Anal. Calcd. for $C_{25}H_{46}$: C, 86.62; H, 13.38. Found: C, 86.87; H, 13.26.

4'-n-Nonyl-m-tercyclohexyl. In a similar manner, hydrogenation of 4'-*n*-nonenyl-*m*-terphenyl[6] gave 4'-*n*-nonyl-*m*-tercyclohexyl, column b.p. 188°/0.25 mm., n_D^{25} 1.4933–1.4937,[18] d_{25}^{25} 0.9044, pour point 15° F., viscosities 222 cs./100° F., 11.6 cs./210° F., heat of combustion 19,667 Btu./lb. Infrared bands: 2.41 (w), 3.48 (s), 3.73 (m), 6.90 (s), 7.24 (m), 7.40 (m), 7.92 (m), 9.64 (w), 10.23 (m), 11.20 (m), 11.78 (m), 13.84 (m) μ.

Anal. Calcd. for $C_{27}H_{50}$: C, 86.55; H, 13.45; Mol. Wt., 374.7. Found: C, 86.87; H, 13.28; Mol. Wt., 371.

Acknowledgment. The authors acknowledge the assistance of Messrs. J. G. Pomonis, M. VanDyke, and Miss E. A. Moore with the large scale syntheses.

DENVER 10, COLO.

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

The Synthesis and Properties of Some α,β-Unsaturated Valerolactams[1]

MAURICE SHAMMA AND PAUL D. ROSENSTOCK

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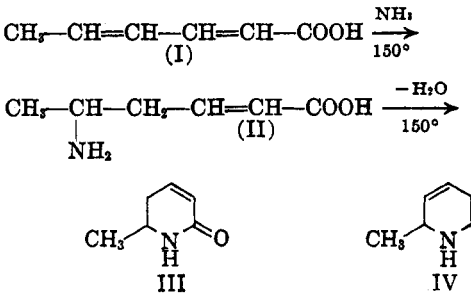
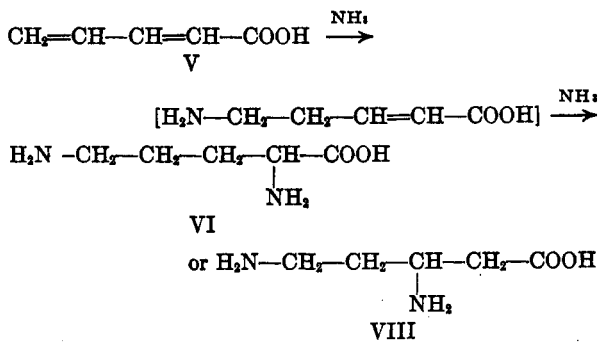
The condensation of sorbic acid (I) and 2-styrylacrylic acid (IX) with a variety of aliphatic and aromatic primary amines led to the formation of 1-substituted 6-methyl-5,6-dihydro-2-pyridone derivatives and 1-substituted 6-phenyl-5,6-dihydro-2-pyridone derivatives, respectively. Reduction of these cyclic lactams with lithium aluminum hydride, lithium aluminum hydride–aluminum chloride, or mixed aluminum hydrides yielded the corresponding substituted piperidines.

Fischer and Schlotterbeck[2] reported in 1904 that the condensation of sorbic acid (I) with ammonia led to the formation of an amino acid (II) which was isolated by means of its mercuric chloride complex. The free amino acid (II) upon heating readily eliminated water and cyclized to yield an unsaturated lactam (III) which had an analysis corresponding to C_6H_9NO. On the basis of a carbon hydrogen analysis, Fischer and Schlotterbeck assigned structure III to the lactam. No degradative studies were undertaken by them to ascertain the position of the double bond and, in a fairly recent review article, Mosher[3] assigned structure IV to the lactam.



In 1905, Fischer and Raske[4,5] also reported that the addition of ammonia to vinylacrylic acid (V) produced a diaminovaleric acid (VI). Subsequently, Riesser[6] claimed that the melting points of the mono- and dipicrates of the diaminovaleric acid (VI) corresponded to those of ornithine (VII). The structure of these products cannot be considered as definitely established, however, for there are substantial theoretical arguments that could predict that VI is actually 3,5-diaminovaleric acid (VIII).



Finally, Riedel[7] reported that the methyl ester of 2-styrylacrylic acid (IX) does not react with amines or ammonia.

In the light of the confusion which existed in the literature concerning the 1,6-addition of amines and ammonia to doubly unsaturated conjugated acids it was of interest to repeat and enlarge the scope of the reported reaction of sorbic acid (I) with ammonia and extend it to 2-styrylacrylic acid (IX).

In the present investigation the method of Fischer and Schlotterbeck was slightly modified. Sorbic acid (I) was condensed with aqueous ammonia to yield the amino acid II which was cyclized, without isolation, to form the monoaddition product III. Little or no reaction occurred between sorbic acid (I) and ammonia at temperatures below 150°, and it was therefore necessary to employ a

(1) This research was supported by Grant No. G5105 from the National Science Foundation.

(2) E. Fischer and F. Schlotterbeck, *Ber.*, **37**, 2357 (1904).

(3) H. S. Mosher, *Heterocyclic Compounds*, R. C. Elderfield, Editor, John Wiley and Sons, Inc., New York, N. Y., 1950, Vol. I, p. 651.

(4) E. Fischer and K. Rask, *Ber.*, **38**, 3607 (1905).

(5) J. W. Ralls, *Chem. Rev.*, 59, 329 (1959).

(6) O. Riesser, *Z. Physiol. Chim.*, **49**, 248 (1906).

(7) A. Riedel, *Ann.*, **361**, 96 (1908).

hydrogenation bomb as an autoclave. Addition of ammonia to sorbic acid (I) occurred readily at 180°. Raising the temperature to 200° had no effect on the yield of III, but in runs below 120° only unchanged sorbic acid (I) could be isolated. No tendency towards bis addition in the reaction could be noted.

6-Methyl-5,6-dihydro-2-pyridone (III) exhibited strong infrared absorption between 6.0 and 6.2 μ and absorbed in the ultraviolet at 252 mμ (log ϵ 3.19). The latter absorption indicates that the lactam function and the double bond are conjugated, as isolated double bonds or isolated lactam functions do not absorb above 210 mμ in the ultraviolet.[8] Thus, on the basis of this ultraviolet absorption the structure proposed by Fischer and Schlotterbeck is correct.

Reduction of III with excess lithium aluminum hydride in tetrahydrofuran yielded 2-methylpiperidine (XII) which was characterized as its hydrochloride and hydrobromide salts.

The condensation of sorbic acid (I) with methylamine produced two products, depending upon the temperature employed. Thus, at 90° the sole product was 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII) while at 150–180° an almost quantitative yield of 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) was obtained. At intermediate temperature varying amounts of XIII and XIV were produced. It was found that the condensation at 90° could be carried out simply in an ordinary reflux set-up equipped with a mercury pressure trap. However, the high temperature condensation had to be run in an autoclave.

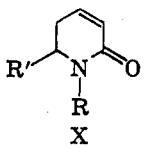
The low temperature condensation product XIII readily absorbed bromine to form a solid dibromide that decomposed in a matter of minutes to a resinous oil that could not be characterized. The lactam exhibited an ultraviolet absorption maximum at 252 mμ (log ϵ 3.14) which indicated that the double bond and the lactam function are conjugated.

Reduction of the unsaturated lactam XIII with lithium aluminum hydride in ether gave 1,2-dimethylpiperidine (XV) in 60% yield, while reduction with lithium aluminum hydride–aluminum chloride gave an almost quantitative yield of the amine XV.

1,6-Dimethyl-4-(*N*-methylamino)-2-piperidone (XIV), which is formed in the high temperature condensation of sorbic acid (I) with methylamine, slowly undergoes elimination of methylamine to yield 1,6-dimethyl-5,6-dihydropyridone (XIII). The presence of the methylamino function in the lactam (XIV) is indicated by a strong peak at 3.1 μ (N—H) in the infrared. In addition, the aminolactam (XIV) readily forms a hydrochloride salt (XVI) and also on exhaustive methylation yields 1,6-dimethyl-4-(*N*-trimethylammonium)-2-piperidone iodide (XVII).

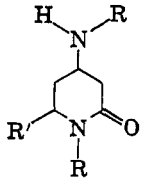
Reduction of XIV with lithium aluminum hydride in ether gave an almost quantitative yield of 1,2-dimethyl-4-(*N*-methylamino)piperidine (XVIII). This amine was characterized by means of its dihydrochloride and dihydrobromide salts.

The condensation of sorbic acid (I) with aniline at 190° yielded predominantly the monoaddition product XIX. In most instances there was a tendency toward some bis addition to form the aminolactam XX as indicated by varying intensities of absorption at 3.1 μ in the infrared spectrum of crude XIX. Raising the temperature above 190° did not appreciably increase the yield of 1-phenyl-4-(*N*-phenylamino)-6-methyl-2-piperidone (XX), and no further attempts were made to isolate this compound. Also, in the few instances where XX was isolated it eliminated in a matter of hours to give aniline and the lactam XIX.



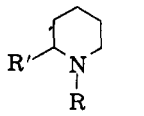
X

Compound	R	R′
XIII	Methyl	Methyl
XIX	Phenyl	Methyl
XXIV	Benzyl	Methyl
XXVII	Methyl	Phenyl
XXX	Benzyl	Phenyl
XXXIII	Phenyl	Phenyl

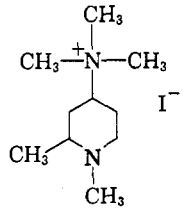


XI

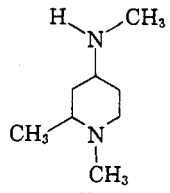
XIV	Methyl	Methyl
XX	Phenyl	Methyl
XXV	Benzyl	Methyl



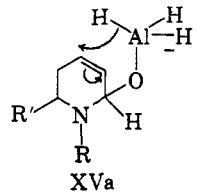
XII	Hydrogen	Methyl
XV	Methyl	Methyl
XXII	Phenyl	Methyl
XXVI	Benzyl	Methyl
XXVIII	Methyl	Phenyl
XXXII	Benzyl	Phenyl



XVII



XVIII



XVa

Catalytic hydrogenation of XIX with a platinum dioxide catalyst consumed one mole of hydrogen to yield 1-phenyl-6-methyl-2-piperidone (XXI). Reduction of XIX with lithium aluminum hydride yielded 1-phenyl-2-methylpiperidine (XXII) in good yield. Reaction of the base XXII with methyl iodide gave a crystalline methiodide derivative. However, the hydrobromide, hydrochloride, and perchlorate salts of the amine were oils.

Treatment of an aqueous hydrobromic acid solution of 1-phenyl-2-methylpiperidine (XXII)

(8) A. E. Gillam and E. S. Stern, *An Introduction to Electronic Absorption Spectrography in Organic Compounds*, Edward Arnold, Inc., London, England, 2nd Edition, 1957, pp. 43 and 47.

with excess bromine led to the formation of a crystalline monobromide hydrobromide derivative XXIII. The ionic bromine in XXIII was immediately precipitated by an aqueous ethanolic solution of silver nitrate. However, the nonionic bromine atom was completely inert toward this reagent and gave no precipitate of silver bromide, even after two days refluxing with excess reagent. The non-ionic bromine was, therefore, assigned to the aromatic ring. On the basic of the fact that anilinium, *N*-methylanilinium, and *N,N*-dimethylanilinium ions are all *meta* directing substituents,[9,10] the nonionic bromine atom has tentatively been assigned to the *meta* position. Thus, the monobromide hydrobromide XXIII is 1-(*m*-bromophenyl)-2-methylpiperidine hydrobromide.

In all of the lithium aluminum hydride reductions run during this investigation unchanged starting materials could be isolated in addition to the desired amines. It appeared that lithium aluminum hydride was not the most efficient reducing agent and, therefore, several other reducing agents were tested in an attempt to improve the yields. The use of tetrahydrofuran as a solvent generally gave lower yields, but it was the only solvent that could be used in the case of 6-methyl-5,6-dihydro-2-pyridone (III) because of the insolubility of this lactam in ether.

1-Phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) was chosen as the model compound for an extensive study of the reduction of α,β-unsaturated lactams with metal hydrides because of its easy availability and the great stability of its reduction product 1-phenyl-2-methylpiperidine (XXII). The results of the reductions with various reducing agents are summarized in Table I.

TABLE I

REDUCTION OF 1-PHENYL-6-METHYL-5,6-DIHYDRO-2-PYRIDONE (XIX) TO 1-PHENYL-2-METHYLPIPERIDINE (XXII)

No.	Reducing Agent[a]	Solvent	% Yield of XXII
1	$LiAlH_4$	Ether	65
2	$LiAlH_4$	Tetrahydrofuran	39
3	$^1/_2$ mole eq. $LiAlH_4$	Ether	46
4	Diethylaluminum hydride	Benzene-hexane	0.5
5	$LiAlH_4$—Al_2Cl_6	Ether	94
6	$LiAl(OC_2H_5)_3H$	Ether	45
7	$LiAl(OC_2H_5)_2H_2$	Ether	70
8	$LiAl(OC_2H_5)H_3$	Ether	84

[a] Unless otherwise stated excess reducing agent was employed.

A gas chromatographic analysis of the product obtained from Run 5 indicated that distillation of the crude amine netted 1-phenyl-6-methylpiperidine (XXII) of better than 99.5% purity. With the exception of the product obtained from Run 3, the infrared spectra of all of the distilled amine products obtained from the various reducing agents were identical. A gas chromatographic analysis of the distilled product from Run 3 indicated that it was composed of 1-phenyl-2-methylpiperidine (XXII) of approximately 96% purity.

From the data in Table I it can be seen that the reducing agents with at least three hydrogen atoms attached to the aluminum gave the best results. It is possible that during the course of the reduction an intermediate such as XVa is formed which, by the electron shifts indicated, ultimately leads to a saturated heterocyclic ring.

Significantly enough reduction of the saturated lactam 1-phenyl-6-methyl-2-piperidone (XXI) with lithium aluminum hydride, a case where no intermediate of the type XVa is required, gave an 84% yield of 1-phenyl-2-methylpiperidine (XXII).

Benzylamine was found to react with sorbic acid (I) to form predominantly the monoaddition product XXIV. Here again there is a tendency toward bis addition to form small amounts of 1-benzyl-4-(*N*-benzylamino)-6-methyl-2-piperidone (XXV).

Reduction of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with excess lithium aluminum hydride in ether yielded 1-benzyl-2-methylpiperidine (XXVI). This amine was characterized as its methiodide and hydrobromide salts.

The results obtained in the reduction of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with various reducing agents are summarized in Table II. As will be noticed by a comparison of the data in Table I with that in Table II, the reduction of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) gave higher yields of the corresponding amine than were obtained in the reduction of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV). However, the same general trend as to the relative effectiveness of each reducing agent was observed.

TABLE II

REDUCTION OF 1-BENZYL-6-METHYL-5,6-DIHYDRO-2-PYRIDONE (XXIV) TO 1-BENZYL-2-METHYLPIPERIDINE (XXVI)

Reducing Agent[a]	% Yield of XXVI
$LiAlH_4$	40
$LiAlH_4$—Al_2Cl_6	66
$LiAl(OC_2H_5)_3H$	32
$LiAl(OC_2H_5)_2H_2$	50
$LiAl(OC_2H_5)H_3$	68

[a] Ether was employed as the solvent and excess reagent was used in all of the reductions.

The condensation of 2-styrylacrylic acid (IX) with methylamine at 180° and 250 psi. gave a 49% yield of 1-methyl-6-phenyl-5,6-dihydro-2-

(9) L. F. Fieser and M. Fieser, *Organic Chemistry*, Reinhold Publishing Corporation, New York, N. Y., Third Edition, 1956, p. 569.

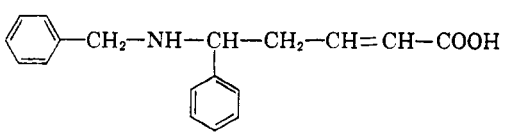
(10) G. W. Wheland, *Resonance in Organic Chemistry*, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 491.

pyridone (XXVII). There was no tendency toward the formation of bis-addition products in any of the reactions of 2-styrylacrylic acid with amines. It was found that little or no reaction occurred between the acid and methylamine below 140°, and in all instances where the condensation was attempted below 110° an almost quantitative recovery of 2-styrylacrylic acid was achieved. An attempted condensation of 2-styrylacrylic acid with ammonia at 190° and 300 p.s.i. gave back only unreacted acid. Evidently, ammonia is not reactive enough to undergo addition to this acid at this temperature.

Reduction of XXVII with excess lithium aluminum hydride in ether yielded 1-methyl-2-phenylpiperidine (XXVIII). The hydrochloride, hydrobromide, perchlorate, and methiodide salts of XXVIII were all oils that could not be crystallized.

A white crystalline dibromide hydrobromide derivative XXIX was obtained when an aqueous hydrobromic acid solution of 1-methyl-2-phenylpiperidine (XXVIII) was treated with excess bromine. The two nonionic bromine atoms were inert toward alcoholic silver nitrate solution, even after two days refluxing, and were therefore assigned to the aromatic nucleus. On the basis of the fact that benzyltrimethylammonium ion is *ortho-para* directing[10] the two bromine atoms have tentatively been assigned to the 2- and 4-positions on the aromatic ring. This assignment is further substantiated by the presence of weak peaks at 8.12, 8.25, 8.30, 8.40, 8.55, and 9.04 μ corresponding to a 1,2,4-trisubstituted benzene nucleus[11] in the infrared spectrum of XXIX. Thus, the dibromide hydrobromide XXIX is probably 1-methyl-2-(2′,4′-dibromophenyl)piperidine hydrobromide.

The reaction of 2-styrylacrylic acid (IX) with benzylamine gave 1-benzyl-6-phenyl-5,6-dihydro-2-pyridone (XXX) in low yields. Large amounts of polymeric material were formed in the course of the condensation of the amine with the acid. This suggests that the intermolecular condensation of the intermediate aminoacid XXXI may be favored over its intramolecular condensation.



XXXI

Reduction of XXX with excess lithium aluminum hydride in ether gave 1-benzyl-2-phenylpiperidine (XXXII), which was characterized as the hydrochloride and hydrobromide salts.

Finally, the condensation of 2-styrylacrylic acid (IX) with aniline yielded small amounts of 1,6-diphenyl-5,6-dihydro-2-pyridone (XXXIII).

EXPERIMENTAL

Infrared spectra were determined on a Perkin Elmer Model 21 double-beam spectrophotometer. All infrared spectra of solids were run as potassium bromide pellets; all liquids were run as films. All melting points are uncorrected. Elemental analyses are by Alfred Bernhardt Mikroanalytisches Laboratorium, Mulheim, Germany.

6-Methyl-5,6-dihydro-2-pyridone (III). The method of Fischer and Schlotterbeck[3] was slightly modified as follows:

Sorbic acid (I) (20 g., 0.18 mole) was heated with 500 ml. of aqueous ammonia (saturated at 0°) in a 1200 ml. hydrogenation bomb for 1 day at 180°. The initial pressure was 500 p.s.i. and the final pressure was 256 p.s.i. At the end of this period the bomb was allowed to cool to room temperature, opened, and the honey colored liquid transferred to a 1 l. distilling flask. The bomb was washed several times with hot methanol and the washings added to the product. The combined product and washings were evaporated under reduced pressure and with heating to a syrupy residue. This residue was dissolved in a minimum amount of hot methanol and transferred to a 100 ml. distilling flask. The flask was placed on an oil bath and heated at 150° for 3 hr. (or until no more ammonia was evolved), cooled, and the resulting residue distilled *in vacuo* at 6 mm. A fraction which tended to solidify in the condenser distilled over at 130–136°. (In order to facilitate the distillation steam was run through the condenser jacket). The distillate was extracted several times into hot hexane, the hexane washings filtered, and evaporated to 300 ml. After cooling for several hours the solution was filtered, the precipitate washed with hexane, and dried on the funnel to yield 6.8 g. (34%) of white crystalline solid; m.p. 93–98°. This product was sufficiently pure for preparative purposes.

A second recrystallization of the product from hexane netted 6.6 g. (31%) of white crystalline solid; m.p. 100–102°. Two additional recrystallizations from the same solvent gave an analytic sample that exhibited a melting point of 103°; reported m.p. 103°. Infrared peaks at: 3.20 (N—H), 5.90–6.05 (amide) and 6.25 μ (conjugated double bond). Ultraviolet absorption maximum at 252 mμ (log ε 3.19).

Anal. Calcd. for C_6H_9NO: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.83; H, 8.18; N, 12.52.

2-Methylpiperidine (XII). Reduction of 10 g. (0.09 mole) of 6-methyl-5,6-dihydro-2-pyridone (III) with 7.6 g. (0.2 mole) of lithium aluminum hydride in tetrahydrofuran resulted in a 0.8 g. (9.2%) yield of 2-methylpiperidine (XII); b.p. 105–110° at 717 mm.; reported[12] b.p. 117–118° at 745. mm.

The infrared spectrum of this compound was identical with that of a sample of known 2-methylpiperidine obtained from The K and K Laboratories.

Treatment of the 2-methylpiperidine (XII) obtained above with dry hydrogen chloride gas gave 2-methylpiperidine hydrochloride; m.p. 209–210°.

Treatment of the 2-methylpiperidine (XII) obtained above with aqueous hydrobromic acid yielded 2-methylpiperidine hydrobromide; m.p. 189–190°.

The 2-methylpiperidine hydrobromide and 2-methylpiperidine hydrobromide prepared above gave undepressed mixed melting points with known samples of 2-methylpiperidine hydrobromide and 2-methylpiperidine hydrochloride, respectively. In addition, the infrared spectra of the corresponding compounds were identical.

1,6-Dimethyl-5,6-dihydro-2-pyridone (XIII). In a 1-l. round bottom flask equipped with a condenser and a mercury

(11) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1958, p. 82.

(12) I. Heilbron and H. M. Bunbury, *Dictionary of Organic Compounds*, Oxford University Press, New York, N. Y., 1953, Vol. IV, pp. 214–215.

pressure trap was placed 40 g. (0.36 mole) of sorbic acid (I) and 800 ml. of 40% aqueous methylamine solution. The mixture was heated at 90° for 15 hr. and, at the end of this period, the solution was evaporated with heating and under reduced pressure to a brown syrupy residue. This residue was then dissolved in a minimum amount of hot methanol, transferred to a 200-ml. distilling flask, and heated on an oil bath at 150° for 3 hr. (or until no more methylamine was evolved). The residue was distilled *in vacuo* and the fraction boiling at 90–100° at 5 mm. was collected. This cut consisted mainly of 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII) contaminated with varying amounts of sorbic acid (I) and 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV). The compound was purified by adding the crude distillate to 200 ml. of 10% sodium hydroxide solution and continuously extracting the resulting solution with ether. The ether extract was then evaporated and residue was added to 200 ml. of 10% hydrochloric acid solution. The acidic solution was continuously extracted with ether for 1 day, the ether layer was dried, filtered, and the ether distilled off at atmospheric pressure. The residue was distilled *in vacuo* to yield 20 g. (44%) of 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII) as a colorless oil; b.p. 92–95° at 5 mm. This product was sufficiently pure for preparative purposes. One additional distillation furnished an analytic sample; b.p. 83–84° at 1 mm. Ultraviolet absorption maximum at 252 mμ (log ε 3.14).

Anal. Calcd. for $C_7H_{11}NO$: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.21; H, 8.71; N, 11.37.

1,2-Dimethylpiperidine (XV). *Method A. Lithium aluminum hydride in ether.* Reduction of 10 g. (0.08 mole) of 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII) with 3.8 g. (0.1 mole) of lithium aluminum hydride in ether yielded 4.2 g. (47%) of 1,2-dimethylpiperidine (XV); b.p. 123–126° at 737 mm.; reported b.p. 126–127° at 742 mm.

Method B. Lithium aluminum hydride-aluminum chloride. The method of Nystrom[13] was slightly modified as follows: The mixed hydride was prepared by introducing 13.3 g. (0.1 mole) of dried granular aluminum chloride in 100 ml. of ether to 3.8 g. (0.1 mole) of lithium aluminum hydride suspended by stirring in 100 ml. of ether. To this reagent was added, with stirring and under a reflux condenser, 10 g. (0.08 mole) of 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII) dissolved in 75 ml. of ether at such a rate so as to cause gentle refluxing. The mixture was stirred for 18 hr. at room temperature and, at the end of this period, the excess of hydride was decomposed by the cautious addition of 100 ml. of water. The mixture was filtered and the precipitate washed well with ether. The precipitate was stirred for 1 hr. with 200 ml. of ether, filtered, and washed with ether. The combined filtrates were dried over anhydrous calcium sulfate, filtered, and distilled at atmospheric pressure. The fraction boiling at 125–128° at 748 mm. was collected to yield 8 g. (91%) of 1,2-dimethylpiperidine (XV).

The infrared spectrum of the reduction product was identical with that of known 1,2-dimethylpiperidine prepared by a Clarke-Eschweiler methylation of 2-methylpiperidine.

Treatment of the 1,2-dimethylpiperidine (XV) prepared above with dry hydrogen chloride gas gave 1,2-dimethylpiperidine hydrochloride; m.p. 258–259°.

This compound gave an undepressed mixed melting point with an authentic sample of 1,2-dimethylpiperidine hydrochloride. Furthermore, the infrared spectra of the two compounds were identical.

1,6-Dimethyl-4-(N-methylamino)-2-piperidone (XIV). Sorbic acid (I) (20 g., 0.18 mole) was heated with 450 ml. of 40% methylamine solution in a 1200 ml. capacity hydrogenation bomb for 1 day at 180°. At the end of this period the bomb was cooled to room temperature, opened, and the honey colored liquid transferred to a 1-l. distilling flask. The bomb was washed several times with hot methanol and the washings added to the product. The combined product and washings were evaporated under reduced pressure and with heating to a syrupy residue. This residue was dissolved in a minimum amount of hot methanol and transferred to a 100 ml. distilling flask. The flask was placed in an oil bath and heated at 150° for 3 hr. (or until no more methylamine was evolved), cooled, and the resulting residue distilled *in vacuo*. A 22-g. (85%) fraction of pale yellow liquid boiling at 120–124° at 4 mm. was collected. Redistillation of this liquid netted 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) as a colorless hygroscopic liquid; b.p. 124–125° at 5 mm.

Anal. Calcd. for $C_8H_{16}N_2O$: C, 61.54; H, 10.27; N, 17.94. Found: C, 62.09; H, 10.03; N, 17.18.

Nitrogen values for this compound were always low, as on standing it eliminates methylamine to form 1,6-dimethyl-5,6-dihydro-2-pyridone (XIII).

1,6-Dimethyl-4-(N-methylammonium)-2-piperidone chloride (XVI). An ethanol solution (3 ml.) of 200 mg. (1.3 mmoles) of 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) was saturated with dry hydrogen chloride gas and a small amount of ether was added. After standing overnight the solution was filtered, the precipitate washed with ether and dried on the funnel to yield 245 mg. (97%) of white crystalline solid; m.p. 166–176°. Recrystallization of the product from methanol-ether gave 231 mg. (94%) of white crystalline hygroscopic solid; m.p. 190–194°. Two additional recrystallizations from the same solvent combination netted an analytic sample that exhibited a melting point of 196–198°.

Anal. Calcd. for $C_8H_{17}N_2OCl$: C, 49.86; H, 8.89; N, 14.54; Cl, 18.40. Found: C, 49.86; H, 8.70; N, 14.52; Cl, 18.02.

1,6-Dimethyl-4-(N-trimethylammonium)-2-piperidone iodide (XVII). Exhaustive methylation of 9 g. (0.05 mole) of 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) with 30 g. of methyl iodide in 20 ml. of dry methanol yielded 12.1 g. (68%) of pale yellow crystalline solid; m.p. 194–198° dec. Five recrystallizations from methanol-ether gave an analytic sample that exhibited a melting point of 211–213° dec.

Anal. Calcd. for $C_{10}H_{21}N_2OI$: C, 38.47; H, 6.78; N, 8.97; I, 40.68. Found: C, 38.85; H, 6.39; N, 9.25; I, 40.60.

1,2-Dimethyl-4-(N-methylamino)piperidone (XVIII). Reduction of 10 g. (0.065 mole) of 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) with 7.6 g. (0.2 mole) of lithium aluminum hydride in ether yielded 8.7 g. (96%) of 1,2-dimethyl-4-(*N*-methylamino)piperidine (XVIII); b.p. 38–39° at 1 mm.

Treatment of the free amine with dry hydrogen chloride gas gave 1,2-dimethyl-4-(*N*-methylamino)piperidine dihydrochloride as a white solid; m.p. 270–273° in a sealed tube. Three recrystallizations from ether-methanol furnished an analytic sample; m.p. 273–276° in a sealed tube.

Anal. Calcd. for $C_8H_{20}N_2Cl_2$: C, 44.65; H, 9.37; N, 13.02; Cl, 32.96. Found: C, 44.52; H, 9.17; N, 12.75; Cl, 32.98.

Treatment of the 1,2-dimethyl-4-(*N*-methylamino)piperidine (XVIII) prepared above with aqueous hydrobromic acid resulted in the formation of 1,2-dimethyl-4-(*N*-methylamino)piperidine dihydrobromide; m.p. 253–258°. One recrystallization from methanol-ether gave a white crystalline solid; m.p. 258–259°. The analytical sample exhibited a melting point of 264–266°.

Anal. Calcd. for $C_8H_{20}N_2Br_2$: C, 31.60; H, 6.63; N, 9.21; Br, 52.56. Found: C, 31.70; H, 6.60; N, 9.13; Br, 52.87.

1-Phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX). Sorbic acid (I) (40 g., 0.36 mole) was heated under reflux with 800 ml. of aniline for 1 day. At the end of this period the solution was evaporated under reduced pressure and with heating to a syrupy residue. This dark brown residue was dissolved in a minimum amount of hot methanol and transferred to a 250 ml. flask. The flask was heated on an oil bath at 190° for 4 hr., cooled, and the resulting tar distilled *in vacuo* at 10 mm. A pale yellow oily fraction distilled over at

(13) R. F. Nystrom, *J. Am. Chem. Soc.*, 77, 2544 (1955); 81, 610 (1959).

180–186°. This fraction consisted mainly of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) contaminated by small amounts of sorbic acid (I) and 1-phenyl-4-(*N*-phenylamino)-6-methyl-2-piperidone (XX). The product was purified by dissolving it in 500 ml. of ether and extracting the etheral solution with three 100-ml. portions of 10% hydrochloric acid solution, three 100-ml. portions of 10% sodium hydroxide solution, and finally with 100 ml. of water. The organic layer was dried over anhydrous calcium sulfate, filtered, and the ether removed on a steam bath under a stream of nitrogen. The residue was distilled *in vacuo* to yield 26 g. (39%) of analytically pure product as a colorless oil; 180–186° at 10 mm.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.67; H, 7.00; N, 7.48. Found: C, 76.61; H, 6.93; N, 7.33.

Hydrogenation of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with a platinum dioxide catalyst in ethanol solution consumed 1 mole of hydrogen to yield 1-phenyl-6-methyl-2-piperidone (XXI); b.p. 180–187° at 10 mm.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.66; N, 7.40. Found: C, 76.47; H, 7.87; N, 7.38.

1-Phenyl-2-methylpiperidine (XXII). *Method A. Lithium aluminum hydride in ether.* Reduction of 9 g. (0.048 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with 3.8 g. (0.1 mole) of lithium aluminum hydride in ether gave a 5.4 g. (65%) yield of pale yellow liquid; b.p. 123–127° at 9 mm. A second distillation netted a colorless analytic sample, b.p. 124–126° at 9 mm.

Anal. Calcd. for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.40; H, 9.30; N, 8.05.

If the same procedure was employed using 0.5 mole of lithium aluminum hydride per mole of lactam the yield of 1-phenyl-2-methylpiperidine (XXII) was only 46%.

Method B. Lithium aluminum hydride in tetrahydrofuran. Reduction of 8.5 g. (0.045 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with 3.8 g. (0.1 mole) of lithium aluminum hydride in tetrahydrofuran yielded 3 g. (39%) of 1-phenyl-2-methylpiperidine (XXII); b.p. 69–78° at less than 0.5 mm.

Method C. Diethylaluminum hydride. A solution of 7.8 g. (0.042 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) in 15 ml. of dry benzene was treated with the equivalent of 10 g. (1.1 moles) of diethylaluminum hydride dissolved in 40 ml. of hexane. The addition was carried out under a stream of nitrogen. After the addition was complete the reaction mixture was stirred for 6 hr. under a stream of nitrogen. At the end of this period the excess hydride was decomposed by the cautious addition of dry *t*-butyl alcohol and the resulting solution was stirred overnight. The following day the solution was triturated with 7 ml. of water, filtered, and the precipitate washed with ether. The precipitate was then stirred for 1 hr. with 100 ml. of ether filtered, and washed with ether. The combined filtrates were dried over anhydrous calcium sulfate, filtered, and the solvents removed on a steam-bath under a stream of nitrogen. The residue was distilled *in vacuo* to yield 0.4 g. (0.55%) of pale yellow liquid; b.p. 124–128° at 9 mm. Large amounts of starting material could also be isolated.

Method D. Lithium aluminum hydride-aluminum chloride. Reduction of 9.3 g. (0.05 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with lithium aluminum hydride-aluminum chloride by the method used to prepare 1,2-dimethylpiperidine (XV) yielded 8.1 g. (94%) of 1-phenyl-2-methylpiperidine (XXII); b.p. 70–76° at less than 0.5 mm.

Method E. Lithium triethoxyaluminum hydride. The method of Brown[14] was employed for the preparation of all mixed ethoxyalumimum hydrides.

Reduction of 9.3 g. (0.05 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with 0.2 mole of lithium triethoxyaluminum hydride in ether gave 3.9 g. (45%) of pale yellow liquid; b.p. 70–74° at less than 0.5 mm.

(14) H. C. Brown, *et al.*, *Tetrahedron Letters*, **3**, 9 (1959).

Method F. Lithium diethoxyaluminum hydride. Reduction of 9.3 g. (0.05 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with 0.2 mole of lithium diethoxyaluminum hydride in ether yielded 6.1 g. (70%) of pale yellow liquid; b.p. 70–80° at less than 0.5 mm.

Method G. Lithium monoethoxyaluminum hydride. Reduction of 9.3 g. (0.05 mole) of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) with 0.2 mole of lithium monoethoxyaluminum hydride in ether yielded 7.3 g. (84%) of pale yellow liquid; b.p. 68–78° at less than 0.5 mm.

Method H. Lithium aluminum hydride in ether and 1-phenyl-6-methyl-2-piperidone (XXI). Reduction of 5 g. (0.028 mole) of 1-phenyl-6-methyl-2-piperidone (XXI) with 3.8 g. (0.1 mole) of lithium aluminum hydride in ether yielded 4.1 g. (81%) of pale yellow liquid; b.p. 69–76° at less than 0.5 mm.

Treatment of the above prepared 1-phenyl-2-methylpiperidine (XXII) (3 g., 0.017 mole) with 4.31 g. (0.03 mole) of methyl iodide in 10 ml. of absolute methanol resulted in the formation of 3.9 g. (70%) of pale purple crystals; m.p. 132–137° dec. Ten recrystallizations from methanol-ether yielded a white crystalline analytic sample; m.p. 136–140° dec.

Anal. Calcd. for $C_{13}H_{18}NI$: C, 49.22; H, 6.36; N, 4.42; I, 40.01. Found: C, 49.21; H, 5.94; N, 4.49; I, 40.02.

1-(m-Bromophenyl)-2-methylpiperidine hydrobromide (XXIII). 1-Phenyl-2-methylpiperidine (XXII) (1 g., 0.0053 mole) was dissolved in an excess of 48% aqueous hydrobromic acid and 3 ml. of bromine was added to the resulting solution. The reaction mixture was allowed to stand at room temperature for 1 day and, at the end of this period, the water was evaporated on a steam bath under a stream of nitrogen. The residue was dried *in vacuo* overnight and recrystallized from methanol-ether to yield 1.5 g. (84%) of pale yellow crystals; m.p. 232–238° dec. Recrystallization from methanol-ether yielded 1.3 g. (71%) of white crystals; m.p. 237–241° dec. Two additional recrystallizations from the same solvent combination gave an analytic sample that exhibited a melting point of 241–244° dec.

Anal. Calcd. for $C_{12}H_{17}NBr_2$: C, 43.01; H, 5.11; N, 4.18; Br, 47.70. Found: C, 42.90; H, 5.20; N, 4.25; Br, 47.78.

1-Benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV). This compound was prepared from 40 g. (0.36 mole) of sorbic acid (I) and 700 ml. of benzylamine by the method used to make 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX). The yield of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) was 31 g. (41%); b.p. 189–197° at 10 mm.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.10; H, 7.20; N, 7.25.

1-Benzyl-2-methylpiperidone (XXVI). *Method A. Lithium aluminum hydride in ether.* Reduction of 10 g. (0.05 mole) of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with 3.8 g. (0.1 mole) of lithium aluminum hydride in ether gave a 3.7 g. (40%) yield of pale yellow oil; b.p. 127–135° at 13 mm. A second distillation netted a colorless liquid analytical sample; b.p. 70–75° at less than 0.5 mm.

Anal. Calcd. for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.59; H, 10.09; N, 7.76.

Method B. Lithium aluminum hydride-aluminum chloride. Reduction of 14 g. (0.07 mole) of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with lithium aluminum hydride-aluminum chloride by the method employed to prepare 1,2-dimethylpiperidine (XV) yielded 8.6 g. (66%) of pale yellow liquid; b.p. 127–135° at 13 mm.

Method C. Lithium triethoxyaluminum hydride. Reduction of 8 g. (0.04 mole) of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with 0.2 mole of lithium triethoxyaluminum hydride in ether gave 2.4 g. (32%) of pale yellow liquid; b.p. 127–135° at 13 mm.

Method D. Lithium diethoxyaluminum hydride. Reduction of 8 g. (0.04 mole) of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with 0.2 mole of lithium diethoxyaluminum hydride in ether gave 3.7 g. (50%) of pale yellow liquid; b.p. 126–135° at 12 mm.

Method E. Lithium monoethoxyaluminum hydride. Reduction of 10 g. (0.05 mole) of 1-benzyl-6-methyl-5,6-dihydro-2-pyridone (XXIV) with 0.2 mole of lithium monoethoxyaluminum hydride in ether led to the formation of 5 g. (68%) of pale yellow liquid; b.p. 126–136° at 12 mm.

1-Benzyl-2-methylpiperidine hydrobromide. 1-Benzyl-2-methylpiperidine (XXVI) (2.19 g., 0.011 mole) was dissolved in an excess of 48% hydrobromic acid solution and the resulting solution was evaporated to dryness on a steam bath under a stream of nitrogen. The residue was dried *in vacuo* for several hours and recrystallized from methanol-ether to yield 1.8 g. (73%) of white crystalline solid; m.p. 190–194° dec. Addition of ether to the filtrate netted a second crop of 0.4 g. of white crystalline solid; m.p. 186–194° dec.

Recrystallization of the first crop from ether-methanol gave 1.62 g. of white crystalline solid; m.p. 199–201° dec. Five additional recrystallizations from the same solvent combination gave an analytic sample that exhibited a melting point of 199–201° dec.

Anal. Calcd. for $C_{13}H_{20}NBr$: C, 57.78; H, 7.46; N, 5.18. Found: C, 57.54; H, 7.21; N, 5.14.

1-Benzyl-2-methylpiperidine methiodide. A solution of 1.8 g. (0.0097 mole) of 1-benzyl-2-methylpiperidine (XXVI) and 2.25 g. (0.015 mole) of methyl iodide in 10 ml. of absolute methanol was allowed to stand at room temperature for 1 day. At the end of this period ether was added to the point of turbidity, whereupon an oil separated. After cooling for several hours at −20° the oil solidified. The solid was filtered and washed well with ethyl acetate to yield 1.3 g. (40%) of pale yellow crystals; m.p. 169–174°. A second crop of 0.4 g. was obtained by addition of ether to the filtrate.

The first crop was purified by dissolving it in a minimum amount of cold methanol and adding ether to the point of turbidity. After standing for several hours at −20° the solution was filtered and the precipitate washed with ethyl acetate and dried on the funnel to yield 1.1 g. (34%) of white crystals; m.p. 170–173°. Six similar treatments of the product netted an analytic sample of white crystals that exhibited a melting point of 183–185°. The product was found to be sensitive to heat, and the analytic sample was dried at room temperature *in vacuo*.

Anal. Calcd. for $C_{14}H_{22}NI$: C, 50.76; H, 6.69; N, 4.23. Found: C, 50.51; H, 6.41; N, 4.31.

2-Styrylacrylic acid (IX). A mixture of 106 g. (167 ml., 1.14 mole) of freshly distilled cinnamaldehyde, 120 g. (1.15 mole) of malonic acid, and 120 g. (122 ml., 1.15 mole) of pyridine was heated for 18 hr. on a steam bath. During this period the color of the solution changed from yellow to orange and all of the malonic acid dissolved. At the end of this period the reaction mixture was cooled to 10° in an ice bath and a cold solution of 42.5 ml. (0.76 mole) of sulfuric acid in 100 ml. of water was added at such a rate that the temperature did not exceed 20°. A bright yellow oily precipitate formed almost immediately. The solution was filtered and the precipitate washed well with water. The crude product was purified by dissolving it in 1 l. of boiling methanol, filtering the resulting solution, and evaporating the methanol to a volume of 450 ml. The solution was slowly cooled to room temperature and placed in the refrigerator for 1 day to complete precipitation. (Seeding greatly speeds the rate of precipitation of the acid.) The solution was filtered and the precipitate washed with 100 ml. of cold methanol and air dried. The yield of pale yellow crystals was 70–79 g. (34–39%); m.p. 159–164°. This product was sufficiently pure for preparative purposes.

Three recrystallizations of a small aliquot of acid from methanol-hexane netted a white crystalline analytic sample; m.p. 165–167°; reported[15] m.p. 165–166°.

Anal. Calcd. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.61; H, 5.86.

(15) Ref. 12, p. 380.

1-Methyl-6-phenyl-5,6-dihydro-2-pyridone (XXVII). 2-Styrylacrylic acid (IX) (60 g., 0.34 mole) was heated with 900 ml. of 40% aqueous methylamine solution in a 3-l. hydrogenation bomb for 1 day at 180°. The reaction mixture was worked up as in the case of 1,6-dimethyl-4-(*N*-methylamino)-2-piperidone (XIV) to yield 33 g. (52%) of pale yellow oil; b.p. 184–190° at 13 mm. A second distillation yielded a colorless analytic sample; b.p. 186–188° at 13 mm.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.67; H, 7.00; N, 7.48. Found: C, 76.37; H, 6.93; N, 7.74.

1-Methyl-2-phenylpiperidine (XXVIII). Reduction of 10 g. (0.053 mole) of 1-methyl-6-phenyl-5,6-dihydro-2-pyridone (XXVII) with 3.8 g. (0.1 mole) of lithium aluminum hydride in ether yielded 4.5 g. (48%) of pale yellow liquid; b.p. 125–130° at 9 mm. A second distillation gave an analytical sample of colorless liquid; b.p. 125–130° at 13 mm.

Anal. Calcd. for $C_{12}H_{15}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.59; H, 9.30; N, 7.95.

1-Methyl-2-(2',4'-dibromophenyl)-piperidine hydrobromide (XXIX). 1-Methyl-2-phenylpiperidine (XXVIII) (1.68 g., 0.0097 mole) was dissolved in an excess of 48% hydrobromic acid and 3 ml. of bromine was added to the resulting solution. The reaction mixture was worked up as in the case of 1-(*m*-bromophenyl)-2-methylpiperidine (XXIII) to yield 3.2 g. (79%) of white crystals; m.p. 181–188° dec. Seven recrystallizations from methanol-ether furnished a white crystalline analytic sample; m.p. 214–215° dec. Weak infrared peaks at: 8.12, 8.25, 8.30, 8.40, 8.55, and 9.04 μ (1,2,4-trisubstituted benzene[11]).

Anal. Calcd. for $C_{12}H_{13}NBr_3$: C, 34.81; H, 3.90; N, 3.38. Found: C, 35.05; H, 4.15; N, 3.38.

1-Benzyl-6-phenyl-5,6-dihydro-2-pyridone (XXX). 2-Styrylacrylic acid (IX) (60 g., 0.34 mole) was heated under reflux with 200 ml. of pyridine and 70 ml. of benzylamine for 1 day. The reaction mixture was worked up as in the case of 1-phenyl-6-methyl-5,6-dihydro-2-pyridone (XIX) to yield 24 g. (27%) of amber colored viscous oil; b.p. 170–180° at less than 0.5 mm. The crude product was purified by redistillation to yield 20 g. (22%) of pale yellow oil that crystallized in the receiver; b.p. 130–160° at less than 0.5 mm. The solid was dissolved in 1 l. of hot hexane, filtered, and the hexane evaporated to a volume of 500 ml. A first crop of 8 g. (9%) of white crystalline solid was obtained; m.p. 100–110°. A second crop of 8.5 g. of pale yellow crystalline solid could be obtained by evaporating the mother liquor to 200 ml.

Three recrystallizations of the first crop from hexane netted a white crystalline analytic sample; m.p. 112–115°.

Anal. Calcd. for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.32. Found: C, 82.17; H, 6.25; N, 5.61.

1-Benzyl-2-phenylpiperidine (XXXII). Reduction of 6 g. (0.0023 mole) of 1-benzyl-6-phenyl-5,6-dihydro-2-pyridone (XXX) with 1.8 g. (0.05 mole) of lithium aluminum hydride in ether yielded 2.8 g. (47%) of pale yellow liquid that solidified in the receiver; b.p. 135–140° at less than 0.5 mm., m.p. 78–82°. This compound was used without further purification for the preparation of derivatives.

Reaction of the above obtained 1-benzyl-2-phenylpiperidine (XXXII) with aqueous hydrobromic acid yielded a white crystalline hydrobromide salt; m.p. 205–217° dec. Recrystallization from methanol-ether raised the melting point to 215–221° dec. and six additional recrystallizations from the same solvent combination yielded an analytical sample that exhibited a melting point of 220–224° dec.

Anal. Calcd. for $C_{18}H_{22}NBr$: C, 65.06; H, 6.67; N, 4.22; Br, 24.05. Found: C, 65.02; H, 6.73; N, 4.25; Br, 24.01.

Reaction of the 1-benzyl-2-phenylpiperidine (XXXII) prepared above with dry hydrogen chloride gas gave a white crystalline hydrochloride salt; m.p. 190–211° dec. Four recrystallizations from methanol-ether yielded an analytic sample that exhibited a melting point of 226–231° dec. in a sealed tube or 201–217° dec. on a block.

Anal. Calcd. for $C_{18}H_{22}NCl$: C, 75.11; N, 7.70; N, 4.48. Found: C, 74.98; H, 7.71; N, 4.50.

1,6-Diphenyl-5,6-dihydro-2-pyridone (XXXIII). 2-Styrylacrylic acid (IX) (70 g., 0.4 mole) was heated under reflux with 1500 ml. of aniline for 1 day. At the end of this period the solution was evaporated under reduced pressure and with heating to a syrupy residue. The residue was heated on an oil bath at 185° for 3 hr., cooled slightly, and dissolved in 1 l. of hot benzene. The benzene solution was extracted with three 200-ml. portions of 10% sodium hydroxide solution, three 200-ml. portions of 10% hydrochloric acid solution, and once with 200 ml. of water. The organic layer was dried over anhydrous calcium sulfate, filtered, and the benzene removed on a steam bath under a stream of nitrogen. The resulting amber colored oily solid was dissolved in 300 ml. of hot methanol, filtered, and cooled. After standing at −10° for 3 hr. crystallization began and was completed after 1 week. The solution was then filtered and the solid washed with a small amount of cold methanol and dried on the funnel to yield 12 g. (12%) of pale yellow crystalline solid; m.p. 165—170°. The crude material was purified by recrystallization from methanol to give 11.2 g. (11%) of cream colored crystals; m.p. 181–187°. Three additional recrystallizations from methanol netted a white crystalline analytic sample; m.p. 187–188°.

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.58; H, 6.07; N, 5.50.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Preparation of t-Acetylenic Chlorides[1]

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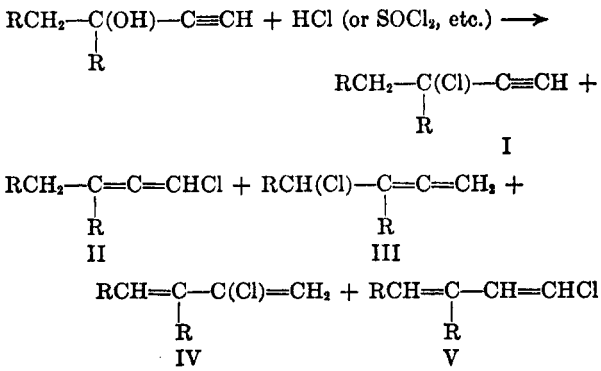
t-Acetylenic chlorides, RR'C(Cl)—C≡CH, were prepared from the corresponding *t*-carbinols by reaction with excess cold concentrated hydrochloric acid containing calcium and cuprous chlorides. The procedure described is the best developed to date with respect to yields and isomer purity of the products.

Earlier work in this laboratory has shown that the *t*-acetylenic chlorides, RR'C(Cl)—C≡CH, are versatile intermediates in organic syntheses.[3] Unfortunately, only a few chlorides of this type have been prepared in good yield and acceptable purity. Where R and R' are small alkyl groups (water and acid soluble *t*-carbinols), chlorides may be prepared in 50–60% yields by treatment of the carbinols with concentrated hydrochloric acid containing calcium chloride.[3] This method has not proved satisfactory, however, where R and (or) R' are larger than ethyl. The difficulty arises largely from the fact that rearrangement products are obtained at the expense of the desired *t*-chloride as shown in the following equation.



Such complex mixtures are easily explained. The carbonium ion ($RR'\overset{+}{C}—C\equiv CH \longleftrightarrow RR'C=C=\overset{+}{C}H$) derived from the alcohol may lead directly to I and II. Dehydration of the alcohol yields the conjugate eneyne hydrocarbon which is converted to III and IV by addition of hydrogen chloride (1,4- and 1,2- addition, respectively). Prototropic rearrangement of II yields V. That mixtures of products are encountered has long been recognized in individual cases.[4]

Favorskaya and co-workers[4] first noted that cuprous chloride has a marked effect on the course of the reaction of the lower *t*-acetylenic carbinols with hydrochloric acid and emphasized that this substance promotes rearrangement of *t*-chlorides

(1) Paper No. 73 on substituted acetylenes; previous paper, G. F. Hennion and C. A. Lynch, *J. Org. Chem.*, 25, 1330 (1960).

(2) Eli Lilly Company Fellow, 1958–60. Abstracted in part from the Ph.D. Dissertation of A. P. B.

(3)(a) G. F. Hennion and D. E. Maloney, *J. Am. Chem. Soc.*, 73, 4735 (1951); (b) G. F. Hennion and E. G. Teach, *J. Am. Chem. Soc.*, 75, 1653, 4297 (1953); (c) G. F. Hennion and J. M. Campbell, *J. Org. Chem.*, 21, 761 (1956); (d) G. F. Hennion and K. W. Nelson, *J. Am. Chem. Soc.*, 79, 2142 (1957); (e) G. F. Hennion and R. S. Hanzel, *J. Am. Chem. Soc.*, 82, 4908 (1960).

(4)(a) A. Favorskii and T. Favorskaya, *Compt. rend.*, 200, 839 (1935); (b) T. Favorskaya, *J. Gen. Chem. U. S. S. R.*, 9, 386 (1939); (c) T. Favorskaya and A. Zakharova, *J. Gen. Chem. U. S. S. R.*, 10, 446 (1940); (d) T. Favorskaya and I. Favorskaya, *J. Gen. Chem. U. S. S. R.*, 10, 451 (1940); (e) T. Favorskaya, *J. Gen. Chem. U. S. S. R.*, 11, 1246 (1941); (f) I. Favorskaya, *J. Gen. Chem. U. S. S. R.*, 18, 52 (1948); (g) C. D. Hurd and W. McPhee, *J. Am. Chem. Soc.*, 71, 398 (1949); (h) G. F. Hennion, J. Sheehan, and D. Maloney, *J. Am. Chem. Soc.*, 72, 3542 (1950); (i) E. Bergmann and D. Herrman, *J. Am. Chem. Soc.*, 73, 4013 (1951); (j) Y. Bhatia, P. Landor, and S. Landor, *J. Chem. Soc.*, 24 (1959); (k) G. F. Hennion and C. A. Lynch, *J. Org. Chem.*, 25, 1330 (1960).