

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

## The Steric Conformations of Nitro- and Nitroso-bis-piperazines

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Attempts have been made to correlate the electric moments of a series of non-cyclic nitramines and nitrosamines with the moments of some homologous dinitroso- and dinitropiperazines. According to the high polarizations these N,N'-disubstituted piperazines exist neither in orthodox crown nor boat conformations and instead are complex oscillators which have been called "flexible" forms. In support of this designation the moment of N,N'-dinitropiperazine in dioxane has been found to increase with rising temperature. All of the nitrosamines and nitramines are found to have high atom polarizations, but these distortion polarizations are minimal in the cyclic polynitramines. It is suggested that this depression of atom polarization is due to synchronized coupling of dipoles in the flexible ring form.

In a recent study it has been found from electric dipole moments that N,N'-disubstituted piperazines are not centrosymmetric.<sup>1</sup> This investigation is now continued with piperazines having nitro and nitroso groups attached at the ring-nitrogen atoms. These substituents are useful not only because they are highly polar but also because a number of simple nitramines are available for comparison. Admittedly comparisons by the notoriously inaccurate "group moment" method of evaluating molecular polarization are of questionable worth. However it is hoped that an ade-

ods described previously.<sup>2,3</sup> Data are available upon request showing that no determination has been accepted unless a linear extrapolation to the dielectric constant ( $\pm 0.001$ ) and specific volume ( $\pm 0.0001$ ) of the solvent has been attained. Distortion polarizations are determined for solids from the linear extrapolations (available upon request) of dielectric constant ( $\pm 0.005$ ) versus pelleted sample thickness. Moments, reproducible to  $\pm 0.01$  debye, calculated from these data for nitrosamines, are shown in Table I.

It is evident from this table that the accuracy of

TABLE I  
PHYSICAL PROPERTIES OF NITROSAMINES AT 20°

Substance	$d_{20}^4$	$P_T$	$n_D^{20}$	Electrical polarization in dioxane			$P_T - \frac{\mu\text{-Debyes}}{R_D P_T - P_{E+A}}$	Spectral extinction strong or medium, $\text{cm.}^{-1}$
				$R_D$ Abbe	$R_D$ additive	$P_{E+A}$ pellets		
Di- <i>n</i> -butylnitrosamine	0.892	444	1.4474	59.4			4.32	1441(S) 1360(S) 1278(M)
Nitrosomorpholine	1.104	223	1.4925	30.5			3.05	1435(S) 1362(S) 1287(M)
1,3,5-Trinitrosotriazine	1.551				38.0	48.8 <sup>a</sup>		1429(S) 1367(M) 1290(S)
1,5-Dinitroso-3,7-methylene-1,3,5,7-tetraazacycloöctane	1.469				44.9	53.3 <sup>b</sup>		1370(S) 1285(S)
N,N'-Dinitrosopiperazine	1.425	129 123 <sup>c</sup>			34.6	38.2	2.08 2.05 <sup>e</sup>	1429(M) 1367(S) 1277(M)
2-Methyl-N,N'-dinitrosopiperazine		132			39.2		2.10	1435(S) 1355(S) 1266(M)
2,5- $\uparrow\uparrow$ -Dimethyl-N,N'-dinitrosopiperazine	1.325	205			43.8	48.0 <sup>e</sup>	2.73	1429(M) 1352(S) 1273(M)
2,5- $\uparrow\downarrow$ -Dimethyl-N,N'-dinitrosopiperazine	1.187	103			43.8	49.2 <sup>f</sup>	1.61	1435(S) 1357(S) 1266(M)

<sup>a</sup>  $\epsilon$  is 3.309. <sup>b</sup>  $\epsilon$  is 3.186. <sup>c</sup> In benzene. <sup>d</sup>  $\epsilon$  is 2.830. <sup>e</sup>  $\epsilon$  is 2.756. <sup>f</sup>  $\epsilon$  is 2.544.

quate substitute for this method may evolve from consideration of data such as we have accumulated.

Dioxane solutions in a field of about 1 e.v. have been used for determination of total polarization, and, whenever possible, compressed solids have been measured for distortion polarization by meth-

(1) M. V. George and G. F. Wright, *Can. J. Chem.*, Jan. (1958).

the determinations cannot equal their precision because of an appreciable atom polarization ( $P_{E+A} - R_D$ ) which varies from 1.8 to 2.7 cc. per nitroso group for the piperazines. But these values are

(2) C. C. Meredith and G. F. Wright, *Can. J. Technol.*, **33**, 182 (1955).

(3) C. C. Meredith, L. Westland and G. F. Wright, *THIS JOURNAL*, **79**, 2385 (1957).

not representative, as may be seen by the 3.6 cc. per nitroso in trinitrosotriazine and the 4.2 cc. per nitroso in 1,5-dinitroso-3,7-methylene-1,3,5,7-tetraza-cyclooctane. Evidently the atom polarization in substances containing the nitrosamine group is strongly dependent on structure. Obviously one cannot guess the deficiency in molecular refraction as an estimate of the distortion polarization of dibutylnitrosamine or nitrosomorpholine.

However, the moments of these substances are sufficiently high that the discrepancy in  $P_A$  is relatively unimportant. Including with the moments of the dibutyl- and morpholinonitrosamines the moment of 3.98 debye reported<sup>4</sup> for dimethylnitrosamine a group moment of about 3.6–3.7 debye may be assigned to the nitroso group. But as may be seen below such group moments are of little value in conformational study of the piperazines. The data show only that nitrosopiperazines cannot be described in the easily-calculated crown forms.

In view of earlier polarization studies of piperazines<sup>1</sup> the moment of 2.08 debye for N,N'-dinitropiperazine in dioxane is not surprising; it is of interest that this moment is almost the same in benzene. The small augmentation in the 2-methyl homolog might be attributed to an equatorial substituent, in which case the somewhat larger 2.73 debye for the 2,5- $\downarrow\downarrow$ -dimethyl homolog might be ascribed to two axially disposed methyl groups, all in the sense of the boat conformation. But these speculations are pointless in view of the low moment (1.61 debye) found for the 2,5- $\uparrow\downarrow$ -homolog. No specific conformation and perhaps no static form at all is adequate to explain these moments.

It might be argued (though not very forcefully because of the magnitude of the moments) that these orientation polarizations were due to activated states of centrosymmetrical crown conformation. In this event a single crystal X-ray diffraction study should be informative. Such a study was attempted with N,N'-dinitropiperazine<sup>5</sup> the extinctions of which showed the space group to be either  $D_{2h}^{12}$ -Pmmn or  $C_{2v}^2$ -Pmn. However, trial structures based on a centrosymmetrical arrangement were unsuccessful. Subsequently a test of the structure factors by the so-called "fly's eye" method<sup>6</sup> showed that in fact the symmetrical space group Pmmn could not apply. Since centrosymmetrical molecules are known<sup>6</sup> not to exist in a non-symmetrical space group, it is doubtful that N,N'-dinitropiperazine exists in the crown conformation. Indeed the observed moment at 20° (2.21 debye) is not widely divergent from that expected for a "boat" conformation in which the symmetrically-opposed methylene-bis-nitramino halves approach the planarity proposed for dimethylnitramine.<sup>7</sup> However, this simple dimensional designation is not justified by the remainder of the data in Table II.

Examination of the moments of aliphatic non-cyclic nitramines in this table seem to show an expected correlation: methyl < propyl < butyl < iso-

propyl from which a *sec*-nitramino group moment of 4.2 debye may be derived. It will be shown subsequently that this moment is about 0.05–0.10 debye too large because of an atom polarization contribution. At best the limited applicability of a group moment is seen among the moments of the N,N'-dinitropiperazine homologs, although they do follow in a qualitative sense the divergence noted for the analogous nitrosamines. In neither series does a simple static structure seem to be applicable.

It would appear that the intuitive designation of static "boats" and "crowns" may be erroneous, at least insofar as ring systems like piperazines are concerned. An alternative to either fixed conformation is the so-called "flexible" form, the dynamic variation of the "boat."<sup>8</sup> With the conformational integrity of the ring minimized in this way, one would expect marked deformation of the cycle by substituent groups. But it follows from these arguments that the moments of such substances ought to vary with respect to temperature.

Inspection of Table II shows that for N,N'-dinitropiperazine the moment increases markedly over the temperature range of 20 to 40°. Moreover the apparent linearity indicates that yet higher moments would be observed at elevated temperatures. The behavior indicates that the N,N'-dinitropiperazines are not rigid, not limited by the steric consequences of the *sec*-nitramine degeneracy postulated by Costain and Cox<sup>7</sup> and not to be described adequately by static structures.

During attempts to understand the nature of these ring structures, the distortion polarizations may be of interest. It may be seen in Table II by comparison among the mononitramines of additive molecular refractions (which agree closely with  $R_D$  determined from refractive index) and the distortion polarization calculated from dielectric constants of nitramines which are solids that the *sec*-nitramino group exhibits a high atom polarization, varying from 7 to 11 cc. per nitramino group. The effect must be roughly additive in non-cyclic compounds since N-methylnitramino-bis-ethane with its two nitramino groups has an atom polarization of 13.9 cc. But in the cyclic polynitramines this atom polarization is markedly diminished. In N,N'-dinitropiperazine (the electronic polarization having been determined from the axial indices in the crystal) the atom polarization per nitramino group is 1.8 cc. In trinitrotriazine (RDX) it is even less (1.1 cc.) while no atom polarization at all can be found in 1,3-dinitro-1,3-diaza-5-oxacyclohexane.

At the present time there is no satisfactory explanation for abnormal atom polarization in organic compounds since the theory of Coop and Sutton<sup>9</sup> has proved to be inadequate in respect of their candidate substance, benzoquinone.<sup>1</sup> Actually in absence of this theory one might expect that a polar linkage like the nitramino group would resemble the polar bonding in inorganic compounds. What requires an explanation is the diminution of the atom polarization in cyclic polynitramines.

(8) W. C. Kumler and A. Huitric, *THIS JOURNAL*, **78**, 3369 (1956), for examples and leading references.

(9) I. E. Coop and L. E. Sutton, *J. Chem. Soc.*, 1269 (1938).

(4) E. G. Cowley and J. R. Partington, *J. Chem. Soc.*, 1252 (1933).

(5) W. R. Kingdon, M.A. Thesis, University of Toronto, 1950.

(6) C. W. Bunn, "Chemical Crystallography," Oxford Press, New York, N. Y., 1946.

(7) W. Costain and E. G. Cox, *Nature*, **160**, 826 (1947).

TABLE II  
 PHYSICAL PROPERTIES OF NITRAMINES

Substance and temp., °C.	$d_{20}^4$	$P_r$	Electrical polarization in dioxane				$\mu$ -Debyes		Spectral extinctions strong or medium, cm. <sup>-1</sup>
			$n_{20}^D$	$R_D$ Abbe	$R_D$ additive	$P_{E.A}$ pellets	$P_r - R_D$	$P_r - P_A$	
Dimethylnitramine, 20		470			21.8		4.61		1529(M) 1274(S) 1124(M) 757.5(S)
Di- <i>n</i> -propylnitramine, 20	0.995	517	1.4370	40.0	39.9		4.76		1504(M) 1304(S) 1111(M) 761.5(M)
Diisopropylnitramine, 20	1.104	548			39.9	51.2 <sup>a</sup>	4.91	4.86	1516(S) 1304(S) 1132(S) 761.5(S)
Di- <i>n</i> -butylnitramine, 20	0.962	538	1.4557	49.3	49.1		4.82		1504(M) 1282(S) 1101(M) 760.5(S)
Nitromorpholine, 20	1.363	248			30.1	38.5 <sup>b</sup>	3.22	3.16	1520(S) 1285(S) 1122(S) 761.5(M)
2-Cyanoctyl-bis-nitramine, 20	1.424	378			38.1	47.1 <sup>c</sup>	4.02	3.96	1520(S) 1299(S) 1092(M) 757.5(M)
N-Methylnitramino-bis- ethane, 20	1.446	315			40.6	54.5 <sup>d</sup>	3.61	3.52	1504(S) 1282(S) 1111(M) 762.3(S)
1,3-Dinitro-1,3-diaza-5- oxacyclohexane, 20	1.824	706			35.4	35.3 <sup>g</sup>	5.64	5.64	
1,3,5-Trinitrotriazine, 20	1.78	751			43.7	47.0	5.79	5.78	
N,N'-Dinitropiperazine, 20	1.638	145	1.617	38.6	38.4	42.1 <sup>h</sup>		2.21 <sup>e</sup>	1548(S)
Same, 25		154						2.33	1287(M)
Same, 30		165						2.46	1099(M)
Same, 40		183						2.68	767(S)
2-Methyl-N,N'-dinitro- piperazine, 20		146			43.0			2.21	1516(S) 1299(M) 1092(W) 762.3(M)
2,5- $\uparrow$ -Dimethyl-N,N'- dinitropiperazine, 20		440			47.6			4.32	1522(S) 1311(S) 1115(W) 751.8(M)
2,5- $\downarrow$ -Dimethyl-N,N'- dinitropiperazine, 20		124			47.6			1.90	1516(S) 1304(S) 1105(W) 763.3(M)

<sup>a</sup>  $\epsilon$  is 2.892. <sup>b</sup>  $\epsilon$  is 2.975. <sup>c</sup>  $\epsilon$  is 2.990. <sup>d</sup>  $\epsilon$  is 3.382. <sup>e</sup> By our error an incorrect value was reported several years ago to Prof. Kuntler.<sup>8</sup> <sup>f</sup> Corr. for atom polarization as found for dinitropiperazine. <sup>g</sup>  $\epsilon$  is 3.790. <sup>h</sup>  $\epsilon$  is 2.933.

We suggest that this diminution may be due to a synchronization of nitramino force-fields in the flexible form which reduces the susceptibility toward external fields.

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M. Bedard, using potassium bromide pellets at the Canadian Armaments Research and Development Establishment, Quebec.

We are grateful to the Wyandotte Chemical Corporation for gifts of substituted piperazines.

#### Experimental<sup>10</sup>

**Piperazine Dihydrochloride.**—A solution of 12.4 g. (0.078 mole) of piperazine hexahydrate in 100 ml. of water

(10) Melting points have been corrected against reliable standards.

saturated with hydrogen chloride was evaporated *in vacuo*. The crude product in quantitative yield was dissolved in a minimum of boiling water, then cooled and precipitated slowly by addition of ethanol, yielding 5.6 g. (63%) of needles, m.p. 318–320° dec.

*Anal.* Calcd. for  $C_4H_{12}Cl_2N_2$ : Cl, 44.6. Found: Cl, 44.4.

**N,N'-Dinitropiperazine.**—To a stirred solution of 12.0 g. (0.188 mole) of 99.3% nitric acid, 21.0 g. (0.206 mole) of acetic anhydride and 11.1 g. (0.188 mole) of acetic acid under nitrogen was added slowly 6.0 g. (0.038 mole) of piperazine dihydrochloride during 22 min. at 0–5°. After 0.5 hr. the reaction system was warmed to 25° and stirred during the next 72 hr. Then the system was treated with 30 ml. of water and evaporated to dryness *in vacuo*. The residue, crystallized from 100 ml. of acetic acid, weighed 5.5 g. (84%) of needles, m.p. 208–214°. This crude dinitropiperazine, giving a positive Franchimont test and a slightly positive test for halogen, was dissolved in 30 ml. of 99.3% nitric acid at 0° and treated with 21 g. of ammonium persulfate. After 3 hr. at 0° and 2 hr. at 25° the system was poured into ice. The precipitate was crystallized from a minimum of boiling water, then washed successively with dilute aqueous sodium carbonate, water and ethanol, 3.1 g. (58%), m.p. 214.8–216°. This halogen-free product formed brilliant white needles, m.p. 214.8–215°, when crystallized from boiling ethyl acetate. Crystallization from hot ethyl acetate or from 70% nitric acid was controlled by varying the rate of cooling and by altering the rate of evaporation of the solvent to give hexagonal needles and some hexagonal platelets which were useful for crystallographic work. Density was determined by flotation during centrifugation in a mixture of carbon tetrachloride and ethylene dibromide,  $d = 1.638 \pm 0.002$  g. per cm.<sup>3</sup>.

Refractive indices along the "a-" and "c"-axes were determined simply by microscopic examination of suitably positioned platelets in media of comparable refraction. Because of a V-shaped edge the third axis could not be determined in this way, so the crystal was glued to the point of a pin so that one of the previously-determined axes was parallel to the axis of the pin. The assembly was mounted on a cell consisting of a microscope slide to which were cemented two polythene strips. One of these strips was drilled to contain two or three drops of immersion medium, the surface tension of which was sufficient to immerse the crystal completely. The other strip served to maintain the pin in a horizontal position. By rotation of the pin the refractive index of the "b"-axis was discovered, like that of "a" and "c", by transparency in an isotropic medium. The indices are  $n_\alpha = 1.585$ ;  $n_\beta = 1.615$ ;  $n_\gamma = 1.655$ . The birefringence ( $n_\gamma - n_\alpha$ ) therefore is 0.075. The molecular refraction calculated from  $(n_\alpha + n_\beta + n_\gamma)/3$  is 38.6 cc. in daylight as compared to 38.4 cc. calculated from group refractions including 9.96 cc. for the N–NO<sub>2</sub> linkage.

Cleavage of the crystals occurred easily only in zones perpendicular to the "a"-axis. Suitable fragments for each axis were obtained for rotation, precession and Weissenberg photographs on zero, first and second layer lines. Orthorhombic cell constants were determined as  $a = 10.82 \pm 0.01$  Å,  $b = 12.02 \pm 0.02$  Å,  $c = 5.374 \pm 0.005$  Å. Correlation of these dimensions with density defines the unit cell content as 4 molecules. All  $hkl$ ,  $0kl$  and  $hk0$  reflections were present but only  $h0l$  reflections when  $h + l = 2n$  and only  $0k0$  reflections when  $k = 2n$ . The space group is probably either  $D_{2h}^{13}$ -Pmmn or  $C_{2v}^7$ -Pmn. A trial structure on the  $hk0$  projection showed that centrosymmetry was absent, thus designating the second of these space groups for dinitropiperazine. Evaluation of intensities from the photographs furnished the structure factors listed in Table III.

**Homologs of N,N'-Dinitropiperazine.**—These methyl homologs were prepared from the hydrochlorides in the manner described for dinitropiperazine. The data for all four substances are recorded in Table IV.

Special comment need be made only for the reaction of 2,5- $\uparrow \downarrow$ -dimethylpiperazinium chloride. A solution of this salt in acetic anhydride and an excess of absolute nitric acid at 5° gave only N-nitro-2,5- $\uparrow \downarrow$ -dimethylpiperazinium nitrate (40%) after 80 hr. This salt melted at 228° but unlike the dinitramine it gave a positive brucine test as well as a Franchimont test. Its electric moment in sodium-dried 2,5-dimethylpiperazine (in which the moment of 2,5-

TABLE III

OBSERVED STRUCTURE FACTORS									
$hkl$	$F_{obs}$	$hkl$	$F_{obs}$	$hkl$	$F_{obs}$	$hkl$	$F_{obs}$	$hkl$	$F_{obs}$
020	0.0	052	17.3	160	9.2	530	2.8	101	0.8
040	19.5	072	4.1	200	31.9	540	4.1	103	1.1
080	0.0	082	4.6	210	2.2	550	1.9	202	2.9
060	17.0	013	8.7	220	2.7	560	3.1	204	1.9
010	0.0	033	9.6	230	1.0	600	0.0	301	1.2
021	3.5	043	2.9	240	11.5	680	2.2	402	20.5
031	22.6	053	2.6	280	4.9	720	4.2	404	2.4
041	16.7	083	5.8	340	0.6	740	1.8	501	1.1
051	10.0	004	5.9	360	3.7	760	1.6	505	1.4
071	16.8	014	3.7	400	14.7	800	8.1	602	9.2
081	5.5	054	3.9	410	1.5	810	1.6	604	1.6
002	19.8	084	3.5	420	2.0	820	3.6	701	1.4
012	7.1	085	1.7	460	1.4	920	3.1	802	1.6
032	7.3	006	0.0	480	5.1	1000	3.9	901	1.6
042	13.6	120	10.6	520	3.0	1020	3.2		

TABLE IV

## PREPARATION OF N,N'-DINITROPIPERAZINES

Information	Unsubs.	2-Methyl	2,5- $\uparrow \downarrow$ -dimethyl	2,5- $\uparrow \downarrow$ -dimethyl
Yield, %	84	74	58	56
M.p., crude, °C.	208–214	165	150	221
M.p., pure, °C.	215	170.5	155.5	228 (dec.)
Cryst. from ethyl acetate, ml./g.	50	5	5	50
Cryst. from water, ml./g.	100	50	75	150
<i>Anal.</i> for	$C_4H_8N_4O_4$	$C_5H_{10}N_4O_4$	$C_6H_{12}N_4O_4$	$C_6H_{12}N_4O_4$
C: calcd., found	27.3, 27.7	31.6, 31.8	35.3, 35.4	35.3, 35.7
H: calcd., found	4.58, 4.63	5.30, 5.34	5.93, 6.00	5.93, 6.12
N: calcd., found	31.8, 31.5	29.5, 29.3	27.5, 27.3	27.5, 27.8

$\uparrow \downarrow$ -dimethylpiperazine at 20° was 4.13 *D*) was found to be 4.91 *D* at 20° (*P*<sub>T</sub>, 407).

*Anal.* Calcd. for  $C_6H_{12}N_4O_5$ : C, 32.6; H, 5.93; N, 25.3. Found: C, 32.2; H, 6.13; N, 25.7.

When this salt was retreated with nitric acid, acetic anhydride and 0.1 equivalent of acetyl chloride, it was converted in 55% yield to the dinitramine.

**The Homologous Dinitrosopiperazines.**—The unsubstituted dinitrosopiperazine was prepared by one method<sup>11</sup> and the remainder by another method.<sup>12</sup> The data pertaining to these preparations are given in Table V.

TABLE V

## PREPARATION OF N,N'-DINITROSOPIPERAZINES

Information	Unsubs.	2-Methyl	2,5- $\uparrow \downarrow$ -dimethyl	2,5- $\uparrow \downarrow$ -dimethyl
M.p., °C.	156–156.5	68.5–69	91–91.5	173–173.5
Crystn. from water, ml./g.	5.6	9	5.5	6.8
<i>Anal.</i> for	$C_4H_8N_4O_2$	$C_5H_{10}N_4O_2$	$C_6H_{12}N_4O_2$	$C_6H_{12}N_4O_2$
C: calcd., found	33.3, 33.1	38.0, 38.1	41.8, 41.6	41.8, 41.8
H: calcd., found	5.60, 5.50	6.38, 6.45	7.03, 7.03	7.03, 6.94
N: calcd., found	38.9, 39.0	35.4, 35.2	32.6, 33.1	32.6, 32.1

**Electrical Polarization Measurements.**—These evaluations have been made by use of the same equipment and methods which have been described previously.<sup>1,3</sup> Calculations have been made according to the method of Halverstadt and Kumler.<sup>13</sup>

**X-Ray diffraction patterns** using Cu K $\alpha$  (Ni filtered) radiation have been determined as relative intensities ( $I/I_1$ ) for  $d$  spacings in ångströms as follows: diisopropyl-nitramine (10) 5.749, (6) 6.458, 4.267, 3.630, 3.162, (5) 4.055, 3.218, [2] 5.035, (1) 3.437, 2.627, 2.562, 2.415; N,N'-dinitrosopiperazine [10] 4.831, 4.607, (9) 3.288, 7 5.257, (5) 2.981, (2) 2.680, (1) 3.140, 2.799, 2.642, 2.169; N,N'-dinitroso-2-methylpiperazine [10] 5.166, [4] 4.805, 3.601, (3) 5.417, 2.873, (1) 2.928, 2.712; N,N'-dinitroso-2,5- $\uparrow \downarrow$ -dimethylpiperazine (10) 5.921, (6) 5.092, (4) 5.352, (2) 3.398, 3.103, (1) 5.196, 3.682; N,N'-dinitroso-2,5- $\uparrow \downarrow$ -dimethylpiperazine (10) 5.901, (9) 4.937, (4) 3.823, 3.638,

(11) A. Ladenburg, *Ber.*, **24**, 2400 (1891).(12) C. Stoehr, *J. prakt. Chem.*, [2] **51**, 449 (1895).(13) I. F. Halverstadt and W. D. Kumler, *This Journal*, **64**, 2988 (1942).

(3) 3.312, 3.156, 2.586, (1) 5.273, 3.682, 3.367, 2.952; N,N'-dinitropiperazine (10) 5.467, (8) 3.790, (7) 3.235, (3) 3.097, (2) 2.650, 2.712, 3.040, (1) 1.922, 5.352; N,N'-dinitro-2-methylpiperazine (10) 5.196, (9) 4.951, (8) 4.019, 3.470, (4) 3.201, 2.824, (2) 3.904, 3.066, (1) 2.928; N,N'-

dinitro-2,5- $\uparrow\uparrow$ -dimethylpiperazine (10) 6.702, (9) 3.195, (8) 5.078, 4.870, (7) 8.185, 3.076, (6) 3.652, (5) 4.010, (4) 5.941, 5.552, 3.524, (1) 7.338, 4.583, 2.523.

ONTARIO, CANADA

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## Detection and Structural Analysis of Furans by Proton Magnetic Resonance

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Measurements are reported herein which show that proton magnetic resonance spectroscopy is a powerful tool for the detection of furan rings and for the location of substituents attached thereto.

The detection of the furan ring system as a constituent of complex organic structures has previously been a difficult matter because of the lack of a generally informative diagnostic method. Chemical and color tests are, at best, only suggestive in this regard because of their lack of specificity and also due to wide variation in the chemical properties of the furan ring system.<sup>3</sup> Ultraviolet spectroscopy is of very limited usefulness because of the rather non-characteristic absorption by furans in that region.<sup>4</sup> Although correlations of certain bands in the infrared spectra of several furans have been made,<sup>5</sup> the nature of the absorption and the necessary assumption that no interfering bands are present render the infrared data of little use when more than corroborative evidence is desired. Another important problem in the case of simple as well as complex structures containing the furan system is the location of substituents on the nucleus. This problem also has resisted solution by physical methods.

In connection with investigations of the structures of certain natural products which are being pursued in these laboratories and also because of the widespread occurrence of furan systems in nature,<sup>5</sup> we have been concerned with these problems and have sought to apply other methods to their solution. In this paper we describe the structural analysis of furans by proton magnetic resonance, a technique which has been conspicuously successful in the cases studied thus far.

Our nuclear magnetic resonance measurements with furan derivatives show that in general the protons attached to the furan nucleus are less shielded than protons attached to double bonds and in this respect are similar to protons attached to benzenoid nuclei.<sup>6</sup> Comparison of furans with vinyl ethers, their non-aromatic structural analogs, indicates

that proton resonance occurs at lower fields for the former than for the latter, as would be anticipated from the occurrence of diamagnetic  $\pi$ -electron currents around the furan ring (*cf.* recent discussions of benzenoid annular currents).<sup>7,8</sup> This difference between furanoid and ethylenic and paraffinic proton resonance, although not unexpected, is a useful and desirable one for purposes of structural analysis. At least of equal significance and utility is the fact that furan  $\alpha$ -hydrogens are usually less shielded than furan  $\beta$ -hydrogens, *i.e.*, resonance occurs at lower fields for the former.

### Experimental

All proton magnetic resonance spectra were determined at 40 mc. rf. with a Varian model V-4300B high-resolution spectrometer fitted with a field-sensing stabilizer ("Super Stabilizer"). The compounds were measured as *ca.* 10% solutions in methylene chloride and in some cases also in deuterio-chloroform, tetrachloroethane or carbon tetrachloride. The chemical shifts expressed herein in c.p.s. relative to water were actually determined relative to methylene chloride, using a concentric-tube cell<sup>9</sup> with methylene chloride in the outer compartment when it was not used as solvent. Subtraction of 26 c.p.s. from shifts relative to methylene chloride was used in figuring shifts in c.p.s. relative to water. Chemical shifts were essentially the same in methylene chloride, tetrachloroethane and deuteriochloroform solutions and generally were *ca.* -15 c.p.s. from those in carbon tetrachloride (*i.e.*, resonance occurred at higher fields in the case of carbon tetrachloride).

The furan compounds studied were in many cases generously supplied by other laboratories: cafestol (Dr. Carl Djerassi), columbin (Dr. Michael Cava), 3-furoic acid and derivatives (Dr. Henry Gilman), menthofuran (A. M. Todd Co.) and 2,5-dimethylfuran (Quaker Oats Co.). Otherwise, purified samples obtained in our laboratories were used.

### Results and Discussion

**Part A.**—The proton magnetic resonance spectrum of furan itself (I) in methylene chloride solution (Table I) is composed of two sharp triplets centered at -113 and -71 c.p.s. with a signal ratio of 1:1. We assign the triplet at -113 c.p.s. to the two  $\alpha$ -hydrogens and that at -71 to the two  $\beta$ -hydrogens. This assignment is that dictated from the inductive unshielding effect of oxygen, expected to be greater for  $\alpha$ - than for  $\beta$ -protons, and is clearly supported by the data on substituted furans. The triplets, anticipated to result from spin-spin coupling between  $\alpha$ - and  $\beta$ -hydrogen

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