Reactions of Amines. XI. Synthesis of α-Amino Ketones from Ketimines[1,2]

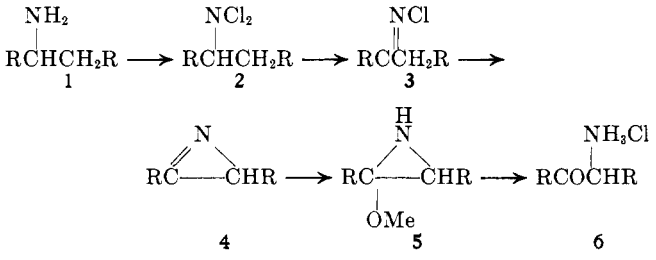
HENRY E. BAUMGARTEN, JAMES M. PETERSEN, AND DONALD C. WOLF

Avery Laboratory, University of Nebraska, Lincoln 8, Nebraska

Received December 26, 1962

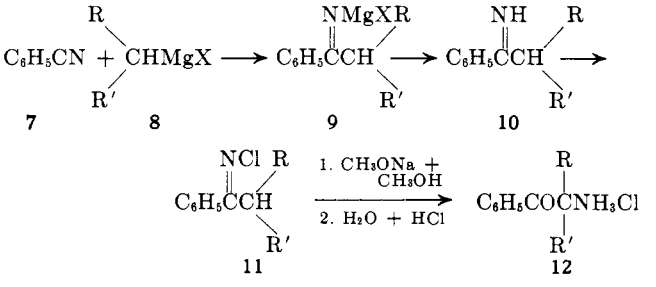
Five α-amino ketones have been prepared by a sequence consisting of (1) the reaction of benzonitrile with an alkylmagnesium halide to form a ketimine, (2) chlorination of the ketimine to form an N-chloroketimine, and (3) base-catalyzed rearrangement of the N-chloroketimine to intermediates which yield α-amino ketone salts on acid hydrolysis.

In earlier papers[3-5] in this series a synthesis of α-amino ketone hydrochlorides (**6**) was described which involved the rearrangement of N,N-dichloro-*sec*-alkylamines (**2**) and for which the following reaction path was proposed.[6]



In a relatively few examples starting material **1** was readily available (*e.g.*, cyclohexylamine), but, in general, **1** had to be prepared from an available starting material, most often from the ketone, $RCOCH_2R$, by chemical or catalytic reductive amination. The purpose of the work described in this communication was to modify the sequence **1** → **6** in such a fashion as to permit the use of more readily available starting materials.

The reaction sequence chosen for study is indicated in the following equations.



Series a, R = H, R′ = H
b, R = CH_3, R′ = H
c, R = $CH_3CH_2CH_2$, R′ = H
d, R = CH_3, R′ = CH_3
e, R = C_6H_5, R′ = H

In this sequence benzonitrile (**7**) is treated with an alkyl Grignard reagent **8** to form the magnesium halide salt of ketimine **9**. The latter is decomposed to the free ketimine **10**, and **10** is chlorinated to form the N-chloro ketimine **11**. Rearrangement of **11** under the conditions of the Neber rearrangement[7,8] or N,N-dichloro-*sec*-alkylamine rearrangement[3-5] gives the amino ketone hydrochloride **12**.

Essentially this same sequence of reactions (different only in the experimental conditions employed and the anticipated product) was studied about thirty years ago by Campbell,[9] who prepared benzyl phenyl N-chloroketimine (**11e**) and attempted without success to convert this substance into 2,3-diphenylazirine (**4**, R = R′ = C_6H_5) by treatment with silver oxide, with potassium hydroxide in ether, and with aqueous sodium hydroxide. Reaction occurred only with the last reagent giving a rather intractable mixture, possibly consisting in part of the condensation products of desylamine (**12e**), plus benzilic acid.

Following Campbell's directions, we prepared **9e** and treated it with hydrogen chloride, obtaining a 57% yield of the hydrochloride of **10e**. This material was treated with ammonia, the resulting **10e** was chlorinated with *t*-butyl hypochlorite to form **11e**, and the latter was treated with methanolic sodium methoxide without isolation of either **10e** or **11e**. From the acidification of the reaction mixture with hydrochloric acid, desylamine hydrochloride (**12e**) was obtained in 66% yield, a yield that compared quite favorably with the 45–46% yield obtained from the rearrangement of N,N-dichloro-1,2-diphenylethylamine.[5]

When the rearrangement of **11e** was stopped before the addition of acid and the intermediate species present were reduced with lithium aluminum hydride, a 48% yield (based on the hydrochloride of **10e**) of *cis*-2,3-diphenylethylenimine was obtained. Similar results have been obtained in the Neber rearrangement[7b] and in the N,N-dichloro-*sec*-alkylamine rearrangement.[4] Assuming that these rearrangements have a common mechanism, the evidence obtained by Hatch and

(1) Paper X, H. E. Baumgarten, *J. Am. Chem. Soc.*, **84**, 4975 (1962). A preliminary report of the present work appeared in Paper VI, H. E. Baumgarten, J. E. Dirks, J. M. Petersen, and D. C. Wolf, *ibid.*, **82**, 4422 (1960).

(2) This work was supported in part by grants G-3689 and G-11339 of the National Science Foundation.

(3) H. E. Baumgarten and F. A. Bower, *J. Am. Chem. Soc.*, **76**, 4561 (1954).

(4) H. E. Baumgarten and J. M. Petersen, *ibid.*, **82**, 459 (1960).

(5) H. E. Baumgarten and J. M. Petersen, *Org. Syn.*, **41**, 82 (1961).

(6) This sequence is arbitrary in the sense that it assumes the Neber–Cram mechanism (*cf.* ref. 4, 7, and 8) for the Neber and N,N-dichloro *sec*-alkyl amine rearrangements. If a mechanism involving nitrene intermediates similar to that suggested by H. O. House and W. F. Berkowitz [*J. Org. Chem.*, **28**, 307 (1963)] were assumed, intermediate **4** would *follow* **5** in those examples in which **4** appeared at all. At present there is no evidence requiring the formation of **4** in any but a few Neber rearrangements in which pyridine rather than an alkoxide was employed as base. Thus far, experiments in progress in this laboratory designed to distinguish between the Neber–Cram mechanism and mechanisms involving nitrene intermediates have proved to be inconclusive. However, it should be noted that (contrary to the statement by House and Berkowitz) an insertion reaction of a simple nitrene to form an ethylenimine has been reported by D. H. R. Barton and L. R. Morgan, Jr. [*Proc. Chem. Soc.*, 206 (1961)].

(7) (a) P. W. Neber and A. Friedolsheim, *Ann.*, **449**, 109 (1962); (b) P. W. Neber and A. Uber, *ibid.*, **467**, 52 (1928); (c) P. W. Neber and A. Burgard, *ibid.*, **493**, 281 (1932); (d) P. W. Neber and G. Huh, *ibid.*, **515**, 283 (1935); (e) P. W. Neber, A. Burgard, and W. Thier, *ibid.*, **526**, 277 (1936).

(8) (a) D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953); (b) M. J. Hatch and D. J. Cram, *ibid.*, **75**, 38 (1953).

(9) K. N. Campbell, *ibid.*, **59**, 2058 (1937).

TABLE I

SYNTHESIS OF α-AMINO KETONE HYDROCHLORIDES

Product, hydrochloride of	R_2CHMgX	Time,[a] **8** → **9**, hr.	Apparent yield of **10**,[b] %	Time,[c] **11** → **12**, min.	Yield of **12**,[d] %	M.p.,[e] of **12**·HCl, °C.	Lit. m.p., °C.
Phenacylamine	CH_3MgBr[f]	6.5	88	60–150	40–51	185–186	186.5[g]
α-Aminopropiophenone	CH_3CH_2MgBr	15	65	25–35	36–45	186–188	188–190[h]
α-Aminovalerophenone	$CH_3CH_2CH_2CH_2MgCl$[f]	10–13	70–86	75–85	70–72	156.5–158	156–158[i]
α-Aminoisobutyrophenone	$(CH_3)_2CHMgBr$	11.5	87	14–20[k]	20–35	186–188	187–188
Desylamine	$C_6H_5CH_2MgCl$	4	57[k]	45	38–50	232–234	232–235[l] 234[m]

[a] Time for reaction of benzonitrile with Grignard reagent; see Experimental. [b] See ref. 13. [c] Time required for negative starch–iodide test; see Experimental. [d] Based on benzonitrile. [e] With decomposition. [f] Commercial 3 *M* solution. [g] Ref. 3–5. [h] F. Ebel and W. Deuschel, *Chem. Ber.*, **89**, 2799 (1956). [i] Hours. [j] H. E. Baumgarten and C. H. Anderson, *J. Am. Chem. Soc.*, **83**, 399 (1961). [k] Yield of crude ketimine hydrochloride. [l] Ref. 7. [m] Ref. 6.

Cram[7b] for the Neber rearrangement suggests that the intermediate being reduced is **5**.

For the preparation of the remaining ketimines (**10a**–**10d**) we chose to take advantage of the careful studies of the Grignard reagent–nitrile reaction that have been carried out in recent years by Pickard and coworkers.[10-11] In their most recent report[11] this group has shown that, because of the insolubility of magnesium alkoxide halides in the usual solvents employed, complexes such as **9** may be decomposed to the free bases **10** by treatment with absolute methanol. Combined with the analytical procedure of Pickard and Iddings,[12] this technique makes it possible to avoid the isolation of the ketimine **10** and still estimate the *apparent yield*[13] of ketimine in the reaction mixture. For the various Grignard reagents **8a**–**8d** and benzonitrile (**7**) the apparent yields of the corresponding ketimines **10a**–**10d** were in the range, 65–91%.

The ketimines were chlorinated (without isolation of **10**) using *t*-butyl hypochlorite and the resulting N-chloroketimines **11** were treated (without isolation of **11**) with methanolic sodium methoxide. Hydrolysis of the reaction mixture with aqueous hydrochloric acid gave the amino ketone hydrochlorides **12** in reasonably good yields (Table I) considering the number of separate steps involved in the sequence **7** → **12**. The examples shown in the Table were chosen to demonstrate the applicability of the reaction to ketimines with methyl, methylene, methinyl, and activated (benzyl) substituents on the ketimine carbon atom.[14]

One interesting result of this work was the surprisingly good yield (40–51%) of phenacylamine hydrochloride (**12a**). Ketimines such as methyl phenyl ketimine (**10a**) are especially difficult to work with because of their tendency toward hydrolysis. Apparently the technique employed here was successful in largely avoiding that destructive side reaction.

Another interesting result was the yield of 20–35% of α-aminoisobutyrophenone hydrochloride (**12d**). Based on their studies of the Neber rearrangement of oxime tosylates, Hatch and Cram[7b] have concluded that that rearrangement requires a methyl or methylene group adjacent to the oximino function. The N-chloroketimine rearrangement would appear to be quite similar similar to the Neber rearrangement and, therefore, to have the same requirements; however, **12d** has only a methinyl group. If the assumption that these rearrangements are quite similar is valid, one must conclude that some factor other than the presence of a methinyl group must be responsible for the results on which Hatch and Cram based their generalization.[15]

When a solution containing **9e** (rather than **10e**) was treated with *t*-butyl hypochlorite, **11e** could be isolated from the reaction mixture in 41% yield; however, attempts to combine the halogenation of **9** and the rearrangement of **11** without the isolation of intermediates were not successful. In some experiments (with **9c**) there was a definite indication of C- rather than N-halogenation during such attempts, but it was not clear whether or not N-halogenation preceded C-halogenation. This and other reactions of **9** are under study.

Experimental

α-Amino Ketone Hydrochlorides (12a–d).—Virtually the same procedure was used for the preparation of all of the α-amino ketone hydrochlorides listed in Table I except **12e**. The specific procedure for the preparation of α-aminovalerophenone hydrochloride is given, for it is the result of a large number of experiments carried out to determine the optimum conditions for the reaction sequence. Deviations from this procedure for the other amino ketone hydrochlorides are given after the procedure. Many of the preparations of the other α-amino ketones were completed before the optimum procedure was developed; therefore, their yields do not necessarily represent the maximum obtainable.

(10) P. L. Pickard and D. J. Vaughan, *J. Am. Chem. Soc.*, **72**, 876, 5017 (1950); P. L. Pickard and C. W. Young, *ibid.*, **73**, 42 (1951); P. L. Pickard and E. F. Engles, *ibid.*, **74**, 7607 (1952); P. L. Pickard and S. H. Jenkins, Jr., *ibid.*, **75**, 5899 (1953); P. L. Pickard and G. W. Polly, *ibid.*, **76**, 5159 (1954).

(11) P. L. Pickard and T. L. Tolbert, *J. Org. Chem.*, **26**, 4886 (1961).

(12) P. L. Pickard and F. A. Iddings, *Anal. Chem.*, **31**, 1228 (1959).

(13) Inasmuch as the analysis gives a measurement of the quantity of all basic species present in solution, it gives only the upper limit of the ketimine content. Traces of alkoxide, ammonia, etc., will cause the apparent yield of ketimine to be higher than the actual yield.

(14) G. H. Alt and W. S. Knowles [*J. Org. Chem.*, **25**, 2047 (1960)] have carried out the rearrangement of N,N-dichlorocyclohexylamine in two distinct steps (**2** → **3** and **3** → **6**) and have isolated N-chlorocyclohexylideneimine in so doing. K. Schmitz [*Angew. Chem.*, **73**, 23 (1961)] also has shown that the latter compound, prepared from cyclohexanone anil and chloramine, can be converted to α-aminocyclohexanone (or one of its derivatives) by treatment with base. Although the procedure of Alt and Knowles is of interest as a technique for the preparation of N-chloro ketimines, it does not appear to have any advantage over the N,N-dichloro-*sec*-alkylamine rearrangement (with which it shares a common starting material) for preparation of α-amino ketones. The extent to which Schmitz procedure can be used for the preparation of α-amino ketones is not known.

(15) The only examples cited specifically by Hatch and Cram which support their conclusion are the unsuccessful rearrangement of α,α-di(*p*-chlorophenyl)acetoxime (A) and the reaction of α,α-diphenylketoxime (B) with pyridine. These examples have both α-CH and α-CH_3 groups. Furthermore, the products of the reaction of A were not completely characterized and the reaction of B involved unusual conditions.

To a solution of 84 ml. (0.25 mole) of 3 *M* *n*-butylmagnesium chloride and 150 ml. of dry ether a solution of 10.3 ml. (0.10 mole) of benzonitrile in 10 ml. of dry ether was added dropwise at such a rate as to maintain a slight reflux. After the addition was complete the gray solution containing a precipitate was heated under reflux for 10 hr. in the oil bath. The oil bath was removed and the mixture was cooled in an ice bath. To this cooled solution, 60 ml. of dry methanol was added dropwise, the first portion being added slowly and cautiously as the reaction was quite vigorous. After the addition was complete, the reaction mixture, containing a finely divided white precipitate, was stirred at room temperature for 20 min. The mixture was then cooled in ice and filtered by suction through a 0.25-in. layer of Celite in a Büchner funnel. The filter cake was washed with three 25-ml. portions of dry ether, which were added to the filtrate. The ether was evaporated from the yellow filtrate in a rotary evaporator, and to the yellowish liquid remaining in the evaporator flask, 80 ml. of dry benzene was added. Usually a small amount of precipitate either remained after evaporation or formed on addition of the benzene, and this was removed by filtering the mixture through a Büchner funnel into a tared flask. The evaporator flask was washed with small portions of dry benzene totaling 30 ml. After weighing the flask plus filtrate and washings, weighed samples of the solution were taken for analysis.[12] The apparent yield of the *n*-butyl phenyl ketimine was 70–86%.

The solution was cooled in an ice–salt bath to 5° and a solution of 12.3 ml. (0.10 mole) of *t*-butyl hypochlorite in 12 ml. of dry benzene was added at such a rate as to maintain the temperature below 10°. After the addition of *t*-butyl hypochlorite was complete, the clear pale yellow solution was stirred at room temperature for 0.5–4 hr. A freshly prepared solution of 4.0 g. (0.17-g.-atom) of sodium in 60 ml. of anhydrous methanol was then added at such a rate as to maintain a gentle reflux. After the addition of the sodium methoxide was complete, the solution was heated under reflux until a test[5] with acidified starch iodide paper was negative (about 75–85 min.). The reaction mixture was cooled in an ice–water bath and the precipitated sodium chloride was removed by filtration through a Büchner funnel. The filter cake was washed with two 25-ml. portions of dry benzene. The combined yellow filtrates were added very slowly with shaking or stirring to 75 ml. of cold (10°) 2 *N* hydrochloric acid solution. The layers were separated and the benzene layer was extracted with three 35-ml. portions of 2 *N* hydrochloric acid. The combined acid extracts were washed twice with 40-ml. portions of ether. The pale yellow aqueous solution was evaporated to dryness at a temperature not greater than 40°. The residue was heated under reflux with 35 ml. of isopropyl alcohol–hydrochloric acid solution[5] for at least 0.5 hr. and was filtered hot through a Büchner funnel. The residual solid was returned to the extraction flask and extracted in the same manner with a 25-ml. portion of the isopropyl alcohol–hydrochloric acid solution. The two extracts were cooled separately in the refrigerator overnight and then filtered on a Büchner funnel. The nearly colorless crystals were washed on the filter with two 25-ml. portions of dry ether. Each of the filtrates was diluted with five volumes of dry ether (165 ml. and 75 ml., respectively) and was allowed to stand in the refrigerator overnight. From these diluted filtrates further crops of crystals were collected. The combined yield of the three to four crops was 15.0–15.5 g. (70–72%), m.p. 155–157° dec.

The principal variations necessary in the preparations of the other α-amino ketone hydrochlorides were in (1) the length of time allowed for the reaction of the Grignard reagent with the benzonitrile, (2) the length of time required to obtain a negative test with starch–iodide in the reaction of the N-chloroketimine with sodium methoxide, and (3) the amount of isopropyl alcohol–hydrochloric acid required to extract the crude α-amino ketone. The variation in these factors for each α-amino ketone is given in Table I.

Other experimental variations studied included the isolation of the intermediate ketimine and variation in the organometallic nitrile pair. All of these experiments were directed toward the preparation of ethyl phenyl ketimine (**10b**). From the combination indicated in the equation, **10b** could be isolated in about 30% yield but of only about 79% actual ketimine content. Chlorination and rearrangement using this material gave a 69% yield of **12b** (based on actual ketimine content). Attempts to prepare **10b** from ethyllithium and **7** from phenylmagnesium bromide and propionitrile gave little or no ketimine. The reaction of phenyllithium with **7** gave a 20–25% yield of **10b**, but the procedure appeared to have no advantage over that employing the Grignard reagent; therefore, it was not studied further. Limited experiments with other ketimines indicated that, in general, for the present purpose it was undesirable to isolate and purify the intermediate ketimine, for the over-all yield invariably suffered under these conditions.

Desylamine Hydrochloride (12e).—Phenyl benzyl ketimine hydrochloride was prepared in 57% yield by the method outlined by Campbell.[8] The product was used without further purification.

A suspension of 11.58 g. (0.05 mole) of phenyl benzyl ketimine hydrochloride in approximately 100 ml. of dry benzene was cooled to 5° in an ice–water bath, and anhydrous ammonia gas was passed into the suspension for 30 min. The precipitated ammonium chloride was removed by filtration, and dry nitrogen was passed through the solution for 15 min. in order to remove entrained ammonia gas. To the solution, cooled to approximately 0° in an ice–salt bath, was added 5.4 g. (6.2 ml., 0.05 mole) of *t*-butyl hypochlorite diluted with 25 ml. of dry benzene at such a rate to maintain a temperature of less than 10°. After the addition was completed, the reaction mixture was stirred at room temperature for 40 min. A freshly prepared solution of sodium methoxide [2.3 g. (0.1 g.-atom) of metallic sodium in 30 ml. of dry methanol] was added to the reaction mixture at such a rate as to maintain a gentle reflux. As the sodium methoxide was added, the solution became dark orange in color before the formation of the sodium chloride was noted. As the sodium chloride was formed the reaction mixture became yellow-orange. After the addition of the sodium methoxide was completed, the reaction mixture was refluxed 45 min. until a negative starch–iodide test was obtained. The precipitated sodium chloride was removed by filtration and washed twice with small portions of dry benzene. The combined benzene solutions were poured into 300 ml. of 2 *N* hydrochloric acid solution. The aqueous phase was separated and the benzene phase was extracted four times with 25-ml. portions of acid. The combined acid extracts were washed twice with ether which was discarded. The acid extracts were yellow in color.

The aqueous solution was worked up in a fashion similar to that described earlier for α-aminovalerophenone. The total yield of desylamine hydrochloride was 8.22 g. (66%), m.p. 232–234° dec. (lit. m.p. 232–235°,[7] 234°[6]).

***cis*-2,3-Diphenylethylenimine.**—The crude phenyl benzyl ketimine hydrochloride (0.025 mole) was chlorinated and treated with base in the same manner as described for the preparation of desylamine hydrochloride. After the addition of sodium methoxide and the reflux period, the benzene filtrate was treated in precisely the same manner as was the benzene filtrate from the rearrangement of N,N-dichloro-1,2-diphenylethylamine.[4] Evaporation of the ethereal solution from the lithium aluminum hydride reduction produced 2.54 g. of material, m.p. 82–84°. Recrystallization of this material from 12 ml. of petroleum ether produced 2.25 g. (48%) of *cis*-2,3-diphenylethylenimine, m.p. 83.5–84.5° (lit.[7b] m.p. 81–82.5°).

Benzyl Phenyl N-Chloroketimine (11e).—To a solution of benzylmagnesium chloride, prepared from 19.3 g. (0.113 mole) of benzyl chloride, 2.8 g. (0.113 g.-atom) of magnesium, and 75 ml. of ether, was added dropwise at such a rate as to maintain reflux a solution of 11.6 g. (0.113 mole) of benzonitrile in 25 ml. of ether. The mixture was heated under reflux for 4 hr., after which time it consisted of a yellow solution and a gray-yellow precipitate. To the mixture, cooled and stirred in ice, was added dropwise a solution of 13.0 g. (0.113 mole) of *t*-butyl hypochlorite in 30 ml. of ether. The solution warmed up somewhat but did not boil. A white precipitate formed below a yellow supernatant liquid.

The mixture was poured into 200 ml. of saturated aqueous ammonium chloride solution in which the precipitate dissolved. The ether layer was separated and the aqueous layer was extracted with 50 ml. of ether. After evaporation of the ether, the residual solid was recrystallized from 120 ml. of ethanol (charcoal). A small amount of bright yellow insoluble solid that formed as the hot solution stood was removed by filtration. The yield of crude benzyl phenyl N-chloroketimine was 15 g. (58%), m.p. 75.5–76.5°. Recrystallization of the crude material from methanol gave 10.6 g. (41%) of benzyl phenyl N-chloroketimine, m.p. 76.5–78° (lit.[9] m.p. 78°) (again accompanied by the formation of some bright yellow methanol-in-

soluble material). Treatment of a pentane solution of the N-chloro compound with dry hydrogen chloride gave a quantitative recovery of benzyl phenyl ketimine hydrochloride, m.p. 209–211° (lit.[9] m.p. 210–211°). Acidification of a methanol solution of the product (1 g./10 ml.) with 1:1 concentrated hydrochloric acid–water liberated chlorine. These observations are in accord with those of Campbell[9]; however, the compound appeared to be much more stable than reported by Campbell.

The Reaction of Hydrazine with 3,6-Diamino-*s*-tetrazine[1]

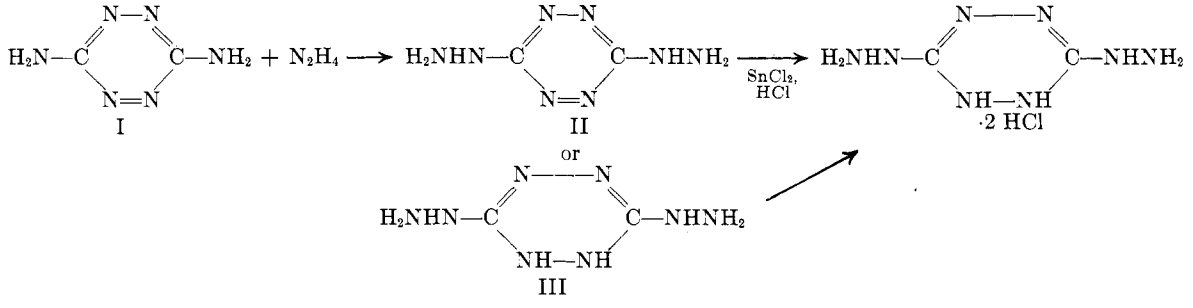
HENRY J. MARCUS AND ALLEN REMANICK

Chemical Products Division, Aerojet-General Corporation, Azusa, California

Received April 12, 1963

The reaction of hydrazine with 3,6-diamino-*s*-tetrazine was investigated. By suitable choice of reaction conditions, either 3,6-dihydrazino-*s*-tetrazine or the reduced form, 3,6-dihydrazino-1,2-dihydro-*s*-tetrazine, was isolated The two products are interconvertible. Several derivatives of each are described.

The reaction of guanidine with hydrazine to yield triaminoguanidine has been reported in the literature.[2] As part of an investigation into the reaction of hydrazine with heterocyclic materials, the reaction of 3,6-diamino-*s*-tetrazine (I) with anhydrous hydrazine was investigated. Depending upon the reaction conditions chosen, it was found that this reaction produced either 3,6-dihydrazino-*s*-tetrazine (II) or 3,6-dihydrazino-1,2-dihydro-*s*-tetrazine (III).



If reaction is carried out at ambient temperatures, with no effort to exclude air, II is obtained. At slightly higher temperatures (40–50°), with rigorous exclusion of air, III results. When II is reduced with stannous chloride in hydrochloric acid, the product is identical with the hydrochloride salt prepared directly from III.

Hydrazine then is capable not only of formally displacing the amino groups from I, but also of acting as a reducing agent for the *s*-tetrazine ring. The reduction actually may have been accomplished by diimide or a substituted species of it,[3] although no effort was made to detect its existence, nor was any attempt made to investigate the reaction of diimide with I or II.

Attempts to verify the structure of II (or of III) by synthesis *via* alternate routes[4,5] were not successful, although some of the methods were not evaluated thoroughly. The structure of II was, however, established unequivocally by elemental analysis of the compound itself and of several derivatives (see Table I), and by conversion back to I. This was accomplished by treating it with nitrous acid to form the diazide, reducing the diazide with stannous chloride to 3,6-diamino-1,2-dihydro-*s*-tetrazime hydrochloride, and oxidizing the latter in aqueous base to yield a red, crystalline solid whose infrared spectrum and melting characteristics[6] proved it to be identical with the starting material. Thus the *s*-tetrazine ring remained intact during the hydrazinolysis of I and the reconversion of II to I.

Characteristics of II and III.—Compound II is a red solid, melting at 160–162° with decomposition. It reduces Fehling's solution in the cold. II crystallizes readily from dimethyl sulfoxide (DMSO) and is preferably recovered by the addition of alcohol. It is moderately soluble in hot sulfolane, dimethyl sulfoxide, and glacial acetic acid. Exothermic decomposition, however, appears to take place in the latter two solvents above 75°. Compound II is very slightly soluble in hot water and hot methanol. It is insoluble in the other aliphatic alcohols, dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, acetonitrile, benzene, dimethylformamide, pyridine, chlorobenzene, and nitrobenzene. It decomposes rapidly in aqueous alkali and slowly in water. It is soluble in dilute hydrochloric

(1) Contribution no. 312:62-105, Chemical Products Division, Aerojet-General Corp.

(2) (a) L. H. Diamond, Dissertation, University of Illinois, 1954, p. 98; (b) L. F. Audrieth and B. A. Ogg, "The Chemistry of Hydrazine," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 215.

(3) E. E. van Tamelen, R. S. Dewey, M. F. Lease, and W. H. Pirkle, *J. Am. Chem. Soc.*, **83**, 4302 (1961).

(4) Among the routes investigated for compound II were the Hunsdiecker reaction with the silver salt of 3,6-dicarboxy-*s*-tetrazine; the bromination of *s*-tetrazine; and the fluorination of 3,6-dicarboxy-*s*-tetrazine. It was intended to replace the halogen of the 3,6-dihalo-*s*-tetrazine (had they been obtained) with hydrazine by direct metathesis. In addition, attempts were made to effect the oxidative ring-closure of S-methylthiocarbohydrazide hydriodide and the amination of I with hydroxylamine-O-sulfonic acid.

(5) Alternate routes investigated for the synthesis of III included the preparation of "*p*-dithiourazine" (prior to the disclosure of its structure as that of the isomeric N-aminodithiourazole) [A. W. Lutz, Abstracts, Division of Organic Chemistry, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March, 1961, p. 3-O, and N. Petri, *Zeitschrift Naturforsch.*, **16B**, 767 (1961)], which was to be followed by alkylation and hydrazinolysis; the nitrosation of I with amyl nitrite, to be followed by reduction; and the hydrazinolysis of 3,6-diamino-1,2-dihydro-*s*-tetrazine. The latter compound, found to be stable in the form of its hydrochloride salt, was immediately oxidized to I in the presence of hydrazine.

(6) I does not melt up to 300°, but sublimes at about 200–240°.