products were analyzed on an 8 ft × 1/4 in. 3% SE-30 column at 120°. Calibration curves with areas of known chlorinated anilines were used to determine per cent yield. The chloropyridines were analyzed on an 8 ft × 1/4 in. column containing 3% Carbowax 20M and 5% KOH at 100°. Morpholine was used as the internal standard for quantitative measurements. For the chloro-*o*-toluidines a 6 ft × 1/8 in. column containing 10% Carbowax 1540 (polyethylene glycol) and 5% KOH at 200° was used. Quantitative measurements were made with aniline as the internal standard. Acetanilide and 4-chloroacetanilide were analyzed on a 6-ft 3% SE-30 column at 170°.

Only two compounds were not commercially available for vpc identification: 2,4-dichloro-6-methylaniline (mp 183–185° of acetanilide derivative, lit.[14] 186°) and 4-chloroacetanilide (mp 177–179°, lit.[15] 179°). The 2,4-dichloro-6-methylaniline was prepared from 4-chloro-2-methylaniline (Aldrich Chemical Co.) by chlorinating the acetanilide derivative.[16]

Registry No.—**1**, 586-96-9; **2**, 611-23-4; **3**, 694-59-7; phosphorus pentachloride, 10026-13-8; phosphoryl chloride, 10025-87-3; phosphorus trichloride, 7719-12-2.

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A Nuclear Magnetic Resonance Study of Some Nitrogen-15 Substituted Azo Heterocycles

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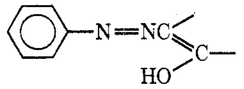
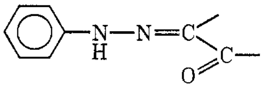
Six ^{15}N-substituted azo heterocycles have been prepared and their tautomeric structures studied by means of nmr spectroscopy. A phenylazo-3-pyrazolone and a phenylazo-4-pyrazolone exist in the azo form in $CDCl_3$, DMSO, and C_5H_5N. Phenylazothioindoxyl and the phenylazo derivative of diphenylbarbituric acid exist predominantly in the phenylhydrazone form in DMSO at room temperature. The phenylazo derivatives of coumaran-2-one and 4-hydroxycoumarin exhibit phenylhydrazone geometric isomerism in DMSO and $CHCl_3$, respectively.

The determination of the structure of azo heterocycles by the usual spectroscopic techniques is often plagued by the ambiguities inherent in peak assignment. In an attempt to eliminate these ambiguities in our own investigations, we have prepared and studied the ^{15}N isotopomers of six heterocycles containing the structural feature A or B.

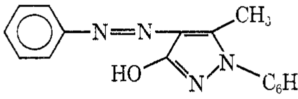

A


B

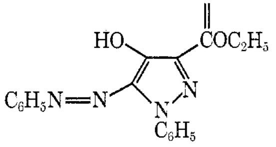
Each of the compounds can exist in at least two different tautomeric forms; all but the above two forms can be eliminated by conventional techniques.

The ^{15}N isotopomers were prepared by diazotization of ^{15}*N*-aniline and coupling to the appropriate heterocycle. The probability of isotopic scrambling under the conditions used (*vide infra*) has been shown to be very low and the heterocycles can therefore be safely assumed to carry the ^{15}N attached to the benzene ring.[1] Since the ^{15}N isotope has a spin quantum number of 1/2, the NH proton resonance of form B would be a low-field doublet with coupling constant of 90–100 Hz. The OH proton resonance of A will be, of course, a low-field singlet. If the compound exists as a mixture of A and B and if the proton exchanges intermolecularly between the ^{15}N of B and the oxygen of A or between two molecules of B, the shape of the peak(s) will depend upon the rate of exchange. If the exchange is fast and intramolecular, the shape depends upon the coupling constant in pure B and the composition of the mixture.[2]

The nmr spectrum of 5-methyl-4-phenylazo-1-phenyl-3-pyrazolone (**1**), whose structure has previously been determined to be the azo form shown (and for which no simple hydrazone tautomeric structure can be written),[3] showed the expected singlet for the acidic proton in both the ^{14}N and ^{15}N derivatives in $CDCl_3$ from 38 to −51°, in DMSO at 38°, and in pyridine at 38 to −23°. The chemical shifts of all compounds are listed in Table I.


1

The acidic proton resonance for 3-carboethoxy-1-phenyl-5-phenylazo-4-pyrazolone (**2**) in all three solvents was a singlet, an observation which could be interpreted as indicative of only the azo form or of rapid intermolecular exchange. The similarity of chemical shifts and peak shapes to those of **1** favors the


2

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(1) A. K. Bose and I. Kugajevsky, *J. Amer. Chem. Soc.*, **88**, 2325 (1966).

(2) G. O. Dudek and E. P. Dudek, *ibid.*, **86**, 4283 (1964).

(3) F. A. Snavely and C. H. Yoder, *J. Org. Chem.*, **33**, 513 (1968).

TABLE I

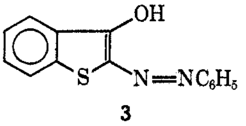
CHEMICAL SHIFTS OF ^{15}N DERIVATIVES

	CDCl$_3$^{a}			DMSO-d_6^{a}			C$_5$H$_5$N-d_5^{a}		
Compd	δ, ppm	m,^{b} J,^{c} $W_{1/2}$^{d}	Temp, °C	δ, ppm	m,^{b} J,^{c} $W_{1/2}$^{d}	Temp, °C	δ, ppm	m,^{b} J,^{c} $W_{1/2}$^{d}	Temp, °C
1	9.4^e	bs (16)	38	10.4^e	bs (20)	38	10.3^e	bs (20)	38
	10.3^e	bs (18)	−51				11.4^e	bs (30)	−23
2	9.5^e	bs (12)	38	9.8^e	bs (30)	38	10.1^e	ss (8)	38
	10.4^e	bs (18)	−51				10.8^e	bs (14)	−21
3				11.0^g	vbd	18	10.9^e	vbs (30)	−38
				10.9^f	bs (30)	38			
				10.7^e	bs (16)	84			
4				14.1^{g,h}	d, 95 (8)	35	14.7^f	bs (40)	38
				14^d	vbs (90)	133			
5				12.1^g	d, 97 (2)	27–40	12.4^g	d, 97 (4)	35–70
				11.0^g	d, 97 (6)				
				12.0^g	bd (8)	80			
				10.9^f	bd (20)				
6	14.2^g	d, 95 (3)	38	14.0^e	bs (20)	38	13^e	vbs (70)	38
	16.4^g	d, 93 (2)		15.6^g	d, 97 (16)				

[a] All solutions 5%, except **1** and **2** in CDCl$_3$ and **3** and **4** in DMSO, which were 10%. [b] ss, sharp singlet; bs, broad singlet; vbs, very broad singlet; d, doublet; bd, broad doublet; vbd, very broad doublet. [c] ±1 Hz. [d] Half height width of peak in hertz given in parentheses. [e] Analogous absorption in ^{14}N derivative has the same shape. [f] Analogous peak in ^{14}N derivative is significantly sharper. [g] ^{14}N derivative has singlet(s) at center of ^{15}N doublet(s). [h] In ^{15}N at 77°, d, 92; 93°, d, 83; 103°, d, 79.

former interpretation, which is in agreement with earlier work.[3]

The room-temperature spectrum of the ^{15}N derivative of 2-phenylazothianapthen-3-one (**3**) in DMSO

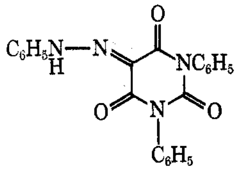


3

shows a broad singlet for the acidic proton resonance, which is considerably broader than the singlet exhibited by the ^{14}N derivative. As the temperature is decreased, the broad ^{15}N singlet degenerates to a broad doublet, while an increase in temperature sharpens the singlet until, at 84°, it is identical in shape with that of the ^{14}N derivative. This behavior is indicative of a temperature-dependent exchange process. Such a process could involve intermolecular exchange between two hydrazone forms, or inter- or intramolecular exchange between a hydrazone and an azo form. The existence of a tautomeric equilibrium for **3** in relatively nonpolar solvents is supported by its visible spectrum (in CHCl$_3$), which contains two peaks at 380 and 499 nm. If the exchange is between two tautomeric forms, the rate of the exchange and the composition of the equilibrium mixture should be affected by a change in temperature. As the composition of the azo–hydrazone mixture changes, a change in chemical shift should occur (unless the NH and OH shifts of forms A and B are identical). The data of Table I indicate that the chemical shift of the acidic proton of **3** is temperature dependent, but changes in intermolecular association could also produce such a change.

In pyridine from 0 to 38° the spectra of both the ^{14}N and ^{15}N derivatives of **3** contain a broad singlet for the low-field proton. This could be interpreted as either rapid intermolecular (hydrazone–hydrazone or hydrazone–azo) exchange or as a shift to the azo form. The latter interpretation is in agreement with earlier conclusions for azo-5-pyrazolones.[4]

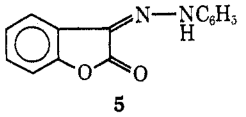
The nmr spectrum of the ^{15}N derivative of 1,3-diphenyl-4-phenylazobarbituric acid (**4**) contains a



4

doublet centered at 14.3 ppm, whose separation (J = 95.6 Hz) remains unchanged from 35 to 65°. At higher temperatures the doublet begins to coalesce until at 133° only a broad singlet remains. In pyridine, the ^{15}N derivative displays a singlet for the acidic proton, which is considerably broader than the ^{14}N singlet. These observations are amenable to the same interpretations discussed for **3**.

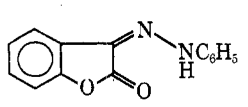
The nmr spectrum of the ^{14}N derivative of 3-phenylazocoumaran-2-one (**5**) contains two low-field singlets



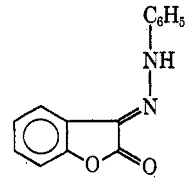
5

at 11.1 and 12.1 ppm with approximately equal areas. The ^{15}N derivative shows two doublets centered at the same positions and with the same areas. The simplest explanation for this observation appears to be the presence of *two* phenylhydrazone forms, presumably the syn and anti isomers shown below. This same type of nmr pattern for an ^{15}N-acetoacetaldehyde phenylhydrazone has been previously attributed to geometrical

(4) G. J. Lestina and T. H. Regan, *J. Org. Chem.*, **34**, 1685 (1969).



syn



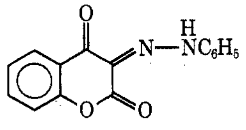
anti

isomerism.[5] The lower field resonance can probably be assigned to the NH proton of the intramolecularly hydrogen bonded syn form.

As the temperature is increased the low-field doublet broadens slightly and the higher field doublet coalesces (at about 120°) to a single broad peak. Apparently the syn form is stabilized by hydrogen bonding, but the anti form undergoes exchange (either with the azo form or with itself).

The low-field pattern for the ^{14}N derivative of **5** in pyridine consists of a singlet, while the ^{15}N derivative shows a doublet (J = 98 Hz), evidence for only one phenylhydrazone form in this solvent.

The nmr spectrum of 3-phenylazo-4-hydroxycoumarin (**6**) in CDCl$_3$ exhibits the same low-field pattern as **5**: two doublets in the ^{15}N derivative, and two singlets in the ^{14}N with integrated ratios of 5:1 (lower field to higher field). Geometrical isomerism in the phenylhydrazone form appears again to be the most reasonable explanation. In DMSO, the low-field spectrum shows a doublet and a broad singlet; in pyridine, only a singlet appears. The explanation above applied to **5** at higher temperatures in DMSO and in pyridine would appear to hold for **6** in these solvents.



6

A comparison of the tautomeric forms of the above azo derivatives, and those studied previously in this laboratory (1,2-diphenyl-4-phenylazo-3,5-pyrazolidinedione,[3] 3-methyl-1-phenyl-4-phenylazo-5-pyrazolone,[3] and 3-methyl-4-phenylazo-5-isoxazolone[6]), with the structures of the heterocycles themselves[7] (*e.g.*, 3-methyl-1-phenyl-5-pyrazolone) shows that, with the probable exception of **6**, the structure of the heterocycle and its azo derivative at room temperature in relatively nonpolar solvents are the same with respect to enolization at the carbon β to the phenylazo group. In other words, if the azo derivative exists in form A (hydroxyazo) under these conditions, the heterocycle also exists in the hydroxy form. The generality of this observation remains to be determined.

Experimental Section

The ^{15}N derivatives were prepared by diazotization of 99% isotopically enriched ^{15}N-aniline at 0° and coupling to the appropriate heterocycle. The melting points of ^{15}N derivatives were identical to within ± 1° with their ^{14}N homologs and were in agreement with literature values (**1**,[8] **2**,[3] **3**,[9] **4**,[10] **5**,[11] **6**[12]).

Nmr spectra were obtained on a Varian A-60D spectrometer. Deuterated solvents were dried over molecular sieves. Integrated areas were in good agreement with the theoretical values.

Registry No.—**1**, 15095-26-8; **2**, 15096-02-3; **3**, 36540-15-5; **4**, 36540-16-6; (*Z*)-**5**, 36540-17-7; (*E*)-**5**, 36540-18-8; **6**, 36540-19-9.

Acknowledgment.—The authors are indebted to the Camille and Henry Dreyfus Foundation for partial support of this work.

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(6) F. A. Snavely and C. H. Yoder, *J. Inorg. Nucl. Chem.*, **33**, 2699 (1971).

(7) For 3-pyrazolones see A. R. Katritsky and F. W. Maine, *Tetrahedron*, **20**, 315 (1964); for 4-pyrazolones see M. J. Nye and W. P. Tang, *ibid.*, **28**, 455 (1972); for 5-pyrazolones and isoxazolones see A. R. Katritsky and F. W. Maine, *ibid.*, **20**, 299 (1964), and A. R. Katritsky, S. Økase, and A. J. Boulton, *ibid.*, **18**, 777 (1962); for others see A. R. Katritsky and A. P. Ambler in "Physical Methods in Heterocyclic Chemistry," Vol. II, A. R. Katritsky," Ed., Academic Press, New York, N. Y., 1963; A. R. Katritsky and J. W. Lagowski in "Advances in Heterocyclic Chemistry," Vol. 2, A. R. Katritsky, Ed., Academic Press, New York, N. Y., 1963.

(8) F. A. Snavely, D. A. Sweigart, C. H. Yoder, and A. Terzis, *Inorg. Chem.*, **6**, 1831 (1967).

(9) K. Auwers and K. Müller, *Justus Liebigs Ann. Chem.* **381**, 276 (1911).

(10) M. A. Whitely, *J. Chem. Soc.*, **91**, 1330 (1907).

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