

Winterfeld and Heinen<sup>23</sup> modification of the lithium aluminum hydride reduction<sup>22</sup> of diethyl  $\beta$ -(2-pyridyl)-ethylmalonate.<sup>31,32</sup> A solution of 92 g. (0.51 mole) of the aminodi-alcohol in 250 ml. of purified dioxane was hydrogenated over 30 g. of copper chromite catalyst at 260° and 300 atm. during 6 hours. The solution was filtered and the filtrate was distilled slowly through a packed column at water-pump pressure. Two fractions were collected after solvent removal: b.p. 80–100° (22 mm.) and 135–155° (12–16 mm.). Refractionation gave 13.4 g. (0.087 mole) of 3-methylquinolizidine, b.p. 75–80° (14 mm.). The higher boiling fraction, b.p. 90–95° (2 mm.), proved to be 3-hydroxymethylquinolizidine,<sup>23</sup> 38.8 g. (0.238 mole).

**Separation of the Racemates of 3-Methylquinolizidine.**—Thirteen grams of 3-methylquinolizidine was distilled slowly through a spinning band column of 26 theoretical plates, fitted with a total condensation, variable take-off distillation head. The pressure was maintained at 14 mm. by means of a manostat, and a reflux ratio of about 10:1 was employed. Cuts of distillate were taken regularly throughout the distillation. The over-all distillation range was 6° (74.5–80.5° (14 mm.)),  $n_D^{20}$  1.4776 to 1.4731: A racemate, b.p. 77.5° (14 mm.),  $n_D^{20}$  1.4757 (15%); B racemate, b.p. 80.5–81° (14 mm.),  $n_D^{20}$  1.4738 (85%).

*Anal.* Calcd. for  $C_{10}H_{19}N$ : C, 78.36; H, 12.50; N, 9.14. Found for A: C, 77.96; H, 12.22; N, 9.50; for B: C, 78.41; H, 12.25; N, 9.36.

**Picrates** were made from the two fractions and recrystallized from ethanol: A picrate, yellow plates, m.p. 194.5–195.5°; B picrate, yellow elongated prisms, m.p. 183–184°.

*Anal.* Calcd. for  $C_{16}H_{25}N_3O_7$ : C, 50.25; H, 5.80; N, 14.61. Found for A: C, 50.42; H, 5.69; N, 14.43; for B: C, 50.37; H, 5.71; N, 14.39.

**Picolonates** of the two fractions were prepared in and recrystallized from ethanol: A picolonate, yellow prisms, m.p. 248–250° dec.; B picolonate, yellow elongated prisms, m.p. 208–209° dec.

*Anal.* Calcd. for  $C_{20}H_{27}N_5O_5$ : C, 57.54; H, 6.52; N, 16.78. Found for A: C, 57.48; H, 6.63; N, 16.53; for B: C, 57.59; H, 6.85; N, 16.69.

(39) W. E. Doering and Ruth A. N. Weil, *THIS JOURNAL*, **69**, 2461 (1947).

**Ethyl  $\alpha$ -Methyl- $\gamma$ -(2-pyridyl)-butyrate (XIII).**—The addition of diethyl methylmalonate to 2-vinylpyridine in the presence of sodium ethoxide and ethanol, led, as in the case of the ethyl homolog,<sup>22</sup> to a decarboxylated product. A 77% yield of ethyl  $\alpha$ -methyl- $\gamma$ -(2-pyridyl)-butyrate was realized, b.p. 111° (2 mm.),  $n_D^{20}$  1.4868.

*Anal.* Calcd. for  $C_{12}H_{17}NO_2$ : C, 69.53; H, 8.27; N, 6.76. Found: C, 69.78; H, 8.38; N, 7.00.

**3-Methylquinolizidine.**—A solution of 150 g. (0.75 mole) of ethyl  $\alpha$ -methyl- $\gamma$ -(2-pyridyl)-butyrate in 270 ml. of purified dioxane was hydrogenated over 22 g. of copper chromite catalyst at 260° and 300 atm. The solution was filtered, the solvent removed and the residue fractionated yielding 66.5 g. (58%) of 3-methylquinolizidine, b.p. 82° (15.5 mm.). The entire product was distilled through a spinning band column, and there was no appreciable change in the refractive index,  $n_D^{20}$  1.4738, through the 23 fractions taken. (The 1-ml. forerun and the pot residue had slightly higher indices.) The picrate was prepared in and recrystallized from ethanol as yellow elongated prisms, m.p. 182–183°, no depression in melting point on mixture with B picrate (above).

**1-Methylquinolizidine (XII).**—A solution of 85 g. (0.29 mole) of 1,3-dicarbethoxy-4-quinolizone (XI)<sup>13</sup> in 400 ml. of purified dioxane was hydrogenated at 260° and 340 atm. over 22 g. of copper chromite catalyst. The product was isolated by distillation, b.p. 75–77° (11 mm.), yield 68%.

**Separation of the Racemates of 1-Methylquinolizidine.**—Sixteen grams of 1-methylquinolizidine was distilled slowly through a spinning band column, as for the separation of the 3-isomers. The over-all distillation range was 10° (79–89° (13 mm.));  $n_D^{20}$  1.4728–1.4758.

**Picrate A** was made from the fraction boiling at 79–81.5° (13 mm.),  $n_D^{20}$  1.4740, and was recrystallized from ethanol as small yellow platelets, m.p. 192.5–193.5°. **Picrate B** was made from the fraction boiling at 85–87° (13 mm.),  $n_D^{20}$  1.4757, and recrystallized from ethanol as small yellow needles, m.p. 161–162°.

*Anal.* Calcd. for  $C_{16}H_{25}N_3O_7$ : C, 50.25; H, 5.80; N, 14.66. Found for A: C, 50.52; H, 5.72; N, 14.50; for B: C, 50.27; H, 6.12; N, 14.47.

The racemate with the higher refractive index made up about 75% of the total 1-methylquinolizidine.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

## Studies on Dihydropyridines. I. The Preparation of Unsymmetrical 4-Aryl-1,4-dihydropyridines by the Hantzsch-Beyer Synthesis<sup>1</sup>

BY JEROME A. BERSON AND EARLENE BROWN

RECEIVED AUGUST 2, 1954

The preparation of some 2'-substituted 4-aryl-1,4-dihydropyridines is described. A consideration of spectra and chemical properties leads to the conclusion that the products of the Hantzsch synthesis arise from "normal" condensation.

In connection with other studies,<sup>2</sup> we have had occasion to prepare a number of dihydropyridines of the types I, II, III and IV.

The classical Hantzsch synthesis<sup>3</sup> of dihydropyridines, involving the condensation of an aldehyde, ammonia and acetoacetic ester or other 1,3-dicarbonyl compound, was modified by Beyer<sup>4</sup> and later by Knoevenagel<sup>5</sup> to allow the preparation of unsymmetrical 1,4-dihydropyridines by condensa-

tion of an alkylidene or arylidene 1,3-dicarbonyl compound with a  $\beta$ -amino- $\alpha,\beta$ -unsaturated carbonyl compound, *e.g.*,<sup>5</sup> ethyl  $\beta$ -aminocrotonate heated with benzylidene acetylacetone gave ethyl 2,6-dimethyl-4-phenyl-5-acetyl-1,4-dihydropyridine-3-carboxylate (IIIa). The present study is concerned with the preparation of some unsymmetrical 4-aryl-1,4-dihydropyridines (in which the 4-aryl group bears an ortho substituent) by these methods and with a consideration of the structures of the products formed.

**The Structure of the Products of the Hantzsch-Beyer Synthesis.**—In the simplest case, condensation of formaldehyde, ammonia and ethyl acetoacetate leads to 2,6-dimethyl-3,5-dicarbethoxy-1,4-

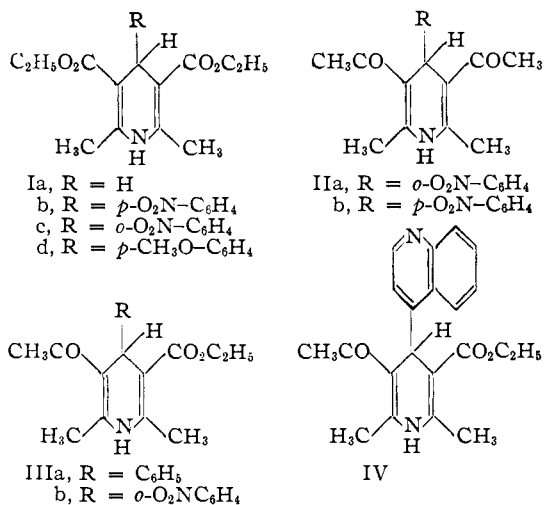
(1) This work was supported in part by a Frederick Gardner Cottrell Grant from Research Corporation.

(2) J. A. Berson and E. Brown, *THIS JOURNAL*, **77**, 447, 450 (1955).

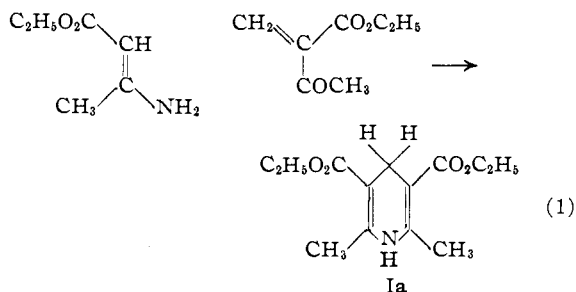
(3) A. Hantzsch, *Ber.*, **17**, 1515 (1884); **18**, 1774, 2579 (1885).

(4) C. Beyer, *ibid.*, **24**, 1662 (1891).

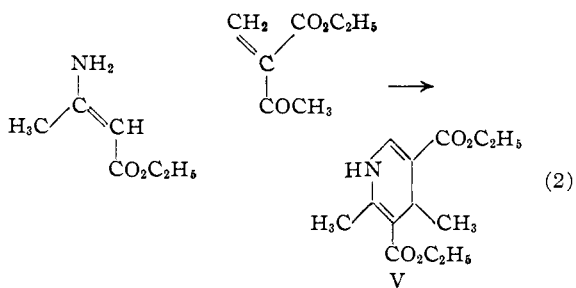
(5) E. Knoevenagel and W. Ruschhaupt, *ibid.*, **31**, 1025 (1898).



dihydropyridine (Ia).<sup>3</sup> The mechanism of the condensation has been represented<sup>4-6</sup> as involving preliminary formation of ethyl β-aminocrotonate and methyleneacetoacetic ester followed by Michael condensation and cyclization (1)



Condensation in the sense of equation 2 would lead to an isomer V. V, however, is inconsistent

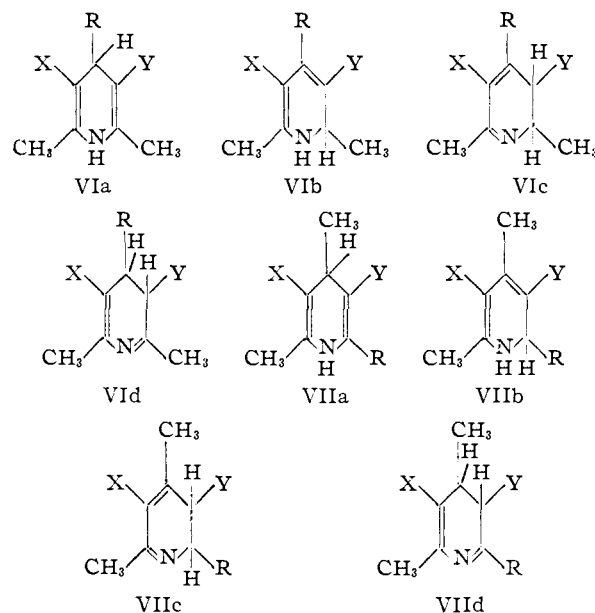


with the degradation of the product to 2,6-lutidine, and consequently structure Ia (or a double bond isomer thereof) is established. It is not clear, however, that reaction in the sense of (1) should always predominate. Indeed, the Hantzsch synthesis often gives low yields, and in some cases, side products (uncharacterized) are isolated.<sup>7</sup> Nevertheless, Hantzsch synthesis products have invariably been formulated in the literature as arising from condensation according to (1), even though independent, unambiguous syntheses or other methods of structure proof were not available.

(6) H. S. Mosher in "Heterocyclic Compounds," edited by R. C. Elderfield, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 462.

(7) I. E. Hinkel, E. E. Ayling and W. H. Morgan, *J. Chem. Soc.*, 1835 (1931).

A mechanistic argument favoring equation 1 over 2 can be made if one assumes that the product-determining step is attack of the α-carbon (equation 1) or the nitrogen (equation 2) of ethyl β-aminocrotonate upon the double bond of the unsaturated carbonyl compound. In this case, since formation of a C-C bond is about 10 kcal. per mole more exothermic than formation of a C-N bond,<sup>8</sup> reaction according to equation 1 would be favored. The complexity of the reaction and the fact that the Michael condensation step is, at least in principle, reversible, make such an argument less compelling than would otherwise be the case. Therefore, the structures which must be considered for the products of the reactions of ethyl β-aminocrotonate with an alkylidene- or arylideneacetoacetic ester or acetylacetone are VIa-d and VIIa-d (R = alkyl or aryl, X and Y = CH<sub>3</sub>CO or COOC<sub>2</sub>H<sub>5</sub>).



Structures VIc, VId, VIIc and VIId can be immediately rejected on the grounds that the Hantzsch products are (i) non-basic and (ii) all show well-defined N-H absorption in the infrared (Table I). The general similarities of the ultraviolet spectra of Table I<sup>9</sup> and, in particular, the occurrence throughout the series of the medium-intensity band at 360-385 mμ, leave little doubt that the same principal chromophoric system is present in all these substances. The Hantzsch products are therefore either 1,4-dihydropyridines (VIa or VIIa) or 1,2-dihydropyridines (VIb or VIIb). The weight of evidence in the literature favors the 1,4-dihydro structure: Thus, while 1,2-dihydropyridines are formed by the reduction of "pyridone methids" (anhydro bases)<sup>10</sup> and react rapidly with

(8) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p. 53.

(9) The general features of all these ultraviolet spectra are in agreement with those reported for another series of dihydropyridines prepared by lithium aluminum hydride reduction of the corresponding pyridines [F. Bohlmann and M. Bohlmann, *Chem. Ber.*, **86**, 1419 (1953)].

(10) O. Mumm, K. Behrens, A. von Fischer-Trauenfeld, G. Hingst, W. Lund, O. Mrozek, J. Sönksen and O. Tonn, *Ann.*, **443**, 272 (1925).

silver nitrate<sup>11,12</sup> and with maleic anhydride,<sup>12,13</sup> 1,4-dihydropyridines (including the Hantzsch products) react sluggishly with silver nitrate<sup>9,12</sup> and slowly<sup>14</sup> or not at all<sup>12</sup> with maleic anhydride.

TABLE I  
ULTRAVIOLET<sup>a</sup> AND INFRARED<sup>b</sup> SPECTRA

	$\lambda_{\max}$ , m $\mu$	$\epsilon$	$\lambda_{\max}$ , $\mu$
Ia	231	6350	3.09
	375	3390	
Ib	234	16890	3.12
	282	11100	
	366	3680	
Ic	237	9830	3.12
	332 <sup>c</sup>	4990	
	<230	...	
Id	275, 278 <sup>d</sup>	3300, 3350	3.11
	357	6360	
	257	16590	
IIa	257	16590	3.14
	382	5490	
IIb	256	24500	3.10
	385	6750	
IIIa	251	13870	3.14
	375	6940	
IIIb	274	8810	3.10
	359	4740	
IV <sup>c</sup>	234	13180	3.14
	305	5000	
	384	4100	

<sup>a</sup> Taken in 95% ethanol with the Beckman spectrophotometer, Model DU. <sup>b</sup> In hexachlorobutadiene mull, taken with the Perkin-Elmer spectrometer, Model 13, NaCl prism. <sup>c</sup> The spectrum closely approximated the sum of those of quinoline and Ia. <sup>d</sup> This band complex corresponds to the peaks of anisole,  $\lambda_{\max}$  266, 272, 278 m $\mu$ ;  $\log \epsilon$  3.15, 3.28, 3.25 [R. A. Friedel and M. Orchin, "Ultra-violet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, curve 55]. <sup>e</sup> The peak is very broad and runs into a pronounced shoulder at 355-365 m $\mu$ ,  $\epsilon$  4700.

A choice between the remaining structures VIa and VIIa is based upon the ultraviolet absorption behavior of the Hantzsch products (Table I). If these substances had the "abnormal" structure VIIa (resulting from condensation according to equation 2), one would expect the spectra to be responsive to the nature of the group R, since it is attached to the chromophoric system. In fact, however, the variation of R over the series of electron-withdrawing and electron-releasing unsaturated groups produces only minor shifts in the position of the long wave length maximum. This is consistent with insulation of these substituents from the chromophore and, we believe, confirms the structure of the Hantzsch products as VIa, derived from the "normal" condensation (equation 1).

### Experimental<sup>15</sup>

2,6-Dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (Ia), prepared from formaldehyde, acetoacetic ester and am-

- (11) P. Karrer and O. Warburg, *Biochem. Z.*, **285**, 297 (1936).  
 (12) O. Mumm and O. Diederichsen, *Ann.*, **538**, 198 (1939).  
 (13) P. Karrer, *Helv. Chim. Acta*, **20**, 72 (1937).  
 (14) (a) D. Craig, L. Schaefgen and W. P. Tyler, *THIS JOURNAL*, **70**, 1624 (1948); (b) D. Craig, A. K. Kuder and J. Efrogmson, *ibid.*, **72**, 5236 (1950).

(15) Melting points are corrected. Boiling points are uncorrected. The analyses are by Messrs. J. Pirie and W. J. Schenck.

monia, had m.p. 175-180°, reported<sup>16</sup> m.p. 175-180°.

4-(4'-Nitrophenyl)-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (Ib), from *p*-nitrobenzaldehyde, ethyl acetoacetate and ethyl  $\beta$ -aminocrotonate, melted at 128-129°, reported m.p. 136°, 118-122°.<sup>17</sup>

4-(2'-Nitrophenyl)-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (Ic), from *o*-nitrobenzaldehyde, ethyl acetoacetate and ethyl  $\beta$ -aminocrotonate, had m.p. 120-120.5°, reported<sup>17</sup> m.p. 119-120°.

4-(4'-Methoxyphenyl)-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (Id) from anisaldehyde, ethyl acetoacetate and ethyl  $\beta$ -aminocrotonate, had m.p. 159-159.5°, reported<sup>18</sup> m.p. 159°.

4-Phenyl-2,6-dimethyl-3-carbethoxy-5-acetyl-1,4-dihydropyridine (IIIa), from ethyl  $\beta$ -aminocrotonate and benzylideneacetylacetone, melted at 165-166°, reported<sup>6</sup> m.p. 167°.

**Synthesis of 2,6-Dimethyl-3,5-diacetyl-4(2'-nitrophenyl)-1,4-dihydropyridine (IIa).**—A solution of 2 g. of acetylacetone, 1.5 g. of *o*-nitrobenzaldehyde and 1.5 cc. of concentrated ammonium hydroxide in 5 cc. of 95% ethanol was heated on the steam-bath for 45 minutes. The solvents were removed in a current of nitrogen and the residue was triturated with ether. The resulting crude solid was recrystallized from 95% ethanol to give 0.88 g. of IIa as lemon-yellow needles, m.p. 224-225°. Further recrystallization raised the m.p. to 225.7-226°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>: C, 64.92; H, 5.76; N, 8.89. Found: C, 64.58; H, 5.88; N, 8.67.

The yield was extremely sensitive to the quantity of ammonia water used in the condensation. In runs using more than 1.5 cc. of ammonia water to 2 g. of acetylacetone, the crude product required treatment with activated charcoal (Norite-A) before purification could be effected. If as much as 4.5 cc. of ammonia water was used, no IIa was isolated.

**Oxidation of IIa to the Corresponding Pyridine.**—A mixture of 0.20 g. of (0.56 mmole) of IIa and 0.3 g. of chloranil (1.2 mmole) in enough benzene to effect complete solution was heated at reflux for 5.5 hours. The solution was extracted with hydrochloric acid, the aqueous layer made basic with sodium carbonate and the precipitated solid collected to give 0.165 g. of 2,6-dimethyl-3,5-diacetyl-4(2'-nitrophenyl)-pyridine, m.p. 141-142°. Recrystallization from aqueous ethanol gave colorless needles melting at 144-144.6°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>16</sub>O<sub>4</sub>N<sub>2</sub>: C, 65.37; H, 5.16; N, 8.97. Found: C, 65.40; H, 5.25; N, 8.98.

**Synthesis of 2,6-Dimethyl-3,5-diacetyl-4(4'-nitrophenyl)-1,4-dihydropyridine (IIb).**—A mixture of 6 g. of *p*-nitrobenzaldehyde, 8 g. of acetylacetone and 10 cc. of concentrated ammonia hydroxide was heated on the steam-bath for 16 hours. The resulting dark red oil was taken up in ethanol, treated with Norite-A, filtered, and treated with ether to give 3.5 g. of IIb, m.p. 200-202°. Recrystallization from ethanol-ether yielded bright yellow needles, m.p. 202-202.4°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>: C, 64.92; H, 5.76; N, 8.89. Found: C, 65.26; H, 5.89; N, 9.11.

**Synthesis of 2,6-Dimethyl-3-acetyl-5-carbethoxy-4(2'-nitrophenyl)-1,4-dihydropyridine (IIIb).**—*o*-Nitrobenzylidene acetylacetone was prepared by allowing a solution of 3.0 g. of *o*-nitrobenzaldehyde, 2.0 of acetylacetone and 4 drops of piperidine to stand at -10° for three days. The benzene solution was washed with dilute hydrochloric acid and dried over magnesium sulfate. The solvent was removed by evaporation and the residual pale yellow oil crystallized from ether-ligroin to give 4.5 g. of faintly yellow plates, m.p. 63-63.5°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>11</sub>O<sub>4</sub>N: N, 6.03. Found: N, 5.78.

A mixture of 1.86 g. of *o*-nitrobenzylideneacetylacetone and 1.04 g. of ethyl  $\beta$ -aminocrotonate was heated on the steam-bath for 16 hours. The resulting burgundy oil was triturated with ether to give 1.82 g. of IIIb as a yellow precipitate. Recrystallization of this material from ether-ethanol (20:1) gave golden yellow rosettes, m.p. 175-175.4°.

(16) A. Singer and S. M. McElvain, in "Organic Syntheses," edited by A. H. Blatt, Coll. Vol. II, John Wiley and Sons, Inc., New York, New York, 1943, p. 214.

(17) R. Lepetit, *Ber.*, **20**, 1338 (1887).

(18) L. E. Hinkel and W. R. Madel, *J. Chem. Soc.*, **135**, 750 (1929).

*Anal.* Calcd. for  $C_{18}H_{20}O_3N_2$ : C, 62.75; H, 5.85; N, 8.17. Found: C, 62.87; H, 5.97; N, 8.13.

An attempt to prepare IIIb directly from *o*-nitrobenzaldehyde, acetylacetone and ethyl  $\beta$ -aminocrotonate gave a mixture of equal amounts of IIa and IIb.

**Synthesis of 2,6-Dimethyl-3-acetyl-5-carbethoxy-4-(4'-quinoliny)-1,4-dihydropyridine (IV).**—The hydrate of cinchoninaldehyde (quinoline-4-aldehyde)<sup>19</sup> was dehydrated by suspending a 1.75-g. sample in benzene and removing the water by azeotropic distillation. The aldehyde gradually dissolved. The benzene solution was cooled and treated with 1.0 g. of acetylacetone and 4 drops of piperidine. After 72 hours at room temperature, large droplets of water had separated from the reaction mixture. The reaction mixture was dried over magnesium sulfate, filtered and evaporated to give a reddish-orange oil. (In one case the product crystallized as waxy, yellow needles.) The crude 4-quinolinyldeneacetylacetone was used without further purification. A mixture of 2.5 g. of this material and 1.3 g. of ethyl  $\beta$ -aminocrotonate was heated on the steam-bath for four hours. The resulting dark red oil was leached with seven successive portions of boiling ether (total 500 cc.). The ethereal solutions were combined, concentrated to a small volume and cooled, whereupon 1.05 g. of a yellow solid separated. This material, m.p. 193–194°, was recrystallized from ether to give golden, pellet-like clusters of needles, m.p. 194.5–195°.

(19) H. Kaplan, *THIS JOURNAL*, **63**, 2654 (1941).

*Anal.* Calcd. for  $C_{21}H_{22}O_3N_2$ : C, 71.97; H, 6.33; N, 7.99. Found: C, 71.48; H, 6.39; N, 7.82.

**Oxidation of IV to the Corresponding Pyridine. A. With Chloranil.**—A solution of 0.20 g. of IV and 0.28 g. of chloranil in benzene was heated under reflux for 16 hours. The benzene solution was extracted with dilute hydrochloric acid, the aqueous layer was made basic with sodium carbonate and the precipitate collected to give 0.188 g. of colorless solid, m.p. 111–112°. Recrystallization from aqueous ethanol gave glistening colorless needles of 2,6-dimethyl-3-carbethoxy-5-acetyl-4-(4'-quinoliny)-pyridine, m.p. 113.5–114°.

*Anal.* Calcd. for  $C_{21}H_{20}O_3N_2$ : C, 72.39; H, 5.79; N, 8.04. Found: C, 72.16; H, 5.90; N, 8.04.

The oxidation was also effected in methylene chloride as solvent (five hours at reflux) or in tetrahydrofuran (two hours at reflux).

**B. With Dichromate.**—A solution of 0.20 g. of IV in 10 cc. of dilute sulfuric acid was treated dropwise with a solution of 1.0 g. of potassium dichromate and 5 cc. of concentrated sulfuric acid in 20 cc. of water until no further reduction of the dichromate was observed. The reaction mixture was made basic with aqueous ammonia, extracted with benzene and the benzene layer dried over magnesium sulfate and evaporated to give the pyridine, m.p. 110°, alone or mixed with a sample prepared as above.

LOS ANGELES 7, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

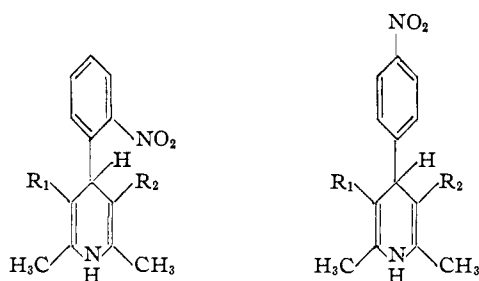
## Studies on Dihydropyridines. II. The Photochemical Disproportionation of 4-(2'-Nitrophenyl)-1,4-dihydropyridines<sup>1</sup>

BY JEROME A. BERSON AND EARLENE BROWN

RECEIVED AUGUST 2, 1954

Irradiation of 4-(2'-nitrophenyl)-1,4-dihydropyridines at 366  $m\mu$  converts these substances to the corresponding 4-(2'-nitrosophenyl)-pyridines. The photochemical reaction appears to be intramolecular.

The qualitative observation<sup>2</sup> that 2,6-dimethyl-3,5-dicarbethoxy-4-(2'-nitrophenyl)-1,4-dihydropyridine (Ia) is sensitive to light has led us to an investigation of the photochemical behavior of this substance and its congeners, Ib, Ic, IIa and IIb.



Ia,  $R_1, R_2 = CO_2C_2H_5$   
 b,  $R_1 = COCH_3; R_2 = CO_2C_2H_5$   
 c,  $R_1, R_2 = COCH_3$   
 IIa,  $R_1, R_2 = CO_2C_2H_5$   
 b,  $R_1, R_2 = COCH_3$

Qualitatively, the members of the 4-(2'-nitrophenyl) series (Ia-c) are indefinitely stable in the dark in the solid state or in solution. However, exposure of the crystals of any of these substances, or of their ethanolic solutions, to even diffuse laboratory light causes rapid and extensive changes.

(1) This work was supported in part by a Frederick Gardner Cottrell Grant from Research Corporation.

(2) L. E. Hinkel, E. E. Ayling and W. H. Morgan, *J. Chem. Soc.*, 1835 (1931).

In contrast, the 4-(4'-nitrophenyl) compounds are stable, even under intense irradiation by sunlight or a mercury arc.<sup>3</sup>

The photochemical decompositions of Ia-c are demonstrated by the absorption curves of Fig. 1. The near-identity of the three degraded spectra strongly implies that the products in all three cases are similar.

The photochemically significant exciting wave length was determined for the case of Ic by isolating the various lines of the mercury spectrum (from a General Electric Type AH-4 source) by means of appropriate optical filters and measuring spectrophotometrically the rate of disappearance of Ic relative to that of a sample irradiated by the entire spectrum. The data bracket the region 360–392  $m\mu$  as the one which probably includes the effective exciting lines. Since virtually all the intensity of the mercury emission spectrum in this region is concentrated in the strong 366  $m\mu$  lines, we conclude that this wave length is the effective one, although the very weak 377  $m\mu$  and 382  $m\mu$  lines may also contribute. We assume that the same wave length light also effects the decomposition of Ia and Ib. This wave length is very close to an absorption

(3) Known members of the 4-(3'-nitrophenyl) series of related 1,4-dihydropyridines [A. P. Phillips, *THIS JOURNAL*, **73**, 2248 (1951)], are not reported to be light sensitive. Dr. Phillips has kindly confirmed (by private communication) that these substances are not qualitatively unstable to light.