MONOSUBSTITUTED FURAZANES.
I. NMR INVESTIGATION

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The ^{1}H, ^{13}C, ^{15}N, and ^{17}O NMR spectral parameters were obtained for monosubstituted furazanes and the ^{13}C NMR chemical shifts of these compounds were correlated with the chemical shifts of monosubstituted benzenes.

Furazanes (1,2,5-oxadiazoles) were first synthesized in 1888 [1] and have been studied in detail [2, 3]. However, there are still some difficulties in identifying these compounds.

In the present work we studied the ^{1}H, ^{13}C, ^{15}N, and ^{17}O NMR spectra of monosubstituted furazanes in order to determine the effect of substituents on the spectral parameters of the furazane ring, thereby facilitating the identification of more complex compounds.

RESULTS AND DISCUSSION

Table 1 gives the ^{3}C NMR spectral data for the furazanes studied. The great difference in the $^{1}J_{CH}$ and $^{2}J_{CH}$ chemical shifts permit an unequivocal assignment of the furazane ring carbon signals. A downfield shift of the signal of substituted C-3 is found for all the compounds studied. Comparison of the effect of substituents on its chemical shift (CS) with the increments of the same substituents in monosubstituted benzenes shows that this effect in furazanes is much less (the correlation coefficient was 0.89; see Fig. 1). On the other hand, the same substituent almost identically alters the magnitude and direction of the chemical shifts of the ortho-carbon atoms in monosubstituted benzenes and the C-4 atoms in furazanes (the correlation coefficient was 0.93; see Fig. 1). This behavior may occur since the electric substituent effects in benzenes and furazanes on the carbon atoms adjacent to the substituted carbon atoms are transmitted through σ bonds and the π-electron density on the ipso-carbon and C-3 does not alter these effects through two bonds.

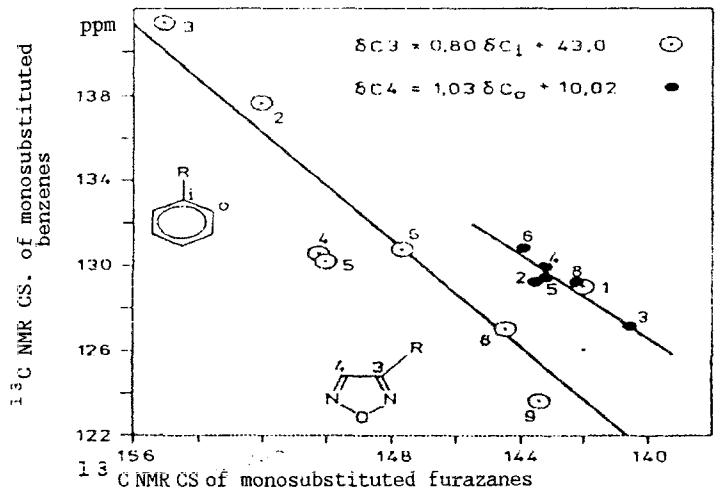

Fig. 1. Correlation of the chemical shifts of the ^{13}C NMR signals in monosubstituted benzenes and furazanes (numbering corresponds to Table 1).

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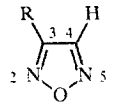
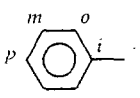
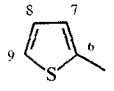
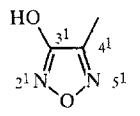
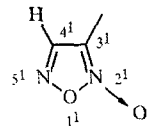
TABLE 1. ^{13}C NMR spectra of Monosubstituted Furazanes



№	R	Chemical shifts (ppm) and ^{13}C-^{1}H coupling constants (Hz)		
		C-3	C-4	other carbon atoms in R
1	H	142,0 ^{1}J=199,9	142,0 ^{2}J=12,34	
2	CH_3	152,1 ^{2}J=11,7 (CH) ^{2}J=7,2 (CH_3)	143,5 ^{1}J=196,5 (CH) ^{3}J=3,1 (CH_3)	8,7 (CH_3) ^{1}J=130,7
3		155,1 ^{2}J=11,1 (CH)	140,5 ^{1}J=197,3	*i* 125,7 *o* 127,9 *m* 129,7 *p* 131,4
4	HOOC	150,2 ^{2}J=10.6	143,2 ^{1}J=203,3	158,8 (C=O)
5	COOMe	150,0 ^{2}J=10,7	143,2 ^{1}J=203,6	158,8 (C=O) 53,9 (OCH_3)
6	CH_2NO_2	147,7 ^{2}J=11,4 (CH) ^{2}J=5,7 (CH_2)	143,9 ^{1}J=202,4 ^{3}J=3,0 (CH_2)	67,9 (CH_2NO_2) ^{1}J=151,3
7		150,7 ^{2}J=11,3	140,7 ^{1}J=199,8	C-6 127,0 C-7 130,7 ^{1}J=171,2; ^{2}J=5,9; ^{3}J=9,5 C-8 128,9 ^{1}J=170,5; ^{2}J=4,3; ^{3}J=4,8 C-9 130,4 ^{1}J=185,5; ^{2}J=7,5; ^{3}J=10,6
8		144,5 ^{2}J=11,4	142,2 ^{1}J=204,2	168,3 (C-3') 138,0 (C-4')
9		143.4 ^{2}J=11,1	140,4 ^{1}J=206,3	107,8 (C-3') 145,3 (C-4') ^{1}J=205,7

Thus, this behavior permits us to predict the chemical shifts in monosubstituted furazanes using the extensive data on substituted benzenes [4]. The use of an additive scheme in the case of disubstituted furazanes may lead to large errors due to substituent interaction as found in ortho-disubstituted benzenes. This question requires special study.

Among the $^{13}C—^{1}H$ coupling constants, we should note the $^{2}J_{(C—H)}$ coupling constant of C-3, which is approximately double the $^{3}J_{(C—H)}$ coupling constant of C-4 with the protons of the methyl and nitromethyl groups. As noted in our previous work [5], this may be used to assign the ^{13}C NMR signals of furazanes.

Satisfactory correlations were not found between the substituent properties and ^{1}H, ^{15}N, and ^{17}O NMR parameters (Tables 2 and 3). We note that, as a rule, the signal for N-2 is upfield relative to the signal for N-5 in the ^{15}N NMR spectra of the compounds studied.

The chemical shifts found for substituted C-3 were used to determine the relative electron delocalization in the furazane ring. The difference in the substituent effect on the ^{13}C NMR chemical shifts in monosubstituted benzenes and heteroaromatic compounds may be used to evaluate the local π-deficiency on the heterocycle carbon atoms, which may be described by the following formula for the case examined according to Jovanovic [6, 7]:

$$^{X}\Delta_f = p_f \ ^{X}\Delta_b + \text{const},$$

where $^{X}\Delta_b$ are the increments of substituents X in monosubstituted benzenes [4], $^{X}\Delta_f$ are the increments of substituents X in monosubstituted furazanes, and p_f is the local π-electron density on the furazane carbon atom (for benzene, p_b = 1.0).

TABLE 2. ^{1}H NMR Spectra of Monosubstituted Furazanes

№*	Chemical shifts (ppm) and ^{1}H-^{1}H coupling constants (Hz)	
	H-4	protons in substituent R
1	7,92 3 (H—H)=0,52	7,92
2	8,41	2,47 (CH_3)
3	8,83	7,8 (*o*); 7,4 (*m*, *p*)
4	9,05	12,1 (COOH)
5	9,09	4,03 ($COOCH_3$)
6	8,92	6,19 (CH_2NO_2)
7	9,06	7,7 (H-7) $^3J_{(H7—H8)}$=3,8; 7,2 (H-8) $^4J_{(H7—H9)}$=1,2; 7,8 (H-9) $^3J_{(H8—H9)}$=5,1
8	9,28	4,4 (OH)
9	9,28	9,31 (H)

*Numbering of compounds given in Table 1.

TABLE 3. ^{15}N and ^{17}O NMR Spectra of Monosubstituted Furazanes

№*	^{15}N NMR chemical shifts (ppm) and ^{15}N-^{1}H chemical shifts (Hz)			^{17}O NMR chemical shifts (ppm)
	N-2	N-5	N-substituent	
1	33,5 ^2J=13,6	33,5 ^3J=1,1		450
2	23,4 ^3J=1,1	34,7 ^2J=13,3 ^3J=5,3 (CH_3)		443
3	22,9 ^3J=0,6	38,7 ^2J=13,3		450
4	43,6 ^3J=1,0	43,5 ^2J=13,6		462
5	—	43,6 ^2J=13,6		—
6	34,1 ^3J=1,0 ^3J=2,5 (CH_3)	40,5 ^2J=13,6 ^4J=0,2 (CH_2)	-6,1 (NO_2) ^2J=2,6 (CH_2)	454 597 (NO_2)
7	18,1 ^3J=0,9	37,8 ^2J=13,4		—
8	32,2 ^3J=0,9	40,2 ^2J=13,5		456 397 (N—O—N) 45 (OH)
9	28,8 ^3J=0,9	41,5 ^2J=13,6	2,1 (N-5) ^2J=12,6 -25,3 (N-2) ^3J=3,7	448 (N—O—N) 363 (N—O)

*Numbering of compounds given in Table 1.

According to the evaluation carried out using the data in Table 1 and Fig. 1, p_f for furazane is 0.8. This result may be taken into account in considering the reactivity of furazane derivatives.

EXPERIMENTAL

The ^{1}H, ^{13}C, ^{15}N, and ^{17}O NMR spectra were taken on a Bruker AM-300 spectrometer for solutions in acetone-d_6. The chemical shifts were determined relative to TMS as an internal standard for the ^{1}H and ^{13}C NMR spectra, acetone-d_6 as the internal standard in the ^{17}O NMR spectra (560 ppm), and CH_3NO_2 as the external standard in the ^{15}N NMR spectra without correction for diamagnetic susceptibility and are given on the δ-scale. In taking the ^{15}N NMR spectra, proton polarization transfer was used according to the INEPT [8] and SPI techniques [9]. The $^3J_{(H—H)}$ coupling constant in unsubstituted furazane was measured for the signals of the ^{15}N satellites in the ^{1}H NMR spectrum. The signals in the thiophene substituted were assigned on the basis of the ^{13}C—^{1}H coupling constants [10]. The IR spectra were taken on a UR-20 spectrometer. The mass spectra were taken on a Varian MAT CH-6 mass spectrometer with direct inlet into the ion source.

Samples of furazane [11], 3-phenyl- [12], 3-nitromethyl-, 3-(3-hydroxyfurazan-4-yl)- and 3-(furoxan-3-yl)furazanes [13] were obtained according to reported methods.

3-Methylfurazane. A sample of 10.2 g (0.1 mole) methylglyoxime was carefully mixed with 18.65 g (0.126 mole) phthalic anhydride and heated on an oil bath at 210-220°C. The product was distilled over into a cooled receiver. The distillate was dried over magnesium sulfate and redistilled, collecting the fraction at 122-130°C. Redistillation gave 3.8 g (45%) product with bp 125-125.5°C, n_D^{20} 1.4124. Mass spectrum, m/z: 84 (M^+), 69 (M^+—CH_3), 54 (M^+—NO). IR spectrum for KBr pellet

(ν, cm^{-1}): 3175, 3130, 1585, 1460, 1405, 1375, 1070, 1000, 890, 845.

Furazane-3-carboxylic Acid. A sample of 47 g (0.3 mole) $KMnO_4$ was added in portions with vigorous stirring to an emulsion of 8.4 g (0.1 mole) 3-methylfurazane in 120 ml 50% sulfuric acid at 10-15°C. The mixture was brought to room temperature, maintained for 0.5 h, heated at 40°C for 1 h, and cooled. The precipitate was filtered off. The filtrate was decolorized by adding oxalic acid, acidified by the addition of sulfuric acid, and extracted with three 120-ml ether portions. Ether was removed. The residue was washed by shaking with 30 ml pentane and dissolved in benzene. Benzene was removed and the residue was washed to give 4.6 g (40%) product with mp 107.5-108.0°C [14]. Mass spectrum, m/z: 70 (M^+—CO_2), 52, 44, 40. IR spectrum for KBr pellet (ν, cm^{-1}): 3120-2840, 1680, 1530, 1465, 1445, 1330, 1230, 1110, 1020, 970, 910, 880.

Methyl Ester of Furazane-3-carboxylic Acid. A sample of 20 ml methanol was saturated with hydrogen chloride and 1.14 g (0.01 mole) furazane-3-carboxylic acid was added. The mixture was heated at reflux with the passage of HCl for 1.5 h, cooled, poured into 50 ml water, extracted with three 20-ml methylene chloride portions, washed with water, dried over anhydrous $MgSO_4$, and filtered. Distillation gave 0.83 g (64.8%) product as a slightly yellowish liquid. Mass spectrum, m/z: 129 (M^+ + I), 115 (M^+—CH_3), 98 (M^+—NO), 97, 79, 70, 59. IR spectrum for KBr pellet (ν, cm^{-1}): 3150, 2970, 1755, 1570, 1465, 1420, 1255, 1140, 995, 910, 830, 810, 785.

3-(Thien-2-yl)furazane. A mixture of 17 g (0.1 mole) thienylglyoxime and 12 g (0.12 mole) succinic anhydride was heated on an oil bath at 120°C until the reaction started. The bath was then removed and the mixture was brought to room temperature. The mass obtained was ground and extracted with 2:1 CH_2Cl_2—pentane. The extract was filtered through silica gel, left over anhydrous $MgSO_4$ and activated charcoal overnight, and then again filtered through silica gel. The solvent was evaporated and the residue was crystallized from hexane to give 9.8 g (64.5%) product with mp 59-60°C. Mass spectrum, m/z: 152 (M^+), 125 (M^+—HCN), 122 (M^+—NO), 109, 95, 70, 69, 58. IR spectrum for KBr pellet (ν, cm^{-1}): 3105, 1570, 1440, 1360, 1210, 1070, 1015, 970, 915, 865, 845, 920, 700.

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