Azido–Tetrazole Tautomerism in the Azole Series

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Summary It is shown, in the case of azidopyrazoles, that for the neutral molecule the equilibrium is displaced towards the azide, whilst for the anion it is displaced towards the tetrazole.

(I)

(two tautomers)

(II)

(three tautomers)

(V)

(III)

(IV)

Scheme

	a	b	c	d	e
R¹	H	H	CO₂Et	CO₂Et	Ph
R²	H	Me	H	Me	H

Previous results indicate that the azido-tetrazole equilibrium is completely displaced towards the azido-tautomer in the azole series: imidazole,[1] pyrazole,[2] s-triazole,[3] v-triazole,[1] tetrazole,[4] benzimidazole.[5]

We have shown that in the pyrazole series the direction of the equilibrium is reversed when the neutral molecule is converted into the anion (Scheme).

The products show, in CHCl₃, EtOH, Me₂SO, and KBr, a very intense peak $\nu_{as}(N_3)$ at 2130 cm^{-1}, characteristic of the azide (I). This band does not alter with time.

In their n.m.r. spectra these same products show the signals normally expected for a structure of type (I) [but equally compatible with the tetrazole form (II)] in CDCl₃, (CD₃)₂SO, and C₆D₆. Nevertheless it is noteworthy that in (CD₃)₂SO coupling of pyrazole protons of positions 4 and 5 with the NH proton is observed (Table); it is the first time
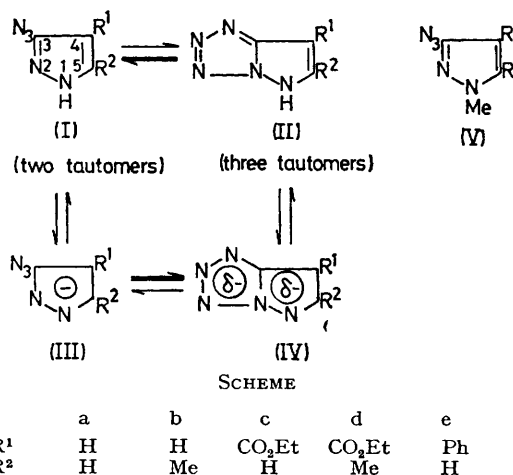
that coupling of this type has been established in pyrazoles[6] (on the other hand it has been observed for pyrrole[7]: $J_{1,2}$ 2·67, $J_{1,3}$ 2·50 Hz).

TABLE

Chemical shifts (p.p.m. from Me_4Si) and coupling constants (Hz) of azidopyrazoles in $(CD_3)_2SO$

		(Ia)	(Ib)	(Ic)	(Id)	(Ie)
NH^1	:	8·8 (b)	11·2 (b)	13·3 (b)	13·5 (b)	12·9 (b)
R^1	:	5·99 (t)	5·74 (m)	$\begin{cases} 1·26\ (t) \\ 4·21\ (q) \end{cases}$	$\begin{cases} 1·29\ (t) \\ 4·21\ (q) \end{cases}$	7·2—7·8 (m)
R^2	:	7·71 (q)	2·19 (d)	8·25 (d)	2·42	8·18 (d)
$J_{1,4}$	:	2·10	2·05	—	—	—
$J_{1,5}$	:	1·45	—	1·80	—	1·80
$J_{4,5}$	:	2·25	0·75	—	—	—

A study of the i.r. spectra of these products in a mixture of EtOH–EtONa shows that the azide peak† diminishes with time following first-order kinetics; the order of the speed of cyclisation of the products is as follows: (Id) > (Ic) >> (Ie) > (Ib) > (Ia). We have verified that these equilibria are reversible [on acidification, the azide peak gradually appeared and the product (I) was finally recovered unchanged] and also that, for the N-methyl derivatives (V), the intensity of the azide peak does not vary with time.

It is possible to follow the phenomenon by n.m.r. spectroscopy since the signals corresponding to R^1 and R^2 appear at different fields for the azide (III)‡ and the tetrazole (IV).‡ Thus in the case of (Ib) we have recorded spectra on a 60 MHz spectrometer every 10 minutes. The methyl

signals resonate at 2·19 (IIIb) and 2·35 (IVb) p.p.m. from Me_4Si. The kinetics are first order, $t_{1/2} = 130$ min.

It is our belief that in basic media the anion (III) is formed in a proportion which depends on the acidity of the pyrazole (I), and that then, in a slow step, (III) cyclises to the anion (IV), which is less basic.

We conclude that in a sufficiently strong basic medium the stable form of the azidopyrazoles, and probably of all the azidoazoles, is the tetrazole anion, which presents interesting possibilities in the study of the reactivity of these products.

† This peak appears at a lower frequency (10 to 15 cm^{-1}) in the anion (III) than in the neutral species (I).

‡ In fact, these are the averaged signals situated between those of the neutral molecule and those of the anion and they are dependent on the acidity of the pyrazole (I) and the tetrazole (II).

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