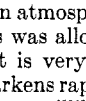
was washed twice with 50-ml. portions of 2*N* hydrochloric acid and then with water. It was dried over magnesium sulfate, treated with some Magnesol to remove color and, concentrated *in vacuo* to give the 5-benzyloxy nitroester as a red oil. The infrared spectrum of this material contained the expected absorptions.

c. *5-Benzyloxytryptophan.* Ethyl α-nitro-β[3-(5-benzyloxyindole)]propionate (3.7 g., 0.01 mole) in 50 ml. of absolute alcohol was hydrogenated at 40 p.s.i. of hydrogen using 1.0 g. of platinum oxide catalyst. Uptake of hydrogen ceased after 1.75 hr. After carefully purging with nitrogen, the bottle was opened and 4.0 g. of a 20% (by weight) solution of sodium hydroxide was added. A hydrogen atmosphere was re-established in the bottle and hydrolysis was allowed to proceed at room temperature overnight. It is very important to exclude air; otherwise, the solution darkens rapidly and purification of the product is difficult. Twenty milliliters of water was added and the catalyst was removed by filtration. The *p*H of the filtrate was adjusted to 6 with glacial acetic acid whereupon a gelatinous solid formed. On heating it gradually changed to solid material. The mixture was cooled and the solid was collected and washed with water to give 2.64 g. of 5-benzyloxytryptophan. The compound is amphoteric and can be partially purified by dissolving in either acid or base, treating with charcoal and then adjusting the *p*H to 6. A small amount was purified in this manner and then crystallized from water containing a little alcohol; m.p. (introduced at 270°) 280° dec. (lit.,[16] m.p. 280° dec.).

d. *5-Hydroxytryptophan.* 5-Benzyloxytryptophan (3.42 g.) was suspended in 50 ml. of alcohol and 50 ml. of water with 1.0 g. of 10% palladium-on-charcoal and hydrogenated at 10 p.s.i. Reduction was rapid and complete. The catalyst was removed by filtration, but the filtrate was dark because of the presence of colloidal catalyst. The filtrate was concentrated to a small volume under vacuum and the resulting dark crystals were dissolved in water. The hot solution was filtered and allowed to crystallize. The crystalline material was still dark; therefore it was recrystallized from water, using a Seitz filter to remove the colloidal catalyst; white crystals were obtained (1.23 g.). A second crop was obtained by concentrating the mother liquor (0.29 g.). Total weight, 1.52 g. (62.5%). A small sample was recrystallized for analysis; m.p. 285° dec.[16] Ultraviolet: 220 sh (23,850); 275 (6,050); 300 (5,750); 312 (3,725). Infrared: OH/NH: 3380, 3240; NH_3^+: 3120, 3060, 2720, 2630, 2510, 2420;  deformation: 1632, 1596, 1403; C=C: 1612, 1495; C—O: 1233, 1221; ar. sub.: 855, 843, 813, 791, 765.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.50; N, 12.73. Found: C, 59.94; H, 5.50; N, 12.47.

Acknowledgment. The authors are indebted to Mr. W. A. Struck and associates of our Microanalytical Laboratory for analyses, to Mr. M. Grostic and Mr. J. Stafford for infrared and ultraviolet spectral data, and to Mr. L. G. Laurian for laboratory assistance. We also wish to thank Dr. M. E. Greig of our department of pharmacology for permission to discuss some of the enzymological data obtained in her laboratory.

KALAMAZOO, MICH.

[CONTRIBUTION FROM THE MEDICAL CENTER, UNIVERSITY OF CALIFORNIA, LOS ANGELES, AND THE DEPARTMENT OF CHEMISTRY, FRESNO STATE COLLEGE]

Syntheses and Resolutions Involving Papain-Catalyzed Reactions between (Hydroxyalkyl)anilines and *N*-Acylamino Acids[1]

JOHN LEO ABERNETHY[2] AND BROTHER MYRON COLLINS[3]

Received June 4, 1959

Papain catalysis provides a means for acylating the amino group of substituted anilines containing an alcoholic hydroxyl without concurrent acylation of the alcoholic hydroxyl. These substituted anilines can be employed for resolution of certain *N*-acylamino acids like carbobenzoxy-DL-alanine, with papain as the catalyst and resolving agent. When the asymmetric center is shifted to the substituted aniline, as with *m*-(1-hydroxyethyl)aniline in its reaction with non-asymmetric hippuric acid, papain does not cause a resolution to take place, but a racemic product is formed in good yield instead. Reduction of *m*-aminoacetophenone to racemic *m*-(1-hydroxyethyl)aniline has been found to occur in good yield by means of lithium aluminum hydride. The optimum *p*H for the papain-catalyzed reaction between *m*-(1-hydroxyethyl)aniline and hippuric acid is about 4.7 for the experimental conditions employed.

Numerous papain-catalyzed syntheses of anilides[4-6] and phenylhydrazides[4,7,8] of *N*-acylamino acids have been studied, especially with reference to resolutions of *dl*-*N*-acylamino acids. Also, rates of precipitation of substituted hippuric anilides[9] have been investigated in relation to the effect of position of a given substituent on the aniline nucleus. However, nothing has been reported on the

(1) Taken mainly from a thesis of Brother Myron Collins to be submitted to the Graduate School of Fresno State College in partial fulfillment of the requirements for the degree of Master of Arts.

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(4) M. Bergmann and H. Fraenkel-Conrat, *J. Biol. Chem.*, 119, 707 (1937).

(5) D. G. Doherty and E. A. Popenoe, Jr., *J. Biol. Chem.*, 189, 447 (1951).

(6) E. Waldschmidt-Leitz and K. Kuhn, *Z. physiol. Chem.*, 285, 23 (1950).

(7) H. B. Milne and C. M. Stevens, *J. Am. Chem. Soc.*, 72, 1742 (1950).

(8) E. L. Bennett and C. Niemann, *J. Am. Chem. Soc.*, 1789 (1950).

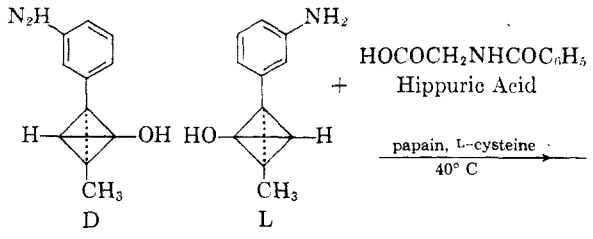
(9) J. L. Abernethy, J. Nakamura, and Bro. M. Collins, *J. Org. Chem.*, 22, 586 (1958).

behavior of *N*-acylamino acids toward substituted anilines containing a hydroxyalkyl substituent.

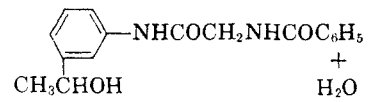
There are at least three significant reasons for such an investigation. First, this provides a procedure for acylating an amino group, without subjecting an alcoholic hydroxyl radical to concurrent acylation. Second, it is of interest to ascertain the ability of (hydroxyalkyl)anilines to bring about resolutions of racemic *N*-acylamino acids under the asymmetric influence of papain. Resolutions do not always occur[5] in reactions between racemic *N*-acylamino acids and aniline when papain is employed as the catalyst and resolving agent. Third, it is of particular value to shift the asymmetric center from the amino acid moiety to the substituted aniline moiety during the formation of the substituted anilide.

The substituted anilines ultimately chosen for investigation were *o*-aminobenzyl alcohol, *m*-aminobenzyl alcohol, *p*-(2-hydroxyethyl)aniline, and *m*-(1-hydroxylethyl)aniline. *N*-Acylamino acids selected were these relatively soluble ones: hippuric acid, benzoyl-DL-alanine, benzoyl-L-alanine, carbobenzoxy-DL-alanine, and carbobenzoxy-L-alanine.

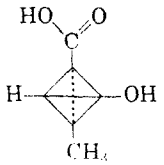
m-(1-Hydroxyethyl)aniline contains an asymmetric center at the carbon bonded to the hydroxyl. Its behavior toward hippuric acid is significant because no asymmetric center exists in hippuric acid.



m-(1-Hydroxyethyl)aniline[10]



Hippuric *m*-(1-hydroxyethyl)anilide



The dependence of yield on *p*H for this reaction was determined, as shown in Fig. 1. As a consequence, all subsequent reactions were conveniently carried out at a *p*H of about 4.7, reasonably close to this optimum.

EXPERIMENTAL

Activation of papain. The procedure described previously for activation[9] of the papain was employed in the activation of separate 50-g. samples of Schwarz and Wallerstein papain.[11] The lightly crushed, dry, activated papain was stored in small, stoppered vials kept in a large brown bottle with a screw cap and refrigerated at about 5°.

(10) Appropriate degradation of the benzene ring would give direct configurational relationship to D-lactic acid.

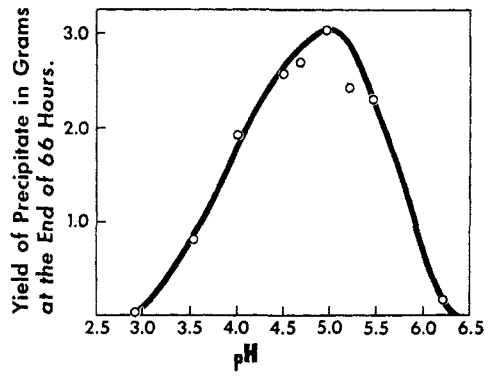


Fig. 1. Dependence of yield on *p*H for the papain-catalyzed synthesis of hippuric *m*-(1-hydroxyethyl)anilide from hippuric acid and *m*-(1-hydroxyethyl)aniline at 40°. Solutions involved: 0.0500 mol. hippuric acid; 0.0500 mol. *m*-(1-hydroxyethyl)aniline; 0.500 g. L-cysteine hydrochloride; 0.250 g. activated Schwarz papain; 250 ml. total solution.

Synthesis of m-(1-hydroxyethyl)aniline. *m*-Aminoacetophenone, practical grade from Eastman Organic Chemicals, was dissolved in a minimum amount of boiling water, treated with carbon black, filtered hot, and the solution was separated from a small amount of insoluble oily substance. Then the solution was evaporated to about one third of its original volume and cooled overnight in a refrigerator. The light yellow solid was removed by filtration and dried first in the atmosphere and subsequently over phosphorus pentoxide. This dried *m*-aminoacetophenone was used for reduction with lithium aluminum hydride.

Lithium aluminum hydride (10 g.) was weighed rapidly on glazed paper and added to a three-neck flask swept free of atmospheric gases by means of a continuous flow of dry nitrogen. Then 13.52 g. of powdered *m*-aminoacetophenone was partly dissolved in 500 ml. of absolute ether and the slurry was added dropwise over a period of 2 hr., with vigorous stirring, to the lithium aluminum hydride. The mixture was stirred for two more hours and allowed to stand overnight. Cautious addition of about 100 ml. of water was followed by addition of 250 ml. of 15% sodium hydroxide solution. The mixture was stirred for 2 hr. and the ether solution was separated. The aqueous layer was extracted with two 300-ml. portions of ether and the combined ether solutions were filtered and dried over anhydrous sodium sulfate. Then the ether solution was stirred with decolorizing carbon, filtered three times, and evaporated to dryness. The residue consisted of 11.0 g. (81% yield) of *m*-(1-hydroxyethyl)aniline, a cream colored product, m.p. 70–71°.

Anal. Calcd. for $C_8H_{11}ON$: N, 10.21. Found: N, 10.41.

Dependence of yield on pH for the formation of hippuric m-(1-hydroxyethyl)anilide from hippuric acid and m-(1-hydroxyethyl)aniline. Hippuric acid (0.050 mol.), *m*-(1-hydroxyethyl)aniline (0.050 mol.) and 0.500 g. of L-cysteine hydrochloride were dissolved in about 230 ml. of hot buffer solution. The solution was cooled to 35° and 0.250 g. of papain was ground with a small amount of the solution and added to it, with rinsing. More buffer was added to make the total volume 250 ml. The *p*H was adjusted to the value desired with the aid of a *p*H meter, then filtered, and incubated at 40° for 66 hr. Hippuric *m*-(1-hydroxyethyl)-anilide was removed by filtration, dried, and weighed. Re-

(11) This papain was generously supplied by the Schwarz Laboratories of Mount Vernon, N. Y., and the Wallerstein Laboratory of New York City.

TABLE I

PAPAIN-CATALYZED REACTIONS BETWEEN *N*-ACYLAMINO ACIDS AND NONASYMMETRIC (HYDROXYALKYL)ANILINES

(Hydroxyalkyl)aniline Reactant[a]	N-Acylamino Acid Reactant[b]			
m-Aminobenzyl Alcohol	Hippuric acid (HA)	Carbobenzoxy-DL-alanine (C-DL-A)	Carbobenzoxy-L-alanine (C-L-A)	Benzoyl-DL-alanine (B-DL-A)
Name of Product	*m*-Hippuramidobenzyl alcohol	2-(Benzyloxycarbonylamino)propionic *m*-(hydroxymethyl)anilide	L-2-(Benzyloxycarbonylamino)propionic *m*-(hydroxymethyl)anilide	2-(Benzoylamino)propionic *m*-(hydroxymethyl)anilide
Wt. of Product				
0–18 hr.	0.33 g.	1.78 g.	1.52 g.	0.00 g.
18–42 hr.	0.85 g.	0.53 g.	0.14 g.	0.00 g.
42–210 hr.	1.52 g.	0.32 g.	0.00 g.	0.00 g.
M.p.	185–186°	133.5–134.0°	133.5–134.0°	
$[\alpha]_D^{25°}$ 2% in pyridine		−31.30°	−33.00°	
% *N* calcd.	9.853	8.506	8.506	
% *N* found	9.73		8.28	
p-(2-Hydroxyethyl)-aniline	(HA)	(C-DL-A)	(C-L-A)	(B-DL-A)
Name of Product	Hippuric *p*-(2-hydroxyethyl)anilide	2-(Benzyloxycarbonylamino)propionic *p*-(2-hydroxyethyl)anilide	L-2-(Benzyloxycarbonylamino)-propionic *p*-(2-Hydroxyethyl)-anilide	2-(Benzoylamino)-propionic *p*-(2-Hydroxyethyl)-anilide
Wt. of Product				
0–18 hr.	1.43 g.	2.45 g.	3.26 g.	1.28 g.
18–42 hr.	1.25 g.	0.185 g.	0.03 g.	0.62 g.
42–210 hr.	0.790 g.	0.280 g.	0.132 g.	0.21 g.
M.p.	173–174°	152–153°	155–155.5°	189–190°
$[\alpha]_D^{25°}$ 2% in pyridine		−43.8°	−44.9°	−76.0°
N calcd.	9.39	8.179	8.179	8.969
% *N* found	9.26		8.41	8.90

[a] 0.020 mol. [b] 0.020 mol. HA; 0.020 mol. C-DL-A; 0.010 mol. C-L-A; 0.020 mol. B-DL-A; 0.500 g. L-cysteine hydrochloride; 0.500 g. activated Wallerstein papain; 125 ml. total solution; pH ≃ 4.6.

sults are shown graphically in Fig. 1. The hippuric *m*-(1-hydroxyethyl)anilide was dissolved in hot ethanol, treated with decolorizing carbon, filtered hot three times, and poured into cold water. The precipitate was washed with hot water and dried over phosphorus pentoxide and then had a melting point of 154–155°.

Anal. Calcd. for $C_{17}H_{18}O_3N_2$: N, 9.39. Found: N, 9.36.

Attempted resolution of m-(1-hydroxyethyl)aniline by means of its papain-catalyzed reaction with hippuric acid. A mixture of 0.05 mol. (8.96 g.) of hippuric acid, 0.05 mol. (6.85 g.) of *m*-(1-hydroxyethyl)aniline, 1.000 g. of L-cysteine hydrochloride, and 200 ml. of buffer solution (*p*H 4.75) was heated to bring about rapid solution and then cooled. Then 0.500 g. of activated Wallerstein papain was added, and the resultant solution was filtered. After making up to a total volume of 250 ml. with more buffer, the solution was incubated at 40°. These weights of hippuric *m*-(1-hydroxyethyl)anilide were obtained: 0–16 hr., 0.00 g.; 16–24 hr., 1.40 g.; 24–48 hr., 2.80 g.; 48–72 hr., 1.56 g.; 72–96 hr., 0.80 g.; 96–120 hr., 0.44 g.; 120–144 hr., 0.21 g.; 144–168 hr., 0.09 g.; 168–336 hr., 0.37 g. After recrystallization the rotation was tested for each precipitate in a 2% solution in pyridine and found to be 0.000° in a Rudolph high-precision polarimeter. No detectable resolution had occurred.

Experiments with o-aminobenzyl alcohol. A series of reaction mixtures was set up using *o*-aminobenzyl alcohol with acylated amino acids in the usual way. No evidence was given that any papain-catalyzed reactions had occurred. The considerable insolubility of the *o*-aminobenzyl alcohol appeared to be a major factor in the failure of the reactions to take place.

Preparation of starting materials. Carbobenzoxy-DL-alanine and carbobenzoxy-L-alanine were synthesized by the method of Carter, Frank, and Johnston.[12] *o*-Aminobenzyl alcohol was prepared by reduction of anthranilic acid[13] and *m*-nitrobenzyl alcohol was reduced to *m*-aminobenzyl alcohol.[14] It was necessary to purify crude *p*-(2-hydroxyethyl)aniline as obtained from Eastman Organic Chemicals. This alcohol was treated with carbon in ethanol and warmed and filtered, and the process repeated five times. Evaporation of the solvent and subsequent cooling yielded white, flaky crystals of the alcohol, m.p. 110–110.5°.

Papain-catalyzed reactions between m-aminobenzyl alcohol and N-acylamino Acids. m-Aminobenzyl alcohol (0.020 mol.) was placed in separate flasks with these acylated amino acids: 0.020 mol. of hippuric acid; 0.020 mol. of carbobenzoxy-DL-alanine; 0.010 mol. of carbobenzoxy-L-alanine; 0.020 mol. of benzoyl-DL-alanine; 0.010 mol. of benzoyl-L-alanine. A total buffered solution of 125 ml. was made up in each case and each contained 0.500 g. of L-cysteine hydrochloride and 0.50 g. of activated Wallerstein papain. Incubation was carried out at 40°. Results of these experiments are tabulated in Table I. No reaction was given with either benzoyl-DL-alanine or benzoyl-L-alanine.

Papain-catalyzed reactions between p-(2-hydroxyethyl)-aniline and N-acylamino acids. The same procedure was followed as in the experiments with *m*-aminobenzyl alcohol except that 0.020 mol. of *p*-(2-hydroxyethyl)aniline was used with: 0.020 mol. of hippuric acid; 0.020 mol. of carbobenzoxy-DL-alanine; 0.010 mol. of carbobenzoxy-L-alanine;

(12) H. E. Carter, R. L. Frank, and H. W. Johnston, *Org. Syntheses*, **Coll. Vol III**, 168 (1955).

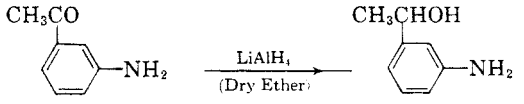
(13) W. G. Brown in "Organic Reactions," Vol. VI, R. Adams, Editor-in-Chief, John Wiley and Sons, Inc., New York, 1951, p. 491.

(14) A. P. Phillips and A. Maggiolo, *J. Org. Chem.*, **15**, 659 (1950).

0.020 mol. of benzoyl-DL-alanine; 0.020 mol. of benzoyl-L-alanine. No reaction was given with benzoyl-L-alanine. Results are tabulated in Table I.

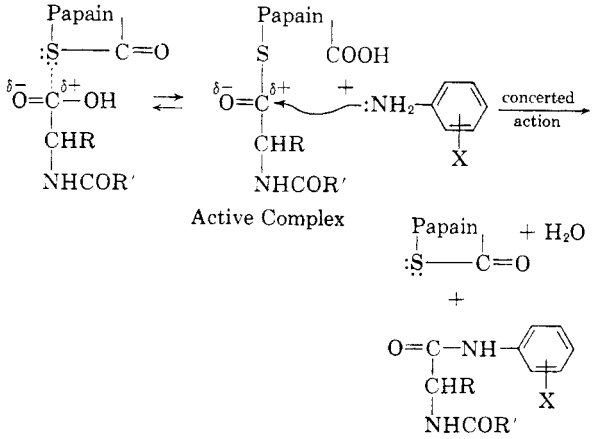
Discussion of results. The original plan of investigation called for a comparison of the rates of precipitation of substituted hippuric anilides formed from *o*-, *m*-, and *p*-aminobenzyl alcohols, as well as possible differences in abilities of these aminobenzyl alcohols to cause resolutions of *N*-acylamino acids. This plan was abandoned because *p*-aminobenzyl alcohol underwent polymerization[14] in an acid medium and *o*-aminobenzyl alcohol proved to be too insoluble. Satisfactory results were obtained in the use of *m*-aminobenzyl alcohol and *p*-(2-hydroxyethyl)aniline, which could be employed under the resolving influence of papain to bring about the resolution of carbobenzoxy-DL-alanine. Only *p*-(2-hydroxyethyl)aniline was able to resolve benzoyl-DL-alanine. Carbobenzoxy-L-alanine reacts with both of these amino alcohols but benzoyl-L-alanine reacts with neither. This is in accord with previous work.[15]

m-(1-Hydroxyethyl)aniline was prepared with ease in a yield of greater than 80% by reduction of *m*-aminoacetophenone with lithium aluminum hydride in dry ether. This substituted aniline was not



resolved in its papain-catalyzed reaction with hippuric acid, but the reaction did produce racemic hippuric *m*-(1-hydroxyethyl)anilide in good yield.

The mechanism of these papain-catalyzed reactions is considered to be essentially a reversal of the mechanism suggested for the hydrolysis of amide linkages.[16] For amide synthesis, this mechanism should be approximately the same as the one proposed for the papain-catalyzed synthesis of N^{α},N^{β}-diacylhydrazines.[15]



(R = —H or —CH_3; R′ = —C_6H_5 or —$OCH_2C_6H_5$; X = —CH_2OH, —$CHOHCH_3$ or —CH_2CH_2OH)

(15) J. L. Abernethy, M. Kientz, R. Johnson, and R. Johnson, *J. Am. Chem. Soc.*, **81**, 3944 (1959).

(16) E. L. Smith, *J. Biol. Chem.*, **223**, 1392 (1958).

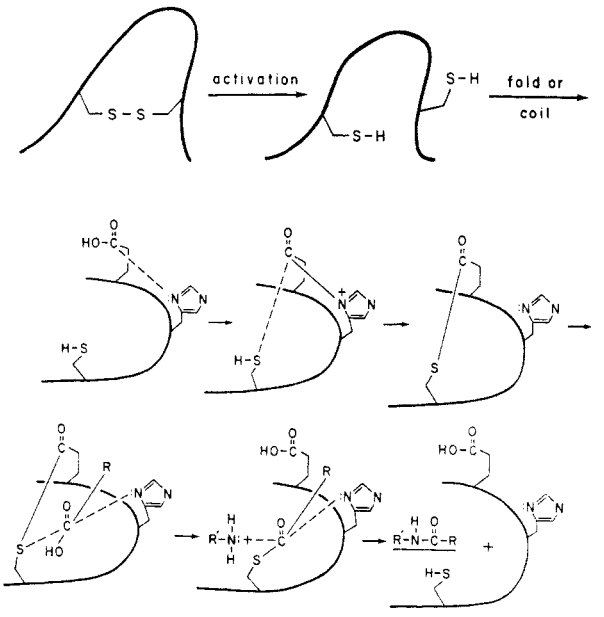


Fig. 2. Mechanism at Papain's active site

It has been suggested[17] that there is insufficient driving force between just a thiolactone and the carboxyl of an *N*-acylamino acid for a reaction to occur with the rapidity of this enzyme action. In view of the recent discovery that one histidine residue is within the active fragment of the papain molecule[18] and that *n*-propyl γ-(4-imidazolyl)thiobutyrate[19] is hydrolyzed exceedingly rapidly due to activation by the anchored imidazole group, it is possible that the imidazole ring performs an activating function here. Some such peptide sequence of amino acid residues, like L-cysteine, L-histidine (with its imidazole ring) and L-glutamic acid might be able to cause thiolactone formation, give a subsequent reaction with an *N*-acylamino acid substrate in producing an external thioester and be activated to undergo a rapid reaction with an amine substrate to form an amide. Also, the configuration of this active center of the enzyme ought to be stereospecific in displaying preference largely toward an L-*N*-acylamino acid substrate. Fig. 2 shows this.

It is possible that the *m*-(1-hydroxyethyl) radical is too far removed from the amino group on the benzene ring to create any stereospecificity at the moment reaction occurs with the active complex formed between the enzyme and the *N*-acylamino acid. It should be recalled, nevertheless, that the asymmetric center of acetyl-DL-phenylalanylglycine is considerably removed from the free carboxyl group, which contacts sulfur at the active center of

(17) Professor Saul Winstein of the UCLA Chemistry Department suggested this in a private conversation with the senior author, J. L. A. The subsequent mechanism was devised by J. L. A. to incorporate this suggestion.

(18) Information given to the senior author, J. L. A., by Professor Emil L. Smith of the College of Medicine, University of Utah, through correspondence.

(19) T. C. Bruice, *J. Am. Chem. Soc.*, **81**, 5444 (1959).

the enzyme. This racemic acid does undergo resolution[20] when subjected to anilide formation in the presence of papain to give acetyl-L-phenylalanylglycine anilide. Evidently some stereospecific contact of the enzyme with the asymmetric region of benzoyl-DL-alanylglycine gives preference to the L-antipode. Such a differentiating contact with racemic *m*-(1-hydroxyethyl)aniline must be absent.

Acknowledgments. This research was supported by grants-in-aid from the Society of Sigma Xi and RESA. The Research Corp. provided funds for the Rudoph high-precision polarimeter. Generous grants from the Fresno County Heart Association and California Heart Association permitted the purchase of chemicals and apparatus. Dr. Robert D. Beech, Dr. Kendall B. Holmes, and Mrs. Joyce Richardson of the Fresno County Heart Association and Dr. John J. Sampson, Dr. Robert H. Maybury, and Miss Phyllis Hecker of the California Heart Association were instrumental in securing these grants. Donations of papain were generously made by the Schwarz Laboratories of Mount Vernon, N. Y., and the Wallerstein Laboratories of New York City.

LOS ANGELES 24, CALIF.

(20) M. Bergmann, O. K. Behrens, and D. G. Doherty, *J. Biol. Chem.*, 124, 7 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF BRITISH COLUMBIA]

The Reaction of 2-Acetonaphthoxime with Carbon Monoxide and Hydrogen. A New Benzoquinoline Synthesis[1]

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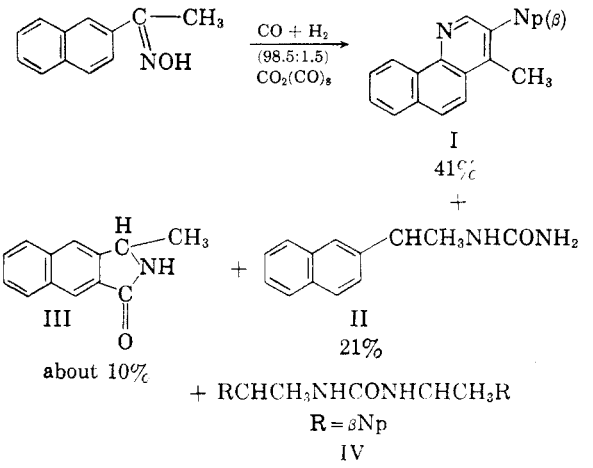
Received August 10, 1959

2-Acetonaphthoxime reacted with carbon monoxide and hydrogen at a pressure of about 4000 p.s.i. and at a temperature of about 220° in the presence of preformed dicobalt octacarbonyl as catalyst to yield 2-(β-naphthyl)-4-methylbenzo[h]quinoline, racemic 1-(β-naphthyl)ethylurea, and 3-methylbenzo[f]phthalimidine. Crystalline hydrochloride, methiodide, picrate and aldehyde derivatives of 2-(β-naphthyl)-4-methylbenzo[h]quinoline were obtained. The infrared and ultraviolet spectra of the aforementioned compounds are described.

This paper is concerned with an extension of our previous study[1,2] of the reaction of carbon monoxide with aromatic ketoximes. In particular, it deals with the reaction of 2-acetonaphthoxime with a mixture of carbon monoxide and hydrogen (98.5:1.5) at a pressure of about 4000 p.s.i. and at a temperature of about 220° in the presence of preformed dicobalt octacarbonyl as catalyst.

Whereas the expected cyclization reaction took place only to the extent of about 10% yielding product III, the main reaction was a condensation one resulting in the formation of 2-(β-naphthyl)-4-methylbenzo[h]quinoline(I) and racemic 1-(β-naphthyl)ethylurea(II).

Products I and II were easily isolated from the reaction mixture by fractional crystallization. 1-(β-naphthyl)ethylurea was slightly soluble in benzene or chloroform, whereas 2-(β-naphthyl)-4-methylbenzo[h]quinoline came down as the second product using ethanol as solvent. Direct chromatographic fractionation of the reaction mixture on alumina using benzene–petroleum ether as developer proved to be the best way to isolate product I (highly fluorescent) in pure form.



The empirical formula of compound I was $C_{24}H_{27}N$. Infrared analyses showed no NH stretching band. As compound I could not be reduced with magnesium in methanol it was assumed that the C=N—group must be part of an aromatic system. On the basis that compound I failed to react with maleic anhydride the linear benzoquinoline structure was eliminated.[3] A peak at 362 mμ in the ultraviolet spectrum of I suggested that the nucleus of

(1) Financial assistance by the National Research Council, Canada, and by the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. Presented at the 136th Meeting of the American Chemical Society, Atlantic City, N. J., September 1959.

(2) A. Rosenthal, R. F. Astbury, and A. Hubscher, *J. Org. Chem.*, 22, 1037 (1958).

(3) W. S. Johnson and F. J. Mathews, *J. Am. Chem. Soc.*, 66, 210 (1944).