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HETEROCYCLES BY INTRAMOLECULAR AZA-WITTIG REACTIONS OF IMINOPHOSPHORANES OBTAINED FROM 2-AZIDOBENZOYL- AND 2-AZIDOBENZYLIDENE DERIVATIVES

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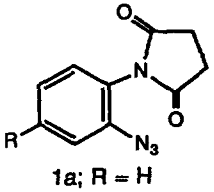
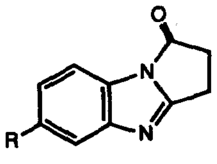
Summary: Iminophosphoranes have been used in intramolecular aza-Wittig reactions to prepare pyrrolo-[1,2-a]benzimidazoles, fused quinazolinones, quinolines, and an isoindolo[1,3,4]benzotriazepinone.

Recent interest[1,2,3] in the intramolecular aza-Wittig reaction of iminophosphoranes, derived from a variety of azides by the Staudinger reaction,[4] as a synthetic route to heterocycles, prompts us to report on our studies in this area.

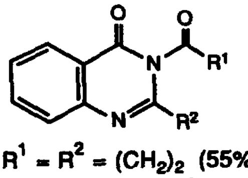
Cyclisation at imide carbonyl has been noted.[2] We have observed[5] similar cyclisations with N-(2-azidoaryl)succinimides (1a[6],b), which, on treatment with triethyl phosphite (TEP) in toluene at room temperature, cyclise directly to the pyrrolo[1,2-a]benzimidazoles (2a,b).



1a; R = H
b; R = Me



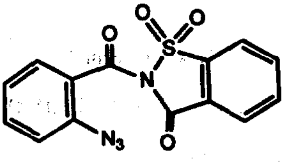
2a; R = H (53%), m.p. 172 °C
(lit.[7] 172 °C)
b; R = Me (72%)[8], m.p. 165° C [9]



3a; $R^1 = R^2 = (CH_2)_2$ (55%)
m.p. > 300°C[9]
b; $R^1 = R^2$ = o-C_6H_4 (60%)
m.p. 241°C (lit.[10] 233°C)

In contrast, the 2-azidobenzoyl derivatives of glutarimide and phthalimide (prepared by acylation of the imides with 2-benzoyl chloride in pyridine solution) yield isolable iminophosphoranes, which cyclise in boiling toluene to the fused quinazolinones (3a,b).

Treatment of N-(2-azidobenzoyl)-1,2-benzoisothiazoline-3-one 1,1-dioxide (4) with TEP in toluene at 25°C effected direct cyclisation to 1,2-benzoisothiazolo[3,2-b]quinazolin-7-one 5,5-dioxide (5) (m.p. 281°C; lit.[11] 276°C) in 88% yield.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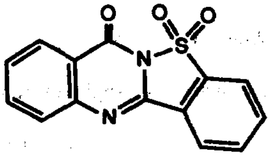
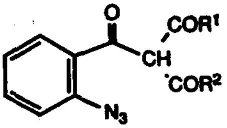

(5)

No product from an alternative cyclisation at the SO_2 function was isolated.

2-Azidobenzoyl derivatives (6a-d)[12] of β-keto-esters and β-diketones with TEP in toluene at room temperature cyclise rapidly (30 mins.) *via* the non-isolable iminophosphoranes to 2,3-disubstituted-4-quinolones (7a-d).[5] Only products resulting from cyclisation at the ketone carbonyl function were formed.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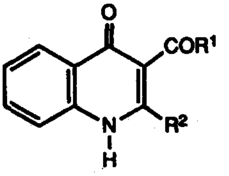
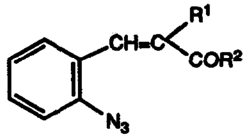

(7)

	Yield (%)	m.p. °C	lit. m.p. °C
a	94	97	101[13]
b	72	236	232[14]
c	81	233	232[15]
d	92	288	289[16]

In a similar manner, 2,3-disubstituted quinolines (9a-e) were obtained directly by reacting the aldol condensation products (8a-e) of 2-azidobenzaldehyde[17] with TEP in toluene at room temperature.

Direct condensation of the 2-azidobenzaldehyde with ethyl nitroacetate to give (8f) by the standard route[23] was troublesome. However, treatment of preformed iminotriphenylphosphorane[24] (10; m.p. 157°C; yield 88%) of 2-azidobenzaldehyde with ethyl nitroacetate in CCl_4 solution at 0°C in the presence of $TiCl_4$[25]

resulted in immediate aldol condensation and intramolecular cyclisation to 3-nitro-2-ethoxyquinoline (9f). In the cases of azides (8, d, e, and f) no products resulting from an alternative cyclisation at the ester or nitro-functions were obtained.



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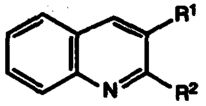
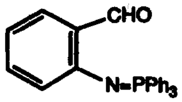


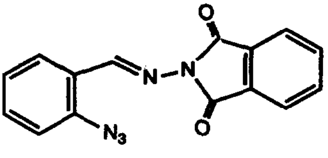
	Yield (%)	m.p.°C	lit.°C
(9) a;	73	oil[9]	-
b;	64	136	135[18]
c;	75	77	76[19]
d;	60	70	72[20]
e;	54	oil	oil[21]
f;	73	69[9]	-[22]



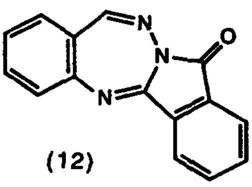
(10)

a) $R^1 = CO_2Et$, $R^2 = OEt$; b) $R^1 = COPh$, $R^2 = Ph$; c) $R^1 = COMe$, $R^2 = Me$;
d) $R^1 = CO_2Et$, $R^2 = Me$; e) $R^1 = CO_2Et$, $R^2 = Ph$; f) $R^1 = NO_2$, $R^2 = OEt$.

Finally, N-(2-azidobenzylidene) phthalimide (11), obtained by condensing 2-azidobenzaldehyde with N-aminophthalimide, with TEP in toluene yielded an isolable iminophosphorane, which on further heating cyclised to the isoindolo[1,2-b][1,3,4]benzotriazepinone (12) (m.p. 223-5°C; 57%).[9]



(11)



(12)

Further studies on the formation of seven-membered rings by this simple method, and on effecting intramolecular cyclisations of iminophosphoranes onto groups other than carbonyl are underway.

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