

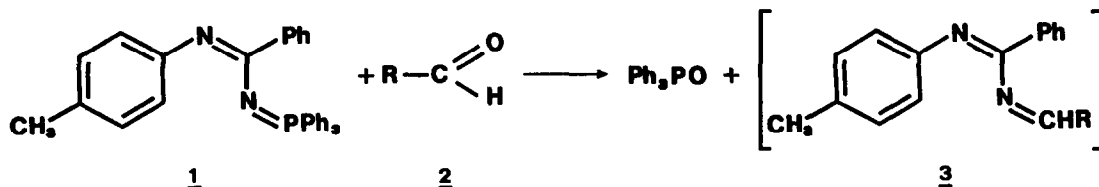
QUINAZOLINES BY ELECTROCYCLIC RING CLOSURE  
OF 1,3-DIAZA-1,3-DIENES

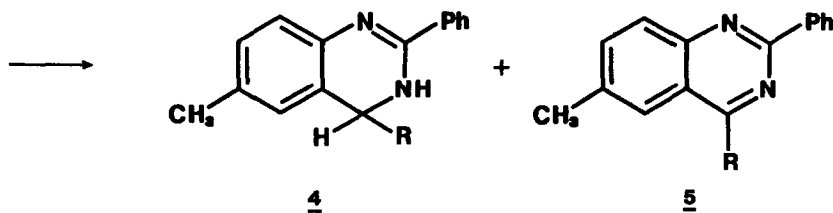
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Summary: N-imidoyliminotriphenylphosphorane reacts with aliphatic and aromatic aldehydes to give via an 1,3-diaza-1,3-diene intermediate 3,4-dihydroquinazolines and quinazolines. The ratio between the reaction products depends from the aldehyde employed.

Recently we reported a new synthetic approach to the quinazoline ring system starting from enamines and S,S-dimethyl-N-(N-arylbenzimidoyl)sulfimides<sup>1,2</sup>. The ready availability of these sulfur-nitrogen ylids and their reactivity as nucleophiles in the reaction with enamines prompted us to also study an other kind of nitrogen ylids derived from N-arylbenzamidines. Phosphorus-nitrogen ylids have been largely studied as reagents for the aza-Wittig reaction<sup>3</sup>. However only few works have been published about the behaviour in this reaction of the N-imidoyliminotriphenylphosphoranes<sup>4</sup>. In this communication we want to report our first results regarding the reaction of N-imidoyliminotriphenylphosphorane 1 and carbonyl compounds. The ylid 1 was easily prepared by a modification of the method described by Yoshida et al.<sup>4</sup> and its reactivity was tested initially with aldehydes and ketones.

The reaction of N-imidoyliminotriphenylphosphorane 1 and aldehydes 2 was performed in boiling xylene using three equivalents of aldehyde. The crude reaction mixture gave, after chromatographic purification over silica gel, the 3,4-dihydroquinazolines 4 and/or the quinazolines 5:

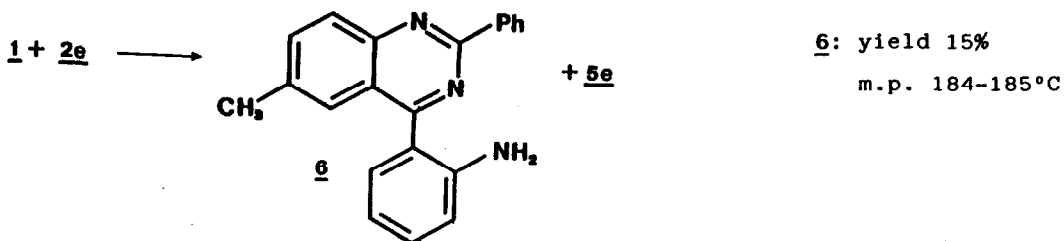




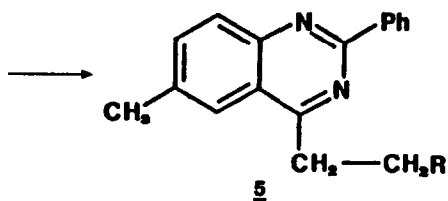
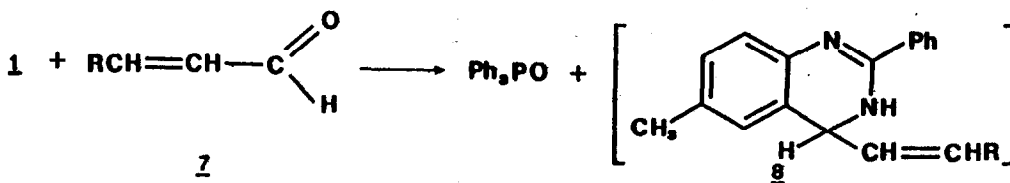
2-5	R	Reaction time	Yield %		m.p. °C	
			4	5	4	5
a	C <sub>6</sub> H <sub>13</sub>	40	31	42	79-82	61-63
b	PhCH <sub>2</sub> CH <sub>2</sub>	24	40	50	134-136	120-125
c	Ph	48	71	0	165-168	-
d	p(NO <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	12	0	70	-	214-217
e	o(NO <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	12	0	46	-	189-190

The mechanism probably involves an aza-Wittig reaction followed by electrocyclic ring closure of the 1,3-diaza-1,3-diene intermediate **3**<sup>6</sup>. The 3,4-dihydroquinazoline **4** thus formed may aromatize spontaneously in the reaction condition to quinazoline **5**. The ratio between compounds **4** and **5** depends probably upon the nature of substituent R, even if further experimental evidences are necessary for a complete understanding of this phenomenon. However, considering that the reaction is stopped when no more iminophosphorane **1** is detectable by tlc, the following comments can be made: when R is an aliphatic group an equimolecular distribution between compounds **4** and **5** is observed; if an aromatic substituent, such a phenyl group is present at C<sub>4</sub> only the 3,4-dihydro derivative **4** is detected. Nevertheless, if an electron withdrawing substituent is present on the aromatic ring the aromatization process is favoured and the quinazoline **5** is the sole reaction product. Furthermore the aromatization seems to be a temperature dependent process. In fact, when the reactions between N-imidoyltriphenylphosphorane **1** and 3-phenylpropionaldehyde **2b** or benzaldehyde **2c** are performed at 200°C (decalin) the ratio between products **4** and **5** decreases.

In the case of the reaction between iminophosphorane **1** and 2-nitrobenzaldehyde **2e** it was possible to isolate the quinazoline **5e** as well as a small amount (15%) of the 6-methyl-4-(2'-aminophenyl)-2-phenylquinazoline **6**, which probably comes from an intramolecular reaction of oxido-reduction:



A similar behaviour was observed when the N-imidoyltriphenylphosphorane **1** was reacted with  $\alpha,\beta$ -unsaturated aldehydes **7**:



5-8	R	Reaction time	Yield %	m.p. °C
f	Ph	50	44	120-125
g	C <sub>3</sub> H <sub>7</sub>	50	34	90-92

In this case the aromatization of undetected 3,4-dihydroquinazoline intermediate 8 occurs via intramolecular rearrangement to quinazoline 5 which is the sole reaction product.

The reactivity of this ylid was tested also with ketones. 1 does not react with acetophenone, diethylketone and cyclohexanone neither in xylene nor in other high-boiling solvents such decalin.

Further work is in progress to screen the reactivity of this kind of ylid and to synthesize new and more reactive nitrogen-phosphorus ylids derived from N-arylbenzamidines.

#### REFERENCES

1. Rossi, E.; Stradi, R. Synthesis 1989, 214.
2. Rossi, E.; Stradi, R.; Visentin, P. Tetrahedron submitted.
3. Johnson, A.W., in: Ylid chemistry, Academic Press, New York 1966, p.217.
4. Yoshida, H.; Ogata, T.; Inokawa, S. Bull.Chem.Soc.J. 1979, 1541 and references cited therein.
5. The reaction was performed by reacting N-chloro-N-(4-methylphenyl)benzamide with triphenylphosphine in  $\text{CH}_2\text{Cl}_2$  at  $-50^\circ\text{C}$  for 10' and then treating with NaOH 2M. (Yield: 70%). Analytical and spectral data are in accordance with reported values<sup>4</sup>.
6. The capability of the 1,3-diaza-1,3-dienes to undergo electrocyclic ring closure was proved via an alternative synthesis described elsewhere (see Ref. 2).

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