Reaction of Azines with Nitriles

José Barluenga, Laudina Muñíz, and Vicente Gotor

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Oviedo, Spain

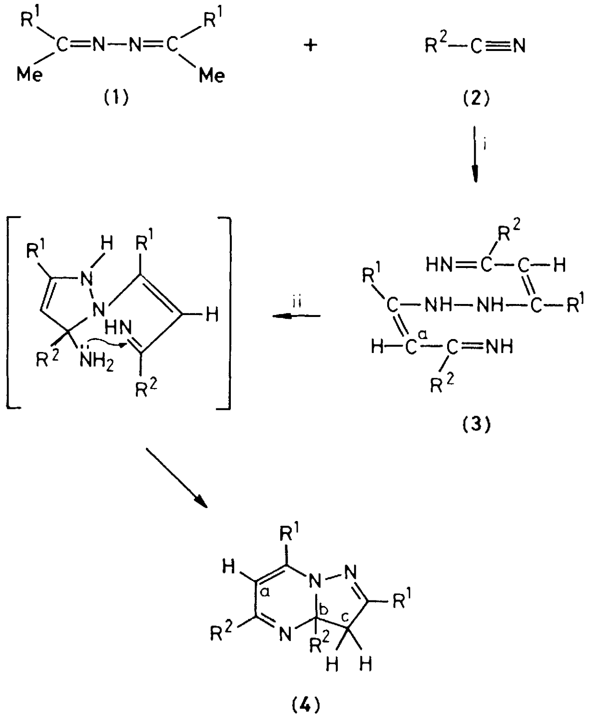
A new method for the synthesis of the hydrazine derivatives (**3**) by reaction of azines with nitriles is described; the hydrolysis of (**3**) yields the 3*H*-pyrazolo[1,5-*a*]pyrimidines (**4**).

Imines react with saturated nitriles in the presence of $AlCl_3$ to give 1-azabutadiene derivatives,[1] which are useful in the synthesis of five- and six-membered heterocyclic rings.[2] In order to produce suitable starting materials for the synthesis of

Table 1. Hydrazine derivatives (**3**) and 3*H*-pyrazolo[1,5-*a*]pyrimidines (**4**) obtained from azines.

	R^1	R^2	% Yield (**3**)	m.p./°C	% Yield (**4**)	m.p./°C	Carbon-13 chemical shifts and multiplicities			
							δ C^a(**3**) (p.p.m.)	δ C^a (**4**) (p.p.m.)	δ C^b (p.p.m.)	δ C^c (p.p.m.)
a	Me	Ph	69	190—191	73	110—112	96.22(d)	94.56(d)	82.39(s)	55.97(t)
b	Me	*p*-MeC_6H_4	72	213—216	78	119—121	95.63(d)	94.76(d)	82.62(s)	56.39(t)
c	Ph	Ph	85	185—186	81	190—191	93.86(d)	98.78(d)	83.61(s)	52.94(t)
d	*p*-ClC_6H_4	Ph	82	204—205	79	206—208	94.24(d)	98.27(d)	82.89(s)	52.90(t)
e	Me	cyclohexyl	77	188—191			92.52(d)			
f	Et	Ph	70	169—171			94.42(d)			

more complex heterocycles we investigated the reactions of the azines (**1**) with the saturated nitriles (**2**) in the presence of lithium di-isopropylamide (LDA) (Scheme 1).† Typically, (**1**) (0.01 mol) in diethyl ether or tetrahydrofuran was added to LDA (0.022 mol). After 20 min the mixture was cooled to −78 °C and (**2**) (0.02 mol) was added. The mixture was warmed to room temperature with stirring and then hydrolysed with water. The compounds (**3**), obtained regioselectively and in excellent yields, were extracted with diethyl ether and purified by recrystallization in hexane–chloroform. 3*H*-Pyrazolo[1,5-*a*]pyrimidines (**4**) were obtained by hydrolysis of (**3**) with 2M H_2SO_4 at room temperature, and were purified by recrystallization in hexane. The results of the syntheses are summarized in Table 1.‡



Scheme 1. *Reagents:* i, lithium di-isopropylamide; ii, H_3O^+.

Structures (**3**) and (**4**) were verified by elemental analysis, i.r., ^1H n.m.r. and mass spectroscopy. In addition these compounds displayed characteristic signals in their ^{13}C n.m.r. spectra. The proton-coupled spectrum of (**3**) contains a doublet centred at δ 93—96 p.p.m. and of (**4**) a doublet at δ 94—98, a singlet at δ 82—83, and a triplet at δ 54—56 p.p.m.

Received, 31st December 1981; Com. 1492

References

1 H. Hoberg and J. Barluenga, *Synthesis*, 1970, 142.
2 J. Barluenga, M. Tomás, J. López-Ortiz, and V. Gotor, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1891; J. Barluenga, V. Rubio, and V. Gotor, *J. Org. Chem.*, 1980, **45**, 2592.

---

† Compounds (**1**) and (**2**) do not react in the presence of $AlCl_3$.

‡ When R^1 = Et, the addition through the C(α)–H of the methyl group only is observed.