Synthesis of 3-Diaminomethylene-2(3H)-furanones by Reaction of 2-Amino-4,5-dihydro-3-furancarboxamides with Amines

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Summary. The reaction of 2-amino-4,5-dihydro-3-furancarboxamides with morpholine in the presence of acetic acid in pyridine or under the influence of ammonium acetate gave the corresponding 3-diaminomethylene-4,5-dihydro-2(3H)-furanones; 4,5-dihydro-2-morpholino-3-furancarboxamides were not isolated. One of the former reacted with benzylamine to give (E)- and (Z)-3-(amino(benzylamino)-methylene)-4,5-dihydro-4-phenyl-2(3H)-furanones and 2-benzylamino-4,5-dihydro-4-phenyl-3-furancarboxamide.

Keywords. Furancarboxamides; Furanones; Amines; Michael addition; Recyclization.

Introduction

Earlier, we have reported on the reaction of 2-amino-4,5-dihydro-3-furancarbonitriles (I) with amines such as morpholine, pyrrolidine, and piperidine to give 4,5-dihydro-2-morpholino-2-pyrrolidino and 2-piperidino-3-furancarbonitriles [1, 2]. This reaction probably occurs via Michael addition to the \(\alpha,\beta\)-unsaturated nitrile moiety of I with amine to form the intermediate adduct which undergoes elimination of ammonia to give the observed products. The reaction suggests the possibility that when 2-amino-4,5-dihydro-3-furancarboxamides 3 are treated with amines, the Michael adduct initially formed may undergo elimination of ammonia to furnish the corresponding 2-amino-4,5-dihydro-3-furancarboxamides. Thus, we have investigated the reaction of 3 with amines.

Results and Discussion

The required tetrahydro-2-oxo-4-phenyl- and -5-phenyl-3-furancarbonitriles (2a and 2b) [3, 4] were obtained by reaction of 2-amino-4,5-dihydro-4-phenyl- and -5-phenyl-3-furancarbonitriles (1a and 1b) [5] with hydrochloric acid. The starting materials 3 were prepared from 2 and concentrated ammonium hydroxide according to Ref. [6] (Scheme 1).

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When a mixture of 3a, morpholine, and acetic acid in pyridine was heated at 80°C, 3-diaminomethylene-4,5-dihydro-4-phenyl-2(3H)-furanone (4a) was obtained in 75% yield, and the expected 4,5-dihydro-2-morpholino-4-phenyl-3-furancarboxamide could not be isolated (Scheme 2). The structure of 4a was deduced from satisfactory elemental analyses and spectroscopic data. The mass spectrum and the results of elemental analyses of 4a indicate that both 4a and 3a have the same molecular composition C_{11}H_{12}N_{2}O_{2}. The IR spectrum of 4a displays a band due to a lactone carbonyl group conjugated with an enamine group [7] at 1660 cm^{-1}. Similarly, the reaction of 3b with morpholine afforded 3-diaminomethylene-4,5-dihydro-5-phenyl-2(3H)-furanone (4b). In order to confirm the structure of 4a, we carried out the reaction shown in Scheme 3. The reaction of 4a with benzoyl chloride gave 3-(amino-(benzamido)-methylene)-2(3H)-furanone 5. Hydrolysis of 5 with hydrochloric acid provided N-benzoyl-3-furancarboxamide 6 which was converted into methyl 2-oxo-4-phenyl-3-furancarboxylate 7 [8] by treatment with concentrated hydrochloric acid and methanol. The structure of 7 was confirmed by direct comparison with an authentic sample which was synthesized by the following methods: methyl 2-amino-4-phenyl-3-furancarboxylate 8 was prepared from 2a and a catalytic amount of sodium methoxide according to Ref. [9]. Hydrolysis of 8 with hydrochloric acid provided the desired compound 7.

The formation of 4 can be explained by the mechanism shown in Scheme 2. The Michael addition of morpholine to 3 gives the adduct A which undergoes recycylation to provide B. B in turn is transformed into the intermediates 11 by elimination of ammonia. The conjugated addition of ammonia to 11 produces the adduct C which undergoes elimination of morpholine to yield 4.

Subsequently, we examined the reaction of the intermediates 11 with ammonia in the presence of acetic acid in order to prove whether or not compounds 4 are formed. Compounds 11 were prepared by successive treatment of 2 with trimethylsilylmorpholine and water. The IR spectra of 11 showed a primary amino bands near 3300 cm^{-1}, but lacked a characteristic nitrile band. The reaction of 11 with ammonium acetate afforded 4 in good yields. In a similar manner, the reaction of 3 with ammonium acetate resulted in the formation of the same compounds 4. Probably, this recycilation takes place through the adduct D.

Finally, we have examined the reaction of 3a with benzylamine in order to explore the scope of this type of reaction. The reaction of 3a with benzylamine