STUDIES WITH REISSERT COMPOUNDS. PART VI.[1] CHANGE OF PATHWAY OCCASIONED BY PHASE TRANSFER CATALYSIS: SUPPRESSION OF N-ACYL PSEUDO-BASE FORMATION IN FAVOUR OF A REISSERT REACTION

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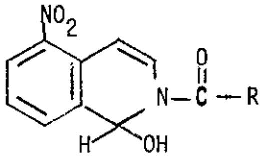
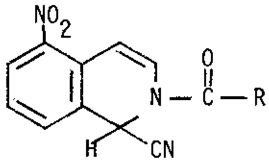
Treatment of phthalazine with p-chlorobenzoyl chloride and potassium cyanide in a two-phase system gives an N-acyl pseudo-base (3, R = 4-ClC_6H_4). Addition of a phase transfer catalyst to the medium changes the reaction pathway to give a Reissert compound (4, R = 4-ClC_6H_4) as major product with only a trace of N-acyl pseudo-base. The same change is observed with 5-nitroisoquinoline and a variety of acid chlorides. Inclusion of a phase transfer catalyst also increases the yields of Reissert compounds in reactions in which N-acyl pseudo-bases are not involved.

We reported earlier[2,3] that an N-acyl pseudo-base of the type (1) is obtained in high yield when 5-nitroisoquinoline is treated with an acid chloride and potassium cyanide in water/methylene chloride, the expected Reissert compound (2) being given in yields of only 5% or less. Similar behaviour, though less marked in some cases, has been reported for analogous isoquinoline,[2,3,4] quinoline,[2,3,5] and 1,3,4-thiadiazole[6] systems, each carrying certain electron-withdrawing features.

In a similar manner we have recently observed that phthalazine with p-chlorobenzoyl chloride and potassium cyanide produces a 55% yield of N-acyl pseudo-base (3, R = 4-ClC_6H_4) and only a trace (<1%) of Reissert compound (4, R = 4-ClC_6H_4). Investigating this reaction further we have examined the effect of adding a phase transfer catalyst[7] to the two-phase system. We found this caused a striking reversal of the previous behaviour. The Reissert compound (4, R = 4-ClC_6H_4) is formed in 72% yield, with less than 1% of N-acyl pseudo-base (3, R = 4-ClC_6H_4).



(1)



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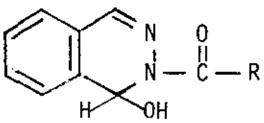

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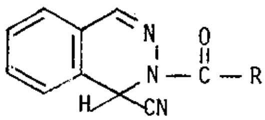

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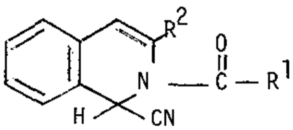

(5)

We have subsequently shown that this change in pathway occurs with 5-nitro-isoquinoline on treatment with a variety of acid chlorides and potassium cyanide in water/methylene chloride containing 1% of benzyltrimethylammonium chloride, $PhCH_2\overset{+}{N}Me_3Cl^-$ with respect to cyanide concentration. N-Acyl pseudo-base formation is completely suppressed and Reissert compound formed. The results are summarised in the Table (entries a - e).

Also included in the Table (entries f - j) is a comparison of cases of normal Reissert compound formation (no pseudo-base involvement) in the absence or presence of the phase transfer catalyst. We have mainly selected cases in which the Reissert reaction proceeds in only low or moderate yield, in the absence of catalyst, such as in the formation of phthalazine Reissert compounds (4) or those prepared from chloroformates (e.g. 5, R^1=OMe, R^2=H). It can be seen that in every case marked improvements in yields are given.

The benzyltrimethylammonium chloride would appear to provide a greatly enhanced selective transport of cyanide ion from the aqueous to the organic medium. This probably results from a favourable soft acid-soft base[8] interaction of the $PhCH_2\overset{+}{N}Me_3$ ion with the ^-CN ion, rather than with the harder ^-OH (or H_2O).

Table N-Acyl pseudo-base and/or Reissert compound formation

	Without $PhCH_2\overset{+}{N}Me_3Cl^-$				With $PhCH_2\overset{+}{N}Me_3Cl^-$	
	N-acyl pseudo-base m.p.	Yield	Reissert compound m.p.	Yield	N-acyl pseudo-base Yield	Reissert compound Yield
a	(3,R=4-ClC_6H_4) 147-148°C(a)	55%	(4,R=4-ClC_6H_4) 201-203°C(a)	<1%	<1%	72%
b	(1,R=4-$MeOC_6H_4$) 167-169°C[3]	70%	(2,R=4-$MeOC_6H_4$) 209-210°C[3]	5%	-	27%
c	(1,R=C_6H_5) 189-190°C[3]	90%	(2,R=C_6H_5) 148-149°C(b)	1%	-	17%
d	(1,R=CH_3) 174-176°C[3]	74%	(2,R=CH_3) 186-187°C[3]	2%	-	24%
e	(1, R=OCH_3) 169-171°C(a)	15%	(2,R=OCH_3) 140-141°C(a)	2%	-	72%

	Without $PhCH_2\overset{+}{N}Me_3Cl^-$			With $PhCH_2\overset{+}{N}Me_3Cl^-$
	Reissert compound	m.p.	Yield	Yield
f	(4,R=4-$CH_3C_6H_4$)	212-213°C(a)	<1%	50%
g	(4,R=CH_3)	167-168 C(a)	22%	54%
h	(5,R^1=OMe, R^2=H)	83-85°C(c)	24%	69%
i	(5,R^1=OMe, R^2=Me)	60-61°C(d)	53%	64%
j	(5,R^1=Ph, R^2=Me)	134-135°C(e)	63%	77%

(a) Satisfactory elemental analyses and spectral data obtained.

(b) lit. m.p. 148°C[9] (c) lit. m.p. 83-85°C[10] (d) lit.m.p. 60-61°C[11]

(e) lit. m.p. 127-128°C[12]

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