H, 5.2; N, 10.2. Found: C, 61.3; H, 5.4; N, 10.5. After removal of anthranilic acid, as above, the acid solution is made alkaline with sodium bicarbonate and extracted with ether. The ethereal solution, when evaporated, leaves behind an oily basic residue which behaves like a pyrrole derivative, imparting a red color to a pine shaving moistened with hydrochloric acid. The alkaline solution is again acidified with sulfuric acid and steam distilled. The steam distillate is acid to congo paper, and after neutralization with sodium hydroxide and evaporation, leaves behind a salt identical to sodium formate. *Anal.* Calcd. for HCOONa: Na, 33.3. Found: Na, 31.8.

Summary

From the Chinese drug, Ch'ang Shan, identified as *Dichroa febrifuga* Lour., there have been isolated umbelliferon, 4-quinazolone, a base with the composition $C_{18}H_{23}O_3N_3$, and a water soluble alkaloid named dichroine. The last compound has the composition $C_{16}H_{21}O_3N_3$ and undergoes easily isomeric change with the formation of three isomerides, which are provisionally named α-, β- and γ-dichroines, being convertible into each other under suitable conditions. Regarding their antimalarial activity, the γ-isomeride shows the greatest, and the α-isomeride the least. Based on the results of oxidation and alkaline hydrolysis, dichroine appears to be composed of 4-quinazolone and a pyrrole derivative which requires further investigation. Dichroine forms both normal and acid salts and a nitroso compound. The isolation of 4-quinazolone from a natural plant, Ch'ang Shan, affords a remarkable coincidence with the chemical research for antimalarials along this line.

RECEIVED JUNE 21, 1947

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

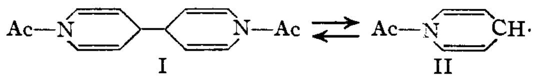
Pyridines. II. The Dissociation of N,N'-Diacetyltetrahydro-4,4'-dipyridyl[1]

BY ROBERT L. FRANK, FLOYD PELLETIER AND FRED W. STARKS

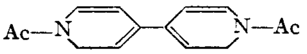
The reductive acetylation of pyridine by means of zinc and acetic anhydride was first reported by Dimroth and Heene[2] to yield the bimolecular product N,N'-diacetyltetrahydro-4,4'-dipyridyl (I). They observed that the compound exists in two interconvertible modifications, one white, the other yellow. Dimroth and Frister[3] later suggested that the yellow color might be due to an impurity, N,N'-diacetyldihydro-4,4'-dipyridyl.

It has occurred to us that either of two phenomena might be responsible for the existence of the two forms of this compound. The easy cleavage of the 4,4' valence bond between the rings in compounds of this type[2–6] suggests that the yellow color is connected with dissociation of the colorless form (I) into radicals (II).[7] On the other hand the work of Mumm and co-workers[5] on N-alkylated tetrahydrodipyridyls and the fact that α-dihydropyridines are yellow while the γ-isomers are colorless[8] presents the alternative proposition that the white and yellow forms may be represented by Structures I and III (or IIIa), respectively, owing to isomerism of double bonds.

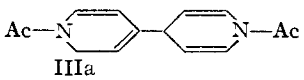
The evidence presented herein favors the dissociation theory and renders unlikely the rearrangement of double bonds.



I II



III



IIIa

The interconversion of the two modifications depends on the solvent and on the temperature. If the white form is dissolved in methanol, ethanol, acetone or dioxane, it stays white until heated, then turns yellow. On cooling it again becomes colorless. In acetic acid or chloroform the white form turns yellow on standing at room temperature, or more quickly on heating.

Both forms have been reported to have the same m. p.[2] The reason for this is that the white crystals can be observed to turn yellow before melting. This change is first evident at about 105° and the material is bright yellow just before melting at 130–131°. This thermal conversion from white to yellow conforms with the idea that the yellow form contains radicals, since dissociation should be more likely at elevated temperatures.

Further, the yellow color in solutions is dispelled by small amounts of air. This is to be expected of radicals,[9] and may signify the formation of a peroxide from the dissociated form. No peroxide has been found, however, and complete air oxidation either of solutions or of the crystalline forms, yields 4,4'-dipyridyl.[2]

Measurements of the magnetic susceptibility of the two crystalline forms further indicate the presence of radicals in the yellow modification. The

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(1) For the previous communication on pyridine chemistry, see Frank, Blegen, Dearborn, Myers and Woodward, THIS JOURNAL, **68**, 1368 (1946).

(2) Dimroth and Heene, *Ber.*, **54**, 2934 (1921).

(3) Dimroth and Frister, *ibid.*, **55**, 1223 (1922).

(4) Emmert, *ibid.*, **53**, 370 (1920).

(5) Mumm, Roder and Ludwig, *ibid.*, **57**, 865 (1924); Mumm and Ludwig, *ibid.*, **59**, 1605 (1926).

(6) Wibaut and Arens, *Rec. trav. chim.*, **60**, 119 (1941).

(7) Structure II represents only one of the several possible resonance forms for such a radical.

(8) Karrer, Schwarzenbach, Benz and Solmssen, *Helv. Chim. Acta*, **19**, 811 (1936).

(9) Gomberg and Cone, *Ber.*, **37**, 3538 (1904).

yellow form was found to be paramagnetic ($K = +0.437 \times 10^{-6}$), while the white is diamagnetic ($K = -0.199 \times 10^{-6}$).

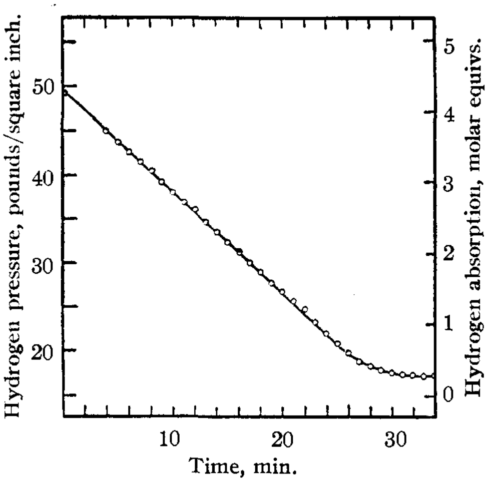

Fig. 1.—Rate of hydrogenation of N,N'-diacetyltetrahydro-4,4'-dipyridyl.

Considering now the data which rule out Structure III (or IIIa) for the yellow form, the rate of complete hydrogenation of yellow N,N'-diacetyltetrahydro-4,4'-dipyridyl over platinum oxide in acetic acid showed that all four double bonds absorb hydrogen at the same rate (Fig. 1). This indicates four unconjugated double bonds, as in Structure I. Structure III would be expected to absorb the last mole of hydrogen more slowly than the first three.

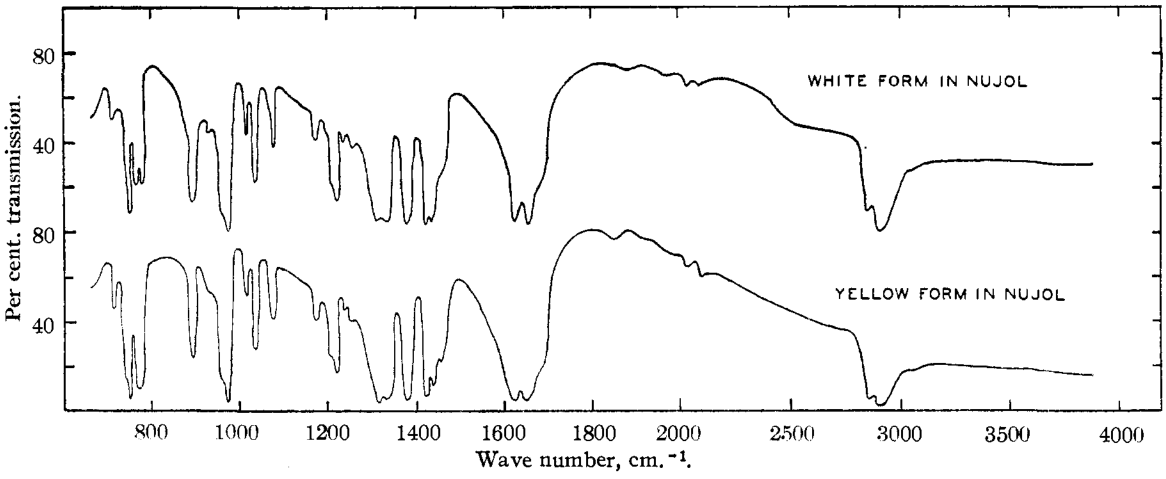

Fig. 2.—Infrared spectra of solid, N,N'-diacetyltetrahydro-4,4'-dipyridyl.

Infrared (Fig. 2) and ultraviolet (maximum at 239 mμ (log ϵ = 3.73)) absorption spectra of both white and yellow forms are essentially identical, which would not be expected if the forms differed in the manner of Structure I and III (or IIIa).[10]

Ozonolysis of the yellow form of N,N'-diacetyltetrahydro-4,4'-dipyridyl gave succinic acid as the only isolable product. Succinic acid would be expected from Structure I, but is not possible from Structures III or IIIa.

Although the above evidence is best interpreted by dissociation of Structure I into free radicals, the amount of dissociation at room temperature is probably slight, since the catalytic hydrogenation of the yellow form gave only N,N'-diacetyl-4,4'-dipiperidyl. No N-acetylpiperidine, the expected reduction product of the radical (II), was found.

One further experiment was considered, the effect of the white and yellow forms on the polymerization of styrene. When a trace of either form was added to styrene and the styrene heated in a sealed viscosimeter at 58°, the solution containing the white form turned yellow, and in either case polymerization of the styrene was completely inhibited.

Experimental

N,N'-Diacetyltetrahydro-4,4'-dipyridyl (I).—A yield of 23.6 g. (20%) of the yellow form was obtained using the directions of Wibaut and Arens[6] from 50.0 g. (0.632 mole) of freshly-distilled pyridine. From this was obtained in 75% yield the colorless modification by means of 0.5% methanolic potassium hydroxide.[6,11] The b. p. of 10.00 ml. of chloroform was raised 0.128° by 0.10995 g. of the compound (yellow in boiling chloroform); mol. wt. 224 (calcd. for undissociated molecule 244).

Behavior in Solutions and in Air.—Small amounts (0.1–1.0%) of colorless N,N'-diacetyltetrahydro-4,4'-dipyridyl dissolved in methanol, ethanol, acetone or dioxane become yellow on warming in a stoppered flask. On cooling, the solution becomes colorless. If the heated flask is opened to the air and shaken, the solution becomes colorless, but gradually turns yellow again if restoppered. The yellow crystalline modification, dissolved (0.1%) in any of these solvents open to the atmosphere at room temperature, becomes colorless in five to ten minutes.

The same properties are exhibited in glacial acetic acid or chloroform, except that in these solvents the yellow

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[10] Barnes, Gore, Liddel and Williams, "Infrared Spectroscopy," Reinhold Publishing Corp., New York, N. Y., 1944, pp. 1–25.

[11] This "conversion" of the yellow to the white form is probably not a conversion at all, but rather the oxidative destruction of the small amount of yellow dissociated material present, with subsequent recovery of the remaining undissociated compound.

color predominates at room temperature as well as at higher temperatures.

Prolonged heating of the yellow acetic acid (or ethanol) solution gives rise to the deep blue color observed and studied by Dimroth and co-workers.[2,3]

In the crystalline form both modifications decompose on standing in air (the yellow form apparently more readily) to give a brown oil having the odor of pyridine. From one such sample was isolated a small quantity of 4,4′-dipyridyl as its crystalline hydrate, m. p. 105–106°; m. p. of picrate 252–254° (Dimroth and Heene[2] have reported the isolation of 4,4′-dipyridyl from air-oxidized ethanolic solutions).

Magnetic Susceptibility.—The measurements were kindly carried out by Mr. Clayton Callis using the apparatus described by Driggs and Hopkins.[12] All measurements were taken at 25° on the two solid forms of N,N′-diacetyltetrahydro-4,4′-dipyridyl and the magnetic susceptibility (*K*) calculated in units per gram.

Quantitative Catalytic Hydrogenation.—Eight and six-tenths grams (0.035 mole) of yellow N,N′-diacetyltetrahydro-4,4′-dipyridyl dissolved in 130 ml. of glacial acetic acid was hydrogenated over 0.2 g. of platinum oxide at room temperature and 50 pounds per square inch initial pressure. Hydrogen was absorbed as shown in Fig. 1. Removal of the solvent under reduced pressure gave a white residue which yielded on recrystallization from dioxane 6.3 g. (74%) of shiny colorless plates of N,N′-diacetyl-4,4′-dipiperidyl, m. p. 173.5–174.5° (reported,[13] 174°). Attempts to hydrogenate N,N′-diacetyltetrahydro-4,4′-dipyridyl using Raney nickel in dioxane or methanol under pressures of 50–1400 pounds per square inch and temperatures of 25–70° generally failed to reduce the compound. Zinc and methanolic sodium hydroxide also failed to effect reduction.

Absorption Spectra.—Infrared determinations were kindly carried out by Mrs. J. L. Johnson using the crystalline white and yellow forms in Nujol. The instrument was a Perkin-Elmer Model 12B infrared spectrometer with rock salt optics.

Ultraviolet determinations were kindly made by Mr. John C. Brantley using a Model D Beckman spectrophotometer with 95% ethanolic solutions of the white (5.22 mg. per liter of solution) and yellow (12.1 mg. per liter of solution) forms.

Ozonolysis.—Five and five-tenths grams (0.025 mole) of yellow N,N′-diacetyltetrahydro-4,4′-dipyridyl dissolved in 40 ml. of glacial acetic acid was ozonized for forty-eight hours at 20° with 3% ozone flowing at a rate of 2.2 ml. per minute. The acetic acid solution was then added dropwise at 0° to 300 ml. of water and 30 ml. of 30% hydrogen peroxide. The mixture was allowed to stand overnight, then heated to 90° for ten minutes. The solvent was removed by distillation, leaving a residue of 3.5 g. of crude yellowish succinic acid, m. p. 160–178°. From this was prepared a *p*-bromophenacyl ester by the method of Shriner and Fuson,[14] m. p. 210–212°. Succinamide was also prepared in 43% yield through the methyl ester from 0.692 g. of the crude acid, using the method of Morrell.[15] The colorless needles, recrystallized from water, melted at 260–261°. A mixed m. p. with an authentic sample was not depressed.

Effect on Polymerization of Styrene.—The flow times of solutions of 0.10 g. of the white and yellow forms of N,N′-diacetyltetrahydro-4,4′-dipyridyl in 13.3 ml. of freshly-distilled styrene were periodically compared with those of pure styrene in Foord-type viscosimeters[16] maintained at 58°. The viscosity of the pure styrene increased steadily, until after two days the liquid was too thick to flow. The flow times of the solutions were unchanged after two days at 58°, and still unchanged after five months at room temperature.

Summary

Evidence is presented to suggest that N,N′-diacetyltetrahydro-4,4′-dipyridyl dissociates into free radicals which give rise to the yellow modification of the compound.

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[12] Driggs and Hopkins, THIS JOURNAL, **47**, 363 (1925).

[13] Emmert and Wolpert, *Ber.*, **74**, 1015 (1941).

[14] Shriner and Fuson, "Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1940, p. 132.

[15] Morrell, *J. Chem. Soc.*, **105**, 2698 (1914).

[16] Foord, *ibid.*, 48 (1940).

URBANA, ILLINOIS RECEIVED FEBRUARY 16, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF INDIANA UNIVERSITY]

The Reaction of Azlactones with Secondary Amines

BY DAVID K. BARNES,[1] E. CAMPAIGNE AND R. L. SHRINER[2]

No systematic study has been made of the reaction of secondary amines with azlactones.[3] Only a few scattered examples of the reaction have been reported in the literature.[4–8] In view of this fact, it was considered desirable to investigate the reactions of 2-phenyl-4-benzal-5-oxazolone (an unsaturated azlactone) and 2-phenyl-4-benzyl-5-oxazolone (a saturated azlactone) with the following series of secondary amines: piperidine, morpholine, dimethylamine, diethylamine, methylaniline, ethylaniline, diphenylamine, indole and carbazole. These amines were chosen because they represented different degrees of basicity.

Erlenmeyer[4] reported that 2-phenyl-4-benzal-5-oxazolone (I) reacted with piperidine to produce α-benzoylaminocinnamapiperidide with a melting point of 178°. In the present work, it has been found that two isomeric products may be isolated from the reaction of 2-phenyl-4-benzal-5-oxazolone[9] with piperidine. When equivalent amounts of the reactants were employed, Piperidide A,

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[1] Taken from part of a thesis submitted by David K. Barnes to the Faculty of the Graduate School in partial fulfillment of the requirements for the Degree, Doctor of Philosophy, in the Department of Chemistry, Indiana University. Present address, Stanolind Oil and Gas Co., Tulsa, Oklahoma.

[2] Present address: Chemistry Department, University of Iowa, Iowa City, Iowa.

[3] Carter, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, 1946, p. 198.

[4] Erlenmeyer, *Ber.*, **33**, 3035 (1900).

[5] Erlenmeyer and Wittenberg, *Ann.*, **337**, 294 (1904).

[6] Erlenmeyer and Stadlin, *ibid.*, **337**, 283 (1904).

[7] Lettre and Fernholz, *Z. physiol. Chem.*, **266**, 37 (1940).

[8] Doherty, Tietzman and Bergmann, *J. Biol. Chem.*, **147**, 617 (1943).

[9] Two isomeric forms, (*cis* and *trans*) of this azlactone have been described by Carter and Risser, *J. Biol. Chem.*, **139**, 255 (1941). Only the readily available higher melting isomer was used by Erlenmeyer and also in the present work.