Anal. Calcd. for $C_{18}H_{20}O_5N_2$: 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 β-aminocrotonate gave a mixture of equal amounts of IIa and IIIb.

Synthesis of 2,6-Dimethyl-3-acetyl-5-carbethoxy-4-(4'-quinolinyl)-1,4-dihydropyridine (IV).—The hydrate of cinchoninaldehyde (quinoline-4-aldehyde)[19] 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-quinolinylideneacetylacetone was used without further purification. A mixture of 2.5 g. of this material and 1.3 g. of ethyl β-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°.

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'-quinolinyl)-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.

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

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

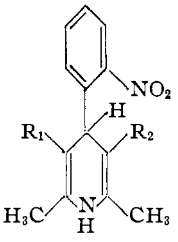
Studies on Dihydropyridines. II. The Photochemical Disproportionation of 4-(2'-Nitrophenyl)-1,4-dihydropyridines[1]

BY JEROME A. BERSON AND EARLENE BROWN

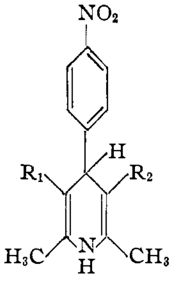
RECEIVED AUGUST 2, 1954

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

The qualitative observation[2] 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. In contrast, the 4-(4'-nitrophenyl) compounds are stable, even under intense irradiation by sunlight or a mercury arc.[3]

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 mμ 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 mμ lines, we conclude that this wave length is the effective one, although the very weak 377 mμ and 382 mμ 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

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[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).

[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.

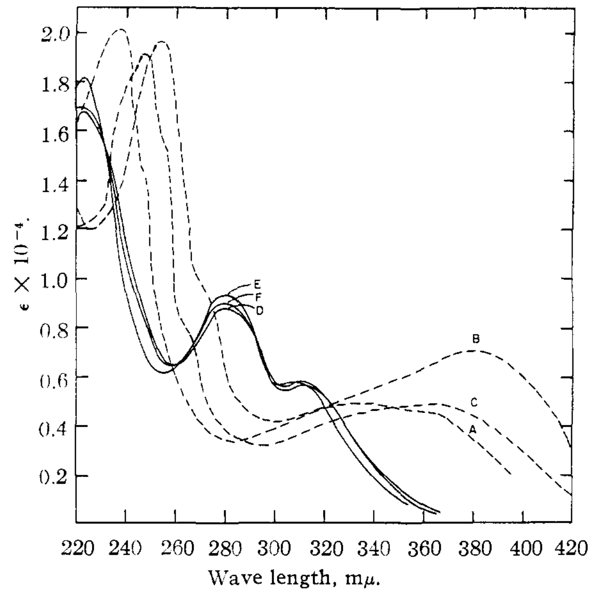
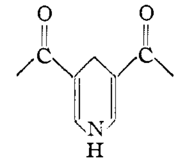


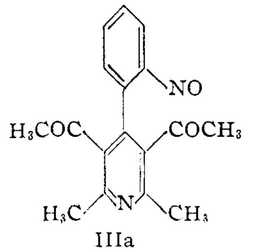
Fig. 1.—Ultraviolet absorption spectra in 95% ethanol: A = Ia; B = Ic; C = Ib; D = IIIa = Ic after irradiation; E = Ia after irradiation; F = Ib after irradiation.

maximum characteristic of the chromophore Id,[4] and is within the absorption band, but not near the maximum, associated with aromatic nitro compounds.[5] The short wave length maximum (237–274 mμ) of the 2′-nitrophenyl-1,4-dihydropyridines appears to be photochemically inactive, since the reaction proceeds in Pyrex glass (opaque below 285 mμ, 40% transmission at 313 mμ for a 2 mm. thickness, virtually transparent at 365 mμ[6]).

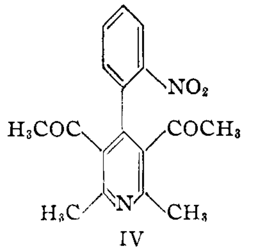


Id

The product of the photochemical decomposition of Ic is a *base*, $C_{17}H_{16}O_3N_2$, resulting empirically from Ic by loss of a molecule of water. We formulate this substance as 2,6-dimethyl-3,5-diacetyl-4-(2′-nitrosophenyl)-pyridine (IIIa) on the basis of the following evidence



IIIa



IV

(i) In contrast to Ic (and other similar 1,4-dihydropyridines) which show no basic properties, the irradiation product is a base. This indicates a pyridine nucleus.

(ii) IIIa gives positive qualitative tests for a nitroso compound.

(iii) The ultraviolet spectrum of IIIa shows a band at 280 mμ, corresponding to that of nitrosobenzene.[7]

(iv) The characteristic monomer–dimer equilibrium of aromatic nitroso compounds[8] is suggested by the isolation of IIIa in two forms: buff needles (presumably dimer) and aquamarine staves (presumably monomer). Both forms show the same ultraviolet spectrum.

(v) Oxidation of IIIa with cold dichromate gives a substance $C_{17}H_{16}O_4N_2$, identical with the nitro compound (IV) obtained[4a] by dehydrogenation of Ic with chloranil.

The photochemical reaction appears to be virtually quantitative, since the crude reaction product is entirely acid-soluble and the ultraviolet spectrum of the total irradiation reaction mixture is indistinguishable from that of IIIa.

Although the new photochemical reaction is unique in that reduction of a nitro group is achieved at the expense of an aromatizing dehydrogenation, it has formal analogies in the photochemical reductions of nitro groups in *o*-nitrobenzaldehyde,[9] *o*-nitroterephthalaldehyde,[10] 2,4-dinitrobenzaldehyde, 2,4,6-trinitrobenzaldehyde,[11] 2,4,6-trinitrotoluene[12] and *o*-nitrobenzylidene glycol.[13]

The mechanism of these changes is uncertain. However, for the case of *o*-nitrobenzaldehyde, Lucy and Leighton[9f] have been able to account theoretically for the observed[9b,c,e] quantum efficiency of 0.5 and for the negative temperature coefficient[9g] in terms of a quantum mechanical model. These authors represent the process as the transfer of an oxygen atom from an activated nitro group to the carbonyl carbon, the transfer occurring by a re-distribution of electrons ("Villars' allegiance exchange") when the nitro and aldehydo groups are coplanar with the aromatic ring. An analogous change in I would lead to V and, by loss of water, to the nitrosophenylpyridine (VI). However, there seems to be no reason to exclude the possibility that, at least in the case of I, the reaction might

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[4] (a) J. A. Berson and E. Brown, THIS JOURNAL, **77**, 444 (1955); (b) F. Bohlmann and M. Bohlmann, *Chem. Ber.*, **86**, 1419 (1953).

[5] P. A. Leighton and F. A. Lucy, *J. Chem. Phys.*, **2**, 756 (1934).

[6] G. W. Morey, "The Properties of Glass," Reinhold Publ. Corp., New York, N. Y., 1938, p. 433. The data do not eliminate the possibility that the strong 313 mμ line of the mercury spectrum is also effective, although the combination Pyrex glass-Corning No. 5874 filter (which readily allows the photochemical reaction) excludes 98% of incident radiation at 313 mμ.

[7] Y. Tuzuki, T. Uemura and N. Hirasawa, *Ber.*, **74**, 616 (1941), report λ_{max} 282 mμ for nitrosobenzene. It is of interest that the position of this band is essentially unchanged by the presence of a substituted 4-pyridyl nucleus *ortho* to the NO group of IIIa. Presumably, this is due to steric inhibition of resonance.

[8] (a) D. L. Hammick, *J. Chem. Soc.*, 3105 (1931); (b) C. K. Ingold and H. A. Piggott, *ibid.*, **125**, 168 (1924).

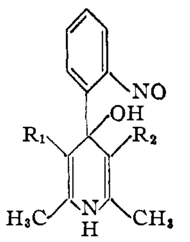
[9] (a) G. Ciamician and P. Silber, *Ber.*, **34**, 2040 (1901); (b) F. Weigert and L. Kummerer, *ibid.*, **46**, 1207 (1913); (c) F. Weigert and L. Brodmann, *Trans. Faraday Soc.*, **21**, 453 (1926); (d) E. J. Bowen, H. Hartley, W. D. Scott and H. G. Watts, *J. Chem. Soc.*, 1218 (1924); (e) P. A. Leighton and F. A. Lucy, *J. Chem. Phys.*, **2**, 756 (1934); (f) F. A. Lucy and P. A. Leighton, *ibid.*, **2**, 760 (1934); (g) K. G. Zimmer, *Z. physik. Chem.*, **23B**, 239 (1933); (h) R. Wegscheider, *Monatsh.*, **62**, 101 (1933).

[10] G. Kögel, *Z. wiss. Phot.*, **24**, 216 (1926); *C. A.*, **20**, 3646 (1926).

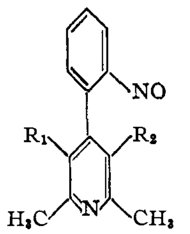
[11] (a) P. Cohn and P. Friedländer, *Ber.*, **35**, 1265 (1902); (b) F. Sachs and R. Kempf, *ibid.*, **35**, 2704 (1902).

[12] G. Schultz and K. L. Ganguly, *ibid.*, **58**, 702 (1925).

[13] I. Tanasescu and H. Tanasescu, *Bull. Soc. stiinte Cluj.*, **2**, 369 (1925); *C. A.*, **20**, 749 (1926).



V



VI

involve transfer of the C_4 hydrogen of I to the nitro group. The uncertainty surrounding the mechanism is increased by the fact that the exciting wave length (366 mμ) is absorbed by both the nitrophenyl and dihydropyridine chromophores. (In *o*-nitrobenzaldehyde, only the nitrophenyl chromophore is excited.[9e])

The structural requirement that the nitro group of the nitrophenyl-1,4-dihydropyridines be in the 2'-position implies that the photochemical reaction is intramolecular.[14] A corollary of this is that the reaction, at constant light flux and "infinite" optical thickness, should obey the kinetic form $(-dc/dt = K)$[15] of the Einstein photochemical equivalence law.[16,17] This is partially confirmed by the observation (Fig. 2) that the decomposition of Ib follows zero-order kinetics to about 60% reaction. The decrease in rate beyond this point is attributable to an inhibition of the reaction by the product, 2,6-dimethyl-3-carbethoxy-5-acetyl-4-(2'-nitrosophenyl)-pyridine (IIIb). The nature of this inhibition we do not yet fully understand. The internal filter effect,[18] due to absorption by IIIb of part of the photochemically significant radiation, would account for part, but apparently not all of the inhibition. Irradiation of a solution 7.49×10^{-4} *M* in Ib and 4.43×10^{-4} *M* in IIIb (Fig. 2) should result in an initial rate for the photochemical process about 0.9 times as fast as that for Ib alone (under the same experimental conditions) if the internal filter effect were the only mechanism of inhibition. Actually, however, the observed initial rate is only about 0.5 times as fast.

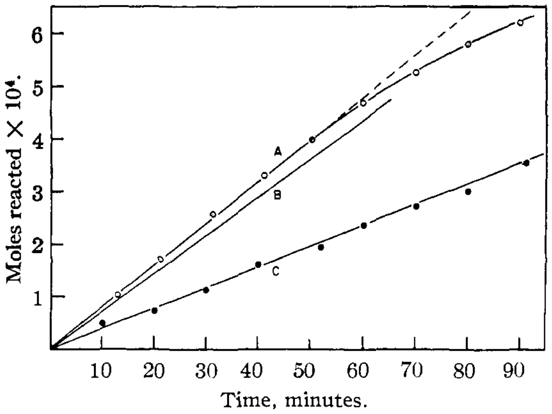


Fig. 2.—Rates of photochemical decomposition of Ib in 95% ethanol: A, at initial concentration 6.25×10^{-4} *M* in Ib; C, initial concentration 7.49×10^{-4} *M* in Ib and 4.43×10^{-4} *M* in IIIb; B, theoretical curve for the "internal filter" effect under conditions in C.

Experimental

Qualitative Behavior of the Dihydropyridines to Light.—The extreme light-sensitivity of the 2'-nitrophenyl compounds (Ia-c)[4a] made it necessary to carry out all operations in a dark room. Spectrophotometric readings of ethanolic solutions of these substances were reproducible, provided that the solutions were exposed only to the spectrophotometric light source (hydrogen or tungsten lamp, Beckman Model DU Spectrophotometer). The quantum output of these sources is apparently low enough so that any photochemical changes were negligible. Ethanolic solutions of Ia-c obeyed Beer's law in the concentration range 10^{-3}–10^{-4} *M*. The values of ϵ_{max} for a given substance were reproducible to better than 1% for varying concentrations. All solutions were masked with metal foil and stored in the dark when not in use. No spectral changes were noted after several weeks of storage. Solid samples of Ia-c faded from the characteristic yellow color of the pure materials to buff and then to brown after an hour or so of exposure to laboratory light.

The 4'-nitrophenyl compounds (IIa, IIb)[4a] showed no evidence of deterioration in the solid state. Ethanolic solutions of these substances were exposed to laboratory light, intense California daylight and a General Electric Type AH-4 mercury arc source without showing any detectable spectrophotometric changes.

The curves of the irradiated products of Fig. 1 were obtained by exposure of the solutions until the spectra showed no further change.

Determination of the Photochemically Significant Wave Lengths.—In these experiments, the extent of decomposition of an ethanolic solution of Ic in a given time when irradiated by filtered light was compared with that in a comparison sample of the same initial concentration exposed to the entire mercury arc spectrum. The two solutions were contained in quartz cuvettes of identical dimensions and the cuvettes were carefully shielded from light except for a rectangular space of the same area on both. The radiation was passed through the filter positioned in front of the test sample, while the comparison sample was placed alongside. Since some of the Wratten filters used have only a limited optical stability, the transmission region for each filter was determined in the Beckman immediately before use. The concentrations of the two samples after a given period of irradiation were determined spectrophotometrically. The results follow (filter/main transmission range/fractional transmission at 366 mμ/approximate rate relative to comparison sample): Wratten No. 35/360–440 mμ/0.24/0.39; Wratten No. 45/430–530 mμ/0.01/0.01; Wratten No. 15/ $>$510 mμ/0/no reaction; sodium nitrite, saturated aqueous solution and Rhodamine B/405–496 mμ/0/no reaction; Corning No. 5874/360–392 mμ/0.54/0.37. The amount of material decomposed per unit time was not detectably different when the reaction was run in a Pyrex flask compared to that in a Vycor No. 790 flask.

Isolation of IIIa.—A solution of 0.15 g. of Ic in 750 cc. of 95% ethanol was irradiated for 16 hours with the General Electric Type AH-4 mercury arc. The solvent was removed *in vacuo* and the residue taken up in dilute hydrochloric acid. The entire residue was acid-soluble. The aqueous solution was made basic with sodium carbonate, whereupon a buff precipitate separated. Ethanol solutions of this material were pale green. When the solution was concentrated, a mixture of buff needles and a few long, sharply-defined aquamarine staves was obtained. We were unable to determine conditions for separating the two forms by crystallization. A sample of the green form was obtained by hand-picking the crystals under the microscope. This material melted at 129.5–130.5° dec. Its ultraviolet spectrum in 95% ethanol was indistinguishable from that of the buff material or the total irradiated solution (Fig. 1).

Anal. Calcd. for $C_{17}H_{16}O_3N_2$: C, 68.90; H, 5.44. Found: C, 68.41; H, 6.14.

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(14) A similar conclusion is inferred[9f] from the fact that o-nitrobenzaldehyde is photochemically unstable, while *m*- and *p*-nitrobenzaldehyde are not.

(15) M. Bodenstein, *Trans. Faraday Soc.*, **21**, 525 (1925).

(16) A. Einstein, *Ann. Physik*, [4] **37**, 832 (1912).

(17) J. Stark, *ibid.*, [4] **38**, 467 (1912).

(18) N. R. Dhar, "The Chemical Action of Light," Blackie and Son, Ltd., London and Glasgow, 1931, p. 25.

The buff needles were recrystallized from benzene–hexane to give material of m.p. 129.5–130.5° dec. with softening at 125–128°. The substance gave a green color with phenol and concentrated sulfuric acid.[19] With sodium pentacyanoammine ferroate, it gave a green color which gradually changed to violet.[20]

Anal. Calcd. for $C_{17}H_{16}O_3N_2$: C, 68.90; H, 5.44; N, 9.46. Found: C, 69.10; H, 5.57; N, 9.68.

Oxidation of IIIa to IV.—To a solution of 0.10 g. of IIIa in 10 cc. of 10% sulfuric acid was added dropwise 6 cc. of a solution of 1 g. of potassium dichromate in 10 cc. of 10% sulfuric acid. The resulting mixture was stirred at room temperature for 4 hours, treated with solid sodium carbonate until basic and extracted with benzene. The benzene solution was dried over magnesium sulfate and evaporated *in vacuo*. The residue was taken up in ethanol, the solution brought to a faint turbidity by the addition of water and then slowly evaporated at room temperature *in vacuo* until the onset of crystallization. The product, 0.05 g. of clustered, colorless needles, melted at 139–141°. The m.p. was not depressed on admixture with an authentic sample of IV.[4a]

Kinetics of the Decomposition of Ib.—The light source was a General Electric Type AH-4 mercury lamp, which operates at 8 atmospheres working pressure. The quantum output of this lamp was essentially constant over periods of several hours. This was demonstrated as follows. The light from the arc was collimated by two slits, 2 × 20 mm., placed 5 and 17 cm. from the lamp. The beam was intermittently interrupted by a rotating sector at a frequency of 1080 cps. A No. 929 blue-sensitive phototube and a Wratten No. 50 filter were used to isolate the 435.7 mμ line. The phototube was operated at 20 volts and the resulting alternating signal amplified in a high gain, highly degenerated, narrow band amplifier. The output was rectified and observed on a 1 milliampere meter. In two separate determinations the initial readings (milliamp.) were 0.82 and 0.83 and the readings after 2 and 3 hours, respectively, were 0.82 and 0.81.

The rate runs of Fig. 2 were followed spectrophotometrically at the absorption maximum of Ib (359 mμ). Since the effective wave length appears to be limited to the 366 mμ line, the beam was not filtered. The optical path was set up vertically, the beam passing through the bottom of the reaction vessel, a Pyrex beaker. The reaction solutions were stirred to eliminate concentration gradients and the solutions were of sufficient depth to provide "infinite" optical thickness (at least 99% absorption of incident radiation) even after 90% reaction and after removal of the necessary aliquots. The aliquots were diluted when necessary to a convenient concentration for spectrophotometry, these operations being carried out rapidly and with minimum exposure to light.

Acknowledgment.—The authors are indebted to Mr. Gerald B. Porter for determining the constancy of the light source.

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[19] C. Liebermann, *Ber.*, **7**, 247 (1874), *et seq.*

[20] (a) O. Baudisch, *ibid.*, **54**, 413 (1921); (b) F. Feigl, "Qualitative Analysis by Spot Tests," Elsevier Publ. Co., Inc., New York, N. Y., 1946, p. 321.

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

Studies on Dihydropyridines. III. An Absolute Asymmetric Synthesis and an Attempted Conversion of Carbon Atom Asymmetry to Biphenyl Asymmetry[1]

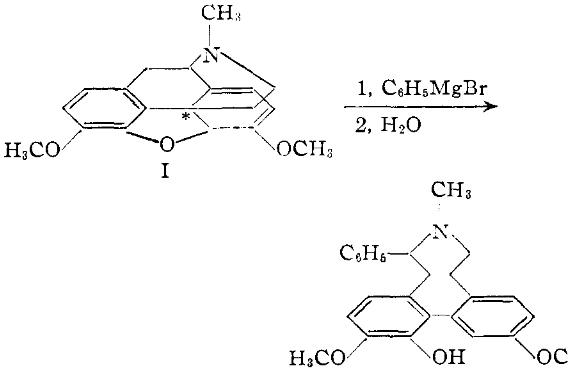
BY JEROME A. BERSON AND EARLENE BROWN

RECEIVED AUGUST 2, 1954

A novel type of asymmetric induction reaction is proposed, *i.e.*, one in which a center of carbon atom asymmetry is destroyed concomitant with the generation of a new center of biphenyl asymmetry. An absolute asymmetric decomposition of a 4-(2′-nitrophenyl)-1,4-dihydropyridine with circularly polarized light is described.

Asymmetric induction is possible whenever products arise *via* diastereomeric transition states. In detail, most asymmetric inductions have involved creation or destruction of a new carbon atom asymmetric center in the presence of a previously existing one in the same molecule[2] or in a molecule of a catalyst[2a,b] or reagent.[2a,b,3] An example which involves creation of a center of molecular (allene) asymmetry is the *d*-camphor-10-sulfonic acid-catalyzed dehydration of 1,3-diphenyl-1,3-di-(1-naphthyl)-propene-2-ol-1.[4]

The present report initiates a study of a little-known type of asymmetric induction, *i.e.*, one in which a center of biphenyl-type asymmetry is created at the expense of destruction of a center of carbon atom asymmetry. As far as we are aware, only two examples of this type of asymmetric "transfer" are known. The conversion of thebaine (I) to phenyldihydrothebaine (II)[5] involves[6] loss



I

II

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

[2] *Cf. inter alia* (a) F. Ebel in "Stereochemie," edited by K. Freudenberg, Vol. II, Franz Deuticke, Leipzig and Vienna, 1932, pp. 580–584; (b) R. L. Shriner, R. Adams and C. S. Marvel in "Organic Chemistry," second edition, edited by H. Gilman, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 308–312. For later literature, see (c) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952); (d) V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953); (e) E. E. Turner and M. M. Harris, *Quart. Rev.*, **1**, 299 (1947); (f) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950).

[3] (a) G. Vavon and B. Angelo, *Compt. rend.*, **224**, 1435 (1947); (b) G. Vavon, C. Riviere and B. Angelo, *ibid.*, **222**, 959 (1946); (c) H. S. Mosher and E. La Combe, THIS JOURNAL, **72**, 3994 (1950); (d) A. Streitwieser, *ibid.*, **75**, 5014 (1953); (e) W. von E. Doering and T. Aschner, *ibid.*, **71**, 838 (1949); (f) W. von E. Doering and R. W. Young, *ibid.*, **72**, 631 (1950); (g) A. Bothner-By, *ibid.*, **73**, 846 (1951).

[4] P. Maitland and W. H. Mills, *Nature*, **135**, 994 (1935).

[5] (a) M. Freund, *Ber.*, **38**, 3234 (1905); (b) L. Small, L. J. Sargent and J. A. Bralley, *J. Org. Chem.*, **12**, 1839 (1947).

[6] R. Robinson, *Nature*, **160**, 815 (1947).