Addition of bromine to 2-methyl-2-azabicyclo[2.2.1]hept-5-ene

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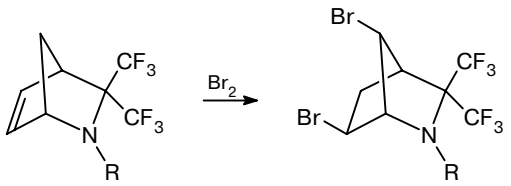
Addition of bromine to 2-methyl-2-azabicyclo[2.2.1]hept-5-ene was studied. Unexpectedly, 3-bromo-1-methyl-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane tribromide was isolated rather than the product of bromine addition to the double bond. The former reacted with the starting alkene in a polar solvent to form the corresponding monobromide.

Key words: azabicycloheptenes, bromination; azoniatricycloheptanes; aziridines; quaternary ammonium bases.

It is known[1—3] that azabicyclo[2.2.1]heptane derivatives exhibit biological activities. Hence, a search for procedures for the introduction of new functional groups into this nitrogen-containing bicycle has attracted considerable interest. One of such approaches involves functionalization of the double bond in azabicyclo[2.2.1]heptenes.

Electrophilic addition of halogenating reagents to 2-azabicyclo[2.2.1]hept-5-enes gives rise to rearrangement products[4,5] (Scheme 1).

Scheme 1



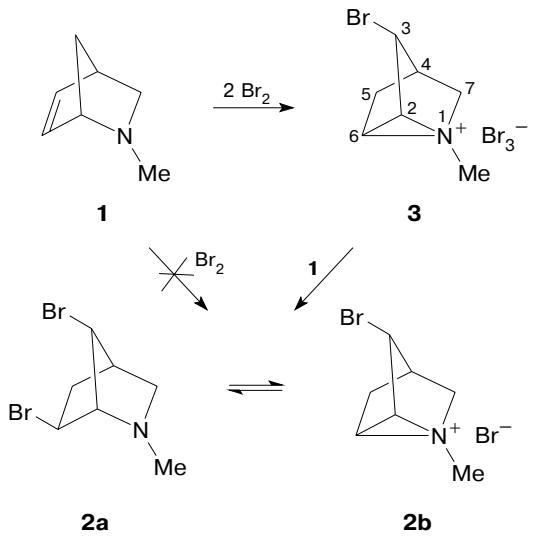
R = H, COOMe, Ts

The reactions of *N*-alkyl-substituted derivatives with electrophilic reagents have not yet been studied.

An attempt to perform the reaction of bromine with 2-methyl-2-azabicyclo[2.2.1]hept-5-ene (**1**) did not afford the expected addition product **2**. However, an orange precipitate of 3-bromo-1-methyl-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane tribromide (**3**) was obtained upon the addition of a twofold excess of Br_2 in CCl_4 to the reaction mixture. The precipitate was stable upon storage (Scheme 2).

The ^{1}H NMR spectral pattern of compound **3** counts in favor of the fact that it has the structure of the quaternary ammonium salt. Thus, the signals of the H(2) and H(6) protons in the ^{1}H NMR spectrum represent an AB system with the spin-spin coupling constant of 4.4 Hz. To the contrary, the signal of the H(4) proton occurs as a broadened singlet.

Scheme 2



The unexpected stability of the resulting aziridinium derivative made it possible to use it in the synthesis of the target dibromide **2**. We found that the reaction mixture was decolorized upon addition of a solution of the initial alkene **1** to compound **3** in a polar solvent. After removal of the solvent *in vacuo*, product **2** was isolated as a white powder, which gradually decomposed in air.

The ^{1}H NMR spectrum of compound **2** contains a set of signals virtually identical with that of compound **3**. This suggests that dibromide **2** in solution also exists as quaternary ammonium salt **2b**. Its instability can be attributed to the fact that the bromide ion, which is not involved in the complex Br_3^- anion, causes the shift of the equilibrium between the covalent and ionic forms to the left (see Scheme 2). Covalent form **2a** (tertiary amine) acts as a base and leads to elimination of HBr from the salt-like form of compound **2b**. The resulting

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alkene is unstable and either undergoes polymerization or is oxidized by atmospheric oxygen.

An attempt to perform the reaction of the initial alkene **1** with one equivalent of bromine in a polar solvent bypassing the stage of formation of compound **3** did not allow us to isolate compound **2b** in the pure form. In this case, the latter contained an admixture of tribromide **3**. Apparently, monobromide **2** in a polar solvent exists in the equilibrium with a mixture of tribromide **3** and the initial alkene **1**.

To summarize, the addition of bromine to 2-methyl-2-azabicyclo[2.2.1]hept-5-ene affords 3-bromo-1-methyl-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane tribromide in 100% yield. The reaction of the latter with the starting alkene gives rise to the corresponding monobromide.

Experimental

The ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Varian VXR-400 spectrometer; the chemical shifts are given relative to HMDS (δ 0.05).

2-Methyl-2-azabicyclo[2.2.1]hept-5-ene (1) was synthesized from a mixture of freshly distilled cyclopentadiene (6.6 g, 100 mmol), $MeNH_2 \cdot HCl$ (8.8 g, 130 mmol), and a formaldehyde solution (13 mL; 30 %, 130 mmoles of CH_2O) according to a procedure reported previously.[6] The yield was 8.53 g (78%), b.p. 37 °C (60 Torr), n_D^{24} 1.4473. ^{1}H NMR ($CDCl_3$), δ: 1.33 (dd, 1 H, *endo*-H(3), J_1 = 1.6 Hz, J_2 = 8.4 Hz); 1.36 (ddd, 1 H, *syn*-H(7), J_1 = 1.6 Hz, J_2 = 3.0 Hz, J_3 = 8.0 Hz); 1.56 (ddd, 1 H, *anti*-H(7), J_1 = 1.6 Hz, J_2 = 1.6 Hz, J_3 = 8.0 Hz); 2.15 (s, 3 H, Me); 2.86 (m, 1 H, H(4)); 3.12 (dd, 1 H, *exo*-H(3), J_1 = 3.0 Hz, J_2 = 8.4 Hz); 3.70 (dd, 1 H, H(1), J_1 = 1.6 Hz, J_2 = 3.0 Hz); 6.00 (dd, 1 H, H(5), J_1 = 2.1 Hz, J_2 = 5.7 Hz); 6.29 (ddd, 1 H, H(6), J_1 = 1.1 Hz, J_2 = 3.0 Hz, J_3 = 5.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 40.6 (C(4)), 43.9 (Me), 48.2 (C(7)), 52.9 (C(3)), 65.6 (C(1)), 130.1 (C(5)), 136.0 (C(6)).

3-Bromo-1-methyl-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane tribromide (3). A solution of Br_2 (3.1 mL, 60 mmol) in CCl_4 (10 mL) was added dropwise with vigorous stirring to a solution of compound **1** (3.27 g, 30 mmol) in dry CCl_4 (30 mL; distilled over P_4O_{10}) at −20 °C. Then the reaction mixture was warmed to ~20 °C. The orange precipitate that formed was filtered off and dried in a desiccator. The yield was 12.8 g (100%), m.p. 117 °C (from 95% EtOH). ^{1}H NMR (CD_3CN), δ: 2.31 (d, 1 H, *syn*-H(5), J = 13.2 Hz); 2.39 (d, 1 H, *anti*-H(5), J = 13.2 Hz); 2.89 (br.s, 1 H, H(4)); 3.21 (s, 3 H, Me); 3.24 (dd, 1 H, *endo*-H(7), J_1 = 1.5 Hz, J_2 = 9.6 Hz); 3.33 (d, 1 H, *exo*-H(7), J = 9.6 Hz); 3.95 (dd, 1 H, H(6), J_1 = 1.5 Hz, J_2 = 4.4 Hz); 4.03 (dd, 1 H, H(2), J_1 = 1.5 Hz, J_2 = 4.4 Hz); 4.49 (dd, 1 H, H(3), J_1 = J_2 = 1.5 Hz). ^{13}C NMR (CD_3CN), δ: 31.0 (Me), 38.4 (C(7)), 40.1 (C(5)), 45.1 (C(4)), 48.0 (C(2)), 48.6 (C(6)), 58.0 (C(3)). Found (%): C, 19.72; H, 2.35; N, 3.04. $C_7H_{11}Br_4N$. Calculated (%): C, 19.61; H, 2.59; N, 3.27.

3-Bromo-1-methyl-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane bromide (2b). A solution of compound **1** (0.55 g, 5 mmol) in MeCN (10 mL) was added dropwise with stirring and cooling with ice to a solution of compound **3** (2.15 g, 5 mmol) in MeCN (20 mL). The solvent was removed *in vacuo*. The yield was 2.70 g (100%), m.p. 128—130 °C. ^{1}H NMR ($CDCl_3$), δ: 2.51 (br.s, 2 H, H(5)); 2.87 (br.s, 1 H, H(4)); 3.51 (d, 1 H, *endo*-H(7), J = 9.1 Hz); 3.68 (s, 3 H, Me); 3.98 (d, 1 H, *exo*-H(7), J = 9.1 Hz); 4.32 (d, 1 H, H(6), J = 4.3 Hz); 4.42 (dd, 1 H, H(2), J_1 = 1.6 Hz, J_2 = 4.3 Hz); 4.90 (dd, 1 H, H(3), J_1 = 1.6 Hz, J_2 = 1.6 Hz).

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