[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

β-ELIMINATIONS OF *syn*- AND *anti*-PIPERONALDOXIME ACETATES WITH POTASSIUM AMIDE IN LIQUID AMMONIA[1]

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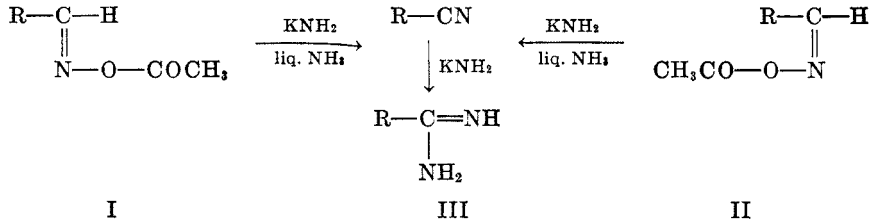
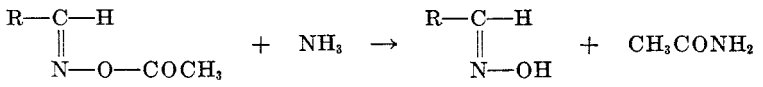
It has previously been shown (1, 2) that *syn*- and *anti*-aldoxime acetates, I and II respectively, undergo with slightly more than one equivalent of potassium amide during ten minutes both β-elimination to form the nitrile and ammonolysis to give the corresponding aldoxime. For example, *syn*- and *anti*-piperonaldoxime acetates (I and II, R = 3, 4-methylenedioxyphenyl) produced the nitrile in yields of 48% and 71% respectively, and the corresponding aldoxime, in yields of 44% and 4% respectively. The higher yield of nitrile from the *anti* acetate is in line with the well known fact that *trans* β-eliminations occur more readily than *cis* β-eliminations; these two types of β-elimination are represented below. The slight excess of the reagent, relatively short reaction time, and inverse addition were employed to minimize the further conversion of the nitrile to the amidine (III).



I III II

It has now been found that, on increasing the excess of the potassium amide to 2.5 equivalents but keeping the reaction time the same (ten minutes), both the *syn*- and *anti*-aldoxime acetates underwent relatively more β-elimination (80–83%). Furthermore, on also increasing the reaction period to one hour, the two acetates exhibited exclusively *cis* and *trans* β-eliminations (90% and 96% respectively). However, much of the nitrile was obtained as the amidine (III).

The exclusive formation of the nitrile and amidine under the last conditions suggest that at least part of the aldoxime obtained under the milder conditions arose from ammonolysis of unreacted acetate by the ammonia after the excess potassium amide was neutralized with ammonium chloride. In agreement with this, both the *syn*- and *anti*-aldoxime acetates were found to undergo ammonolysis in the absence of the potassium amide under otherwise similar conditions to form the corresponding aldoxime and acetamide. The ammonolysis of the *syn*-acetate may be represented by the equation,



[1] Supported by the Duke University research council.

Although exclusive β-elimination was realized with 2.5 equivalents of potassium amide in one hour, the *syn-* and *anti*-piperonaldoxime acetates yielded with sodium amide under similar conditions some of the corresponding aldoxime, 24% and 13% respectively, in addition to the nitrile, 63% and 81% respectively.

It should be pointed out that the β-eliminations of aldoxime acetates with alkali amides are not entirely unique for esters since even certain ordinary esters undergo such a reaction. For example, β-phenylethyl acetate is converted by excess potassium amide in liquid ammonia to styrene (3). It is possible that, as in the latter reaction (3), an α-hydrogen of the acyl portion of the aldoxime acetate is first ionized by the amide ion to form the ester anion which then undergoes β-elimination with excess of the amide ion. However, this is probably not required with the aldoxime acetates, since even the O-methyl ethers of *syn-* and *anti*-benzaldoximes undergo β-elimination under similar conditions (1).

EXPERIMENTAL

anti-Piperonaldoxime acetate with excess potassium amide. To a stirred suspension of 2.0 g. (0.0097 mole) of *anti*-piperonaldoxime acetate (m.p. 84–85°) in 350 ml. of anhydrous ether (cooled to −35°) was added (inverse addition) 2.5 equivalents (0.0287 mole) of potassium amide in liquid ammonia. After stirring one hour, 1.45 g. (0.03 mole) of solid ammonium chloride was added and the reaction mixture then was evaporated to dryness (40–60 minutes). The residue was stirred with water and ether, and the aqueous and ethereal layers were separated. The ether layer, after extraction with 2 *M* sodium hydroxide, was dried over magnesium sulfate and the ether was evaporated to give 0.63 g. (47%) of 3,4-methylenedioxybenzonitrile, m.p. 89–91°; reported m.p. 93–94° (1). Saturation of the alkaline extracts with gaseous carbon dioxide precipitated no oxime. The original aqueous solution, after filtering, was diluted with water to 500 ml. in a volumetric flask. A 50-ml. aliquot then was treated with 3 ml. of glacial acetic acid followed by 50 ml. of a saturated aqueous picric acid solution. The resulting yellow precipitate was collected on a funnel and sucked dry yielding 0.14 g. of the corresponding amidine picrate, m.p. 255–256° dec., equivalent to a 49% yield of amidine. The total yield of elimination products (nitrile plus amidine) was 96%.

An analytical sample of the amidine picrate melted at 257–258° dec.

Anal.[2] Calc'd for $C_{14}H_{11}N_5O_9$: N, 17.81. Found: N, 17.88.

When the reaction was repeated, and the ammonium chloride added after only 10 minutes, there were obtained 21% of the nitrile, m.p. 89–91° and 62% of the amidine picrate, m.p. 256° dec. The total yield of elimination products was 83%. There was also isolated, on saturating the alkaline extracts with gaseous carbon dioxide, 0.23 g. (16%) of *anti*-piperonaldoxime, m.p. 141–142°; reported m.p. 146° (1).

When a blank experiment was carried out with the *anti*-aldoxime acetate in the absence of potassium amide, and the ammonium chloride was added after 10 minutes, there was obtained on working up the reaction mixture (40–60 minutes) an 85% yield of the *anti*-aldoxime, m.p. 143–145°. This melting point was not depressed on admixture with an authentic sample of the *anti*-acetate.

syn-Piperonaldoxime acetate with excess potassium amide. The reaction of this *syn*-acetate (m.p. 105°) was carried out essentially as described above for the *anti* isomer.

When the reaction time was one hour there was obtained 18% of the nitrile, m.p. 88–91°, and 72% of the amidine picrate, m.p. 255–257° dec. No aldoxime was found.

When the reaction time was 10 minutes, there was obtained 19% of the nitrile, m.p. 87–89° and 61% of the amidine picrate, m.p. 255–256° dec. (total yield of elimination prod-

[2] Analysis by Galbraith Laboratories, Knoxville, Tenn.

ucts, 80%). In addition, saturation of the alkaline extracts with carbon dioxide gave a 15% yield of *syn*-piperonaldoxime, m.p. 110°; reported m.p. 110° (1).

When a blank experiment was carried out with the *syn*-aldoxime acetate in the absence of potassium amide (ammonium chloride added after 10 minutes) there was obtained on working up the reaction mixture a good yield of *syn*-piperonaldoxime, m.p. 110°. This melting point was not depressed on admixture with an authentic sample of *syn*-piperonaldoxime. From the original aqueous solution, on evaporating to dryness under reduced pressure and extracting with chloroform, there was isolated 0.75 g. (85%) of acetamide, m.p. 80–81°; reported m.p. 82° (4).

In another blank experiment the reaction mixture was worked up without adding ammonium chloride to give a 76% yield of the oxime, 22% of the *syn*-aldoxime, m.p. 105°, being recovered.

syn- and anti-Piperonaldoxime acetates with excess sodium amide. Addition of 2.5 equivalents of sodium amide in 150 ml. of liquid ammonia to a stirred ether suspension of 2.0 g. of *anti*-piperonaldoxime acetate gave, on adding ammonium chloride after one hour, an 81% yield of the nitrile, m.p. 89–90°, and a 13% yield of *anti*-piperonaldoxime, m.p. 141–142°. No appreciable amidine picrate was obtained.

Under similar conditions, *syn*-piperonaldoxime acetate gave a 63% yield of the nitrile, m.p. 89–90°, and a 24% yield of *syn*-piperonaldoxime, m.p. 110°.

SUMMARY

1. *syn-* and *anti*-piperonaldoxime acetates were found to exhibit exclusively *cis* and *trans* β-elimination with excess potassium amide under appropriate conditions, although much of the resulting nitrile was converted to the amidine.

2. With sodium amide under similar conditions the aldoxime acetates yielded mainly the nitrile and some of the corresponding aldoxime.

3. In the absence of an alkali amide, the aldoxime acetates underwent ammonolysis to form the corresponding aldoximes and acetamide.

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