22.1. Calc. for $C_7H_{12}OS$: S, 22,2); IR ν_{max} cm^{-1}: 1684 (C=O), 1624 (C=C); ^1H NMR: δ 1.68 (6H, *s*), 2.28 (3H, *s*), 3.5 (2H, *d*, $J = 8$ Hz), 5.19 (1H, *t*, $J = 8$ Hz, $J = 1.5$ Hz). MS: M^+ *m/e* 144.0610 (16%) (calc. for $C_7H_{12}OS$ 144.0609), 101.0418 (30%) (calc. for C_5H_9S 101.0425), 69.0716 (100%) (calc. for C_5H_9 69.0705), 43.0152 (3%) (calc. for C_2H_3O 43.0184).

S-(3-Methyl-2-butenyl)-3-methyl butanethioate **3**. MS: M^+ *m/e* 186.1082 (8%) (calc. for $C_{10}H_{18}OS$ 186.1079), 129.0370 (4%) (calc. for C_6H_9OS 129.0374), 101.0418 (8%) (calc. for C_5H_9S 101.0425), 85.0648 (69%) (calc. for C_5H_9O 85.0653), 69.0676 (80%) (calc. for C_5H_9 69.0704), 57.0715 (100%) (calc. for C_4H_9 57.0704), 41.0366 (70%) (calc. for C_3H_5 41.0391).

Synthesis of **3**. 3-Methylbut-2-enethiol (2.5 ml) in Py (15 ml) was reacted with 3-methylbutanoyl chloride (6 ml) as described above to give 1.7 g **3**, bp 88–92°/4 mm Hg. (Found: S, 16.9. Calc. for $C_{10}H_{18}OS$: S, 17.2); IR ν_{max} cm^{-1}: 1682 (C=O), 1627 (C=C); ^1H NMR: δ 0.95 (6H, *d*, $J = 6$ Hz), 1.7 (6H, *s*), 2.16 (1H, *m*, $J = 6$ Hz), 2.42 (2H, *d*, $J = 7$ Hz), 3.53 (2H, *d*, $J = 7$ Hz), 5.22 (1H, *t*, $J = 7$ Hz, $J = 1.5$ Hz). MS: M^+ *m/e* 186.1084 (19%) (calc. for $C_{10}H_{18}OS$ 186.1079), 129.0369 (1%) (calc. for C_6H_9OS 129.0374), 101.0416 (11%) (calc.. for C_5H_9S) 101.0425), 85.0636 (79%) (calc. for C_5H_9O 85.0653), 69.0672 (95%) (calc. for C_5H_9 69.0704), 57.0748 (100%) (calc. for C_4H_9 57.0704), 41.0417 (74%) (calc. for C_3H_5 41.0391).

S-(3-Methyl-2-butenyl)-2-methyl propanethioate (**1**). MS: M^+ *m/e* 172.0921 (19%) (calc. for $C_9H_{16}OS$ 172.0922), 129.0374 (11%) (calc. for C_6H_9OS 129.0374), 101.0417 (18%) (calc. for C_5H_9S 101.0425), 71.0457 (85%) (calc. for C_4H_7O 71.0497), 69.0678 (100%) (calc. for C_5H_9 69.0704).

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PANAXYDOL, A NEW POLYACETYLENIC EPOXIDE FROM *PANAX GINSENG* ROOTS

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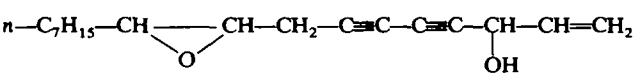
Key Word Index—*Panax ginseng*; Araliaceae; polyacetylenic alcohol; 9,10-epoxy-3-hydroxyheptadeca-1-en-4,6-diyne; synthesis.

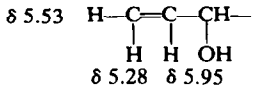
A new polyacetylenic compound named panaxydol was isolated from *Panax ginseng* C. A. Meyer roots together with falcarinol, 3-hydroxyheptadeca-1,9c-dien-4,6-diyne (**1**), previously described by Bohlmann [1, 2], Takahashi [3] and Jones [4]. Spectroscopic data showed the compound to be a derivative of a polyacetylenic alcohol with a structure similar to **1**.

The existence in **1** of a terminal olefinic bond and of unsaturation equivalent to 5 mol of hydrogen was demonstrated by ozonolysis and catalytic hydrogenation. Bands at 2270 and 1650 cm^{-1} in the IR spectrum indicated the presence of acetylenic and olefinic bonds. The chemical shifts and coupling constants of three of the protons were identical to those of the terminal structure of falcarinol (Scheme 1).

Since no other olefinic or acetylenic protons were observed in the ^1H NMR spectrum, the remaining multiple bonds were assigned to two conjugated acetylenic bonds. The IR band at 2270 cm^{-1} is characteristic of conjugated diacetylenes directly bonded to the —CHOH group [5]. Analysis of the ^1H NMR spectrum, together with the conversion of panaxydol



Panaxydol **2**



Scheme 1.

to the corresponding chlorhydrin, suggest the presence of an oxirane ring. The identified structural fragments of panaxydol suggest that its structure is similar to that of falcarinol and can be formulated as **2**.

The proposed structure was confirmed by two independent syntheses. Selective epoxidation of the C_9 double bond in falcarinol was achieved by oxidation with *m*-chloroperbenzoic acid. The IR and MS spectra, as well as the elemental analysis of the compound obtained, confirm structure **2** and are consistent with those of the natural product isolated from *P. ginseng* roots.

As shown by the ^{1}H NMR, synthetic falcarinol contains a significant amount of the *trans* isomer besides the required *cis* form. Moreover it was found that the IR spectra of dodeca-4-en-1-yne, an intermediate of falcarinol synthesis, showed characteristic absorption of *cis* (720 cm^{-1}) and *trans* (965 cm^{-1}) olefins. Hence, synthetic panaxydol also consists of two isomers which we could not separate chromatographically. ^{1}H NMR and IR spectra of the natural compound are identical with those of the synthetically obtained isomer mixture.

The second method of synthesis of **2** was from the epoxidation of dodeca-4-en-1-yne. The synthesis and the subsequent steps establish the carbon skeleton and the positions of all functional groups. By GC–MS it was found that both *cis* and *trans* isomers of 4,5-epoxydodeca-1-yne were present but the difference between the retention times of the two isomers was too small to separate them on a preparative scale. The final compound was identical with epoxidized falcarinol and natural **2**.

EXPERIMENTAL

^{1}H NMR spectra were determined using TMS as int. standard. TLC, PLC and column chromatography was carried out on Si gel. TLC plates were visualized by spraying with conc H_2SO_4 and charring at 110°. GLC was carried out on a glass column (2 m, i.d. 10 mm), packed with 25% SE-30 on Chromosorb W at 180° with argon as carrier gas.

Extraction and isolation. Dry, powdered root of Korean *P. ginseng* (3 kg) was extracted with 50% EtOH. The extract was concentrated *in vacuo* and the fraction of interest was extracted into petrol. Column chromatography with petrol–Me_2CO–wet Et_2O (40:1:1) on Si gel (300g, Suchardt 100/200 mesh) furnished **1** (0.92 g) and **2** (1.32 g). Vacuum distillation of **2** (120°/0.05 mm Hg) yielded 200 mg of unstable yellowish oil, homogeneous by TLC and GLC.

Panaxydol (**2**). ^{1}H NMR (100 MHz, $CDCl_3$): δ 5.95 (1H, *m*, C-2), 5.33 (1H, *m*, C-1), 5.28 (1H, *m*, C-1), 4.91 (1H, *d*, J = 6 Hz, C-3), 3.06 (1H, *m*, C-9), 2.96 (1H, *m*, C-10), 2.7 (1H, *dd*, J_1 = 16 Hz, J_2 = 5 Hz, C-8), 2.35 (1H, *dd*, J_1 = 16 Hz, J_2 = 7 Hz, C-8), 1.48 (2H, *m*, C-11), 1.3 (10H, –$(CH_2)_5$–), 0.92 (3H, *t*, C-17) ppm. IR cm^{-1} 2270, 2165 C≡C); 3415 (OH); 935 (CH=CH_2). Low resolution MS (probe) 70 eV *m/e* (composition, rel. int.): 129 ($C_8H_{17}O$, 12), 57 (C_3H_5O, 32), 41 (C_5H_5, 100). Found: C, 77.3, H, 9.6, $C_{17}H_{24}O_2$ requires: C, 78.4; H, 9.2%.

Hydrogenation. **2** (100 mg) in 10 ml EtOH was hydrogenated using Adam's Pt catalyst. 2.08 mmol H_2 was absorbed. In the ^{1}H NMR spectrum the intensity of the Me triplet was doubled.

Chlorohydrin of **2**. **2** (100 mg) in 30 ml of 96% EtOH was treated with 0.1 ml conc HCl. After 30 min at room temp. the solvent was removed. The residue on PLC gave 80 mg of oily product, ^{1}H NMR (100 MHz, $CDCl_3$): δ 4.1 (1H, *m*, C-10), 3.86 (1H, *td*, J_1 = 6Hz, J_2 = 3 Hz, C-9), 2.65 (2H, *d*, J = 6 Hz, C-11), 1.81 (2H, *m*, C-8); other signals were the same as those of **2**.

Epoxidation of **1**. **1** was synthesized by the method of ref. [2] and 310 mg was dissolved in 5 ml $CHCl_3$ with the addition of *m*-chloroperbenzonic acid (160 mg). The reaction was carried out for 20 hr at room temp. After removal of $CHCl_3$ the product was taken up in 10 ml of hexane. Column chromatography (20 g MN-Kieselgel 60, petrol–Me_2CO tone, 6:1) yielded starting material (50 mg) and **2** (115 mg) (41% theoretical yield).

Epoxidation of dodeca-4-en-1-yne. The compound (770 mg) was epoxidized with excess *m*-chloroperbenzoic acid (20%) in the manner described above. Upon removal of the solvent, distillation of the residue gave 4,5-epoxydodeca-1-yne (450 mg) bp 105–110° (7 mm Hg), 55% theoretical yield. ^{1}H NMR (80 Hz, $CDCl_3$): δ 2.91 (2H, *m*, C-4, C-5), 2.45 (2H, *m*, C-3), 2.02 (1H, *m*, C-1), 1.47 (2H, *m*, C-5), 1.27 (10H, *m*,—$(CH_2)_5$—), 0.87 (3H, *m*, C-1). IR cm^{-1} 3315, 2135 (C≡CH). Low-resolution MS (GC–MS) 70 eV *m/e*, (composition, rel. intensity): 141 ($M^+ - 39$, 2), 81 ($M^+ - 89$, 40).

Synthesis of **2** *from Cadiot–Chodkiewicz coupling.* 4,5-Epoxydodeca-1-yne (237 mg) was dissolved in 0.7 ml MeOH and 0.2 ml dioxane with addition of NH_2OH–HCl (7.6 mg), $EtNH_2$ (0.2 ml 70% aq soln) and Cu_2Cl_2 (2.6 mg). 1-Bromo-3-hydroxypent-4-en-1-yne (212 mg) in 1.3 ml MeOH was then added. The soln was kept overnight at 30°. The mixture was treated with H_2O and extracted with 3 × 15 ml hexane. Column chromatography (80 g MN-Kieselgel 60; petrol–Et_2O, 6:1) yielded starting material (50 mg) and **2** (97 mg), 35% theoretical yield. All spectroscopic data of this compound (^{1}H NMR, IR, MS) were in agreement with those for the natural product.

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SYNTHÉSE DU (±)-DOLICHODIAL *TRANS-CIS*

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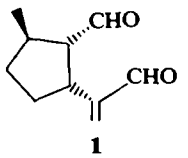
Key Word Index—*Teucrium marum;* Labiatae; *trans-cis*-(±)-dolichodial; monoterpenoid; synthesis.

Deux monoterpènes cyclopentaniques stéréoisomères, les dolichodials **1** (*cis-trans*) et **2** (*trans-cis*) ont tout d'abord été isolés à partir des sécrétions défensives de phasmes et de fourmis [1, 2]. Ils sont aussi abondants dans l'huile essentielle de *Teucrium marum* L. de Sardaigne [3] et de Corse [4, 5], Labiées qui présentent de fortes propriétés attractives chez les chats et induisent chez eux une hyperexcitabilité, une mydriase avec salivation abondante, suivie d'une myorelaxation en phase terminale [4, 5]. Cette ivresse est très comparable à celle provoquée par *Nepeta cataria* L. [6, 7].

Des essais préliminaires réalisés avec diverses fractions de l'essence de *Teucrium marum* [4, 5] ont démontré que les substances impliquées dans l'activité physiologique chez les félidés correspondent aux dolicholactones issues des dialdéhydes **1** et **2**.

Dans le but d'obtenir des quantités suffisantes de ces lactones, dont les précurseurs sont les composés **1** et **2**, nous avons mis au point une nouvelle synthèse simple et stéréospécifique de l'un de ces iridoïdes dialdéhydiques: le (±)-dolichodial *trans-cis* **2**.

La précédente synthèse des dolichodials par Cavill et Whitfield [8] se développait en dix étapes à partir du D-(+)-citronellal, (Rdt global voisin de 5%, mélange de trois isomères *cis-trans*/*trans-cis* et *trans-trans*). Le point de départ de cette nouvelle synthèse est le photocitral A **4a**, obtenu par cyclisation photochimique du citral [9, 10]. Nous avons déterminé les conditions optimales de cyclisation pour obtenir en une seule fois, une concentration maximale en photocitrals (voisine de 90%; photocitral A: photocitral B = 87 : 13). Le citral résiduel (8%) est éliminé par combinaison bisulfitique. A partir du photocitral **4a**, la



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synthèse du (±)-dolichodial *trans-cis* **2** se développe suivant le Schéma 1.

Le composé **4a** est transformé en présence d'éthanol et d'orthoformiate d'éthyle [11] en acétal diéthylique **5**. L'acétal **5**, oxydé par SeO_2 [12–14] conduit à l'aldéhyde-acétal **6**. La fonction aldéhyde est régénérée par traitement en milieu acide. Le dialdéhyde obtenu présente des données spectroscopiques (RMN et IR) identiques à celles du dolichodial **2** isolé de *Teucrium marum* de Corse. Notons qu'au cours de l'étape d'oxydation par SeO_2, il apparaît du dialdéhyde **2**. Ceci est dû à la fragilité du groupement protecteur employé et à la présence d'acide sélénique dans SeO_2. En conclusion, cette synthèse permet d'atteindre avec un rendement global de 10% le (±)-dolichodial **2**, le plus stable (équilibration par MeONa, MeOH) de configuration *trans-cis*.

PARTIE EXPÉRIMENTALE

Cyclisation photochimique du citral. On irradie 40 g de citral dans 760 ml d'EtOH absolu, pendant 350 hr (réacteur Hanovia, avec lampe UV moyenne pression de 100 W). La réaction est suivie par GLC (détecteur FID; N_2 à 20 ml/min; Isotherme 130°; Carbowax 20 M 5%). Elle est arrêtée lorsque la quasi totalité du citral est cyclisé. Le milieu réactionnel