

[7+2]- AND [11+2]-CYCLOADDITION REACTIONS OF DIAZO-AZOLES  
WITH ISOCYANATES TO AZOLO[5,1-d][1,2,3,5]TETRAZINE-4-ONES <sup>1)</sup>

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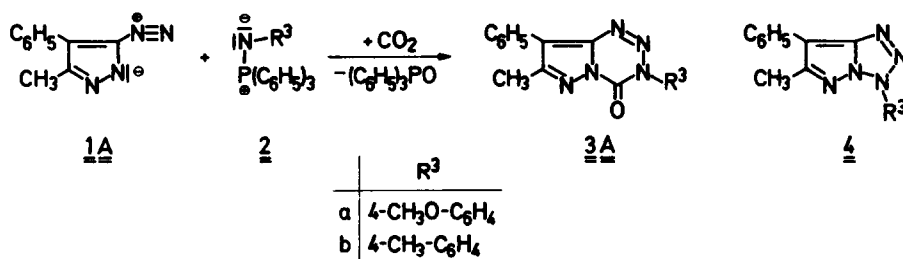
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Diazo-azoles react as 1,7- or 1,11-dipoles with isocyanates to form the hitherto unknown pyrazolo[5,1-d][1,2,3,5]tetrazine-4-ones, [1,2,3,5]tetrazino[5,4-b]indazole-4-ones and [1,2,3]triazolo[5,1-d][1,2,3,5]tetrazine-4-ones in a [7+2]- or [11+2]-cycloaddition reaction.

Recently we reported cycloadditions of diazo-azoles with ylides of the diazoalkane-, phosphonium-, sulfonium-, pyridinium- or sulfene-type with the formation of 3H-azolo[5,1-c][1,2,4]-triazoles <sup>2)</sup>.

In attempts to use phosphanimines 2 as ylides in the reaction with the diazo-pyrazole 1A we did not obtain the expected 3H-pyrazolo[1,5-d]tetrazoles 4, but instead we isolated the carbonyl-containing species 3A with a strong infrared carbonyl absorption at 1750 cm<sup>-1</sup> (scheme 1, cf table 1).

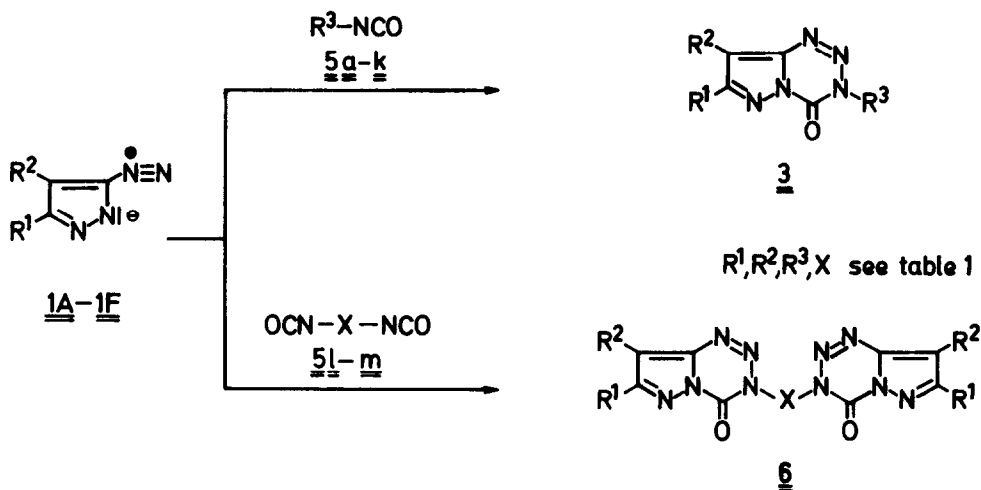
Scheme 1



Suggesting how these compounds could have been formed, a reasonable reaction sequence seems to involve isocyanates resulting from reaction of phosphanimines 2 with carbon dioxide from the air <sup>3)</sup>. In fact, we obtained the same products 3Aa and 3Ab from the diazo-pyrazole 1A with the isocyanates 5a and 5b, respectively. In order to show the scope of this reaction various combinations of diazo-azoles with isocyanates have been investigated. Thus a solution of the diazo-pyrazoles 1A - 1E in dichloromethane was added dropwise to an ice-cold solution of the

mono-isocyanates 5a - 5k or of the di-isocyanates 5l - 5m also in dichloromethane. Usually after 12 h at room temperature no diazo-pyrazole could be detected by attempted coupling with 2-naphthol. After removal of the solvent and addition of ether the pyrazolo[5,1-d][1,2,3,5]-tetrazine-4-ones 3Aa - 3Ak, 3Bc - 3Ec, 3Eg, 6Al - 6Am are obtained in good yields and nearly pure (scheme 2 and table 1).

Scheme 2

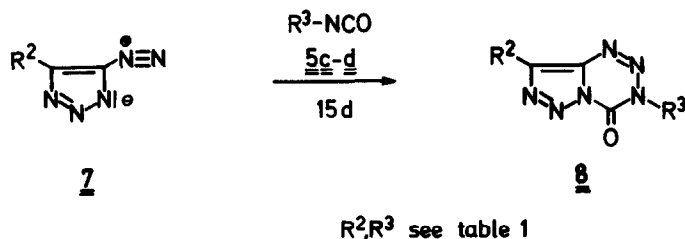


This reaction can be understood as a [7+2]cycloaddition of the diazo-pyrazole to the electron deficient hetero-double bond of the isocyanate<sup>4,5</sup>). Alternatives to the concerted [7+2]cycloaddition are two step mechanisms consisting of (i) a ring nitrogen acylation to a 1,9-dipole followed by intramolecular coupling or (ii) a [3+2]cycloaddition of the diazo-pyrazole to the isocyanate with subsequent [1,5]acylshift.

Surprisingly the diazo-indazole 1F ( $R^1-R^2$ :  $CH=CH-CH=CH$ ) did react as a 1,11-dipole with the mono-isocyanates 5c - 5d and with the di-isocyanate 5m in a [11+2]cycloaddition to the [1,2,3,5]tetrazino[5,4-b]indazole-4-ones 3Fc - 3Fd and 6Fm (scheme 2 and table 1), although the stability of 1F against electron deficient multiple bonds has been stated<sup>5c</sup>). But the reaction time for 1F with minimal 24 h was markedly longer than in the case of the diazo-pyrazoles 1A - 1E.

Even more slowly was the reaction rate of 4-diazo-5-phenyl-[1,2,3]triazole 7 with the isocyanates 5c - 5d to the [1,2,3]triazolo[5,1-d][1,2,3,5]tetrazine-4-ones 8c - 8d (scheme 3 and table 1).

Scheme 3

Table 1 : Data of the azolo[5,1-d][1,2,3,5]tetrazine-4-ones 3, 6 and 8 [a].

	$\text{R}^1$	$\text{R}^2$	$\text{R}^3/\text{X}$	yield [%]	m.p. [°C]	$\nu(\text{CO})$ [cm <sup>-1</sup> ]
<u>3Aa</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub>	86	182-184	1750
<u>3Ab</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	97	171-172	1750
<u>3Ac</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	79	143-144	1775
<u>3Ad</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	98	190-192	1755
<u>3Ae</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	4-Cl-C <sub>6</sub> H <sub>4</sub>	62	178-182	1755
<u>3Af</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	2,4,6-(CH <sub>3</sub> ) <sub>3</sub> C <sub>6</sub> H <sub>2</sub>	96	176-178	1760
<u>3Ag</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	84	134	1750
<u>3Ah</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	ClCH <sub>2</sub> CH <sub>2</sub>	68	95-96	1745
<u>3Ai</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	(CH <sub>3</sub> ) <sub>2</sub> CH	62	83-84	1765
<u>3Aj</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub> -(CH <sub>2</sub> ) <sub>3</sub>	86	oil	1775
<u>3Ak</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	(CH <sub>3</sub> ) <sub>3</sub> C	37	153-154	1775
<u>3Bc</u>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	88	120-121	1755
<u>3Cc</u>	H	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	95	185-186	1760
<u>3Dc</u>	C <sub>6</sub> H <sub>5</sub>	H	C <sub>6</sub> H <sub>5</sub>	80	198-200	1755
<u>3Ec</u>	H	COOC <sub>2</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	88	145-148	1770, 1720
<u>3Eq</u>	H	COOC <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	30	137-138	1765, 1715
<u>3Fc</u>	CH=CH-CH=CH		C <sub>6</sub> H <sub>5</sub>	82	160-162	1745
<u>3Fd</u>	CH=CH-CH=CH		4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	85	166-168	1750
<u>6Al</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	-(CH <sub>2</sub> ) <sub>6</sub> -	95	174-176	1750
<u>6Am</u>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>		97	216-220	1765
<u>6Fm</u>	CH=CH-CH=CH			70	172-173	1760
<u>8c</u>		C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	41	140-142	1775
<u>8d</u>		C <sub>6</sub> H <sub>5</sub>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	70	147-148	1790

[a] The analytical data (microanalyses and UV, IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR) of all products are in accordance with the assigned structures.

The azolo[5,1-d][1,2,3,5]tetrazine-4-ones 3, 6 and 8 are colourless to yellow compounds showing strong fluorescence in the solid state or in dichloromethane solution in the long wavelength UV region. At their melting points they decompose partially with gas evolution. The bicyclic and tricyclic compounds 3, 6 and 8 contain the [1,2,3,5]tetrazine ringsystem that has been regarded as unstable<sup>6)</sup> and which has been synthesized just recently<sup>7)</sup>, whilst condensed [1,2,3,5]tetrazines were hitherto unknown.

The azolo[1,2,3,5]tetrazine-4-ones are heteroanalogous to benzo[1,2,3]triazine-4-ones that have widespread use, for instance as diuretics, sedatives, tranquilizers and inflammation inhibitors<sup>8)</sup>.

At present, we are investigating cycloaddition reactions of diazo-azoles with other heterocumulenes and fragmentation reactions of the cycloadducts continuing earlier studies<sup>9)</sup>.

#### References and notes:

- 1) Reactions with diazo-azoles, 3rd communication. We are grateful to the BASF Aktiengesellschaft and the Bayer AG for gifts of chemicals. - 2nd communication: Ref. 2).
- 2) G. Ege and K. Gilbert, *Tetrahedron Lett.* 1979, 1567.
- 3) H. Staudinger and J. Meyer, *Helv. Chim. Acta* 2, 635 (1919); herein the reaction is performed at the melting points of the phosphanimines.
- 4) In an analogous manner some electron deficient ethenes and dimethyl acetylendicarboxylate give a cycloaddition with 3-diazo-5-phenyl-pyrazole cf M.H. Elnagdi, M.R.H. Elmoghayar, S.M. Fahmy, M.K.A. Ibraheim and H.H. Alnima, *Z. Naturforsch.* 33b, 216 (1978).
- 5) For cycloadditions of diazo-azoles to electron rich multiple bonds cf a) W.L. Magee and H. Shechter, *J. Am. Chem. Soc.* 99, 633 (1977); b) G. Ege, K. Gilbert and H. Franz, *Synthesis* 1977, 556; c) H. Dürr and H. Schmitz, *Chem. Ber.* 111, 2258 (1978).
- 6) H. Neunhoeffer and P.F. Wiley, *Chemistry of [1,2,3]Triazines, and [1,2,4]Triazines, Tetrazines, and Pentazines*, Wiley and Sons, New York, 1978, p. 1296.
- 7) K. Kubo, T. Nonaka and K. Odo, *Bull. Chem. Soc. Japan* 49, 1339 (1976).
- 8) See ref. 6), p. 165 - 167.
- 9) G. Ege, Ph. Arnold, E. Beisiegel, I. Lehrer, H. Suschitzky and D. Price, *Liebigs Ann. Chem.* 1976, 946.

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