The Formation of Formic Anhydride with N, N′-Dicyclohexylcarbodiimide

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It has been reported that various acid anhydrides can be obtained from acids by treatment with *N, N′*-dicyclohexylcarbodiimide (DCC)[1-3] under mild conditions. This suggests the possibility of a successful dehydration of formic acid to yield formic anhydride, when DCC is used as a dehydrating reagent in an inert solvent at low temperature. Formic anhydride is unstable and has not yet been prepared by the usual method. In the present investigation, the dehydration reaction of formic acid with DCC was studied in order to ascertain the formation of formic anhydride.

When formic acid was treated with DCC in ether at room temperature, the evolution of a gas took place rapidly and the precipitate of *N, N′*-dicyclohexylurea was formed in a good yield (Eqs. 1 and 2). When the reaction was carried out below -5°C in the molar ratio according to Eq. 1, no evolution of gas was observed, but the urea was formed in nearly the theoretical yield. Therefore, it was suspected that formic anhydride was formed without decomposition by this reaction.

$$2\ \mathrm{HCOOH} + \mathrm{C_6H_{11}{-}N{=}C{=}N{-}C_6H_{11}} \rightarrow$$

$$\mathrm{HCO{-}O{-}COH} + \mathrm{C_6H_{11}{-}NHCONH{-}C_6H_{11}} \quad (1)$$

$$\mathrm{HCO{-}O{-}COH} \rightarrow \mathrm{HCOOH} + \mathrm{CO} \quad (2)$$

To confirm the existence of formic anhydride, a part of the solvent was removed from the filtrate under reduced pressure, and the remaining liquid was added into a solution of L-leucine in formic acid or of *p*-nitrophenol in ether; *N*-formyl-L-leucine and *p*-nitrophenyl formate respectively were obtained in good yields. On the other hand, the reactions of formic acid and L-leucine or *p*-nitrophenol in the absence of DCC did not give the formyl compounds. It was concluded from these results that formic anhydride can be obtained from formic acid with DCC at a low temperature, though it has not yet been isolated.

Experimental

***N*-Formyl-L-leucine.**—Into 3.8 ml. (100 mmol.) of formic acid dissolved in 20 ml. of ether, 10.3 g. (50 mmol.) of DCC in 38 ml. of ether was added with stirring in such a way that the temperature did not exceed -5°C. After the stirring had been continued for 3 hr., *N, N′*-dicyclohexylurea (10.57 g., 94%) was filtered off. Most of the ether in the filtrate was removed at water-pump pressure. During these procedures the temperature of the mixture was held below -5°C. The residual liquid was added into a solution of 1.31 g. (10 mmol.) of L-leucine in 3 ml. of formic acid. After it had been stirred for 2.5 hr. at 0°C, the mixture was concentrated under reduced pressure. The oily residue was recrystallized from ethyl acetate. Yield, 1.27 g. (80%). M. p. 138∼139°C. It was identified by comparison with *N*-formyl-L-leucine[4] [m. p. 139∼141°C, $[\alpha]_D^{20}$ -17.7° (*c* 4.97, ethanol)], which was obtained with formic acetic anhydride. When 1.31 g. of L-leucine was treated with 8 ml. of formic acid in the same manner without DCC, no formyl compound was yielded.

***p*-Nitrophenyl Formate.**—Nineteen grams (0.41 mol.) of formic acid was treated with 41.2 g. (0.2 mol.) of DCC in 300 ml. of ether as above. *N, N′*-Dicyclohexylurea (43.1 g., 0.192 mol.) was filtered off, and the filtrate was concentrated in an ice-salt bath under reduced pressure to a volume of 170 ml. The resulting solution was added to 9.73 g. (70 mmol.) of *p*-nitrophenol in 20 ml. of ether. Stirring was continued for 2.5 hr. at -10∼0°C. After it had stood overnight at room temperature, the mixture was concentrated under reduced pressure to a syrup. Recrystallization of the residue from tetrahydrofuran gave 6.99 g. (41.8 mmol., 60%) of *p*-nitrophenyl formate; m. p. 73∼74°C[5]; IR spectrum (in carbon tetrachloride): 1750, 1200, 1090 cm^{-1} (ester). The same run in the absence of DCC did not give the formate, but the *p*-nitrophenol was recovered.

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