[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF REED COLLEGE AND THE UNIVERSITY OF NORTH CAROLINA]

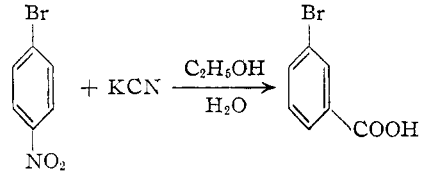
Studies on the Conditions, Scope and Mechanism of the von Richter Reaction[1]

BY J. F. BUNNETT, MICHAEL M. RAUHUT, DAVID KNUTSON AND GEORGE E. BUSSELL

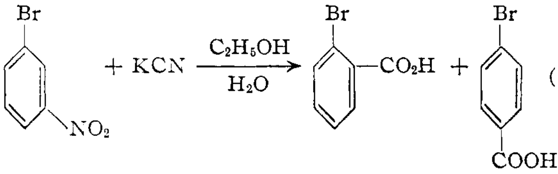
RECEIVED JULY 9, 1954

Experiments with deuterium compounds show that in the reaction of 1-chloro-4-nitrobenzene with ethanolic potassium cyanide to form *m*-chlorobenzoic acid, and in the transformation of nitrobenzene to benzoic acid, hydrogen exchange with the solvent occurs. Efforts to isolate a nitrile intermediate have been unsuccessful, but it is shown that nitriles are hydrolyzed rapidly under the conditions of the reaction. Dibromonitrobenzenes having bromine *ortho* to nitro react poorly, but those with unflanked nitro groups give fair yields. A tarry, amorphous by-product is shown to contain carboxyl groups. Optimum conditions for the reaction have been defined. The mechanism is discussed.

The von Richter reaction is exemplified by the reaction (equation 1) of *p*-bromonitrobenzene with potassium cyanide in aqueous alcoholic medium to form *m*-bromobenzoic acid. *m*-Bromonitrobenzene gives, under the same treatment, a mixture of *o*- and *p*-bromobenzoic acids (equation 2), and *o*-bromonitrobenzene gives a tiny yield of *m*-bromobenzoic acid.[2] This reaction was discovered by von Richter[3] some eighty years ago, but received relatively little attention until Bunnett, Cormack and McKay[4] confirmed many of von Richter's findings and found that the reaction is given by a variety of aromatic nitro compounds.



(1)



(2)

The first part of this paper records experiments which led to an improved technique for conducting the reaction, the second part describes the behavior of several additional nitro compounds with potassium cyanide, and the last part deals with experiments bearing directly on the mechanism.

Development of Improved Conditions.—Table I summarizes a number of experiments in which nitrobenzene or its *p*-chloro or *p*-bromo derivative was allowed to react with potassium cyanide in various solvents under various conditions. The following conclusions can be drawn from the data: (a) aqueous alcoholic solvents are superior to those solvents of other types which were tried; (b) of the alcohols, ethanol is the best[5]; (c) the conversion is higher when a large excess of potassium cyanide is used; and (d) the reaction can be run at the comparatively low temperature of refluxing 48% ethanol. This last fact, which was discovered relatively late in this work, is the key to a satisfactory general procedure for the reaction, a goal which we long sought. Earlier it was evident that larger conversions were obtained with a great excess of cyanide, but attempts to use large amounts of cyanide in 48% ethanol *in sealed tubes* always led to explosive bursting of the tubes. In refluxing 48% ethanol, one can combine the advantages of a favorable solvent influence, of performing the reaction on a large scale, of employing a great excess of cyanide, and of operating, safely and conveniently, in an open apparatus. These, then, are the conditions of choice for the reaction.

We found that addition of sodium nitrite, cuprous oxide or manganese dioxide to the reaction mixture had little effect on the yield of *m*-chlorobenzoic acid from *p*-chloronitrobenzene, but that addition of potassium ferricyanide or sodium sulfite prevented the usual reaction. Ferricyanide inhibited attack on the nitro compound, allowing a large recovery of starting material, but sulfite caused tars to be formed so that only 12% of the *p*-chloronitrobenzene could be recovered.

Descriptive Studies.—The behavior of several additional nitro compounds with potassium cyanide under the conditions of the von Richter reaction is summarized in Table II. Most of these compounds have not been subjected to such treatment before.

In giving a substantial yield of the expected acid product, 1-iodo-4-nitrobenzene resembled its 1,3-isomer[3] and also its chlorine and bromine analogs, all of which give satisfactory von Richter reactions. In surprising contrast, the two fluoronitrobenzenes failed to furnish fluorobenzoic acids. The failure of 1,4-dinitrobenzene to furnish an acid product was less surprising, for Lobry de Bruyn and van Geuns[6] isolated, from the action of potassium cyanide on 1,4-dinitrobenzene in aqueous or alcoholic media, only azo or azoxy compounds resulting from reduction of nitro groups or ethers resulting from the replacement of nitro groups by alkoxide ions. The disinclination of cyanide ions to straightforwardly replace normally replaceable substituents has been noted before.[4,7] It is particularly re-

---

[1] Part of this work was presented at the American Chemical Society Meeting, Chicago, Ill., September, 1953.

[2] Prior to the present study, efforts to isolate an acid product from the action of potassium cyanide on *o*-bromonitrobenzene had been unsuccessful.

[3] V. von Richter, *Ber.*, **4**, 21, 459, 553 (1871); **7**, 1145 (1874); **8**, 1418 (1875).

[4] J. F. Bunnett, J. F. Cormack and F. C. McKay, *J. Org. Chem.*, **15**, 481 (1950).

[5] It is interesting to note that for the related reaction of 1,3-dinitrobenzene with alcoholic potassium cyanide to form 2-alkoxy-6-nitrobenzonitriles, methanol is the favored solvent; *cf.* A. Russell and L. M. Addison, THIS JOURNAL, **65**, 2379 (1943).

[6] C. A. Lobry de Bruyn and J. W. van Geuns, *Rec. trav. chim.*, **23**, 26 (1904).

[7] However, F. M. Beringer, A. Brierley, M. Drexler, E. M. Gindler and C. C. Lumpkin, THIS JOURNAL, **75**, 2708 (1953), have reported that sodium cyanide reacts with 2- or 3-nitrodiphenyliodonium bromide to form, respectively, 2- or 3-nitrobenzonitrile. (They actually isolated the corresponding benzoic acids after hydrolysis of the original products.)

TABLE I

THE YIELD IN VON RICHTER REACTIONS AS AFFECTED BY CHANGES IN EXPERIMENTAL CONDITIONS

Wt. nitro cpd., g.	Wt. KCN, g.	Solvent[a]	Conditions	Conversion,[b] %	Starting material recovd., %
		A. Experiments on *p*-bromonitrobenzene			
4.0	2.6	50% methanol (25 cc.)	Sealed tube, 150°, 1 hr.	12.5	55
4.0	10.4	50% methanol (25 cc.)	Sealed tube, 150°, 1 hr.	21	0
4.0	2.6	48% ethanol (25 cc.)[c]	Sealed tube, 150°, 1 hr.	22	35
4.0	8.1	48% ethanol (34 cc.)	Reflux, 48 hr.	37	0
4.0	2.6	50% 1-propanol (25 cc.)	Sealed tube, 150°, 1 hr.	11	55
4.0	2.6	50% 2-propanol (25 cc.)	Sealed tube, 150°, 1 hr.	10	72
4.0	2.6	50% 1-butanol (25 cc.)	Sealed tube, 150°, 1 hr.	2.5	85
4.0	15.0	95% pinacol (50 g.)	Reflux, 1 hr.	1.5	60
4.0	15.0	90% diethyleneglycol (75 cc.)	Reflux, 2.5 hr.	2.5	0
4.0	15.0	99% 2-methyl-2-hexanol (30 cc.)	Reflux, 2.5 hr.	0	65
4.0	15.0	98% 5-methyl-5-decanol	Reflux, 2.5 hr.	0	70
		B. Experiments on nitrobenzene			
2.5	2.6	75% pyridine (25 cc.)	Sealed tube, 150°, 1 hr.	0	96
2.5	5.0	80% dioxane (25 cc.)	Sealed tube, 160°, 2 hr.	0	88
2.5	5.0	48% ethanol (25 cc.)	Sealed tube, 160°, 1.5 hr.	10	12
		C. Experiments on *p*-chloronitrobenzene			
2.5	5.0	48% ethanol (25 cc.)	Sealed tube, 150°, 50 min.	38	0
3.15	200.0	48% ethanol (600 cc.)	Reflux, 48 hr.	42	0
3.15	10.3	48% ethanol (75 cc.)	Reflux, 18 hr.	20	19
3.15	20.0	95% ethanol (75 cc.)	Reflux, 48 hr.	14	33
3.00	6.45	48% ethanol (26 cc.)	Reflux, 48 hr.	40	0
3.15	20	50% methanol (75 cc.)	Reflux, 48 hr.	20	0
3.15	20	33% methanol (75 cc.)	Reflux, 48 hr.	15	6
3.15	20	50% 2-propanol (75 cc.)	Reflux, 48 hr.	9	47
3.15	10.3	53% ethanol 22% benzene (90 cc.)	Reflux, 20 hr.	0	61
3.15	20	50% acetonitrile (75 cc.)	Reflux, 45 hr.	0	[d]
3.15	2.6	50% glycerol, 25% ethanol (75 cc.)	Sealed tube, 150°, 1 hr.	0	79
3.15	2.6	50% dioxane (75 cc.)	Sealed tube, 150°, 1 hr.	7	56

[a] The rest of the solvent was water; percentages by volume are given. [b] Conversion is the yield without allowing for recovered starting material. [c] This experiment from ref. 4. [d] Not recorded.

markable in the cases of 1-fluoro-4-nitrobenzene and 1,4-dinitrobenzene because in these compounds the fluorine atom and a nitro group, respectively, are normally replaced by nucleophilic reagents with exceptional ease.[8]

The behavior of all six dibromonitrobenzenes was studied in order to gain a better insight into the effect of neighboring substituents on the reaction. As shown in Table II, fair yields (16 and 18%) were obtained from the two dibromonitrobenzenes whose nitro groups were not flanked by any *o*-bromine atoms, small yields (1 to 7%) were obtained from the three isomers having one bromine *ortho* to the nitro group, and the one isomer having bromine atoms in both positions *ortho* to the nitro group was quite unaffected by the reagent. Since the total electronic effect of the bromine atoms on the positions attacked (positions *ortho* to nitro) is of the same general order of magnitude in all six isomers, the results affirm our earlier observation[4] that substituents *ortho* to the nitro group have a most unfavorable effect on the reaction.

It may be noted that von Richter[3] described 1,4-dibromo-2-nitrobenzene as being especially reactive, and as giving a substantial yield (20%) of 2,5-dibromobenzoic acid. Our results do not indicate outstanding reactivity for this compound, nor were we able to reproduce his yield. However, 1,4-dibromo-2-nitrobenzene did give a somewhat better yield than other *o*-bromonitrobenzene derivatives.

The pattern of reactivity of the dibromonitrobenzenes provides support for our view[4] that the carboxyl group always enters *ortho* to the position vacated by the nitro group, and not *para*. Thus, 1,2-dibromo-3-nitrobenzene gave 3,4-dibromobenzoic acid, whereas entry of carboxyl at the free position *para* to nitro would have given 2,3-dibromobenzoic acid. Also, 1,3-dibromo-5-nitrobenzene yielded 2,4-dibromobenzoic acid and not 2,6-dibromobenzoic acid. In experiments with 1,3-dichloro-5-nitrobenzene, the 2,4-dichlorobenzoic acid product was obtained in a high state of purity directly as first isolated; there was no suggestion of contamination by the isomeric 2,6-dichlorobenzoic acid. Nor were 2,6-dichlorobenzamide nor 2,6-dichlorobenzonitrile, which might be expected to be isolable in this instance because of the hydrolysis-hindering effect of two bulky *o*-substituents, discovered amongst the products of reaction. Particularly in the 1,3-dihalo-5-nitrobenzenes, the conditions are favorable for attack

---

[8] (a) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 333 (1951); (b) N. B. Chapman and R. E. Parker, *J. Chem. Soc.*, 3301 (1951).

TABLE II

THE VON RICHTER REACTION ON VARIOUS SUBSTITUTED NITROBENZENES

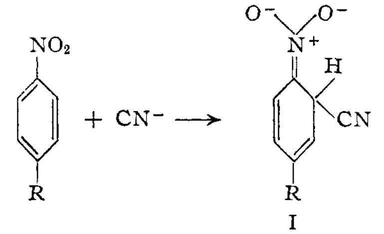
Starting benzene deriv.	Product benzene deriv.	Conditions	Conversion, %	Starting material recovd., %	Tar formation
1-Iodo-4-nitro	1-Iodo-3-carboxy	Sealed tube	40	0	[e]
1,3-Dichloro-5-nitro	1,3-Dichloro-4-carboxy	Sealed tube	30	0	Much
1-Fluoro-3-nitro	No acid	Sealed tube	0	74	None
1-Fluoro-4-nitro	No acid[a]	Sealed tube[b]	0	14	Much
1,4-Dinitro	No acid[a]	Sealed tube	0	6	[e]
1,2-Dibromo-3-nitro	1,2-Dibromo-4-carboxy	Reflux	1	0	Little
1,2-Dibromo-4-nitro	1,2-Dibromo-3-carboxy	Sealed tube	16	0	Much
1,3-Dibromo-2-nitro	No acid	Sealed tube	0	93	None
1,3-Dibromo-4-nitro	1,3-Dibromo-5-carboxy	Reflux	2	0	Little
1,3-Dibromo-5-nitro	1,3-Dibromo-4-carboxy	Sealed tube	18	32	Much
1,4-Dibromo-2-nitro	1,4-Dibromo-2-carboxy[c]	Sealed tube[d]	7	23	Much
1-Bromo-2-nitro	1-Bromo-3-carboxy	Reflux	2	44	Little

[a] *p*-Nitrophenetole was obtained in 5% yield. [b] A run at reflux produced much acidic tar but no fluorobenzoic acids. [c] In this case the structure of the product does not reveal the occurrence of cine-substitution. [d] Similar results were obtained in a run at reflux. [e] Not recorded.

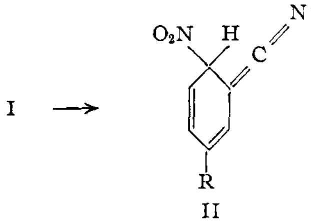
of the cyanide *para* to the nitro group if such attack can occur. Though it may be too early to conclude that a von Richter reaction involving *para* attack can never occur, it is clear that the structure of every product so far obtained is consistent with the hypothesis of exclusive *ortho* attack, and that products of *para* attack have not been formed under conditions apparently favorable to such a reaction.

Concerning a Nitrile Intermediate for the Reaction.—Neither we nor von Richter have ever isolated a nitrile as a product from a von Richter reaction, though both he and we have supposed nitriles to be intermediates. In a determined attempt to isolate *m*-chlorobenzonitrile from the action of potassium cyanide on *p*-chloronitrobenzene, we prepared a number of sealed tubes containing identical charges of ingredients. Each of these was placed in the hot furnace (150°) and after a measured time quickly removed and thrust into a tub of cold water. From these runs, only unreacted *p*-chloronitrobenzene and/or the usual product, *m*-chlorobenzoic acid, were isolated, and each was obtained directly (by steam distillation) in a state of high purity. Since the tube which had been heated 20 minutes furnished 64% of unreacted nitro compound and only 4% of acid product, while that which had been heated 35 minutes gave 35% of acid with no recovery of starting material, hydrolysis of the supposed intermediate must be very rapid indeed.

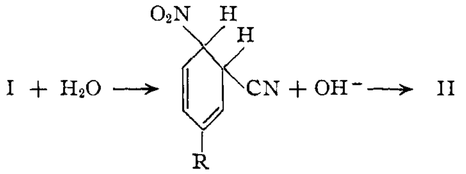
To test this conclusion, *m*-chlorobenzonitrile (0.0058 mole) was added to a typical von Richter reaction mixture containing 0.0108 mole of *p*-chloronitrobenzene. The sealed tube was heated 38 minutes at 150°. No starting materials were recovered, and 0.0079 mole of *m*-chlorobenzoic acid was obtained; this is equivalent to a quantitative hydrolysis of the nitrile plus 19% yield from *p*-chloronitrobenzene. It is thus clear that nitriles are rapidly hydrolyzed under the conditions of the von Richter reaction, and therefore it is reasonable to consider them as intermediates even though they have not been isolated from the reaction mixtures.



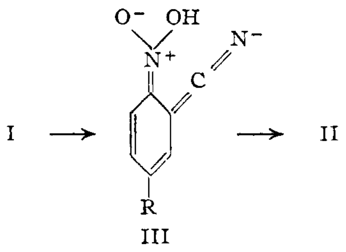
(3)



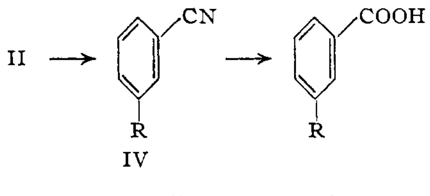
(4a)



(4b)



(4c)



(5)

Experiments with Deuterium-containing Materials.—One of the steps in the mechanism envisaged by Bunnett, Cormack and McKay was the direct migration (equation 4a) of a hydrogen atom from the carbon atom in I bearing the cyano group to the carbon atom bearing the nitro group, forming II. This mechanism would predict that if the reaction were run in a solvent of D_2O and C_2H_5OD, the acid product would be deuterium-free (after equilibration of the carboxyl hydrogen atoms with ordinary water). Several reactions[9] have been shown, by such experiments, to involve direct transfer of hydrogen from one carbon atom to another without involvement of hydrogen atoms from a hydroxylic solvent.

We submitted ordinary nitrobenzene to the von Richter reaction in a solvent of D_2O and C_2H_5OD. The benzoic acid produced contained, after equilibration of its carboxyl hydrogen atoms with ordinary water, 0.72 deuterium atoms per molecule. Recovered nitrobenzene was nearly deuterium-free (0.02D). Thus, hydrogen atoms from the solvent do become attached to aromatic carbon during the von Richter reaction. Step 4a in the mechanism of Bunnett, Cormack and McKay is therefore untenable unless hydrogen exchange with the solvent occurs either before or after the transformation of I to II.

As a further check on this same point, we submitted 1-chloro-4-nitrobenzene, deuterium-labeled in the 3- and 5-positions, to the action of potassium cyanide in aqueous alcohol of common isotopic composition. This experiment was run independently in both the Reed and North Carolina laboratories. The first step in preparing deuterium-labeled 1-chloro-4-nitrobenzene was, in both laboratories, the acid-catalyzed exchange of hydrogen isotopes between *p*-chloroaniline and heavy water. Under the conditions we employed, exchange is known[10] to occur only in positions *ortho* and *para* to the amino group. Since the *para* position was blocked by chlorine, deuterium was introduced only at the positions *ortho* to the amino group, that is, at positions to be *ortho* to the nitro group in the final product. At Reed, the deuterated *p*-chloroaniline was oxidized by persulfate to *p*-chloronitrosobenzene and thence by peracetic acid to *p*-chloronitrobenzene. At North Carolina, the deuterium-labeled *p*-chloroaniline was diazotized and the diazo group replaced by nitro by means of sodium cobaltinitrite. In Table III, the action of potassium cyanide on the two samples of deuterated 1-chloro-4-nitrobenzene is summarized.

TABLE III

THE VON RICHTER REACTION ON 1-CHLORO-4-NITROBENZENE DEUTERIUM-LABELED IN THE 3- AND 5-POSITIONS

Laboratory	Deuterium count, atoms/molecule in Starting material	Product[a]	Recovd. starting material
Reed	1.02	0.42	
N. C.	0.99	.38	0.95

[a] Carboxyl hydrogen in the product, *m*-chlorobenzoic acid, was fully equilibrated with ordinary water before analysis.

In these experiments, too, there was extensive exchange of hydrogen isotopes with the solvent during the von Richter reaction. The conclusion of the earlier experiment is upheld.[11]

Experiments with Nitrosobenzene.—The fact that aromatic nitroso compounds undergo the Piria reaction,[12] to which the von Richter reaction might seem to be related, suggested these experiments. The action of potassium cyanide on nitrosobenzene in 48% ethanol under our usual sealed tube conditions furnished no benzoic acid, but there was a small yield of azobenzene. In 75% dioxane, there was again no formation of benzoic acid, but azoxybenzene was formed in small amount. Since nitrobenzene does form benzoic acid under the conditions of the run in ethanol, nitrosobenzene is shown not to be an intermediate in the von Richter reaction.

Amorphous By-products.—It should be noted (Table I) that yields of acids in von Richter reactions have not exceeded 50%, even when the starting nitro compound has been completely consumed. Most of the rest of the starting material can be accounted for in amorphous by-products which inevitably form during successful reactions (see also Table II). The most common type of by-product appears regularly upon acidification of the filtered, water-diluted reaction mixture. It melts in hot water, and solidifies on cooling. All attempts to isolate pure compounds from it have failed.

The amorphous by-product formed during the reaction of 1-chloro-4-nitrobenzene with a large excess of cyanide in refluxing 50% ethanol was examined with some care. It was separated into hot-water-soluble, water-insoluble-but-ethanol-soluble and water-and-ethanol-insoluble fractions. These fractions were, respectively, tan, light brown and dark brown in color.

All three fractions were acidic, as shown by their solubility in dilute alkali. They could be titrated potentiometrically with dilute sodium hydroxide. The titration curves did not break sharply, but by scrutiny of them it was possible to locate end-points. Two titrations on the water-insoluble-but-alcohol-soluble fraction gave neutral equivalents of 232 and 236. The infrared spectrum of this same fraction showed only one well-defined absorption band, at 6.00 μ. This is evidently the carbonyl band of a carboxyl group; the same band at the same wave length was found in the infrared spectrum of *m*-chlorobenzoic acid. Thus we conclude that the amorphous material contains carboxyl groups.

A preliminary quantitative analysis has shown the presence of substantial percentages of chlorine and nitrogen in this fraction.

On the basis of the above evidence and other experience, we are led to believe that the amorphous by-products are mixtures, that they are probably polymeric in nature, that their carboxyl groups originated in the cyanide reagent, and that neither the introduction of the carboxyl groups nor the formation of linkages between monomer units has

---

[9] W. von E. Doering, T. I. Taylor and E. F. Schoenewaldt, THIS JOURNAL, **70**, 455 (1948); H. Fredenhagen and K. F. Bonhoeffer, *Z. physik. Chem.*, **A181**, 379 (1938).

[10] A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 28 (1938); 239 (1946).

[11] It is surprising that the *m*-chlorobenzoic acid product had *less than half* the deuterium content of the 1-chloro-4-nitrobenzene. A full explanation of this is not obvious.

[12] W. M. Lauer, M. M. Sprung and C. M. Langkammerer, THIS JOURNAL, **58**, 225 (1936); see also reference 8a, p. 398.

involved extensive loss of either chlorine or nitrogen from the starting *p*-chloronitrobenzene. The evidence now available does not, however, allow any detailed conclusions about the structure of these by-products to be drawn.

Discussion.—Bunnett, Cormack and McKay[4] proposed a mechanism for the von Richter reaction which involved these steps: attack of cyanide ion on the nitro compound to form intermediate ion I (equation 3), transformation of this into intermediate II, expulsion of nitrite ion from II to form nitrile IV, and hydrolysis of IV to the acid which is isolated (equation 5). Except for their conception of the means of transformation of I into II, all their views find additional confirmation in the present experiments, as we have in some cases already remarked. We shall therefore confine our attention to the mechanism of transformation of I into II.

Bunnett, Cormack and McKay proposed a direct migration of a hydrogen atom from one carbon to another (equation 4a); as we have seen, our experiments with deuterated compounds vitiate this transformation unless it is preceded or followed by hydrogen exchange with the solvent. Another possibility, briefly mentioned by Bunnett and Zahler,[13] is an addition–elimination sequence (equation 4b). In his discussion of the von Richter reaction, Ingold[14] advocated mechanism 4b, which he characterized as "Michael-like," as more plausible than the "Cannizzaro-like" mechanism 4a. A third possibility (mechanism 4c) is that hydrogen might be removed from the position occupied by the cyano group before it becomes attached to the position occupied by the nitro group. The intermediate IV which we have pictured would, of course, be in mobile equilibrium with other species differing only in the number of protons on oxygen atoms.

We have remarked that mechanism 4a is tenable only if the direct hydrogen migration is preceded or followed by hydrogen exchange with the solvent. Such exchange would necessarily require abstraction of a proton either from the cyano position in I or from the nitro position in II, followed by return of a proton from the medium. In either of these exchanges, an intermediate of type III would be involved. Thus mechanism 4a must now be regarded as a particularly complicated version of mechanism 4c, and as such mechanism 4a is logically unattractive.

We conclude, then, that the transformation of I into II goes either by the proton-abstraction-and-return mechanism 4c, or by the Michael-like addition–elimination mechanism 4b. It is interesting to note that, in endorsing mechanism 4b, we are essentially returning to the mechanism first proposed by von Richter 79 years ago.

Bunnett and Zahler[13] observed that the von Richter reaction bears a formal resemblance to a number of other aromatic nucleophilic substitution reactions in which the entering group takes a position other than that vacated by the displaced group. They dubbed all reactions of this type "cine-substitutions." One of the other cine-substitutions, the substitution with rearrangement that occurs when aryl halides react with sodamide in liquid ammonia, has been examined recently in regard to its mechanism by Roberts and coworkers.[15] These authors proposed a mechanism involving an extraordinary "benzyne" intermediate. There is no reason to consider such a mechanism for the von Richter reaction. On the other hand, it is not clear that our mechanism 4b or 4c has application to other cine-substitutions.

The comparatively low yields in von Richter reactions are a consequence of the operation of several competing reactions: (a) hydrolysis or alcoholysis of cyanide ions; (b) reduction of nitro compounds by the alkaline alcoholic medium or by cyanide ions; and (c) formation of amorphous, acidic by-products. Competing reaction (a) is serious when a relatively low ratio of cyanide to nitro compound is used, and causes unreacted nitro compound to be isolable at the end of the reaction. Reaction (b) probably operates in ethanol solutions of low water content. Under such conditions, the von Richter reaction gives a small yield of acid in a messy reaction mixture (Table I). Blom[16] has shown that the reduction of nitro compounds by alcoholic alkali is favored by a low concentration of water in the medium.

Competing reaction (c) appears to be intimately related to the von Richter reaction. It forms an acidic, though amorphous, product, and the most reasonable source for the carboxyl groups in this product is the cyanide reagent. Thus both reaction (c) and the von Richter reaction involve attack of cyanide ions upon the nitro compound. Indeed, it is not unlikely that the two reactions share one or more initial steps in common, and that somewhere along the reaction path there is a fork, one branch of the path leading to well-defined acids and the other to amorphous by-products. In accord with this view is the close parallel between production of well-defined acids and production of tars in the reactions of dibromonitrobenzenes with potassium cyanide (Table II).

Lacking a detailed understanding of the structure of the amorphous by-products and of the mechanism of their formation, we are unable to understand the factors that determine the fraction of the presumed common intermediate which may proceed to well-defined acid products, and the fraction which is diverted to by-products. We can predict, however, that some of these factors are constitutional, and are fixed once a particular nitro compound has been chosen for the reaction. Other influences may relate to reaction conditions such as temperature, solvent, etc. It is possible that changes in reaction conditions may increase the proportion of formation of well-defined acids, and thus improve the yields.

Experimental

Preparation of Materials.—Nitrosobenzene, 2-methyl-2-hexanol, pinacol, *p*-dinitrobenzene and *p*-chloro-, *p*-bromo-, *p*-iodo-, *p*-fluoro- and *o*-bromonitrobenzene were prepared

---

(13) Reference 8a, p. 390.

(14) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 812.

(15) J. D. Roberts, H. E. Simmons, L. A. Carlsmith and C. W. Vaughan, THIS JOURNAL, **75**, 3290 (1953).

(16) A. V. Blom, *Helv. Chim. Acta*, **4**, 297 (1921).

by standard methods or were commercial products repurified. A sample of *m*-fluoronitrobenzene was donated by Dr. Arthur Roe, to whom we are sincerely grateful.

m-**Chlorobenzonitrile**, m.p. 39–41° (lit.[17] 40.5°), was prepared by the method of Clarke and Read.[18] **5-Methyl-5-decanol**, b.p. 108–112° (17 mm.), n^{22}D 1.4360 (lit.[19] b.p. 106–107° (15 mm.), n^{20}D 1.4369), was made by a Grignard procedure. **1,3-Dichloro-5-nitrobenzene**, m.p. 63.8–64.2°, was prepared by the method of Kremer and Bendich,[20] who reported m.p. 65.4°. **1,2-Dibromo-3-nitrobenzene**, m.p. 85° (lit.[21] 84°), was prepared by the method of Holleman[21] except that the diazotization of 2-bromo-6-nitroaniline was performed according to Hodgson and Walker's technique.[22] **1,2-Dibromo-4-nitrobenzene**, m.p. 56–58° (lit.[23] 58.6°), was made by bromination of 1-bromo-4-nitrobenzene according to the procedure of Derbyshire and Waters.[24]

1,3-Dibromo-2-nitrobenzene.—2,6-Dibromoaniline[25] was diazotized in 9.5 *M* hydrochloric acid with precautions to keep the temperature below 0°. The diazonium cobaltinitrite was prepared and decomposed as described by Hodgson and Marsden.[26] There resulted 1,3-dibromo-2-nitrobenzene, m.p. 81–83° (lit.[27] 83°), in 22% yield based on 2,6-dibromoaniline.

1,3-Dibromo-4-nitrobenzene.—*m*-Bromoacetanilide was nitrated according to Case and Sloviter,[28] and the mixture of products deacetylated by acid hydrolysis. The crude mixture of 3-bromo-4-nitroaniline and 3-bromo-6-nitroaniline was diazotized[22] and the diazonium salts were treated with cuprous bromide. The resulting 1,3-dibromo-4-nitrobenzene (both bromonitroanilines furnish the same dibromonitrobenzene) was recrystallized from ethanol; m.p. 59–61° (lit.[27] 62°).

1,3-Dibromo-5-nitrobenzene, m.p. 105–106°, was synthesized essentially according to the method of Shepherd,[29] who reported m.p. 106°.

1,4-Dibromo-2-nitrobenzene, m.p. 81–83° (lit.[30] 84°), was made by nitration of *p*-dibromobenzene; the mixed m.p. with *p*-dibromobenzene (m.p. 87°) was strongly depressed.

Deuterium-labeled 1-Chloro-4-nitrobenzene.—Ten grams of deuterium oxide (99.5% D_2O, Stuart Oxygen Co.) and 12.8 g. of *p*-chloroaniline hydrochloride were sealed in a tube and heated at 120° for 112 hours (at Reed), or at 150° for 24 hours (at North Carolina).

At Reed, a solution of Caro's acid was prepared by adding 43 cc. of cold concentrated sulfuric acid to 50 g. of potassium persulfate, allowing the mixture to stand in an ice-bath with occasional stirring for one hour, pouring the mixture onto 300 g. of crushed ice, and neutralizing with a saturated solution of sodium carbonate. The sealed tube containing the deuterated *p*-chloroaniline hydrochloride was opened, the contents were neutralized with 6 *M* sodium hydroxide, and about 40 cc. of dioxane[31] were added to make the mixture homogeneous. This solution was added slowly with stirring to the solution of Caro's acid. The nitroso compound separated in light yellow flocs which were collected by filtration. After 90 minutes the additional crop of nitroso compound which had separated from the filtrate was collected by filtration. The two crops were combined in 200 cc. of glacial acetic acid, to which were added 200 cc. of 30% hydrogen peroxide, 200 cc. of glacial acetic acid and 13 cc. of nitric acid (sp. gr. 1.42). The resulting green solution was heated on the steam-bath until it turned orange (45 min.) and then poured into 1500 cc. of water. The nitro compound separated as cream-colored flocs which were recrystallized from ethanol; 6.2 g. (39%), m.p. 74–78°, were obtained. For deuterium analysis, part of this was further recrystallized to m.p. 81.5–82.5°.

At North Carolina, the contents of the sealed tube containing deuterated *p*-chloroaniline hydrochloride were combined with dilute hydrochloric acid and diazotization was performed in the usual way. The diazonium cobaltinitrite was formed and decomposed as described by Hodgson and Marsden,[26] and the resulting nitro compound was purified by steam distillation and crystallization from ethanol; 2.6 g. (21%), m.p. 83–84°, were obtained.

Ethanol-O-*d*.—Ethyl borate[32] (10.8 g., 0.074 mole) and deuterium oxide (5.0 g., 0.25 mole) were combined in the distillation flask of an all-glass distillation apparatus. After hydrolysis of the ester had been allowed to proceed overnight, the deuterated ethanol (doubtless accompanied by some heavy water) was distilled away from the residue of boric acid. The distillate was stored in sealed ampoules; it was not analyzed.

von Richter Reactions.—The experiments summarized in Table I were carried out essentially according to the "standard procedure" of Bunnett, Cormack and McKay. The sealed tube reactions of Table II were performed the same way, using two moles of cyanide per mole of nitro compound, 48% ethanol (usually about 50 cc.) as the solvent, and a reaction time of one hour at 150°. In the reflux reactions of Table II, 20 g. of potassium cyanide and 4.0 g. of the dibromonitrobenzene were combined in 100 cc. of 48% ethanol and the mixture was refluxed 48 hours. The dibromobenzoic acids were found to have such low volatility that separation of them from the tars by steam distillation was not practical. The following procedure, reminiscent of that of von Richter, was used to isolate the pure dibromobenzoic acids: The reaction mixture was diluted to 300 cc. with water and filtered to remove unreacted starting material and neutral amorphous by-products. Unreacted starting material was recovered by crystallization of the filter cake from ethanol, in which the neutral amorphous by-products are insoluble. The filtrate was heated to boiling, acidified, digested 15 minutes on the steam-bath, reheated to boiling and filtered. Tarry acidic by-products were often separated by this process; the dibromobenzoic acids were soluble in the volume of hot water used. The filtrate was made alkaline with sodium carbonate, evaporated to 50 cc., acidified almost to the point of precipitation and treated repeatedly with decolorizing charcoal until the color had changed to yellow (from dark red). The solution was then acidified, cooled and filtered. The filter cake was dissolved in dilute ammonium carbonate solution, and the solution was treated with decolorizing charcoal, acidified, cooled and filtered. This last cycle was repeated several times until a white acid was obtained.

In the following list, we give detailed information about the products of the reactions of Table II, and confirmation of the structures assigned to them.

m-**Iodobenzoic acid** (from 1-iodo-4-nitrobenzene): m.p. 182–183° (lit.[33] 186.7°).

2,4-Dichlorobenzoic acid (from 1,3-dichloro-5-nitrobenzene): m.p. 158.5–159.5°; mixed m.p. with authentic 2,4-dichlorobenzoic acid of m.p. 159.5–160° (Matheson Co. product once more recrystallized), 158.5–159.5°.

p-**Nitrophenetole** (from 1-fluoro-4-nitrobenzene): m.p. 57–59°; mixed m.p. with authentic *p*-nitrophenetole (Eastman Kodak) was not depressed. A liquid recovered from the product mixture was identified as unreacted 1-fluoro-4-nitrobenzene by reduction and benzoylation to form *p*-fluorobenzanilide, m.p. 182–184° (lit.[34] 184°).

p-**Nitrophenetole** (from 1,4-dinitrobenzene): m.p. 55–58°; mixed m.p. with authentic sample not depressed.

3,4-Dibromobenzoic acid (from 1,2-dibromo-3-nitrobenzene): m.p. 225–227° (lit.[35] 232°); the amide, prepared by conventional means, had m.p. 149–151° (lit.[36] 151.5°).

2,3-Dibromobenzoic acid (from 1,2-dibromo-4-nitrobenzene): m.p. 144–148° (lit.[37] 149–150°); the acid chloride,

---

[17] A. Korczynski and B. Fandrich, *Compt. rend.*, **183**, 422 (1926).

[18] H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 514.

[19] F. C. Whitmore and F. E. Williams, THIS JOURNAL, **55**, 408 (1933).

[20] C. B. Kremer and A. Bendich, *ibid.*, **61**, 2658 (1939).

[21] A. F. Holleman, *Rec. trav. chim.*, **27**, 156 (1908).

[22] H. H. Hodgson and J. Walker, *J. Chem. Soc.*, 1620 (1933).

[23] W. Koerner, *Gazz. chim. ital.*, **4**, 370 (1874).

[24] D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, 573 (1950).

[25] M. K. Seikel, *Org. Syntheses*, **24**, 47 (1944).

[26] H. H. Hodgson and E. Marsden, *J. Chem. Soc.*, 22 (1944).

[27] A. F. Holleman, *Rec. trav. chim.*, **25**, 197 (1906).

[28] F. H. Case and H. A. Sloviter, THIS JOURNAL, **59**, 2382 (1937).

[29] R. G. Shepherd, *J. Org. Chem.*, **12**, 281 (1947).

[30] J. Booy and J. W. Dienske, *Rec. trav. chim.*, **45**, 450 (1926).

[31] *Cf.* J. McIntyre and J. C. E. Simpson, *J. Chem. Soc.*, 2606 (1952).

[32] J. J. Etridge and S. Sugden, *ibid.*, 989 (1928).

[33] H. P. Klug, E. Mack and F. C. Blake, THIS JOURNAL, **51**, 2881 (1929).

[34] G. Schiemann and R. Pillarsky, *Ber.*, **62**, 3041 (1929).

[35] A. K. Miller, *J. Chem. Soc.*, **61**, 1033 (1892).

[36] H. Hübner and J. W. Raveill, *Ann.*, **222**, 187 (1884).

[37] J. B. Cohen and I. H. Zortmann, *J. Chem. Soc.*, **89**, 47 (1906).

prepared by conventional means and recrystallized from petroleum ether, had m.p. 60–62° (lit.[37] 60–62°).

3,5-Dibromobenzoic acid (from 1,3-dibromo-4-nitrobenzene): m.p. 219–220° (lit.[38] 219–220°); the amide, prepared by conventional means, had m.p. 184–186° (lit.[39] 187°).

2,4-Dibromobenzoic acid (from 1,3-dibromo-5-nitrobenzene): m.p. 163–167° (lit.[37] 168–169°); the amide, prepared by conventional means, had m.p. 195–196° (lit.[39] 195°).

2,5-Dibromobenzoic acid (from 1,4-dibromo-2-nitrobenzene): m.p. 151–153° (lit.[40] 157°); the mixed m.p. with an authentic sample (from permanganate oxidation of Eastman Kodak 2,5-dibromotoluene) of m.p. 156° was 152–155°.

***m*-Bromobenzoic acid** (from 1-bromo-2-nitrobenzene): m.p. 151–153°; mixed m.p. with an authentic sample (Eastman Kodak) was 152–155°.

Products from Reactions of Nitrosobenzene.—The reaction of nitrosobenzene with 2.6 g. of potassium cyanide in 25 cc. of 48% ethanol for one hour at 155° furnished a small crop of red needles which, after crystallization from ethanol, weighed 0.3 g. and had m.p. 65–66°. These were recognized as azobenzene (m.p. 68°) by reduction (tin and hydrochloric acid) to benzidine (m.p. 117–120°) which did not depress the mixed m.p. with an authentic sample.

The run in 75% dioxane yielded a yellowish neutral material of m.p. 29–31°; the mixed m.p. with an authentic sample of azoxybenzene (m.p. 31.5–32.2°) was 30–31.5°.

Experiments with Deuterium-labeled Compounds.—A tube was charged with 5.0 g. of nitrobenzene, 5.0 g. of anhydrous potassium cyanide, 5 cc. of the ethanol-O-*d* preparation described above, and 5 cc. of heavy water. It was sealed, heated one hour at 150–160°, and cooled. By our usual procedure, about 3 g. of nitrobenzene were recovered, and 0.380 g. of benzoic acid was obtained. After crystallization from common distilled water, and then sublimation, the acid showed m.p. 120.5–121°. It was quantitatively diluted with repurified reagent grade benzoic acid, and the mixture was sublimed to give the analytical sample.

At Reed, a tube containing 2.2 g. of deuterium-labeled 1-chloro-4-nitrobenzene, 5 g. of potassium cyanide and 30 cc. of 48% ethanol was sealed and heated at 160–170° for 75 minutes. The tube exploded as it was being opened, but a good deal of the product could be isolated from the lower part of the tube which did not shatter. The *m*-chlorobenzoic acid product, m.p. 151–152°, was isolated in the usual way and purified by crystallization from water. It was quantitatively diluted with repurified Eastman Kodak *m*-chlorobenzoic acid, and the mixture was recrystallized from water to give the analytical sample. At North Carolina, essentially the same procedure was followed except that a lower ratio of cyanide to nitro compound was employed.

The deuterium analyses were done in the Division of Steroid Biochemistry, Sloan-Kettering Institute for Cancer Research, by Josephine Leong under the supervision of Dr. David K. Fukushima and Dr. Thomas F. Gallagher.

Acknowledgments.—We thank the Research Corporation for support of this research during its early stages, and the Office of Ordnance Research, U. S. Army, for financial assistance more recently. We are also grateful to Dr. David K. Fukushima for his interest and advice.

CHAPEL HILL, N. C.

---

(38) M. T. Bogert and W. F. Hand, THIS JOURNAL, **25**, 942 (1903).

(39) J. J. Sudborough, *J. Chem. Soc.*, **67**, 594 (1895).

(40) S. A. Koopal, *Rec. trav. chim.*, **34**, 148 (1915).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

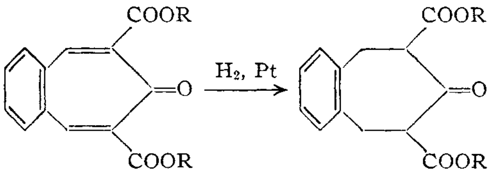
A Rearrangement Involving Aromatization. The Condensation of Δ^4-Tetrahydrophthalaldehyde with Diethyl Acetonedicarboxylate[1]

BY D. S. TARBELL AND BERNARD WARGOTZ[2]

RECEIVED JUNE 2, 1954

The condensation of Δ^4-tetrahydrophthalaldehyde with diethyl acetonedicarboxylate in the presence of piperidine acetate yields, by a rearrangement involving aromatization, 5,8-dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (IX). The structure of this product has been established by converting it to the following compounds, which have been synthesized: the lactone of 2-hydroxy-1-naphthaleneacetic acid (XIII), 2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester and 5,6,7,8-tetrahydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester. The ultraviolet and infrared spectra of the compounds are in agreement with the assigned structures, and the mechanism of the aromatization is discussed. An improved procedure for preparing Δ^4-tetrahydrophthalaldehyde is described, which involves the lithium aluminum hydride reduction of N,N,N′,N′-tetramethyltetrahydrophthalamide. It is found that a basic ion-exchange resin is a good catalyst for the condensation of phthalaldehyde and diethyl acetonedicarboxylate.

The condensation of phthalaldehyde with diethyl acetonedicarboxylate leads to the dicarbethoxybenzocycloheptadieneone[3] I, and a similar reaction between phthalaldehyde and hydroxy- or methoxyacetone yields β,γ-benzotropolone[4] or its methyl ether.[5] The use of Δ^4-tetrahydrophthalaldehyde in similar condensation reactions might be expected to lead to compounds offering interesting possibilities for further synthetic operations in the tropolone and colchicine fields. The present paper reports a study of the condensation product from tetrahydrophthalaldehyde and diethyl acetonedicarboxylate; it is shown that the product does not contain a seven-membered ring, as expected, but is actually a dihydronaphthalene derivative. The condensation reaction therefore involves a molecular rearrangement with the formation of a benzenoid instead of a seven-membered ring.



I VII

The preparation of Δ^4-tetrahydrophthalaldehyde by addition of butadiene to maleic or fumaric dialdehyde was described previously.[6] A more convenient method has been found to be the lithium

---

[1] This research was aided by a grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] Abbott Laboratories Fellow, 1953–1954.

[3] J. Thiele and J. Schneider, *Ann.*, **369**, 287 (1909).

[4] D. S. Tarbell, G. P. Scott and A. D. Kemp, THIS JOURNAL, **72**, 379 (1950).

[5] (a) D. S. Tarbell and J. C. Bill, *ibid.*, **74**, 1234 (1952); (b) G. A. Nicholls and D. S. Tarbell, *ibid.*, **74**, 4935 (1952).

[6] D. L. Hufford, D. S. Tarbell and T. R. Koszalka, *ibid.*, **74**, 3014 (1952).