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

M. FREIFELDER, R. W. MATTOON, AND Y. H. NG

Organic Chemistry and Physical Chemistry Departments, Research Division, Abbott Laboratories, North Chicago, Illinois

Received April 16, 1964

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

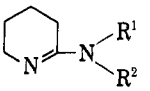
VI VIa

(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.

TABLE I



No.	R^1	R^2	Yield,[a] %	B.p., °C.	mm.	$n^{25}D$	Hydrochloride m.p., °C.	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
II	C_2H_5	C_2H_5	71.8	124–126	47	1.4884		$C_9H_{18}N_2$	70.07	69.91	11.76	11.76	18.13	18.07
				108	38									
							103[b]	$C_{13}H_{24}N_2O_4$[c]	57.33	57.33	8.88	8.83	10.28	10.36
IV	CH_3	CH_3	60	95–97	30	1.4952								
				84–87	22	1.4951		$C_7H_{14}N_2$	66.62	66.59	11.18	11.07	22.92	22.92
							124–126[d]	$C_7H_{15}ClN_2$	51.68	51.48	9.28	9.22	17.22	17.04
VI	H	CH_3	60	104–105	14–16	*e*		$C_6H_{12}N_2$	64.23	63.45[f]	10.78	10.89	24.88	24.63
							162[d]	$C_6H_{13}ClN_2$	48.47	48.29	8.81	8.67	18.84	18.82

[a] The yields could be increased by continuous extraction. [b] Succinate salt. [c] Oxygen was also run. Calcd., 23.50. Found, 23.89. [d] The hydrochloride salts were extremely hygroscopic. They had to be weighed in a dry atmosphere to obtain good analyses. [e] Material solidified. [f] The base absorbed carbon dioxide rapidly. Analysis had to be carried out immediately after distillation. Carbon value of the same material analyzed 2 hr. later dropped to 61%.

n.m.r. spectra of the base in chloroform, dimethyl sulfoxide, and water[4] showed the N-methyl protons as a sharp singlet. The signal in the spectrum of the hydrochloride salt in water or of a solution in water and acid to pH 0.8 was still a singlet.[5]

No real evidence is seen for either structure. However, a comparison of the n.m.r. spectra of II and IV, each with a fixed endocyclic bond, with that of VI (VIa) shows the C-6 protons of the three compounds as essentially symmetric triplets (J = 5 c.p.s.) with almost identical chemical shifts. This suggests that the latter compound exists primarily in the *endo* form.

Experimental

The reaction of 2-bromopyridine and diethylamine to form I is typical of the method used to prepare III and V. Each of the starting substituted aminopyridines is known. However, the difficulty in separating any contaminating 2-bromopyridine from the products made elemental analysis necessary so that only pure products would be used for subsequent ring reduction.

2-Diethylaminopyridine (I).—A solution of 79 g. (0.5 mole) of 2-bromopyridine and 146 g. (2.0 moles) of diethylamine in 350 ml. of ethyl alcohol was heated and shaken in a 1-l. rocker-type bomb for 20 hr. at 175°.[6] After removal of the material from the bomb, the mixture was concentrated. The residue was treated with anhydrous ether. After diethylamine hydrobromide was filtered from the solution, the solvent was distilled and the residue fractionated. The yield of the fraction collected at 116–119° (32 mm.), $n^{25}D$ 1.5357–1.5360, was 72%. The described boiling point is 208–214°, at atmospheric pressure.[6]

2-Dimethylaminopyridine (III), b.p. 105–107° (40–41 mm.),[7] $n^{25}D$ 1.5547–1.5551, was obtained in 81–84% yield.

2-Methylaminopyridine (V), b.p. 94–96° (15 mm.),[8] $n^{25}D$ 1.5716, was obtained in 81.5% yield. It has an affinity for carbon dioxide. Unless it was analyzed immediately after distillation, carbon values were always low.

2-Diethylamino-3,4,5,6-tetrahydropyridine (II).—A solution of 22.5 g. (0.15 mole) of I in 100 ml. of glacial acetic acid was hydrogenated under 3 atm. in the presence of 9.0 g. of 5% rhodium on alumina.[9] Uptake did not proceed beyond 2 equiv. (2 hr.). The solution, after removal of catalyst, was concentrated under reduced pressure to a thick mass. Water was added, and the solution was made strongly basic with 50% sodium hydroxide solution. The mixture was cooled and thoroughly extracted with ether, and the ether extract was dried over anhydrous magnesium sulfate. After removal of the drying agent, the solution was concentrated, and the residue was distilled. Compounds IV and VI were similarly prepared from III and V (see Table I for physical constants).

When the reduction of I was run in the presence of 0.45 g. of platinum oxide[9] uptake was slow. When 1.2 g. was used the rate increased. In each case only 2 equiv. were absorbed.

The infrared spectra of II, IV, and VI showed the presence of a C=N band at 6.15–6.28 μ and the absence of pyridine ring. In addition, there was an NH band at 2.9 μ for VI.[10]

N.m.r. Spectra of the 3,4,5,6-Tetrahydropyridines (δ).—**2-Diethylamino derivative II**: methyl protons of the ethyl group, triplet centered at 1.07 (J = 7 c.p.s.), integration, 6; methylene protons, quartet, 3.11, 3.23, 3.35, 3.47 (J = 7 c.p.s.); C-3 protons,[11] triplet with fine splitting, centered at 2.22, integration, 2; C-4 and C-5 protons, multiple peaks with fine splitting, 1.33–2.00, integration, 4; C-6 protons,[11] triplet centered at 3.51 (J = 5 c.p.s.), partially obscured by one of the methylene peaks at 3.47 (this and the methylene quartet integrate to 6).

2-Dimethylamino compound IV: methyl protons, singlet, 2.87, integration, 6; C-3 protons,[11] triplet centered at 2.23 (J = 6 c.p.s.), integration, 2; C-4 and C-5 protons, multiple peaks, 1.50–2.03, integration, 4; C-6 protons,[11] triplet centered at 3.53 (J = 5 c.p.s.), integration, 2.

Compound VI (VIa) in chloroform[12]: methyl protons, sharp singlet, 2.79; NH, 3.97 (disappears on addition of D_2O); C-3, C-4, and C-5 protons, multiple split peaks 1.37–1.97 and a possible triplet centered at 2.13, integration, 6[13]; C-6 protons,[11] triplet centered at 3.50 (J = 5 c.p.s.).

In dimethyl sulfoxide and in water the separation between the C-3 and the C-4 and -5 signals was better defined. The N-methyl

(4) Basic amines of the type CH_3NHR do not always show a doublet for the methyl protons. "High Resolution N.M.R. Catalog," Vol. 2, N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, Varian Associates, Palo Alto, Calif.; example 652 shows splitting while example 489 does not. Some unpublished spectra from this laboratory of similar type compounds show singlets in some instances, doublets in others. In the spectrum of V, the signal is a doublet (J = 5 c.p.s.).

(5) L. M. Jackman, "Application of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon Press, Inc., New York, N. Y., 1959; section 5.2 points out that methylamine hydrochloride does not show splitting because of rapid exchange of the amino proton with water.

(6) British Patent 265,167 (1928); the reaction was carried out with 2-chloropyridine at 225° for 8 hr. When we used an 8-hr. period at 150° with 2-bromopyridine, a mixture of I and bromopyridine was obtained. The longer reaction period and higher temperature were used to ensure complete conversion.

(7) A. E. Chichibabin and I. L. Knunianz [*Ber.*, **61**, 427 (1928)] give 88° (15 mm.).

(8) F. W. Bergstrom, H. G. Sturz, and H. W. Tracy [*J. Org. Chem.*, **11**, 239 (1946)] give 100–102° (18 mm.).

(9) Available from Engelhard Industries, Newark, N. J.

(10) Infrared spectra run by A. Kammer and W. Washburn of this laboratory.

(11) Adjacency to the double bond should move the C-3 signal further downfield than that of the C-4 and C-5 protons. The C-6 protons should be seen farthest downfield because of proximity to the heterocyclic nitrogen atom. Each should be a triplet split by the C-4 and C-5 protons, respectively.

(12) When the spectrum was run in $CDCl_3$, no signal for NH was seen, but a very strong chloroform peak appeared at 7.47. Evidence of exchange was confirmed by infared when the solution showed almost total elimination of NH at 2.9 μ and ND appeared at 3.9 μ. All other points in the n.m.r. spectra in $CDCl_3$ and $CHCl_3$ were identical.

(13) The triplet is not too well defined. There is a definite separation between it and the multiplet. The portion further downfield which we assign to the C-3 protons (see ref. 11) integrates to 2, while the multiplet integrates to 4.

protons in each solvent were represented by a single peak. The C-6 protons in each instance appeared as a triplet (J = 5 c.p.s.).[14]

Attempted Hydrolysis of VI (VIa).—The material was heated for about 4 hr. with 18% hydrochloric acid, cooled, made basic, and extracted with ether. Similarly, hydrolysis with a 20% sodium hydroxide solution was carried out. The cooled solution was extracted with ether. The two extracts were dried and concentrated. The residues were examined. Their n.m.r. spectra were unchanged. However, when hydrolysis was carried out in 20% sodium hydroxide for 18–20 hr., a sample of the solution submitted for n.m.r. showed complete removal of the methyl protons.

Acknowledgment.—The authors are indebted to Dr. John Tadanier of the Organic Research Department of this laboratory and to Professor Peter Beak of the University of Illinois at Urbana for the discussions of the n.m.r. data while trying to develop the structure of VI (VIa).

(14) The spectrum of VI (VIa) in dimethyl sulfoxide to which a few drops of concentrated hydrochloric acid were added showed the N-methyl protons as a doublet, 2.83 and 2.92 (J = 5 c.p.s.), and the C-6 protons were seen as an unsharp group with separate peaks (J = 2 c.p.s.) suggestive of two overlapping triplets probably caused by protonation of the heterocyclic nitrogen. The spectrum in concentrated hydrochloric acid also showed a doublet, 2.89 and 2.97 (J = 5 c.p.s.), for the N-methyl protons and split peaks, 3.45 and 3.49 (J = 2 c.p.s.), amid an unsharp group for the C-6 proton signal. These two spectra only establish that the protonated form of VI (VIa) exists as a resonance stabilized hybrid.

Microbial Hydroxylation of 5,6-Dihydrosolasodine

YOSHIO SATO, JAMES A. WATERS, AND HIDEHIKO KANEKO[1]

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda 14, Maryland

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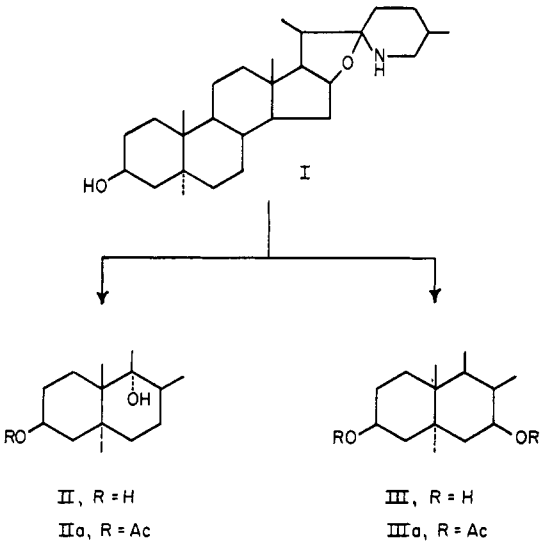
The hydroxylation of diosgenin, the well-known steroidal sapogenin,[2] with the fungus, *Helicostylum piriforme* (ATCC, 8992), leads to the formation of 7β,11α-dihydroxy- (10–15% yield) and 11α-hydroxy-7-oxodiosgenin (5–10% yield).[3] However, when the same fungus was incubated with the 5,6-dihydro derivative of diosgenin, *i.e.*, tigogenin, no detectable amount of hydroxylation was observed.[3]

In view of this somewhat surprising effect of the saturated 5,6-dihydro steroid in suppressing hydroxylation, it became of some interest to study the behavior of 5,6-dihydrosolasodine[4] (solasodan-3β-ol) since its precursor solasodine has previously been shown to hydroxylate readily to form 9α- (*ca.* 35%), 11α- (*ca.* 1%), and 7β-hydroxysolasodine (*ca.* 1%).[5]

The hydroxylation of 5,6-dihydrosolasodine (I), contrary to our expectation, was not altered to any appreciable degree in comparison with solasodine; the corresponding 9α-hydroxy- (II) and 7β-hydroxy-5,6-dihydrosolasodine (III) were obtained. The yields were roughly comparable with that obtained in the hydroxylation of solasodine. The diol II formed the expected O,N-diacetylhydroxy derivative, IIa, and III, the O,O,N-triacetate IIIa, upon acetylation.



The identity of diol II was determined by comparison with a sample of 9α-hydroxy-5,6-dihydrosolasodine prepared by the catalytic reduction of 9α-hydroxysolasodine.[5] The location of the hydroxyl function in the latter has been authenticated. The structure of the second diol III was likewise ascertained by comparison with a specimen of 7β-hydroxy-5,6-dihydrosolasodine obtained from the catalytic reduction of 7β-hydroxysolasodine.[5] Molecular rotation data was also in agreement for a 7β-configuration.

The seemingly contradictory data observed in the hydroxylation of tigogenin (5,6-dihydrodiosgenin) and 5,6-dihydrosolasodine attest to the necessity for more fundamental knowledge concerning the mechanism of microbiological hydroxylation.

Experimental[6]

Microbiological Hydroxylation of 5,6-Dihydrosolasodine.—Erlenmeyer flasks (500-ml.) each containing 200 ml. of corn steep medium,[5] were inoculated with newly formed spores of the fungus *H. piriforme* and agitated on a platform shaker at 29–30° for 67 hr. A solution of 25 mg. of dihydrosolasodine (m.p. 205–208°) in 2.0 ml. of ethanol was added to each flask. The flasks were incubated at 29–30° for 100 hr. The mycelium from the combined flasks was removed by filtration through a thin layer of Celite, and then washed with ethanol. The filtrate was made basic with ammonium hydroxide and extracted with chloroform. Thus in a typical run 1.5 g. of dihydrosolasodine yielded 2.0 g. of light brown, resinous residue, which was shown to consist principally of a lipid material and of three steroidal components by thin layer chromatography (silica gel G, *n*-heptane–ethyl acetate–triethylamine, 2:4:4).

The extract was chromatographed on 50 g. of neutral alumina (grade II, Woelm) with the following eluents: absolute ether, 0.5, 1.0, and 2.0% methanol in ether, finally chloroform. Each fraction was tested by t.l.c. The 0.5% methanol in ether eluate gave 50 mg. of the starting material. The 2% methanol in ether eluate yielded 542 mg. of crude crystalline material which through repeated fractional crystallization from chloroform–ether and from methanol furnished 350 mg. of rhombic prisms: m.p. 221–223°, $[\alpha]^{20}D$ −64.3 ± 2° (*c* 0.86, $CHCl_3$), $\lambda_{max}^{CHCl_3}$ 2.78 and 2.91 μ (OH and NH). It was identical in properties (melting point, mixture melting point, and infrared spectrum) with an authentic specimen of 9α-hydroxydihydrosolasodine (II).

(1) Visiting Scientist (1963–1964), National Institutes of Health.

(2) R. E. Marker, T. Tsukamoto, and D. L. Turner, *J. Am. Chem. Soc.*, **62**, 2525 (1940).

(3) S. Hayakawa and Y. Sato, *J. Org. Chem.*, **28**, 2742 (1963).

(4) L. H. Briggs, R. P. Newbold, and N. E. Stace, *J. Chem. Soc.*, 3 (1942).

(5) Y. Sato and S. Hayakawa, *J. Org. Chem.*, **28**, 2739 (1963).

(6) Melting points were taken on the Kofler block and are uncorrected. Microanalyses were performed by the Microanalytical Services Unit of this laboratory under the direction of Dr. W. C. Alford. The infrared spectra were taken on the Model 21 Perkin-Elmer infrared spectrometer by Mr. H. K. Miller and Mrs. A. H. Wright of this laboratory.