LITERATURE CITED

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STUDY OF THE ELECTRON INTERACTIONS OF POLYSUBSTITUTED AZOLES BY PMR AND IR SPECTROSCOPY

N. N. Zatsepina, I. F. Tupitsyn, A. I. Belyashova, A. A. Kane, N. S. Kolodina, and G. N. Sudakova

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The IR and PMR spectra of an extensive series of methyl derivatives of aromatic and heteroaromatic compounds were investigated. With a few exceptions, the experimental data on the chemical shifts of the protons (δ^{CH_3}) and the intensity of the band of the symmetrical stretching vibration [$(A_{CH})^{1/2}$] for five- and six-membered heterorings can be united in a single reaction series with polysubstituted toluenes within the framework of an additive scheme. The $(A_{CH})^{1/2}$ values correlate satisfactorily with the calculated (by the CNDO/2 method) total charges on the carbon and hydrogen atoms of the methyl group. In contrast to the intensities of the IR bands, linear relationships between the chemical shifts and the charges on the hydrogen atoms are observed only within the limits of particular reaction series. The lack of a unified relationship was interpreted as being the result of the effect of the ring current, the contribution of which to the δ^{CH_3} value depends on the nature of the heteroatom.

In our previous papers [1, 2] we demonstrated the applicability of the principle of additivity for the characterization of the contributions of the individual substituents and heteroatoms to the changes in the kinetic and spectroscopic parameters of the methyl group in the polysubstituted toluenes and their heteroanalogs. In the present research we made an attempt to extend the indicated approach to the IR and PMR spectroscopic characteristics of methyl derivatives of five-membered aromatic heterocycles and to ascertain the possibility of a quantum-chemical description of the trend of the change in these parameters.

Applicability of the Additive Scheme

PMR Spectra. The chemical shifts of both aromatic protons and the protons of methyl groups bonded to the heteroaromatic ring in azoles have been studied in a number of papers (for example, see [3-19]). However, in the overwhelming majority of cases only the effect of variable substituents on the δ value as the nature and position of the heteroatomic groupings built into the ring remain fixed has been investigated. The experimental data presented in Table 1 make it possible to thoroughly analyze the entire set of data on the change in the shielding constants of the protons of the methyl group in azoles of various types.

As in [2], we used a variant of the additive scheme in which the effect of each substituent in the azole ring characterizes the $\Delta\delta_i$ increment, which reflects its contribution to the δ^{CH_3} value in the corresponding monosubstituted toluene; the contributions of the heteroatomic $-O-$, $-S-$, $-N(CH_3)-$, and $-N=$ groups are conveyed by the magnitude of the $\Delta\delta^{CH_3}$ chemical shift in the furan, thiophene, N-methylpyrrole, and pyridine rings with respect to toluene as the standard compound ($\delta^0 = 2.34$ ppm). Moreover, in conformity with the generally accepted concepts regarding the transmission capacities of the $-O-$, $-S-$, and $-NH-$ heteroatoms in five-membered rings [20], all of the azole ring positions adjacent to them are considered to be ortho-like, the 1-3(4), 2-4, and 3-5 positions are considered to be meta-like, and the 2-5 positions are considered to be para-like positions of the benzene ring.

State Institute of Applied Chemistry, Leningrad 197198.

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TABLE 1. Chemical Shifts of the Protons of the Methyl Group Bonded to the Heteroring (ppm)[a]

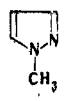
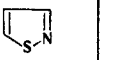
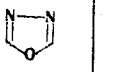
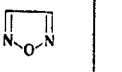
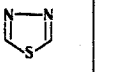
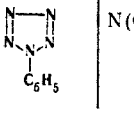
Compound No.	Heterocycle	Substituents[b]					δ CH$_3$		ΔΔδ[e]
		R_1	R_2	R_3	R_4	R_5	meas.[c]	calc.[d]	
1	2	3	4	5	6	7	8	9	10
1		O	CH_3	—	—	—	2,27	2,29	−0,02
2		O	CH_3	—	—	COCl	2,45	—	—
3		O	CH_3	—	—	CHO	2,40	—	—
4		O	CH_3	—	—	COOR	2,40	2,34	0,06
5		O	CH_3	—	—	NO_2	2,44	2,44	0
6		O	CH_3	—	—	CH_3	2,20	2,21	−0,01
7		O	—	CH_3	—	—	1,94	2,08	−0,14
8		S	CH_3	—	—	—	2,44	—	—
9		S	—	CH_3	—	—	2,18[f]	—	—
10		S	CH_3	—	—	CHO	2,48	—	—
11		S	CH_3	—	—	CH_3O	2,28	2,38	−0,10
12		S	CH_3	—	—	Cl	2,34	2,42	−0,08
13		S	CH_3	—	—	CH_3	2,35	2,38	−0,03
14		$N(CH_3)$	CH_3	—	—	—	2,16	2,10	0,06
15		$N(CH_3)$	—	CH_3	—	—	2,05	2,02	0,03
16		$N(CH_3)$	N	CH_3	—	—	2,23[f]	2,23	0
17		$N(CH_3)$	N	—	CH_3	—	2,04[f]	2,00	0,04
18		$N(CH_3)$	N	CH_3	—	CH_3	$2,17_{(3)}$[g]	2,19	−0,02
19							$2,17_{(5)}$	2,03	0,14
								2,27[h]	(−0,10)
20		$N(CH_3)$	N	CH_3	Br	CH_3	$2,22_{(3)}$[f]	2,23	−0,01
21							$2,24_{(5)}$[f]	2,07	0,17
								(2,31)[h]	(−0,07)
22		$N(CH_3)$	N	—	CH_3	CH_3	$1,96_{(4)}$[f]	1,91	0,05
23							$2,16_{(5)}$[f]	1,98	0,18
								(2,22)[h]	(−0,06)
24		$N(CH_3)$	N	CH_3	CH_3	CH_3	$2,14_{(3)}$[f]	2,20	0,04
25							$1,89_{(4)}$[f]	1,82	0,07
26							$2,12_{(5)}$[f]	1,94	0,18
								(2,18)[h]	(−0,06)
27		$N(CH_3)$	N	COOEt	—	CH_3	2,32[f]	2,14	0,16
								(2,38)[h]	(−0,06)
28		$N(CH_3)$	N	COOEt	Br	CH_3	2,32[f]	2,18	0,14
								(2,42)[h]	(−0,10)
29		$N(CH_3)$	N	CH_3	—	Cl	2,26[f]	2,30	−0,04
30		$N(CH_3)$	N	CH_3	Br	Cl	2,24[f]	2,34	−0,10
31		$N(CH_3)$	N	CH_3	Br	—	2,20[f]	2,27	−0,07
32		$N(CH_3)$	N	CH_3	Cl	—	2,25[f]	2,26	−0,01
33		$N(CH_3)$	N	CH_3	—	Br	2,23[f]	2,21	0,02
34		$N(CH_3)$	N	CH_3	Br	Br	2,24[f]	2,25	−0,01
35		$N(CH_3)$	N	—	—	CH_3	2,22[f]	2,07	0,15
								(2,31)[h]	(−0,09)
36		$N(CH_3)$	N	Br	—	CH_3	2,23[f]	2,05	0,18
								(2,29)[h]	(−0,06)
37		$N(CH_3)$	N	—	Br	CH_3	2,24[f]	2,11	0,13
								(2,35)[h]	(−0,11)
38		$N(CH_3)$	N	Br	Br	CH_3	2,28[f]	2,09	(−0,18)
								(2,33)[h]	(−0,05)
39		$N(CH_3)$	N	CH_3	CH_3	—	$2,17_{(3)}$[f]	2,14	0,03
40							$1,96_{(4)}$[f]	1,91	0,05
41		$N(CH_3)$	N	CH_3	Cl	CH_3	$2,20_{(3)}$[f]	2,22	−0,02

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
42							$2,23_{(5)}$ [f]	2,06 (2,30) [h]	0,17 (−0,07)
43		$N(CH_3)$	N	CH_3	NO_2	CH_3	$2,46_{(3)}$ [f]	2,43	0,03
44							$2,61_{(5)}$ [f]	2,29 (2,53) [h]	0,32 (0,08)
45		$N(CH_3)$	N	CH_3	CH_3	Cl	$2,15_{(3)}$ [f]	2,16	−0,01
46							$1,91_{(4)}$ [f]	1,94	−0,03
47		$N(CH_3)$	CH_3	N	—	—	2,30	2,31	−0,01
48		$N(CH_3)$	CH_3	N	Cl	Cl	2,30 [i]	2,31	−0,01
49		O	CH_3	N	—	—	2,40	2,48	−0,08
50		O	—	N	CH_3	—	2,17	2,29	−0,12
51		O	CH_3	N	CH_3	CH_3	$2,27_{(2)}$	2,38	−0,11
52							$1,95_{(4)}$	2,16	−0,21
53							$2,14_{(5)}$	2,10	−0,04
54		O	N	CH_3	—	—	2,28	2,29	−0,01
55		O	N	—	—	CH_3	2,42	2,35 (2,48) [h]	0,07 (−0,06)
56		O	N	CH_3	—	CH_3	$2,24_{(3)}$	2,25	−0,01
57							$2,40_{(5)}$	2,24 (2,37) [h]	−0,16 (0,03)
58		O	N	CH_3	—	CH_3O	2,10	2,26	−0,16
59		O	N	CH_3	NO_2	CH_3	$2,49_{(3)}$	2,51	−0,02
60							$2,77_{(5)}$	2,60 (2,73) [h]	0,17 (0,04)
61		O	N	CH_3	NH_2	CH_3	$2,00_{(3)}$ [f]	1,89	0,11
62							$2,10_{(5)}$	1,98 (2,11) [h]	0,12 (−0,01)
63		O	N	CH_3	CH_3	CH_3	$2,12_{(3)}$	2,16	−0,04
64							$1,85_{(4)}$	1,96	−0,11
65							$2,25_{(5)}$	2,21 (2,34) [h]	0,04 (−0,09)
66		O	N	CH_3	CN	CH_3	$2,38_{(3)}$	2,46	−0,08
67							$2,62_{(5)}$	2,51 (2,64) [h]	0,11 (−0,02)
68		O	N	CH_3	C_6H_5	CH_3	$2,22_{(3)}$	2,29	−0,07
69							$2,37_{(5)}$	2,30 (2,43) [h]	0,07 (−0,06)
70		O	N	CH_3	CH_3	NH_2	$2,03_{(3)}$	2,06	−0,03
71							$1,65_{(4)}$	1,65	0
72		O	N	OH	CH_3	CH_3	$1,83_{(4)}$	1,82	0,01
73							$2,22_{(5)}$	2,15 (2,28) [h]	0,07 (−0,06)
74		O	N	CH_3	Cl	CH_3	$2,17_{(3)}$	2,28	−0,11
75							$2,33_{(5)}$	2,33 (2,46) [h]	0 (−0,13)
76		O	N	C_6H_5	CH_3	CH_3O	1,60	1,86	−0,26
77		O	N	CH_3O	CH_3	CH_3	$1,74_{(4)}$	1,77	−0,03
78							$2,20_{(5)}$	2,22 (2,35) [h]	−0,02 (−0,15)
79		S	CH_3	N	CH_3	—	$2,67_{(2)}$	2,61	0,06
80							$2,38_{(4)}$	2,34	0,04
81		S	CH_3	N	—	—	2,74 [f]	2,70	0,04
82		S	—	N	CH_3	—	2,45	2,39	0,06
83		S	—	N	—	CH_3	2,49	2,51	−0,02
84		S	CH_3	N	CH_3	—	$2,61_{(2)}$	2,61	0
85							$2,33_{(4)}$	2,34	−0,01
86		S	CH_3	N		CH_3	$2,54_{(2)}$	2,59	−0,05
87							$2,36_{(5)}$	2,36	0
88		S	—	N	CH_3	CH_3	$2,35_{(4)}$	2,28	0,07

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
89							$2,31_{(5)}$	2,24	0,07
90		S	CH_3	N	CH_3	CH_3	$2,51_{(2)}$	2,55	−0,04
91							$2,24_{(4)}$	2,25	−0,01
92							$2,21_{(5)}$	2,27	−0,06
93		S	—	N	CH_3	NO_2	2,80 [f]	2,64	0,16
94		S	CH_3	N		CH_3	$2,70_{(2)}$ [f]	2,75	−0,05
95					NO_2		$2,62_{(5)}$ [f]	2,62	0
96		S	CH_3	N	CH_3	NO_2	$2,70_{(2)}$ [f]	2,78	−0,08
97							$2,74_{(4)}$ [f]	2,61	0,13
98		S	N	CH_3	—	—	2,41 [f]	2,38	0,03
99		S	N	—	CH_3	—	2,17 [f]	2,15	0,02
100		S	N	—	—	CH_3	2,41	2,51	−0,10
101		S	N	CH_3	Cl	—	2,46	2,41	0,05
102		S	N	CH_3	NO_2	—	2,74	2,64	0,10
103		S	N	Cl	CH_3	—	2,28	2,18	0,10
104		S	N	—	Cl	CH_3	2,43	2,54	−0,11
105		S	N	—	NO_2	CH_3	2,88	2,67	0,21
106		S	N	CH_3	—	CH_3	$2,31_{(3)}$	2,34	−0,03
107							$2,48_{(5)}$	2,47	0,01
108		S	N	CH_3	CH_3	—	$2,31_{(3)}$	2,29	0,02
109							$2,18_{(4)}$	2,06	0,12
110		S	N	—	CH_3	CH_3	$2,12_{(4)}$	2,06	0,06
111							$2,36_{(5)}$	2,42	−0,06
112		S	N	CH_3	CH_3	CH_3	$2,22_{(3)}$	2,25	−0,03
113							$1,97_{(4)}$	1,97	0
114							$2,28_{(5)}$	2,38	−0,10
115		O	CH_3	N	N	CH_3	2,48	2,49	−0,01
116		O	N	CH_3	CH_3	N	2,32	2,27	0,05
117		S	CH_3	N	N	CH_3	2,74	2,56	0,18
118		N(CH_3)	CH_3	N	N	N	2,58 [f]	2,30 (2,50) [h]	0,28 (0,08)

[a] The δ values for compounds 1-6 were taken from [5], the values for compounds 8-13 were taken from [6], the values for compounds 7, 14, and 15 were taken from [2] the values for compounds 16-42 were taken from [7], the values for compounds 43-46 were taken from [8], the value for compound 48 was taken from [9], the values for compounds 49-53 were taken from [10], the values for compounds 54-78 were taken from [11], the values for compounds 79-92 were taken from [12], the values for compounds 93-97 were taken from [13], the values for compounds 98-100 were taken from [14], the values for compounds 101-105 were taken from [15], the values for compounds 106-114 were taken from [16], the values for compound 118 was taken from [17, 18], and the values for compounds 47 and 115-117 were measured by us.

[b] The heteroatoms were considered to be substituents.

[c] The solvent was CCl_4.

[d] $\delta' = 2,34 + \Sigma\Delta\delta_i$; the $\Delta\delta_i$ values were taken from [2].

[e] $\Delta\Delta\delta = \delta - \delta'$.

[f] In $CDCl_3$.

[g] Here and subsequently, when there are two nonequivalent methyl groups in the ring, the position of the "indicator" CH_3 group is indicated in parentheses.

[h] The $\Delta\delta_{2N}$ increment was used in place of $\Delta\delta_{4N}$.

[i] In $CH_2Cl_2 + CHCl_3$ (3 : 1).

As seen from Table 1, the additivity ratio

$$\delta' = \delta^0 + \Sigma\Delta\delta_i \quad (1)$$

in the overwhelming majority of cases satisfactorily conveys the effect of some of the substituents and the heteroatoms on the δ^{CH_3} value in five-membered rings:

$$\delta^{CH_3} = 0.16 + 0.93\delta' \quad (r = 0.963,\ n = 93).* \quad (2)$$

One must note only the following violation of this rule. In contrast to pyridine derivatives, in which the presence of a nitrogen heteroatom in the 4 position practically does not exert its characteristic electron-acceptor effect on the shift of the protons of the methyl group [2], its activating effect on the para-like position of the isoxazole, pyrazole, and tetrazole rings in most cases is almost as intense as on the ortho position ($\Delta\delta \sim 0.15$ ppm). The observed intensification of the electron-acceptor capacity is evidently associated with the polarizing effect of the second heteroatom in the ring adjacent to the nitrogen atom, which displays pronounced electron-donor properties via a conjugation mechanism.

IR Spectra. The results of measurements of the intensity of the band of the symmetrical C–H stretching vibration of the methyl group [$(A_{CH}s)^{1/2}$] in the IR spectra of the series of investigated azoles are presented in Table 2. Their treatment via a similar scheme with allowance for the previously obtained data on the intensity of the C–H vibrational bands in a series of substituted toluenes and methyl derivatives of six-membered nitrogen heterocycles [2, 21, 22] has shown that in this case also the effect of several of the substituents and heteroatoms is subject to the additivity principle:

$$(A_{CH}s)^{1/2} = 4.8 + 0.8\Sigma\,(A_{CH}s)^{1/2}_{calc} \quad (r = 0.946,\ n = 18). \quad (3)$$

In summarizing the above material, it can be concluded that, with few exceptions, the experimental data on the δ^{CH_3} and $(A_{CH}s)^{1/2}$ values for a large number of substituted azoles can be united in a single reaction series with analogous data for polysubstituted toluenes and six-membered nitrogen heterocycles within the framework of a common additive scheme.

Quantum-Chemical Examination

IR Spectra. In recent years the CNDO/2 and INDO methods have come to be used more and more extensively for the calculation of the derivatives of the dipole moment with respect to the nuclear coordinates ($\partial\mu/\partial Q$) and consequently for the description of the integral intensity of the bands of various vibrations ($A^{1/2}$) in the IR spectra of polyatomic organic molecules (for example, see [23-31]). However, the applicability of the indicated approaches for the comparative study of the intensities of bands in extensive series of compounds is fraught with certain difficulties associated primarily with the considerable expenditure of computer time.†

In the case of similarly constructed compounds the practical realization of quantum-chemical expressions for the $A^{1/2}$ values can be simplified substantially when there is approximate conformity between the changes in the $\partial\mu/\partial Q$ derivatives and the distribution of the electron density on the atoms that participate in the vibrations.

Our calculation by the CNDO/2 method of the surplus electronic charges on the carbon ($\Delta q_C^{\sigma+\pi}$) and hydrogen (ΔQ_{H_1}) atoms and of the overall charge on the C and H atoms of the methyl group ($\Delta q_{CH_3} = 3\Delta q_{H_1} + \Delta q_C^{\sigma+\pi}$) showed (Tables 2-4)‡ that identical expressions

$$(A_{CH}s)^{1/2} = 31.1 - 370\Delta q_{CH_3} \quad (r = 0.907,\ n = 26), \quad (4)$$

$$(A_{CH}s)^{1/2} = 34.7 - 597.3\Delta q_{H_1} \quad (r = 0.917,\ n = 26), \quad (4a)$$

$$(A_{CH}s)^{1/2} = 34 - 725.3\Delta q_{H_1} - 89.1\Delta q_C^{\sigma+\pi} \quad (R = 0.919,\ n = 26) \quad (4b)$$

can be successfully used for the description of the trend of the change in the intensity of the band of the symmetrical C–H vibration of the methyl groups of both aromatic (substituted toluenes) and five- and six-mem-

* Compounds for which $\Delta\Delta\delta > 0.1$ ppm were excluded from the correlation treatment (see Table 1).

† The obtaining of one $\partial\mu/\partial Q$ value on the basis of numerical differentiation requires the calculation of 10-15 configurations in the vicinity of the equilibrium state of the molecules.

‡ In most cases the basis of the calculation of the investigated methyl derivatives has been the experimental geometry of the corresponding unsubstituted heterocycles [32-40]; the idealized geometry parameters recommended by Pople and Gordon [41] have been used for the substituents. The calculations were made with a BÉSM-6 computer from a program composed in the department of quantum chemistry of Leningrad State University.

TABLE 2. Intensity of the Band of the Symmetrical C–H Vibration of the Methyl Group in Five-Membered Heteroaromatic Monocyclic Compounds ($\nu_{CH} = 2935 \pm 10$ cm^{-1})

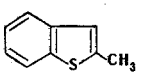
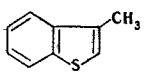
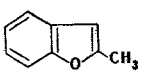
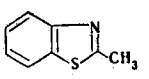
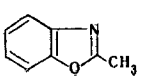
Compound No.	Heterocycle	Substituents					A_{CH}[a]		$\Delta\Delta A_{CH}^{1/2}$[c]	Δq_{CH_3}, au
		R_1	R_2	R_3	R_4	R_5	meas.[a]	calc.[b]		
1	2	3	4	5	6	7	8	9	10	11
1		$N(CD_3)$	CH_3	N	—	—	23,0	26,8	−3,8	0,0020
2		$N(CD_3)$	CH_3	N	—	NO_2	17,0[e]	17,1	−0,1	0,0236
3		$N(CD_3)$	N	CH_3	—	CH_3	28,8	31,6	−2,8	0,0088
4		$N(CD_3)$	N	CH_2	Cl	CH_3	25,6	26,9	−1,3	
5		$N(CD_3)$	N	CH_3	NO_2	CH_3	18,9[e]	18,4	0,5	0,0616
6		$N(CD_3)$	N	CH_3	Br	CH_3	24,6	23,0	1,6	—
7		$N(CD_3)$	N	CH_3	NH_2	CH_3	29,4	35,4	−6,0	−0,0020
8		$N(CD_3)$	N	CH_3	I	CH_3	27,0	—	—	—
9		O	CH_3	N	CH_3	CH_3	23,5	26,4	−3,1	0,0120
10		O	N	CH_3	—	CH_3	25,0	22,0	3,0	0,0144
11		O	N	CH_3	Br	CH_3	15,8	13,4	2,4	0,0289
12		O	N	CH_3	NO_2	CH_3	11,6[e]	7,9	3,7	0,0580
13		O	N	CH_3	Ph—N=N	CH_3	18,6	15,4	3,2	—
14		S	CH_3	N	CH_3	—	26,2	24,6	1,6	0,0234
15		S	CH_3	N	—	CH_3	26,2	25,4	0,8	0,0183
16		S	—	N	CH_3	—	25,6	24,3	1,3	0,0121
17		S	—	N	—	CH_3	27,4	26,1	1,3	0,0100
18		S	CH_3	N	N	CH_3	17,3	19,1	−1,8	0,0289
19		O	CH_3	N	N	CH_3	18,7	16,6	2,1	0,0362
20		O	N	CH_3	CH_3	N	17,0	22,4	−5,5	—
21		O		CH_3	CH_3	N	14,0	18,0	−4,0	—
22		$N(CD_3)$	CH_3	N	CH_3	N	23,2	21,4	1,8	—
23		$N(C_6H_5)$	CH_3	N	N	N	15,3	15,8	−0,5	0,0309

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
24		S	CH_3	—	—	—	29,5[f]	—	—	0,0140
25		S	—	CH_3	—	—	32,5[f]	—	—	0,0019
26		O	CH_3	—	—	—	27,0[f]	—	—	0,0110

[a]This is the integral intensity of the ν_{CHs} vibrational band referred to a single methyl group (in liters per mole per square centimeter). The IR spectra of 0.01-0.05 mole/liter of the compound in CCl_4 were recorded (IKS-16 instrument).
[b]$(A_{CHs})^{1/2} = 33.6 + \Sigma\Delta A^{1/2}$. The $\Delta A^{1/2}$ values were calculated from the data in [2, 21, 22], as were the increments for the oxygen heteroatom in the 3 position ($\Delta A^{1/2} = -4.0$) and the heteroatomic $N(CH_3)$ grouping in the 2 and 3 positions ($\Delta A^{1/2} = 1.8$ and $\Delta A^{1/2} = 7.2$, respectively), which were determined from the data in the present table.
[c]These are the differences between the measured and calculated $(A_{CHs})^{1/2}$ values.
[d]Referred to a single methyl group.
[e]The presented value is evidently too high because of partial overlapping of the bands belonging to the stretching vibrations of the methyl and nitro groups.
[f]Taken from [22].

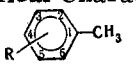
TABLE 3. Intensity of the Symmetrical C–H Vibration of the Methyl Group in Five-Membered Heteroaromatic Rings

Comp. No.	Compound	$(A_{CHs})^{1/2}$, [a] liter$^{1/2}$ · mole^{-1} · cm^{-2}	Δq_{CH}, au
1		28,4	0,0153
2		28,0	0,0013
3		26,6	0,0161
4		18,0	0,0372
5		17,5	0,0433

[a]Taken from [22].

membered heteroaromatic compounds. In conformity with the conclusions obtained on the basis of the results of correlation analysis [21, 22], the existence of the indicated dependences indicates that electronic effects play the leading role in the change in the intensity of the bands of the C–H stretching vibrations.

PMR Spectra. Although there have frequently been attempts [42-44] to investigate the relationship between the chemical shift of the protons of the methyl groups and the changes in the electron density on the hydrogen atoms and on the carbon atoms that constitute their immediate envioronment, a theoretically substanti-

TABLE 4. Spectroscopic and Quantum-Chemical Characteristics of the Methyl Group in Substituted Toluenes 

Comp. No.	R	δ_{CH_3}, ppm	[a] $(A_{CH}^s)^{1/2}$, [b] liter$^{1/2}$ · mole$^{-1/2}$ · cm^{-2}	Δq_H, au	Δq_C, $\sigma+\pi$ au	Δq_{CH_3}, au
1	H	2,34	33,2	0,0046	−0,0185	−0,0047
2	3-CH_3O	2,31	31,2	0,0067	−0,0206	−0,0005
3	3-CH_3	2,30	35,0	0,0046	−0,0191	−0,0053
4	4-CH_3	2,28	34,4	0,0033	−0,0169	−0,0070
5	3-F	2,36	31,7	0,0084	−0,0209	0,0043
6	4-F	2,33	31,0	0,0045	−0,0156	−0,0021
7	4-CN	2,44	—	0,0076	−0,0199	0,0029
8	3-NO_2	2,50	26,6	0,0119	−0,0201	0,0156
9	4-NO_2	2,51	23,5	0,0132	−0,0233	0,0163
10	2-N	2,55	25,0	0,0144	−0,0337	0,0095
11	3-N	2,32	29,8	0,0053	−0,0180	0,0021
12	4-N	2,31	25,6	0,0085	−0,0248	0,0004

[a]Taken from [2].
[b]Taken from [21].

TABLE 5. Charges on the H and C Atoms of the Methyl Group in Five-Membered Heterocycles

Compound No. in Table 1	Δq_{H_1} au	$\Delta q_C^{\sigma+\pi}$ au	Compound No. in Table 1	Δq_{H_1} au	$\Delta q_C^{\sigma+\pi}$ au
1	0,0176	−0,0418	53	0,0120	−0,0343
3	0,0224	−0,0455	59	0,0304	−0,0455
6	0,0157	−0,0401	60	0,0416	−0,0545
7	0,0046	−0,0137	74	0,0190	−0,0446
8	0,0116	−0,0208	75	0,0265	−0,0338
9	0,0044	−0,0113	81	0,0240	−0,0374
10	0,0165	−0,0250	82	0,0134	−0,0281
11	0,0089	−0,0161	83	0,0106	−0,0212
12	0,0132	−0,0194	86	0,0224	−0,0359
13	0,0099	−0,0191	87	0,0081	−0,0193
14	0,0055	−0,0231	94	0,0331[a]	−0,0383[a]
18	0,0117	−0,0274	96	0,0353	−0,0425
19	0,0135	−0,0306	97	0,0321	−0,0340
41	0,0136	−0,0290	98	0,0154	−0,0323
43	0,0251	−0,0355	99	0,0039	−0,0051
44	0,0491	−0,0640	100	0,0153	−0,0279
47	0,0180	−0,0518	102	0,0284	−0,0361
49	0,0282	−0,0491	105	0,0474	−0,0693
50	0,0100	−0,0207	115	0,0277[b]	−0,0469[b]
51	0,0269	−0,0482	116	0,0174[c]	−0,0293[c]
52	0,0068	−0,0178	117	0,0237	−0,0422
			118	0,0271	−0,0504

[a]For 2-Methyl-4-nitrotriazole.
[b]For 2-methyloxadiazole.
[c]For 2-methylfurazan.

ated analytical expression of this dependence has not yet been established. In the series of compounds that we examined the best correlation was found by contrasting the δCH_3 values with surplus charges on the hydrogen atoms (Table 5). The dependences thus obtained have the following form:

For substituted toluenes and six-membered nitrogen-containing heterocycles

$$\delta = 2.21 + 21.3\Delta q_{H_1} \quad (r = 0.864,\ n = 13); \tag{5}$$

for thiophene, thiazole, isothiazole, and thiadiazole derivatives

$$\delta = 2.19 + 15.9\Delta q_{H_1} \quad (r = 0.944,\ n = 16), \tag{6}$$

$$\delta = 2.18 + 13.9\Delta q_{H_1} - 1.6\Delta q_C^{\sigma+\pi} \quad (R = 0.945,\ n = 16); \tag{6a}$$

for pyrazole, imidazole, and tetrazole derivatives

$$\delta = 1.96 + 19.1\Delta q_{H_1} \quad (r = 0.973,\ n = 6), \tag{7}$$

$$\delta = 1.96 + 19.4\Delta q_{H_1} + 0.3\Delta q_C^{\sigma+\pi} \quad (R = 0.973,\ n = 6); \tag{7a}$$

for furan, oxazole, isoxazole, and oxadiazole derivatives

$$\delta = 1{,}92 + 18{,}4\Delta q_{H_1} \quad (r = 0{,}926,\ n = 15), \tag{8}$$

$$\delta = 1{,}96 + 13{,}2\Delta q_{H_1} - 0{,}8\Delta q_C^{\sigma+\pi} \quad (R = 0{,}866,\ n = 11). \tag{8a}$$

The fact that, in contrast to the intensity of the IR bands, the changes in the chemical shift of the protons of the methyl group cannot be described within the framework of a single correlation relationship is an indirect confirmation of the concept of the substantial effect of changes in the ring current on the δ^{CH_3} value, the relative contribution of which to the shielding constants of the protons of the methyl group depends on the type of heteroatom. The character of the shift of correlation lines (6)-(8) relative to line (5) corresponds to a successive decrease in the aromatic character of the five-membered rings in the order benzene > thiophene > pyrrole > furan [45-48].

Worthy of special mention is the fact that in all of the investigated reaction series the introduction of a pyridine nitrogen heteroatom in the five- and six-membered ring does not give rise to appreciable deviations of the corresponding compounds from correlation ratios (5)-(8). Despite the point of view regarding the predominant contribution of the magnetic anisotropic effect and the effect of the electrical field of the unshared pair of the $-N=$ heteroatom that has been expressed in the literature, [44], the character of the dependences obtained in this research constitutes an argument in favor of the conclusion of the primarily electronic nature of its effect on the δ^{CH_3} value.

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EFFECT OF N-ALKYL AND N-ARALKYL SUBSTITUENTS ON NUCLEOPHILIC SUBSTITUTION IN THE BENZIMIDAZOLE SERIES

M. M. Medvedeva, V. N. Doron'kin, A. F. Pozharskii, and V. N. Novikov

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It is shown in the case of the Chichibabin reaction and exchange of chlorine in 2-chlorobenzimidazoles by a piperidine residue that N-alkyl and N-aralkyl groups are arranged in the following order with respect to their effect on the rate of the process (in the order of decreasing rates): $CH_3 > C_6H_5CH_2$, $C_2H_5 >$ iso-C_3H_7, $(C_6H_5)_2CH >$ n-$C_9H_{19} >$ tert-C_4H_9. The overall decrease in the rate on passing to compounds with branched N-substituents is low. It follows from this that steric hindrance to nucleophilic substitution in the 2 position is only of small significance.

In a previous study of the Chichibabin reaction in the benzimidazole series it was qualitatively concluded that α-branched N-substituents (iso-C_3H_7, $C_6H_5CH_2$, cyclohexyl, benzhydryl, and particularly tert-butyl) have a passivating effect on the course of the process; this was ascribed to steric factors [1-5]. In the present research we set out to make a quantitative study of the effect of N-alkyl and N-aralkyl groups on the two most typical nucleophilic substitution reactions in the benzimidazole series: amination with sodium amide (the Chichibabin reaction) and exchange of chlorine by a secondary amine residue (for which we selected piperidine).

Chichibabin Reaction

The results of measurements of the rate of gas evolution and the composition of the gas in the amination of 1-substituted benzimidazoles Ia-g with sodium amide in o-xylene or dimethylaniline at various temperatures are presented in Figs. 1 and 2 and Table 1. It should be noted that the composition of the gas was determined only at the end point of the reaction from the results of titration of the ammonia formed. Thus the curves in Figs. 1-3 were constructed from the results of measurements of the total volume of hydrogen and ammonia.

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