ACYLATION AND CYCLODEHYDRATION
OF BENZOFURAN-, BENZOTHIOPHENE-, AND
INDOLYL-3-ACETIC ACID ARYLAMIDES.
SYNTHESIS OF NOVEL BENZOFURO[2,3-c]-,
BENZOTHIENO[2,3-c], AND INDOLO[2,3-c]-
PYRILIUM AND PYRIDINE DERIVATIVES

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The acylation of benzo[b]furan-, benzo[b]thiophene, and indolyl-3-acetic acid arylamides using acetic anhydride in the presence of 70% perchloric acid occurs at the α-position of the heterocycle to give 2-acetylbenzo[b]furan-, 2-acetylbenzo[b]thiophene, and 2-acetylindolyl-3-acetic acid arylamides. Depending on the amount of perchloric used in the reaction they undergo cyclodehydration to 3-arylamino-1-methylhetero[2,3-c]pyrilium salts and to N-aryl-1-methyl-3(2H)hetero[2,3-c]pyridones.

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α-Acylation and subsequent dehydration of β-oxoalkyl derivatives of aromatic and heterocyclic systems give condensed pyrilium salts [1]. This reaction has been used by us previously in the benzofuran, benzothiophene, and indole series [2-4]. The acylation and cyclodehydration of benzofuran-, benzothiophene-, and indolyl-3-acetic acid arylamides has not been studied previously. This reaction is of interest since the amides described above have two reactive nucleophilic centers (CO and NH) and hence acylation-cyclodehydration can occur by two routes to yield pyrilium salts and pyridine bases.

We have studied the acylation of the arylamides of the benzo[b]furan-3-acetic acid 1a-e, benzo[b]thiophene-3-acetic acids 2a,b, and indolyl-3-acetic acids 3a-c in the system acetic anhydride–70% perchloric acid with different perchloric acid content. The acylation takes place at the α-position of the heterocycle. The intermediately formed 2-acetylheteryl-3-acetic acid arylamides 4-6 are cyclodehydrated to the corresponding 3-arylamino-1-methylpyrilium perchlorates 7-9. We have found that the yields of the pyrilium salts 7-9 depend on the amount of perchloric acid taken in the reaction. The maximal yields for the pyrilium salt (90%) are observed with a two fold excess of perchloric acid. It was interesting to find that the NH group in the 3-arylaminopyrilium salts is not acylated, even upon prolonged holding of compounds 7-9 in the acylating mixture.
In contrast to the acylation of the benzo[b]furan-3-acetic acid arylamides 1a-e and the benzo[b]thiophene-3-acetic acid arylamides 2a, b that of the indolyl-3-acetic acid arylamides occurs with significant tarring. Since we could not prepare the corresponding pyrilium salts in the pure state, we carried out an alternative method for their synthesis consisting of the cyclization of the 2-acetylindolyl-3-acetic acid arylamides 6a-c in a mixture of acetic anhydride and 70% perchloric acid. The 2-acetylheteryl-3-acetic acid arylamides 4-6 were prepared by the reaction of the 1-methylhetero[2,3-c]pyrones 10a-c with anilines in DMF. Cyclodehydration of the keto amides 4a-e, 5a,b, 6a-c in an acylating mixture with an excess of 70% perchloric acid gave the corresponding pyrilium salts 7a-e, 8a,b, 9a-c in greater than 90% yield. The pyrilium perchlorates 7-9 synthesized by this method were identical to the pyrilium salts obtained by the acylation of the benzofuran- and benzothiophene-3-acetic acid arylamides. The structure of the 3-arylamino-1-methylpyrilium perchlorates 7-9 was confirmed using elemental analytical analysis and from their $^{1}H$ NMR spectra (Tables 1 and 2).

A study of the cyclodehydration of the keto amides 4a-e, 5a,b, 6a-c in the acylating mixture with an equivalent amount of 70% perchloric acid showed that, along with the pyrilium salts 7a-e, 8a,b, 9a-c, the reaction mixture contained the corresponding N-aryl-1-methyl-3(2H)hetero[2,3-c]pyridones 11-13. Thus a chromatographic investigation of the composition of the reaction mixture (after separation of the pyrilium salt) showed that the product of cyclodehydration of the 2-acetyl-6-methyl-(4-methylphenyl)amide of benzo[b]furan-3-acetic acid (4b) using 70% perchloric acid in acetic anhydride gave both the pyrilium salt 7b (yield 40%)