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TRICHOCLIN, A NEW FUROCOUMARIN FROM *TRICHOCLINE INCANA*

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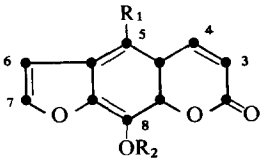
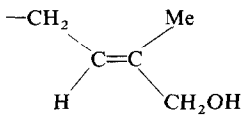
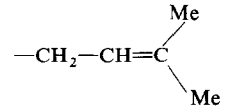
Key Word Index—*Trichocline incana*; Compositae; furocoumarin; trichoclin; structural determination.

Abstract—The structure for trichoclin, (*E*)-8-(3-methyl-4-hydroxy-2-butenyloxy)-psoralen, a new furocoumarin isolated from *Trichocline incana*, has been established. Phellopterin and isopimpinellin were also obtained. The new side chain of trichoclin was confirmed by synthesis.

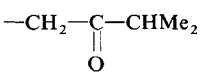
In the course of an investigation of *Trichocline incana* we isolated a new furocoumarin, trichoclin (**1**), in addition to two known members of this class of compounds, phellopterin [1] (**2**) (0.23%), and isopimpinellin [2] (**3**) (0.1%). The isolation and structure elucidation of trichoclin are reported in this communication.

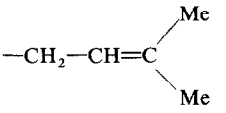


(**1**) R1 = H R2 = 

(**2**) R1 = OMe R2 = 

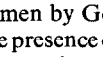
(**3**) R1 = Me R2 = —Me

(**4**) R1 = H R2 = 

(**5**) R1 = H R2 = 

Trichoclin (**1**), $C_{16}H_{14}O_5$, is a new furocoumarin isolated in 0.88% yield from leaf and stem material of *T. incana*. Its UV spectrum [λ_{max}^{MeOH} 219, 248, 262 and 299 nm (log ε:4.39, 4.35, 4.12 and 4.05 respectively)] is typical of a linear furocoumarin and similar to pabularinone (**4**) [3] and imperatorin (**5**) [2] (8-alkoxy analogs of psoralen) while the IR spectrum revealed OH (3400 cm^{-1}), coumarin carbonyl (1725, 1700) and benzofuran (1030, 880) groups. The PMR (60 MHz, $CDCl_3$) showed the coumarin doublets at δ6.33 and 7.79 (J = 9.5 Hz each), the α-furan proton at δ7.68 (1H, *d*, J = 2.5 Hz), the β-furan proton at δ6.8 (1H, *d*, J = 2.5 Hz) with a single aromatic proton (5-position) at δ7.35 (1H, *s*). The one-proton triplet at δ5.8 (J = 7.5 Hz) has been assigned to the olefinic hydrogen and the two-proton doublet at δ5.05 (J = 7.5 Hz) to the allylic methylene group adjacent to the phenoxy group. The 3 protons at δ1.73 (*brs*) have been attributed to the olefinic Me group and the two protons at δ4.03 (*brs*) to the allylic hydroxymethylene group; the signal at 2.45 (1H, *brs*) disappears in D_2O and can therefore be assigned to the OH proton.

Catalytic hydrogenation (Pd-C/H_2 in MeOH) of **1** afforded tetrahydro-8-hydroxypsoralen (**6**), $C_{11}H_{10}O_4$, and 2-methylbutane which was identified with a synthetic specimen by Gorey GC–MS.

The presence of the primary OH group as () was corroborated from the formation of trichoclin acetate**7**. Signals at δ2.05 (3H, *s*) was assigned to the acetyl group and the acetyloxymethylene protons now appeared downfield at δ4.47 (2H, *brs*).

To ascertain the geometrical configuration of the side chain, the following syntheses were attained. (*E*)-2-Methyl-4-chloro-2-butenal-1 (**10**) [4] was derived from 2-hydroxy-2-methyl-3-butenal dimethylacetal (**9**) and (*E*)-2-methyl-4-chloro-2-butenyl acetate (**12**) was synthesized from the aldehyde (**10**) via the alcohol (**9**). On the other hand 8-hydroxypsoralen (**8**) [5], was derived from trichoclin by acid hydrolysis [6]. To the 8-hydroxypsoralen Na salt (prepared from (**8**) and NaH) in dry DMF was added the allyl chloride (**12**) and an acetate was obtained, which was identical in all respects (IR, PMR, mmp and TLC) to authentic trichoclin acetate (**8**) which was derived from trichoclin by acetylation.

From the available data, the structure for trichoclin was determined as (*E*)-8-(3-methyl-4-hydroxy-2-buteny-loxy) psoralen, (**1**).

EXPERIMENTAL

Isolation. Dried and ground leaf and stem material (450 g) of *T. incana* (collected on 14 January 1975 in Salta Province,

Argentina) was extracted with $CHCl_3$ and worked up in the usual way [7]; yield of crude syrup: 18 g. The syrup (16.8 g) was chromatographed on a Si gel column (670 g) which was packed with C_6H_6 and then eluted with 9 fractions (each 150 ml) of C_6H_6–Me_2CO (10:1), and 10–25 fractions of C_6H_6–Me_2CO (5:1), all of which were monitored by TLC (Si gel G). Fractions 4–5 yielded 1.7 g of crude crystals which, on recrystallization from EtOAc, afforded 1.04 g of prisms, mp 100–101°, whose PMR, IR and UV spectra were identical with those of phellopterin (**2**). Fractions 6–8 yielded 0.61 g of crude crystals which, on recrystallization from EtOAc, afforded 452 mg of crystals, mp 145–146°, whose PMR, IR and UV spectra were identical with those of isopimpinellin (**3**). Fractions 14–18 yielded 6.21 g of crude crystals which, on recrystallization from EtOAc (twice), gave 3.96 g mg of pure trichoclin (**1**), mp, 123.5–124°, $[\alpha]_D^{18}$ 0.0 ($CHCl_3$), UV, λ_{max}^{MeOH} nm (log ε): 219 (4.39), 248 (4.35), 262 (4.12) and 299 (4.05), IR (nujol): 3400 (OH), 1725, 1700 (coumarin carbonyl) and 1030, 880 cm^{-1} (benzofuran). MS 70eV, *m/e* (rel. int.): 284 $(M-2)^+$ (0.2), 203 (24), 202 (100), 174 (25), 146 (4), 145 (4), 90 (6), 89 (10) and 63 (6). (Found: C, 67.40; H, 5.11. $C_{16}H_{14}O_5$ requires C, 67.13; H, 4.93%).

Acetylation of (**1**). Under standard conditions (Py–Ac_2O), trichoclin gave an acetate (**7**), mp, 107–108° (from EtOAc). IR, (nujol): 1735 (acetate), 1582, 1235, 1138, 1080, 1060, 1030, 985 and 942 cm^{-1}. PMR ($CDCl_3$): δ7.76 (1H, *d*, *J* = 9.5 Hz for 4-H), 7.65 (1H, *d*, *J* = 2.5 Hz for 7-H), 7.35 (1H, *s*, for 5-H), 6.79 (1H, *d*, *J* = 2.5 Hz for 6-H), 6.33 (1H, *d*, *J* = 9.5 Hz for 3-H), 5.89 (1H, *br t*, *J* = 7.5 Hz for olefinic-H of side chain), 5.04 (2H, *br d*, *J* = 7.5 Hz for allylic methylene), 4.45 (2H, *s*, for allyic acetyloxymethylene group), 2.05 (3H, *s*, for acetate Me) and 1.72 (3H, *br s*, for olefinic Me group) MS 70eV, *m/e* (rel. int): 328 M^+ (0.3), 269 (0.5), 203 (18), 202 (60), 174 (18), 127 (75), 89 (15), 85 (15) and 43 (100).

Tetrahydro-8-hydroxypsoralen (**6**) *and 2-methylbutane from* **1**. A soln of **1** (160 mg) in 15 ml MeOH was hydrogenated at room temp. under atmos. pres. in the presence of 20 mg of activated Pd-C. The reaction was stopped after the uptake of *ca* 4 equivs of H_2 (48.2 ml) After filtration of the catalyst, the filtrate was concd *in vacuo* to yield, after Si gel TLC (C_6H_6–Me_2CO, 4:1) and recrystallisation from EtOAc, 95 mg of pale crystals of tetrahydro-8-hydroxypsoralen (**6**), mp, 135–136°, IR. (nujol): 3380 (OH), 1765 (δ-lactone), 1250, 1145, 1090 and 1000 cm^{-1}. PMR ($CDCl_3$): δ6.55 (1H, *s*, for 5-H), 4.63 (2H, *t*, *J* = 8.5 Hz for 7-H), 3.16 (2H, *t*, *J* = 8.5 Hz for 6-H), 2.82 (4H, *m*, for 3,4-H), MS, *m/e* (rel. int.) 206 M^+ (49), 165 (10), 164 (100), 163 (8), 108 (5), 79 (8) and 77 (7) A small portion of the filtrate (2μl) was analysed by GLC (Ucon-LB-55OX) using a 45 m Gorey column (stainless steel) at 30°. A peak at R_t 5.2 min was identical with 2-methylbutane [8] by GLC-MS.

8-Hydroxypsorlen (**8**) *from* **1**. A soln of 150 mg of **1** in 1% HCl–EtOH (15 ml) was kept for 3 hr at 50°. After evaporation of the solvent the reactant was treated with H_2O–EtOAc. The EtOAc layer was washed with satd. aq. $NaHCO_3$ and the aq. layer was acidified with HCl to pH 1 then extracted with EtOAc. The EtOAc layer was dried and concd to give 81 mg of crude crystals. Recrystallization from 95% EtOH yielded 49 mg of **8**. mp, 247–249°, IR (nujol): 3250 (OH), 1705 (coumarincarbonyl), 1592, 1295, 1150, 1090, 1030 cm^{-1}. PMR (CD_3COCD_3). δ9.40 (1H, *br s*, for 8-OH), 7.97 (1H, *d J* = 9.5 Hz, for 4-H), 7.88 (1H, *d*, *J* = 2.5 Hz for 7-H), 7.4 (1H, *s*, for 5-H), 6.93 (1H, *d*, *J* = 2.5 Hz for 6-H), 6.29 (1H, *d*, *J* = 9.5 Hz for 3-H).

(E)-*2-Methyl-4-chloro-2-butenal-1* (**10**) *from 2-hydroxy-2-Methyl-3-butenal dimethyacetal* (**9**) To a soln of C_6H_6 (15 ml) containing **9** (10 g) $CuCl_2$ (0.34 g) and NaCl (3.43 g) was added dropwise 13.6 g of 35% HCl at 0°. The reaction mixture was then kept at 50° for 5 hr. The mixture was then washed with C_6H_6–H_2O, and the C_6H_6 layer concd and distilled to give **9** 6.41 g as oil (74–76°/16 mmHg), $[n]_D^{18}$ 1.4923. IR (film) 1690 (aldehyde), 1255, 1145, 1003 cm^{-1}. PMR ($CDCl_3$): δ9.37 (1H, *s*, for —CHO), 6.50 (1H, *dt*, *J* = 1.5, 7 Hz, for olefinic-H), 4.28 (2H, *d*, *J* = 7 Hz for $—CH_2Cl$), 1.81 (3H, *d*, *J* = 1.5 Hz, for $—CH_3$).

(E)-*2-Methyl-4-chloro-2-buten-1-ol* (**11**) *from* **10** To **10** (4.3 g) in MeOH (40 ml) was added $NaBH_4$ (2.06 g) at 0° and the mixture then kept for 1 hr under stirring. The reaction mixture was poured into ice-H_2O and extracted with C_6H_6. Distillation gave **11** (3.29 g) (133–142°/16 mmHg), $[n]_D^{20°}$ 1.4953. IR., (film): 3360 (OH), 1460, 1390, 1070, 1030 cm^{-1}. PMR. ($CDCl_3$) δ5.65 (1H, *dt*, *J* = 1.5, 7 Hz, for olefinic-H), 4.08 (2H, *d*, *J* = 7 Hz, for $—C\underline{H}_2Cl$), 4 (2H, *s*, for $—CH_2OH$), 1.71 (3H, *d*, *J* = 1.5 Hz, for $—CH_3$)

(E)-*2-Methyl-4-chloro-2-butenyl acetate* (**12**) *from* **11** Acetylation of **11** (2.5 g) by Py (1.97 g), AcCl (1.95 g) at 0° gave the crude acetate. Purification by Si gel chromatography (C_6H_6) gave the acetate (**12**), 1.88 g, $[n]_D^{20.5}$ 1.4700. IR, (film): 1740 (carbonyl), 1445, 1370, 1230, 1025, 860 cm^{-1}. PMR ($CDCl_3$): δ5.65 (1H, *dt*, *J* = 1.5, 7 Hz for olefinic-H), 4.44 (2H, *s*, for $—CH_2OAc$), 4.07 (2H, *d*, *J* = 7 Hz for $—CH_2Cl$), 2.05 (3H, *s*, for acetyl—CH_3), 1.74 (3H, *brs*, for olefinic—CH_3).

Synthesis of **7** *from* **8** *and* **12**. To 8-hydroxypsoralen (**8**) (40 mg), in dry DMF (5 ml) containing 5.7 mg of NaH, was added dropwise the chloroacetate **12** (38.6 mg) at room temp and the mixture maintained at 90° for 2 hr The mixture was then washed with Et_2O–H_2O and the Et_2O layer purified by Si gel TLC (C_6H_6–Me_2CO, 4:1) R_f 0.6, gave a crystalline product (38 mg), which upon recrystallization from EtOAc gave **7**, mp, 108–109° which was identical in all respects (IR, PMR., mmp and TLC) with the synthetic specimen which was derived from trichoclin (**1**) by acetylation.

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