pyrazine[11] in 200 ml. of chloroform. The temperature rose to near the boiling point, and the color became yellow, then yellow-brown, and finally light yellow again. The chlorine was passed in at a moderate rate for a total of 0.5 hr. Most of the chloroform was removed and 150 ml. of ether was added. The light yellow hygroscopic solid that separated was filtered and washed with ether.

Recrystallization was effected by dissolving the solid in 150 ml. of hot acetonitrile and adding ether until turbid. Crystals quickly separated and were filtered and washed with 1:1 acetonitrile–ether. The almost white crystals weighed 8.8 g., m.p. 155–157°; $\lambda_{\max}$ (hydrochloride in ethanol) 260 mμ (log ϵ 4.05) and 332 (3.76). A second crop weighed 1.5 g., m.p. 150–153°, to give a total of 10.2 g. (45.9%).[12]

Anal. Calcd. for $C_8H_{12}ClN_3 \cdot HCl$: C, 43.26; H, 5.90; N, 18.92. Found: C, 43.17; H, 6.16; N, 18.64.

In another run using prolonged reaction time and increased rate of chlorine addition, a sparingly soluble, weakly basic polychlorination reaction product was obtained in 20% yield. Two recrystallizations from 2-propanol afforded material of constant melting point (113–115°). The analysis corresponded fairly closely to a tetrachloro derivative. Only three halogens could be replaced by silver nitrate in ethanol. N.m.r. studies showed proton resonances at 2.63 and 3.08 p.p.m., with the integrated intensities being in the proportion 1:2, respectively. The above data are consistent with a compound in which three of the chlorines are located on one methyl group and one chlorine is on the ring.

Anal. Calcd. for $C_8H_9Cl_4N$: C, 33.25; H, 3.14; N, 49.08. Found: C, 33.54; H, 3.38; N, 48.60.

2-Dimethylamino-5-chloro-3,6-dimethylpyrazine Hydrochloride (Xa). Method B.—A solution of 5.1 g. (0.03 mole) af 2-dimethylamino-3,6-dimethylpyrazine 4-oxide,[13] 100 ml. of benzene, and 15 ml. of phosphorus oxychloride was maintained at reflux for 15 min. The reddish solution was freed of benzene and most of the excess phosphorous oxychloride. On the addition of 200 ml. of ether to the viscous residue, tan crystals gradually formed. The solid was filtered, washed with 20 ml. of ether, and dried in a vacuum desiccator to give 2.5 g. (37.5%) of white crystals, m.p. 149–152°.

Recrystallization from acetonitrile–ether afforded an analytical sample melting at 153–154°. The infrared spectrum was identical with that of the product obtained by direct chlorination.

2-Dimethylamino-5-methoxy-3,6-dimethylpyrazine Hydrochloride (Xb).—A solution of 0.06 mole of sodium methoxide and 5.55 g. (0.0297 mole) of 2-dimethylamino-5-chloro-3,6-dimethylpyrazine in 50 ml. of methanol was heated in a Carius tube at 125° for 18 hr. Sodium chloride was removed by filtration and the solvent was removed on a rotary evaporator. Water was added and the separated oil was extracted into ether. The dried ($MgSO_4$) yellow-green solution was treated with dry hydrogen chloride to give a yellow, partly crystalline solid. This was filtered and washed with 20 ml. of ether to give 4.4 g. of a hygroscopic solid.

Recrystallization from 25 ml. of hot ethyl acetate gave 1.5 g. (23.3%) of light yellow crystals melting at 128° with bubbling and resolidification and remelting at 232–234°. Further recrystallization from ethyl acetate gave a product which melted at 154–156° and resolidified and remelted at 232–234°.

Anal. Calcd. for $C_9H_{15}N_3O \cdot HCl$: C, 49.65; H, 7.41; N, 19.30. Found: C, 49.67; H, 7.67; N, 19.17.

2-Dimethylamino-5-hydroxy-3,6-dimethylpyrazine Hydrochloride (Xc).—A solution of 8.0 g. (0.0398 mole) of 2-dimethylamino-5-methoxy-3,6-dimethylpyrazine hydrochloride in 100 ml. of concentrated hydrochloric acid was maintained at reflux for 3 hr. and evaporated to dryness on a rotary evaporator. The remaining crude brown solid was sublimed at 140° (0.01 mm.) to give 4.5 g. (56%) of orange sublimate, m.p. 225–230°.

Recrystallization from 100 ml. of ethyl acetate gave 3.2 g. of a light orange solid, m.p. 235–240°; $\lambda_{\max}^{H_2O}$ 230 mμ (log ϵ 3.94) and 323 (3.76). Infrared absorption of a mull showed strong bands at 1636 and 1684 cm.$^{-1}$, indicating that the material exists largely as a lactam.

Anal. Calcd. for $C_8H_{13}N_3O \cdot HCl$: C, 47.17; H, 6.93; N, 17.41. Found: C, 47.28; H, 7.01; N, 17.40.

2,5-Bis(dimethylamino)-3,6-dimethylpyrazine Dihydrochloride (Xd).—A mixture of 11.1 g. (0.05 mole) of 2-dimethylamino-5-chloro-3,6-dimethylpyrazine and 50 ml. of liquid dimethylamine was heated in a steel bomb for 18 hr. at 200°. The solvent was removed. The oily residue was treated with 50 ml. of water and 100 ml. of 50% potassium carbonate and extracted with 800 ml. of ether. The dried (K_2CO_3) solution was filtered and the ether was evaporated to give 3.4 g. of a light yellow oil. This was dissolved in 35 ml. of 2-propanol and treated with dry hydrogen chloride. The light yellow solid was filtered and washed with 2-propanol and ether to give 4.2 g. (32%) of white solid, m.p. 173–175° dec.

Recrystallization from ethanol–ether (1:1) afforded 3.9 g. of analytically pure material, m.p. 176–178°; $\lambda_{\max}$ (hydrochloride in ethanol) 263 mμ (log ϵ 4.03) and 337 (3.77).

Anal. Calcd. for $C_{10}H_{18}N_4 . 2HCl$: C, 44.95; H, 7.55; N, 20.97. Found: C, 45.06; H, 7.84; N, 20.74.

Acknowledgment.—We wish to acknowledge the services of the Analytical and Physical Chemistry Section, under the supervision of Mr. Arnold D. Lewis, for physical analytical data. In particular we want to thank Mr. Thomas Wilderman, Mrs. Unni Zeek, and Miss Awilda Calenti for microanalyses; Mrs. Barbara Kane, Mr. Robert Puchalski, and Mr. Joseph Brooks for infrared and ultraviolet spectra and interpretations; and Miss Marianne Garofalo for gas–liquid chromatograms. The technical assistance of Mr. Jerry Cetenko and Mr. George Conrad is also gratefully acknowledged.

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[11] H. Gainer, M. Kokorudz, and W. K. Langdon, *J. Org. Chem.*, **26**, 2360 (1961).

[12] A 70% crude yield was subsequently obtained by using a solution of chlorine (slight excess) in chloroform and maintaining the temperature at 35°.

[13] Prepared similarly to IIb, this material melted at 89–91°; $\lambda_{\max}^{1\,N\text{ HCl}}$ 212 mμ, (log ϵ 3.89), 252 (4.30), and 358 (3.78). *Anal.* Calcd. for $C_7H_{11}N_3O$: C, 54.88; H, 7.24; N, 27.43. Found: C, 55.00; H, 7.53; N, 27.54.

6-Cyano-1,2,5,6-tetrahydropyridines in the Preparation of 1,2-Dihydropyridines. Tautomerism of the Dienes

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In the study of a 1,2-dihydropyridine for use in the synthesis of a β-benzomorphan, rearrangements leading to both a *cis*- and *trans*-2,3-dialkyldihydropyridine were encountered.[1] It was demonstrated that the *cis*-dialkylimonium salt was formed by stepwise migration of double bonds, whereas the *trans* isomer probably resulted from a concerted rearrangement of the ammonium salt. This note presents other examples of stepwise rearrangements in 1,2-dihydropyridine systems together with another example of control of the 2,3-dialkyl steric relationship. Perhaps of more general interest is a description of the use of the cyano as a protecting group in the preparation of 1,2-dihydropyridine bases by both the Grignard and borohydride reagents.

Recent work with the borohydride reagent on N-alkylpyridines suggests that, after the initial dihydro stage is reached, further reduction depends on the tautomerism of an α,β double bond to the imonium form and that unless this transformation is inhibited

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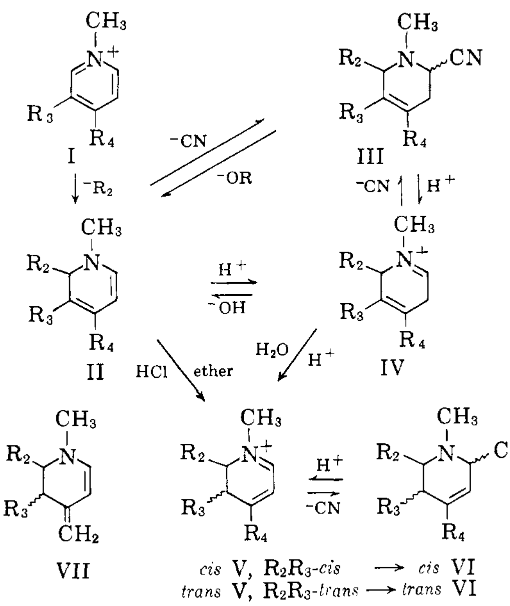
[1] E. M. Fry, *J. Org. Chem.*, **28**, 1869 (1963).

CHART I



the end result is a tetrahydropyridine.[2] Substrates with N-phenyl[3] or N-glucoside[4] groups or with a substituent on the unsaturated α-[5] or β-carbon[2,6] appear to resist reduction beyond the dihydro stage and some degree of success in stopping at this point has been achieved in alkaline[4,5] solutions and by the use of other hydride reagents.[4,7]

Cyanide proved to be an effective competitor for the second active site when it was present in large excess in the alkaline sodium borohydride solution of pyridine, γ-picoline, and 3,4-lutidine N-methyl quaternary salts. Isolation of the nitriles was facilitated by means of ether and by the insolubility of these oils in the aqueous medium; small amounts of the tetrahydro products also were obtained. As is well known, nitrile groups on carbon α to tertiary nitrogen are subject to removal by hydride reagents and to what extent and under what conditions the nitriles described here might be made to survive in a homogeneous medium is not known. But as a practical matter the distribution of any imonium salt and its product cyano base between polar and nonpolar immiscible solvents should make this separation generally feasible.

The structures of the di- and tetrahydro N-methylpyridines shown in Chart I are based on spectral evidence correlated with data obtained for members of the 2-benzyl-1,3,4-trimethyl series which were uniquely identified by ultimate conversion to α- and β-benzomorphans.[1]

The tetrahydronitriles III, obtained both through the Grignard reagent and by the action of borohydride on the pyridinium salts I, are characterized by lack of a maximum in the ultraviolet above 220 mμ. Making a solution weakly alkaline caused development of a band, characteristic of II, at 330 mμ[8] and acidification of the nitrile solution gave a developing band at 290 mμ marking the formation of V. In compounds with a 3-substituent the position of the double bond and hence the site of attack was determined by n.m.r. The bases II were usually prepared by the action of alcoholic potassium ethoxide on the nitriles III. All of the bases examined were oils and had characteristic bands at 6.05 and 6.3 μ. Acidification of alcohol solutions of the bases gave the salts IV, each characterized by lack of a maximum above 220 mμ. Solutions of the perchlorates (IV) in methylene chloride showed characteristic bands at 5.85 and 5.95 μ. Both bands lie in the absorption region reported for Δ^1-tetrahydropyridinium perchlorates.[9] Only in the case of the unsubstituted ring did the infrared absorption fail to yield this evidence. Heating the nitriles III in acid gave the dienes V except for the two examples lacking a 4-substituent. The products in these cases remain unidentified. Presumably IV is the intermediate in the rearrangement to V and it is the form usually isolated from the Grignard reaction after decomposition with acid, but one instance (R_2 = $PhCH_2$, R_3 = H, R_4 = CH_3) was encountered in which the product of acid decomposition was the conjugated diene V.

Dienes IV and V were easily distinguishable not only in the ultraviolet but by means of the derived nitriles III and VI. The latter always had a very strong band at 11.2 μ, but otherwise was like the III isomer in that it had no maxima above 220 mμ and readily lost the cyano group in acidic or basic solution. In the above case, when decomposition of the Grignard solution was carried out in aqueous sodium cyanide solution the nitrile III was obtained. The II bases were not as a rule recoverable from the V salts or the VI nitriles by the action of base. Instead, oils absorbing at 6.2 μ and 300 mμ were obtained. By analogy with the 2-benzyl-1,3,4-trimethyl derivative these probably are the *exo*-methylene bases VII.[10]

The experimental conditions necessary for the preparation of *trans* V (R_2, R_3, R_4 = CH_3) were limited compared with those which gave *trans* V (R_2 = $PhCH_2$; R_3, R_4 = CH_3). The addition of ethereal hydrogen chloride to an ethereal solution of 1,2-dihydro-1,2,3,4-tetramethylpyridine (II) under conditions which provided mixing at high dilution gave an oil which rapidly crystallized to give a 48% yield of *trans* V (R_2, R_3, R_4 = CH_3). As in the case of the 2-benzyl analog, the hydrochloride of II (R_2, R_3, R_4 = CH_3) rearranged in the aprotic solvent methylene chloride, whereas the perchlorate, structure IV, proved to be stable in this solvent.

Isomers *cis* V and *trans* V were distinguished by means of the tetrahydro bases obtained by replacing the cyano groups of the respective nitriles VI with hydrogen. These gave crystalline picrates having a similar melting range which was not depressed on admixture. However, the bases gave different infrared diagrams and could be

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(2) R. E. Lyle, D. A. Nelson, and P. S. Anderson, *Tetrahedron Letters*, (**13**), 553 (1962).

(3) M. Saunders and E. H. Gold, *J. Org. Chem.*, **27**, 1439 (1962).

(4) (a) J. J. Panouse, *Bull. soc. chim. France*, D, 60 (1953); (b) J. J. Panouse, *Thèse de Doctorat ès Sciences* (Paris) (1952).

(5) N. Kinoshita and T. Kawasaki, *J. Pharm. Soc. Japan*, **83**, 126 (1963).

(6) W. Traber and P. Karrer, *Helv. Chim. Acta*, **41**, 2066 (1958); K. Schenker and J. Druey, *ibid.*, **42**, 1960, 2571 (1959); K. Wallenfels, H. Schüly, and D. Hofmann, *Ann.*, **621**, 106 (1959); T. Tsukamoto, N. Kinoshita, and A. Ando, *J. Pharm. Soc. Japan*, **82**, 1317 (1962); N. Kinoshita, M. Hamana, and T. Kawasaki, *ibid.*, **83**, 115 (1963).

(7) E. Wenkert, R. A. Massy-Westropp, and R. G. Lewis, *J. Am. Chem. Soc.*, **84**, 3732 (1962).

(8) The infrared and ultraviolet absorption values given in the text are only approximate. For individual compounds see Experimental.

(9) N. J. Leonard and F. P. Hauck, Jr., *J. Am. Chem. Soc.*, **79**, 5279 (1957).

(10) No equilibrium observations were made. For a discussion of thermodynamic stability in cisoid *vs.* transoid cyclohexadienes, see R. B. Bates, R. H. Carnighan, and C. E. Staples, *ibid.*, **85**, 3030 (1963).

separated on a vapor column. The chromatograms of each revealed traces of the other along with a trace of the Δ^3-isomer.

Experimental

Microanalyses are by the Analytical Services Section of this Laboratory, Harold McCann, director. Ultraviolet spectra are by a Cary recording spectrophotometer, Model 14, and infrared spectra are by a Perkin-Elmer Infracord, Model 137. N.m.r. spectra, 60 Mc., are with tetramethylsilane as internal reference standard. Melting points are uncorrected.

6-Cyano-1,2,5,6-tetrahydropyridines (III). A. By Sodium Borohydride Reductions in Cyanide Solutions. 6-Cyano-1,4-dimethyl-1,2,5,6-tetrahydropyridine Hydrochloride.—Fifty milliliters of 6 *N* hydrochloric acid was added slowly to a solution of 50 g. (0.77 mole) of potassium cyanide in 100 ml. of water, layered with 150 ml. of ether, and kept below 15°. Fifty grams (0.21 mole) of γ-picoline methiodide was dissolved in the cold solution and 10 g. (0.26 mole) of sodium borohydride was added. The milky, mildly effervescing solution was allowed to warm to 25° and then held at this temperature by occasional cooling. After a total of 5 hr. the ether was separated, washed with water, chilled, and treated with 2 ml. of methyl iodide which reacted over 30 min. at 5° with over-reduced material to give a precipitate of 1,1,4-trimethyl-1,2,5,6-tetrahydropyridinium iodide. The ethereal solution was decanted into a stirred solution of 33 ml. of 6.5 *N* absolute ethanolic hydrochloric acid with separation of a crystalline solid, 27.2 g. (74%), m.p. 131–133°.

Anal. Calcd. for $C_8H_{13}ClN_2$: C, 55.65; H, 7.59; N, 16.23. Found: C, 55.29; H, 7.61; N, 16.11.

6-Cyano-1,3,4-trimethyl-1,2,5,6-tetrahydropyridine, made as above from 3,4-lutidine methiodide, was obtained crystalline in 49% yield from a cold petroleum ether (30–60°) solution of the crude product. It melted at 43–45°. The integrated n.m.r. spectrum showed no vinylic hydrogen and an unsplit C–CH_3 band (6H). Replacement of cyano by benzyl has been reported.[1]

Anal. Calcd. for $C_9H_{14}N_2$: C, 71.96; H, 9.39; N, 18.65. Found: C, 71.78; H, 9.49; N, 18.41.

2-Cyano-1-methyl-1,2,3,6-tetrahydropyridine hydrochloride, prepared by the detailed procedure above from pyridine methiodide, was freed of oil with cold acetone and stored over sodium hydroxide to remove adhering hydrogen chloride. The yield of product, m.p. 115–118° (gas), was 50%.

Anal. Calcd. for $C_7H_{11}ClN_2$: C, 53.00; H, 6.99; N, 17.66; Cl, 22.35. Found: C, 53.66; H, 7.05; N, 17.06; Cl, 21.98.

B. By the Action of Cyanide on Grignard Products (Evidence bearing on low yields is given in the last experiment in this section). **6-Cyano-1,2,3-trimethyl-1,2,5,6-tetrahydropyridine Perchlorate.**—The mixture from the action of methylmagnesium iodide on 1,3-dimethylpyridinium iodide was poured with stirring into a perchloric acid–ice mixture, the ether separated, and cold sodium cyanide solution added in excess to the cold acid solution. Alternately the Grignard mixture was poured into a sodium cyanide solution with stirring. The crude oily nitrile in ether solution was converted to the crystalline perchlorate by the addition of 9 *N* perchloric acid. After purification from acetone–ether, it melted at 116–121° and was obtained in 28–31% yield. Both procedures gave the same recovery. Recrystallized from 9 *N* perchloric acid, the salt melted at 165–168° (gas). A return to the lower melting form was made in acetone. Infrared diagrams of the bases recovered from the dimorphic salts were identical.

Anal. Calcd. for $C_9H_{15}ClN_2O_4$: C, 43.12; H, 6.03; N, 11.18. Found: C, 43.23; H, 6.26; N, 10.98.

2-Benzyl-6-cyano-1,4-dimethyl-1,2,5,6-tetrahydropyridine.—A cold aqueous solution of sodium cyanide was added with stirring to the chilled suspension resulting from the action of the benzyl Grignard reagent on 1,4-dimethylpyridinium iodide. The ether was separated and distilled, the last portion being removed under reduced pressure. A solution of the oil in petroleum ether (30–60°) deposited crystals which, after trituration in cold alcohol to remove oil, were recovered in 23–29% yield. Recrystallized from petroleum ether, the material melted at 76–78°.

Anal. Calcd. for $C_{15}H_{18}N_2$: C, 79.61; H, 8.02. Found: C, 79.83; H, 7.98.

6-Cyano-1,2,3,4-tetramethyl-1,2,5,6-tetrahydropyridine was obtained in the same way as was described for the 1,2,3-trimethyl analog. The oily hydrobromide separated on passing hydrogen bromide into a solution in ether. It was induced to crystallize from cold acetone and was obtained in 36–41% yields. It melted at 152–153° (gas).

Anal. Calcd. for $C_{10}H_{17}BrN_2$: Br, 32.60. Found: Br, 32.55.

The **perchlorate** crystallized on addition of perchloric acid to an aqueous solution of the hydrobromide. It melted at 150–152°.

Anal. Calcd. for $C_{10}H_{17}ClN_2O_4$: C, 45.37; H, 6.48. Found: C, 45.17; H, 6.70.

2,5-Dihydropyridinium (IV) Perchlorates.—The only member of this group which has been obtained crystalline is the previously described 2-benzyl-1,3,4-trimethyl-2,5-dihydropyridinium perchlorate.[1] The others are characterized by the infrared absorption of the perchlorates, made *in situ* in methylene chloride, and by the absence of significant maxima in the ultraviolet immediately after acidification of the bases (II) (Table I).

TABLE I

R_2	R_3	R_4	Infrared,[a] μ
H	H	CH_3	5.80 (m), 5.95 (w)
H	CH_3	CH_3	5.79 (m), 5.91 (m)
CH_3	CH_3	H	5.84 (w), 5.96 (m)
CH_3	CH_3	CH_3	5.84 (m), 5.95 (m)
$PhCH_2$	H	CH_3	5.85 (m), 5.97 (m)
$PhCH_2$	CH_3	CH_3[b]	5.86 (m), 5.96 (m)

[a] m, medium; w, weak. [b] Previously reported in ref. 1.

To what extent an accompanying absorption at 6.24 μ is due to water in solvent methylene chloride is not known.

1,2-Dihydropyridines (II).—These bases are oils subject in varying degree to self-condensation (loss of volatility) and oxidation (development of color). They were most satisfactorily obtained by the action of 2.6 *N* potassium ethoxide (10 vol.) on the nitriles at room temperature. Under these conditions the condensation was minimized. The progress of the reaction was marked by precipitation of a salt, presumably potassium cyanide, over several hours, and could be followed in the ultraviolet. Finally, the alcohol solution was diluted with an equal volume of petroleum ether (30–60°), water added and mixed, the petroleum ether layer separated, and the solvent removed under reduced pressure. The recorded ultraviolet values were obtained by diluting 0.02 ml. of the preparative solution with ethanol; the infrared observations were made on the neat oils unless otherwise noted (Table II).

TABLE II

R_2	R_3	R_4	Infrared,[a] μ, all strong bands	Ultraviolet, mμ (ϵ)
H	H	H	6.08, 6.35 (CH_2Cl_2)	335 (2100)
H	H	CH_3	6.05, 6.33	330 (2200)
H	CH_3	CH_3	6.02, 6.26	322 (2500)
CH_3	CH_3	H	6.08, 6.32	330 (4200)
CH_3	CH_3	CH_3	6.05, 6.30	323 (4000)
$PhCH_2$	H	CH_3	6.06, 6.24 (sh), 6.35	330 (3500) 253 (hump)
$PhCH_2$	CH_3	CH_3[b]	6.05, 6.23 (sh), 6.32	275 (4100) 325 (3800)

[a] sh, shoulder. [b] Previously reported in ref. 1.

4-Methylene-1,2,3,4-tetrahydropyridines (VII).—The bases were obtained by the action of potassium ethoxide on the nitriles VI, or by sodium hydroxide on the salts V. All were oils and were characterized by ultraviolet and infrared bands (Table III). Contamination by the endocyclic dienes was usually evident, more so with the bases derived from the *cis* V salts than with those from the *trans*, and, in one case (R_2 = $PhCH_2$, R_3 = H, R_4 = CH_3), the presence of the exocyclic base was dubious.

2,3-Dihydropyridinium (*cis* and *trans* V) Chlorides.—The nitriles III lost hydrogen cyanide in hot 2.2 *N* hydrochloric acid to give the imonium salts *cis* V, and the reaction was readily followed by development of absorption in the ultraviolet. The infrared data are on oils obtained either by chloroform extraction of the aqueous acid solutions, or from the action of alcoholic acid on the nitriles VI (Table IV). The *trans* V sample (R_2 = R_3 = R_4 = CH_3) was formed rapidly when hydrogen chloride was passed

TABLE III

R_2	R_3	R_4		Infrared,[a] μ	Ultraviolet, mμ (ε)
H	H	CH_3		6.09 (m), 6.18 (m), 6.36 (m)	292 (2700)
H	CH_3	CH_3		6.0 (sh); 6.14 (s), 6.25 (sh)	291 (5700)
CH_3	CH_3	CH_3	*cis*	6.05 (sh), 6.18 (m), 6.3 (sh)	302 (6000)
			trans	6.16 (s)	299 (15000)
$PhCH_2$	CH_3	CH_3[b]	*cis*	6.06 (s), 6.18 (sh), 6.32 (s)	282 (4600) 300–315 (4400)
			trans	6.17 (s)	302 (14200)

[a] s, strong; m, medium; w, weak; sh, shoulder. [b] Reported in ref. 1.

TABLE IV

R_2	R_3	R_4		Infrared,[a] μ	Ultraviolet, mμ (ε)
H	H	CH_3		5.96 (m), 6.22 (s)	288 (7100)
H	CH_3	CH_3		5.99 (m), 6.26 (s)	288 (5200)
CH_3	CH_3	CH_3	*cis*	6.0 (m), 6.25 (s)	292 (5500)
			trans	6.0 (m), 6.24 (s)	290 (6800)
$PhCH_2$	H	CH_3		6.0 (m), 6.24 (s)	285 (5700)
$PhCH_2$	CH_3	CH_3[b]	*cis*	6.01 (m), 6.29 (s)	298 (4400)
			trans	6.0 (m), 6.26 (s)	282 (5800)

[a] s, strong; m, medium. [b] Reported in ref. 1.

into a methylene chloride solution of the base II; the bands characteristic of the imonium salts IV were not observed. Its preparation is given below.

***trans*-1,2,3,4-Tetramethyl-2,3-dihydropyridinium** (*trans* **V) Chloride.**—To 30 ml. of 0.01 *N* dry ethereal hydrogen chloride, contained in a three-neck flask equipped with two graduated separatory funnels and a stirrer, was added dropwise simultaneously through each funnel 3 ml. of a solution of the base in ether and 3 ml. of an ethereal solution of an equivalent amount of hydrogen chloride. The slightly oily crystalline material which formed was filtered and washed free of oil with acetone. In this manner 0.23 g. of 1,2,3,4-tetramethyl-1,2-dihydropyridine (II) gave 0.14 g. (48%) of the hydrochloride (*trans* V). The salt was hygroscopic. It was recrystallized by adding acetone to a solution in methylene chloride, m.p. 129–135°.

Anal. Calcd. for $C_9H_{16}ClN$: C, 62.23; H, 9.29; Cl, 20.41. Found: C, 61.47; H, 9.48; Cl, 20.25.

6-Cyano-1,2,3,6-tetrahydropyridines (VI).—These were made simply by adding enough aqueous sodium or potassium cyanide to cold solutions of salts V so that the final solution was alkaline. The nitriles were recovered with ether or petroleum ether and except for the following example were oils. **6-Cyano-1,4-dimethyl-1,2,3,6-tetrahydropyridine** was obtained crystalline in 60% yield. Recrystallized from petroleum ether (30–60°) it melted at 46–49°. The infrared spectra is given in Table V.

TABLE V

R_2	R_3	R_4		Infrared, μ, all strong bands
H	H	CH_3		11.37
H	CH_3	CH_3		11.25
CH_3	CH_3	CH_3	*cis*	11.27
			trans	11.27
$PhCH_2$	H	CH_3		11.32
$PhCH_2$	CH_3	CH_3[a]	*cis*	11.23
			trans	11.31

[a] Reported in ref. 1.

Anal. Calcd. for $C_8H_{12}N_2$: C, 70.55; H, 8.88; N, 20.57. Found: C, 71.06; H, 9.00; N, 19.83.

1,2,3,4-Tetramethyl-1,2,5,6-tetrahydropyridine, obtained by the action of sodium borohydride on the nitrile as previously described,[1] gave a picrate in 55% over-all yield. Recrystallized from alcohol it melted at 155–158°. The integrated n.m.r. diagram of the base showed two unsplit methyl groups at τ 8.4, and one split methyl group centered at 8.9.

Anal. Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47. Found: C, 49.23; H, 5.27.

***cis*-1,2,3,4-Tetramethyl-1,2,3,6-tetrahydropyridine picrate**, obtained as above in 60% yield, melted at 167–169°, slight previous sinter. It did not depress the melting point of the Δ^3-compound. The n.m.r. diagram showed one vinylic hydrogen at τ 4.7.

Anal. Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47. Found: C, 48.85; H, 5.27.

***trans*-1,2,3,4-Tetramethyl-1,2,3,6-tetrahydropyridine.**—The crude material, obtained as above from the nitrile, was distilled at about 60° (10 mm.). It was converted to the picrate in 41% over-all yield (five steps) starting from the isomeric nitrile III. The base n.m.r. diagram showed one vinylic hydrogen at τ 4.6. The picrate melted at 162–165° and the melting point was not depressed on admixture with the *cis* isomer.

Anal. Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47. Found: C, 49.10; H, 5.56.

1,2,3-Trimethyl-1,2,5,6-tetrahydropyridine was obtained in like manner from the crystalline perchlorate of the cyano derivative (III). After distillation at <100° (9 mm.), it was converted to the picrate in an over-all yield of 45%. Recrystallized from alcohol, it melted 194–195°. Its n.m.r. spectrum showed one vinylic hydrogen at τ 4.55. This picrate was obtained also from the noncrystalline portion of the preparation of the nitrile III perchlorate in an amount that signified a yield increase of 50% over that represented by crystalline material. Diastereoisomerism of the nitriles is thereby indicated.

Anal. Calcd. for $C_{14}H_{18}N_4O_7$: C, 47.46; H, 5.10. Found: C, 47.46; H, 5.11.

Rearrangements of Alkoxypyridine 1-Oxides

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Although a number of 2-alkoxypyridine 1-oxides are known,[2,3] thermal rearrangements of these compounds are, to our knowledge, unreported.[4] It was of interest to determine whether rearrangement of 2-alloxypyridine 1-oxide (I) would give a mixture of products such as had been obtained from 2-alloxypyridines[5] and 4-alloxypyrimidines,[6] or whether exclusive rearrangement to either the 3-carbon or 1-oxygen atom would occur.

For this purpose, I was prepared by treatment of 2-chloropyridine 1-oxide[7] (II) with the sodium salt of allyl alcohol under mild conditions, a procedure similar to that previously used by Gardner and Katritzky for the preparation of other 2-alkoxypyridine 1-oxides.[3] Rearrangement of I took place under very mild conditions to give 1-alloxy-2-pyridone (III) in nearly quantitative yield.

The identification of I is based on infrared and ultraviolet spectral data as well as on the method of synthesis. The infrared spectrum of I has sharp absorption bands in the 1200–1300-cm.$^{-1}$ region characteristic of

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[1] Allied Chemical Corp. Fellow, 1963.

[2] E. Shaw, *J. Am. Chem. Soc.*, **71**, 67 (1949).

[3] J. N. Gardner and A. R. Katritzky, *J. Chem. Soc.*, 4375 (1957).

[4] It should be noted that Shaw[2] observed the formation of 1-benzyloxy-2-pyridone as a minor product resulting from an acid-catalyzed debenzylation of 2-benzyloxypyridine 1-oxide.

[5] F. J. Dinan and H. Tieckelmann, *J. Org. Chem.*, **29**, 892 (1964).

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[7] A. R. Katritzky, *J. Chem. Soc.*, 191 (1957).