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Equilibrium of Acetyl Transfer between Pyridine *N*-Oxides and Their Acetylonium Salts

V. I. Rybachenko, K. Yu. Chotii, V. V. Kovalenko, and H. Schroeder

Litvinenko Institute of Physical Organic Chemistry and Coal Chemistry, National Academy of Sciences of Ukraine, Donetsk, Ukraine

Mickiewicz University, Poznan, Poland

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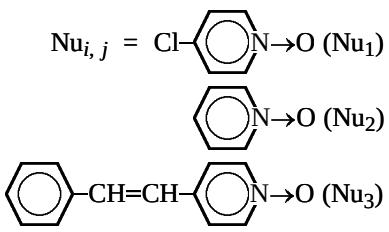
Abstract—The equilibrium constants of acetyl transfer between *O*-acetylonium salts of a series of pyridine *N*-oxides and 4-(4-dimethylaminostyryl)pyridine *N*-oxide in acetonitrile and methylene chloride were determined. The equilibrium constants correlate with the acid–base characteristics of the *N*-oxides and with the heats of reactions calculated quantum-chemically.

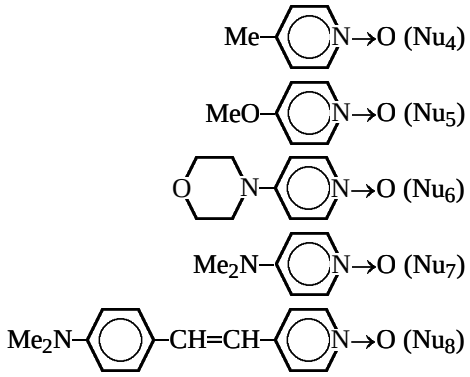
Previously we studied the kinetic characteristics of a wide range of acyl transfer reactions (1) between *N*,*O*-acylonium salts and heterocyclic bases (Acyl = AcO, MeOCO, Me_2NCO, etc.; Nu_i and Nu_j are pyridines, their *N*-oxides, etc.) [1, 2].

$$\text{Acyl–Nu}_i^+, X^- + \text{Nu}_j \overset{K}{\rightleftarrows} \text{Acyl–Nu}_j^+, X^- + \text{Nu}_i \quad (1)$$

Evidences were obtained that transfer of, in particular, acyl group in these compounds occurs by the concerted mechanism, i.e., in one stage without formation of a stable tetrahedral intermediate [3]. This fact allows such transformations to be considered as reactions similar to those of proton [4] and methyl [5] transfer, extensively studied in organic chemistry and largely controlled by the thermodynamic factor [6, 7]. For reactions (1), the values of the thermodynamic driving forces are unknown, since in the literature data on the equilibrium characteristics of such reactions are lacking, except a few values of heat [8].

In this work, using UV spectroscopy, we determined the equilibrium constants of acetyl transfer (1) in MeCN and CH_2Cl_2 at 298 K (i = 1–7, j = 8, X^- = BPh_4^-). The formulas of Nu_i and Nu_j are given below:





The choice of these pairs of nucleophiles was governed by the convenience of analysis, as 4-(4-dimethylaminostyryl)pyridine *N*-oxide (Nu_8, λ_{max} 395 nm) and its *O*-acetyl salt (λ_{max} 510 nm) have strong (ε 36 000 and 59 000 l mol^{-1} cm^{-1}, respectively) absorption bands which do not overlap with each other and with absorption bands of the other reactants. It is particularly important to determine the constants accurately, because by summing up in pairs the reactions with $Nu_i(1) \equiv Nu_j(2)$ it is possible to estimate all the elements of the 8×8 matrix (i = 1–8, j = 1–8) many of which cannot be determined by a direct experiment.

The resulting equilibrium constants are listed in Table 1. It is interesting that the values obtained for system 5 in different solvents (MeCN and CH_2Cl_2) coincide. We observed the similar trend previously when studying the heats of acyl transfer [8]. The insensitivity of the equlibrium constants to the nature of the solvent is due to the fact that the differences

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Table 1. Equilibrium constants K of acetyl transfer in MeCN (Nu_i = Nu_1–Nu_7, Nu_j = Nu_8, 298 K)

System	i	$pK_{BH^+}(Nu_i)$[a]	K	System	i	$pK_{BH^+}(Nu_i)$[a]	K
1	1	0.38	535 ± 30	5	5	2.05	$(4.5 \pm 0.3) \times 10^{-2}$
2	2	0.79	58 ± 4				$(4.5 \pm 0.4) \times 10^{-2}$ [b]
3	3	1.10	7.3 ± 0.4	6	6	3.25	$(1.6 \pm 0.1) \times 10^{-4}$
4	4	1.29	3.0 ± 0.2	7	7	3.88	$(5.5 \pm 0.3) \times 10^{-6}$

[a] The values of pK_{BH^+} in water were taken from [9]. The value of pK_{BH^+} for Nu_6 in water at 298 K was determined spectrophotometrically in our laboratory by N.G. Korzhenevskaya, similarly to [10]. [b] In CH_2Cl_2.

Table 2. Thermal effects of acetyl transfer calculated by the AM1 and PM3 methods and the free energies ΔG_0 determined from the equilibrium constants at 298 K (kJ mol^{-1})

System	Determination method			System	Determination method		
	AM1	PM3	ΔG_0		AM1	PM3	ΔG_0
1	–59.0	–41.8	–15.5	5	–23.0	–14.2	7.70
2	–49.0	–40.0	–10.1	6	4.6	10.9	21.7
3	–21.8	–13.4	–4.94	7	14.2	7.1	30.0
4	–37.2	–28.9	–2.72				

Table 3. Equilibrium constants (K) of acetyl transfer between pyridine N-oxides Nu_i, Nu_j in MeCN (i, j = 1–8, 298 K)

Nu_i	Nu_j							
	1	2	3	4	5	6	7	8
1	1	9.1	72	1.8×10^2	1.2×10^4	3.3×10^6	9.5×10^7	525
2	0.11	1	7.9	19	1.3×10^3	3.6×10^5	1.1×10^7	58
3	1.4×10^{-2}	0.13	1	2.4	1.6×10^2	4.6×10^4	1.3×10^6	7.3
4	5.7×10^{-3}	5.2×10^{-2}	0.41	1	67	1.9×10^4	5.5×10^5	3.0
5	8.6×10^{-5}	7.8×10^{-4}	6.2×10^{-3}	1.5×10^{-2}	1	2.8×10^2	8.3×10^3	4.5×10^{-2}
6	3.0×10^{-7}	2.8×10^{-6}	2.2×10^{-5}	5.3×10^{-5}	3.6×10^{-3}	1	29	1.6×10^{-4}
7	1.0×10^{-8}	9.5×10^{-8}	7.5×10^{-7}	1.8×10^{-6}	1.2×10^{-4}	3.4×10^{-2}	1	5.5×10^{-6}
8	1.9×10^{-3}	1.7×10^{-2}	1.4×10^{-1}	0.33	22	6.3×10^3	1.8×10^5	1

between the energies of solvation and of ionic bonds in the ion pairs for the initial species and products in Eq. (1) are insignificant, i.e., the thermodynamic characteristics of reaction (1) mainly depend on the structural factors. It is seen that, depending on the structure of the salt cation, the equilibrium constants vary in a very wide range (up to 8 orders of magnitude). There is a good linear correlation (2) between $\log K$ and pK_{BH^+} of the leaving group in the salt cation:

$$\log K = (3.92 \pm 0.14) - (2.74 \pm 0.06)pK_{BH^+};$$
$$n\ 7,\ r\ 0.998,\ s_0\ 0.21. \qquad (2)$$

From relation (2) it follows that the equilibrium of acyl transfer, as compared to proton transfer, is considerably more sensitive to structural features. This correlation allows evaluation of the basicity of the N-oxide group in 4-(4-dimethylaminostyryl)pyridine N-oxide in which, according to [10], the nitrogen atom of the dimethylamino group is protonated first, with $pK_{BH^+}[NMe_2]$ 4.30 [9]. For Nu_8 $\log K = 0$, and $pK_{BH^+}(N \rightarrow O) = 1.43 \pm 0.06$.

The structural similarity between the initial species and products in reaction (1) suggests that in this reaction the entropy factor does not affect significantly the position of the equilibrium. Indeed, the entropies of reactions in systems 1–7, calculated quantum-chemically, vary within the range 3–5 J mol^{-1} deg^{-1}, i.e., are practically constant. In this connection, it is interesting to compare the free energies and heats of reaction (1). Calorimetric measurement of the heats of reactions (1) for i = 1–7 is difficult because of the poor solubility of the reactants in aprotic solvents and low thermal effects [8]. Therefore, we calculated the heats of acetyl transfer quantum-chemically. The results of the AM1 and PM3 calculations of the ΔH values of the reactions listed in Table 1 are given in Table 2. The calculated heats of the reactions and the

experimentally determined (from the equilibrium constants) free energies of acetyl transfer are poorly consistent but satisfactorily correlate with each other [Eqs. (3), (4)], which allows equilibrium (1) to be classed with isoentropic processes.

$$\text{AM1: } -\Delta H = (-7.2 \pm 0.7) + (1.5 \pm 0.2)\Delta G_0; \quad n\ 7,\ r\ 0.961,\ s_0\ 1.9. \tag{3}$$

$$\text{PM3: } -\Delta H = (-5.2 \pm 0.8) + (1.2 \pm 0.2)\Delta G_0; \quad n\ 7,\ r\ 0.931,\ s_0\ 2.0. \tag{4}$$

The equilibrium constants of reactions (1) for all the combinations of Nu_i and Nu_j, determined by summation of the reactions below, are listed in Table 3.

$$Ac\text{–}Nu_i^+ + Nu_8 = Ac\text{–}Nu_8^+ + Nu_i, \quad K_{i8},$$

$$Ac\text{–}Nu_8^+ + Nu_j = Ac\text{–}Nu_j^+ + Nu_8, \quad K_{8j},$$

$$Ac\text{–}Nu_i^+ + Nu_j = Ac\text{–}Nu_j^+ + Nu_i, \quad K_{ij} = K_{i8}K_{8j}.$$

EXPERIMENTAL

The electronic absorption spectra were taken on a Specord UV-Vis spectrophotometer. The optical densities of solutions were measured on an SF-26 spectrophotometer in a temperature-controlled cell (298 ± 0.1 K).

Quantum-chemical calculations were performed by the AM1 and PM3 methods using the MOPAC 97 program.

All the salts except $AcNu_8^+BPh_4^-$ were prepared and purified as in [11]. The *N*-oxides were distilled or recrystallized before use. Acetonitrile and methylene chloride (Aldrich) were stored over molecular sieves (3 Å).

The equilibrium constants for systems 1–5 were calculated from the equilbrium concentrations of two reagents in reaction (1), which, in turn, were determined from the optical densities of the solutions at 395 [$Ac\text{–}Nu_8^+$] and 510 nm [Nu_8]. For systems 6 and 7 we determined only the equilibrium concentrations of Nu_8, λ 510 nm.

1-Acetyloxy-4-(4-dimethylaminostyryl)pyridinium tetraphenylborate. To a solution of 0.075 g of 4-(4-*N*,*N*-dimethylaminostyryl)pyridine *N*-oxide in 3 ml of acetic anhydride, we added in the dark a fourfold excess of sodium tetraphenylborate (~0.42 g) and vigorously stirred for 10–15 min. Then about 100 ml of diethyl ether was added, and after 30–40 min the dark violet crystalline precipitate was filtered off; yield ~0.14 g (~80%). Found, %: C 81.5; H 6.7; N 4.8. $C_{41}H_{39}BN_2O_2$. Calculated, %: C 81.7; H 6.5; N 4.6. The salt is light-sensitive and was handled in the dark.

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