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A NOVEL VON RICHTER REACTION

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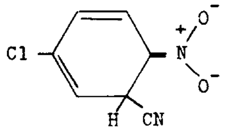
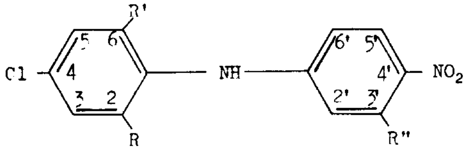
The reaction of p-chloronitrobenzene (I) with potassium cyanide in aqueous alcohol to give m-chlorobenzoic acid as the major product was discovered by von Richter,[1] and studies by Bunnett[2] and others[3-6] have elucidated its mechanism. We now report that when dimethyl sulfoxide (DMSO) is used as solvent, the reaction takes a completely different course, and a novel series of products is formed.

The reaction of I with excess cyanide in DMSO is complete in two hours at 100° (compared with 48 hours for the reaction in refluxing aqueous alcohol[2]) and gives a complex mixture from which we have isolated five crystalline products in a combined yield of 40%.[7] A, B and C are neutral, and D and E are acidic; all appear to be new compounds.

Product A, $C_{13}H_8ClN_3O_2$,[8] m.p. 266°, contains nitrile and conjugated nitro groups. The marked bathochromic shift in alkali, from 379 to 506 mμ, suggested a diphenylamine structure with conjugated electron-withdrawing groups, such as IIIa, and the n.m.r. spectrum was consistent with this. Hydrolysis of the nitrile A gave an acid (IIIb), $C_{13}H_9ClN_2O_4$,[8] identical with the product of an Ullman reaction of 5-chloroanthranilic acid and p-bromonitrobenzene; hence A is 2-cyano-4-chloro-4'-nitrodiphenylamine (IIIa).



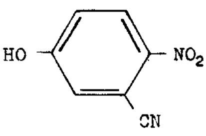


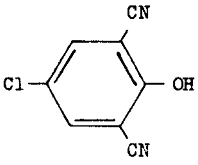
IIIa R = CN, R' = H,R" = H
b R = COOH,R' = H,R" = H
c R = $CONH_2$,R' = H,R" = H
d R = $CONH_2$,R' = $CONH_2$,R" = H
e R = $CONH_2$,R' = H,R" = $CONH_2$

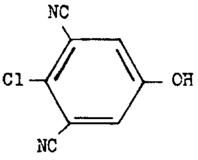
Product B, m.p. 241°, has a very similar U.V. spectrum to A ($\lambda_{max.}$ 385 mμ (pH 7), 500 mμ (pH 13)), and the I.R. spectrum suggested that it contained an amide group in place of a nitrile group. This was confirmed by elementary analysis ($C_{13}H_{10}ClN_3O_3$, i.e. A + H_2O) and hydrolysis to the same acid, IIIb, which had been obtained from A. Hence B is the corresponding amide (IIIc).

Analytical and spectral data showed that C, $C_{14}H_{11}ClN_4O_4$, m.p. 224°, was similar to B, but containing an additional amide group. Examination of the most likely structures, IIId and IIIe, indicates that these would have very different n.m.r. spectra, A_2X_2 with an additional singlet (IIId), and a complex ABC/A'B'X pattern (IIIe). The spectrum of C is complex and definitely rules out structure IIId but appears to be consistent with structure IIIe.

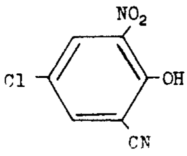
Product D, m.p. 201°, is cyanonitrophenol, $C_7H_4N_2O_3$ (pK_a 6.63). There are ten possible isomers, but only one (IV) is consistent with the n.m.r. spectrum (details of which will be reported elsewhere).


IV


V


VI

Product E, $C_8H_3ClN_2O$,[8] m.p. 193° is also a phenol containing nitrile groups and has a very low pK_a (2.57). The n.m.r. spectrum has but a single peak (1.75), showing that the two aromatic protons are symmetrically placed. There are two possible structures, V and VI. Comparison of the n.m.r. spectrum with that of 2-nitro-4-chloro-6-cyano-phenol (VII) and with the calculated value for VI (Table 1) indicates that E is 2,6-dicyano-4-chlorophenol (V). When the reaction was carried out under strictly anhydrous conditions, D and E were not isolated, and one can conclude that the phenolic oxygen is derived from water and not from the solvent; dimethylsulphide is not produced.


VII

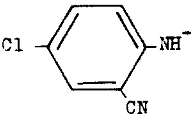

VIII

TABLE 1

^1H n.m.r. Spectra of substituted cyanochlorophenols[9]

Experimental		Calculated
E	VII	VI
1.75	1.63	2.69

To account for the formation of the products, it is suggested that the reaction is initiated by nucleophilic attack of cyanide ion on I to give II, which then undergoes reduction by hydride transfer (from another molecule of II) to give reactive nucleophilic species such as VIII. Condensation with starting-material would yield IIIa. Alternatively, intramolecular transfer of oxygen from the nitro to the adjacent nitrile group[10] and reduction would give a similar intermediate containing the amide function, and hence IIIc. Products IV and V can readily be derived from II; reaction of intermediates with water under the alkaline conditions in dimethyl sulfoxide seems reasonable. The mode of formation of the second amide group in IIIe remains to be elucidated.

It will be of interest to study the scope of the reaction described, its usefulness in preparing novel diphenylamines, and to determine the effect of using other dipolar aprotic solvents.[11]

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4. M. Rosenblum, J. Am. Chem. Soc., 82, 3796 (1960).
5. E.F. Ullman and E.A. Bartkus, Chem. and Ind., 93 (1962).
6. K.M. Ibne-Rasa and E. Koubek, J. Org. Chem., 28, 3240 (1963).
7. Yields of m-chlorobenzoic acid in the normal von Richter reaction are 10-40% depending on the reaction conditions.
8. Satisfactory analytical data were obtained.

9. Values are based on a first-order analysis.

10. Such as has been shown to occur during the catalytic reduction of o-nitrobenzonitrile (H. Musso and H. Schröder, Ber., 98, 1562 (1965)).

11. This work was presented, in part, at the meeting of the Chemical Society in Nottingham, September 1965.