polymer particles the rate of polymerization of styrene is proportional to the number of polymer particles present and is in dependent of the persulfate concentration. This can best be interpreted as indicating that the average number of free radicals per particle is a constant and equal to one-half. Thus from the rate of polymerization per particle and the concentration of monomer in the particle reported herein, the chain propagation constant for styrene has been calculated to be $3.5 \times 10^{10} \exp(-11{,}700/RT)$ l. mole^{-1} sec.$^{-1}$.

A study of the number of polymer particles produced has shown that the factors favoring production of a large number of particles are high soap concentration, high persulfate concentration and high temperature. The number of particles produced agrees satisfactorily with the theoretical law.

$$N = k(\rho/\mu)^{2/5}(a_s S)^{3/5}$$

where N is the number of particles formed per cc. of water up to the time that the soap is completely adsorbed on the polymer particles, k is a numerical constant with a value between 0.37 and 0.53, ρ is the rate of formation of free radicals per cc. of water solution, μ is the rate of increase in volume of a polymerizing swollen polymer particle, a_s is the interfacial area occupied by one gram of adsorbed soap when micelles are present and S is the initial concentration of the soap in the aqueous phase.

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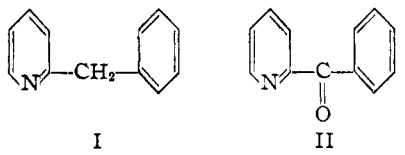
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Beckmann Rearrangement of the Oximes of Phenyl 2-Pyridyl Ketone (2-Benzoylpyridine)

BY ERNEST H. HUNTRESS AND HENRY C. WALTER[1,2,3]

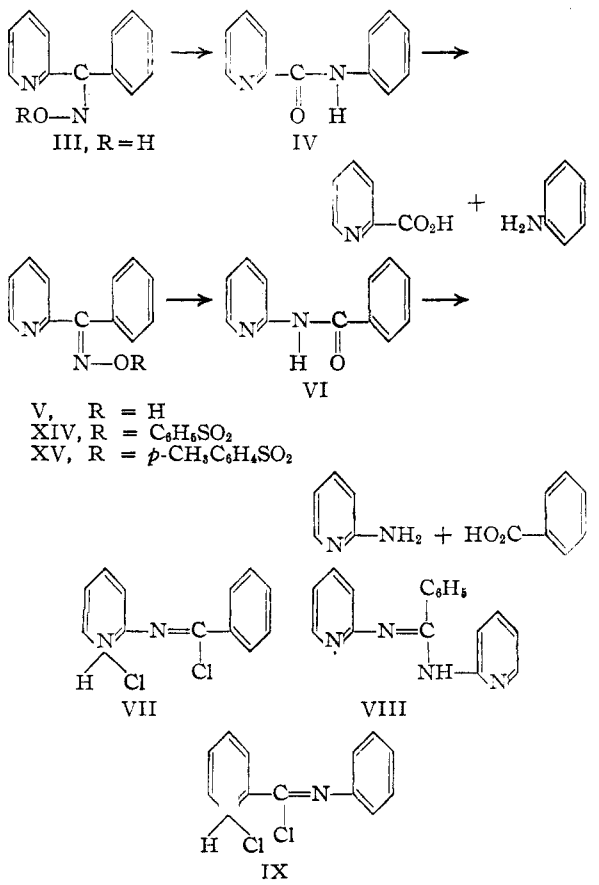
2-Benzoylpyridine (II), easily obtained from 2-benzylpyridine (I) by oxidation, was first oximated by Tschitschibabin,[4] who isolated different forms melting at 150–152° and 165–167°, respectively, but made no attempt to establish their configurations. From the observation that the lower melting form gave colored complexes with metal salts whereas the higher melting form did not, Tschugaeff[5] surmised that the former might be the *anti*-phenyl stereomer (III); the higher melting, the *syn*-phenyl stereomer (V).



I II

In 1930 Pfeiffer and Buchholz[6] suggested a nitrone structure for the complex salts of the lower melting form. No other work on these oximes has been reported.

In the light of modern views of the Beckmann rearrangement, including that of the *trans* interchange of radicals, a study of this reaction of these stereomers seemed of value. Rearrangement of the *syn*-phenyl stereomer (V) should yield 2-(benzoylamino)-pyridine (VI) hydrolyzable to benzoic acid and 2-aminopyridine. Similarly, the *anti*-phenylsteromer (III) should yield picolinic anilide



III, R = H IV

V, R = H
XIV, R = $C_6H_5SO_2$
XV, R = p-$CH_3C_6H_4SO_2$

VII VIII

IX

(1) This paper is constructed from part of a dissertation submitted by Henry C. Walter to the Faculty of the Massachusetts Institute of Technology in September, 1946, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(3) du Pont Fellow, June-December, 1943; November, 1945–June, 1946.

(4) Tschitschibabin, *J. Russ. Phys.-Chem. Soc.*, **33**, 700 (1901); *Chem. Zentr.*, **73**, I, 206 (1902).

(5) Tschugaeff, *Ber.*, **39**, 3382 (1906).

(6) Pfeiffer and Buchholz, *J. prakt. Chem.*, [2] **124**, 137 (1930).

(IV) hydrolyzable to picolinic acid and aniline. Both of these expectations have been fully realized. Within the stated premise, therefore, the configuration of the lower melting oxime may now be regarded as the *syn*-phenyl (V), the higher melting oxime as the *anti*-phenyl (III), thus reversing the earlier view as has so frequently happened since the establishment of the generality of *trans* Beckmann rearrangement.

Oximation of 2-benzoylpyridine (II) gave in almost quantitative yield a mixture of both stereoisomeric oximes. From this material extraction with chloroform followed by recrystallization from ethanol readily gave 50–56% yields of pure lower melting stereomer (V). From the residues of the above process the higher melting stereomer (III) was obtained by a procedure involving solution in dilute acid, precipitation as the sparingly soluble copper salt of all residual lower melting oxime, removal of excess cupric ion as copper sulfide, and precipitation of the higher melting form by neutralization. The melting points of the two forms obtained by these methods were identical with those first reported[4] where the method of separation was not specified.

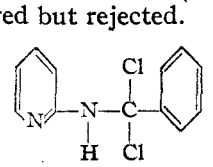
Both forms of phenyl 2-pyridyl ketoxime were hydrolyzed slowly but eventually by boiling 6 *N* hydrochloric acid to give 2-benzoylpyridine and hydroxylamine. The oximes themselves did not reduce Tollens reagent, but the lower melting form gave with it a yellow precipitate which was not further examined. The lower melting stereomer was also found to yield a crystalline bisulfate salt.

Beckmann rearrangement of the oximes was studied with various reagents including thionyl chloride, sulfuric acid and phosphorus pentachloride. Best results and maximum convenience were achieved with thionyl chloride which in chloroform solution reacted smoothly, vigorously, and with little side reaction. The material obtained by such rearrangement of pure low-melting oxime (V) gave on hydrolysis excellent yields of benzoic acid and 2-aminopyridine, while that obtained from crude oxime mixture gave also picolinic acid and aniline. Rearrangement of the oximes with strong (85–96%) sulfuric acid was negligible below 100° and at high temperatures was accompanied by much charring and discoloration. At 140° for several hours, however, pure samples of either lower melting or higher melting oximes rearranged and hydrolyzed giving picolinic acid and sulfanilic acid. Neither benzoic acid nor 2-(benzoylamino)-pyridine could be detected although in one experiment benzoic acid was intentionally added and recovered. These results, considered in the light of those with thionyl chloride, show that sulfuric acid must effect an isomerization of the low-melting oxime (V) to the higher melting form (III) which then rearranges normally. Rearrangement of the oximes with phosphorus pentachloride was impracticable in dry ether, but in chloroform proceeded smoothly. From pure lower melting isomer (V) such rearrangement followed by hydrolysis gave 90% yields of benzoic acid and 2-aminopyridine.

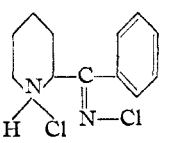
Both the benzenesulfonyl (XIV) and *p*-toluenesulfonyl esters (XV) of the lower melting oxime (V) were also rearranged by heat alone. When executed merely by heating above their melting points, rearrangement was violently exothermal, but when carried out in solvents (such as methylene (di)chloride, chloroform, acetylene tetrachloride, or benzene) proceeded smoothly. The resultant oil was not itself characterized but upon acid hydrolysis invariably gave benzoic acid and 2-aminopyridine. When the benzenesulfonate ester (XIV) of the lower melting oxime (V) was heated with 6 *N* hydrochloric acid for three hours, examination of the reaction mixture disclosed that partial rearrangement (followed by hydrolysis) had occurred even under these conditions for there was obtained not only benzoic acid and 2-aminopyridine but also picolinic acid and aniline. Furthermore, although the solid aryl sulfonate esters were solids apparently stable at room temperature for short periods, they gradually suffered spontaneous rearrangement on protracted standing.

During the study of the rearrangement of the lower melting oxime (V) with thionyl chloride, two intermediate reaction products were isolated and characterized. The proposed formulas for these intermediates are N-(2-pyridyl)-benzimidyl chloride hydrochloride (VII) and N,N′-di-(2-pyridyl)-benzamidine (VIII).

The N-(2-pyridyl)-benzimidyl chloride hydrochloride (VII) was obtained directly from the reaction of the lower melting oxime (V) with thionyl chloride in chloroform in the form of white prisms melting over a range (153–157°) which could not be narrowed. It structure was deduced from its mode of formation, analysis, and very ready hydrolysis to 2-(benzoylamino)-pyridine. Several isomeric structures (VII-A and VII-B) were considered but rejected.



VII-A



VII-B

Structure VII-A was considered unlikely since such dichlorides readily lose hydrogen chloride, a process which would be especially favored by the presence of an additional basic nitrogen in the pyridyl section of the molecule to give structure VII. Structure VII-B is highly improbable especially since such N-chloroiminoketones do not undergo Beckmann rearrangements but upon hydrolysis regenerate the original ketone.[7] Attempts to synthesize structure VII from 2-(benzoylamino)-pyridine by the action of thionyl chloride or phosphorus pentachloride were unsuccessful, such

(7) Peterson, *Am. Chem. J.*, **46**, 325–344 (1911).

reactions giving only 2-(benzoylamino)-pyridinium chloride.

The N,N'-di-(2-pyridyl)-benzamidine (VIII), a white solid melting at 173.5–174°, was isolated after hydrolysis of the chloroform solution from reaction of the lower melting oxime (V) with thionyl chloride. Its structure was deduced from its analysis, molecular weight, and hydrolysis to benzoic acid and 2-aminopyridine in a molar ratio approaching 1:2. The same compound was synthesized from 2-aminopyridine and N-(2-pyridyl)-benzimidyl chloride hydrochloride (VII) by condensation in chloroform.

The formation of amidines during Beckmann rearrangement has been previously recognized.[8] In our case, however, its formation was not observed when the solvent was evaporated directly after the thionyl chloride reaction, but only when the reaction solution was extracted with water. This suggests that in our work amidine formation was a secondary reaction involving the water, such as the condensation of a molecule of N-(2)-pyridyl)-benzimidyl chloride hydrochloride (VII) with a molecule of 2-(benzoylamino)-pyridine (VI). Experiment showed that these reactants in chloroform did in fact give a small yield (8%) of the amidine (VIII).

During our study of the rearrangement of the higher melting oxime (III) by thionyl chloride, a third intermediate (IX) was isolated as yellow crystals melting at 128–131°. From its analysis and ready hydrolysis to picolinicanilide it was shown to be N-phenylpicolinimidyl chloride hydrochloride, analogous to N-(2-pyridyl)-benzimidyl chloride hydrochloride (VII) from the lower melting oxime (V).

The 2-benzoylpyridine (II) required for this work was obtained in excellent yields by the oxidation with aqueous permanganate of 2-benzylpyridine (I) essentially according to the method of Crook and McElvain.[9] For convenient purification of the initial 2-benzylpyridine (I) we have preferred recrystallization of the beautifully crystalline 2-benzylpyridinium nitrate (X).

Experimental Work[10]

2-Benzylpyridinium Nitrate (X).—2-Benzylpyridine (I) (169 g., 1.0 mole) dissolved in a mixture of concentrated nitric acid (100 g.) and water (500 ml.) gave on cooling an abundant precipitate of white crystals. After recrystallization from hot water (200 ml.) 173 g. (74.5% yield) of white crystalline salt resulted. A further purification from a mixture of ethyl acetate (500 ml.) with ethanol (100 ml.) gave 168 g. (72.5% yield) of m. p. 113–114°, uncor. (recorded[11] 116°, cor.), and this was not changed by further recrystallization from acetone. The neutralization equivalent was determined in alcohol solution.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$ (*i. e.*, $C_{12}H_{11}N\cdot HNO_3$): neut. equiv., 232. Found: neut. equiv., 232.5, 233.5.

2-Benzoylpyridine (II).—2-Benzylpyridine (I) (254 g., 1.5 moles) ($n^{20}D$ 1.5793) suspended in water (2 l.) in a 3-l. ring neck flask equipped with a thermometer, reflux condenser, and liquid-sealed stirrer was oxidized with potassium permanganate (320 g., 2.03 moles) in the general manner reported in the literature.[9] In the final distillation after a preliminary fraction taken up to 130° at 1–2 mm., ($n^{20}D$ 1.6005), the main product (235 g., 86% yield) was obtained at 130–133° at 1–2 mm.; $n^{20}D$ 1.6056.

Subsequently, this reaction was carried out on a larger scale using 507 g. (3 moles) of 2-benzylpyridine, 640 g. (4.05 moles) of potassium permanganate in 3 l. of water in a 5-l. flask. Reflux was not employed, the temperature being kept just below boiling. The oil was not extracted with benzene but instead the manganese dioxide sludge was filtered off and the oil separated directly from the aqueous solution. The preliminary fraction from such runs amounted to 50 g.; the main fraction, b. p. 130–135° at 1–2 mm., amounted to 430 g. or 78.5% yield.

Phenyl 2-Pyridyl Ketone *p*-Nitrophenylhydrazone (XI).—This derivative was prepared from the ketone by refluxing with alcoholic *p*-nitrophenylhydrazine containing a little hydrochloric acid as catalyst. From ethanol or dilute acetic acid it crystallized in golden yellow needles, m. p. 199.0–199.5°.

Anal. Calcd. for $C_{18}H_{14}N_4O_2$: N, 17.6. Found: N, 17.2, 17.6.

Phenyl 2-Pyridyl Ketone 2,4-Dinitrophenylhydrazone (XII).—This derivative was prepared in a fashion analogous to the *p*-nitrophenylhydrazone. The direct product consists of a mixture of two stereoisomeric forms melting 187–220°. Recrystallization from slightly diluted acetic acid followed by further purification from ethyl acetate yielded a lower melting form as silky orange-yellow needles, m. p. 196.5–197.5°. Dilution with water of the original alcoholic mother liquor or that from acetic acid recrystallization, followed by further purification from benzene/petroleum ether, gave a higher melting form as agglomerated orange microcrystals, m. p. 230–231°.

Anal. Calcd. for $C_{18}H_{13}N_5O_4$: N, 19.3. Found: for lower melting form, N, 19.0, 19.1; for higher melting form, N, 19.2, 19.3.

By refluxing with acetic acid, either the lower or the higher melting forms could in part be changed to the other and both forms isolated.

Phenyl 2-Pyridyl Ketoxime (III + V).—2-Benzoylpyridine (183 g., 1.0 mole) dissolved in 95% ethanol (300 ml.) was treated with a solution of hydroxylammonium sulfate (85 g., 0.52 mole) in water (400 ml.), the dilution of the alcohol causing some precipitation of ketone. To the reaction mixture was added a hot solution of sodium hydroxide (85 g., 2.13 moles) in water (400 ml.). The clear hot red solution was further heated almost to boiling, cooled and gradually acidified with glacial acetic acid. Upon the first evidence of clouding the solution was seeded with previously obtained oxime, and acidification continued to faint acidity toward litmus. After allowing to stand several hours at room temperature, the pale pink precipitate was filtered, thoroughly washed with water and dried at 50–60°. The yield of mixed stereoisomeric oximes was 191 g. (96.5% yield) melting over the range 116–145°.

***syn*-Phenyl 2-Pyridyl Ketoxime (V).**—The above mixture of stereoisomers was refluxed ten to fifteen minutes with dry chloroform (250 ml.). Cooling and filtration gave 123 g. (62% yield) of crystals, m. p. 139–152.5°. Recrystallization of this material from the minimum quantity of hot ethanol (260 ml.) yielded 109 g. (55%) of m. p. 148.5–152.5°, and another recrystallization from alcohol gave 101 g. (51%) pure white crystals, m. p. 150.5–152.5°.

***syn*-Phenyl 2-Pyridyl Ketoxime Hydrogen Sulfate (XIII).**—The *syn* form (V) of the oxime of 2-benzoylpyridine (2 g.) dissolved in concentrated sulfuric acid (4 ml.) and poured over ice gave a white precipitate, easily soluble in water but recrystallizable from hot alcohol and ethyl acetate, giving 1.57 g. of shining white flakes, m. p. 188–

(8) Stephen and Bleloch, *J. Chem. Soc.*, 886 (1931).

(9) Crook and McElvain, THIS JOURNAL, **52**, 4006 (1930).

(10) All melting points are uncorrected; they were taken on a 360° rod form thermometer immersed to its 0° mark in a sulfuric acid bath.

(11) Bryans and Pyman, *J. Chem. Soc.*, 550, 552 (1929).

189° dec. Aqueous solutions of this salt were acid, and with barium chloride precipitated barium sulfate. On treatment with alkali followed by acidification with acetic acid the original oxime was regenerated. The salt titrated sharply with 0.1 *N* sodium hydroxide using phenolphthalein indicator.

Anal. Calcd. for $C_{12}H_{10}N_2O \cdot H_2SO_4$: neut. equiv., 148.1. Found: neut. equiv., 147.0, 147.3.

***syn*-Phenyl 2-Pyridyl Ketoxime O-benzenesulfonate (XIV).**—The *syn* ketoxime (V) (19.8 g., 0.1 mole) dissolved in aqueous 10% sodium hydroxide solution (100 ml.) and additional water (50 ml.) was treated at 14–17° with benzenesulfonyl chloride (23 g., 0.13 mole) in acetone (75 ml.). Addition required one and one-half hours and stirring was continued a further twenty minutes. The crude pale tan precipitate after washing and air drying amounted to 33.5 g. (99% yield) and melted 98–99° dec. Recrystallization from benzene by precipitation with petroleum ether gave 31.5 g. (94% yield), m. p. 97–98° dec.

Anal. Calcd. for $C_{18}H_{14}N_2O_3S$: N, 8.29; sapn. equiv., 338. Found: N, 8.33, 8.34; sapn. equiv., 336.1, 336.3.

***syn*-Phenyl 2-Pyridyl Ketoxime O-*p*-toluenesulfonate (XV).**—In a completely analogous fashion the *syn*-oxime (V) (19.8 g., 0.1 mole) in water (150 ml.) containing sodium hydroxide (10 g.) was esterified with *p*-toluenesulfonyl chloride (24 g., 0.125 mole) in acetone (75 ml.). The crude ester (29.5 g., 84% yield), m. p. 101–102° dec., on recrystallization from benzene/petroleum ether gave 27.5 g. (78% yield) of white needles, m. p. 101.5–102.5° dec.

Anal. Calcd. for $C_{19}H_{16}N_2O_3S$: N, 7.96; sapn. equiv., 352. Found: N, 8.02, 8.07; sapn. equiv., 355.2, 357.9.

***anti*-Phenyl 2-Pyridyl Ketoxime (III).**—The residue (81.5 g.) obtained by evaporation of both the chloroform and alcohol filtrates from recrystallization of the *syn*-phenyl stereoisomer (above) after extraction with ether was diminished to 61.5 g. (0.31 mole). It was dissolved in a mixture of concentrated hydrochloric acid (50 ml.) and water (150 ml.) and treated with an aqueous solution of hydrated copper sulfate (40 g., 0.32 equiv.). After several hours the bright green precipitate of copper derivative was filtered off, washed with water and the filtrate treated with excess hydrogen sulfide. After removal of the precipitated copper sulfide, the filtrate was cautiously treated with ammonium hydroxide, care being taken to keep it faintly acid. The resultant white crystalline precipitate (21 g., 11% of total oxime) melted at 158–162°, but after two further recrystallizations from alcohol showed m. p. 165–167°. Additional amounts of less pure stereomer were obtained by suitable treatment of the pink precipitate resulting from addition of excess ammonia to the filtrate from precipitation of the copper.

Beckmann Rearrangement of the Oximes with Thionyl Chloride in Chloroform

Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime. (a) Without Isolation of Intermediate Products.—To *syn*-phenyl 2-pyridyl ketoxime (V) (3.96 g., 0.02 mole) in chloroform (20 ml.) was added slowly a slight excess of pure thionyl chloride (3.3 g., 0.028 mole). Vigorous exothermal reaction occurred with evolution of sulfur dioxide. Evaporation of the resultant yellow solution first in a dry air stream and afterward at reduced pressure gave a yellow solid. Hydrolysis of this material by refluxing for two and one-half hours with 6 *N* hydrochloric acid (40 ml.) gave benzoic acid (91% yield) and 2-aminopyridine (crude 91%, pure 76%).

(b) With Isolation of 2-(Benzoylamino)-pyridine (VI).—Using the same procedure and quantities described in (a), the solid obtained upon evaporation of the chloroform was dissolved in water and the solution made alkaline with sodium hydroxide. After seeding the resultant oil with an authentic sample, it gave 3.92 g. (99% yield) of crude product. After recrystallization from dilute alcohol there resulted 2.79 g. (70.5% yield) of 2-(benzoylamino)-pyridine, m. p. 80–83°.[12]

(12) Huntress and Walter, *J. Org. Chem.*, **13**, 736 (1948).

(c) With Isolation of N-(2-Pyridyl)-benzimidyl Chloride Hydrochloride (VII).—In a 500-ml. 3-necked flask, fitted with dropping funnel, reflux condenser and mercury-sealed stirrer, *syn*-phenyl 2-pyridyl ketoxime (V) (19.8 g., 0.1 mole) was dissolved and suspended in dry chloroform (100 ml.). To the stirred mixture was added a solution of thionyl chloride (12 g., 0.1 mole) in chloroform (10 ml.) at such a rate as to keep the solution boiling but under control. The white precipitate initially formed dissolved to give a clear yellow solution. Most of the chloroform was evaporated in a stream of dry air and acetone was then added. The resultant crystalline solid weighed 21.8 g. corresponding to 86% yield of the intermediate. After several recrystallizations from chloroform/acetone, chloroform/petroleum ether, or dioxane the melting point was raised to a maximum of 152–157° dec.

The compound was found to contain nitrogen and chlorine but no sulfur. It readily dissolved in water giving an acid solution containing chloride ion. The acidic character was titratable with standard sodium hydroxide; the chloride was precipitable from a solution of the compound in dilute nitric acid by addition of silver nitrate.

Anal. Calcd. for $C_{12}H_{10}Cl_2N_2$: Cl, 28.0; neut. equiv., 126.5. Found: Cl, 27.8, 28.0; neut. equiv., 125.2, 125.8.

The compound is fairly stable in air but does slowly hydrolyze. A sample originally melting 153–157° showed no change after five days' exposure but after sixteen days it melted at 140–152° and after a month at 140–178°. Alkaline hydrolysis readily yielded 2-(benzoylamino)-pyridine, m. p. 80.5–82°[12] and not depressing the melting point of an authentic sample.

(d) With Isolation of N,N'-Di-(2-pyridyl)-benzamidine (VIII).—In the general manner of (c) above *syn*-phenyl 2-pyridyl ketoxime (19.8 g., 0.1 mole) was rearranged with thionyl chloride (15 g.) in dry chloroform (100 ml.). After reaction the solution was cooled and stirred with water (70 ml.). After separation the chloroform layer was stirred with 2 *N* hydrochloric acid (70 ml.), the organic layer again separated, and the solvent evaporated. That portion of the remaining viscous oil which was then insoluble in hydrochloric acid had a strong odor of benzoyl chloride and was shown to be such by conversion to benzamide which did not depress the melting point of an authentic specimen. The acid soluble portion of the oil on making alkaline gave 10.6 g. of a semi-solid mass. After treatment with ether there remained a solid (3.24 g., m. p. 154–167°) which upon further purification from dilute ethanol gave white needles, m. p. 173.5–174.0°, of N,N'-di-(2-pyridyl)-benzamidine.

Anal. Calcd. for $C_{17}H_{14}N_4$: N, 20.4; mol. wt., 274. Found: N, 20.2, 20.4; mol. wt. (Rast), 254, 287.

This compound dissolved in dilute aqueous acids and was reprecipitated by bases. Upon hydrolysis with hot 6 *N* hydrochloric acid, it gave benzoic acid and 2-aminopyridine neither of which depressed the respective melting points of authentic samples. Careful working up of the hydrolyzate showed that considerably more than one mole of 2-aminopyridine was formed for each mole of benzoic acid. The identity of the material was confirmed by its failure to depress the melting point of a synthetic sample (m. p. 172.5–173.5°) prepared by condensation in chloroform solution of equivalent amounts of 2-aminopyridine or its benzoyl derivative with N-(2-pyridyl)-benzimidyl chloride hydrochloride.

Rearrangement of *anti*-Phenyl 2-Pyridyl Ketoxime (III). (a) Without Isolation of Intermediates.—The *anti*-stereomer was treated in chloroform with thionyl chloride in the amounts and manner described for the *syn* isomer. After removal of the chloroform on a steam-bath in a stream of air, the red residue solidified on cooling. After hydrolysis with hot 6 *N* hydrochloric acid for three hours, there was isolated by conventional procedures 1.86 g. (86.5% yield) of aniline confirmed by color reactions and by formation of acetyl, benzoyl and benzenesulfonyl derivatives. Acidification of the alkaline solution with acetic acid and treatment with hot cupric acetate

solution gave eventually 2.0 g. (58% yield) of copper picolinate.

(b) With Isolation of N-(Phenyl)-picolinimidyl Chloride Hydrochloride (IX).—A smaller sample of the *anti*-phenyl 2-pyridyl ketoxime (3.96 g., 0.02 mole) was rearranged with thionyl chloride (3.2 g., 0.028 mole) in chloroform (20 ml.) as before. After removal of most of the solvent addition of dry acetone precipitated bright yellow crystals (3.4 g., 67% yield) of solid melting at 128–131° after sintering at 115–128°. Further purification failed to raise or sharpen this melting range.

Anal. Calcd. for $C_{12}H_{10}Cl_2N_2$: Cl, 28.0; neut. equiv., 126.5. Found: Cl, 27.9, 28.5; neut. equiv., 127.0, 127.3.

The neutralization equivalent was determined by titration in dilute ethanol with 0.1 *N* hydroxide using phenolphthalein. The resulting solutions were acidified with dilute nitric acid and the chlorine determined gravimetrically. Hydrolysis of the compound (0.52 g.) by solution in cool dilute hydrochloric acid followed by addition of sodium hydroxide gave picolinanilide (0.38 g., 93% yield), m. p. 75–76°. Recrystallization from dilute ethanol gave a product, m. p. 76–77°, which did not depress that of an authentic sample prepared from picolinoyl chloride and aniline.

Beckmann Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime with Phosphorus Pentachloride.—To *syn*-phenyl 2-pyridyl ketoxime (V) (3.96 g., 0.02 mole) in chloroform (30 ml.) was added slowly a slight excess of phosphorus pentachloride (4.5 g., 0.022 mole). A vigorous exothermal reaction occurred. Evaporation of the resultant red solution in a stream of dry air gave a red oil soluble in water. When such a solution was made alkaline with sodium hydroxide a viscous red oil came out which could not be crystallized even after seeding with 2-benzoylaminopyridine. Hydrolysis of this oil by refluxing for three hours with dilute hydrochloric acid gave benzoic acid (96% yield) and 2-aminopyridine (crude 95%, pure 50% yield).

Beckmann Rearrangement of the Oximes with Sulfuric Acid

Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime.—In a typical experiment *syn*-phenyl 2-pyridyl ketoxime (V) (5.0 g., 0.025 mole) dissolved in concentrated sulfuric acid (10 ml.) was heated in an oil-bath at 135–145° for two and one-half hours. On pouring the pale brown solution over ice, a white precipitate (3.10 g., 71% yield) of sulfanilic acid was obtained. Its identity was demonstrated by positive tests for both nitrogen and sulfur, by absence of sulfate, and by neutralization equivalent (173.2) of the dehydrated material.

On making the acid filtrate alkaline and extracting with ether, there was obtained a small amount (0.41 g.) of oil which by conversion of its *p*-nitrophenylhydrazone (XI) (m. p. 197–199°) and mixed melting point comparison with an authentic sample proved to be 2-benzoylpyridine (II).

Acidification of the alkaline solution gave a trace (0.10 g., 2%) of unreacted oxime which was filtered off. Addition of hot cupric acetate solution then precipitated the highly characteristic shiny dark blue crystals of copper picolinate (3.16 g., 73% yield). Its identity was confirmed by conversion to free picolinic acid which after recrystallization from ethanol melted 136–137° as recorded.

Rearrangement of *anti*-Phenyl 2-Pyridyl Ketoxime.—This stereomer (III) (3.96 g., 0.02 mole) in concentrated sulfuric acid (8 ml.) was rearranged and worked up exactly as with the preceding case. It gave similarly sulfanilic acid (2.37 g., 68.5% yield) and copper picolinate (1.97 g., 57% yield). No benzoic acid was found.

Beckmann Rearrangement of Arylsulfonyl Esters of *syn*-Phenyl 2-Pyridyl Ketoxime

Thermal Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime O-Benzenesulfonate.—In a typical run the benzenesulfonate ester (XIV) of the *syn*-stereomer (6.76 g., 0.02 mole) dissolved in chloroform (20 ml.) was refluxed for one hour, by which time the initially pale yellow solution had become red-brown. Evaporation of the solvent gave a taffy-like residue which was hydrolyzed by refluxing two and one-half hours with 6 *N* hydrochloric acid (40 ml.). After cooling benzoic acid (2.20 g., 90% yield) was obtained. By working up the hydrochloric acid filtrate there resulted 1.62 g. (86.5% yield) of crude 2-aminopyridine readily purified to 1.24 g. (66% yield) of pure material of m. p. 58–59°.

Thermal Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime O-*p*-Toluenesulfonate.—From an entirely analogous experiment carried out on the *p*-toluenesulfonate ester (XV) (7.04 g.) there was likewise obtained both benzoic acid (92% yield) and 2-aminopyridine (71% yield crude, 53% pure).

Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime O-Benzenesulfonate on Standing. A sample of the benzenesulfonate ester (XIV) of the *syn*-oxime which initially melted at 97–98° was found after standing at room temperature in the dark for two months to melt over the range 92–120°. Extraction of this material (2.46 g.) with dry benzene (15 ml.) at room temperature left a residue of 1.32 g. (54%) melting at 128.5–132°. Further purification by precipitation from chloroform with petroleum ether sharpened the melting point to 129–130°. Water solutions of the compound were acidic and when made alkaline deposited 2-benzoylaminopyridine. Titration with alkali gave a neutralization equivalent (358, 360) suggesting that the product was 2-benzoylaminopyridine benzenesulfonate (neut. equiv. 356). This was confirmed by syntheses from authentic materials yielding a salt which melted at 128–129° and which was not depressed when mixed with rearrangement product.

Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime O-Benzenesulfonate in 6 *N* Hydrochloric Acid.—The ester (XIV) (6.76 g., 0.02 mole) dissolved in 6 *N* hydrochloric acid to give a pale yellow solution whose appearance was unchanged after refluxing for three hours. On cooling, some benzoic acid separated and more was recovered by extraction with ether; the total amount was 1.04 g. or 42% yield. On addition of excess sodium hydroxide to the acid filtrate an emulsion separated which eventually was found to contain a mixture (1.8 g., 96% yield) of 2-aminopyridine and aniline. These were separated by shaking with a mixture of water (20–25 ml.) and ether (10 ml.). The 2-aminopyridine was dissolved by the water, and on separation and treatment with benzoyl chloride and alkali gave 2-(dibenzoylamino)-pyridine,[12] m. p. 167.0–169°. The aniline was dissolved by the ether which on similar treatment gave benzanilide, m. p. 156–158°. Both benzoylation products were confirmed by mixed melting points with authentic samples. The alkaline solution from which these amines had been extracted was acidified with acetic acid, concentrated to about 75 ml. and treated with hot cupric acetate solution. Deep blue crystals of copper picolinate (0.17 g., 5% yield) slowly separated.

Rearrangement of *syn*-Phenyl 2-Pyridyl Ketoxime O-*p*-Toluenesulfonate in 6 *N* Hydrochloric Acid. A sample of this ester (XV) was rearranged with 6 *N* hydrochloric acid as described for its lower homolog (XIV). On working the products there was obtained benzoic acid (25%), 2-aminopyridine plus aniline (83%) and copper picolinate (32%) all expressed in fractions of theoretical yield.

Summary

1. A procedure for oximation of 2-benzoylpyridine and for convenient separation by a chemical method of the two resulting stereoisomeric oximes has been devised.

2. Beckmann rearrangement of both stereoisomeric oximes has been effected with thionyl chloride and with sulfuric acid, and for the lower melting stereomer also with phosphorus pentachloride.

3. Such rearrangement of pure lower-melting

stereomer with thionyl chloride followed by hydrolysis gives excellent yields of benzoic acid and 2-aminopyridine. Either stereomer (or their mixture) with concentrated sulfuric acid undergoes not only Beckmann rearrangement but also hydrolysis, giving, however, exclusively picolinic acid and sulfanilic acid, the latter by incidental sulfonation of the corresponding aniline.

4. On the current premise of *trans* interchange of radicals during Beckmann rearrangement, these results require for the higher-melting oxime the *anti*-phenyl configuration; for the lower-melting oxime, the *syn*-phenyl configuration.

5. The benzenesulfonate and *p*-toluenesulfonate esters of the lower-melting oxime have been prepared and shown to undergo thermal Beckmann rearrangement directly, in solvents, or even slowly on standing at ordinary temperature.

6. Treatment of the lower-melting oxime with thionyl chloride leads under specified conditions to the hydrochlorides of N-(2-pyridyl)-benzimidyl chloride or of N,N'-di-(2-pyridyl)-benzamidine. The higher-melting stereomer with thionyl chloride can be caused to give the hydrochloride of N-phenylpicolinimidyl chloride.

7. In the course of this work the *p*-nitrophenylhydrazone and both stereoisomeric 2,4-dinitrophenylhydrazones of 2-benzoylpyridine, together with the bisulfate salt of the low melting form of 2-benzoylpyridine oxime, have incidentally been characterized.

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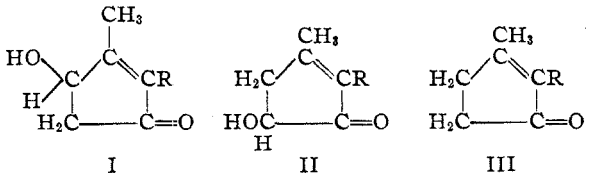
Constituents of Pyrethrum Flowers. XXII. Synthesis and Relative Toxicity of Two Isomers of Cinerin I

BY F. B. LAFORGE, NATHAN GREEN AND W. A. GERSDORFF

It has been shown that the hydroxyl group in dihydrocinerolone (Ia) and tetrahydropyrethrolone (Ib), and hence in cinerolone (Ic) and pyrethrolone (Id), occupies position 4, in the nucleus instead of position 5 as formerly accepted.



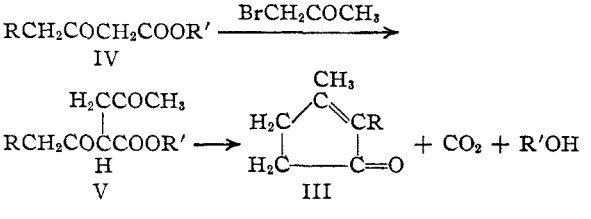
I II III

a, R = —*n*-C_4H_9
b, R = —*n*-C_5H_{11}
c, R = —$CH_2CH{=}CHCH_3$
d, R = —$CH_2CH{=}CH{-}CH{=}CH_2$
e, R = —$CH_2CH_2CH{=}CH_2$

This revision in their structures resulted from the fact that 2-butyl-5-hydroxy-3-methyl-2-cyclopentene-1-one (IIa) was not identical with dihydrocinerolone[1] and from the synthesis of the 2-butyl[2] and 2-amyl-4-hydroxy compounds[3] (Ia and Ib), identical with dihydrocinerolone and tetrahydropyrethrolone, respectively. The synthesis of the last two compounds was accomplished by the bromination of dihydrocinerone (IIIa) and tetrahydropyrethrone (IIIb) in the allylic, 4, position with N-bromosuccinimide and subsequent replacement of the bromine with hydroxyl.

Owing to the presence of an unsaturated side chain, this method is not available for a synthesis of cinerolone, where the reagent causes complete decomposition of cinerone (IIIc). Since no other method has yet been found for the introduction of hydroxyl in position 4 in cinerone itself, we have undertaken to prepare the 5-hydroxycinerone (IIc) and its analog with a 3-butenyl side chain (IIe), and have compared the toxicities of their chrysanthemum monocarboxylic acid esters with those of cinerin from natural sources and the pyrethrum standard. The results of such tests would show the effect of the transposition of the acyl group from position 4 to position 5 in the nucleus, and of the double bond from 2 to 3 in the side chain.

For the synthesis of IIc and IIe the starting compounds are cinerone (IIIc) and 2-(3-butenyl)-3-methyl-2-cyclopenten-1-one (IIIe), the syntheses of which have been described by Harper,[4] and are based on the general procedure of Hunsdiecker.[5] The steps involved are illustrated by the scheme



IV V III

For the synthesis of cinerone (IIIc) we have found it more convenient to prepare the intermediate, ethyl 3-oxo-6-octenoate, by a series of reactions different from those employed by Harper.

The reaction of crotyl chloride with ethyl acetoacetate followed by decarbethoxylation furnished

(1) LaForge and Soloway, THIS JOURNAL, **69**, 186 (1947).
(2) LaForge and Soloway, *ibid.*, **69**, 989 (1947).
(3) Dauben and Wenkert, *ibid.*, **69**, 2074 (1947).
(4) Harper, *J. Chem. Soc.*, 892 (1946).
(5) Hunsdiecker, *Ber.*, **75B**, 455 (1942).