

REACTIONS BETWEEN HYDROXYLAMINES AND AROYL CYANIDES

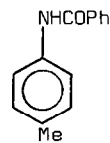
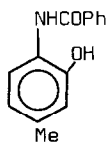
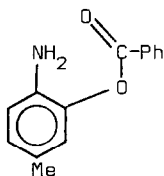
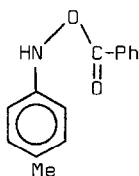
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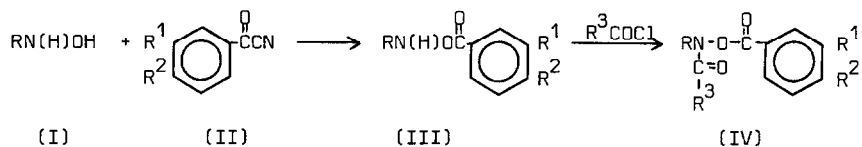
Summary Aromatic hydroxylamines and sterically bulky aliphatic hydroxylamines react with aroyl cyanides to give exclusively the O-acyl derivatives

The construction of phenanthridines and benzo(c)phenanthridines involving photolysis of C,N-diaryl hydroxamic acids was recently reported.¹ It was subsequently found² that suitably substituted C,N-diaryl hydroxamic acids cyclise smoothly in conc sulphuric acid to afford phenanthridones. Benzoyl cyanide is a good acylating agent³ and it was expected that this class of compound can be utilised to prepare sensitive C,N-diaryl hydroxamic acids from aryl hydroxylamines under neutral and mild conditions. Our results (TABLE) show that, in marked contrast to aroyl chlorides, aroyl cyanides react exclusively on the oxygen atom of N-aryl hydroxylamines to give O-acylated products. Thus phenylhydroxylamine with veratroyl cyanide (entry 1) yielded III⁴ (unstable oil⁵, no colour reaction with FeCl₃, i.r. 1730 cm⁻¹) which on acetylation gave the corresponding N-acetyl derivative, identical with the product obtained from N-phenyl aceto-hydroxamic acid and veratroyl chloride⁶

Variation in the electronic character of the substituents in the aroyl cyanide does not have effect in the nature of the product formed. However when the aryl hydroxylamine carried an electron-donating substituent (entry 7) the products obtained were the 2-hydroxy-4-methylbenzanilide (3, 46%), 4,4'-dimethylazoxybenzene (18%) and 4-methylbenzanilide (4, 10%)



TABLE



	I	II		III		IV		
	R	R ¹	R ²	Yield (%)	I.R. (cm ⁻¹)	R ³	M.p. (°C)	I.R. (cm ⁻¹)
1	C ₆ H ₅	CH ₃ O	CH ₃ O	> 90	1730	CH ₃	132-134	1760, 1690
2	C ₆ H ₅	H	H	88	1735	4-NO ₂ -C ₆ H ₅	136-138	1770, 1690
3	C ₆ H ₅	H	CH ₃	83	1735	4-NO ₂ -C ₆ H ₅	123, 5-125, 5	1770, 1695
4	C ₆ H ₅	O-CH ₂ -O		86	1725	CH ₃	97-99	1760, 1695
5	4-Br-C ₆ H ₅	CH ₃ O	CH ₃ O	87	1730	-	-	-
6	4-Br-C ₆ H ₅	H	H	83	1730	4-NO ₂ -C ₆ H ₅	142-144	1770, 1680
7	4-CH ₃ -C ₆ H ₅	H	H	0	-	-	-	-
8	C(CH ₃) ₃	CH ₃ O	CH ₃ O	91	1710	C ₆ H ₅	011	1760, 1670
9	CH(CH ₃) ₂	CH ₃ O	CH ₃ O	87	1710	C ₆ H ₅	011	1770, 1670
10	CH ₃	CH ₃ O	CH ₃ O	0 ⁺	-	-	-	-
11	H	CH ₃ O	CH ₃ O	0 ⁺	-	-	-	-

(+) Corresponding hydroxamic acid obtained (80%).

The production of the phenol 3 (under non acidic conditions) implies the initial formation of the O-benzoyl derivative (1) which either by a 1-aza-1'-oxa [3,3] sigmatropic rearrangement, or, as seems more likely, by heterolytic cleavage⁷ of the N-O bond and subsequent recombination of the ion-pair, gives rise to the o-aminobenzoate (2). O to N migration of the benzoyl group generates (3).

The decomposition of N-aryl hydroxylamines to give azoxybenzenes and anilines is well-known⁸ and the product (4) results from benzoylation of the p-toluidine formed.

Whereas the sterically bulky aliphatic hydroxylamines (entries 8 and 9) afforded exclusively the O-aroylated products,⁹ the other two hydroxylamines (entries 10 and 11) yielded only the corresponding hydroxamic acids by direct N-attack on the aroyl cyanide

When N-methylhydroxylamine was allowed to react with benzoyl cyanide in CDCl_3 at -40°C and the reaction monitored by n.m.r. only the N-CH_3 signal ($\delta 3.41$ s) of the corresponding hydroxamic acid was observed. Thus in the absence of steric congestion about the nitrogen atom of the hydroxylamines, aryl cyanides react directly on the nitrogen to give the N-acylated products¹⁰

Theoretical studies are underway to explain the marked difference in reactivity between aryl cyanides and aryl chlorides towards hydroxylamines, and the differing ambident properties the latter.

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- 1 S Prabhakar, A M Lobo and M R.Tavares, J C.S., Chem.Comm , 1978, 884
- 2 S Prabhakar, A.M Lobo and M.R.Tavares, 2nd Portuguese National Meeting of Chemistry, Comm. 5 E 32, Oporto, 1979
3. M Havel, J.Velek, J.Pospisek and M Soucek, Coll Czech Chem Comm., 44, 2443 (1979)
- 4 Preferential O-acylation of hydroxylamine in aqueous solution occurs with diaceto-hydroxamic acid (92%) and acetylimidazole (86%) (cf. W.P Jencks, J.Am.Chem Soc., 80, 4581 (1958)).
5. Typically a toluene solution of the O-acylated aromatic hydroxylamine showed little decomposition when kept in the ice-chest for a week, but showed extensive decomposition

when kept at room temperature.

6. Confirmation of the structures of O-acylated products was obtained in analogous manner
7. D.Gutschke and A Heesing, Chem.Ber., 106, 2379 (1973).
8. P A,Smith in "Open Chain Nitrogen Compounds", vol 2, p. 4, W A Benjamin, 1966
9. Hydroxylamines I (entries 8 and 9) with acyl chloride gave a mixture of O- and N-acylated products. For example, I (entry 8) when reacted with veratroyl chloride gave rise to the corresponding hydroxamic acid and the O-acylated compound (yields respectively 40% and 60%), whereas I (entry 9) with the same acylating agent gave essentially the hydroxamic acid
10. Benzoyl cyanide has been found to exhibit steric discrimination towards primary, secondary and tertiary alcohols (cf for example ref. 3)

Aroyl cyanides reported in this paper were prepared either from the corresponding cyano-hydrins by oxidation with pyridinium chlorochromate in dichloromethane, or from the corresponding acid chloride with cyanide under phase transfer conditions (K E Koenig and W.P.Weber, Tetrahedron Letters, 2275 (1974)) The former method consists of addition of the appropriate cyanohydrin (5.2 mmole) in dry dichloromethane (10 ml) to a rapidly stirred suspension of pyridinium chlorochromate (7.8 mmole) in dry dichloromethane (10 ml) at room temperature. After 24 hours the mixture is filtered and the solid obtained on evaporation of the solvent crystallised from benzene-n-hexane

Acylation of hydroxylamines was carried out by adding a solution of aroyl cyanide (1.2 eq) to a stirred solution of the hydroxylamine (1 eq) in an aprotic solvent (benzene, toluene or dichloromethane) at room temperature. The presence of NaHCO₃ (1 eq.) was found to offer no special advantage The product obtained was isolated in virtually pure state by evaporating the solvent under reduced pressure

All new compounds were satisfactorily characterised by microanalysis and spectral data (n m r and m s)

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