HETEROCYCLES, Vol 24, No 1, 1986

SYNTHESIS OF TERPENOIDAL ALKALOID, FABIANINE

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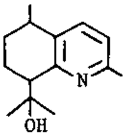
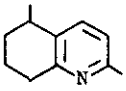
Abstract —— Synthesis of a terpenoidal alkaloid, fabianine, was accomplished by application of Diels-Alder reaction of 1,2,3-triazine with enamine.

Fabianine (1) and 2,5-dimethyl-5,6,7,8-tetrahydroquinoline (2) are alkaloids isolated and characterized in 1962 by Edwards and Elmore from a South American plant, Fabiana imbricata.[1]
These alkaloids have been synthesized by Rouillier[2a] and Soccolini.[2b] In this paper we report the synthesis of fabianine as an extension of our recent work concerning Diels-Alder reaction of 1,2,3-triazine with enamines,[3] and in the preceding paper, we described the synthesis of 2,5-dimethyl-5,6,7,8-tetrahydroquinoline.

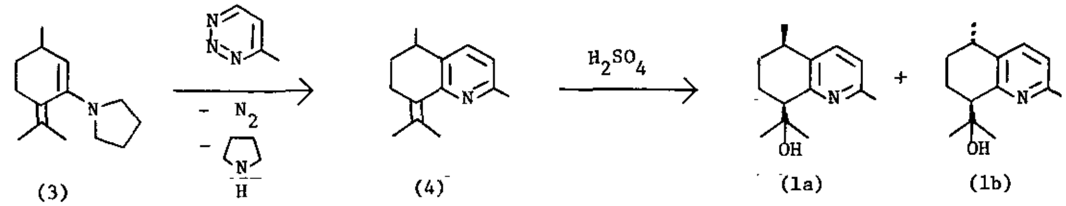
Pyrrolidine enamine (3) (290mg, 1.4mmol) of pulegone, which was synthesized by general method,[4] was treated with 4-methyl-1,2,3-triazine (95mg, 1mmol) in dry $CHCl_3$ in a sealed glass tube at 100°C (bath temperature) for 2 h. The crude products obtained were separated by preparative thin layer chromatography on silica gel to give 2,5-dimethyl-8-isopropylene-5,6,7,8-tetrahydroquinoline (4)[5] in 37% yield (46% based on a consumed starting material, 4-methyl-1,2,3-triazine). In addition, we obtained pulegone (58mg) which was prepared by the hydrolysis of enamine (3). The cycloaddition occurs at N-3/C-6 of the 1,2,3-triazine nucleus, and the nucleophilic carbon of the enamine attaches to C-6 of the 1,2,3-triazine. Hydration of (4) with 80% sulfuric acid at 60-70°C gave fabianine (1) (21%) and unreacted (4) (46%). We found that fabianine existed as a mixture of diastereoisomers (1a) and (1b)[6] in equivalent amounts based on the examination of NMR spectrum and HPLC.[7] Spectroscopic properties of the diastereoisomeric mixture showed good agreement with those described in the literature.[2a]



(1)



(2)



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5. IR$_{max}^{CHCl_3}$ cm^{-1} : 1620, 1570 ; ^{1}H-NMR($CDCl_3$) δ : 1.26(3H, d, J=7Hz, 5-Me), 1,87 and 2.18(3Hx2, s each, Mex2), 2.52(3H, s, 2-Me), 2.71(1H, m, 5-H), 6.93(1H, d, J=8Hz, 3-H), 7.38(1H, d, J=8Hz, 4-H) ; MS m/z : 201.1511(M$^+$, calcd for $C_{14}H_{19}N$, 201.1516).

6. IR$_{max}^{CHCl_3}$ cm^{-1} : 3200, 1590, 1570 ; ν$_{max}^{EtOH}$ nm : 281(sh), 273, 215 ; MS m/z : 220.1681([MH]$^+$, calcd for $C_{14}H_{22}NO$, 220.1699) ; ^{1}H-NMR($CDCl_3$) δ : (1a)- 0.97 and 1.02(3Hx2, s each, -C(OH)Me_2), 1.23(3H, d, J=7Hz, 5-Me), 2.49(3H, s, 2-Me), 6.98 or 7.02(1H, d, J=8Hz, 3-H), 7.37 or 7.55(1H, d, J=8Hz, 4-H) : (1b)- 1.29(3H, d, J=7Hz, 5-Me), 1.32 and 1.34(3Hx2, s each, -C(OH)Me_2), 2.49(3H, s, 2-Me), 6.98 or 7.02(1H, d, J=8Hz, 3-H), 7.37 or 7.55(1H, d, J=8Hz, 4-H).

7. HPLC was preformed with a Shimadzu LC-3A liquid chromatograph system under the folloing conditions : column, Cosmosil $5C_{18}$ (4.6mm x 150mm) ; solvent, CH_3OH-H_2O (70:30 v/v) ; flow rate, 1.0 ml/min ; detection, UV.

Received, 6th September, 1985