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REACTION OF SOME HETEROCYCLIC KETONES WITH ACETONITRILE IN AN ACID MEDIUM

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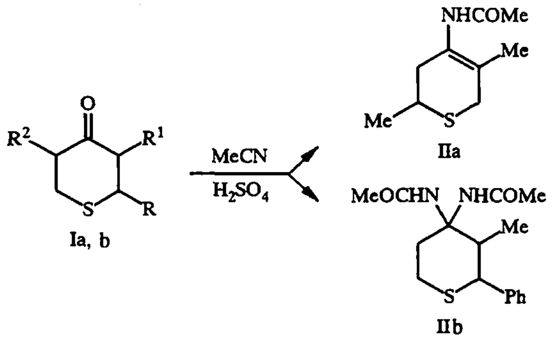
In previous work [1], we have shown that the reaction of substituted 4-piperidones with four equivalents of acetonitrile in the presence of sulfuric acid leads to the formation of the corresponding bisamides, namely, 4,4-diacetylaminopiperidines. We then undertook a study of the feasibility of obtaining bisamides from other saturated heterocyclic ketones.

We attempted to obtain bisamides by analogy with our previous procedure [1] from several tetrahydro-4-thiopyranones and tetrahydro-4-pyranones.



I, IIa R = R^2 = Me, R^1 = H; b R = Ph, R^1 = Me, R^2 = H

2,5-Dimethyl- (Ia) and 3-methyl-2-phenyltetrahydro-4-thiopyranones (Ib) were found to react with acetonitrile over 24 h at 20°C. The reaction ratio was 1:4 or 1:2. In the case of ketone Ia, extraction of the reaction mixture with hot hexane gave 4-acetylamino-3,6-dimethyl-5,6-dihydro-2H-thiopyran (IIa) in 30% yield, mp 107-108°C (from hexane). IR spectrum: ~1510 (NH def), 1630-1670 (amide C=O and C=C), ~3200 cm^{-1} (NH, stretching). PMR spectrum in $CDCl_3$: 1.28 (3H, d, 6-CH_3), 1.7 (3H, s, 3-CH_3), 2.04 (3H, s, $COCH_3$), 2.15 and 2.63 (5-CH_2), 2.92 and 3.45 (2-CH_2), 3.05 (1H, m, 6-H_a), 6.75 ppm (1H, br.s, NH), $J_{2a2e} = J_{5a5e} = 17.1$, $J_{5a6a} = 10.2$, $J_{5e6a} = 3.9$, $J_{6aCH_3} = 6.84$ Hz. Under the same conditions, ketone Ib gives a mixture of compounds. PMR spectroscopy indicated that the major component is diamide IIb. PMR spectrum in $CDCl_3$: 0.86 (3H, d, 3-CH_3), 1.99 (3H, s, $COCH_3$), 2.16 (3H, s, $COCH_3$), 2.7-3.3 (5-CH_2 and 6-CH_2), 3.82 ppm (1H, d, 2-H_a). However, attempts to isolate pure diamide IIb were unsuccessful.

The reaction of 3,5-dimethyl-2,6-diphenyltetrahydro-4-pyranone with acetonitrile in acid medium under the same conditions is accompanied by ring opening and formation of a mixture of alicyclic compounds as indicated by PMR spectroscopy. The structures of these products were not studied.

It is interesting to note that 1-acetyl-4-piperidone (III) was recovered quantitatively in all cases when we attempted to carry out the reaction of this piperidone with acetonitrile in acid medium at 20°C over 12 days and at 60°C over 2 h (the reagent ratio was 1:2 or 1:4). Thus, a reduction in basicity makes the formation of bisamides impossible even for 4-piperidones.

We attempted to convert 1-methyl-4-piperidone (IV) into the corresponding amidoketone, namely, 2-(4-acetylamino-1-methyl-4-piperidyl)-1-methyl-4-piperidone by analogy with the results of Kochetkov et al. [2], who discovered a similar reaction for cyclohexanone. However, piperidone IV does not undergo reaction under these conditions. When the piperidone –

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acetonitrile ratio was 1:4, piperidone IV was converted into 4,4-diacetylamino-1-methylpiperidine (V) [1]. We should note that using the procedure for obtaining bisamides from aldehydes proposed by Kochetkov [2], who carried out this reaction with two equivalents acetonitrile per equivalent aldehyde at 20°C over 10 days, we obtained pure bisamide V in 56% yield, mp 230-231°C. Found: C, 55.54; H, 8.62; N, 19.09%. Calculated for $C_{10}H_{19}N_3O_2$: C, 56.31; H, 8.98, N, 19.70%. PMR spectrum in $CDCl_3$: 1.93 (6H, s, $COCH_3$), 2.27 (3H, s, $N-CH_3$), 2.40 (8H, br.s, ring protons), 6.34 ppm (2H, s, NH).

Thus, the formation of bisamides from ketones is not a general reaction and depends strongly on the nature and structure of the starting compounds.

REFERENCES

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