**N-Quaternary Compounds. Part II.* Deuterium Labelling of Thiazolo[3,2-a]pyridinium Betaines**

TORE LÆRUM, GUNNAR ARNFINN ULSAKER and KJELL UNDHEIM

Department of Chemistry, University of Oslo, Oslo 3, Norway

Reaction between 1,1,2,2-tetrabromoethane and 3-hydroxypyridine-2-thione has yielded 2-bromo-thiazolo[3,2-a]pyridinium-8-olate. The bromo derivative allows selective deuteriation on C-2 and C-3. The $^{13}$C NMR spectra are discussed.

Simple pyridinium systems are resistant towards electrophilic substitution. The thiazolo- and dihydrothiazolo[3,2-a]pyridinium systems are activated by an 8-hydroxy group for electrophilic substitution in the pyridine ring. The thiazole ring in thiazolo[3,2-a]pyridinium-8-olates is not activated for direct electrophilic substitution thus excluding direct halogenation. We herein report a method for the synthesis of a bromo-substituted thiazole derivative. The latter also allows regioselective deuterations in the thiazole ring (Scheme 2). Deuterations in the pyridine ring have previously been reported.

* Part L, see Ref. 1.

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\[ \text{Scheme 1.} \]

in 10 % acetic acid to the 3-deutero isomer 6d.

The $^1$H NMR spectra (D$_2$O) are in accordance with structure 3a assigned to the bromo isomer. Thus H-3 (6c, $\delta$ 8.30) resonates at lower field than H-2 (6d, $\delta$ 7.94); which is the same relative order of the chemical shifts as for the thiazole protons in isomeric 2,5- and 3,5-dimethyl homologues of 6a, and therefore supports the structural assignment. A bromine substituent in benzene has little effect on the chemical shifts of the $\alpha$-protons, which is also apparent in the present series by comparison of the chemical shift for H-3 in the bromo derivative ($\delta$ 8.35) and 6c ($\delta$ 8.30).

Gated-(1) decoupled spectra were useful in the relative assignment of $^{13}$C chemical shifts (Fig. 1). The signals for C-8 and C-9 were identified by the lack of one-bond coupling and by the high chemical shifts. C-8 is long-range coupled with H-6, $^3J_{CH}$ 8.6 Hz. The meta coupling for C-9 to H-7 was not resolved in agreement with previous observation that pyridines without the lone pair of electrons are poorly resolved, which has been attributed to $^{14}$N-$^{13}$C couplings.

Similarly the signals from the $\alpha$-carbons in the pyridine ring in dihydrothiazolo[3,2-$\alpha$]pyridine derivatives are unresolved. C-7 is meta coupled to H-5, $^3J_{CH}$ 7.2 Hz, and C-6 is ortho coupled to H-5, $^3J_{CH}$ 4.2 Hz. The size of the latter coupling corresponds closely to the values (ca. 4 Hz) reported for $^3J_{CH}$ in other pyridinium-olates. The ortho couplings between the $\beta$, $\gamma$-positions in the pyridine ring were too small to be seen under the recording conditions.

The one-bond carbon-hydrogen coupling $^1J_{CH}$ is highest for the $\alpha$-carbons on pyridines, and is further increased on protonation or quaternisation. The broad signals with $^1J_{CH}$ ca. 200 Hz can therefore be assigned to C-3 and

Fig. 1. $^{13}$C NMR spectral data.
C-5. Further differentiation, besides the magnitude of the long range couplings, follows from comparison with the spectra of the 2- and 3-deutero derivatives 6c and 6d. The relative chemical shifts of C-2 and C-3 follow the order in thiazole itself. The increase Jca 10 Hz in the one-bond coupling can perhaps be compared with the increase JCH for the α-carbons in pyridine when the heteroatom carries a positive charge as discussed above. The increase in JCH for both C-2 and C-3 may indicate that both heteroatoms in the thiazole ring in δ are partially charged. The ortho coupling for C-2 JCH 9.8 Hz is considerably less than the corresponding coupling ca. 16 Hz in thiazole, and is reminiscent of the decrease in JCH between C-α and H-β in pyridines when the heteroatom is charged. The ortho coupling JCH 7.2 Hz for C-3, however, corresponds closely to the corresponding coupling in thiazole. The effect on the chemical shifts of the bromine atom in 3a is almost as in the corresponding 5-bromothiazole, viz. ca. 10 ppm shielding at C-2 and ca. 1 ppm deshielding at C-3.

EXPERIMENTAL

1H NMR spectra were recorded in D2O on a 60 MHz spectrometer. The 13C NMR spectra were recorded in D2O (1.5–2.0 g in 2 ml) by means of a Yeol FX60 Fourier transform spectrometer operating at 25.2 MHz. The temperature was ca. 30 °C. Proton-noise decoupled and gated-(1) decoupled spectra were obtained. The shifts are related to TMS.

2-Bromo-3-hydroxythiazolo[3,2-a]pyridinium fluoroaborate 3a-HEBF4. A mixture of 3-hydroxy-2-thione (1.27 g, 0.01 mol), 1,1,2,2-tetramethylethane (20 ml) and potassium carbonate (6.0 g) in DMF (100 ml) was stirred at room temperature. The progress of the reaction was monitored by TLC. (Silica gel; n-BuOH: EtOH: NH3 1:1:1). At 4-day intervals, further additions of 1,1,2,2-tetramethylethane (10 ml) and potassium carbonate (3.0 g) were carried out. All the pyridine-2-thione had been consumed after 20 days. The reaction mixture was then filtered and the filtrate diluted with water (200 ml) and extracted with chloroform (2x50 ml). The aqueous solution was next passed over a strong cation exchanger (Amberlite IR-120 (H+)); the salts were washed out with water and the bromo derivative 3a eluted withaq. 0.3 M ammonia, yield 0.40 g (17%). For elemental analysis the product was converted to its hydrofluoroborate by addition of boronfluoric acid in ether to a methanolic solu-

REFERENCES

5. Ref. 4, p. 236.

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