6.94 *br dd*
H-9	7.04 *br d*	7.06 *br d*
H-10	2.03 *dt*	1.28 *d*

J (Hz): compound **42**: 2,3 = 4.5; 2,10 = 3,10 = 1.5; 3,4 = 7; 5,6 = 8.5; 5,7 = 1; 6,7 = 12; 7,9 = 2.5; compound **43**: 1,10 = 7; 5,6 = 8; 6,7 = 12; 7,9 = 2.5.

Grindelia paludosa Greene (voucher RMK 8401, deposited in the U.S. National Herbarium). The roots (80 g) afforded 4 mg **2**, 6 mg **5**, 4 mg **6**, 6 mg **8**–**10** (*ca* 2:1:2), 6 mg **37**, 2 mg **40** (Et_2O–petrol, 1:20), 3 mg **42** (Et_2O–petrol, 1:10), 1 mg **43** (Et_2O–petrol, 1:10) and 8 mg **44**, while the aerial parts (900 g) gave 5 mg bornyl acetate, 7 mg chrysanthemyl acetate, 2.5 g **11a**, 100 mg **12a**, 20 mg **13a**, 6 mg **15a**, 5 mg **18a**, 7 mg **20a**, 4 mg **22a**, 10 mg **33a** (all acids isolated as their methyl esters), 4 mg **38**, 1 mg **39** (Et_2O–petrol, 1:20), 4 mg **40** and 3 mg **41**.

Grindelia camporum Greene (voucher RMK 8427, deposited in the U.S. National Herbarium). The roots (250 g) afforded 120 mg **11a**, while the aerial parts (650 g) gave 70 mg germacrene D, 40 mg β-farnesene, 70 mg α-humulene, 80 mg bisabolene and after esterification of the polar fractions 2.7 g **11b**, 30 mg **12b**, 50 mg **13b**, 70 mg **15b**, 60 mg **16b**, 20 mg **20b**, 60 mg **22b**, 30 mg **33b** and 70 mg **36b**.

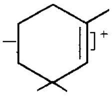
Methyl-6α-hydroxy-grindeloate (**15b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO_2R); MS *m/z* (rel. int.): 350.246 $[M]^+$ (14) ($C_{21}H_{34}O_4$), 332 $[M - H_2O]^+$ (6), 317 $[332 - Me]^+$ (2), 226 [M –  $]^+$ (100) (RDA), 208 $[226 - H_2O]^+$ (51), 197 $[226 - CHO]^+$ (60), 135 $[208 - CH_2CO_2Me]^+$ (62).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-28.2 \quad -28.7 \quad -34.2 \quad -63.6} \quad (c = 0.57, \text{CHCl}_3).$$

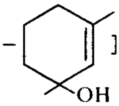
Methyl-6α-formyloxy-grindeloate (**16b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 348.230 $[M - CH_2O]^+$ (4) ($C_{21}H_{32}O_4$), 333.243 $[M - OCHO]^+$ (4) ($C_{21}H_{33}O_3$), 69 $[C_5H_9]^+$ (100); CIMS (*iso*-butane): 379 $[M + 1]^+$ (19), 349 $[379 - CH_2O]^+$ (67), 333 $[379 - HCO_2H]^+$ (24), 145 $[C_7H_{13}O_3]^+$ (100), 127 $[145 - H_2O]^+$ (39).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-27.5 \quad -27.5 \quad -32.5 \quad -52.5} \quad (c = 0.4, \text{CHCl}_3).$$

To 4 mg **16b** in 1 ml MeOH 50 mg K_2CO_3 in 0.2 ml H_2O was added. Usual work-up after 1 hr afforded **15b**.

Methyl-3β-hydroxy-grindeloate (**17b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640 (OH), 1740 (CO_2R); MS *m/z* (rel. int.): 350.246 $[M^+]$ (1.6) ($C_{21}H_{34}O_4$), 332 $[M - H_2O]^+$ (2), 301 $[332 - OMe]^+$ (2), 210 [M –  $]^+$ (100) (RDA).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-23.0 \quad -26.9 \quad -34.6 \quad -61.5} \quad (c = 0.13, \text{CHCl}_3).$$

Methyl-4α-hydroxy-18-norgrindeloate (**18b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1740 (CO_2R); MS *m/z* (rel. int.): 336.229 $[M]^+$ (0.5) ($C_{20}H_{32}O_4$), 318 $[M - H_2O]^+$ (1), 210 [M –  $]^+$ (100) (RDA).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-32.5 \quad -35.0 \quad -40.5 \quad -70.5} \quad (c = 0.2, \text{CHCl}_3).$$

Methyl-4α-formyloxy-18-norgrindeloate (**19b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (CO_2R); MS *m/z* (rel. int.): 334 $[M - CH_2O]^+$ (5) ($C_{20}H_{30}O_4$), 210 [RDA] (100); CIMS (*iso*-butane): *m/z* 365 $[M + 1]^+$ (7), 335 $[365 - CH_2O]^+$ (100), 319 $[365 - HCO_2H]^+$ (33).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-35 \quad -38 \quad -45 \quad -75} \quad (c = 0.1, \text{CHCl}_3).$$

Methyl-19-hydroxy-grindeloate (**20b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640 (OH), 1745 (CO_2R); MS *m/z* (rel. int.): 350.246 $[M]^+$ (1) ($C_{21}H_{34}O_4$), 319 $[M - CH_2OH]^+$ (0.6), 210 [RDA] (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-103.5 \quad -107.8 \quad -123.8 \quad -214.5} \quad (c = 0.5, \text{CHCl}_3).$$

Methyl-18-oxo-grindeloate (**21b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2710, 1750 (CHO), 1735 (CO_2R); MS *m/z* (rel. int.): 348.230 $[M]^+$ (0.3) ($C_{21}H_{32}O_4$), 210 [RDA] (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-30.9 \quad -32.9 \quad -38.8 \quad -65.9} \quad (c = 0.34, \text{CHCl}_3).$$

Methyl-18-acetoxygrindeloate (**22b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1235 (OAc), 1740 (CO_2R); MS *m/z* (rel. int.): 392.256 $[M]^+$ (1) ($C_{23}H_{36}O_5$), 332 $[M - AcOH]^+$ (3), 210 [RDA] (100).

Methyl-18-isovaleryloxygrindeloate (**23b**). Colourless oil, not free from **25b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 434.303 $[M]^+$ (0.5) ($C_{26}H_{42}O_5$), 210 [RDA] (100).

Methyl-18-[2-methylbutyryloxy]-grindeloate (**24b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R); MS *m/z* (rel. int.): 434.303 $[M]^+$ (1) ($C_{26}H_{42}O_5$), 332 $[M - RCO_2H]^+$ (1.5), 317 $[332 - Me]^+$ (1), 210 [RDA] (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-15.0 \quad -16.0 \quad -19.5 \quad -38.5} \quad (c = 0.4, \text{CHCl}_3).$$

Methyl-18-isobutyryloxy-grindeloate (**25b**). Colourless oil, not free from **23b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 420.288 $[M]^+$ (0.7) ($C_{25}H_{40}O_5$), 210 [RDA] (100).

Methyl-17-acetoxy-grindeloate (**26b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R); MS *m/z* (rel. int.): 392.256 $[M]^+$ (2) ($C_{23}H_{36}O_5$), 268 [RDA] (100), 208 $[268 - AcOH]^+$ (74), 176 $[208 - MeOH]^+$ (95).

Methyl-17-propionyloxy-grindeloate (**27b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, (CO_2R); MS *m/z* (rel. int.): 406.272 $[M]^+$ (0.6) ($C_{24}H_{38}O_5$), 282 [RDA] (38), 208 $[282 - RCO_2H]^+$ (48), 134 $[208 - MeCO_2Me]^+$ (53), 57 $[Et_2CO]^+$ (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-21.5 \quad -26.5 \quad -34.0 \quad -58.5} \quad (c = 0.2, \text{CHCl}_3).$$

Methyl-17-*isovaleryloxy-grindeloate* (**28b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 434.303 $[M]^+$ (0.5) ($C_{26}H_{42}O_5$), 310 [RDA] (48), 208 $[310 - RCO_2H]^+$ (83), 176 $[208 - MeOH]^+$ (100), 134 $[208 - MeCO_2Me]^+$ (82).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-18.4 \quad -19.1 \quad -22.0 \quad -38.3} \quad (c = 1.35,\ \text{CHCl}_3).$$

Methyl-17-[*2-methylbutyryloxy*]-*grindeloate* (**29b**). Colourless oil, not free from **28b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 434.303 $[M]^+$ (0.7) ($C_{26}H_{42}O_5$), 310 [RDA] (44), 208 $[310 - RCO_2H]^+$ (87), 176 $[208 - MeOH]^+$ (100), 134 $[208 - MeCO_2Me]^+$ (72), 85 $[C_4H_9CO]^+$ (20).

Methyl-17-*isobutyryloxy-grindeloate* (**30b**). Colourless oil, not free from **29b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R); MS *m/z* (rel. int.): 420.288 $[M]^+$ (0.5) ($C_{25}H_{40}O_5$), 296 [RDA] (50), 208 $[296 - RCO_2H]^+$ (90), 176 $[208 - MeOH]^+$ (100).

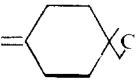
Dimethyl-18-*oic grindeloate* (**31b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1747, 1740 (CO_2R); MS *m/z* (rel. int.): 378.241 $[M]^+$ (0.5), $C_{22}H_{34}O_5$, 319 $[M - CO_2Me]^+$ (0.5), 305 $[M - CH_2CO_2Me]^+$ (1), 210 [RDA] (100), 136 $[210 - MeCO_2Me]^+$ (11).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-15.3 \quad -16.1 \quad -19.0 \quad -34.6} \quad (c = 0.52,\ \text{CHCl}_3).$$

Methyl-18-*acetoxy*-6-*oxo-grindeloate* (**32b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R), 1680 (C=CCO); MS *m/z* (rel. int.): 406.236 $[M]^+$ (2) ($C_{23}H_{34}O_6$), 224 [RDA] (100).

Methyl-7α-*hydroxy*-7,8-*dihydro*-8(17)-*dehydrogrindeloate* (**33b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500 (OH), 1745 (CO_2R); MS *m/z* (rel. int.): 350.246 $[M]^+$ (10) ($C_{21}H_{34}O_4$), 332 $[M - H_2O]^+$ (12), 236 (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-9.5 \quad -9.7 \quad -11.1 \quad -15.6} \quad (c = 1.0,\ \text{CHCl}_3).$$

Methylgrindelistrictoate (**34b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1740 CO; MS *m/z* (rel. int.): 294.220 $[M - CO_2]^+$ (8) ($C_{18}H_{30}O_3$), 265 $[M - CH_2CO_2Me]^+$ (8), 173 [HO=  $CO_2Me]^+$ (62), 109 $[C_8H_{13}]^+$ (100); CI (*iso*-butane): 339 $[M + 1]^+$ (100).

Methyl strictanonoate (**35b**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (CO_2R), 1715 (C=O); MS *m/z* (rel. int.): 366.241 $[M]^+$ (17) ($C_{21}H_{34}O_5$), 335 $[M - OMe]^+$ (7), 308 $[M - Me_2CO]^+$ (37), 293 $[308 - Me]^+$ (25), 280 $[308 - CO]^+$ (12), 69 $[C_5H_9]^+$ (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-7.6 \quad -7.6 \quad -9.5 \quad -14.2} \quad (c = 0.21,\ \text{CHCl}_3).$$

Modhephenepoxide (**39**). Colourless oil, MS *m/z* (rel. int.): 220.183 $[M]^+$ (7) ($C_{15}H_{24}O$), 215 $[M - Me]^+$ (14), 177 $[215 - CO]^+$ (18), 55 $[C_4H_7]^+$ (100). Modhephene (4 mg) in 1 ml CH_2Cl_2 was stirred with 10 mg $NaHCO_3$ and 4 mg *m*-chloroperbenzoic acid for 30 min. TLC (Et_2O–petrol, 1:15) afforded 2 mg **39**, identical with the natural compound (^1H NMR, TLC).

1-*Methyl*-7-*methoxytetralin* (**40**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2880, 1620, 1510, 1390, 1140; MS *m/z* (rel. int.): 176.120 $[M]^+$ (100) ($C_{12}H_{16}O$), 161 $[M - Me]^+$ (95). ^1H NMR ($CDCl_3$, 400 MHz): 2.88 (*br ddq*, H-1), 1.88 *m*, 1.50 (*m*, H-2), 1.85 *m*, 1.69 (*m*, H-3), 2.69 (*m*, H-4), 6.99 (*br d*, H-5), 6.67 (*dd*, H-6), 6.71 (*d*, H-8), 1.27 (*d*, H-9), 3.77 (*s*, OMe), [*J* (Hz): 1,2 = 1,9 = 7; 5,6 = 8.5; 6,8 = 2.5].

Palutropone (**42**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1640, 1580, 910; MS *m/z* (rel. int.): 172.089 $[M]^+$ (8) ($C_{12}H_{12}O$), 144.094 $[M - CO]^+$ (38) ($C_{11}H_{12}$), 129 $[144 - Me]^+$ (100).

Dihydropalutropone (**43**). Colourless oil, MS *m/z* (rel. int.): 174.104 $[M]^+$ (17), ($C_{12}H_{14}O$), 146 $[M - CO]^+$ (16), 131 $[146 - Me]^+$ (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+18 \quad +19 \quad +20 \quad +34} \quad (c = 0.1,\ \text{CHCl}_3).$$

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