Exchange of Nitrile and Carboxyl Groups in Aromatic Compounds

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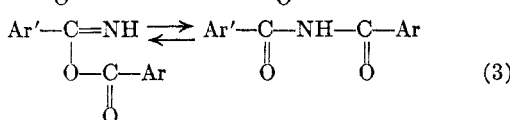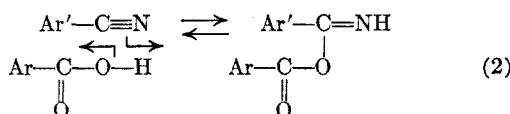
A method has been found to exchange quantitatively carboxylic acid and nitrile functions in aromatic compounds. The method involves heating a higher boiling nitrile with a lower boiling acid to form an equilibrium mixture containing the lower boiling nitrile and higher boiling acid. The equilibrium is displaced by distilling out the lower boiling nitrile. A mechanism of the exchange involving the isoimide intermediate is proposed. The general preparative value of the reaction and its application to the synthesis of iso- and terephthalic acids from the corresponding tolunitriles and xylenes are discussed.

The reactions between nitriles and carboxylic acids have been known for some time.[1-6] Our work has shown that the reaction between aromatic nitriles and aromatic acids can be carried out to give nearly quantitative yields of the exchange products (Equation 1).

$$ArCO_2H + Ar'CN \longrightarrow ArCN + Ar'CO_2H \quad (1)$$

We believe that the reaction of carboxyl and nitrile groups proceeds via Equations 2 and 3. In Equation 2

$$
\begin{array}{cc}
Ar'{-}C{\equiv}N & Ar'{-}C{=}NH \\
\rightleftarrows & \\
Ar{-}C{-}O{-}H & Ar{-}C{-}O \\
\parallel & \parallel \\
O & O
\end{array}
\quad (2)
$$

$$
\begin{array}{cc}
Ar'{-}C{=}NH & Ar'{-}C{-}NH{-}C{-}Ar \\
\rightleftarrows & \\
O{-}C{-}Ar & O \quad\quad O \\
\parallel & \\
O &
\end{array}
\quad (3)
$$

the acidic proton becomes attached to the cyanide nitrogen and, more or less simultaneously, the carboxylate oxygen forms a bond with the cyanide carbon. The isoimide intermediate then rearranges via Equation 3 to the dicarboximide. The mechanism proposed here is similar to that proposed by Davidson and Skovronek[7] for the reaction between anhydrides and amides. Their work indicates that the isoimide is, indeed, in equilibrium with dicarboximide, nitrile, carboxylic acid, and amide and anhydride. We did not examine our reaction mixtures for amide and anhydride, but we have no reason to doubt their presence. Other workers have also demonstrated that dicarboximide is in equilibrium with nitrile and carboxylic acid.[5] However, these authors do not mention the isoimide as an intermediate.

The work described in References 5 and 7 and our own work appear to be explained best by the mechanism above including the isoimide intermediate. The fact that electron-withdrawing groups accelerate the forward reaction[5] can be explained by this mechanism since withdrawing electrons increases the acidity of the acid, which, in turn, would facilitate protonation of the cyanide nitrogen. A striking example of the effect of a strong electron-withdrawing group is that trichloroacetic acid and its nitrile form the dicarboxamide quantitatively; i.e., the equilibrium is shifted in favor of the dicarboxamide to a much greater extent in this case.

The reverse of Equations 2 and 3 does not show the exchange of nitrile and acid functions. However, when the original aromatic groups are different, the equilibrium mixture will, of course, contain both types of nitriles and acids, three types of dicarboxamides, and four types of isoimides, as well as amides and anhydrides. The actual distribution of components in equilibrium will depend upon the substituents on the aromatic groups. In our experiments, we used a simple device to avoid the tedious separation of such a mixture. The method depends upon the fact that nitriles invariably have lower boiling points than the corresponding acids. Thus, by starting with a high boiling nitrile and an acid, we can separate by distilling directly from the reaction vessel the lowest boiling component of the mixture; i.e., the lower boiling nitrile. This route does more than simplify the preparation. The selective removal of the lowest boiling component shifts the equilibria in its favor and results in a nearly quantitative conversion to the new nitrile and new acid in a very short time. This has been done for various pairs of aromatic acids and nitriles in which the aromatic group was phenyl, tolyl, methoxyphenyl, chlorophenyl, cyanophenyl, and carboxyphenyl (Table I).

The reaction works well with equivalent quantities of acid and nitrile. However, when the lower boiling nitrile is the desired product, it is convenient to use an excess of higher boiling nitrile. A variation involves the use of a dinitrile as the source of nitrogen. This often results in an easy separation by virtue of large boiling point differences. A simple distillation column suffices for this purpose.

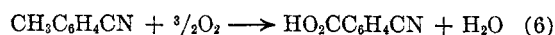The rates and energies of activation for these

(1) A. Gautier, Compt. rend., 67, 1255 (1868); Ann., 150, 187 (1869).

(2) C. E. Colby and F. O. Dodge, Am. Chem. J., 13, 1 (1891).

(3) E. H. Miller, J. Am. Chem. Soc., 16, 433 (1894).

(4) J. A. Mathews, J. Am. Chem. Soc., 20, 648 (1898).

(5) R. H. Wiley and W. B. Guerrant, J. Am. Chem. Soc., 71, 981 (1949).

(6) The Distillers Co. Ltd., British Patent 722,843, February 2, 1955.

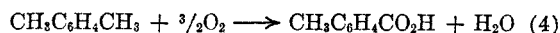(7) D. Davidson and H. Skovronek, J. Am. Chem. Soc., 80, 376 (1958).

TABLE I

Examples of Nitrile Formation by Exchange

Reactants		Reaction Temp., °C.	Time, Hr.	Overhead Distillation Temp., °C.	Yield of[a] New Nitrile, % of Theory	Physical Constants of Crude Product
Acid, moles	Nitrile, moles					
Benzoic, 0.1	Isophthalo-, 0.2	237–287	3	190–194[b]	100	...
p-Toluic, 0.74	p-Carboxybenzo-, 0.68	230–242	3	210–216[c]	93	Neutral
Benzoic, 1.0	p-Chlorobenzo-, 0.4	240	1.5	191–195[b]	89	$n_D^{20} = 1.5298^f$
p-Chlorobenzoic, 0.5	Isophthalo-, 1.0	259–294	0.7	220–223[d]	93	m.p. 88–91°[g]
Anisic, 0.5	Isophthalo-, 1.0	283–297	1.0	261–264[e]	95	Neutral, m.p. 53–60°[h]

[a] These yields do not include product which remained in the reaction vessel, column, and head. [b-h] Literature values for constants: [b] 190.7°, [c] 217°, [d] 223°, [e] 257°, [f] 1.5289, [g] 92°, [h] 62°.

equilibria have not been measured. We do know, however, from the literature and our own work that the reaction proceeds slowly at 150–175°, but rapidly at 200° and above. Under the latter conditions, the rate of formation of new products is usually limited by the rate of removal of the product, rather than by the rate of reaching equilibrium.

This interchange has been employed in a novel route to phthalic acids from xylenes.[8] In the oxidation of the xylenes to the phthalic acids, the toluic acids are intermediates. However, the toluic acids are oxidized more slowly to the phthalic acids than are toluic acid derivatives such as esters, anhydrides,[9,10] and nitriles. With the aid of the nitrile exchange reaction, tolunitrile is an excellent substitute for toluic acid. The tolunitrile is obtained in a cyclic process by nitrile-carboxyl exchange between the toluic acid and the tolunitrile oxidation product, cyanobenzoic acid. In this manner, xylene is oxidized to phthalic acid via tolunitrile with essentially complete conservation of nitrile groups. Equations 4–6 show the reactions involved:

(8) W. G. Toland, California Research Corp., U. S. Patent **2,795,599**, June 11, 1957.

(9) I. E. Levine, California Research Corp., U. S. Patent **2,653,165**, September 22, 1953.

(10) Imhausen and Co., British Patent **727,989**, April 13, 1955.

$$CH_3C_6H_4CH_3 + {}^3/_2O_2 \longrightarrow CH_3C_6H_4CO_2H + H_2O \quad (4)$$

$$CH_3C_6H_4CO_2H + NCC_6H_4CO_2H \longrightarrow$$
$$CH_3C_6H_4CN + HO_2CC_6H_4CO_2H \quad (5)$$

$$CH_3C_6H_4CN + {}^3/_2O_2 \longrightarrow HO_2CC_6H_4CN + H_2O \quad (6)$$

EXPERIMENTAL

A typical example of the nitrile exchange reaction is described below. The equipment and procedures are identical for all the examples listed in Table I. The reaction vessel is a 500-ml. round bottomed flask equipped with a thermowell for temperature readings and a standard taper joint for a column connection. The flask is heated with a Glas-Col mantle. The column is a 20-cm. length of 12-mm. glass tubing heated externally with Nichrome wire and packed with one-fourth inch glass helices. Above the column is a simple distillation head provided with a water condenser and a stopcock for control of reflux ratio.

p-Chlorobenzonitrile. A mixture of 128 g. (1 mole) of isophthalonitrile and 78.2 g. (0.5 mole) of p-chlorobenzoic acid was heated in the flask. As the flask temperature reached 259°, distillation began at 220° overhead. The pot temperature rose from 259° to 294° over a period of 40 min., while 64 g. of distillate was collected from 220° to 223°. The melting point of the crude product is 88° to 91°. Literature values for p-chlorobenzonitrile are: m.p. 92°, b.p. 223°. The yield of p-chlorobenzonitrile is 93%, but it should be noted that additional nitrile was present in the flask, column, and head.

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