

(70%) of product as a colorless liquid, b.p. 88–89° (0.3 mm.),  $n_D^{20}$  1.4848,  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  256  $\mu$  ( $\epsilon$  3640) with a shoulder at 320  $\mu$  ( $\epsilon$  1450),  $\lambda_{\text{max}}^{\text{CCl}_4}$  1725  $\text{cm}^{-1}$  (conj. ester C=O).

Anal. Calcd. for  $\text{C}_{11}\text{H}_{14}\text{O}_3$ : C, 67.32; H, 8.22. Found: C, 67.38; H, 8.16.

*Ethyl 4-ethoxy-2,5-dihydrobenzoate* (III). A solution of 3.05 g. of ethyl 4-ethoxy-2,5-dihydrobenzoate and 10 ml. of absolute ethanol was added with stirring to a solution of sodium ethoxide prepared from 0.3 g. of sodium and 15 ml. of absolute ethanol. The deep red solution was stirred at room temperature for 5 hr. before being diluted with water. The product was isolated by extraction with ether and distillation of the dried ether extract, under reduced pressure, gave 2.7 g. (88%) of a colorless liquid, b.p. 88–89° (0.3 mm.),  $n_D^{20}$  1.5180,  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  322  $\mu$  ( $\epsilon$  11,500) with no appreciable absorption in the 256- $\mu$  region.  $\lambda_{\text{max}}^{\text{CCl}_4}$  1727  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{11}\text{H}_{14}\text{O}_3$ : C, 67.32; H, 8.22. Found: C, 67.00; H, 7.99.

*4-Ethoxybenzoic acid*. A mixture of 3.0 g. of 10% palladium-on-charcoal and 5.0 g. of ethyl 4-ethoxy-2,5-dihydrobenzoate in 75 ml. of xylene was refluxed for 6 hr. The catalyst was removed by filtration and the distillate was distilled to give 3.4 g. (68%) of ethyl 4-ethoxybenzoate as a colorless liquid, b.p. 82–87° (0.25 mm.),  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  259  $\mu$  ( $\epsilon$  10,500),  $\lambda_{\text{max}}^{\text{CCl}_4}$  1730  $\text{cm}^{-1}$ . A small amount of ethyl 4-ethoxybenzoate was refluxed with 20 ml. of a 10% sodium hydroxide solution for 11 hr. On acidification with hydrochloric acid, 4-ethoxybenzoic acid precipitated, which after recrystallization from benzene-petroleum ether (b.p. 40–60°) melted at 194.5–196.5° (lit.,<sup>9</sup> m.p. 195–196°),  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  254.5  $\mu$  ( $\epsilon$  16,500).

*4-Carboethoxy-3-cyclohexenone* (II). A solution of 66.6 g. (0.34 mole) of ethyl 4-ethoxy-2,5-dihydrobenzoate, 200 ml. of tetrahydrofuran, 35 ml. of concd. sulfuric acid, and 160 ml. of water was stirred at room temperature for 1 hr. before being diluted with more water. The product was isolated by extraction with ether, the ether extract washed with a saturated solution of sodium bicarbonate, dried, and distilled to give 40.5 g. (71.5%) of 4-carboethoxy-3-cyclohexenone as a colorless liquid, b.p. 83–84.5° (0.3 mm.),  $n_D^{20}$  1.4789,  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  215  $\mu$  ( $\epsilon$  8300),  $\lambda_{\text{max}}^{\text{CCl}_4}$  1725  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_9\text{H}_{12}\text{O}_4$ : C, 64.27; H, 7.19. Found: C, 64.49; H, 7.38.

An orange-red *2,4-dinitrophenylhydrazone* was formed in ethanol solution, m.p. 124–124.5°,  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  373  $\mu$  ( $\epsilon$  25,750). The orange-red color of this derivative and the suspiciously high wave length of the ultraviolet spectrum raise the possibility that it may actually be the 2,4-dinitrophenylhydrazone of 4-carboethoxy-2-cyclohexenone.

Anal. Calcd. for  $\text{C}_{15}\text{H}_{16}\text{N}_4\text{O}_6$ : C, 51.72; H, 4.63; N, 16.08. Found: C, 51.68; H, 4.79; N, 15.83.

*4-Carboethoxycyclohexanone*. Hydrogenation of 1.16 g. of 4-carboethoxy-3-cyclohexenone in 15 ml. of ethanol with 0.07 g. of palladium-on-charcoal was completed in 2 hr. (one molecular equivalent of hydrogen was absorbed). The catalyst was removed by filtration, and the filtrate was added to a boiling ethanolic solution of 2,4-dinitrophenylhydrazine hydrochloride to give in essentially quantitative yield *4-carboethoxycyclohexanone 2,4-dinitrophenylhydrazone* which on recrystallization from ethanol melted at 121–122°,  $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$  361  $\mu$  ( $\epsilon$  26,000).

Anal. Calcd. for  $\text{C}_{15}\text{H}_{18}\text{N}_4\text{O}_6$ : C, 51.42; H, 5.18; N, 15.99. Found: C, 51.42; H, 5.29; N, 16.15.

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(9) J. B. Cohen and H. W. Dudley, *J. Chem. Soc.*, 97, 1741 (1910).

## The Preparation of *N*-Phenyl-1,2-dihydropyridine<sup>1,2</sup>

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Pullman, San Pietro, and Colowick, and others, have shown that *N*-methyldihydropyridine and similar dihydropyridines have the 1,4-dihydro structure.<sup>3–9</sup> In the present paper we wish to report the preparation, characterization, and unambiguous structural assignments of the *N*-phenyldihydropyridines I and II.



Although previous reports of reduction of simple *N*-alkylpyridinium salts with sodium or potassium borohydride<sup>10</sup> indicate that only the tetrahydro compounds are formed, reduction of *N*-phenylpyridinium cation by sodium or potassium borohydride in alkaline aqueous solution gave a solid I, m.p. 82.5–83.5°, in 60% yield. The NMR spectrum clearly showed that this was the 1,2-isomer. Since the 1,2-isomer had previously been reported by Weitz<sup>11</sup> and subsequently by Karrer<sup>12</sup> who reported that it had been prepared by sodium amalgam reduction of the *N*-phenylpyridinium cation; we repeated this work and obtained compound II. The melting point and physical properties of II corresponded to those previously reported.

Even cursory examination of the NMR spectra

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(2) Part of a Ph.D. thesis to be submitted to Yale University.

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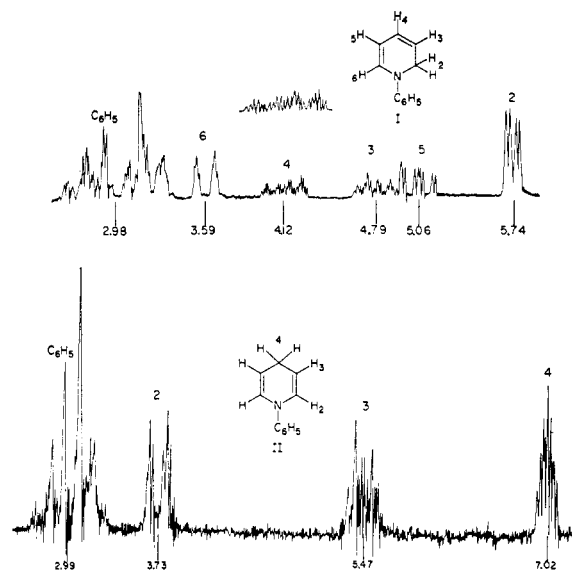


Fig. 1. The proton magnetic resonance spectra of *N*-phenyl-1,2-dihydropyridine (I) (in carbon tetrachloride) and *N*-phenyl-1,4-dihydropyridine II (in carbon tetrachloride)

of I and II as shown in Fig. 1, permits the definite assignment of structures, since the spectrum of II shows aliphatic hydrogen and only two kinds of olefin, while the spectrum of I shows four distinct olefin hydrogens. A more detailed analysis of the fine structure allows the assignment of spin-spin coupling constants as reported in Table I. The most

TABLE I

THE NMR COUPLING CONSTANTS BETWEEN THE PROTONS IN *N*-PHENYL-1,2-DIHYDROPYRIDINE (I) AND *N*-PHENYL-1,4-DIHYDROPYRIDINE (II)

Coupling constants in cycles per second

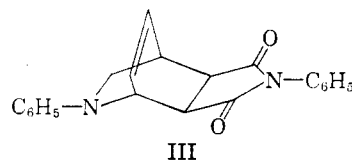
	I	II
$J_{23}$	3.6	9.0
$J_{24}$	1.5	1.6
$J_{34}$	7.7	3.9
$J_{25} = J_{26}$	0	
$J_{45}$	4.5	
$J_{56}$	6.9	
$J_{35} = J_{36} = J_{46}$	0.9	

interesting multiplet is that which we have assigned to proton 4 in I. We would expect, *a priori*, that the spectrum of 4 would be split into a triplet by the  $\text{CH}_2$  group at 2. Each further proton which interacted with 4 could double the number of lines. This would lead to 24 lines if *none* of the lines were to overlap. The observed multiplet contains 23 distinctly observable lines. On close examination it becomes clear that in the very center of the pattern is a composite line formed by overlapping of the two extreme lines of left and right subpatterns. Its intensity coincides with this view.

*N*-Phenyl-1,4-dihydropyridine (II) shows one maximum at  $286 \text{ m}\mu$  ( $\log \epsilon 4.2$ ),<sup>13</sup> whereas the 1,2-

isomer (I) shows two maxima at 239 and  $350 \text{ m}\mu$  ( $\log \epsilon 3.9$  and 4.1, respectively). Both spectra were taken in absolute ethanol.

We attempted reaction of these isomers with maleic anhydride without obtaining characterizable product. However, reaction of I with *N*-phenylmaleimide did yield a crystalline 1:1 adduct to which we assigned structure III. II yielded no product under the same conditions.<sup>14</sup> As in the case of other dihydropyridines,<sup>15</sup> both compounds appeared very sensitive to acid and were extremely easily oxidized. However, both compounds could be readily purified by sublimation and handled conveniently *in vacuo*.



All attempts at alkylation of either I or II have so far failed. Treatment with methyl iodide led to production of *N*-phenylpyridinium iodide, possibly through a free radical path as shown by similar oxidations of Hantzsch bases reported by Kurz, Hutton, and Westheimer.<sup>16</sup> Triethyloxonium fluoroborate apparently produced polymeric product. The difficulty in alkylation appears to be due to the ease of other reactions which can occur rather than any intrinsic barrier to the alkylation itself.

Some comment on the specificity of these two reactions is in order. Properties of these molecules suggest that they are not in equilibrium under the conditions of either reaction, and therefore, that both results are due to kinetic control. In the formation of compound I, sodium borohydride evidently adds a hydride mainly in the alpha position. It is suggestive that the addition occurs at the site closest to the positive nitrogen and, therefore, most favored by coulombic attraction. The fact that the reduction stops readily at the dihydro stage, is probably due to the immediate precipitation of the dihydro compound from solution as it is formed. It seems probable that the sodium amalgam reduction of *N*-phenylpyridinium occurs *via* initial addition of two electrons to give a doubly allylic resonance-stabilized carbanion which then abstracts a proton from the solvent water. The forma-

(13) Karrer *et al.* (see ref. 2) reports one maximum (0.001 *N* sodium hydroxide in ethanol) at  $285 \text{ m}\mu$  ( $\log \epsilon 5.0$ ).

(14) O. Mumm and J. Diedrichsen, *Ann.*, **538**, 195 (1939), reported that 1,2-dihydro-1,2,6-trimethyl-4-phenyl-3,5-dicarbethoxypyridine gives a 1:1 adduct with maleic anhydride, whereas the 1,4- isomer does not.

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(16) J. L. Kurz, R. Hutton, and F. H. Westheimer, *J. Am. Chem. Soc.*, **83**, 584 (1961).

tion of an unconjugated isomer on protonation of such a species has many analogies.

EXPERIMENTAL<sup>17</sup>

*N*-Phenylpyridinium chloride was prepared according to the method of Grigor'eva *et al.*<sup>18</sup>

*N*-Phenyl-1,2-dihydropyridine (I). To a stirred solution containing 7.4 g. (0.041 mole) of *N*-phenylpyridinium chloride and 4.6 g. (0.082 mole) of potassium hydroxide dissolved in 1 l. of water, 0.584 g. (0.0155 mole) of sodium borohydride in 50 ml. of water was added all at once. The reaction mixture was stirred for 16 hr. under a nitrogen atmosphere and then filtered, yielding 6.4 g. of a yellow solid containing approximately 20% of the 1,4 isomer (crude m.p. 77–80°). The product was recrystallized three times from methanol (2.8 g., m.p. 81.5–82.5°). Another 1.3 g. was obtained from two recrystallizations of the combined mother liquor. The combined 1,4-free yellow plates, were sublimed at 60°/0.1 mm., yielding 3.9 g. (60%) of yellow crystals, melting at 82.5–83.5°.

*Anal.* Calcd. for C<sub>11</sub>H<sub>11</sub>N: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.97; H, 7.30; N, 9.17.

*N*-Phenyl-1,4-dihydropyridine (II). A solution of 10.0 g. (0.0555 mole) of *N*-phenylpyridinium chloride in 1 l. of water was stirred with 400 g. (0.26 mole) of 3% sodium amalgam for 12 hr. under a nitrogen atmosphere. The reaction mixture was filtered, and the solid product was sublimed twice at 30°/0.1 mm., yielding 6.1 g. (70%) of white crystals, melting at 48–50° (lit.,<sup>11,12</sup> m.p. 48–50°).

*Oxidation of N-phenyl-1,2-dihydropyridine. A. With iodine.* To a stirred solution of 0.1 g. (0.637 mole) of *N*-phenyl-1,2-dihydropyridine dissolved in 10 ml. of chloroform, 0.161 g. (0.637 mole) of iodine, dissolved in 25 ml. of chloroform was added dropwise for 1 hr. The solution was extracted six times with 10-ml. portions of hot water. Evaporation of the water yielded 0.05 g. (29%) of a white crystalline solid melting at 190–200°. One recrystallization from ethanol raised the melting point to 210–211° (lit.,<sup>11</sup> m.p. 210°). A mixed melting point with an authentic sample of *N*-phenylpyridinium iodide was undepressed. Infrared, ultraviolet and NMR spectra were identical to those of the known iodide.

*B. With methyl iodide.* A 0.1-g. sample (0.637 mole) of *N*-phenyl-1,2-dihydropyridine was dissolved in 2 ml. of methyl iodide and allowed to react for 5 days. The well formed white plates that precipitated from the solution weighed 0.04 g. (22%) and melted at 209–210° without recrystallization. The compound was identical with the known *N*-phenylpyridinium iodide.

*C. With silver nitrate.* An ethanolic solution of silver nitrate turned black instantaneously in the cold, upon addition of a few milligrams of *N*-phenyl-1,2-dihydropyridine.

*Oxidation of N-phenyl-1,4-dihydropyridine with methyl iodide.* In a similar manner, from 0.1 g. of *N*-phenyl-1,4-dihydropyridine in 2 ml. of methyl iodide, *N*-phenylpyridinium iodide was obtained in 14% yield.

*N*-Phenylmaleimide adduct of *N*-phenyl-1,2-dihydropyridine (III). A 0.363-g. sample (2.1 moles) of *N*-phenylmaleimide was placed in a flask which was then evacuated to 10<sup>-6</sup> mm.

(17) All melting points are uncorrected. Infrared spectra were taken with a Perkin-Elmer Model 221 recording spectrophotometer. Ultraviolet spectra were taken with a Cary Model 11S recording spectrophotometer. NMR spectra were taken with a Varian Associates 60-mc. high resolution spectrometer. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside 17, N. Y.

(18) N. E. Grigor'eva and M. D. Yavlinskii, *Ukrain. Khim. Zhur.*, 18, 82 (1952); N. E. Grigor'eva, A. B. Oganes'yan, and I. A. Mysh, *Zhur. Obshchei Khim.*, 27, 1956 (1957).

From a side arm, 0.300 g. (1.9 moles) of *N*-phenyl-1,2-dihydropyridine was sublimed into the flask. After sublimation was complete, 10 ml. of degassed ethyl ether was distilled into the mixture, giving a clear yellow solution. After a short time, a white solid began to form. The mixture was allowed to stand for 6 hr., after which the mixture was filtered and washed with ethyl ether, yielding 0.450 g. (71%) of the white adduct, melting at 212–215°. Recrystallization from a benzene–methylcyclohexane mixture raised the melting point to 215–216°.

*Anal.* Calcd. for C<sub>21</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.45; H, 5.64; N, 8.78.

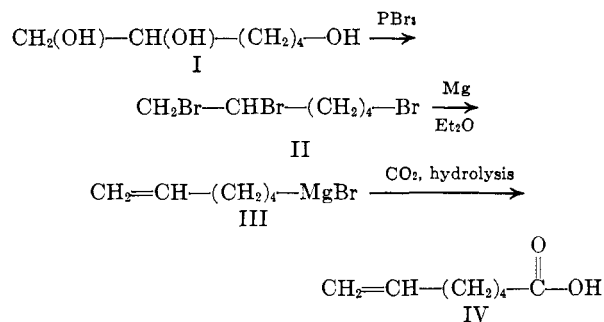
The infrared spectrum showed the imide carbonyl stretch at 1766 and 1701 cm.<sup>-1</sup>, as well as the expected phenyl absorption. The NMR spectrum showed four main areas at 2.92 (10), 3.52 (2), 4.94 (1), and 6.77 (5)  $\tau$  (parts per million referred to tetramethylsilane as 10.00).

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1,2,6-Tribromohexane, 5-Hexenylmagnesium Bromide, and 6-Heptenoic Acid<sup>1</sup>

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Recently we have used a new method (in the accompanying scheme) to prepare 6-heptenoic acid (IV). The procedure appears to be the simplest yet reported:



Producing Grignard reagents from tribromides, where two bromine atoms are *vicinal*, was developed years ago by von Braun and co-workers.<sup>2</sup> However, application of this procedure to 1,2,6-tribromohexane appears to be new.

The more obvious precursors to III would be 6-bromo-1-hexene<sup>3</sup> and 6-chloro-1-hexene.<sup>4</sup> 6-Bromo-1-hexene has been obtained by the reduction of 6-

(1) This work was supported by the National Science Foundation, NSF-G11277.

(2) Julius von Braun and G. Kirschbaum, *Ber.*, 52, 1713 (1919); J. von Braun and Z. Koehler, *Ber.*, 51, 79 (1913); J. von Braun, H. Deutsch, and A. Schmatloch, *Ber.*, 45, 1246 (1912); J. von Braun and H. Deutsch, *Ber.*, 44, 3699 (1911); J. von Braun and W. Sobekij, *Ber.*, 44, 1938 (1911).

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