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THE POLYACETYLENIC FALCARINOL AS THE MAJOR ALLERGEN IN *SCHEFFLERA ARBORICOLA*

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Key Word Index—*Schefflera arboricola*; Araliaceae; falcarinol; allergic contact dermatitis; polyacetylene.

Abstract—*Schefflera arboricola* has been reported to cause allergic contact dermatitis. The major allergen is now isolated and identified as falcarinol, heptadeca-1,9(*Z*)-dien-4,6-diyn-3-ol. The isolation of (*E*)-β-farnesene, phytol and 24β-ethylcholesta-5,22(*E*)-diene-3β-ol (poriferasterol) is also reported.

INTRODUCTION

The genus *Schefflera* (Araliaceae) is widespread in tropical and subtropical regions [1]. *Schefflera* species have recently become popular as ornamental plants in Europe and at the same time allergic contact dermatitis caused by these plants has been reported [2–4]. This communication describes the isolation and structural elucidation of the major allergen of *Schefflera arboricola* (Hayata) Merrill as falcarinol, heptadeca-1,9(*Z*)-dien-4,6-diyn-3-ol, previously described by Takahashi *et al.* [5, 6] and Bohlmann [7]. Falcarinol is known from Pittosporaceae [8] and occurs frequently in Umbelliferae [9], but both its presence in a *Schefflera* and its allergenic activity are novel observations. Additionally we have isolated and identified (*E*)-β-farnesene [10–12], phytol [13, 14] and poriferasterol [15, 16].

RESULTS AND DISCUSSION

The ether extract of fresh leaves and stems of *S. arboricola* was subjected to column chromatography on silica gel. The fractions were examined by TLC and on this basis 18 fractions were selected for patch testing on a volunteer occupationally sensitized towards the plant. The volunteer showed a positive reaction to two of the fractions as well as to the crude extract. From TLC analysis it could be seen that the two active fractions differed from the others in containing one major component giving an intense black colour upon spraying with 1% of vanillin in conc. H_2SO_4. This component was isolated by silica gel/caffeine column chromatography and by semi-preparative HPLC. UV, IR, mass, ^1H and ^{13}C NMR spectroscopy identified the compound as falcarinol [17, 18]. The pure falcarinol was tested on the volunteer and elicited allergic contact dermatitis.

Falcarinol is chemically reactive and it seems reasonable to propose falcarinol as an alkylating agent. If its hydroxyl group by proton assistance is removed as a neutral leaving group, an extremely stable carbocation is formed which can easily react with mercapto and amino groups in proteins forming haptens. An example of the reactivity of falcarinol is its synthetic reaction with *p*-toluenesulphonic acid in benzene in which the rearranged carbocation as an electrophile readily alkylates benzene [19].

Microscopic investigation of leaf sections located falcarinol in the cuticle. When the sections were treated with a solution of 1% of vanillin in conc. H_2SO_4 and observed for 3.5 hr, only the cuticle became coloured. Thus falcarinol may have a protective role in *S. arboricola*; in *Daucus carota* the fungitoxic falcarindiol dominates in the peridermis [20] and the allergenic principles, 5-alkenylresorcinols, of *Philodendron scandens* subsp. *oxycardium* are thought to be associated with the leaf cuticle [21].

Falcarinol is also present in the roots of *S. arboricola* and the isolation from this plant part is easier. A concentrated ethanol–ether extract of finely crushed roots was partitioned between dichloromethane and water and the dichloromethane fraction was separated by preparative TLC to give almost pure falcarinol.

None of the other *Schefflera* species reported to cause allergic contact dermatitis has to our knowledge been examined for the presence of falcarinol, although it is known that C_{17}-polyacetylenes closely related to falcarinol are common in species of Araliaceae and Umbelliferae reported to cause allergic contact dermatitis [9, 22, 23]. It is of interest to examine the possible existence and role of falcarinol as an allergen in these plants.

EXPERIMENTAL

The plant material was obtained as potted plants from the plant nursery A. Blæsbjerg, Nistedvej 31, DK-5270 Odense N. TLC was performed with precoated silica gel plates (Kieselgel 60, F-254 Merck) and the spots were detected by spraying with 1% of vanillin in conc. H_2SO_4 followed by heating to 110° for 5 min. The semi-prep. HPLC was performed on a partly rebuilt Waters Prep. TLC System 500 A. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as int. standard.

Isolation and purification of falcarinol from leaves and stems. Fresh leaves and stems (718 g fr. wt) were finely crushed and extracted with EtOH. The solvent was removed *in vacuo* and the residue extracted with Et_2O. Evaporation of the ether yielded 9.6 g of extract. The extract was subjected to CC on silica gel (200 g) and eluted with hexane alone and with increasing

amounts of Et_2O, and then finally with MeOH. The 48 fractions (25 ml) obtained were examined by TLC and 18 fractions representing all compounds detectable with the spray reagent were selected for patch testing. Two fractions gave a positive response on the sensitized volunteer and were subjected to separation on silica gel/caffeine column (1:9; 45 g) with Et_2O–hexane (5:95) and semi-preparative HPLC on Porasil A with Et_2O–hexane (1:4) as eluant. Flow rate: 50 ml/min. R_t 6 min. Detection: UV (254 nm). By these methods 305 mg were obtained.

Isolation of falcarinol from the roots. Fresh roots (200 g) were finely crushed and extracted with Et_2O–EtOH (1:1). The concd extract was partioned between CH_2Cl_2 and H_2O. The CH_2Cl_2-soluble fraction was subjected to prep. TLC on silica gel plates (Et_2O–hexane, 2:3). The separation yielded almost pure falcarinol with R_f, UV and MS properties identical to those of falcarinol isolated from the leaves and stems. From the absorption in UV at 242 nm the total amount of falcarinol from the roots was calculated to be 110 mg.

Falcarinol. R_f (Et_2O–hexane, 1:4) 0.35. UV λ_{max}^{hexane} nm (ε): 256 (445), 242 (739), 230 (986). IR ν_{max} cm^{-1}: 3350, 3075, 2940, 2910, 2840, 2240, 1635, 1455, 1410, 987, 925. ^1H NMR (270 MHz): δ0.88 (3H, *t*, J = 6.7 Hz, 17-Me), 1.27 (10H, *m*, 12-CH_2–16-CH_2), 2.02 (2H, *dt*, J_d = 6.7 Hz J_t = 6.7 Hz, 11-CH_2), 3.03 (2H, *d*, J = 7.0 Hz, 8-CH_2), 4.90 (1H, *d*, J = 5.3 Hz, H-3), 5.24 (1H, *ddd*, J = 10.2, 1.6, 0.9 Hz, H-1), 5.37 (1H, *dtt*, J_d = 10.2 Hz, J_t = 6.7 Hz, J_t = 1.3 Hz, H-10), 5.46 (1H, *ddd*, J = 17.5, 1.6, 0.9 Hz, H-1), 5.51 (1H, *dtt*, J_d = 10.2 Hz, J_t = 7.0 Hz, J_t = 1.3 Hz, H-9), 5.94 (1H, *ddd*, J = 10.2, 17.5, 5.3 Hz, H-2). ^{13}C NMR (67.9 MHz): δ13.96 (C-17), 17.57 (C-8), 22.52 (C-16), 27.09 (C-11), 29.06 (3C, C-13, C-14, C-15), 31.70 (C-12), 63.43 (C-3), 63.90 (C-6), 71.20 (C-5), 74.13 (C-7), 80.17 (C-4), 116.89 (C-1), 121.78 (C-9), 132.99 (C-10), 136.07 (C-2). MS *m/z* (rel. int.): 244 $[M]^+$ (0.6), 159 (63), 131 (32), 117 (40), 115 (30), 91 (59), 57 (32), 55 (100), 43 (61).

(E)-β-Farnesene. From the hexane fractions of the silica gel CC of the extract of leaves and stems 194 mg pure *(E)-β*-farnesene was obtained as a yellow oil. R_f (hexane) 0.81. The MS, ^1H and ^{13}C NMR data of the isolated compound are in agreement with the data previously reported for *(E)-β*-farnesene [10–12].

Phytol. By silica gel CC of the leaves and stems 100 mg of pure phytol was obtained from the fractions slightly more polar than those containing falcarinol. R_f (Et_2O–hexane, 1:1) 0.50. The phytol was identified by IR, ^1H NMR and MS [13, 14].

Poriferasterol (24β-ethylcholesta-5,22(E)-diene-3β-ol). Two fractions slightly more polar than those containing phytol yielded upon further CC (silica gel, 50 g; Et_2O–hexane, 1:24) 7.5 mg of poriferasterol. Mp 155–156°. R_f (Et_2O–hexane, 1:1) 0.39. The isolated compound was identified as poriferasterol by comparing the IR, ^1H NMR, ^{13}C NMR and MS spectra and the mp with data previously reported for poriferasterol and related compounds [15, 16].

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