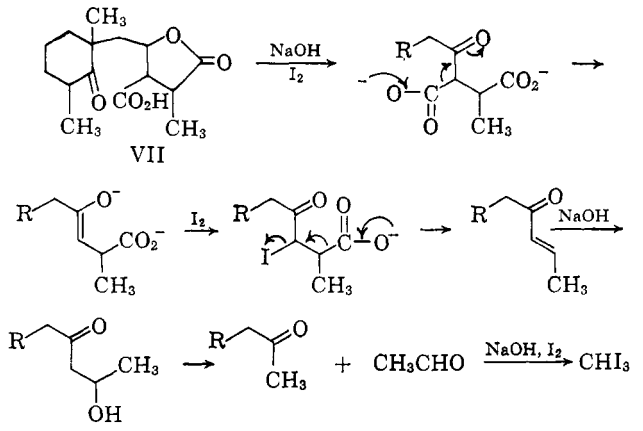
SCHEME I



field in the spectrum of dihydroalantolactone but the doublets at 5.1 and 1.1 p.p.m., attributed to the C-6 proton and the C-4 methyl group, remain. It is noteworthy that neither alantolactone (I) nor isoalantolactone (II) show appreciable $H_{13}/H_{13'}$ spin–spin coupling.[11]

We repeated the low-temperature hydrobromination of dihydroisoalantolactone (III) and obtained Nakazawa's[6] 120–121° bromo derivative which, on the basis of its n.m.r. spectrum, is 4-bromotetrahydroalantolactone. Since the same bromo compound is obtained by hydrobromination of dihydroalantolactone (V),[6] it is clear that this reaction is accompanied by double-bond (or carbonium ion) rearrangement. We were unable to prepare the 189–191° bromo derivative which is reported[6] for both dihydroalantolactone (V) and dihydroisoalantolactone (III). All attempts produced colored oils which evolved hydrogen bromide on exposure to air and during attempted crystallization at room temperature or below. Similar behavior was noted for the 120–121° bromo derivative.

Hydrochlorination of dihydroisoalantolactone (III)[5] was effected smoothly and afforded a mixture of isomeric 4-chlorotetrahydroalantolactones in good yield. The chloro compounds were easily handled and showed no tendency to dehydrochlorinate. Therefore, structural conclusions based on these derivatives[3] must be considered more compelling than conclusions based on the hydrobromides.[6]

The lactone keto acid obtained by ozonation of dihydroalantolactone (V)[7] must now be formulated as VII. A reasonable pathway for the formation of iodoform from this compound is pictured (R = 1,3-dimethyl-2-ketocyclohexyl) in Scheme I.

Experimental[12]

Alantolactone was purchased from Chemicals Procurement Laboratories, Inc., College Point, N. Y. The commercial material was about 60% isoalantolactone which was largely removed by crystallization from aqueous methanol. The remaining alantolactone was purified to the reported melting point[3] by numerous recrystallizations, first from hexane and finally ethanol at −20°. This material retained 5–10% of isoalantolactone (detected by the n.m.r. spectrum and estimated by integration) which could not be removed by further crystallization.[1]

Alantolactone (I) gave $\delta_{TMS}^{CCl_4}$ 6.06 (H-13 doublet, J = 2 c.p.s.), 5.52 (H-13′ doublet, J = 1.8 c.p.s.), 5.14 (H-6 doublet, J = 4 c.p.s.), 4.73 (H-8 multiplet), 3.53 (H-7 multiplet), 1.18 (C-10 CH_3), and 1.11 (C-4 CH_3 doublet, J = 7 c.p.s.) p.p.m.; m.p. 78.5–80°, lit.[3] m.p. 78–79°.

Isoalantolactone (II) gave $\delta_{TMS}^{CCl_4}$ 6.02 (H-13 doublet, J = 0.8 c.p.s.), 5.55 (H-13′ doublet, J = 0.6 c.p.s.), 4.76, 4.55 (C=CH_2), 4.45 (H-8), and 0.82 (C-10 CH_3) p.p.m.; m.p. 112–113°, lit.[3] m.p. 111–113°.

Dihydroisoalantolactone (III) gave $\delta_{TMS}^{CCl_4}$ 4.78, 4.51 (C=CH_2) 4.3–4.6 (H-8), 1.17 (C-11 CH_3 doublet, J = 7 c.p.s.), and 0.82 (C-10 CH_3) p.p.m.; m.p. 172–173°, lit.[7] m.p. 171–172°. This material was prepared by hydrogenation of isoalantolactone over reduced platinum oxide in methanol until 1 mole equiv. was taken up.

Dihydroalantolactone (V) gave $\delta_{TMS}^{CCl_4}$ 5.18 (H-6 doublet, J = 3 c.p.s.), 4.5–4.8 (H-8), 1.22 (C-10 CH_3), and 1.17 (C-4 CH_3 and C-11 CH_3 doublet, J = 8 c.p.s.) p.p.m.; m.p. 132–132.5°, lit.[7] m.p. 133.5–134°. This material was prepared in the manner described for dihydroisoalantolactone.

4-Bromotetrahydroalantolactone gave $\delta_{TMS}^{CCl_4}$ 4.2–4.5 (H-8), 1.78 (C-4 CH_3), 1.18 (C-10 CH_3), and 1.18 (C-11 CH_3 doublet, J = 7 c.p.s.) p.p.m.; m.p. 119–121°, lit.[6] m.p. 120–121°. This material was obtained in only 10% yield by hydrobromination of dihydroisoalantolactone at 0° according to the published method.[6]

Hydrobromination of dihydroisoalantolactone at room temperature by the published procedure[6] afforded a brown oil which fumed in air. Crystallization of the oil could not be induced and dissolution in ether and hexane was attended by fuming and separation of a red-brown oil.

4-Chlorotetrahydroalantolactone gave $\delta_{TMS}^{CCl_4}$ 4.6–4.2 (H-8), 1.52 (C-4 CH_3), 1.20 (C-11 CH_3 doublet, J = 7 c.p.s.), and 1.00 (C-10 CH_3) p.p.m.; m.p. 142–145°, lit.[5] m.p. 145°. The procedure of Hansen[5] was followed using 0.50 g. of dihydroisoalantolactone. The crude hydrochloride, m.p. 104–137°, was obtained in 97% yield. Several recrystallizations from ethanol afforded 0.10 g., m.p. 142–145°.

The mother liquors were evaporated and the residue was recrystallized from ethanol. A second recrystallization afforded 0.05 g., m.p. 127–136°. This material is a mixture of 4-chloro isomers since the n.m.r. spectrum exhibited a new peak at 0.81 p.p.m. (C-10 CH_3) in addition to intense peaks at 1.52 (C-4 CH_3) and 1.00 p.p.m. (C-10 CH_3) present in the 145° isomer.

The chloro derivatives (in distinct contrast to the bromo derivatives) showed no tendency to fume. Solution in boiling 95% ethanol could be effected with no sign of decomposition.

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(11) This result might be expected if the C-13 H–C–H bond angle assumes a value near 125° (ref. 9, p. 310).

(12) Melting points were taken on a Fisher-Johns hot stage and are corrected. N.m.r. spectra were determined with a Varian A-60 spectrometer.

Preparation of Triaminoguanidine

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During the course of a research program involving the use of triaminoguanidinium salts, a convenient method for the preparation of triaminoguanidine was discovered. The synthesis of this compound in its

free-base form has not been reported in the literature.[1] A simple reaction of triaminoguanidinium chloride with liquid ammonia results in the formation of ammonium chloride and a precipitate of triaminoguanidine. Al-

$$[(NH_2NH)_3C]^+Cl^- + NH_3 \xrightarrow{\text{liq. } NH_3} NH_2NHC(=NNH_2)NHNH_2\downarrow + NH_4Cl$$

though triaminoguanidine is a much stronger base than ammonia, its very low solubility in liquid ammonia,[2] together with the use of a large excess of ammonia, causes the reaction to go to completion.

Triaminoguanidine is a white crystalline solid which is stable when stored *in vacuo* or in an inert atmosphere. In air it undergoes slow decomposition of an unknown nature, becoming pink and ultimately deep purple in color. Perhaps owing to greater purity, some samples have initially been more resistant to this decomposition. A relatively small amount of decomposition, not detected by a change in infrared spectrum, imparts rather intense color to the material. Samples which become colored after exposure to air usually revert to a nearly colorless state again when resealed and allowed to stand. However, the color reappears very rapidly when the container is again opened. Triaminoguanidine is extremely soluble in water, insoluble or sparingly soluble in common organic solvents. In water it hydrolyzes to carbohydrazide and hydrazine (half-life at 25° about 14 hr.).[3] Titration of its aqueous solution gives the neutralization curve characteristic of a strong base.

Experimental[4]

The apparatus used consisted of a 125-ml., three-neck, round-bottom flask with a sealed-in sintered-glass disk and draw-off tube in the bottom, equipped with a drying tube and two gas outlet adapters. Seven grams (0.05 mole) of triaminoguanidinium chloride was placed in the flask, the flask was purged with nitrogen, and about 30 ml. of anhydrous liquid ammonia was introduced. The mixture was stirred with a magnetic stirrer for about 10 min. and then the ammonium chloride solution was removed by applying vacuum to the draw-off tube. During the filtration, nitrogen was passed through the flask. The solid remaining in the flask was treated twice more with liquid ammonia in this manner, then nitrogen was drawn through the white crystalline product until it warmed to room temperature. It was dried *in vacuo* over P_2O_5 at 40°, yield 4.7 g. (90%). On a Fisher-Johns block the compound turned red and melted with gas evolution at about 100°. In an evacuated capillary, melting with decomposition began at 141°.

Anal. Calcd. for CH_8N_6: C, 11.54; H, 7.74; N, 80.72; equiv. wt., 104.1. Found: C, 11.61; H, 7.52; N, 80.76; equiv. wt., 103.2 (titration in acetic acid–acetonitrile with perchloric acid).

The infrared spectrum (Nujol mineral oil and halocarbon mulls) showed absorption maxima at 3310 (sh), 3275 (s) (NH_2 asymmetric stretch), 3165 (s) (NH_2 symmetric stretch), 2860 (vw), 1677 (ms) (C=N stretch), 1643 (s) (NH_2 deformation), 1632 (sh), 1485 (s), 1443 (m), 1355 (w), 1343 (w), 1316 (w), 1177 (ms), 1130 (ms), 1002 (m), 954 (s, broad), 868 (m, broad), 753 (ms, broad), 699 (m) cm.$^{-1}$.

Purification of impure material has not been easily accomplished because of the sensitivity of the base to air and moisture, and its low solubility in solvents other than water. The bulk of the colored decomposition products can be removed by washing with anhydrous methanol. Recrystallization then can be carried out by stirring the solid in dimethylformamide (*ca.* 25 ml./g.) at 80° and adding water until it dissolves (*ca.* 6 ml./g.). Subsequent cooling of the solution to −10° usually yields nearly colorless crystals.

Acknowledgment.—This research was supported by the Advanced Research Projects Agency, Propellant Chemistry Office, and was monitored by the Bureau of Naval Weapons, RMMP, under Contract No. NOrd 18728.

(1) Early in 1959, Dr. V. P. Wystrach and Mrs. J. H. Smalley at these laboratories prepared aqueous solutions of triaminoguanidine by passing solutions of the hydrochloride through a strongly basic anion-exchange resin. Isolation of the free base from such solutions was reported that same year in the classified literature by Mrs. P. D. Oja and Mr. G. E. Hartzell of the Dow Chemical Co. This was accomplished by low-temperature concentration and precipitation.

(2) This is in contrast to related strong organic bases such as guanidine, guanylurea, and biguanide, which are reported to be soluble in liquid ammonia: *cf.* W. H. Hill, U. S. Patent 2,274,412 (Feb. 24, 1942).

(3) G. S. Sprague and E. A. Takacs, unpublished work.

(4) Microanalyses were performed by Mr. J. H. Deonarine and Miss J. Schuler, titrations by Dr. C. A. Streuli and Mr. S. Sandler. Infrared spectral data was determined by Mr. N. B. Colthup.

Hydrogenation in the Pyridine Series. II. Catalytic Reduction of 2-Monoalkyl- and 2-Dialkylaminopyridines

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Numerous 2-substituted pyridines have been converted to the corresponding piperidines, but in the catalytic hydrogenation of 2-aminopyridine only 2 molar equiv. are absorbed, yielding 2-iminopiperidine. Further uptake gives only hydrogenolysis.[1] In a study of catalytic debenzylations, Birkhofer did not obtain 2-aminopyridine from 2-benzylaminopyridine. He described the resultant product as 2-benzylamino-3,4,5,6-tetrahydropyridine.[2]

It was anticipated that 2-diethylaminopyridine (I), incapable of tautomerizing, could be reduced to the corresponding piperidine. However, under the most favorable reaction conditions—hydrogenation in glacial acetic acid in the presence of a high ratio of rhodium-on-alumina catalyst—only 2 molar equiv. were absorbed. The reduction product was shown to be 2-diethylamino-3,4,5,6-tetrahydropyridine (II) by the absence of vinyl proton absorption in the n.m.r. spectrum[3] and by infrared examination: $\lambda_{max}^{CHCl_3}$ 6.28 μ, strong (C=N), no bands for NH or pyridine ring.

2-Dimethylamino- and 2-methylaminopyridine were hydrogenated to determine whether smaller substituents would lead to piperidines. In each reduction only 2 equiv. were absorbed giving the corresponding tetrahydropyridines IV and VI (VIa).

The reduction product from V can exist as an *endo* or *exo* double-bonded cyclic amidine. The results of

VI VIa

(1) T. B. Grave, *J. Am. Chem. Soc.*, **46**, 1468 (1924).

(2) L. Birkhofer, *Ber.*, **75**, 429 (1942).

(3) The n.m.r. spectra were run by Mr. R. Kriese on a Varian A-60 spectrometer at 60 Mc./sec. with tetramethylsilane as internal standard and, unless stated, with deuteriochloroform as solvent.