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11-EPI-AZADIRACHTIN H FROM *AZADIRACHTA INDICA*

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Key Word Index—*Azadirachta indica*; Meliaceae; seeds; 11-epi-azadirachtin.

Abstract—A new tetranortriterpenoid 11-epi-azadirachtin H has been isolated from the methanolic extracts of *Azadirachta indica* seeds. Its structure is proposed on the basis of various spectral analyses.

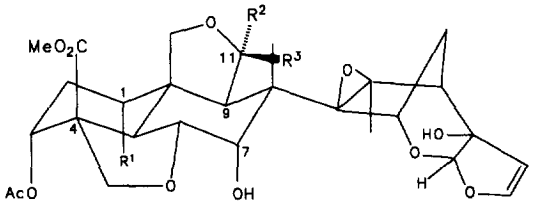
INTRODUCTION

Azadirachtin [1, 2] and its analogues [3–7] are potent insect antifeedants and ecdysis inhibitors and are among the more interesting constituents of *Azadirachta indica* A. Juss. We report here on the isolation of 11-epi-azadirachtin H (**1**), i.e. the 11-epimer of azadirachtin H (**2**) reported earlier [8–10].

RESULTS AND DISCUSSION

The ^{1}H NMR spectrum of **1** is very similar to that of **2** in terms of the following signals: (i) the two olefinic protons H-22 and H-23 (δ 5.05 and 6.45) of the dihydrofuran ring and a low-field singlet for H-21 at δ 5.66; (ii) the four spin system H-15, H-16α,β and H-17 (δ 4.57, 1.68, 1.28 and 2.35); (iii) the four spin system H-1, H-2α,β and H-3 (δ 5.36, 2.39, 2.30 and 5.52); (iv) the AB system of H-28α,β and H-19α,β at δ 4.09 and 3.74; (v) the three spin system H-5, H-6 and H-7 (δ 3.36, 4.46 and 4.65), and (vi) the two methyl signals H-18 and H-30 (δ 1.98 and 1.32).

The proton connectivities were established by ^{1}H–^{1}H COSY spectra and the multiplicities of all carbon signals were assigned by SEFT experiments. Unlike the ^{1}H NMR spectrum of **2**, the spectrum of **1** exhibited a coupling between H-11 (δ 5.4) and the hydroxyl at C-11 (δ 3.1), which disappeared on D_2O exchange. The coupling between H-9 and H-11 observed in **2** was absent in **1** [8–10]. The bond angle between H-9 and H-11 as determined from the MM2 minimized structure (Alchemy molecular model program), was found to be 118.2°, indicating a very small or absence of any detectable coupling between the two. This clearly indicated a β orientation of H-11 and an α orientation of the hydroxyl at C-11. This was further supported by the strong NOE (NOESY) between H-11 and H-30 and between H-1 and the hydroxyl at C-11. The stereochemistry at the other centres were identical to that of **2** as indicated by the ^{1}H NMR, ^{13}C NMR, H–H COSY and NOESY spectra.



1 R^1=Tig R^2=OH R^3=H
2 R^1=Tig R^2=H R^3=OH

EXPERIMENTAL

Neem seeds were collected in Tamilnadu, India, during December 1994. The MeOH extract of the defatted neem seed kernels (1.5 kg) was partitioned between aq. MeOH and EtOAc. The EtOAc-soluble material was purified by repeated CC over silica gel (100–200 mesh) with $CHCl_3$–Me_3CN to afford **1** (30 mg). Microcrystalline solid, mp 170–173°; $[\alpha]_D^{25}$ 28.3° ($CHCl_3$, $c = 0.6$). FAB MS: 685 $[M + Na]^+$ ($C_{33}H_{42}O_{14}$), 645 $(MH^+ - H_2O]^+$, 627 $[645 - H_2O]^+$; UV λ_{max} nm (log ε): 247 (2.42); IR ν_{max} cm^{-1}: 3400 (OH), 1720, 1710 (C=O), 1640 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.36 (1H, *t*, $J = 2.9$ Hz, H-1), 2.30 (1H, *dt*, $J = 16.8$, 3.3 Hz, H-2a), 2.39 (1H, *dt*, $J = 16.8$, 3.3 Hz, H-2b), 5.52 (1H, *t*, $J = 2.7$ Hz, H-3), 3.36 (1H, *t*, $J = 12$ Hz, H-5), 4.46 (1H, *dd*, $J = 12.4$, 2.7 Hz, H-6), 4.65 (1H, *brd*, $J = 2.3$ Hz, H-7), 2.64 (1H, *s*, H-9), 5.4 (1H, *brd*, $J = 3.7$ Hz, H-11), 4.57

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(1H, *d*, $J = 3.4$ Hz, H-15), 1.69 (1H, *ddd*, $J = 13$, 3.8, 5.5 Hz, H-16a), 1.28 (1H, *d*, $J = 12$ Hz, H-16b), 2.35 (1H, *d*, $J = 5.7$ Hz, H-17), 1.98 (3H, *s*, H-18), 3.74 (1H, *d*, $J = 8.7$ Hz, H-19a), 4.09 (1H, *d*, $J = 87$ Hz, H-19b), 5.66 (1H, *s*, H-21), 5.05 (1H, *d*, $J = 2.9$ Hz, H-22), 6.45 (1H, *d*, $J = 2.9$ Hz, H-23), 3.74 (1H, *d*, $J = 8.7$ Hz, H-28a), 4.09 (1H, *d*, $J = 8.7$ Hz, H-28b), 1.32 (3H, *s*, H-30), 2.69 (1H, *brs*, OH-7), 3.1 (1H, *brd*, $J = 4.5$ Hz, OH-11), 2.94 (1H, *brs*, OH-20), 3.79 (3H, *s*, CO_2Me-12), 1.86 (3H, *s*, OAc), 6.98 (1H, *qq*, $J =$ 7.3, 1.4 Hz, H-3′), 1.76 (3H, *brd*, $J = 7.3$ Hz, H-4′), 1.84 (3H, *brs*, H-5′); ^{13}C NMR (100.62 MHz, $CDCl_3$); δ (ppm) 72.25 (C-1), 30.7 (C-2), 67.1 (C-3), 52.3 (C-4), 37.03 (C-5), 72.94 (C-6), 74.06 (C-7), 43.3 (C-8), 48.1 (C-9), 47.7 (C-10), 100.9 (C-11), 69.9 (C-13), 69.9 (C-14), 76.2 (C-15), 25.2 (C-16), 48.8 (C-17), 18.64 (C-18), 72.99 (C-19), 83.4 (C-20), 108.59 (C-21), 107.56 (C-22), 147.1 (C-23), 76.66 (C-28), 173.5 (C-29), 20.9 (C-30), 52.64 (CO_2Me), 166.6 (C-1′), 128.7 (C-2′), 138.09 (C-3′), 14.3 (C-4′), 11.8 (C-5′).

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