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OXIDATION OF SECONDARY AMINES TO α-CYANOAMINES

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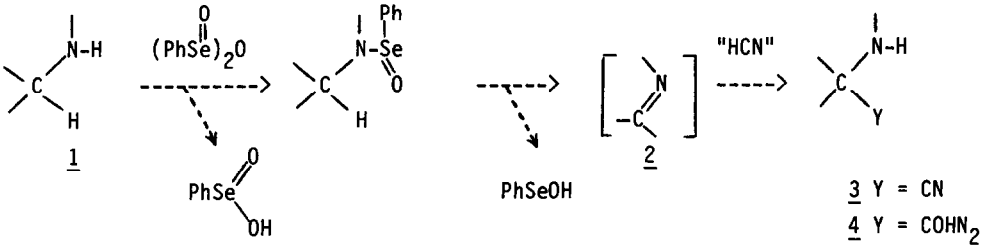
Summary : The dehydrogenation of secondary amines with phenylseleninic anhydride or acid under mild conditions in the presence of either sodium cyanide or trimethylsilylcyanide gives good yields of α-cyanoamines. These compounds[1-3] can be regarded as protected imines, or as a source of α-amino-acids.

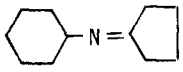
Conversion of secondary amines to the corresponding imines can be achieved by several methods[1a]. The reactivity of phenylseleninic anhydride towards nitrogen containing compounds is now well established[4-8] and is a potentially mild procedure to this end.

In classical methods for the oxidation of secondary amines 1 to imines 2 final yields are often low because the primary product tends to be further oxidised. We thought that trapping of the intermediate imines with hydrogen cyanide or its equivalent could circumvent this limitation by "stabilising" the imine as an α-cyanoamine 3, less oxidizable than the parent amine[1b,2] (Scheme), and hydrolysable to stable amides 4. The trapping of closely related iminium ions derived from tertiary amines with $CN^{\ominus}$ has been shown to be a valuable approach to the preparation of synthetically useful iminium salt equivalents[3].



Scheme

We first showed that imine 5 was quantitatively converted into the corresponding α-cyanoamine 6 at 20°C in THF or EtOAc in the presence of dry NaCN (2.5 eq.) and HOAc (3.5 eq.) or with HOAc as solvent. Compound 6 was characterised by IR, NMR and M.S. spectra, but was unstable towards chromatography.



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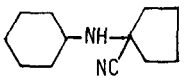


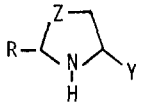
6

$(PhSe)_2$

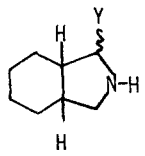
7

PhSeCN

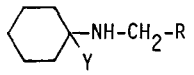
8



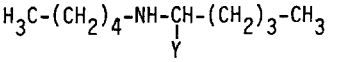
	Y	Z	R
9	H	$-(CH_2)-$	H
10	H	$-(CH_2)_2-$	H
11	H	$-(CH_2)_2-$	CH_3
12	H	$-(CH_2-O-)-$	H
13	H	-(CH=CH)-	H
14	CN	$-(CH_2)-$	H
15	CN	$-(CH_2)_2-$	H
16	CN	$-(CH_2)_2-$	CH_3
17	CN	$-(CH_2-O-)-$	H
18	H	-(CH=CH)-	CN
30	$CONH_2$	$-(CH_2)-$	H
31	$CONH_2$	$-(CH_2)_2-$	H
32	$CONH_2$	$-(CH_2)_2-$	CH_3
33	H	-(CH=CH)-	$CONH_2$



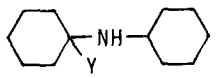
	Y
34	H
35	CN
36	$CONH_2$



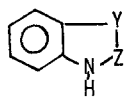
	Y	R
19	H	H
20	CN	H
21	H	CN
22	$COHN_2$	H
23	H	$CONH_2$



	Y
24	H
25	CN
26	$CONH_2$



	Y
27	H
28	CN
29	$CONH_2$



	Y	Z
37	$-(CH_2)-$	$(CH_2)-$
38	CH	CH
39	CSePh	CH

Two methods were used to oxidise secondary amines.- Method I : To the amine (1) (2 mmol) in dry THF (10 ml) under argon at 0°C were added phenylseleninic anhydride (1 mmol), dry sodium cyanide (5 mmol) and acetic acid (7 mmol). After 5 days at 20°C the mixture was made alkaline (diluted with aq. NaOH or $NaHCO_3$) and continuously extracted with CH_2Cl_2 for 18 hrs. Thus was obtained a mixture of α-cyanoamine 3, diphenyldiselenide 7 and phenylselenocyanide 8 (IR 2150 cm^{-1}, MS M^+ 183, m/z 156, 103, 77). The mixture was hydrolyzed (HCl(5N), 100°C, 18 hrs) and the products 7, 8 and the corresponding amide 4 isolated by chromatography on silica gel. Method II : To the amine 1 (2 mmol) in dry CH_2Cl_2 (10 ml) under argon were added at 20°C phenylseleninic anhydride (1 mmol) and trimethylsilylcyanide[9] (3 mmol). After 2 days at room temperature the mixture was treated as in method I giving 3, 7 and 8. The crude mixture was subjected to hydrolysis (sealed tube, HCl 5N, 100°C, 18 hrs) and the products 7, 8 and 4 isolated by chromatography on silica gel. The results are summarised in the Table[10].

Better yields (almost quantitative in α-cyanoamine) were obtained with Method II. In the case of indoline 37 aromatisation does not allow introduction of the cyano group. The formation of 39 has been previously explained[4].

In a large scale experiment piperidine 10 (0.1 M) was oxidised with phenylseleninic acid (0.1 M) in CH_2Cl_2 (250 ml) containing molecular sieves 4Å and trimethylsilylcyanide (0.15 M) at 20°C for 70 hrs. Distillation gave α-cyanoamine 15 (Eb 130°C/25 mm Hg) in good yield (77%).

Control experiments showed that i) PhSeCN does not come from attack on $(PhSe)_2$ by $CN^{\ominus}$, ii) $(PhSe)_2$ obtained at the end of the reaction can be oxidized to water soluble compounds by treatment with H_2O_2 (30%) at -30°C in CH_2Cl_2 for several minutes, iii) the α-cyanoamine and PhSeCN are stable to this treatment.

Although we are sure that Se^{IV} is implicated in the oxidation of the amine, phenylseleninic anhydride is not necessarily the only oxidant. The reaction

Table

Amine	Method	Products (%)	Amide (%, based on Amine)
9	I	14 -	30 (40)
	II	(95)[a]	(50)
10	I	15 -	31 (20)
	II	-	(68)
11	I	16 (32)[b]	32[d]
	II	(95)	
12	II	17 (90)[a]	c
13	I	18 (12)[b]	33[d]
19	I	20	22 (28),
	II	20 + 21	22 (28) + 23 (33)
24	II	25	26 (58)
27	II	28	29 (60)
34	I	35	36 (56)
	II	(95)[a]	
37	I	38 (30)[b]	
		+ 39 (49)[b]	

a) determined by IR with standard solution of pure α-cyanoamine.
b) by chromatography.
c) hydrolysis of α-cyanoamine led to complete decomposition.
d) yield not determined.

of phenylseleninic anhydride with NaCN in THF containing HOAc for 48 hrs gives a mixture which does not contain phenylseleninic anhydride (as judged by I.R.), but is still capable of oxidizing pyrrolidine giving, after a further 48 hrs, the usual results.

References

1. a) J.R. Malpass in "Comprehensive Organic Chemistry", Vol.6, p.45, D.H.R. Barton and W.D. Ollis, Ed. I.O. Sutherland, Pergamon Press, (1979) and references therein; b) ibid., p. 531.
2. D.H.R. Barton, W.B. Motherwell, E.S. Simon and S.Z. Zard, J. Chem. Soc., Chem. Comm., 337 (1984).
3. M. Bonin, J.R. Romero, D.S. Grierson and H.P. Husson, J. Org. Chem., 49, 2392 (1984) and references therein.
4. D.H.R. Barton, X. Lusinchi and P. Milliet, Tetrahedron Lett., 4949 (1982).
5. D.H.R. Barton, D.J. Lester and S.V. Ley, J. Chem. Soc. Perkin I, 1212 (1980).
6. T.G. Back, S. Collins and R.G. Kerr, J. Org. Chem., 46, 1564 (1981).
7. M.R. Czarny, J. Chem. Soc., Chem. Comm., 81 (1976).
8. J.P. Marino and R.D. Larsen Jr., J. Amer. Chem. Soc., 103, 4642 (1981).
9. Trimethylsilylcyanide is conveniently prepared by the method of S. Hunig and G. Wehner, Synthesis, 522 (1979).
10. All new isolable compounds gave satisfactory microanalysis and spectral data (IR, NMR, M.S.).

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