tography (TLC) (Silufol UV-254) and PMR spectroscopy; all of the compounds gave satisfactory results of analysis for carbon, hydrogen, and nitrogen. Compounds I-III, VIII, XII, and XV were recrystallized from alcohol, IV, V, VII, and XI were recrystallized from benzene, VI was recrystallized from alcohol–DMF, IX and X were recrystallized from benzene–CCl_4, XIV was recrystallized from aqueous alcohol, and XVI was recrystallized from CCl_4. The melting points of the tautomeric compounds were not constant and depended on the rate of melting, the peculiarities of crystallization, etc.

LITERATURE CITED

1. S. A. Stekhova, V. V. Lapachev, and V. P. Mamaev, No. 4, 530 (1981).
2. V. V. Lapachev, O. A. Zagulyaeva, and V. P. Mamaev, No. 3, 395 (1977).
3. V. V. Lapachev, O. A. Zagulyaeva, S. F. Bychkov, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 11, 1544 (1978).
4. V. V. Lapachev, O. A. Zagulyaeva (Zagulajeva), S. F. Bichkov, and V. P. Mamaev, Tetrahedron Lett., No. 33, 3055 (1978).
5. M. I. Kabachnik, Zh. Vsesoyuzn. Khim. Obshchestva, No. 2, 263 (1962).
6. J. R. Jones, The Ionization of Carbon Acids, Academic Press, London (1973), p. 63.
7. A. Pross and L. Radom, in: Progress in Physical Organic Chemistry, Vol. 13 (1981), p. 1.
8. J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, The Tautomerism of Heterocycles, Academic Press, New York (1976), p. 84.
9. A. Pollak, B. Stanovnik, M. Tisler, and J. Venetic-Fortuna, Monatsh. Chem., 100, 473 (1975).
10. J. Niwa, M. Yamazaki, and T. Takeuchi, Chem. Lett., No. 7, 707 (1975).
11. S. A. Stekhova, O. A. Zagulyaeva, V. V. Lapachev, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 6, 822 (1980).
12. O. A. Zagulyaeva, O. A. Grigorkina, V. I. Mamatyuk, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 3, 397 (1981).
13. J. Riand, M. T. Chenon, and N. Lumbroso-Bader, J. Am. Chem. Soc., 99, 6838 (1977).

TAUTOMERISM OF AZINE DERIVATIVES.

7.* THERMODYNAMIC PARAMETERS OF THE 1,3-PROTOTROPIC TAUTOMERIC EQUILIBRIUM OF AZAHETARYLMETHANES

O. P. Petrenko, S. F. Bychkov,
V. V. Lapachev, and V. P. Mamaev

UDC 547.852.2'26'854.9'26:541.623'127.3

The constants of the hetaryl–ylidene tautomeric equilibrium in $CDCl_3$ over a wide range of temperatures were measured for azinylmalonic and azinylcyanoacetic acid esters. High-temperature sensitivity of the position of the equilibrium for 2-pyrimidinylcyanoacetic acid esters was demonstrated. The differences in the ΔS values of the equilibrium for derivatives of malonic and cyanoacetic acid esters were explained by different freedoms of rotation about the exocyclic C–C bond in the aromatic tautomeric form.

In the course of a systematic study of the tautomerism of azines we have determined for the first time the thermodynamic characteristics of the prototropic equilibrium of the A $\rightleftarrows$ B type in the azahetarylmethane series. We used ethyl 5-methoxy-2-pyrimidinylcyanoacetate (I), ethyl 5-dimethylamino-2-pyrimidinyl cyanoacetate (II), dimethyl 2-methyl-4-pyrimidinylmalonate (III), dimethyl 3-pyridazinylmalonate (IV), and ethyl 6-methoxy-3-pyridazinylcyanoacetate (V) as models. Comparable amounts of tautomeric forms A and B are observed for I-V from PMR

*See [1] for communication 6.

Novosibirsk Institute of Organic Chemistry, Siberian Branch. Academy of Sciences of the USSR, Novosibirsk 630090.

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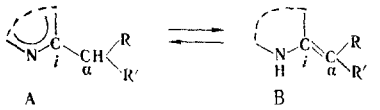
spectroscopic data for solutions in $CDCl_3$, and this makes it possible to determine the tautomeric equilibrium constants with high accuracy.



A B

The differences in the enthalpies ($\Delta H = H_B - H_A$) and entropies ($\Delta S = S_B - S_A$) of the tautomers presented in Table 1 were obtained from the temperature dependence of the equilibrium constant K_T from the usual equation

$$\Delta H - T\Delta S = RT \ln K_T, \text{ where } K_T = [B]/[A]$$

An extremely large difference in the entropies of the tautomers and high sensitivity of the position of the equilibrium to a change in the temperature are observed for I and II. Thus K_T = 0.34 (75% form A) at 370°K for II, whereas K_T = 19.5 (5% form A) at 238°K. We have not found an example of prototropy with such a significant difference in the entropies in the literature. For example, the $S_{keto} - S_{enol}$ difference is only 12.5-16 J/mole-deg for the keto-enol equilibrium of benzoylacetic acid esters [2], and $S_{oxo} - S_{hydroxy}$ = 8.3 J/mole-deg for the oxo-hydroxy tautomerism of 2-hydroxypyrimidine [3]. The $-\Delta S$ values that we found (60-70 J/mole-deg) for the tautomers of I and II are comparable only with the differences in entropy in the case of the azido—tetrazole equilibrium, which does not involve prototropy. Thus, $S_{azido} - S_{tetrazole}$ = 73 J/mole-deg (calculated in conformity with the data in [4]) for 2-azido-4,6-dimethylpyrimidine. Such an unfavorable change in entropy on passing to ylidene tautomer B is evidently associated primarily with the loss of freedom of rotation about the exocyclic C_i—C_α bond. An approximate evaluation made in conformity with [5] shows that the loss of freedom of rotation of the CH(CN)COOR fragment should be accompanied by an entropy change of no less than 40 J/mole-deg.

In contrast to cyanoacetic acid esters I and II, the tautomers of azinylmalonic acid esters III and IV have substantially smaller differences in entropy. If one assumes that rotation about the C_i—C_α bond is absent in form B in all cases, the observed difference in the ΔS values is evidently associated with smaller freedom of rotation of the —CHRR' fragment (form A) in malonic acid esters III and IV as compared with cyanoacetic acid esters I and II. In fact, it is apparent from Fig. 1, in which the effective van der Waals radii of the atoms in accordance with [6] are depicted, rotation about the C_i—C_α bond in tautomers IIIA and IVA should occur with much greater difficulty than in IA and IIA.

In Fig. 1 the heteroring and the ester group are depicted in a single plane, which is least favorable for rotation. It follows from an examination of Stuart—Briegleb models that a decrease in steric hindrance via turning of the plane of the ester group is possible in cyanoacetic acid esters IA and IIA, whereas the possibility of this sort of decrease in the steric hindrance is virtually absent in malonic acid esters IIIA and IVA.

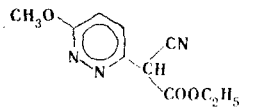
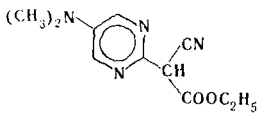
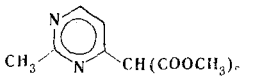
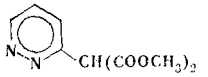
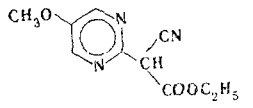
Thus, tautomers IA and IIA differ from IIIA and IVA both with respect to the effective volume of the substituted methyl group and with respect to the steric environment of the C_i atom (Fig. 1). If the explanation of the change in entropy given above is correct, the entropy of the equilibrium should take on an intermediate (between I and II and III and IV) value when only one factor — the ortho orientation of the C_i atom or the substituents in the methyl group — is varied.

We therefore synthesized pyridazinylcyanoacetic acid ester V, in which the side chain is the same as in I and II, but a >C—H fragment, which has greater steric requirements, appears in the ortho position in place of a heteroatom. We found that in this case the difference in the entropies of the tautomers actually has an intermediate value. This confirms the substantial dependence of the ΔS value on the relative freedom of rotation of the substituted methyl group —CHRR' in tautomer A.

EXPERIMENTAL

The PMR spectra of ~1% solutions of the compounds in $CDCl_3$ were recorded with a Bruker WP-80 spectrometer. The equilibrium constants were determined for I, II, and IV over the 240-367°K range at ~20°K intervals, for ester III over the 308-378°K range, and for ester V over the 227-303°K range at ~10°K intervals. The ampuls were sealed for work in the high-

TABLE 1. Thermodynamic Parameters of the Tautomeric Equilibrium of Azinylmethanes I-V in $CDCl_3$

Compound	Form A	ΔH, kJ/mole	−ΔS, J/mole-deg
I		21,1±0,2	62±1
II		23,2±0,2	71±1
III		12,2±0,6	38±2
IV		4,7±0,8	24±2,5
V		7,9±0,6	47±2

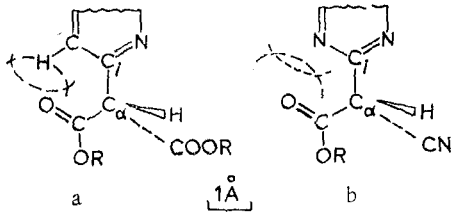


Fig. 1. Steric hindrance in rotation about the C_1—C_α bond for derivatives of malonic (a) and cyanoacetic (b) acid esters.

temperature range. Recording was carried out under pulse conditions; the time lag between pulses (10-15 sec) exceeded by a factor of approximately three the relaxation time of the ring protons and the protons of the methyl groups. The synthesis of I and II was realized by the method in [1], and esters III and IV were synthesized by the method in [7].

Ethyl 6-Methoxy-3-pyridazinylcyanoacetate (V). A 0.5-g (3.5 mmole) sample of 3-methoxy-6-chloropyridazine was added to a solution of the sodium salt of ethyl cyanoacetate in 4 ml of hexamethylphosphoric triamide (HMPT)[obtained from 1.1 g (10 mmole) of ethyl cyanoacetate and 0.5 g (10 mmole) of a 50% suspension of NaH in oil], and the mixture was heated with stirring for 2 h at a bath temperature of 100-110°C. The mixture was then cooled and poured into 50 ml of water, and the aqueous mixture was acidified with concentrated HCl and extracted with benzene. The extract was washed with small portions of water to remove the HMPT and dried over $MgSO_4$. The product was purified by means of preparative TLC on silica gel [elution with $CHCl_3$—ethyl acetate (1:1), R_f ~0.8] to give 0.5 g (50%) of a product with mp 188-190°C (from ethanol). Found: N 19.4%. $C_{10}H_{11}N_3O_3$. Calculated: N 19.0%.

LITERATURE CITED

1. V. V. Lapachev, O. A. Zagulyaeva, O. P. Petrenko, S. F. Bychkov, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 6, 827 (1984).
2. D. G. Zheglova, B. A. Ershov, and A. I. Kol'tsov, Zh. Org. Khim., 10, 18 (1974).

3. P. Beak, F. S. Fry, J. Lee, and F. Steele, J. Am. Chem. Soc., 98, 191 (1976).
4. C. Temple and J. A. Montgomery, J. Am. Chem. Soc., 86, 2946 (1964).
5. D. Stall, A. Westrum, and H. Zincke, The Chemical Thermodynamics of Organic Compounds [Russian translation], Mir, Moscow (1971), p. 120.
6. L. Pauling, The Nature of the Chemical Bond, Cornell University Press, Ithaca, New York (1960).
7. O. P. Petrenko, V. V. Lapachev, and V. P. Mamaev, Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 3, 88 (1983).

CATION RADICALS — INTERMEDIATES IN THE VILSMEIER–HAACK REACTION

V. G. Koshechko and A. N. Inozemtsev

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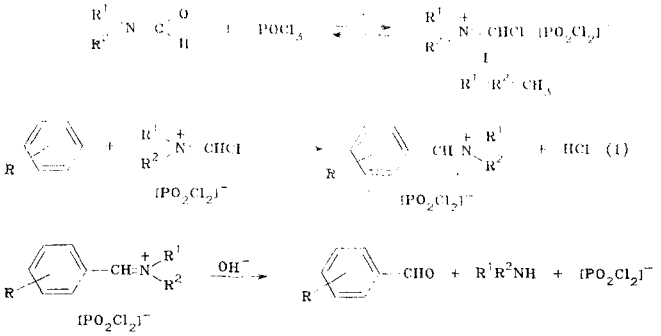
It was observed that cation radicals are intermediate particles in the formylation of N,N'-alkyl- or -aryldihydrophenazines with dimethylformamide in the presence of $POCl_3$. The observed instantaneous cation-radical concentrations in the investigated reactions depend substantially on the concentrations and ratios of the starting reagents and may reach 50-90% based on the substrate undergoing formylation.

The convenient method of obtaining aromatic aldehydes via the Vilsmeier–Haack reaction [1] is finding wide application in organic synthesis [2, 3]. Polycyclic hydrocarbons, aromatic nitrogen-, sulfur-, and oxygen-containing compounds, and a number of other organic substrates can undergo formylation by means of substituted formamides and $POCl_3$, $SOCl_2$, or $COCl_2$ [4]. Despite the extensive utilization of such processes, their mechanism has not yet been elucidated definitively. It is usually assumed [2, 5] that the active electrophilic particle in Vilsmeier–Haack formylation is the cation of iminium salt $R_1R_2\overset{+}{N}{=}CHCl$, X^- (R_1, R_2 = Alk, Ar; X = PO_2Cl_2, Cl, SO_2Cl), which is formed in the reaction of substituted formamides with oxy halides.



We have previously shown [6] that the reaction of some substituted aromatic amines, dihydrophenazines, and phenothiazine with a number of classical electrophilic reagents (HNO_3, Br_2, and $NOBF_4$) may include a step involving electron transfer from the substrate to the electrophile with the formation of intermediate cation radicals. It seemed of interest to ascertain the possibility of the realization of this process in reactions involving formylation with the participation of Vilsmeier complex I. Our electrochemical studies of complex I, which showed that it has a potential ($E^{red}_{1/2}$ = 0.15 V relative to Ag/AgCl, CH_3CN + 0.5 M $NaClO_4$, Pt) sufficient for the oxidation of many organic compounds, served as a prerequisite for this. As the subject of our investigation we used 5,10-dimethyl-5,10-dihydrophenazine (II), since, on the one hand, it readily forms the corresponding aldehyde IV in quantitative

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