Chemistry of Heterocyclic Compounds, Vol. 38, No. 6, 2002

N-AMINATION OF 4-PYRIMIDONES BY MESITYLENESULFONYL HYDROXYLAMINE

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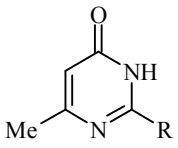
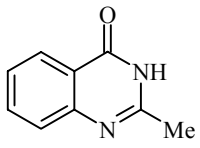
The 3-amino derivatives are formed exclusively during the amination of the anions of 6-methyl-4-pyrimidones and 2-methyl-4-quinazolone by mesitylenesulfonyl hydroxylamine.

Keywords: pyrimidones, quinazolone, N-amination.

The direct amination of nitrogen heterocycles is a convenient method for the production of heterocyclic systems containing an amino group at the annular nitrogen atom. At the same time the regioselectivity of the amination of nitrogen heterocycles by two non-equivalent nitrogen atoms has been studied comparatively little.



1a,b

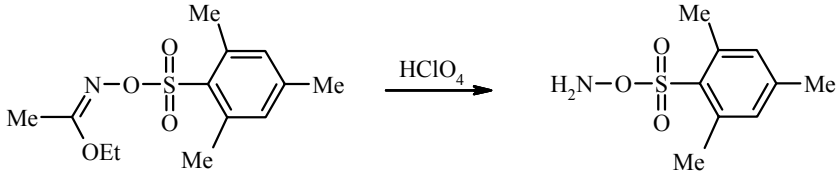


1c

1 a R = Me; **b** R = Ph

We investigated the amination of the pyrimidones **1a**,**b** and the quinazolone **1c** by mesitylenesulfonyl hydroxylamine (MSHA) [1].

According to data in [2], MSHA is explosive in the dry form. The quantity of MSHA required for amination was therefore synthesized from compound **2** just prior to use in the reaction and was not isolated in the pure form.



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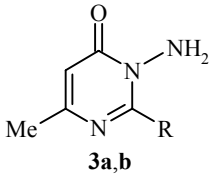
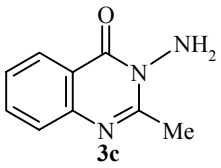
 0009-3122/02/3806-0710$27.00

Compounds **1a-c** were aminated in the form of the sodium salts in methanol at room temperature, using a twofold excess of MSHA.

In all cases the single products **3a-c** were obtained with high yields.



3a,**b**



3c

3 a R = Me; **b** R = Ph

The aminoquinazolone **3c** was identical with the known 3-amino-2-methyl-3,4-dihydro-4-quinazolone, obtained by the method in [3] from N-acetylanthranilic acid and hydrazine.

For evidence for the structure of the aminopyrimidones **3a**,**b** we used the ^{13}C NMR spectra, obtained without proton decoupling, and also the ^{13}C NMR spectra with selective proton decoupling (Fig. 1). In the downfield region of the ^{13}C NMR spectrum of the aminopyrimidone **3a** there are signals for the $C_{(6)}$, $C_{(4)}$, and $C_{(2)}$ atoms. The signal of the $C_{(6)}$ atom (162.2 ppm) in the spectrum recorded without proton decoupling (Fig. 1) is split on account of spin–spin coupling with the protons of the $C_{(6)}$–CH_3 group (6.0 Hz) and the $C_{(5)}$–H proton (1.0 Hz). The signal of the $C_{(4)}$ atom (160.6 ppm) is a multiplet as a result of coupling with the protons of the NH_2 group (1.5 Hz) and the $C_{(5)}$–H proton (2.0 Hz). The signal of the $C_{(2)}$ atom (158.6 ppm) is a multiplet on account of coupling with the protons of the NH_2 (3 Hz) and $C_{(2)}$–CH_3 (6.5 Hz) groups.

The assignment of the signals in the spectrum and the position of the amino group are confirmed by the ^{13}C NMR spectrum, recorded with selective proton decoupling of the NH_2 group (Fig. 1). In this spectrum the form of the $C_{(6)}$ signal did not change, while the form of the signals of the $C_{(2)}$ and $C_{(4)}$ atoms was significantly simplified. The signal of the $C_{(4)}$ atom is a doublet on account only of spin–spin coupling with the $C_{(5)}$–H proton, while the signal of the $C_{(2)}$ atom is a regular quartet on account only of spin–spin coupling with the protons of the $C_{(2)}$–CH_3 group. These facts indicate that the amino group is close to the $C_{(2)}$ and $C_{(4)}$ atoms and distant from the $C_{(6)}$ atom, i.e., is situated at the $N_{(3)}$ atom.

The ^{13}C NMR spectra of the aminopyrimidone **3b** look the same. The signal of the $C_{(6)}$ atom (162.6 ppm) in the spectrum recorded without proton decoupling is a multiplet on account of spin-spin coupling with the protons of the $C_{(6)}$–CH_3 group (6 Hz) and the $C_{(5)}$–H proton (1 Hz). The signal of the $C_{(4)}$ atom (161.6 ppm) is a multiplet on account of coupling with the protons of the NH_2 group (1.5 Hz) and the $C_{(5)}$–H proton (2 Hz). The signal of the $C_{(2)}$ atom (158.7 ppm) is a complex multiplet on account of coupling with the protons of the NH_2 and $C_{(2)}$–C_6H_5 groups.

In the ^{13}C NMR spectrum recorded with selective proton decoupling from the NH_2 group the form of the signal of $C_{(6)}$ did not change, while the form of the signals of the $C_{(2)}$ and $C_{(4)}$ atoms was simplified. The signal of the $C_{(4)}$ atom is a doublet on account of only spin–spin coupling with the $C_{(5)}$–H proton, while the signal of the $C_{(2)}$ atom is a multiplet on account of only spin–spin coupling with the protons of the $C_{(2)}$–C_6H_5 group. This indicates that the amino group is close to the $C_{(2)}$ and $C_{(4)}$ atoms and distant from the $C_{(6)}$ atom, i.e., is situated at the $N_{(3)}$ atom.

Thus, we established that during amination of all three investigated compounds the reaction is directed at the nitrogen atom adjacent to the carbonyl group.

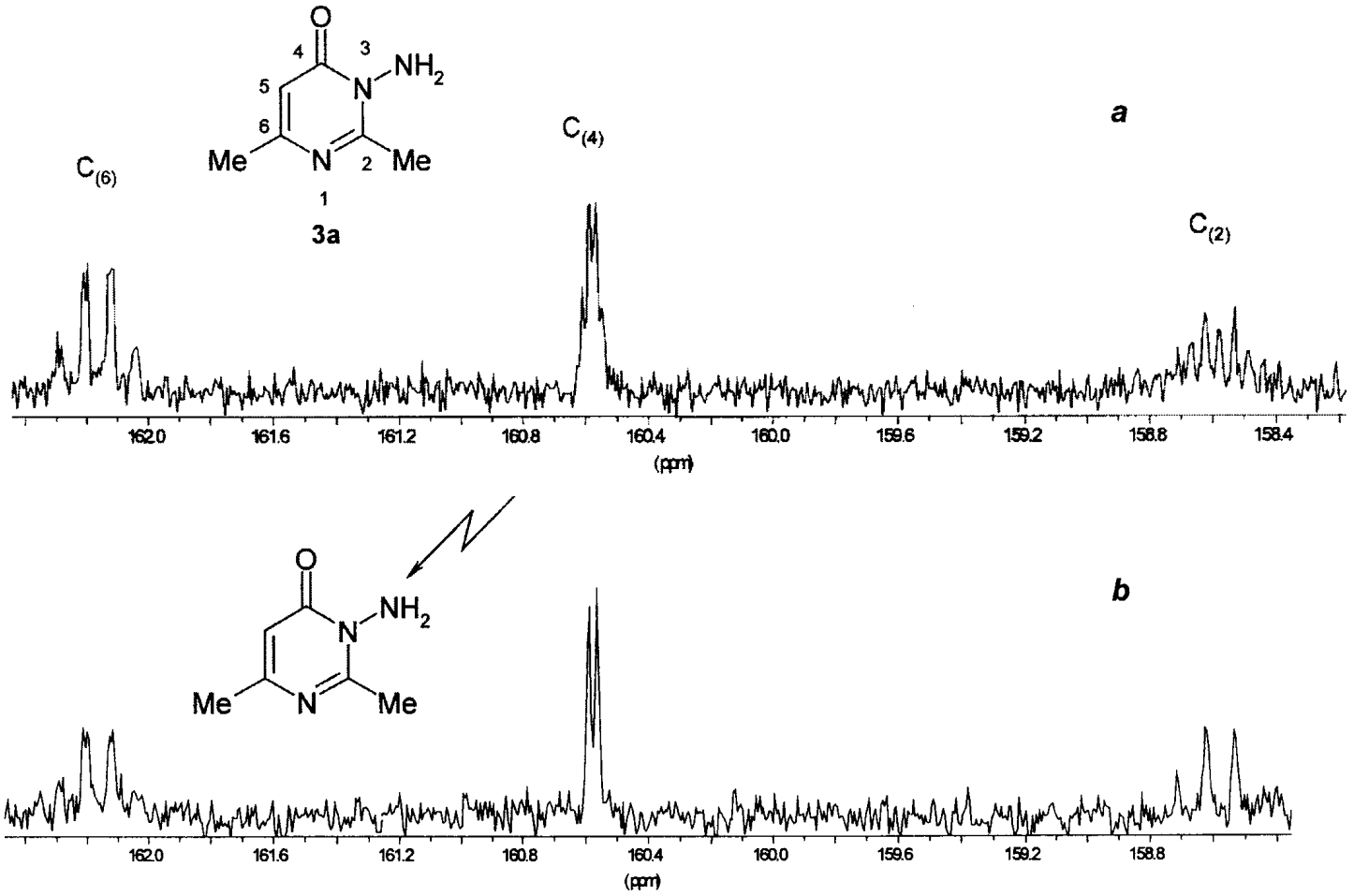


Fig. 1. The ^{13}C NMR spectrum of aminopyrimidone **3a**:
a) without proton decoupling; b) with selective proton decoupling from the NH_2 group.

EXPERIMENTAL

The NMR spectra were obtained on a Bruker DPX-300 spectrometer at 300 MHz. The solvent was DMSO-d_6.

3-Amino-2,6-dimethyl-4-pyrimidone (3a). To a solution of the pyrimidone **1a** (1.0 g, 8 mmol) in methanol (8 ml) we added sodium acetate (8 mmol) in methanol (2.1 ml) and MSHA obtained from compound **2** (2.8 g, 10 mmol). The next day the same amounts of sodium methoxide in methanol and MSHA were added to the solution. After two days the solvent was distilled, and the residue was treated with chloroform. The precipitated sodium mesitylenesulfonate was filtered off, and the filtrate was evaporated under vacuum. The solid residue was washed with ether, and 0.9 g (6.5 mmol, 80%) of 3-aminopyrimidone **3a** was obtained; mp 134°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.16 (3H, s, CH_3); 2.46 (3H, s, CH_3); 5.86 (2H, s, NH_2); 6.21 (1H, s, 5-H). Found %: C 51.79; H 6.46; N 30.31. $C_6H_9N_3O$. Calculated %: C 51.79; H 6.52; N 30.20.

3-Amino-6-methyl-2-phenyl-4-pyrimidone (3b). The compound was obtained similarly to compound **3a**. Yield 84%; mp 143°C (methanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.22 (3H, s, CH_3); 5.73 (2H, s, NH_2); 6.38 (1H, s, 5-H); 7.3-7.9 (5H, m, Ph). Found %: C 65.63; H 5.69; N 20.63. $C_{11}H_{11}N_3O$. Calculated %: C 65.66; H 5.51; N 20.88.

3-Amino-2-methyl-3,4-dihydro-4-quinazolone (3c). The compound was obtained similarly to compound **3a**. Yield 78%; mp 146°C (mp 148°C [3]).

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