[Contribution from the Department of Chemistry, Duke University]

DEHYDRATION OR BECKMANN REARRANGEMENT OF ALDOXIMES WITH BORON FLUORIDE. CONVERSION OF ALDOXIMES TO CORRESPONDING AMIDES[1]

DAVID S. HOFFENBERG[2] and CHARLES R. HAUSER

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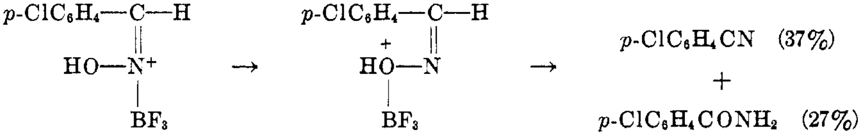
In the preceding investigation (1) it was shown that *syn-p*-chlorobenzaldoxime is converted by boron fluoride at room temperatures to the N-coordination complex of the *anti*-aldoxime (I) which was observed to be stable even at 135°.

In the present investigation, it was found that, although relatively stable, complex I undergoes dehydration or Beckmann rearrangement at 150° or at 115–120° in acetic acid solution. It was shown in a previous paper (2) that the Beckmann rearrangement of the boron fluoride N-coordination complex of benzophenone oxime similarly requires high temperatures.

The thermal decomposition of the solid complex I will first be considered. On heating to 150°, this complex melted and underwent a vigorous exothermic reaction to form mainly *p*-chlorobenzonitrile (37%) and *p*-chlorobenzamide (27%). These products were evidently formed from I by dehydration and the Beckmann 1,2-shift of hydrogen respectively. The corresponding O-coordination complex (II) is assumed to be the reactive intermediate; such an intermediate has been postulated in the Beckmann rearrangement of the N-coordination complex of benzophenone oxime (2). It is possible that the amide arose through the nitrile (see below); if so, only an apparent Beckmann rearrangement occurred.



I II

The thermal decomposition of complex I also produced a little (6%) *p*-chloroformanilide. This product must have arisen from the Beckmann rearrangement of the N-coordination complex of the *syn*-aldoxime (III), a little of which would be in equilibrium with complex I; presumably the corresponding O-coordination

III IV

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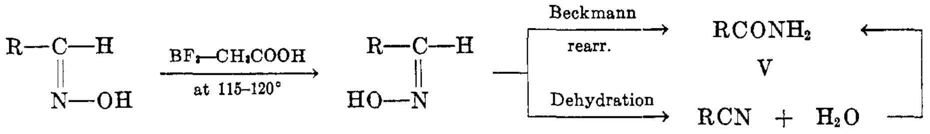
[2] Allied Chemical and Dye Corporation Fellow, 1954–1955.

complex (IV) is the reactive intermediate. Apparently the equilibrium between the N-coordination complexes I and III is not quite so far on the side of I at 150° as at 25° at which temperature the *anti*-aldoxime is obtained almost exclusively with sodium bicarbonate (1).

Whereas the thermal decomposition of the solid complex I produced three products, the reaction of *syn*- or *anti*-*p*-chlorobenzaldoxime with boron fluoride in acetic acid at 115–120°, which would undoubtedly involve the intermediate formation of complex I, yielded exclusively *p*-chlorobenzamide (95–99%). Actually a commercial[3] boron fluoride-acetic acid complex, consisting of one molecule of boron fluoride and two of acetic acid, was employed. The formation of the *p*-chlorobenzamide from the anti-aldoxime may be accounted for by the Beckmann 1,2-shift of hydrogen. The amide may arise from the *syn*-aldoxime in the same manner after preliminary isomerization to the *anti*-isomer. However, the amide might also be formed through *trans* dehydration of the *anti*-aldoxime, followed by addition of the by-product water to the resulting nitrile. It is shown in another paper (3) that the nitrile is indeed converted to the amide in equally good yield under similar conditions. These two possible courses of reaction are represented below employing general formulas, the amide obtained being designated V.



Although the Beckmann rearrangement might appear more likely, the dehydration course of reaction evidently occurs to some extent. Thus, some of the nitrile (5%) was isolated along with the amide (17%) from the reaction mixture of *syn*-*p*-chlorobenzaldoxime and the reagent on stopping the reaction before completion. A blank experiment indicated that the yield of the nitrile from the aldoxime should have been approximately equal to that of the amide if the dehydration course of reaction occurred exclusively. The fact that less nitrile than amide was isolated might be ascribed either to some Beckmann rearrangement or merely to the greater difficulty of isolation of nitrile in the experiment with the aldoxime than in the blank (see experimental).

Similarly the reactions of certain other *syn*-aromatic aldoximes and of heptaldoxime with boron fluoride-acetic acid reagent produced amides of type V in good to excellent yields (Table I). At least one of these reactions, that of *p*-dimethylaminobenzaldoxime to form *p*-dimethylaminobenzamide (VI), appears to be of preparative value. The over-all yield of this amide from commercial *p*-dimethylaminobenzaldehyde was 90% or better. The amide has previously been prepared from the corresponding acid chloride but no yield was reported (4). The acid was prepared recently in 44% yield by the Cannizzaro reaction in the presence of alkali and silver (5), and in 87% yield by the reductive

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[3] Available from the General Chemical Division, Allied Chemical and Dye Corporation.

TABLE I

CONVERSION OF ALDOXIMES TO AMIDES WITH BORON FLUORIDE-ACETIC ACID COMPLEX[a]

Aldoxime[a]	Amide	Yield, %	M.P.,[b] °C.	Lit. M.P., °C.
Benz-	Benz-	98	124–127	128
p-Chlorobenz-	*p*-Chlorobenz-	95 (98)[c]	177–178	179
p-Dimethylaminobenz-	*p*-Dimethylaminobenz-	95	207–208	206
m-Nitrobenz-	*m*-Nitrobenz-	98	139–140	142
Salicyl-	Salicyl-	47	138–139	140
Anis-	Anis-	70	152–154	156–158
Hept-	Hept-	74 (85)[d]	92–94	96
Piperon-		Tar		

[a] Except where noted the aldoxime obtained directly from the aldehyde and hydroxylamine was employed; in the aromatic series, it would have the *syn* configuration. [b] The products on which the yields are based melted at these temperatures. [c] Obtained from the *anti*-aldoxime. [d] This product melted at 82–86°. A 92% yield of the amide was obtained recently with polyphosphoric acid (ref. 8), but the melting point on which this yield was based was only 78–81°.

methylation of *p*-aminobenzoic acid (6). The acid has also been obtained from *p*-dimethylaminobenzaldoxime by dehydration followed by hydrolysis of the resulting nitrile (7).

$$p\text{-}(CH_3)_2NC_6H_4CHO \xrightarrow{H_2NOH} p\text{-}(CH_3)_2NC_6H_4CH{=}NOH \xrightarrow[CH_3COOH]{BF_3} \underset{\text{VI}}{p\text{-}(CH_3)_2NC_6H_4CONH_2}$$

It should be mentioned that polyphosphoric acid has previously been shown (8) to effect the conversion of benzaldoxime and of heptaldoxime to the corresponding amides but the yield was equal to that obtained with boron fluoride only with the latter aldoxime. It is possible that nitriles are intermediates also when polyphosphoric acid is employed since this reagent was shown recently (9) to effect the conversion of nitriles to amides. It has long been known (8, 10) that the usual Beckmann rearrangement reagents, such as phosphorus pentachloride, dehydrate aldoximes to form nitriles.

EXPERIMENTAL[4]

Thermal decomposition of boron fluoride complex of p-chlorobenzaldoxime (I). The solid complex I (10 g.) prepared from *syn*- or *anti-p*-chlorobenzaldoxime as described in the preceding paper (1), was placed in a flask which was immersed in an oil-bath. On heating the oil-bath to 150°, the complex melted and underwent a vigorous exothermic reaction evolving a gas. The temperature inside the molten reaction mixture rose to 210°. After cooling, the mixture was steam-distilled, yielding 2.37 g. (37%) of *p*-chlorobenzonitrile, which solidified in the condenser. This product melted at 93–94°; lit. m.p. 93–94° (11). The residue from the steam-distillation, which contained 100–300 ml. of water, was allowed to

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[4] Melting points are uncorrected.

cool to room temperature, and then chilled in an ice-bath. The resulting white needles were separated from some tarry material and were recrystallized from water to give 1.2 g. (20%) of *p*-chlorobenzamide, m.p. 177–179°; lit. m.p. 179° (12).

In another experiment employing 10 g. of complex I, the *p*-chlorobenzonitrile (37%) was removed by steam-distillation and the residue was made strongly basic with 100 ml. of 20% sodium hydroxide. After refluxing 12 hours (ammonia evolved), the resulting alkaline mixture was steam-distilled until 750 ml. of distillate had been collected. Extraction of the distillate with ether, and evaporation of the solvent yielded 0.4 g. (6%) of *p*-chloroaniline, m.p. 69–71°, which was derived from the hydrolysis of *p*-chloroformanilide. Recrystallization of the *p*-chloroaniline from water produced white prisms m.p. 71°; lit. m.p. 70° (13). Acidification of the residue from the second steam-distillation with 12 *M* hydrochloric acid precipitated 2.0 g. (27%) of *p*-chlorobenzoic acid, m.p. 242–243°; lit. m.p. 242–243° (12). This acid was derived from hydrolysis of the *p*-chlorobenzamide.

In a third experiment employing 3 g. of complex I, the *p*-chlorobenzonitrile was removed by steam-distillation and the residue was refluxed with alkali. Benzoyl chloride then was added, and the resulting mixture was shaken until the odor of the acid chloride was no longer detected. There was isolated 0.31 g. (6%) of *p*-chlorobenzanilide, m.p. 186–188°. Recrystallization from 95% ethanol gave white needles, m.p. 192°; lit. m.p. 192° (13). This product resulted from the benzoylation of the *p*-chloroaniline which was produced by the hydrolysis of *p*-chloroformanilide.

The *p*-chlorobenzamide was shown not to have resulted from the hydrolysis of *p*-chlorobenzonitrile by carrying out two appropriate blank experiments. In one blank, the nitrile was steam-distilled in the presence of 45% fluoboric acid solution, and in the other, the nitrile was converted to its boron fluoride coordination complex (precipitated from benzene) and the complex then was hydrolyzed. In both blanks the original nitrile was recovered in 90–95% yield.

Conversion of aldoximes to amides with boron fluoride-acetic acid complex. The aldoxime (2–3 g.) was dissolved in 20 g. of commercial[3] boron fluoride-acetic acid complex. The solution was heated at 115–120° for 10 minutes, cooled with stirring (mechanical stirrer) in an ice-bath, and made basic with 100 ml. of 6 *N* sodium hydroxide (added over a 20–30 minute period). The resulting mixture was extracted three times with 100-ml. portions of a mixture of equal volumes of ether and ethyl acetate. The extracts were combined, refluxed with Norit if colored, and dried over Drierite. The solvents were removed leaving the amide. The yields and melting points are given in Table I. If the melting points were low, the amides were recrystallized from appropriate solvents.

In the experiment with *p*-dimethylaminobenzaldoxime, the mixture obtained when the solution was made basic with sodium hydroxide was filtered, and the solid was recrystallized from water to give the amide (VI). A sample of this amide was hydrolyzed with 20% sulfuric acid to form *p*-dimethylaminobenzoic acid, m.p. 238°; lit. m.p. 237–238° (6).

Isolation of intermediate nitrile. To 20 g. of boron fluoride-acetic acid complex, which had been preheated to 115–120°, was added 3 g. of *syn*-*p*-chlorobenzaldoxime and, after swirling for 10–15 seconds, the solution was poured rapidly (10 seconds) into 100 ml. of 6 *N* sodium hydroxide containing crushed ice. The precipitate was taken up in a mixture of ether and ethyl acetate, and after drying, the solvents were removed. The residue was steam-distilled, and the solid which came over in the distillate was purified by sublimation to give 0.15 g. (5%) of *p*-chlorobenzonitrile, m.p. 90–92°. This melting point was not depressed on admixture with an authentic sample of the nitrile. The residue from the distillate yielded, on cooling, 0.55 g. (17%) of *p*-chlorobenzamide, m.p. 178–179°, which was not depressed on admixture with an authentic sample of the amide.

In a blank experiment, 3 g. of *p*-chlorobenzonitrile and an equimolar quantity of water was added to 20 g. of the boron fluoride-acetic acid complex under similar conditions. There was isolated 1.5 g. (50%) of unreacted *p*-chlorobenzonitrile, m.p. 90–92°, and 1.6 g. (47%) of *p*-chlorobenzamide, m.p. 178–179°.

SUMMARY

1. Boron fluoride in acetic acid was found to convert *syn*-aldoximes through the *anti*-isomers to the corresponding amides. The formation of these products might involve either the Beckmann 1,2-shift of hydrogen or dehydration followed by addition of the byproduct water to the resulting nitrile. Evidence was obtained that at least some of the amide arose in the latter manner.

2. The solid boron fluoride N-coordination complex of *anti*-*p*-chlorobenzaldoxime was found to decompose at 150° to form mainly *p*-chlorobenzonitrile and *p*-chlorobenzamide.

3. The conversion of *syn*-*p*-dimethylaminobenzaldoxime to *p*-dimethylaminobenzamide by boron fluoride appears to be of preparative value.

DURHAM, NORTH CAROLINA

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