In conclusion, the authors thank I. A. Krasavin for providing us with samples of oxides VII and VIII and T. M. Ivanov and R. V. Linko for recording the x-ray electron spectra.

LITERATURE CITED

1. V. M. Dziomko and A. V. Ivashchenko, Khim. Geterotsikl. Soedin., No. 9, 1190 (1973).
2. A. V. Ivashchenko, V. T. Lazareva, E. K. Prudnikova, S. P. Ivashchenko, and V. G. Rumyantsev, Khim. Geterotsikl. Soedin., No. 2, 236 (1982).
3. I. A. Mazur, P. M. Kochergin, and G. S. Tkachenko, Khim. Geterotsikl. Soedin., No. 5, 82 (1970).
4. B. A. Priimenko and P. M. Kochergin, Khim. Geterotsikl. Soedin., No. 9, 1243, 1255 (1971).

UNUSUAL CLEAVAGE OF PHENACYL-SUBSTITUTED BENZIMIDAZOLIUM SALTS. SYNTHESIS OF 1,4-DIARYLIMIDAZOLES

T. A. Kuz'menko, V. V. Kuz'menko, A. M. Simonov, M. S. Korobov, and S. A. Filippov

UDC 547.785.5.07

The action of ammonium acetate in acetic acid on 1-alkyl(aralkyl)-3-phenacylbenzimidazolium bromides leads, in addition to the formation of a new imidazole ring, to cleavage of the benzimidazole fragment of the molecule at the 1,2 bond to give 1-alkyl(aralkyl)aminoaryl-4-arylimidazoles. 1,2-Dimethyl-3-(p-nitrophenacyl)benzimidazolium bromide is converted under similar conditions to the corresponding 2-methylimidazole. 4,4'-Dimethyl-2,2'-bis(p-nitrophenyl)-1,1'-dipyrrolo[1,2-a]benzimidazole was isolated as a side product of this reaction.

Up until recently the action of ammonium acetate in acetic acid on phenacyl-substituted salts of nitrogen heterocycles with unsubstituted μ-carbon atoms had been studied only in the case of pyridine, quinoline, and isoquinoline. According to the data in [1], phenacylpyridinium bromide does not react with ammonium acetate when the compounds are heated in solution in acetic acid, whereas the corresponding quinolinium and isoquinolinium salts are converted under the indicated conditions to three-ring systems, viz., 4,5-dihydroimidazo-[1,2-a]quinoline and 5,10-dihydroimidazo[1,2-b]isoquinoline [2-5].

In the opinion of Kröhnke and Zecher [1], the decreased reactivity of phenacylpyridinium bromide is due chiefly to the insufficient magnitude of the positive charge on the μ-carbon atom of its cation. In this connection, it seemed expedient to investigate the action of ammonium acetate in acetic acid on phenacyl-substituted benzimidazolium salts, the cations of which have higher electrophilicity as compared with salts of azines [6].

The starting 1-alkyl(aralkyl)-3-phenacylbenzimidazolium bromides (Ia-k) were obtained by a known method [7-9]. As a rule, the quaternization of 1-alkyl(aralkyl)benzimidazoles by ω-bromoacetophenones takes place at 20°C, and prolonged refluxing of an alcohol solution of the components is necessary only for 1-methyl-5-nitrobenzimidazole.

The action of ammonium acetate on a solution of 1-methyl-3-phenacylbenzimidazolium bromide (Ia) in acetic acid initially gives rise to the development of a brown coloration, which is probably due to the formation of the anhydro base described in [8], after which it leads to a colorless low-melting compound that is resistant to the action of acids and alkalis. In analogy with [2], we did not exclude the possibility of the formation in this case of the known 9-methyl-2-phenyl-2,3-dihydroimidazo[1,2-a]benzimidazole (II) [10]. However, a comparison of the melting points of the hydrochlorides of the compound obtained and II showed that they are not identical, although they do have the same elementary composition.

Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 388-392, March, 1982. Original article submitted May 4, 1981.

0009-3122/82/1803-0293$07.50

TABLE 1. 1-Alkyl-3-phenacylbenzimidazolium Bromides (I)

Compound	mp, °C (alcohol)	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Br	N		C	H	Br	N	
Ib	245	58,9	5,0	23,0	8,0	$C_{17}H_{17}BrN_2O$	59,2	4,9	23,1	8,1	87
Ic	195—197	56,3	4,5	22,5	7,8	$C_{17}H_{17}BrN_2O_2$	56,5	4,7	22,2	7,8	85
Id	233—234	52,3	4,0	31,2*	7,6	$C_{16}H_{14}BrClN_2O$	52,5	3,8	31,6*	7,7	90
Ie	223—224	51,3	3,4	21,0	11,6	$C_{16}H_{14}BrN_3O_3$	51,1	3,7	21,2	11,2	71
Ih	253—254	54,2	4,6	18,9	10,3	$C_{19}H_{20}BrN_3O_3$	54,6	4,8	19,1	10,0	83
Ii	238—240	50,5	3,9	19,5	10,0	$C_{17}H_{16}BrN_3O_4$	50,3	3,9	19,7	10,3	91
Ij	235—236	45,3	2,8	19,3	13,0	$C_{16}H_{13}BrN_4O_5$	45,6	3,1	19,0	13,3	76
Ik	226—227	55,8	4,6	15,4	8,5	$C_{24}H_{22}BrN_3O_5$	56,2	4,3	15,6	8,2	80

* This is the combined percentages of Br and Cl.

TABLE 2. 1,4-Diarylimidazoles (III-a-k)

Compound	mp,* °C	IR spectrum, ν_{NH}, cm^{-1}	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIIa	87—88	3450	77,0	5,9	17,0	$C_{16}H_{16}N_2$	77,1	6,0	16,9	28
IIIb	129—130	3430	77,8	6,5	16,1	$C_{17}H_{17}N_3$	77,6	6,4	16,0	17
IIIc	128—129	3440	73,0	6,0	14,9	$C_{17}H_{17}N_3O$	73,1	6,1	15,1	16
IIId	149—150	3230	67,9	5,0	15,0	$C_{16}H_{14}ClN_3$	67,7	4,9	14,8	36
IIIe	204—206	3200	65,5	4,6	19,2	$C_{16}H_{14}N_4O_2$	65,3	4,8	19,0	90
IIIf	167—168	3330	58,7	4,5	13,0	$C_{16}H_{14}BrN_3$	58,5	4,3	12,8	29
IIIg	187—188	3320	65,4	4,9	18,9	$C_{16}H_{14}N_4O_2$	65,3	4,8	19,0	68
IIIh	159—160	3380	68,0	6,1	16,8	$C_{19}H_{20}N_4O_2$	67,9	6,0	16,7	51
IIIi	164—165	3390	63,1	5,0	17,2	$C_{17}H_{16}N_4O_3$	63,0	4,9	17,3	58
IIIj	251—252	3445	56,4	4,0	20,5	$C_{16}H_{13}N_5O_4$	56,6	3,8	20,7	98
IIIk	195—196	3420	66,7	5,3	13,3	$C_{24}H_{22}N_4O_4$	67,0	5,1	13,1	38

* The compounds were recrystallized: IIIa-d from octane, IIIe-i from alcohol, IIIj from aqueous DMF, and IIIk from benzene.

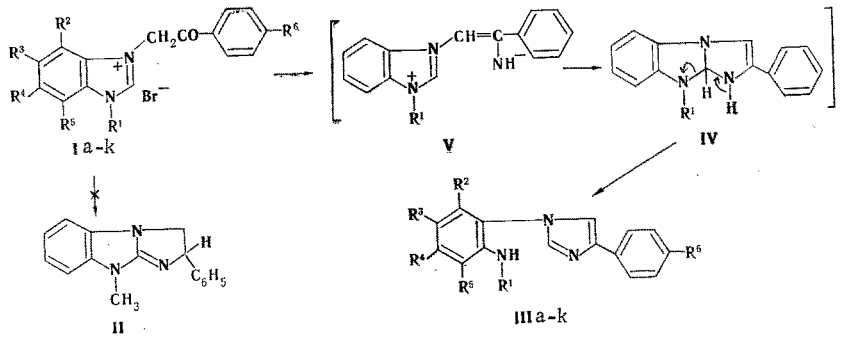
TABLE 3. PMR Spectra of 1,4-Diarylimidazoles (IIIa,d,f,h,j,k,*l*)

Compound	Solvent	Chemical shifts, ppm			
		N—CH_3	N—H	aromatic protons	2-H
IIIa	$CDCl_3$	2,68 d (3H) 2,68* s (3H)	3,73 —	7,25 m (11H)	— —
	CF_3COOH	2,95 s (3H)	—	7,2—7,6 m (10)	8,77 s
IIId	$CDCl_3$	2,7 d (3H) 2,7* s (3H)	3,98 —	6,6—7,5 m (10H) 7,17—7,5 m (10H)	— —
	CF_3COOH	2,92 s (3H)	—	7,17—7,5 m (9H)	8,75 s
IIIf	$CDCl_3$	2,6 d (3H) 2,6* s (3H)	5,3 —	6,63—7,76 m (10H)	— —
IIIh	C_5D_5N	0,98 t (3H) 3,0 m (2H) 0,98* t (3H) 3,0 q (2H)	3,4 —	6,6 s (1H), 6,73 s (1H), 7,82—8,05 m (6H)	— —
IIIj	CF_3COOH	2,59 s (3H)	—	6,56 d (1H), 7,25 m (6H), 7,93 s (1H), 8,0 d (1H)	8,50 s
IIIk	$CDCl_3$	3,63 s (2H) 3,63* s (2H)	4,3 —	6,3 d (1H), 6,75 d (1H), 6,95—7,35 m (6H), 7,85 d (2H), 8,17 d (2H)	7,55 s
III*l*	$CDCl_3$	2,78 d (3H) 2,78* s (3H)	3,83 —	6,75—7,4 m (5H), 7,75 d (2H), 8,1 d (2H)	— —

* After deuteration.

The PMR spectrum ($CDCl_3$) of the compound that we isolated does not contain signals of methylene protons, and the signal of the N—CH_3 group shows up in the form of a doublet (2.68 ppm, J = 5 Hz). A broad signal of the proton of the NH group, which vanishes after deuteration (the doublet corresponding to the N—CH_3 group is converted to a singlet), is present at 3.73 ppm. The signals of 11 aromatic protons are found at 6.58-7.72 ppm. The characteristic (for the imidazolium cation [11]) decoupling of the 2-H proton from the aromatic multiple to weak field (8.77 ppm) occurs in the PMR spectrum recorded in CF_3COOH. A distinct band of stretching vibrations of an NH group at 3450 cm^{-1} is observed in the IR spectrum of the reaction product.

These data make it possible to conclude that the formation of a new imidazole ring, which is accompanied by cleavage of the benzimidazole fragment of the molecule at the 1,2 bond, which leads to 1-(2-methylaminophenyl)-4-phenylimidazole (IIIa), occurs under the reaction conditions. In our opinion, the precursor of imidazole IIIa is cyclic intermediate IV, which arises as a result of the addition of the amino group of enamine V to the C=N bond of the benzimidazolium cation. The inertness of 1,3-dimethyl- and 1-methyl-3-acetonylbenzimidazolium salts to ammonium acetate constitutes indirect evidence for primary participation of this intermediate in the reaction rather than the product of the addition of ammonia to the μ-carbon atom of the heteroring.

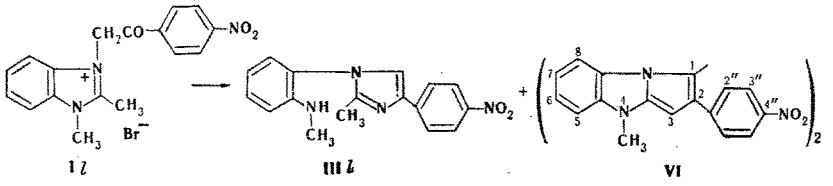


I, III a $R^1=CH_3$, $R^2=R^3=R^4=R^5=R^6=H$; b $R^1=R^3=CH_3$, $R^2=R^4=R^5=R^6=H$; c $R^1=CH_3$, $R^3=OCH_3$, $R^2=R^4=R^5=R^6=H$; d $R^1=CH_3$, $R^3=Cl$, $R^2=R^4=R^5=R^6=H$; e $R^1=CH_3$, $R^3=NO_2$, $R^2=R^4=R^5=R^6=H$; f $R^1=CH_3$, $R^2=R^3=R^4=R^5=H$, $R^6=Br$; g $R^1=CH_3$, $R^2=R^3=R^4=R^5=H$, $R^6=NO_2$; h $R^1=C_2H_5$, $R^2=R^5=H$, $R^3=R^4=CH_3$, $R^6=NO_2$; i $R^1=CH_3$, $R^3=OCH_3$, $R^2=R^4=R^5=H$, $R^6=NO_2$; j $R^1=CH_3$, $R^2=R^4=R^5=H$, $R^3=R^6=NO_2$; k $R^1=CH_2C_6H_5$, $R^2=R^5=OCH_3$, $R^3=R^4=H$, $R^6=NO_2$

The introduction of substituents with various electronic natures in the benzimidazole and phenacyl fragments of starting salts Ia-j does not affect the overall pathway of the reaction but has an appreciable effect on the yields of the corresponding imidazoles. Thus, whereas salt Ia is converted to imidazole IIIa in 28% yield after heating for 8 h, the yields of the corresponding imidazoles IIIb, c from salts that contain donor substituents (CH_3, OCH_3) in the benzimidazole ring are almost halved (see Table 2). On the other hand, salts with acceptor groups (Cl, NO_2) are considerably more active than Ia. Thus 1-methyl-5-nitro-3-phenacylbenzimidazolium bromide (Ie) is converted almost completely to imidazole IIIe after 3 h. Electron-acceptor substituents (NO_2, Br) in the phenacyl residue promote an increase in the reactivity of salts I to a lesser extent (compare the yields of IIIe and IIIg). However, the yields of reaction products range from 40 to 60% even when donors are present in the benzimidazole ring. The structures of the imidazoles obtained were confirmed by means of PMR and IR spectroscopy (see Table 3).

1,2-Dimethyl-3-(p-nitrophenacyl)benzimidazolium bromide (II) [9] is also converted to the corresponding 2-methyl-1,4-diarylimidazole (III) in 31% yield via the scheme presented above. However, in addition to the latter, we observed the formation of a deeply colored high-melting product (VI) as a side product.

Considering the fact that phenacyl-substituted 1,2-dialkylbenzimidazolium salts are readily converted to the corresponding pyrrolobenzimidazoles by the action of bases [9], one might have assumed that VI is a previously unknown derivative of this heterocycle. In fact, a substance identical to VI is formed in almost quantitative yield when a genuine sample of 4-methyl-2-(p-nitrophenyl)pyrrolo[1,2,-a] benzimidazole is heated briefly in acetic acid. The mass-spectrometric determination of the molecular mass of VI showed that it has a dimeric structure. Signals of α-pyrrole protons [12] are absent in the PMR spectrum ($CDCl_3$) of the compound, which indicates fusion of the fragments at the 1,1' positions.



Since 4-methyl-2-phenyl-pyrrolo[1,2-a]benzimidazole is not dimerized when it is heated in acetic acid, one must probably include not only the high π-surplus character of pyrrolobenzimidazoles but also the presence in the molecule of an electron-acceptor nitro group, which ensures greater stability of the radical formed during the reaction, among the structural peculiarities that are responsible for the dimerization.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer with hexamethyldisiloxane as the internal standard. The mass spectrum was recorded with a Varian MAT-CH8 spectrometer.

1-Benzyl-4,7-dimethoxy-3-(p-nitrophenacyl)benzimidazolium Bromide (Ik). A solution of 2.68 g (0.01 mole) of 1-benzyl-4,7-dimethoxybenzimidazole [13] and 2.43 g (0.01 mole) of p-nitrophenacyl bromide in 30 ml of acetone was allowed to stand at 20°C for 8 h, after which the precipitate was removed by filtration and washed with acetone. Salts Ib-d, h, i (Table 1) were similarly obtained.

1-Methyl-5-nitro-3-phenacylbenzimidazolium Bromides (Ie, j). These compounds were formed by heating equimolar amounts of 1-methyl-5-nitrobenzimidazole and the corresponding phenacyl bromides in alcohol for 6 h.

1-(2-Methylaminophenyl)-4-phenylimidazole (IIIa). A solution of 3.31 g (0.01 mole) of 1-methyl-3-phenacylbenzimidazolium bromide (Ia) [7] and 6.16 g (0.08 mole) of ammonium acetate in 10 ml of glacial acetic acid was refluxed for 8 h, after which the mixture was cooled and poured into 30 ml of water. The aqueous mixture was neutralized with sodium bicarbonate and extracted with benzene. The extract was chromatographed with a column filled with Al_2O_3 by elution with benzene. Evaporation of the solvent gave a viscous oil that began to crystallize in a vacuum desiccator over P_2O_5. Data on IIIa, as well as IIIb-d, f-i, k, which were similarly obtained, are presented in Table 2.

IIIa Hydrochloride. The hydrochloride was obtained by treatment of a benzene solution of IIIa with gaseous HCl. The colorless needles had mp 218-220°C (from water). Found: C 67.5; H 5.4; Cl 12.5; N 14.6%. $C_{16}H_{15}N_3 \cdot HCl$. Calculated: C 67.3; H 5.6; Cl 12.4; N 14.7%.

1-(2-Methylamino-5-nitrophenyl)-4-phenylimidazole (IIIe). A solution of 3.76 g (0.01 mole) of salt Ie and 6.16 g (0.08 mole) of ammonium acetate in 10 ml of glacial acetic acid was refluxed for 3 h, after which it was cooled, and the precipitate was removed by filtration to give 2.2 g of product. Dilution of the mother liquor with water gave an additional 0.45 g of precipitate for an overall yield of 2.65 g (Table 2).

Imidazole IIIj was similarly obtained, but the heating time was 2 h.

Reaction of 1,2-Dimethyl-3-(p-nitrophenacyl)benzimidazolium Bromide (II) with Ammonium Acetate in Acetic Acid. A solution of 3.89 g (0.01 mole) of salt II and 6.16 g (0.08 mole) of ammonium acetate in 10 ml of glacial acetic acid was refluxed for 5 h, after which it was cooled, and the precipitated dimer VI was removed by filtration to give 0.35 g (12%) of shiny dark-violet crystals with mp 298°C (from alcohol–DMF). Found: C 70.5; H 4.2; N 14.6%; M^+ (by mass spectroscopy) 580. $C_{34}H_{24}N_6O_4$. Calculated: C 70.3; H 4.1; N 14.5%. PMR spectrum ($CDCl_3$): 7.9 (2H, d, J = 8 Hz, 3H"): 7.45 (2H, d, J = 8 Hz, 2H"), 6.63-7.0 (4H, m, 5, 6, 7, 8H), and 6.0 ppm (1H, s, 3H). The filtrate was neutralized with 22% NH_4OH, and the resulting dark-green precipitate was removed by filtration, washed with water, and purified by chromatography with a column filled with Al_2O_3 (elution with benzene). The yield of imidazole IIIl was 0.7 g (31%). The yellow prisms had mp 197-198°C (from alcohol). Found: C 66.0; H 5.4; N 18.1%. $C_{17}H_{16}N_4O_2$. Calculated: C 66.2; H 5.2; N 18.2%.

4,4'-Dimethyl-2,2'-bis(p-nitrophenyl)-1,1'-dipyrrolo[1,2-a]benzimidazole (VI). A solution of 0.29 g (1 mmole) of 4-methyl-2-(p-nitrophenyl)pyrrolo[1,2-a]benzimidazole [9] in 5 ml of glacial acetic acid was refluxed for 40 min, and the precipitate was removed by filtration and washed with water to give 0.27 g (90%) of a product that was identical to dimer VI described in the preceding experiment with respect to its physicochemical properties.

LITERATURE CITED

1. F. Kröhnke and W. Zecher, Chem. Ber., 95, 1128 (1962).
2. R. F. Cookson, D. P. Novotnik, and R. T. Parfitt, Chem. Commun., No. 21, 911 (1974).
3. R. F. Cookson, D. P. Novotnik, R. T. Parfitt, J. F. Airey, and A. S. Kende, J. Chem. Soc., Perkin Trans. I, No. 2, 201 (1976).
4. U. Habermalz, B. Reinshagen, and F. Kröhnke, Chem. Ber., 108, 984 (1975).
5. H. J. Linder and B. Kitschke, Tetrahedron Lett., No. 24, 2091 (1977).
6. A. F. Pozharskii, Doctoral Dissertation, Rostov State University, Rostov-on-Don (1972), p. 37.
7. H. Ogura and K. Kikuchi, J. Org. Chem., 37, 2679 (1972).
8. R. M. Palei and P. M. Kochergin, Khim. Geterotsikl. Soedin., No. 6, 1075 (1969).
9. R. M. Palei and P. M. Kochergin, Khim. Geterotsikl. Soedin., No. 3, 536 (1967).
10. V. A. Anisimova, A. M. Simonov, and T. A. Borisov, Khim. Geterotsikl. Soedin., No. 6, 791 (1973).

11. A. F. Pozharskii, V. V. Kuz'menko, Yu. V. Kolodyazhnyi, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 9, 1252 (1972).
12. P. M. Kochergin, Yu. N. Sheinker, A. A. Druzhinina, R. M. Palei, and L. M. Alekseeva, Khim. Geterotsikl. Soedin., No. 6, 826 (1971).
13. A. F. Pozharskii, V. V. Kuz'menko, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 8, 1105 (1971).

INVESTIGATION OF THE ELECTROPHILIC REACTIONS OF 5-HYDROXYPYRIMIDINE

S. B. Gashev and L. D. Smirnov

UDC 547.854'855

The possibility of the electrophilic substitution of various positions of the 5-hydroxypyrimidine ring in a weakly basic medium is demonstrated in the case of aminomethylation and diazo coupling. It was found that the ortho positions of 5-hydroxypyrimidine are more reactive than the para position with respect to the hydroxy group.

Electrophilic substitution reactions have not yet been described for 5-hydroxypyrimidine. In addition, it has been reported that 5-hydroxypyrimidine cannot undergo electrophilic substitution because of its low stability in acidic media.

We have previously demonstrated the possibility of electrophilic substitution of the 5-hydroxypyrimidine ring in the case of the aminomethylation and diazo coupling of 4,6-dimethyl-5-hydroxypyrimidine, which were carried out in alkaline media [1].

In this connection, it seemed of interest to extend the indicated reactions to unsubstituted 5-hydroxypyrimidine and in this way to ascertain the relative reactivities of the various positions of the hydroxypyrimidine ring.

It is known that the aminomethylation of phenol takes place initially in the ortho positions and subsequently in the para position [2]. In addition, an aza analog of phenol – 3-hydroxypyridine – is aminomethylated in only one ortho position and subsequently in the para position, and this made it possible to conclude that the ortho positions in the hydroxypyridine ring are not equivalent [3].

In the case of 5-hydroxypyrimidine, the structure of which, in contrast to 3-hydroxypyridine, is distinguished by its symmetry, one might have expected an orientation in aminomethylation similar to that in phenol.

We confirmed this assumption during an experimental study of the aminomethylation of 5-hydroxypyrimidine, which was carried out with N,N,N',N'-tetramethylmethylenediamine as the aminomethylating agent. When it was heated with 5-hydroxypyrimidine, the starting compound gradually passed into solution, which, depending on the treatment time, contained a mixture of mono- and bis(dimethylaminomethyl) derivatives in various ratios. The individual Mannich bases were isolated by chromatography. Since they were uncrystallizable liquids, they were identified and analyzed in the form of the hydrochlorides, which proved to be rather hygroscopic.

Morpholinomethyl derivatives of 5-hydroxypyrimidine were obtained by the method in [4] by refluxing with the calculated amounts of morpholine and paraformaldehyde in chlorobenzene in the presence of triethylamine.

The PMR spectrum of the starting 5-hydroxypyrimidine consists of two singlets belonging to the protons in the 2 and 4(6) positions of the pyrimidine ring with an integral intensity ratio of 1:2. In the spectrum of monoaminomethyl derivative I, however, the intensity of the 4-H signal is half the intensity of the signal observed for the starting compound, and the appearance of a signal of a CH_2 group and signals of the aliphatic part of the amine in the form of a singlet (dimethylamine) or two multiplets (morpholine) is observed.

Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow 117334. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 393-396, March, 1982. Original article submitted June 15, 1981.

0009-3122/82/1803-0297$07.50