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HALOCYCLIZATION OF 2-ALLYLTHIOPYRIDINE

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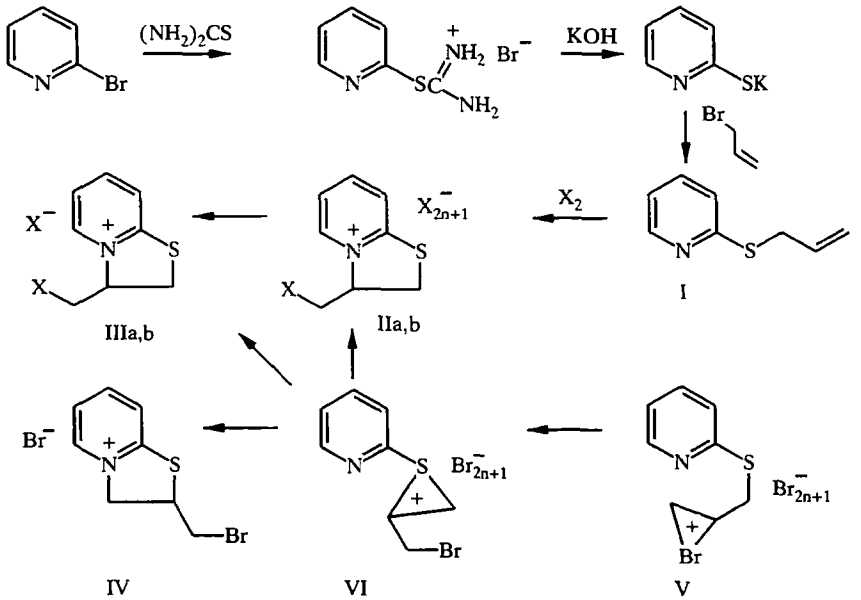
2-Allylthiopyridine reacts with iodine to form 3-iodomethyl-2,3-dihydrothiazolo[3,2-a]pyridinium triiodide, but in reaction with bromine a mixture of 3- and 2-bromomethyl-2,3-dihydrothiazolo[3,2-a]pyridinium bromides is obtained.

Substituted 2-allylthiopyridines (I) have been demonstrated [1-4] to react with bromine and iodine to form dihydrothiazolo[3,2-*a*]pyridinium systems. In the present work, new results on the halogenation of the unsubstituted allyl sulfide I are presented [5].

The sulfide I was prepared by the reaction of 2-bromopyridine with thiourea, KOH, and allyl bromide, the intermediates 2-pyridylisothiuronium bromide and 2-pyridinethione being not isolated (single-pot synthesis).

Reaction of I with excess of iodine produces 3-iodomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium triiodide (IIa), which reacts with NaI or with allyl sulfide I to form 3-iodomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium iodide (IIIa). If the reagents are used in equimolar ratio, a mixture of IIa and IIIa is formed; along with increase of the duration of the reaction the yield of triiodide IIa decreases and that of iodide IIIa increases. This suggests that iodide IIIa is formed by reaction of triiodide IIa with allyl sulfide I and that iodocyclization occurs through the iodonium cation, the counter ion of which is triiodide anion.



II a X = I, n = 1, b X = Br, n = 0; III a X = I, b X = Br

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In contrast to iodine, bromine reacts with allyl sulfide I to give a mixture of 3- (IIIb) and 2-bromomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium (IV) bromides. Bromides IIIb and IV were identified by comparing their PMR spectra with those of iodide IIIa and bromide IV prepared by bromocyclization of 1-allyl-2-pyridinethione. For bromide IIIb, like for iodide IIIa, the signals of the 3-H proton are observed at weaker field (6.0 ppm) than those of SCH_2 and CH_2Br (3.8-4.4 ppm). However, for bromide IV the signals of NCH_2 protons are at weaker field (5.20 ppm) than those of 2-H (4.7 ppm) and CH_2Br (3.95 ppm).

Apparently bromocyclization of sulfide I occurs through bromonium ion V, which isomerizes into the thiiranium ion VI. At intramolecular nucleophilic attack of the nitrogen atom on the tertiary carbon atom IIIb is formed; at the attack on the secondary carbon atom, bromide IV is obtained.

EXPERIMENTAL

IR spectra were recorded on a Specord IR-75 spectrometer in vaseline oil. PMR spectra of I were taken on a Tesla spectrometer (80 MHz); of II-IV, on a Tesla (100 MHz) spectrometer; of a mixture of IIIb and IV, on a Bruker (250 MHz) spectrometer. The internal standard was TMS.

2-Allylthiopyridine (I). Mixture of thiourea (7.6 g, 0.1 mol), ethanol (50 ml), and 2-bromopyridine (15.8 g, 0.1 mol) was boiled for 2 h. Solution of KOH (16.8 g, 0.3 mol) in water (30 ml) was added. Allyl bromide (12.6 g, 0.1 mol) was added over 10 min. Boiling was continued for 2 h. Solvent was distilled *in vacuo*. The residue was extracted with $CHCl_3$ and dried over $CaCl_2$. Chloroform was distilled off. The oil was distilled *in vacuo*. Yield 10.92 g (72%) of sulfide I; bp 107-108°C (1333 Pa), n_D^{20} 1.5819. According to [6] bp 85-87°C (399 Pa), n_D^{20} 1.5811. IR spectrum: 1640 (C=C), 1580, 1550, 1460 cm^{-1} (ring). PMR spectrum in CCl_4: 3.80 (2H, d, SCH_2), 5.15 (2H, m, $=CH_2$), 5.95 (1H, m, CH=), 6.9-7.5 (3H, m, 3-, 4-, and 5-H), 8.35 ppm (1H, m, 6-H).

3-Iodomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium Triiodide (IIa). Solution of 2-allylthiopyridine (0.60 g, 4 mmol) in 5 ml of propan-2-ol (ethanol) was treated under stirring with solution of iodine (1.93 g, 8 mmol) in 25 ml of propan-2-ol (ethanol). After 24 h a precipitate formed. It was filtered off, dissolved in acetone, and reprecipitated with ether. Yield 2.47 g (94%) of IIa; mp 78°C (dec.). IR spectrum: 1450, 1540, 1580 cm^{-1} (ring). PMR spectrum in $(CD_3)_2CO$: 3.85-4.55 (4H, m, CH_2I, SCH_2), 5.95 (1H, m, 3-H), 7.93 (1H, m, 6-H), 8.22 (1H, m, 8-H), 8.53 (1H, m, 7-H), 9.14 ppm (1H, d, J = 6.1 Hz, 5-H). Found, %: S 4.68; I 77.35. $C_8H_9I_4NS$. Calculated, %: S 4.87; I 77.05.

3-Iodomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium Iodide (IIIa). A. Solution of triiodide IIa (0.66 g, 1 mmol) in acetone (5 ml) was treated with solution of $NaI \cdot 2H_2O$ (0.38 g, 2 mmol) in acetone (10 ml). Precipitate of iodide IIIa formed immediately. Yield 0.38 g (94%); mp 151°C (dec.).

B. Solution of triiodide IIa (0.17 g, 0.25 mmol) in acetone (5 ml) was treated with solution of sulfide I (0.11 g, 0.75 mmol) and left for 24 h. Yield 0.15 g (75%) of iodide IIIa.

C. Solution of sulfide I (0.30 g, 2 mmol) in acetone (5 ml) was treated with solution of iodine (0.5 g, 2 mmol) in acetone (7 ml). After 3 h solution of $NaI \cdot 2H_2O$ (0.19 g, 1 mmol) in acetone (7 ml) was added. Yield 0.52 g (64%) of iodide IIIa.

PMR spectrum in DMSO-d_6: 3.5-4.4 (4H, m, SCH_2, CH_2I), 5.70 (1H, m, 3-H), 7.7-8.5 (3H, m, 6-, 7-, and 8-H), 9.03 ppm (1H, d, J = 6.2 Hz, 5-H). Found, %: S 7.81; I 62.85. $C_8H_9I_2NS$. Calculated, %: S 7.92; I 62.66.

2-Bromomethyl-2,3-dihydrothiazolo[3,2-a]pyridinium Bromide (IV). Solution of 1-allyl-2-pyridinethione (0.151 g, 1 mmol) in CCl_4 (7 ml) was treated under stirring with solution of bromine (0.055 ml, 1 mmol) in CCl_4 (7 ml). The precipitate formed was washed with acetone. Yield 0.12 g (38%); mp 162°C. PMR spectrum in DMSO-d_6: 3.95 (2H, m, CH_2Br), 4.76 (1H, m, 2-H), 5.20 (2H, m, NCH_2), 7.78 (1H, m, 6-H), 8.15-8.45 (2H, m, 7- and 8-H), 8.99 ppm (1H, d, 5-H). Found, %: S 10.35; Br 51.21. $C_8H_9Br_2NS$. Calculated, %: S 10.31; Br 51.39.

3-Bromomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium (IIIb) and 2-Bromomethyl-2,3-dihydrothiazolo[3,2-a]pyridinium (IV) Bromides. Solution of sulfide I (0.30 g, 2 mmol) in 5 ml of $CHCl_3$ (CCl_4) was treated at 5°C with solution of bromine (0.11 ml, 2 mmol) in 10 ml of $CHCl_3$ (CCl_4). The separated oil was washed with acetone and crystallized from propan-2-ol. IR spectrum: 1470, 1550, 1600 cm^{-1} (ring). PMR spectrum in

DMSO-d_6: (bromide IIIb) 3.8-4.4 (4H, m, SCH_2, CH_2Br), 6.01 (1H, m, 3-H), 7.70 (1H, m, 6-H), 8.15-8.45 (2H, m, 7- and 8-H), 9.10 ppm (1H, d. d, 5-H); (bromide IV) 3.95 (2H, m, CH_2Br), 4.75 (1H, m, 2-H), 5.22 (2H, m, NCH_2), 7.70 (1H, m, 6-H), 8.15-8.45 (2H, m, 7- and 8-H), 9.10 ppm (1H, d. d, 5-H). Found, %: S 10.12; Br 51.45. $C_8H_9Br_2NS$. Calculated, %: S 10.31; Br 51.39.

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