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SYNTHESIS OF (±)-3-DESOXY-16-AZAEQUILENIN

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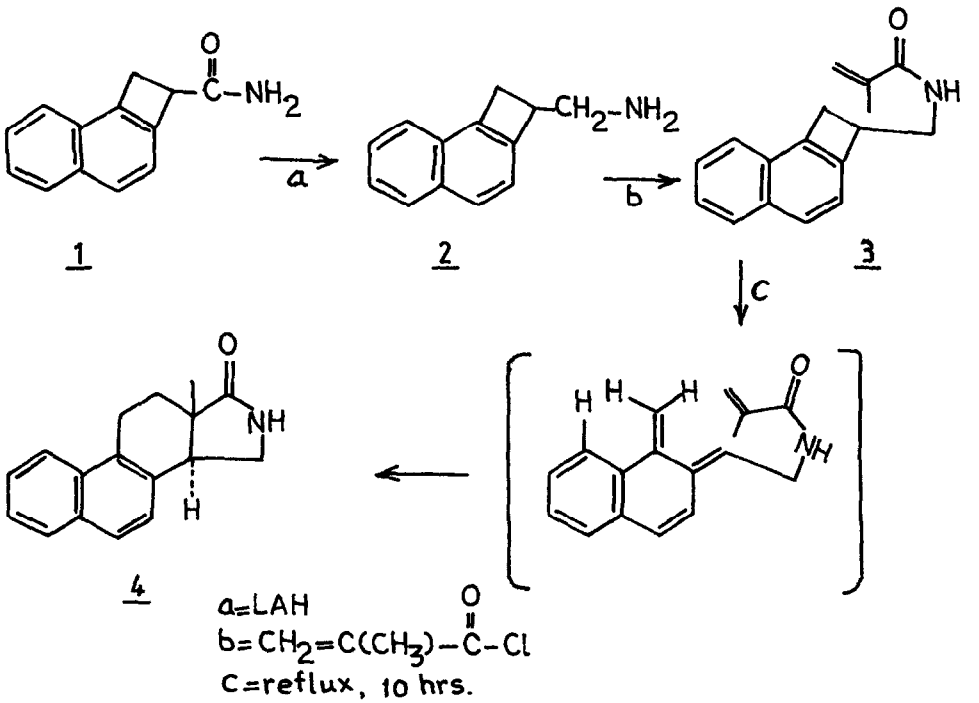
Abstract: Condensation of methacrylyl chloride with the amine obtained on lithium aluminium hydride reduction of 1,2-naphthocyclobuten-3-carboxamide gave a propenamide which on refluxing in O-dichlorobenzene cyclised to (±)-3-desoxy-16-azaequilenin.

Intramolecular [4+2] cycloaddition of quinodimethanes derived from benzocyclobutenes has been extensively used for synthesis of steroids and other polycyclic systems.[1,2,3] It was of interest to see if 1,2-naphthocyclobutenes, readily available by [2+2] photoaddition to naphthalenes[4], undergo similar reactions and with what stereochemical outcome. Here the additional peri steric interaction can distort the reversibly formed quinodimethane and also alter its life time. In the first instance synthesis of (±)-3-desoxy-16-azaequilenin[5] was attempted.

Lithium aluminium hydride reduction of 1,2-naphthocyclobutene-3-carboxamide[4] (1) gave the amine 2 which was reacted with methacrylyl chloride in benzene containing triethylamine. Column chromatography over silica gel gave the propenamide[6] 3 as a thick oil; PMR ($CDCl_3$-d_1/TMS : 90MHz)δ1.95(s,3H), 2.97-3.8 (m,5H),5.3(s,1H),5.6 (s,1H),·6.1 (br s,1H), 7.2-8.0 (m,6H); IR (cm^{-1}) 1620,1660,1710. The amide 3 was refluxed (oil bath at 180-185°) in O-dichlorobenzene for 10 hrs. The usual work up and chromatography over alumina yielded (33%) (±) -3-desoxy-16-azaequilenin (4),m.p. 231-232°; IR(cm^{-1}; KBr) 1670,1730; PMRδ0.95 (s,3H,-CH_3), 1.83-2.4 (m,2H-C_{12}), 3.3-3.9 (m;2H-C_{11},H-C_{14},2H-C_{15}), 6.55 (br s,1H,-N-H; D_2O exchangeable), 7.1-8.1 (m,6H,ArH); MS (m/e) 251 (M^+); UV (λ_{max}; C_2H_5OH) 277, 286 nm.



Bachmann et al. have reported[7] preparation of both trans (±)-3-desoxy-16-azaequilenin (m.p., 234-236°) and its cis epimer (m.p., 205-206°). Since the cis epimer is thermodynamically more stable, the formation[8] of the desired trans isomer in the present cyclisation must be kinetically controlled.

References and Notes

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8. Presence of a small proportion of the cis isomer cannot be ruled out.

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