Chemistry of Heterocyclic Compounds, Vol. 36, No. 1, 2000

QUATERNIZATION OF ELECTRON-DEFICIENT PYRIDINES CONTAINING TWO ELECTRON-WITHDRAWING SUBSTITUENTS

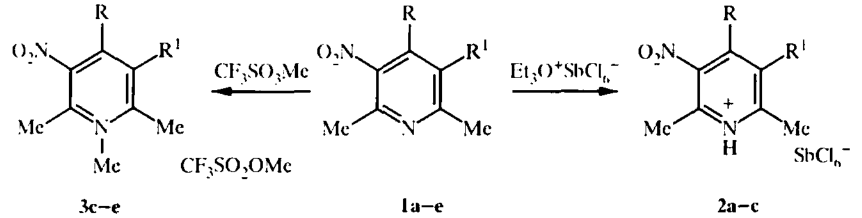
O. D. Mit'kin and M. A. Yurovskaya

Methyl triflate is an efficient agent for the quaternization of nitropyridines containing an additional electron-withdrawing substituent. When triethyloxonium hexachloroantimonate is used as the quaternizing agent, β-elimination occurs with formation of protic pyridinium salt and ethylene.

Keywords: ethoxycarbonylnitropyridines, acetylnitropyridines, cyanonitropyridines, quaternization, nitropyridinium salts.

Electron-deficient nitropyridines are quaternized by methyl iodide or dimethyl sulfate under rather vigorous conditions (at 80-100°C) [1]. Thus, the question arises on feasibility of the quaternization of nitropyridines containing additional electron-withdrawing substituents. The use of such quaternizing agents as methyl iodide or dimethyl sulfate requires elevated temperature for successful proceeding of this reaction and, thus, these agents are unsuitable in light of their thermal instability.

Oxonium salts are strong quaternizing agents [2]. We studied the quaternization of 5-ethoxycarbonyl-2,6-dimethyl-3-nitro-4-(3-nitrophenyl)pyridine (**1a**) by triethyloxonium salts. The reaction was carried out in dichloroethane in a sealed ampoule. Triethyloxonium tetrafluoroborate proved ineffective since only a slight amount of quaternary salt was present in the mixture after heating for 24 h at 100°C. The reaction proceeds over 24 h at room temperature using triethyloxonium hexachloroantimonate but leads to the formation of protic pyridinium salt **2a**. 3-Nitropyridines with a stronger electron-withdrawing substituent at $C_{(4)}$ also give protic salts upon attempted quaternization using this reagent. Thus, 2,5,6-trimethyl- (**1b**) and 4-ethoxycarbonyl-2,6-dimethyl-3-nitropyridines (**1c**) give protonated pyridines **2b** and **2c** in 34 and 52% yield, respectively. The β-elimination involving such weak bases as nitropyridines is probably facilitated by the large bulk of the hexachloroantimonate anion in the oxonium salt ion pair.



3c–e **1a–e** **2a–c**

1, 2, 3 a R = 3-$NO_2C_6H_4$, R^1 = CO_2Et; **b** R = CO_2Et, R^1 = Me; **c** R = CO_2Et, R^1 = H;
d R = C_6H_5, R^1 = CN; **e** R = 3-$NO_2C_6H_4$, R^1 = $COCH_3$

M. V. Lomonosov Moscow State University, 119899 Moscow, Russia; e-mail: yumar@org.chem.msu.su.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 53-54, January, 2000. Original article submitted March 9, 1999.

The quaternization of such pyridines was achieved using methyl triflate. 3-Nitropyridines with electron-withdrawing substituents at $C_{(4)}$ (**1b**) and $C_{(5)}$ (**1d,e**) give quaternary salts in good yield upon heating with this reagent at 100°C.

EXPERIMENTAL

The PMR spectra were taken on a Bruker AM-300 spectrometer in DMSO-d_6 with TMS as the internal standard. Starting nitropyridines **1b** and **1c** were obtained according to procedure [3], while **1a, 1d,** and **1e** were obtained according to Stradyn' et al. [4].

1-H-3-Ethoxycarbonyl-2,6-dimethyl-5-nitro-4-(3-nitrophenyl)pyridinium Hexachloroantimonate (2a). Solution of triethyloxonium hexachloroantimonate (230 mg, 0.525 mmol) in dichloroethane (2 ml) was added to solution of 3-ethoxycarbonyl-2,6-dimethyl-5-nitro-4-(3-nitrophenyl)pyridine **1a** (180 mg, 0.52 mmol) in dichloroethane (2 ml) and left for 24 h. The crystalline precipitate was filtered off and washed with dichloroethane to give 280 mg of compound **2a** (79%); mp 222-224°C. PMR spectrum: 0.90 (3H, t, $C\underline{H}_3CH_2$); 2.60, 2.63 (6H, 2s, 2-, 6-CH_3); 4.05 (2H, q, $CH_3C\underline{H}_2$); 7.79 (2H, m, 2'-, 3'-H); 8.13 (1H, d, J_m = 2 Hz, 4'-H); 8.36 ppm (1H, dt, J_o = 7.5, J_m = 2 Hz, 1'-H). Found, %: C 28.35; H 2.37; N 6.00. $C_{16}H_{16}Cl_6N_3O_6Sb$. Calculated, %: C 28.33; H 2.37; N 6.17.

1-H-4-Ethoxycarbonyl-3-nitropyridinium Hexachloroantimonates. Solution of 4-ethoxycarbonyl-3-nitropyridine **1b** or **1c** (4 mmol) and triethyloxonium hexachloroantimonate (6 mmol) in dichloroethane (6 ml) was heated in a sealed ampoule for 24 h at 100°C and then dissolved in ether (12 ml). The precipitate was washed with ether. Elemental analyses were not carried out due to admixture of chloride ion.

1-H-4-Ethoxycarbonyl-2,5,6-trimethyl-3-nitropyridinium Hexachloroantimonate (2b) was recrystallized from dichloroethane. The yield of **2b** 34%; mp 144-146°C. PMR spectrum: 1.33 (3H, t, $C\underline{H}_3CH_2$); 2.30 (3H, s, 5-CH_3); 2.58, 2.60 (6H, 2s, 2-, 6-CH_3); 4.35 ppm (2H, q, $CH_3C\underline{H}_2$).

1-H-4-Ethoxycarbonyl-2,6-dimethyl-3-nitropyridinium Hexachloroantimonate (2c) was recrystallized from ethyl acetate. The yield of **2c** 52%. PMR spectrum: 1.34 (3H, t, $C\underline{H}_3CH_2$); 2.54, 2.63 (6H, 2s, 2-, 6-CH_3); 4.35 (2H, q, $CH_3C\underline{H}_2$); 7.58 ppm (1H, s, 5-H).

1-Methylpyridinium Trifluoromethanesulfonates. Solution of corresponding 3-nitropyridine (1 mmol) and methyl triflate (1.1 mmol) in dichloroethane (3 ml) was heated in a sealed ampoule for 24 h at 100°C and then evaporated. The residue was triturated with ether. The precipitate was filtered off and washed with ether.

3-Cyano-1,2,6-trimethyl-5-nitro-4-phenylpyridinium Trifluoromethanesulfonate (3d) was obtained in 79% yield; mp 232-233°C (acetonitrile–ethyl acetate). PMR spectrum: 2.95, 3.19 (6H, 2s, 2-, 6-CH_3); 4.33 (3H, s, 1-CH_3); 7.53 (2H, d, 2'-, 6'-H); 7.70 ppm (3H, m, 3'-, 4'-, 5'-H). Found, %: C 45.92; H 3.21; N 10.22. $C_{16}H_{14}F_3N_3O_5S$. Calculated, %: C 46.05; H 3.38; N 10.07.

3-Acetyl-1,2,6-trimethyl-5-nitro-4-(3-nitrophenyl)pyridinium Trifluoromethanesulfonate (3e) was obtained in 89% yield; mp 213-214°C. PMR spectrum: 2.24 (3H, s, CH_3CO); 2.87, 2.90 (6H, 2s, 2-, 6-CH_3); 4.31 (3H, s, 1-CH_3); 7.76-8.19 ppm (4H, m, H_{arom}). Found, %: C 42.31; H 3.29; N 8.82. $C_{17}H_{16}F_3N_3O_8S$. Calculated, %: C 42.59; H 3.36; N 8.77.

4-Ethoxycarbonyl-1,2,6-trimethyl-5-nitropyridinium Trifluoromethanesulfonate (3c) was obtained in 64% yield; mp 174-175°C (ethyl acetate). PMR spectrum: 1.33 (3H, t, $C\underline{H}_3CH_2$); 2.80, 2.98 (6H, 2s, 2-, 6-CH_3); 4.20 (3H, s, 1-CH_3); 4.45 (2H, q, $CH_3C\underline{H}_2$); 8.55 ppm (1H, s, 5-H). Found, %: C 37.28; H 3.89; N 7.00. $C_{12}H_{15}F_3N_2O_7S$. Calculated, %: C 37.12; H 3.89; N 7.21.

REFERENCES

1. M. A. Yurovskaya, A. Z. Afanas'ev, S. L. Druzina, and Yu. G. Bundel', *Khim. Geterotsikl. Soedin.*, No. 6, 805 (1989).
2. H. Meerwein, *Angew. Chem.*, **67**, 374 (1955).
3. M. A. Yurovskaya and O. D. Mytkin, *Khim. Geterotsikl. Soedin.*, No. 11, 1502 (1997).
4. Ya. Stradyn', R. Gavars, L. Baumane, B. Vigante, and G. Duburs, *Khim. Geterotsikl. Soedin.*, No. 8, 1079 (1993).