Studies on the Synthesis of Allylic Diamines from Allylic Dihalides

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A greatly simplified procedure for the synthesis of allylic diamines from the corresponding allylic dibromides is reported. For example, *trans*-1,4-dibromo-2-butene in liquid ammonia gave 2-butene-1,4-diamine in moderate yield. On the other hand, *cis*-1,4-dibromo-2-butene under similar reaction conditions failed to produce diamine.

A FEW studies have been reported on reactions of allylic dihalides with ammonia to give allylic diamines. One of the earliest of these was conducted by Amundsen *et al.* (*2*) and concerned the reaction of *trans*-1,4-dichloro-2-butene with aqueous ammonia, ammonia in ethanol and water, and liquid ammonia. Very low yields of 2-butene-1,4-diamine were obtained in the first two cases, and in the latter case, liquid ammonia and the dichloride produced only tars and polymeric material. In a later investigation of the reaction of *cis*-1,4-dichloro-2-butene in ethanol-water-ammonia solution, Amundsen, Bobbit, and Steiner (*1*) observed the formation of 3-pyrroline and the unexpected 5-azaspiro[4.4]nona-2,7-dienium chloride, formed from the condensation of 3-pyrroline and the cis dichloride. No diamine was isolated. Under the conditions used in these studies, *trans*-1,4-dichloro-2-butene apparently reacted very slowly with liquid ammonia, inasmuch as a considerable quantity of the dichloride was recovered after the ammonia had evaporated. No diamine was isolated.

DeTar and LePome (*5*) have patented their method for converting *trans*-1,4-dibromo-2-butene to the corresponding allylic diamine. Their complex experimental procedure involved the addition of the dihalide to a large excess of liquid ammonia in an autoclave under high nitrogen pressure and at temperatures ranging from 0° to 100° C. They did not study the amination of *cis*-1,4-dibromo-2-butene.

EXPERIMENTAL

***trans*-1,4-Dibromo-2-butene.** The synthesis of this compound is discussed by Hatch, Gardner, and Gilbert (*6*); other references are included in their article. The purity of the compound was confirmed by gas chromatographic analysis under the following conditions: column, 6 feet × 0.25 inch diameter, packed with 2.5% SE-30 on 60 to 80 Chromosorb W at approximately 60° C.; helium flow rate, 750 ml. per minute. An Aerograph 90-P3 chromatograph was used. [Boiling points and melting points are uncorrected.]

***cis*-1,4-Dibromo-2-butene.** This compound was prepared according to the procedure of Valette (*8*). The purity of the cis dibromide was confirmed by gas chromatographic analysis under the conditions reported for the trans isomer. The cis dibromide was very sensitive to rearrangement. To avoid rearrangement, the distillation was conducted at low pressure and the dibromide was condensed and collected at the Dry Ice temperatures. NMR data on *cis*-1,4-dibromo-2-butene and *trans*-1,4-dibromo-2-butene have been presented (*9*).

1,4-Dibromo-2-methyl-2-butene. The synthesis of 1,4-dibromo-2-methyl-2-butene is reported by Sheppard and Johnson (*7*); other references are included in their article. Previously unreported work from this laboratory seems to indicate that 1,4-dibromo-2-methyl-2-butene consists of about 21% cis isomer and 74% trans isomer.

Amination of Allylic Dihalides—General Procedure. Four liters of liquid ammonia was added to a 5-liter, round-bottomed flask, which contained a paddle stirrer slightly beneath the surface of the ammonia and a magnetic stirring bar in the bottom of the flask. To this ammonia solution was added, in very rapid dropwise fashion, 0.234 moles of the allylic dihalide dissolved in 500 ml. of absolute ether. After addition, the ammonia was allowed to evaporate, and to the remaining salts was added a saturated solution of a base such as sodium hydroxide or potassium carbonate until the salts were converted to free amine. Anhydrous potassium carbonate was now added to absorb excess water, and the remaining solution was extracted with ethanol. The ethanol was removed on a fractionation column, and the remaining amine was distilled.

Amination of *trans*-1,4-Dibromo-2-butene. The general procedure was followed. The 2-butene-1,4-diamine, b.p. 70° C. (3.5 mm.), n_D^{25} 1.4867, yield, 37%, reacted with phenylisothiocyanate to give a thiourea derivative, which gave the correct analysis for $C_{18}H_{20}N_4S_2$, m.p. 192.5–194° C. Anal. Calcd. for $C_{18}H_{20}N_4S_2$: C, 60.60; H, 5.61; N, 15.70. Found: C, 60.79; H, 5.80; N, 15.75.

The structure of the 2-butene-1,4-diamine was confirmed by reduction with hydrogen and platinum to known putrescine. The diamine obtained by reduction of 2-butene-1,4-diamine reacted with phenylisothiocyanate to give thiourea derivative which melted at 175–176° C. The thiourea derivative from authentic putrescine melted at 174.5–175° C. A mixed melting point was not lowered.

Amination of *cis*-1,4-dibromo-2-butene. The general procedure was followed. Although the reaction was repeated several times, no diamine was isolated. A low yield (3.8%) of 3-pyrroline was obtained, and was confirmed by the boiling point, 89–91° C. [lit. (*4*) b.p. 90–91° C.], and the melting point of the picrate 157.5° C. [lit. (*3*) m.p. 156° C.].

Several higher boiling products were formed, which were not identified. It was confirmed, however, that they were not *cis*-2-butene-1,4-diamine. Gas chromatographic analysis of the basic product on a Polypak column showed a trace of a compound with nearly the same retention time as *trans*-2-butene-1,4-diamine, which may have been *cis*-2-butene-1,4-diamine.

Amination of 1,4-Dibromo-2-methyl-2-butene. The general procedure was followed. 2-Methyl-2-butene-1,4-diamine, which was obtained in approximately 25% yield, b.p. 63–64° C. (1.8 mm.), n_D^{25} 1.4847, reacted with phenylisothiocyanate to give a thiourea derivative which gave the correct analysis for $C_{19}H_{22}N_4S_2$, m.p. 155–156° C. Anal Calcd. for $C_{19}H_{22}N_4S_2$: C, 61.59; H, 5.99; N, 15.12; S, 17.31. Found: C, 61.73; H, 6.14; N, 14.99; S, 17.25.

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The structure of 2-methyl-2-butene-1,4-diamine was confirmed by reduction with hydrogen and platinum to 2-methylbutane-1,4-diamine, which formed a picrate, m.p. 228° C. A mixed melting point with the picrate of authentic 2-methylbutane-1,4-diamine, m.p. 227–228° C., was not lowered.

DISCUSSION

The authors became interested in finding a relatively simple method of preparing allylic diamines from the corresponding dihalides, specifically the diamines derived from *trans*- and *cis*-1,4-dibromo-2-butene and from 1,4-dibromo-2-methyl-2-butene. Allylic diazides rearrange extensively and, therefore, would not provide a suitable route for the synthesis of diamines since a mixture would be formed on reduction of the diazides (*9*). Also, the addition of 1,4-dibromo-2-methyl-2-butene to ammonia in ethanol produced only white polymeric material.

On the other hand, preliminary investigations on the reaction of *trans*-1,4-dibromo-2-butene with liquid ammonia contained in an open, round-bottomed flask, indicated that moderate yields of diamines could be obtained under greatly simplified conditions. Since *trans*- and *cis*-1,4-dibromo-2-butene could be obtained in pure form, their reactions in liquid ammonia were studied in detail. The results of these studies show that *trans*-1,4-dibromo-2-butene reacts with liquid ammonia to give the corresponding diamine in approximately the same yield as reported by DeTar and LePome (*5*).

In contrast to this, *cis*-1,4-dibromo-2-butene gave only a low yield of 3-pyrroline and not more than a trace of diamine, as indicated by gas chromatographic analysis. No explanation can be given for the fact that the cis dibromide failed to give diamine. The dibromide definitely seemed to react, inasmuch as a white solid remained when the ammonia had evaporated, and there was no indication of the intensely lachrymal effect of the dibromide. Conceivably, 3-pyrroline is formed initially which then reacts with more starting dihalide to form 5-azaspiro[4.4]-nona-2,7-dienium bromide, similar to the chloride reported by Amundsen, Bobbit, and Steiner (*1*).

Similar studies on the amination of 1,4-dibromo-2-methyl-2-butene showed that the corresponding diamine was formed, but in lower yield.

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Synthesis of Some *N*-Cyano and *N,N'*-Dicyanobenzamidines Using Cyanogen Bromide

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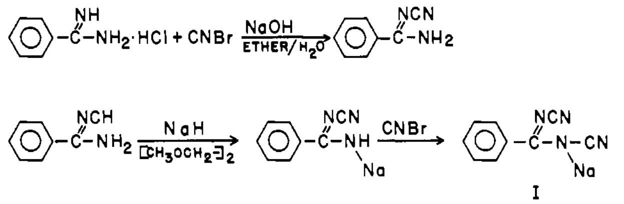
A convenient procedure to convert some benzamidine hydrochlorides to *N*-cyanobenzamidines using cyanogen bromide is given. The latter are converted to sodium *N,N'*-dicyanobenzamidines (I) using cyanogen bromide and sodium hydride in an aprotic solvent.

A COURSE of investigation required a small amount of potassium *N,N'*-dicyanobenzamidine (II). This compound has been prepared in one step by the reaction of cyanogen chloride and benzamidine hydrochloride in the presence of potassium hydroxide using acetone as a solvent (*4*). Several attempts to prepare II from the more readily available and more easily handled cyanogen bromide under the same reaction conditions gave only a very small amount of *N*-cyanobenzamidine and no II. Apparently, a strongly competing hydrolysis reaction (*5*) takes place when cyanogen bromide and sodium hydroxide are in contact with each other. Cyanogen chloride seems to be less reactive and more selective under the same conditions. Compound II could not be prepared from *N*-cyanobenzamidine, cyanogen bromide, and potassium hydroxide using acetone as the solvent. The authors decided to pursue this system to determine if II could be prepared from cyanogen bromide under other conditions. Equations 1 and 2 summarize a two step method which appears to be general for benzamidines—I is obtained rather than the potassium salt.



I

The first step is a modification of the method of Goerdeler and Loevenich (*1*) and gave *N*-cyanobenzamidines in good yield. These workers used cyanogen bromide and dry benzamidine free base in an anhydrous ether system with powdered sodium hydroxide. The method shown in Equation 1 uses benzamidine hydrochlorides (the typical product of the Pinner synthesis) and a two-phase ether-water sys-