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SYNTHESIS OF ETHYL 1-PHENYL- AND 2-METHYL-6H-FURO[2,3-d][1]BENZAZEPINE-5-CARBOXYLATES[1)]

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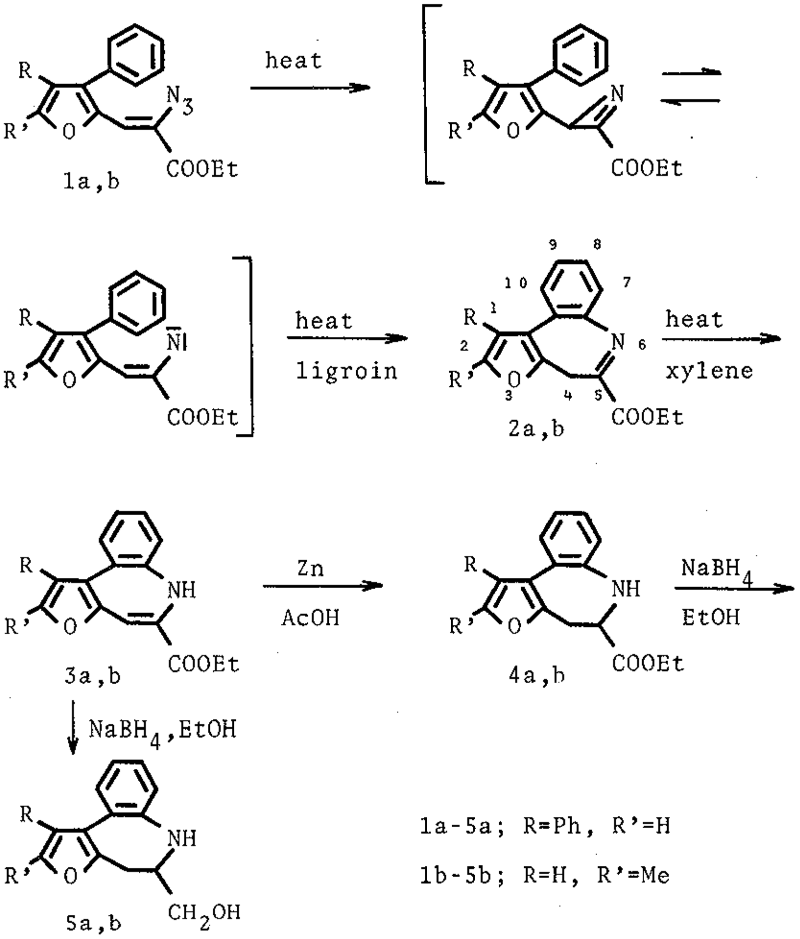
Thermolysis of ethyl α-azido-β-(3-phenylfuryl-2)-acrylates (1a,b) in ligroin gave ethyl 1-phenyl- or 2-methyl-4H-furo[2,3-d][1]benzazepine-5-carboxylates (2a,b). Further thermolysis of 2a and 2b in boiling xylene yielded ethyl 1-phenyl- and 2-methyl-6H-furo-[2,3-d][1]benzazepine-5-carboxylates (3a,b), respectively.

It is known that thermolysis of α-azidovinyl esters bearing aromatic ring systems produces pyrrole ring *via* the intermediacy of azirines.2) Moreover, Taniguchi et al.3) had recently reported that phenyl group which substituted at cyclization position forming five membered ring of 3-benzofuranyl-1-azirines, was attacked by vinyl nitrene affording seven membered ring. In this paper we describe a thermal reaction of ethyl α-azido-β-(3-phenylfuryl-2)acrylates (1a,b) which leads to the formation of the hitherto unknown furo[2,3-d][1]benzazepine ring which is attacked by intramolecular vinyl nitrene.

Ethyl α-azido-β-(3,4-diphenylfuryl-2)acrylate (1a) [mp 109° (decomp), (ether); ir ν (KBr) 2120 and 1701 cm^{-1}; mass *m/e* 359 (M^+) and nmr δ ($CDCl_3$) 7.74 (1H,s,furan-H), 7.24 (10H,m,phenyl-H x 2), 6.78 (1H,s,vinyl-H)4) and 4.30, 1.31 (5H,C_2H_5)] was prepared in 35% yield by condensation of 3,4-diphenylfurfural5) with ethyl azidoacetate in the presence of sodium ethoxide. Ethyl α-azido-β-(5-methyl-3-phenylfuryl-2)acrylate (1b) [mp 97° (decomp), (ether); ir ν (KBr) 2090 and 1695 cm^{-1}; mass *m/e* 297 (M^+) and nmr δ ($CDCl_3$) 7.37 (5H,s,phenyl-H), 6.90 (1H,s,vinyl-H), 6.24 (1H,s,furan-H),6) 4.28, 1.32 (5H,C_2H_5) and 2.44 (3H,s,CH_3)6)] was obtained in 29% yield by similar method after Vilsmeier formylation of 2-methyl-4-phenylfuran.7) Thermolysis of 1a and 1b in ligroin at 95° for 0.5-1.5 hr gave ethyl 1-phenyl-4H-furo[2,3-d][1]benzazepine-5-carboxylate (2a), yellow oil [ir δ (film) 1712 cm^{-1}; mass *m/e* 331 (M^+) and nmr δ ($CDCl_3$) 7.60-6.93 (4H,m,C_{7-10}-H), 7.42 (1H,s,C_2-H), 7.28 (5H,s,phenyl-H), 4.40, 1.43 (5H,C_2H_5) and 3.68 (2H,s,C_4-H)] and ethyl 2-methyl-4H-furo[2,3-d][1]benzazepine-5-carboxylate (2b), yellow oil [ir ν (film) 1710 cm^{-1}; mass *m/e* 269 (M^+) and nmr δ ($CDCl_3$) 7.68-7.24 (4H,m,C_{7-10}-H), 6.38 (1H,s,C_1-H), 4.41, 1.42 (5H,C_2H_5), 3.70 (2H,s,C_4-H) and 2.35 (3H,s,CH_3)] in good yields, respectively. However, thermal reaction of 1a and 1b in boiling xylene for 5-10 hr gave ethyl 1-phenyl-6H-furo-[2,3-d][1]benzazepine-5-carboxylate (3a) [mp 114-115° (ethanol); ir ν (KBr) 3350 and 1695 cm^{-1}; mass *m/e* 331 (M^+) and nmr δ ($CDCl_3$) 7.41 (1H,s,C_2-H), 7.33 (5H,s,phenyl-H), 7.11-6.55 (5H,m,C_4- and C_{7-10}-H), 5.78 (1H,bs,NH) and 4.29, 1.34 (5H,C_2H_5)] and ethyl 2-methyl-6H-furo[2,3-d][1]benzazepine-5-carboxylate (3b) [mp 30-31°;



1a-5a; R=Ph, R'=H

1b-5b; R=H, R'=Me

ir ν (KBr) 3340 and 1685 cm^{-1}; mass *m/e* 269 (M^+) and nmr δ ($CDCl_3$) 7.04-6.31 (5H,m,C_4- and C_{7-10}-H), 6.06 (1H,s,C_1-H), 5.44 (1H,bs,NH), 4.24, 1.32 (5H,C_2H_5) and 2.25 (3H,s,CH_3)] in 76 and 63% yields, through 2a and 2b, respectively.$^{8)}$ In fact, 2a and 2b were readily converted into 3a and 3b, respectively (under reflux in xylene, 5 hr). The easy isomerization of 2 to 3 is probably due to the effect of the carbonyl group.$^{3)}$

Continuously, reduction of 3a and 3b with zinc powder in acetic acid gave saturated esters (4a) [mp 104-105°; nmr δ ($CDCl_3$) 3.89 (1H,dd,J=4, 11 Hz,C_5-H), 3.51 (1H,dd,J=4, 16.2 Hz,C_4-H) and 3.21 (1H,dd,J=11, 16.2 Hz,C_4-H)] and (4b) [mp 60-61°; nmr δ ($CDCl_3$) 3.91 (1H,dd,J=3, 10.5 Hz,C_5-H), 3.53 (1H,dd,J=3, 15.7 Hz,C_4-H) and 3.19 (1H,dd,J=10.5, 15.7 Hz,C_4-H)] by treatment on silica gel column chromatography with benzene in 60-65% yield. Also, reaction of 3a and 3b with excess sodium borohydride in ethanol gave saturated alcohols (5a) [mp 131-132° (ether); nmr δ ($CDCl_3$) 3.62 (2H,m,CH_2), 3.30 (3H,m,C_5-H,NH and OH) and 2.89 (2H,m,C_4-H)] and (5b) [mp 139-140° (ether); nmr δ ($CDCl_3$) 3.63 (2H,m,CH_2), 3.22 (3H,m,C_5-H,NH and OH) and 2.84 (2H,m,C_4-H)] in 70-75% yields, respectively. Both of them were also obtained on sodium borohydride reduction of 4a and 4b.

There would be possibilities for the application of this method to the other fused benzazepine derivatives.

References

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6) On the nmr spectra of compounds 1b-5b, the "CH_3" singlet and the "furan-H" singlet are broadened by long range coupling to each other.

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8) 2a has the nmr singlet at δ 3.68 (δ 3.70 in 2b) assignable to the isolated methylene group. In the cases of 3a and 3b, this methylene signal is not observed, but instead a broad singlet due to a NH group is observed at δ 5.78 in 3a (δ 5.44 in 3b). Clearly, the presence of a NH group in 3a is also supported by its ir spectrum having an absorption maximum at 3350 cm^{-1}(ν_{max} 3340 cm^{-1} in 3b). Also, the C_4-H and the benzene-H overlap at δ 6.64 in nmr spectrum of 3a (δ 6.36 in 3b).

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