

[7 + 2]- and [11 + 2]-Cyclocondensation Reactions of Diazoazoles with
Acyltriphenylphosphonium Methylides to Azolo[5,1-c][1,2,4]triazines

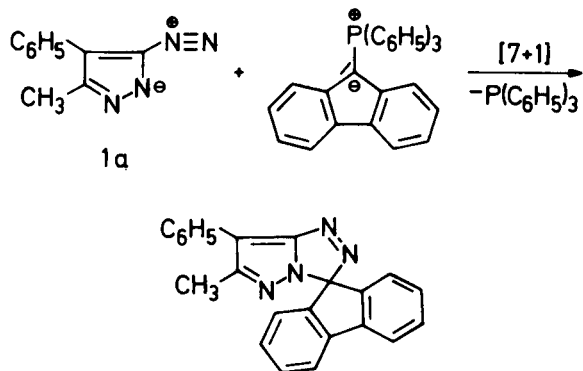
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Acyltriphenylphosphoniummethylides react with diazoazoles in a [2 + 7]- or [2 + 11]-cycloaddition reaction followed by elimination of triphenylphosphane oxide to yield azolo[5,1-c][1,2,4]triazines.

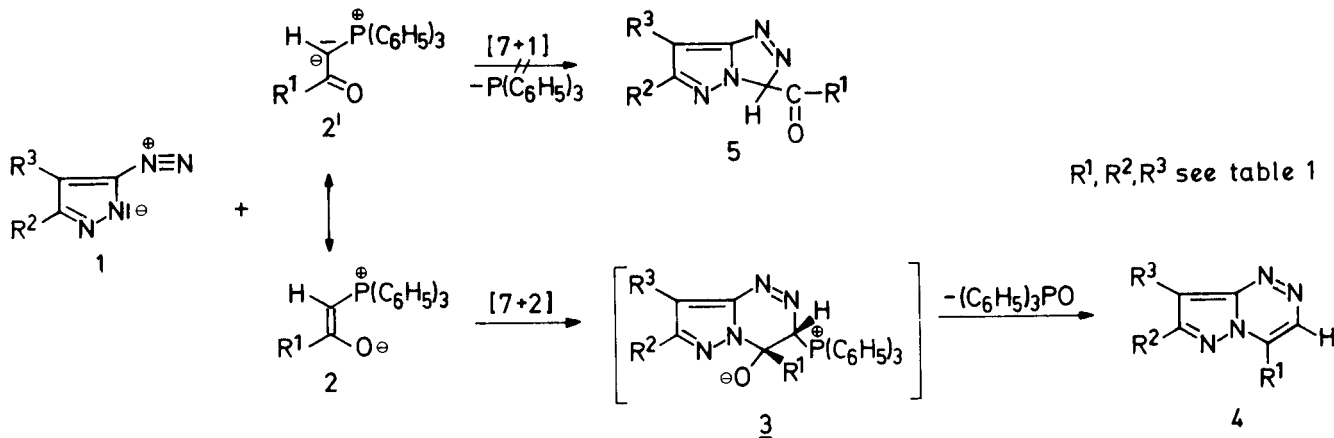
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Diazoazoles **1** (**2**) are known to react as 1,7- or 1,11-dipoles with a variety of ylides in [7 + 1]- or [11 + 1]-cycloadditions forming 3*H*-azolo[5,1-c][1,2,4]triazoles. Thereby the ylides behave as 1-nucleophile-1-electrophiles. In the case of triphenylphosphoniumfluorenylidene triphenylphosphane is eliminated (**3**).



Scheme 1

In order to verify the scope of this reaction we attempted to apply acylsubstituted phosphonium ylides **2** as 1-nucleophile-1-electrophiles (form **2'**, Scheme 2) expecting 3-acyl-3*H*-azolo[5,1-c][1,2,4]triazoles **5** as reaction products or a tautomer thereof. However, acylphosphonium ylides **2** may alternatively behave as 1-nucleophile-2-electrophiles, because they exist, according to ¹H-nmr, to a large extent as phosphonium enolates **2** (**4**). Indeed, it is this form which explains the reaction products of **2** with 1,3-dipolarophilic azides (**5**) or nitrilimines (**6**).



Scheme 2

Treatment of ice-cold solutions of the acyl ylides **2** in dichloromethane with freshly prepared diazoazoles **1** in dichloromethane (method A) or in the two phase system dichloromethane-water (method B) leads to an increasing darkening colour showing the rapid progress of the reaction. After 1 hour, the organic layer is concentrated and filtered through silicagel with dichloromethane as eluent. The yellow or red filtrate yields the pure and crystalline azolo[5,1-c][1,2,4]triazines **4** in 40-73% yield. On further elution with chloroform triphenylphosphane oxide is obtained.

The constitution of the azolotriazines **4** follows from elemental analysis (Table 1) and their spectroscopic data (uv and ¹H-nmr in Table 2; ir: no absorption in the carbonyl region).

The cyclocondensation reaction presumably involves the betaine **3** formed in a [7 + 2]- or [11 + 2]-cycloaddition reaction between **1** and phosphonium enolate **2** which

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Table 1

Yields, Melting Points and Analytical Results of Azolo[5,1-c][1,2,4]triazines **4** (a)

4	R ¹	R ²	R ³	Method	Yield [%]	M.p. [°C]	Colour	Formula	Analysis Found (Calcd.) [%]			
									C	H	N	OCH ₃
a	C ₆ H ₅	CH ₃	C ₆ H ₅	A	51	192-193 (b)	red	C ₁₈ H ₁₄ N ₄	75.35 (75.50)	5.06 (4.93)	19.34 (19.57)	—
b	C ₆ H ₅	H	C ₆ H ₅	A	59	144-145 (b)	red	C ₁₇ H ₁₂ N ₄	75.12 (74.98)	4.57 (4.44)	20.48 (20.58)	—
c	C ₆ H ₅	C ₆ H ₅	H	A	63	157-158 (b)	yellow	C ₁₇ H ₁₂ N ₄	75.20 (74.98)	4.71 (4.44)	20.70 (20.58)	—
d	C ₆ H ₅	H	H	B	56	111-112 (c)	yellow	C ₁₁ H ₈ N ₄	67.10 (67.34)	4.30 (4.11)	28.29 (28.55)	—
e	C ₆ H ₅	CH=CH	— CH=CH	A	73	165 (b)	orange	C ₁₅ H ₁₀ N ₄	73.05 (73.16)	4.20 (4.09)	22.86 (22.75)	—
f(d)	C ₆ H ₅	N=N	— C=C C ₆ H ₅ C ₆ H ₅	A	71	254-255 (b)	orange	C ₂₅ H ₁₆ N ₆	75.19 (74.98)	4.25 (4.03)	20.96 (20.99)	—
g	4-CH ₃ O-C ₆ H ₄	H	3-F ₃ C-C ₆ H ₄	A	65	165-166 (b)	red	C ₁₉ H ₁₃ F ₃ N ₄ O	61.83 (61.62)	3.79 (3.54)	15.12 (15.13)	8.44 (8.38)
h	4-O ₂ N-C ₆ H ₄	H	4-CH ₃ O-C ₆ H ₄	A	40	231-232 (b)	purple	C ₁₈ H ₁₃ N ₅ O ₃	62.11 (62.25)	3.84 (3.77)	20.33 (20.16)	9.18 (8.93)
i	CH ₃	CH ₃	C ₆ H ₅	A	47	127-128 (b)	orange	C ₁₃ H ₁₂ N ₄	69.52 (69.63)	5.54 (5.39)	24.79 (24.98)	—
j	CH ₃	H	H	B	56	100-101 (c)	light yellow	C ₆ H ₆ N ₄	53.63 (53.72)	4.76 (4.51)	41.72 (41.77)	—
k	CH ₃	CH=CH	— CH=CH	A	71	243-244 (b)	yellow	C ₁₀ H ₈ N ₄	65.47 (65.21)	4.64 (4.38)	30.27 (30.41)	—

(a) Note 9. (b) Recrystallized from ethanol/benzene. (c) Sublimed at 90° and 0.1 Torr. (d) Note 10.

Table 2

Uv and ¹H-nmr Data of Azolo[5,1-c][1,2,4]triazines **4**

4	Uv λ max [nm] (ε)	¹ H-nmr δ
a	422 (4700), 298 sh (9200), 269 sh (17800), 247 (25300)	2.71 (s, 3H, 7-CH ₃), 7.3-7.7 (m, 6H, aromat. H), 7.8-8.0 (m, 2H, <i>ortho</i> -H of 8-phenyl), 8.1-8.3 (m, 2H, <i>ortho</i> -H of 4-phenyl), 8.85 (s, 1H, 3-H)
b	428 (5600), 300 sh (10400), 272 sh (17200), 247 (23800)	7.2-7.7 (m, 6H, aromat. H), 8.0-8.3 (m, 4H, <i>ortho</i> -H of 4- and 8-phenyl), 8.51 (s, 1H, 7-H), 8.87 (s, 1H, 3-H)
c	400 sh (4500), 346 (6500), 291 sh (24900), 267 (31600)	7.3-7.7 (m, 7H, 8-H and aromat. H), 7.9-8.1 (m, 2H, <i>ortho</i> -H of 7-phenyl), 8.2-8.4 (m, 2H, <i>ortho</i> -H of 4-phenyl), 8.87 (s, 1H, 3-H)
d	382 (5200), 356 sh (4300), 298 sh (3200), 276 sh (6700), 236 (28700)	7.29 (d, J = 2.5 Hz, 1H, 8-H), 7.5-7.7 (m, 3H, aromat. H), 8.1-8.4 (m, 3H, 7-H and <i>ortho</i> -H of 4-phenyl), 8.92 (s, 1H, 3-H)
e	433 (5600), 364 (7400), 350 sh (6500), 299 sh (20000), 282 (32900), 253 sh (13000)	7.4-7.8 (m, 5H, aromat. H), 7.9-8.05 (m, 1H, 7-H), 8.2-8.4 (m, 2H, <i>ortho</i> -H of 4-phenyl), 8.5-8.7 (m, 1H, 10-H), 9.18 (s, 1H, 3-H)
f	459 sh (5000), 384 (16500), 281 sh (23600), 249 (31600)	7.2-7.8 (m, 13H, aromat. H), 8.35-8.55 (m, 2H, <i>ortho</i> -H of 4-phenyl), 9.40 (s, 1H, 3-H)
g	426 (9100), 325 (13200), 275 sh (11500), 244 (25200)	3.90 (s, 3H, OCH ₃), 7.0-7.3 (m, 2H, 3-H and 5-H of 4-[4-CH ₃ O-C ₆ H ₄]), 7.5-7.7 (m, 2H, 5-H and 6-H of 8-[3-F ₃ C-C ₆ H ₄]), 8.15-8.35 (m, 2H, 2-H and 6-H of 4-[4-CH ₃ O-C ₆ H ₄]), 8.4-8.5 (m, 2H, 2-H and 4-H of 8-[3-F ₃ C-C ₆ H ₄]), 8.57 (s, 1H, 7-H), 8.96 (s, 1H, 3-H)
h	472 (5600), 315 sh (13700), 274 (33300), 254 sh (25200)	3.86 (s, 3H, OCH ₃), 6.95-7.1 (m, 2H, 3-H and 5-H of 8-[4-CH ₃ O-C ₆ H ₄]), 8.1-8.2 (m, 2H, 2-H and 6-H of 8-[4-CH ₃ O-C ₆ H ₄]), 8.43 (s, 4H, aromat. H of 4-[4-O ₂ N-C ₆ H ₄]), 8.53 (s, 1H, 7-H), 8.92 (s, 1H, 3-H)
i	388 (3200), 297 (2900), 261 sh (19500), 242 (25300)	2.69 (s, 3H, 7-CH ₃), 2.74 (s, 3H, 4-CH ₃), 7.2-7.6 (m, 3H, aromat. H), 7.75-7.95 (m, 2H, <i>ortho</i> -H of 8-phenyl), 8.58 (s, 1H, 3-H)
j	356 (2300), 338 sh (2100), 300 sh (1100), 290 (1600)	2.84 (s, 3H, 4-CH ₃), 7.21 (d, J = 2.5 Hz, 1H, 8-H), 8.27 (d, J = 2.5; 1H, 7-H), 8.70 (s, 1H, 3-H)
k	398 (3000), 352 (7800), 338 (6600), 292 sh (11400), 271 (26500), 235 (19900)	2.98 (s, 3H, 4-CH ₃), 7.3-8.1 (m, 3H, 7-H, 8-H and 9-H), 8.5-8.7 (m, 1H, 10-H), 8.96 (s, 1H, 3-H)

upon elimination of triphenylphosphane oxide leads to compounds **4**. Thus, acylphosphonium ylides **2** react as 1-nucleophile-2-electrophiles (7). Compounds **4** formally represent cycloaddition products of diazoazoles **1** and propyne or phenylethyne which, however, do not react in an analogous manner (8).

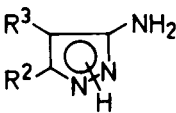
The azolotriazines **4** are yellow to red compounds; the yellow and orange ones show fluorescence in the long wavelength uv. Compounds **4** with an aryl group in the 8-position ($R^3 = \text{aryl}$) are red and do not fluoresce. This bathochromic shift (46 nm in **4b** referred to 7,8-unsubstituted **4d**) is substantially reduced (to 18 nm) if the aryl group is located in position 7 (**4c**, $R^2 = \text{phenyl}$) instead of 8. Presumably this effect may be due to a reduced conjugation between the heterocyclic system and the 7-phenyl group. The bathochromic effect is, as expected, increased by donor-acceptor groups in the para positions of the 4- and 8-phenyl substituents as shown by example **4h** with a 44 nm shift referred to **4b**.

In the $^1\text{H-nmr}$ spectra of all compounds **4** with phenyl substituents in position 4 and/or 7 or 8 the *ortho* protons are shifted downfield (Table 2) which is due to the anisotropy of the heteroaromatic system being effective in a nearly coplanar conformation (11). In all compounds of Table 2 the $^1\text{H-nmr}$ signal for 3-H is the most downfield shifted one. This downfield shift is still more increased by benzo or pyridazino annulation (**4e**, **4k** and **4f**).

EXPERIMENTAL

Melting points were determined on a Bock-Monoscop and are uncorrected. The uv spectra were taken on a Beckman 25 spectrometer in dichloromethane solution. The $^1\text{H-nmr}$ spectra were recorded on a Varian EM 390 spectrometer at 90 MHz using deuteriochloroform as solvent and TMS as an internal standard.

The azolamines corresponding to the diazoazoles **1** and the acylphosphonium ylides **2** were obtained by procedures from the literature.

Azolamines	R^2	R^3	Lit.
	CH_3	C_6H_5	(12a)
	H	C_6H_5	(12b)
	C_6H_5	H	(12c)
	H	H	(12d)
	H	$3\text{-F}_2\text{C-C}_6\text{H}_4$	(12b)
	H	$4\text{-CH}_3\text{O-C}_6\text{H}_4$	(12b)
	$\text{CH}=\text{CH}$	$\text{CH}=\text{CH}$	(12e)
	$\text{N}=\text{N}$	$\text{C}=\text{C}$	(8a)
		C_6H_5 , C_6H_5	
		C_6H_5 , C_6H_5	
Acylphosphonium ylides 2	R^1		Lit.
	C_6H_5		(13a)
	CH_3		(13a)
	$4\text{-CH}_3\text{O-C}_6\text{H}_4$		(13b)
	$4\text{-O}_2\text{N-C}_6\text{H}_4$		(13b)

Pyrazolo[5,1-c][1,2,4]triazines **4a-d** and **4g-j**, [1,2,4]Triazino[4,3-b]indazoles **4e** and **4k**, and 4,9,10-Triphenylpyridazino[3',4'-3,4]pyrazolo[5,1-c][1,2,4]triazine (**4f**).

General Procedure.

To an ice-cold solution of azolamine (10 mmoles) in water (10 ml.) and concentrated hydrochloric acid (5 ml.) was added dropwise a solution of sodium nitrite (0.7 g., 10 mmoles) in water (3 ml.) at $0-5^\circ$. After stirring at this temperature for 30 minutes ice-cold dichloromethane (100 ml.) was added and the mixture made alkaline with a saturated solution of sodium carbonate in water.

Method A.

After neutralization the organic layer containing the diazoazole **1** was separated, dried with sodium sulfate and filtered. The filtrate was dropped into a solution of the acyl ylides **2** (10 mmoles) in dichloromethane (50 ml.) at about 10° .

Method B.

In the case of the water soluble 3-diazopyrazole the two phase system water-dichloromethane was directly used after neutralization by adding a solution of the acyl ylides **2** (10 mmoles) in dichloromethane (50 ml).

The coloured mixture was stirred for one more hour until a coupling test with β -naphthol was negative. The dichloromethane solution was then concentrated, the residue filtered through silicagel (100 g.) with dichloromethane as eluent, and the yellow or red filtrate was evaporated *in vacuo* giving almost pure and crystalline compounds **4**. On further elution with chloroform triphenylphosphane oxide in yields comparable to **4** was obtained.

Yields and melting points of azolotriazines **4** are given in Table 1.

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