REACTIONS OF 5-METHYLPHENANTHRIDINIUM IODIDE WITH NUCLEOPHILES AND REACTION PRODUCTS CONVERSION

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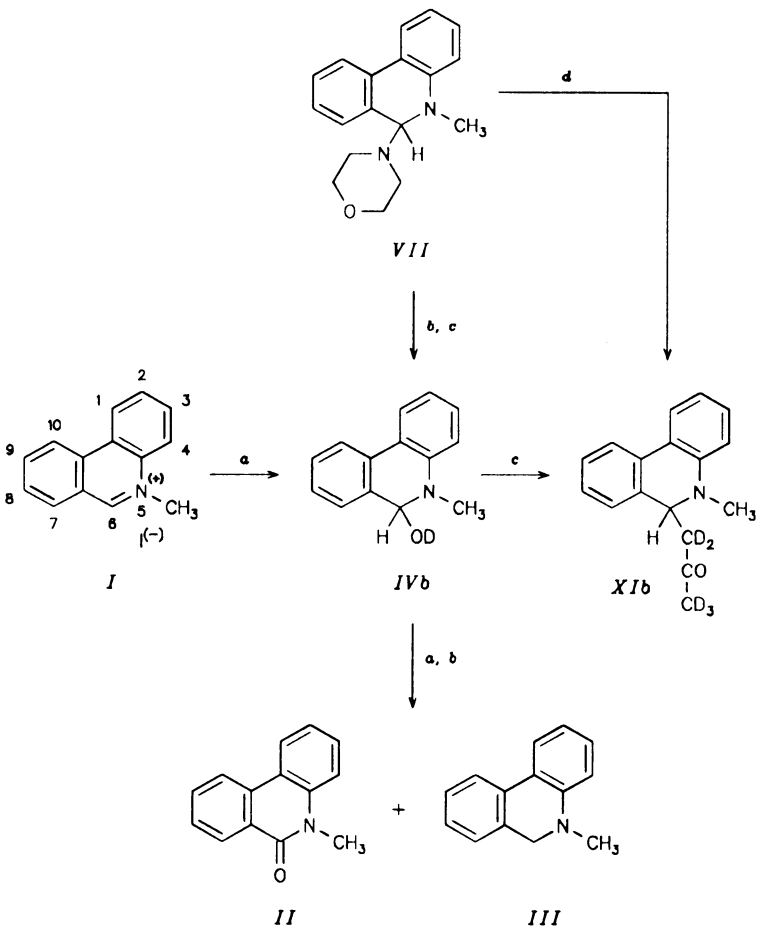
Reactions of 5-methylphenanthridinium iodide (*I*) with oxygen, nitrogen, and carbon nucleophiles, respectively, were studied. 5-Methylphenanthridinium iodide (*I*) yielded in the basic aqueous medium 5-methyl-6-phenanthridone (*II*) and 5,6-dihydro-5-methylphenanthridine (*III*). By NMR spectroscopy in the D_2O–CD_3CN solution 5,6-dihydro-6-deuteroxy-5-methylphenanthridine (*IVb*) (pseudobase) was observed as an immediate unstable product. 5-Methylphenanthridinium iodide (*I*) gave the corresponding adducts with methoxide and ethoxide anions, morpholine, piperidine, pyrrolidine, cyanide anion and acetone. Their structure was determined by IR, ^1H and ^{13}C NMR spectroscopy. Reactions of 5,6-dihydro-5-methyl-6-morpholinophenanthridine (*VII*) were followed by NMR spectroscopy. Morpholino adduct *VII* gave in the CD_3CN–D_2O solution pseudobase *IVb* and its products of disproportionation: oxophenanthridine *II* and dihydrophenanthridine *III*. Treatment of 5,6-dihydro-5-methyl-6-morpholinophenanthridine (*VII*) with H_2O/D_2O in $(CH_3)_2CO/(CD_3)_2CO$ led to CH_3COCH_2–/CD_3COCD_2– adduct *XIa/XIb* formation, respectively.

Quaternary N-alkylisoquinolinium, quinolinium salts and their fused benzoderivatives display a considerable sensitivity towards nucleophilic attack in the position α or γ to the heteroatom unless it is occupied. Reactions of these quaternary heterocycles with hydroxide anion are denoted as pseudobase formation[1]. Reaction of quaternary benzo[*c*]phenanthridine alkaloids with hydroxide is mostly used to isolate the alkaloids from plant extracts. Pseudobases of these alkaloids were characterized partially only but their structure has not been fully established up to now[2]. Our aim was to study similar reactions on a simpler system: 5-methylphenanthridinium cation (*I*).

It is known for a long time from literature[3] that 5-methylphenanthridinium iodide (*I*) gives two products under hydroxide ion action: 5-methyl-6-phenanthridone (*II*) and 5,6-dihydro-5-methylphenanthridine (*III*). The primary hydroxy adduct (pseudobase) *IVa* is probably disproportionating. The mechanism of these conversions is compared to the Cannizzaro reaction[4].

So far, 5,6-dihydro-6-hydroxy-5-methylphenanthridine (*IVa*) has not been described as a chemical individuum, only UV spectra[5] and fluorescence spectra[6] of 5-methylphe-

nanthridinium iodide (*I*) in dependence upon pH have been published. In ref.[7] the picrate of pseudobase *IVa* is mentioned with m.p. 234 °C. This information is rather unreliable as the compound *IVa* cannot likely exist in a strong acid solution (picric acid, pK_a



a NaOD, D_2O, CD_3CN; **b** D_2O, CD_3CN; **c** D_2O, $(CD_3)_2CO$; **d** $(CD_3)_2CO$, morpholine

SCHEME 1

= 0.4). Moreover, in ref.[8] 5-methylphenanthridinium picrate is described with the identical m.p. 234 °C.

EXPERIMENTAL

Melting points were determined on a Mettler FP 51 apparatus and are uncorrected. IR spectra were recorded on a Unicam SP 1000 spectrophotometer (wavenumbers in cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker WP 80 SY (80/20 MHz) and a Tesla BS 567 (100/25 MHz) spectrometers in $(CD_3)_2CO$ unless indicated otherwise. The chemical shifts measured in $(CD_3)_2CO$ were referred to the solvent signal. For other solvents TMS was used as an internal standard. Chemical shifts are in ppm, coupling constants (J) in Hz. Mass spectra were recorded on a Varian Mat 445 spectrometer. TLC was performed on Silufol plates (Kavalier, Votice) in ether–cyclohexane 1 : 1 (v/v) and detected in UV light (254 nm). Preparative column chromatography was performed on Silikagel L 5 – 40 μm (Lachema, Brno) with nitrogen overpressure (0.1 MPa). Phenanthridine was product of Janssen Chimica (Belgium). Potassium cyanide was finely powdered, triturated several times with absolute ethanol and dried in vacuo at 40 °C. Organic solvents were dried prior to use.

5-Methylphenanthridinium Iodide (*I*)

Phenanthridine (1.0 g; 5.58 mmol) was dissolved in chloroform with approximately 10% molar excess of iodomethane (0.4 ml; 6.42 mmol). The mixture was refluxed for 3 – 4 h. On cooling the quaternary salt crystallized out. Product was recrystallized from chloroform (1.70 g; 95%). M.p. 205.5 – 206.5 °C. IR spectrum (KBr): 3 030, 3 000 (Ar–H); 1 625 (C=N^+); 1 575, 1 530, 1 510 (C=C); 1 460, 1 340, 1 260, 1 165, 1 030, 755. ^1H NMR spectrum ($(CD_3)_2SO$): 4.68 s, 3 H ($N–CH_3$); 8.11 – 9.19 m, 8 H (arom.); 10.31 s, 1 H (H-6). ^{13}C NMR spectrum ($(CD_3)_2SO$): 44.80 ($N–CH_3$), 154.70 (C-6), 118.76, 122.04, 123.59, 129.13, 129.27, 130.84, 131.50, 136.77 (C–H arom.); 122.48, 124.43, 133.03, 133.35 (Cq arom.).

Reaction of *I* with KOH

5-Methylphenanthridinium iodide (*I*) (3.5 g; 10.89 mmol) was dissolved in water and a concentrated solution of KOH (2.0 g; 36.29 mmol) was added dropwise. A milk-like mixture was extracted with ether, organic layer was dried with Na_2SO_4 and evaporated in vacuo. The residue was dissolved in a chloroform–cyclohexane 2 : 1 mixture and separated on a column of silica gel (20 g). Elution was performed with the same solvent mixture. The first fractions afforded 5,6-dihydro-5-methylphenanthridine (*III*) as a slightly yellowish syrup (0.5 g; 47%). The following fractions gave 5-methyl-6-phenanthridone (*II*), that was crystallized from cyclohexane (0.6 g; 53%).

5-Methyl-6-phenanthridone (II): M.p. 110 – 111 °C (cyclohexane). IR spectrum (KBr): 3 070, 3 030 (Ar–H); 1 650 (s, C=O); 1 615, 1 590, 1 495 (C=C); 1 445, 1 345, 1 290, 1 140, 1 100, 1 040, 1 005. ^1H NMR spectrum: 3.76 s, 3 H ($N–CH_3$); 7.41 – 8.49 m, 8 H (arom.). ^{13}C NMR spectrum: 30.10 ($N–CH_3$); 161.53 (C=O); 116.02, 122.79, 123.08, 124.12, 128.61, 129.21, 130.50, 133.20 (C–H arom.); 119.67, 126.54, 134.43, 139.10 (Cq arom.).

5,6-Dihydro-5-methylphenanthridine (III): IR spectrum (neat): 3 060, 3 030 (Ar–H); 2 960, 2 870, 2 800, 2 740 (C–H); 1 610, 1 590, 1 510 (C=C); 1 440, 1 340, 1 290, 1 210. ^1H NMR spectrum: 2.88 s, 3 H ($N–CH_3$); 4.18 s, 2 H (CH_2); 6.73 – 7.78 m, 8 H (arom.). ^{13}C NMR spectrum: 38.43 ($N–CH_3$); 55.06 (CH_2); 112.90, 118.96, 122.71, 123.89, 126.28, 127.53, 128.17, 129.70 (C–H arom.); 123.60, 132.70, 133.88, 147.97 (Cq arom.).

Spectra were identical with *III* prepared by reduction of 5-methylphenanthridinium iodide (*I*) with sodium borohydride[9].

5,6-Dihydro-6-deuteroxy-5-methylphenanthridine (*IVb*)

Quaternary iodide *I* (28 mg; 87 μmol) was dissolved in the D_2O–CD_3CN (1 : 1) solution in a NMR tube. Then NaOD (18 mg; 439 μmol) in D_2O was added and the spectrum recorded. ^1H NMR spectrum (CD_3CN–D_2O, 1 : 1): 5.85 s, 1 H (H-6); 3.20 s, 3 H (N–CH_3). ^{13}C NMR spectrum (CD_3CN–D_2O, 1 : 1): 98.73 (C-6); 39.44 (N–CH_3).

5,6-Dihydro-6-methoxy-5-methylphenanthridine (*V*)

Quaternary iodide *I* (1.5 g; 4.67 mmol) was dissolved in methanol and a solution of sodium methoxide (0.45 g; 8.33 mmol) in methanol was added dropwise. The solution promptly became colourless. Methanol was evaporated in vacuo and the rest was extracted with benzene. Filtrate was evaporated in vacuo to give a colourless syrup getting yellow in the air (0.9 g; 86%). IR spectrum (neat): 3 070, 3 040 (Ar–H); 2 960 (C–H); 1 610, 1 570, 1 510 (C=C); 1 450, 1 395, 1 310, 1 230, 1 100 (C–O–C). ^1H NMR spectrum: 2.97 s, 3 H (O–CH_3); 3.27 s (N–CH_3); 5.67 s, 1 H (H-6); 6.89 – 8.06 m, 8 H (arom.). ^{13}C NMR spectrum: 37.75 (N–CH_3); 52.41 (O–CH_3); 90.63 (C-6); 112.97, 118.65, 122.43, 123.49, 127.17, 128.42, 129.17, 129.78 (C–H arom.); 120.85, 130.20, 131.74, 143.48 (Cq arom.).

5,6-Dihydro-6-ethoxy-5-methylphenanthridine (*VI*)

Preparation analogous to *V*. Yield 65%. IR spectrum (neat): 3 060, 3 040 (Ar–H); 2 950 (C–H); 1 610, 1 570, 1 505 (C=C); 1 450, 1 390, 1 325, 1 300, 1 220, 1 110 (C–O–C). ^1H NMR spectrum: 0.87 t, 3 H (C–CH_3, J = 7.5 Hz); 3.14 s, 3 H (N–CH_3); 3.15 q, 2 H (CH_2, J = 7.5 Hz); 5.60 s, 1 H (H-6); 6.79 – 7.95 m, 8 H (arom.). ^{13}C NMR spectrum: 14.22 (C–CH_3); 36.39 (N–CH_3); 59.54 (CH_2); 88.54 (C-6); 111.79, 117.28, 121.17, 122.21, 125.91, 126.95, 127.74, 128.41 (C–H arom.); 119.71, 129.68, 130.31, 142.22 (Cq arom.).

5,6-Dihydro-5-methyl-6-morpholinophenanthridine (*VII*)

Quaternary iodide *I* (0.5 g; 1.55 mmol) was suspended in acetonitrile. The thirty-fold molar excess of morpholine (4.05 g; 46.48 mmol) was added dropwise under nitrogen atmosphere. The reaction mixture became colourless and clear. Acetonitrile and an excess of morpholine were removed in vacuo. The rest was extracted with benzene. Filtrate was evaporated in vacuo to give a solid residue. The product was crystallized from petroleum ether (0.29 g; 66%). M.p. 109 – 111 °C. IR spectrum (KBr): 3 020 (Ar–H); 2 900, 2 850, 2 810, 2 770 (C–H); 1 595, 1 490 (C=C); 1 440, 1 320, 1 290, 1 205, 1 105. ^1H NMR spectrum: 2.20 – 2.50 m, 4 H (H-3′ + H-5′); 3.30 – 3.60 m, 4 H (H-2′ + H-6′); 3.22 s, 3 H (N–CH_3); 5.15 s, 1 H (H-6); 6.50 – 8.15 m, 8 H (arom.). ^{13}C NMR spectrum: 38.92 (N–CH_3); 49.20 (C-3′, C-5′); 67.53 (C-2′, C-6′); 81.19 (C-6); 112.13, 117.75, 122.26, 123.52, 127.18, 128.69, 128.94, 130.13 (C–H arom.); 121.80, 129.78, 132.68, 145.67 (Cq arom.). MS (EI-PEIU), *m/z* (%): 280 (M^+, 0.27), 209 (8.7), 195 (24), 194 (100), 179 (13), 152 (10), 97 (3.8), 87 (22), 57 (29.5), 44 (2).

5,6-Dihydro-5-methyl-6-piperidinophenanthridine (*VIII*)

Preparation analogous to *VII*. Yield 72% of a syrupy substance. IR spectrum (neat): 3 080, 3 050 (Ar–H); 2 960 s, 2 830 (C–H); 1 610, 1 570, 1 510 (C=C); 1 455, 1 375, 1 335, 1 300, 1 210, 1 160, 1 125, 1 085. ^1H NMR spectrum: 1.05 – 1.65 m, 6 H (H-3′, H-4′, H-5′); 2.10 – 2.50 m, 4 H (H-2′, H-6′); 3.17 s, 3 H (N–CH_3); 5.13 s, 1 H (H-6); 6.55 – 8.00 m, 8 H (arom.). ^{13}C NMR spectrum: 25.27 (C-4′); 27.05 (C -3′, C-5′); 38.79 (N–CH_3); 49.60 (C-2′, C-6′); 81.52 (C-6); 111.76, 117.35, 121.98, 123.31, 128.29, 128.77, 129.92 (C–H arom.); 120.78, 130.37, 132.53, 145.72 (Cq arom.).

5,6-Dihydro-5-methyl-6-pyrrolidinophenanthridine (*IX*)

Preparation analogous to *VII*. Yield 76% of a syrupy substance. IR spectrum (neat): 3 050, 3 020 (Ar–H); 2 960 s, 2 900, 2 810 (C–H); 1 605, 1 560, 1 494 (C=C); 1 440, 1 360, 1 325, 1 290, 1 215, 1 165, 1 105, 1 085. ^{1}H NMR spectrum: 1.35 – 1.55 m, 4 H (H-3′, H-4′); 2.17 – 2.40 m, 4 H (H-2′, H-5′); 3.17 s, 3 H (N–CH_3); 5.20 s, 1 H (H-6); 6.67 – 7.97 m, 8 H (arom.). ^{13}C NMR spectrum: 26.02 (C-3′, C-4′); 37.36 (N–CH_3); 47.25 (C-2′, C-5′); 60.20 (C-6); 113.87, 118.72, 123.25, 123.79, 126.64, 128.25, 128.89, 129.96 (C–H arom.); 123.15, 131.42, 136.56, 145.27 (Cq arom.).

5,6-Dihydro-6-cyano-5-methylphenanthridine (*X*)

Quaternary iodide *I* (2.0 g; 6.22 mmol) was dissolved in acetonitrile. A suspension of freshly purified KCN (0.5 g; 7.68 mmol) in acetonitrile was added dropwise. The mixture promptly became clear and discoloured. Acetonitrile was evaporated in vacuo and the rest was extracted with benzene. Filtrate was evaporated in vacuo to give a solid residue. Product was crystallized from benzene–cyclohexane (0.92 g; 67%). M.p. 119 – 121 °C. IR spectrum (KBr): 3 070, 3 030 (Ar–H); 2 900, 2 830 (C–H); 2 220 (w, CN); 1 605, 1 490 (C=C); 1 455, 1 440, 1 375, 1 360, 1 270, 1 200, 1 125, 1 090. ^{1}H NMR spectrum: 3.09 s, 3 H (N–CH_3); 5.70 s, 1 H (H-6); 6.95 – 8.00 m, 8 H (arom.). ^{13}C NMR spectrum: 37.57 (N–CH_3); 55.52 (C-6); 117.18 (CN); 114.93, 121.39, 124.07, 124.67, 127.03, 128.74, 130.56, 130.56 (C–H arom.); 123.53, 129.45, 132.20, 144.37 (Cq arom.). MS (EI-PEIU), *m/z* (%): 220 (M^+, 3.8), 210 (16.3), 209 (96), 196 (6), 195 (45.6), 194 (100), 180 (19.5), 178 (31.5), 165 (6.5), 152 (26), 139 (4.3), 104 (4.3), 97 (15), 87 (8.7), 76 (8.7), 61 (12.5).

6-Acetonyl-5,6-dihydro-5-methylphenanthridine (*XIa*)

Method A: Quaternary iodide *I* (2.0 g; 6.22 mmol) was suspended in acetone (60 ml) and a solution of K_2CO_3 (1.8 g; 13 mmol) in 2 ml of water was added. The mixture was refluxed for 3 h in nitrogen atmosphere. The yellow colouring was slowly turning pale. The colourless solution was concentrated in vacuo, extracted with benzene and dried with Na_2SO_4. Filtrate was evaporated in vacuo to give a slightly yellowish syrup (1.3 g; 83%).

Method B: Compound *VII* (0.3 g; 1.07 mmol) was dissolved in the mixture of acetone (24 g; 413 mmol) and water (0.7 g; 38.85 mmol). The mixture was kept standing under nitrogen at room temperature. After 20 days acetone was evaporated in vacuo. The residue was extracted with benzene and dried with Na_2SO_4. Filtrate was evaporated in vacuo to give a colourless syrup (0.2 g; 74%). IR spectrum (neat): 3 060, 3 020 (Ar–H); 2 940, 2 890, 2 820, 2 790 (C–H); 1 705 (s, C=O); 1 600, 1 565, 1 500 (C=C); 1 450, 1 350, 1 330, 1 300, 1 210, 1 160, 1 120, 1 090. ^{1}H NMR spectrum: 1.91 s, 3 H (CO–CH_3); 2.40 – 2.90 m, 2 H (CH_2); 2.97 s, 3 H (N–CH_3); 4.80 dd, 1 H (H-6, J = 5 Hz, J = 8 Hz), 6.60 – 7.87 m, 8 H (arom.). ^{13}C NMR spectrum ($CDCl_3$): 31.44 (CO–CH_3), 37.34 (N–CH_3); 44.63 (CH_2); 59.85 (C-6); 113.29, 118.35, 122.87, 123.32, 126.01, 127.15, 127.78, 129.32 (C–H arom.); 122.40, 130.61, 135.50, 144.31 (Cq arom.); 207.49 (C=O).

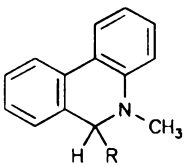
6-(1,1,3,3,3-Pentadeuterioacetonyl)-5,6-dihydro-5-methylphenanthridine (*XIb*)

^{1}H NMR spectrum: 2.96 s, 3 H (N–CH_3); 4.80 br s, 1 H (H-6); 6.60 – 7.87 m, 8 H (arom.). ^{13}C NMR spectrum: 37.19 (N–CH_3); 44.38 qi (CD_2, J = 19.4 Hz); 60.22 (C-6); 113.92, 118.78, 123.17, 123.67, 126.54, 127.60, 128.33, 129.96 (C–H arom.); 122.93, 131.21, 136.16, 145.08 (Cq arom.); carbon resonances of the CD_3 and C=O groups could not be read due to overlap with $(CD_3)_2CO$.

RESULTS AND DISCUSSION

In spite of the fact that the reaction of 5-methylphenanthridinium cation (*I*) with hydroxide is known, we have repeated it. Our results confirmed the above mentioned facts.

The reaction with hydroxide anion in aqueous solution proceeded immediately. Preparative column chromatography permitted us to obtain 5-methyl-6-phenanthridone (*II*) and 5,6-dihydro-5-methylphenanthridine (*III*) in the molar ratio close to 1 : 1. Phenanthridone *II* was in a slight excess because dihydrophenanthridine *III* is easily oxidized[10] into *II*. Phenanthridone *II* displayed the typical IR absorption of the lactam group at 1 650 cm^{-1} and in ^{13}C NMR spectrum a resonance of the C=O carbon at 161.53 ppm.



IVa : R = OH; ***IVb*** : R = OD; ***V*** : R = OCH_3;
VI : R = OCH_2CH_3; ***VII*** : R = 4–morpholinyl;
VIII : R = 1–piperidyl; ***IX*** : R = 1–pyrrolidinyl;
X : R = CN; ***XIa*** : R = CH_2COCH_3; ***XIb*** : R = CD_2COCD_3

But ^1H NMR spectroscopy enabled us to catch signals of the assumed intermediate *IV* (pseudobase) (see below).

Reactions with methoxide and ethoxide anions were carried out in absolute alcohol. The reactions proceeded quite rapidly. The products *V* and *VI* were obtained as colourless, in UV light fluorescent, syrupy substances. Both of them decomposed in the presence of air moisture to give oxo derivative *II* and dihydro derivative *III*. IR spectra of *V* and *VI* showed asymmetrical C–O–C stretching vibration bands near 1 100 cm^{-1}. ^1H NMR spectra in $(CD_3)_2CO$ contained signals of $N–CH_3$ and H-6 at 3.27 and 5.67 ppm for methoxy adduct *V* and 3.14 and 5.60 ppm for ethoxy adduct, respectively.

Reactions with morpholine, piperidine and pyrrolidine were carried out in acetonitrile using an excess of the nucleophile. The reactions also proceeded fast. 5,6-Dihydro-5-methyl-6-morpholinophenanthridine (*VII*) was obtained as a crystalline substance and was found quite stable in this form. Analogous piperidino adduct *VIII* and pyrrolidino adduct *IX* were syrupy fluorescent species. They easily decomposed in the presence of air moisture to *II* and *III*. This decomposition is clearly seen in ^1H NMR spectrum where additional signals of phenanthridone *II* (3.76; $N–CH_3$) and dihydrophenanthridine *III* (2.88, $N–CH_3$; 4.18, CH_2) start arising on standing the sample.

IR spectra of *VII*, *VIII* and *IX* contained C–H stretching vibration bands from a cyclic amine in the 2 810 – 3 000 cm^{-1} region and further C–H bending vibration bands near 1 440 cm^{-1}. In ^1H NMR spectrum one can find signals of H-6 atoms shifted higher-field (near 5.15 ppm) compared with alkoxy derivatives *V* and *VI* because of a less electronegative nitrogen atom attached to the C-6 carbon. The N–CH_3 signals of these adducts as well as of the other ones were found in a narrow range (3.17 – 3.22 ppm) and corresponded with the structure (see Experimental).

5,6-Dihydro-6-cyano-5-methylphenanthridine (*X*) was prepared with freshly purified KCN in acetonitrile. The cyano group of *X* displayed a weak band at 2 220 cm^{-1} in the triple-bond stretching region. Electron attracting N–CH_3(Ph) group attached in α-position to the cyano group reduces considerably the intensity of absorption. The H-6 signal in ^1H NMR spectrum is shifted down-field at 5.70 ppm. The ^{13}C NMR resonance of C≡N function at 117.18 ppm was within the expected nitrile range (115 – 125 ppm).

The cyano derivative *X* is stable towards nucleophilic attack of water and therefore it does not disproportionate.

Because the cyanide anion according to HSAB theory is a soft base (the other used nucleophiles are examples of hard bases) and the C-6 carbon atom of the iminium bond $C=N^+$ in compound *I* may be considered as a relatively soft acid centre then reaction product (complex) *X* of quaternary salt *I* with cyanide anion might be expected to be the most stable compound from the prepared adducts. Therefore in this case under the same conditions as for derivative *VII* (see below) no products of disproportionation were observed in the CD_3CN–D_2O solution. Thus, the stability of the adduct *X* seems to be in a good agreement with HSAB concept.

A few-hour reflux of *I* in acetone containing a base is necessary to get the acetonyl adduct *XIa*. The product was obtained as a fluorescent syrup readily decomposing to *II* and *III*. There was a typical ketone band at 1 705 cm^{-1} in IR spectrum. The ^{13}C NMR resonance of the C=O carbon was found at 207.49 ppm in deuteriochloroform.

The same acetonyl derivative *XIa* was prepared by standing the morpholino adduct *VII* in aqueous acetone at room temperature.

NMR Spectroscopy-Monitored Reactions

In order to make sure about expected unstable hydroxy adduct some reactions of the starting quaternary salt *I* and the morpholino adduct *VII* were carried out and scanned in a NMR tube. The singlets of the H-6 and N–CH_3 protons provided the good outline on proceeding conversions.

5-Methylphenanthridinium iodide (*I*) in the D_2O–CD_3CN (1 : 1) solution instantly gave with NaOD (five-fold molar excess) the deuterated pseudobase, 6-deuteroxy-5,6-dihydro-5-methylphenanthridine (*IVb*). The ^1H NMR signals of *IVb* were: a singlet of H-6 at 5.85 ppm and a singlet of N–CH_3 at 3.20 with the integral ratio 1 : 3. The value of 5.85 is the most down-field H-6 signal of the prepared derivatives because of the

strongly electronegative deuteroxy group. The calculation of this methine shift according to increments in ref.[11] resulted in 5.5 ppm. The signals belonging to the products of disproportionation i.e. 3.76 s ($N–CH_3$, phenanthridone *II*) and 4.18 s (CH_2); 2.88 s ($N–CH_3$); (integrals 2 : 3, dihydrophenanthridine *III*) appeared with the pseudobase *IVb* signals simultaneously. Within three days the signals of pseudobase *IVb* disappeared and the reaction mixture showed the signals of compounds *II* and *III* only.

The experiment confirmed hydroxy adduct (pseudobase) as an unstable product of the reaction of *I* with hydroxide anion in basic aqueous solutions (Scheme 1, path *a*).

Another spectroscopic evidence of pseudobase *IVb* was gained after addition of D_2O (twenty-fold molar excess) into a solution of morpholino adduct *VII* in CD_3CN (Scheme 1, path *b*).

The signals of deuterated pseudobase *IVb* instantly appeared in addition to the resonances of the starting adduct *VII* (3.22 s, $N–CH_3$; 5.15 s, H-6; integrals 3 : 1). Within three days the signals of *VII* and pseudobase *IVb* disappeared completely. The ^1H NMR spectrum contained only the signals of phenanthridone *II*, dihydrophenanthridine *III* and free deuterated morpholine (2.67 – 2.87 m, $CH_2–ND–CH_2$; 3.55 – 3.74 m, $CH_2–O–CH_2$). Because oxygen was supposed to be probable hydrogen/deuterium transmitter we carried out the reaction in a sealed evacuated tube. But the conversion proceeded the same way described above. When following ^{13}C NMR spectrum the signals 98.73 ppm (C–6) and 39.44 ppm ($N–CH_3$) for *IVb* were observed. Calculation of the C-6 chemical shift in *IVb* according to increments[11] led to the value of 97.10 ppm.

5,6-Dihydro-5-methyl-6-morpholinophenanthridine (*VII*) in $(CD_3)_2CO$ with D_2O (twenty-fold molar excess) yielded pseudobase *IVb*. Within two days the transient adduct *IVb* in the presence of the liberated morpholine changed into $CD_3COCD_2–$ derivative *XIb* (Scheme 1, path *c*). ^1H NMR spectrum displayed a broad singlet at 4.80 ppm belonging to the H-6 hydrogen. The ^{13}C NMR resonance of the C-6 carbon was 60.22 ppm, CD_2 signal was a quintet at 44.38 ppm, CD_3 and C=O signals were overlapped by the solvent signal.

In spite of the fact that compound *IVa/IVb* neither could be isolated nor monitored with TLC the spectroscopic measurements described above approved an existence of the pseudobase as an unstable species formed from HO^- hard base and soft acid.

Although water is a relatively weak nucleophile the C-6 carbon in *VII* is characterized with a rather significant electronic deficit. Its transformation to pseudobase *IVb* in the presence of D_2O is probably nucleophilic substitution. Similar mechanism we could expect in the reaction of acetonyl anion generated from acetone in the presence of morpholine (Scheme 1, path *d*). Such an opinion might be supported by the following experiment.

Morpholino adduct *VII* was dissolved in $(CD_3)_2CO$ and absolute morpholine (threefold molar amount) was added and the sample was allowed to stand at room tempe-

rature. Within 24 h the signals of perdeuterated acetonyl adduct *XIb* appeared. The molar ratio of *XIb* to *VII* was 1 : 3 (Scheme 1, path *d*).

In order to exclude an air moisture effect (path *c*) a reference sample was made. It contained only morpholino adduct *VII* in the same concentration in $(CD_3)_2CO$ without morpholine. No changes were observed under these conditions.

REFERENCES

1. Bunting J. W.: Adv. Heterocycl. Chem. *25*, 1 (1979).
2. Dostál J., Potáček M.: Collect. Czech. Chem. Commun. *55*, 2840 (1990).
3. Pictet A., Patry E.: Ber. Dtsch. Chem. Ges. *35*, 2534 (1902).
4. Katritzky A. R.: *Handbook of Heterocyclic Chemistry*, p. 170. Pergamon Press, Oxford 1985.
5. Bunting J. W., Meathrel W. G.: Can. J. Chem. *52*, 981 (1974).
6. Walterová D., Preininger V., Grambal F., Šimánek V., Šantavý F.: Heterocycles *14*, 597 (1980).
7. Höft E., Rieche A., Schultze H.: Justus Liebigs Ann. Chem. *697*, 181 (1966).
8. Brook P. R., Blumer F., Krishna H. J. V., Schnell S., Karrer P.: Helv. Chim. Acta *39*, 667 (1956).
9. Bunting J. W., Luscher M. A.: Can. J. Chem. *66*, 2524 (1988).
10. Karrer P., Szabo L., Krishna H. J. V., Schwyzer R.: Helv. Chim. Acta *33*, 294 (1950).
11. Pretsch E., Clerc T., Seibl J., Simon W.: *Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden*, pp. C 10, H 15. Springer, Berlin 1986.

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