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NEUE GUAJANOLIDE AUS *EUPATORIUM ROTUNDIFOLIUM**

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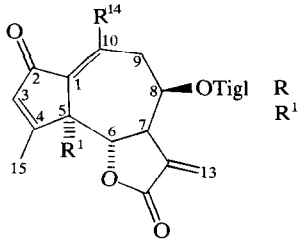
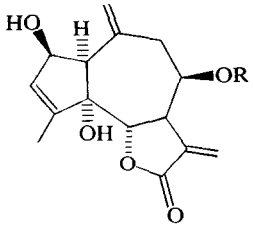
Key Word Index—*Eupatorium rotundifolium*; Compositae; sesquiterpene lactones; new guaianolides.

Die Gattung *Eupatorium* ist bereits recht gut untersucht [1, 2]. Wir haben jetzt erneut *E. rotundifolium* L. ssp. *ovatum* (Bigel.) Montg. et Fairbr. untersucht. Neben bereits früher isolierten Verbindungen [3, 4] haben wir zwei Guajanolide isoliert, die offenbar noch nicht bekannt sind. Die ^{1}H-NMR-Daten zeigen, dass es sich um **1b** und **2** handelt. **1b** ist das 5α-Hydroxy-Derivat von Eupasessifolid B (**1a**) [1]. Entsprechend erhält man mit Mangandioxid den Aldehyd **1c**. Alle ^{1}H-NMR-Daten (s. Tabelle 1) lassen sich eindeutig zuordnen. Sie entsprechen weitgehend denen von Eupasessifolid B (**1a**). Durch die 5α-OH-Gruppe wird jedoch das Signal für 7α-H deutlich zu tieferen Feldern verschoben, was bei einer β-ständigen OH-Gruppe nicht zu erwarten wäre. Auch das Spektrum von **1c** entspricht wiederum weitgehend dem des aus **1a** erhaltenen Aldehyds. Doppelresonanz-Experimente stützen die Zuordnung. Bei dem zweiten Lacton sind die ^{1}H-NMR-Daten weitgehend identisch mit denen des bereits bekannten Tiglinsäureesters **2a** [3], so dass die Struktur gesichert sein dürfte.



	1a [1]	1b	1c
R	CH_2OH	CH_2OH	CHO
R^1	H	OH	OH



2 R = Ang
2a R = Tigl [3]

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Tabelle 1. ^{1}H-NMR-Daten von **1a, 1b, 1c** und **2** (270 MHz, $CDCl_3$, TMS als innerer Standard)

	1a		1b		1c		2	
1-H		—		—		—	*d*	2,98
2-H		—		—		—	*d(br)*	4,85
3-H	*dq*	6,29	*q*	6,24	*q*	6,37	*dq*	5,80
5-H	*d(br)*	3,60		—		—		—
6-H	*dd*	4,14	*d*	4,30	*d*	4,43	*d*	4,80
7-H	*d(br)*	3,17	*d(br)*	4,00	*d(br)*	4,05	*dddd*	3,73
8-H	*d(br)*	5,78	*d(br)*	5,71	*d(br)*	5,86	*ddd*	5,55
9-H	*dd*	3,17	*dd*	2,96	*dd*	3,66	*dd*	2,94
9′-H	*d(br)*	2,71	*d(br)*	3,12	*d(br)*	2,64	*dd*	2,84
13-H	*d*	6,26	*d*	6,22	*d*	6,25	*d*	6,34
13′-H	*d*	5,58	*d*	5,52	*d*	5,61	*d*	5,59
14-H	*dd*	4,54	*d(br)*	4,61	*s*	10,92	*s(br)*	5,16
14′-H	*dd*	4,42	*d(br)*	4,19		—	*s(br)*	5,13
15-H	*s(br)*	2,41	*d*	2,37	*d*	2,43	*s(br)*	1,79
OCOR	*qq*	6,73	*qq*	6,68	*qq*	6,60	*qq*	6,06
	d(br)	1,77	*d(br)*	1,75	*d(br)*	1,72	*d(br)*	1,93
	s(br)	1,75	*s(br)*	1,71	*s(br)*	1,68	*s(br)*	1,95

J (Hz): Bei **2**: 1, 2 = 6,5; 2, 3 = 3, 15 ~ 1,5; 6, 7 = 9; 7, 8 = 3,5; 7, 13 = 3,5; 7, 13′ = 3; 8, 9 = 8, 9′ = 7; 9, 9′ = 14; bei **1a, 1b**: 3, 15 = 1, 3; 6, 7 = 10; 7, 13 = 3,5; 7, 13′ = 3; 8, 9 = 6; 9, 9′ = 15; 14, 14′ = 17; OCOR: 3′, 4′ = 7; 3′, 5′ = 1,5.

EXPERIMENTELLES

IR Beckmann IR 9, $CHCl_3$; ^{1}H-NMR: Bruker WH 270; MS: Varian MAT 711. Die zerkleinerten Pflanzenteile (150 g oberirdische Teile, gesammelt in West Virginia, Herbar im U.S. National Herbarium) extrahierte man bei RT mit Ether–Petrol, 1:2 und trennte den erhaltenen Extrakt durch SC und weiter durch mehrfache DC (Si gel GF 254). Neben bereits früher isolierten Substanzen erhielt man 5 mg **1b** (Ether, 4×entwickelt) und 5 mg **2** (Ether–CH_2Cl_2, 4:1).

5α-Hydroxy-eupasessifolid B (**1b**). Zähes, farbloses Öl, IR cm^{-1}: 3600 (OH), 1780 (γ-Lacton), 1720 (C=CCO_2R). MS: M^+ *m/e* 374.137 (4%) ($C_{20}H_{22}O_7$); $-RCO_2H$ 274 (15); $C_4H_7CO^+$ 83 (100). 5 mg **14** in 2 ml Ether rührte man 1 hr mit 50 mg MnO_2. Nach DC erhielt man 3 mg **14a**, zähes, farbloses Öl, ^{1}H-NMR s. Tabelle 1.

5α-Hydroxy-8β-angeloyloxy-preeupatundin (**2**). Zähes, farbloses Öl, IR cm^{-1}: 3600 (OH), 1770 (γ-Lacton), 1720 (C=CCO_2R). MS: M^+ *m/e* 360.157 (4%) ($C_{20}H_{24}O_6$); $-H_2O$ 342 (5); $-RCO_2H$ 260 (10); 260 $-H_2O$ 242 (23); $C_4H_7CO^+$ 83 (100).

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EUCANNABINOLIDE AND OTHER CONSTITUENTS OF *SCHKUHRIA VIRGATA**

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Key Word Index—*Schkuhria virgata*; Bahiinae, Heliantheae; Compositae; heliangolides; eucannabinolide; sesquiterpene lactones; pectolinarigenin; antileukemic activity.

Abstract—Isolation of eucannabinolide, its 3-isovaleroyl analog and pectolinarigenin from *Schkuhria virgata* (La Llave *et* Lex.) DC. is reported. The identity of eucannabinolide, which exhibits *in vivo* antileukemic activity, with 'hiyodorilactone A', '20-hydroxychromolaenide' and 'schkuhrin I' is discussed.

Schkuhria, an American genus of about 15 taxa [1], has recently been moved, together with its relatives in subtribe Bahiinae, from tribe Helenieae (Compositae) to Heliantheae [2]. We now report isolation of eucannabinolide (**1a**), its 3-isovaleroyl analog **1b** and pectolinarigenin from *Schkuhria virgata* (La Llave *et* Lex) DC.† and attempt to clear up some confusion concerning **1a** which exists in the literature. Eucannabinolide exhibited significant activity against lymphoxytic leukemia P 388 in the mouse.‡

The major lactone constituent of *S. virgata* was a gum, $C_{20}H_{28}O_8$ (high resolution MS), which on the basis of its mass, ^1H and ^{13}C NMR spectrum (Tables 1 and 2) was clearly the des-sarracinoyl derivative **1a** of provincialin (**1b**) [14]. In particular the chemical shift of H-3′, similar to that of tiglic acid, indicated the *E*-configuration for the five carbon-ester side chain and the chemical shifts of H-3′, H-4′, and H-5′ corresponded closely to those of appropriate signals in the ^1H NMR spectrum of eupaformosanin (**2**) whose structure has been established by X-ray crystallography [5].§

A substance to which structure **1a**, has been assigned has been isolated from several sources recently‖ and named variously 20-hydroxychromolaenide [7], hiyodori lactone A [8] and schkuhrin I [9]. Its spectral properties are indistinguishable from those of our material. Takahashi *et al.* [8] recognized a possible relationship of their 'hiyodorilactone A' to eucannabinolide, a gummy substance which was isolated previously [10] from *E. cannabinum* and was assigned [4, 11] structure **1a** on the basis of NMR data, but with side-chain stereochemistry unspecified in the printed formulas [9, 10]. Because the 4.00 ppm chemical shift reported [10] for H-4′ of eucannabinolide

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† Our collection came from Honduras and was labelled *S. guatemalensis* Standl. *et* Steyermark. For synonymy of the only *Schkuhria* species occurring in central America see [3].

‡ Tests were carried out under the auspices of the Division of Cancer Treatment of the National Cancer Institute.

§ Liatripunctin [6] which contains the same five carbon-ester side chain was incorrectly drawn as the *Z*-isomer in ref. [5].

‖ *Isocarpha oppositifolia* (L) R. Br. [7], *Eupatorium sachalinense* Mak. [8] and an African collection of *Schkuhria pinnata* (Lam.) Kuntze [9].