STUDY OF SUBSTITUENT EFFECTS IN N-PHENYL-N',N'-DIMETHYLUREA

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IR, ^{1}H-NMR, and mass spectra of 12 ring-substituted derivatives of N-phenyl-N',N'-dimethyl-urea have been measured. The ^{1}H-NMR chemical shifts of protons of NH and CH$_3$ groups, wave numbers of valence vibrations of N—H and C=O bonds, and fragmentation velocity of the molecular ion have been correlated with the Hammett substituent constants.

Spectral methods allow quick evaluation of substituent effects at various positions of a molecule, which is hardly possible by other methods. In our previous papers[1-4] we showed how it is possible to influence the magnitude of polar effects on some spectral parameters of groups by a change of medium, especially for the groups able of hydrogen bond formation. The present study has been carried out with the aim of evaluation of substituents effects in the benzene ring of N-phenyl-N',N'-di-methylurea on the valence vibrations of N—H and C=O bonds, ^{1}H-NMR chemical shifts of NH and CH$_3$ groups, and fragmentation velocity of the molecular ion. Problems of study of urea derivatives by IR, NMR and mass spectroscopical methods are summarized in ref.[5].

EXPERIMENTAL

The IR spectra were measured with a UR-20 spectrophotometer (Zeiss, Jena) in tetrachloro-methane and acetonitrile solutions in 14 mm and 1 mm cells. The ^{1}H-NMR spectra were mea-sured with a 60 MHz spectrometer Varian A 60 in hexadeuteriodimethyl sulphoxide, using tetra-methylsilane as the internal standard. The mass spectra were measured with an A.E.I. MS 902 spectrometer at the electron energy 70 eV using the direct inlet. Temperature of the ionic source varied within 120 to 140°C for the various substances.

Mass Spectra of N-Phenyl-N',N'-dimethylurea Derivatives m/e (% rel. int. of ion labelling)

I, R = H: 28 (1), 30 (2·5), 38—45 (1, 5, 1, 1, 5, 2, 17*b*, 7·5*d*), 50—52 (1·3, 4, 1), 56 (2·3), 63—66 ⟨2·2, 3*f*, 7·8*i*, 2), 72 (100*a*), 73 (4·2), 77 (5·3*n*), 91—93 (4·3*e*, 3*b'*, 4 h), 106 (2·6*k*), 107 (1), 119 (8·3*c*), 120 (2·5), 147—149 (2*g*, 1·2*m*, 1*j*), 163—165 (2·5*l*, 37 M$^{+\cdot}$, 5).

II, R = 3-CH$_3$: 28 (2), 30 (1), 32 (1), 38—46 (1, 4, 1, 2·1, 4·8, 2, 18·5*b*, 13*d*, 1), 50—53 (2·2, 3·8, 2·3, 1), 56 (2·2), 62—65 (0·8, 2, 1·2, 4), 71—73 (1, 100*a*, 4), 77—80 (7*f*, 5·2, 2·5*i*, 1), 88—91 (1, 1, 0, 5*n*), 104—108 (2·8*e*, 1·3, 3*b′*, 3*h*), 120 (2·6*k*), 132—134 (2·7, 7*c*, 2), 146 (1*g* — CH$_3^+$), 161—163 (2·8*g*, 1*m*, 1*j*), 177—179 (2, 35 M$^{+\cdot}$, 5).

III, R = 3-OCH$_3$: 28 (1), 30 (1·2), 32 (1), 39 (3·8), 41—45 (3·6, 5, 14, 14*b*, 10·5*d*), 50—52 (1·2, 3·7, 3·8), 56 (2), 58 (4), 63—65 (2·6, 3, 2), 72 (100*a*), 73 (4), 77—79 (3, 3, 2), 91 (3 C$_6$H$_5$ — (+)· — N), 92 (2·1), 95 (2·5*h* — HCN), 106 (2*e* — CH$_3^+$), 107 (1·5*n* + [*b′* — CH$_3^+$]), 119 (4 C$_6$H$_5$—N= =C=O$^{(+)\cdot}$), 120 (1·5), 122—124 (2·2*h*, 2·6*b′*), 136 (1·5*k*), 148—150 (1·6, 13·5*c*, 2·6), 177—179 (2, 1, 1), 193—195 (2, 28 M$^{+\cdot}$, 3).

IV, R = 3-CF$_3$: 28 (1·5), 30 (1), 32 (0·6), 39 (1), 41—45 (1, 5·5, 2·5, 12*b*, 2*d*), 56 (2), 63 (2), 72 (100*a*), 73 (4), 83 (1), 92 (1), 113 (1·2*f* — F$^\cdot$), 114 (1), 133 (1*i*), 140 (1*e* — F$^\cdot$), 145 (2*n*), 159 to 161 (1*e*, 1*b′* + [*k* — F$^\cdot$], 1*h*), 168 (1·5*c* — F$^\cdot$), 179 (0·5*k*), 188 (2*c*), 213—217 (1·5 M — F$^\cdot$, 0·3, 0·3*g*, 0·3, 0·3*j*), 231—233 (1, 20 M$^{+\cdot}$, 2).

V, R = 3-COCH$_3$: 27—29 (1·8, 2·8, 1), 38 (1), 39 (2·5), 41—45 (2·5, 5, 14, 15*b*, 5·5*d*), 50—52 (1, 1, 1), 55—58 (1, 2, 2, 1, 1), 62—64 (2·5*f* — COCH$_3^+$, 2, 2), 69 (1), 71—73 (1, 100*a*, 4), 76—78 (1, 1·8, 1·5), 90—92 (2·6*e* — COCH$_3^+$, 2·2, 1) 118—120 (2*c* — COCH$_3^+$, 1·3*n* + [*c* — COCH$_2$], 1), 134 (0·8*b′*), 135 (0·8*h*), 146 (4*c* — CH$_3^+$), 148 (1*k*), 161—163 (2*c*, 0·8, 1·5 M — COCH$_3^+$) 189 (0·5*g*), 191 (0·5*j*), 205—207 (1, 21 M$^{+\cdot}$, 2·8).

VI, R = 3-NO$_2$: 27—30 (2·2, 2·5, 1, 1·2), 38 (1·6), 39 (3), 41—45 (2·4, 7, 8·6 *b*, 2·8 *d*), 50—52 (2, 1, 1·2), 55—58 (1, 2·2, 1, 2·3), 62—65 (1,3 *f* — NO$_2^\cdot$, 2·8, 1·2), 69 (1), 71—79 (1, 100 *a*, 5,1·2, 1·3, 2, 1, 0·8, 0·8), 81 (1), 90—92 (3*e* — NO$_2^\cdot$, 1·3, 1), 106 (1*c* — NO$^\cdot$ — CO), 118 (1*c* — — NO$_2^\cdot$, 0·8), 134 (0·5*c* — NO$^\cdot$), 151 (0·5*k*), 164 (2*c*), 192—194 (0·8*g*, 0·8*m*, 0·7*j*), 208—210 (1, 13·5 M$^{+\cdot}$, 2·4)

VII, R = 4-NO$_2$: 27—30 (1·2, 1·2, 0·5, 2·5), 37—45 (0·5, 1, 2·4, 1, 2, 6·8, 6·7, 12*b*, 2·5*d*), 50—53 (1·8, 1, 1, 0·8), 55—58 (1,2·8, 1, 1·2), 62—65 (0·8, 3*f* — NO$_2^\cdot$, 2·4, 1), 69 (1), 72—75 (100*a*, 4, 1·2, 1·2, 1·3), 78 (0·8), 90 (4*e* — NO$_2^\cdot$), 91 (1·3), 106 (1*c* — NO$^\cdot$ — CO), 118 (0·8*c* — NO$_2^\cdot$), 134 (2*c* — NO$^\cdot$), 151 (0·5*k*), 164 (2*c*), 191—194 (0·6 M — H$_2$O, 0·5*g*, 0·6*m*, 0·5*j*), 208—210 (1, 12 M$^{+\cdot}$, 2)

VIII, R = 3-Cl: 28 (1·8), 30 (1), 32 (0·5), 39 (2), 41—45 (2, 5·3, 4, 12*b*, 3*d*), 50 (1), 56 (2·5), 62—65 (1, 3, 1·8, 1), 69 (1), 72—75 (100*a*, 4, 1, 2·4), 81 (1), 90 (2), 91 (1), 99 (2·5*i*), 111 (1·2*n*), 125—127 (1*e*, 0·8*b′*, 2*h*), 140 (0·8*k*), 153—155 (3·8*c*, 1, 1·2), 162 (1 M — HCl), 181 (0·8*g*), 183 (0·7*j*), 197—200 (1, 16 M$^{+\cdot}$, 2·2, 5·4)

IX, R$_1$ = 3-Cl, R$_2$ = 4-OCH$_3$: 26—30 (2·3, 6·8, 5·3, 3, 5·4), 35—46 (13, 73 HCl, 4, 25, 5·3, 5·5, 7·2, 21, 17, 100*b*, 60*d*, 2·6) 50—58 (2·5, 8·5, 11, 4, 2, 1·8, 2, 1·6), 60—65 (1·2, 2, 2·4, 5, 2, 4), 69 (2), 72 (88*a*), 73 (4), 75—81 (1, 2·2, 1·2, 10, 5, 4, 1), 86—92 (1·8, 3*f* — CH$_3^+$ — CO, 1, 1, 2·2, 1, 1, 1·5), 99 (1·6), 114—116 (20*e* — CH$_3^+$ — CO, 1·8, 7), 140 (2·2*i*), 141—145 (76*e* — CH$_3^+$, 6·6, 26, 2·2), 149 (1·2), 156—160 (2·5, 41*e* + *b′*, 5*h*, 14), 168 (4*c* — CH$_3^+$), 170 (2*k*), 183—185 (12*c*, 2, 4), 227—230 (1, 15 M$^{+\cdot}$, 2, 5)

X, R$_1$ = 3-Cl, R$_2$ = 4-SCH$_3$: 26—30 (1, 6·8, 4, 4, 6·5), 32 (0·5), 35—46 (10, 58 HCl, 2·8, 15', 5·3, 5, 7, 20, 22, 94*b*, 53*d*, 2·5), 50—52 (3·8, 4, 4), 55—58 (2·6, 2·8, 2·2, 1), 60—63 (1, 1, 1·2, 3)' 69 (2·6), 71—79 (1·2, 100*a*, 5, 1·2, 1, 2, 5, 17, 2), 95 (1·3), 121 (1·2), 122 (1·2), 149 (2), 172 (1·5), 174 (1·5), 184 (6*c* — CH$_3^+$), 186 (2·6), 196 (0·8*k*), 199—201 (21*c*, 2·6, 8·6), 244—246 (18 M$^{+\cdot}$, 2·6, 6·5)

Mass spectra — Continued

RESULTS AND DISCUSSION

Table I gives the wave numbers of valence vibrations of N—H and C=O bonds (amide I band), ^{1}H-NMR chemical shifts of NH and CH_3 groups, and logarithms of the intensity ratio of the molecular ion and the ion with m/e 72 for the studied derivatives. Correlations of the IR data with the respective Hammett substituent constants had the following form:

$$\nu(N\text{—}H) = 3473 - 4.8\sigma, \quad R = 0.853, \quad s = 0.70 \,(CCl_4 \text{ solutions}) \quad (1)$$

$$\nu(N\text{—}H) = 3410 - 20.8\sigma, \quad R = 0.980, \quad s = 1.00 \,(CH_3CN \text{ solutions}) \quad (2)$$

$$\nu(C\text{=}O) = 1669 + 9.1\sigma, \quad R = 0.755, \quad s = 1.88 \,(CH_3CN \text{ solutions}) \quad (3)$$

The correlation of $\nu(N\text{—}H)$ obtained in CCl_4 solutions is not satisfactory. As in other cases, acetonitrile also here causes an amplification of the polar substituent effects, and the correlation is markedly improved. The dependence of $\nu(C\text{=}O)$ on the substituent constants can be called only a qualitative one. The 4-nitro derivative was not involved in the calculation; back calculation gave the Yukawa–Tsuno factor $r = 0.45$ for 4-nitro group in this set.

TABLE I

Wave-Numbers of Valence Vibrations of N—H and C=O Bonds, Chemical Shifts of Protons of NH and CH_3 Groups and Relative Intensities of Z Ions

Substituent	$\nu(N\text{—}H)$		$\nu(C\text{=}O)$ CH_3CN	$\delta(NH)$	$\delta(CH_3)$	$\log Z^a$
	CCl_4	CH_3CN		DMSO		
3-CH$_3$	3 473	3 411	1 669	8·33	3·10	0·441
H	3 472·5	3 410	1 669	8·41	3·10	0·422
4-Br	3 472	3 406	1 671	8·53	3·10	—
4-Br-3-CH$_3$	3 472	3 406	1 669	8·47	3·10	—
3-CF$_3$	3 471	3 402	1 674	8·75	3·11	0·699
3-OCH$_3$	3 474	3 410	1 671	8·38	3·10	0·521
3-Cl	3 471·5	3 402	1 674	8·60	3·11	0·739
3-Cl, 4 SCH$_3$	3 471·5	3 401	1 669	8·61	3·11	0·740
3-Cl, 4-OCH$_3$	3 471·5	3 407	1 668	8·43	3·10	0·758
3-NO$_2$	3 469	3 395	1 675	8·93	3·13	0·848
4-NO$_2$	3 468	3 389	1 676	9·10	3·13	0·885
3-COCH$_3$	3 471	3 403	1 675	8·60	3·11	0·649

^{a} $Z = a/M^+$.

The Hammett correlations of the NH and CH_3 protons chemical shift had the following form:

$$\delta(\text{NH}) = 8\cdot36 + 0\cdot76\sigma, \quad R = 0\cdot971, \quad s = 0\cdot04 \text{ ppm} \tag{4}$$

$$\delta(\text{CH}_3) = 3\cdot10 + 0\cdot04\sigma, \quad R = 0\cdot916, \quad s = 0\cdot004 \text{ ppm} \tag{5}$$
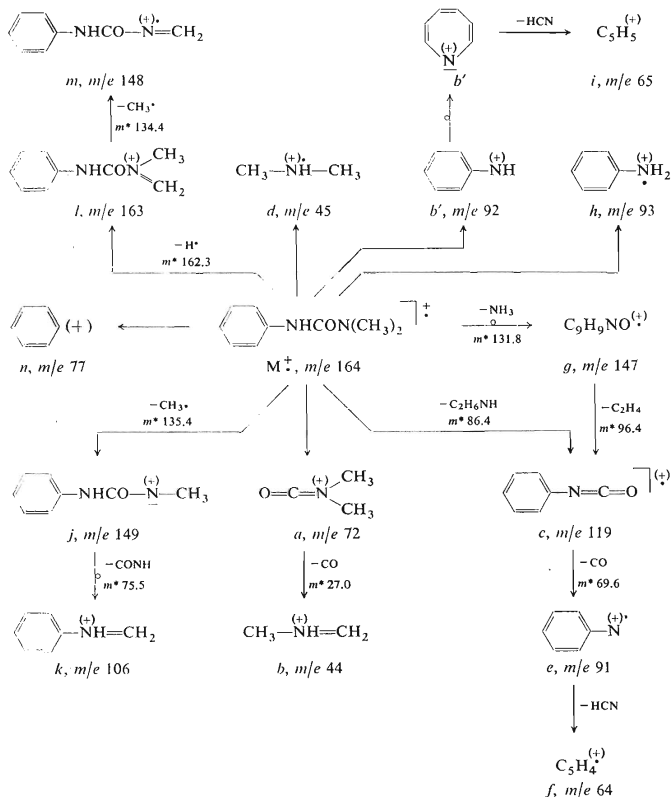
SCHEME 1

Again 4-nitro derivative was not involved in calculation of the constants of Eqs (4) and (5); back calculation gave the Yukawa–Tsuno factor $r = 0.41$ for 4-nitro group in this set. The low value $d\delta/d\sigma$ in Eq. (5) shows that the substituent effects on the CH_3 chemical shifts are markedly weakened by the grouping NH—CO—N (the value is six times lower than that of the substituted toluenes[6,7]). The substituent effects on the NH proton chemical shift of the urea derivatives are comparable with those of acetanilides and methansulfonylanilides[3].

The mass spectra of the studied derivatives are shown in a shortened form in Experimental. Mass spectral fragmentation of urea and its derivatives was studied by Baldwin and coworkers[8] who also gave some general fragmentation processes leading to formation of the ions $a\,(R^1R^2—N=C=O)$, $b\,(R^1R^2N^+)$, $c\,([R^3N=C=$ $=O]^+)$ and $d\,([R^1R^2NH]^+)$. The mass spectrum of N-phenyl-N',N'-dimethylurea given in ref.[8] is considerably different from that measured by us under similar conditions. The main peak of the published[8] spectrum is that of the ions $PhNH_2^+$ (m/e 93) making almost 40% of the total ionic current. The other ions, except for the molecular ion, form peaks of relative intensities below 10%. The ions $d\,((CH_3)_2NH)^+$ are not recorded in the spectrum at all. The ions $a\,((CH_3)_2N^+=C=O)$, making the main peaks with the urea derivatives measured by us (except for N-(3-chloro-4-methoxy)phenyl-N',N'-dimethylurea where they form a peak of relative intensity 88%), form a peak of relative intensity about 2% in the published spectrum[8]. We analyzed the measured spectra by means of metastable peaks, by measurements with high resolving power, and by measurement of the compound labelled by deuterium at nitrogen. The basic fragmentation can be shown in the case of the non-substituted derivative. The fragmentations proceed in several parallel series beginning from the molecular ion. The ions a forming the basic peak are further split into ions b. The ions c eliminate CO to give the ions e, and after splitting off of HCN the ions f are formed. The ions c are formed from both the molecular ions and the ions g (C_9H_9. $.NO^+$, m/e 147) which were formed by elimination of NH_3 directly from the molecular ions. This elimination of NH_3 can be observed with all the derivatives measured by us except for 3-chloro-4-methoxy derivative, although intensity of the peaks formed is relatively low. By mass spectral measurement of N-deuterio-N-phenyl-N',N'-dimethylurea we found that the eliminated NH_3 consisted of three quarters N atom one quarter N' atom. We suppose that the ion b' formed from the molecular ion and containing an even number of electrons is rearranged[9] to form a seven-membered ring which eliminates HCN to give the ion i. Elimination of $CH_3^•$ from the molecular ion gives the ion j which is rearranged to the ion k. The ions k form little intensive peaks of the spectra, nevertheless they are characteristic for the urea derivatives measured by us. From the measurements of N-deuterio-N-phenyl-N',N'-dimethylurea it follows that the ions k contain exclusively the atom N. Elimination of hydrogen from the molecular ion leads to the ion 1 (m/e 163) which then splits off $CH_3^•$

to give the ion *m*. Measurement of the deuterium analog showed that hydrogen is split off from some of the methyl groups during formation of the ion *1*. Fragmentation of the other measured urea derivatives is roughly the same, although the ring substituents give the fragmentation specific impress. The spectra of the isomeric nitro derivatives are almost identical and differ only on the basis of elimination of water from the molecular ions of the 4-nitro derivative.

The ratio of peak intensities of the molecular ion and the ion *a* $(m/e\ 72)$, characterizing the decomposition velocity of the molecular ion by this pathway, was correlated with the Hammett substituent constants. The equation reads as follows: $\log Z = \log a/M^+ = 0{\cdot}445 + 2{\cdot}8\sigma$. In accord with the presumption, the decomposition velocity of the molecular ion by this pathway increases with increasing electron-acceptor ability of the substituent. The elimination of ammonia from the molecular ions is affected by substituents in the opposite way.

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