were kept at room temperature during the period of measurement.

Acknowledgment.—The authors wish to express their appreciation to Dr. Paul D. Sternglanz, Miss Ruth Thompson and Mr. Yao Nan Sheng for the analytical and ultraviolet absorption spectra data, to Mr. D. James Kay for the bacteriological tests, to Mr. Frank Tranner for the riboflavin and antiriboflavin tests, and to Mr. John J. Masterson for assistance in the preparation of these compounds.

SOUTH NORWALK, CONN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

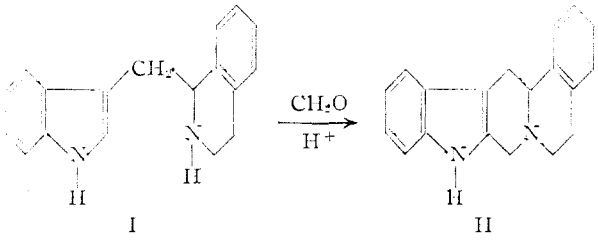
The Synthesis of 1,2-Benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine[1]

BY V. BOEKELHEIDE AND CHU-TSIN LIU

RECEIVED APRIL 29, 1952

The pentacyclic molecule, 1,2-benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine (II), has been synthesized by two different methods. Although II was prepared as a model for certain of the calabash curare alkaloids, the quaternary salts of II possess only slight curare activity, indicating that this probably is not the correct type of nucleus for these alkaloids. Unexpectedly, it was found that catalytic hydrogenation of 1-skatylisoquinoline derivatives in acid effects reduction of a benzene ring rather than the pyridine ring.

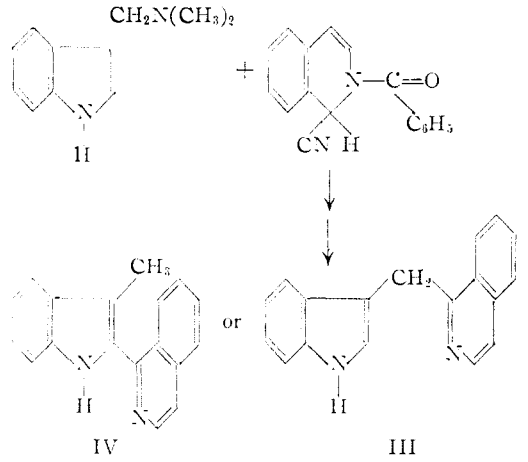
In a previous communication,[2] we reported on some preliminary studies directed toward the synthesis of 1,2-benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine (II), a possible model for certain of the calabash curare alkaloids. The final step in the projected synthesis, as previously outlined, involved the cyclization of 1-skatyl-1,2,3,4-tetrahydroisoquinoline (I) with formaldehyde, as shown below. Since no logical explanation could be advanced to explain the failure encountered in attempts to accomplish this reaction, we have reexamined the steps leading to I to see whether the structure assigned might be incorrect.



I II

One of the steps, which appeared open to question, was the alkylation of 1-cyano-1,2-benzoyl-1,2-dihydroisoquinoline with gramine followed by alkaline hydrolysis to produce 1-skatylisoquinoline (III).[2] As Snyder and Eliel have shown in the case of 1-methylgramine,[3] allylic rearrangement can occur in alkylations with gramine derivatives and the possibility existed that our product had structure IV rather than III. That this was not the case was clearly demonstrated when our product was shown to be identical with a sample of 1-skatylisoquinoline prepared independently by the decarboxylation of 1-(2′-carboxyskatyl)-isoquinoline[2] using copper chromite as catalyst.

In view of these results the only step open to question appeared to be the catalytic hydrogenation of 1-skatylisoquinoline. Although Skita has found that the reduction of isoquinoline using platinum in acetic acid leads to 1,2,3,4-tetrahydroisoquinoline[4] and the reduction of 1-skatylisoquinoline would seem to be analogous, it appeared desirable that this be confirmed by reducing 1-skatylisoquinoline in quantity using the older sodium–alcohol procedure.[5] Despite a coincidence in melting points of derivatives of the two samples of reduced amines, it was obvious from a comparison of their infrared spectra that the product obtained by catalytic hydrogenation was different from that resulting from the sodium–alcohol reduction. The latter product showed the properties of a secondary amine and, in keeping with structure I, it readily underwent cyclization with formaldehyde to give the desired base (II) in excellent yield.



IV III

When the cyclization of I was attempted using an excess of formaldehyde, the main product of the reaction corresponded to a hydroxymethyl derivative of II. This material showed the properties of a carbinol amine and is assumed to be the result of addition of formaldehyde at the indole nitrogen. In support of this, the hydroxymethyl derivative was easily cleaved by aqueous acid to give back the parent compound, II. When acetaldehyde was substituted for formaldehyde in the cyclization

(1) Aided by a grant from the United Cerebral Palsy Association.

(2) V. Boekelheide and C. Ainsworth, THIS JOURNAL, **72**, 2134 (1950).

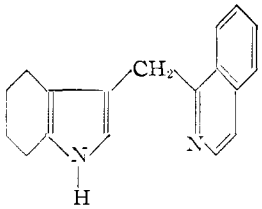
(3) H. R. Snyder and E. L. Eliel, *ibid.*, **70**, 1857 (1948).

(4) A. Skita, *Ber.*, **57**, 1977 (1924); *cf.* B. Witkop, THIS JOURNAL, **70**, 2617 (1948).

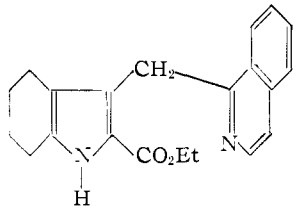
(5) E. Bamberger and W. Dieckmann, *Ber.*, **26**, 1205 (1893); *cf.* R. Wegler and W. Frank, *ibid.*, **70**, 1279 (1937).

step, the 6-methyl homolog of II was likewise obtained in good yield.

Although the structure of the tetrahydro derivative obtained by the catalytic hydrogenation of 1-skatylisoquinoline has not been established, it appears likely that it should be represented by structure V. This is suggested by the elegant work of Schwarz and Schlittler,[6] who found that catalytic reduction with platinum in acid of various β-carboline derivatives led to reduction of the benzene ring rather than the pyridine ring. Similarly, the tetrahydro derivative obtained by catalytic hydrogenation of 1-(2′-carbethoxyskatyl)-isoquinoline is probably best represented by formula VI.

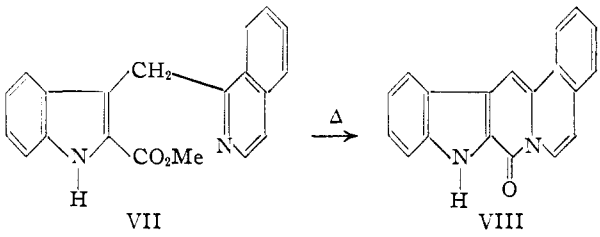


V



VI

The fact that the tetrahydro derivative of 1-(2′-carbethoxyskatyl)-isoquinoline obtained by catalytic hydrogenation undergoes cyclization on heating to give a lactam is not reliable evidence for the presence of a secondary amine group. We have found that 1-(2′-carbomethoxyskatyl)-isoquinoline (VII) can also be cyclized in a similar fashion to yield a lactam. This interesting lactam must be assigned structure VIII, inasmuch as it was converted by reduction with sodium and butanol to 1,2-benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine (II). The product obtained in this way was identical in all respects with that obtained by the cyclization of 1-skatyl-1,2,3,4-tetrahydroisoquinoline with formaldehyde.



VII VIII

The methochloride of II was found to have curariform activity in mice only at dose levels of 45 mg./kg.[7] The weak activity of this quaternary salt was not entirely unexpected in view of the recent chemical evidence of Schmid, Ebnöther and Karrer[8] that the basic structure of the calabash curare alkaloids is not of this type but rather is probably related to that of the strychnos alkaloids.

Experimental[9]

1-Skatyl-1,2,3,4-tetrahydroisoquinoline (I).—To a boiling solution of 3.0 g. of 1-skatylisoquinoline[3] in 150 cc. of *n*-butanol, there was added 9.0 g. of sodium in small portions. The solution was heated until all of the metal had dissolved and then the *n*-butanol was removed by steam distillation. The brown precipitate remaining was collected, pulverized, washed thoroughly with water and air-dried. The crude product (3.0 g.) was purified by converting it to the corresponding hydrochloride salt and regenerating the free base from the purified hydrochloride. Crystallization of the purified base from an ethanol–water mixture gave 1.3 g. (42%) of white crystals, m.p. 55–57°.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.40; H, 6.92. Found: C, 82.42; H, 7.23.

The hydrochloride of 1-skatyl-1,2,3,4-tetrahydroisoquinoline was prepared by treating the crude base in absolute ethanol with dry hydrogen chloride. The crude solid, which precipitated, was washed with absolute acetone and then was crystallized from a methanol–acetone mixture to give colorless prisms, m.p. 250–251°.

Anal. Calcd. for $C_{18}H_{19}N_2Cl$: C, 72.35; H, 6.41. Found: C, 72.40; H, 6.46.

The phenylurea derived from 1-skatyl-1,2,3,4-tetrahydroisoquinoline was obtained by treating the free base in ether with phenyl isocyanate. The resulting solid, on crystallization from methanol, gave colorless crystals, m.p. 225–226°.

Anal. Calcd. for $C_{25}H_{23}N_3O$: C, 78.68; H, 6.07. Found: C, 78.89; H, 6.33.

The picrate of 1-skatyl-1,2,3,4-tetrahydroisoquinoline was obtained by treating the free base with a methanolic picric acid solution. The resulting solid, on crystallization from ethanol, gave golden crystals, m.p. 210–211° dec.

Anal. Calcd. for $C_{24}H_{21}N_5O_7$: C, 58.65; H, 4.31. Found: C, 59.12; H, 4.23.

Although the derivatives of the tetrahydro compound obtained by catalytic reduction in acetic acid with Adams catalyst of 1-skatylisoquinoline[3] (hydrochloride, m.p. 248–250°; picrate, m.p. 210–211° dec.) had similar melting points to those obtained in this preparation and although a mixture of the two hydrochlorides showed no depression of melting point, the infrared spectra of the two bases were clearly different. Thus, in this case, catalytic reduction must occur elsewhere than at the pyridine ring.

1,2-Benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine (II).—To a solution of 230 mg. of 1-skatyl-1,2,3,4-tetrahydroisoquinoline in 30 ml. of 1 *N* hydrochloric acid there were added 0.075 ml. of formalin (35%) and sufficient aqueous sodium acetate (10%) to bring the *p*H of the solution to 5.5. The clear solution was allowed to stand at room temperature for five days, during which some yellow solid separated. After removal of this precipitate (residue A), the solution was made basic with aqueous ammonia and extracted with ether. The ethereal solution was dried over sodium sulfate and the solvent was removed. Crystallization of the residue from absolute ethanol gave 80 mg. of white needles, m.p. 205–206°.

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.16; H, 6.61; N, 10.23. Found: C, 83.05; H, 6.68; N, 9.85.

The yellow solid (residue A), on crystallization from methanol, gave 100 mg. of white crystals, m.p. 280–282°. This proved to be the **hydrochloride** of II, as shown by its composition and conversion to the free base, and thus the total yield of product in this reaction was 71%.

Anal. Calcd. for $C_{19}H_{19}N_2Cl$: C, 73.41; H, 6.16. Found: C, 73.50; H, 6.32.

The picrate of II was prepared using methanolic picric acid and, after crystallization from methanol, it was obtained as yellow needles, m.p. 225°.

Anal. Calcd. for $C_{25}H_{21}N_5O_7$: C, 59.64; H, 4.21. Found: C, 60.08; H, 4.70.

1,2-Benzo-7,8-(2′,3′-indolo)-5-methyltetrahydroquinolizinium Chloride.—A solution of 1.0 g. of II in 10 ml. of benzene was treated with an excess of methyl iodide and warmed for a short time over a steam-bath. The precipitate, which formed, was collected and crystallized from an acetone–methanol mixture. This gave 1.10 g. of the **methiodide of II**, m.p. 242–243° (*Anal.* Calcd. for $C_{20}H_{21}N_2I$: C, 57.71; H, 5.08. Found: C, 58.26; H, 5.45).

To a solution of 250 mg. of the methiodide of II in 25 ml. of methanol, there was added 180 mg. of freshly precipitated silver chloride. The solution was shaken vigorously and then allowed to stand in the dark for three hours. The

(6) H. Schwarz and E. Schlittler, *Helv. Chim. Acta*, **34**, 629 (1951); see also, M-M. Janot, J. Keufer and J. LeMen, *Bull. soc. chim. France*, 230 (1952).

(7) We are indebted to Dr. I. H. Slater, Dept. of Pharmacology, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., for the pharmacological testing.

(8) H. Schmid, A. Ebnöther and P. Karrer, *Helv. Chim. Acta*, **33**, 1486 (1950).

(9) Analyses by Miss Claire King.

precipitate was then removed and the solution was concentrated to a small volume. The precipitate, which resulted on addition of ether, was collected and crystallized from a methanol–ether mixture to yield 150 mg. (77%) of white crystals, m.p. 238–239°. A mixture of this and the starting methiodide melted over a range beginning at 229°.

Anal. Calcd. for $C_{20}H_{21}N_2Cl$: C, 73.96; H, 6.52. Found: C, 74.06; H, 6.69.

1,2-Benzo-7,8-(1′-hydroxymethyl-2′,3′-indolo)-tetrahydroquinolizine.—A solution was prepared by adding 200 mg. of 1-skatyl-1,2,3,4-tetrahydroisoquinoline to 10 ml. of water containing 3 drops of concd. hydrochloric acid. To the clear solution there were added 1 ml. of formalin (35%) and sufficient aqueous sodium acetate to adjust the *p*H of the solution to 5.5. After the solution had been allowed to stand at room temperature for two days, a white solid separated. This precipitate (residue A) was collected, and the solution was made basic with aqueous ammonia. The resulting precipitate was collected and, after crystallization from benzene, it yielded 95 mg. of white crystals, m.p. 169–170°.

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.91; H, 6.62. Found: C, 78.64; H, 6.65.

When residue A was crystallized from a methanol–acetone mixture, it gave 70 mg. of white needles, m.p. 250–252°. This was shown to be the hydrochloride of 1,2-benzo-7,8-(1′-hydroxymethyl-2′,3′-indolo)-tetrahydroquinolizine.

Anal. Calcd. for $C_{20}H_{21}N_2OCl$: C, 70.49; H, 6.21. Found: C, 70.73; H, 6.39.

The methiodide was prepared by treating the free base in benzene with an excess of methyl iodide. The resulting precipitate, on crystallization from water, gave pale yellow crystals, m.p. 204–205°.

Anal. Calcd. for $C_{21}H_{23}N_2OI$: C, 56.65; H, 5.19. Found: C, 56.64; H, 5.10.

When the free base (50 mg.) obtained by this method was heated with 25 ml. of 4 *N* sulfuric acid for one hour and the resulting solution was then made basic, a yellow solid separated which, on crystallization from benzene, gave white needles, m.p. 205–206°. A mixture of this material and compound II showed no depression of melting point. Also the hydrochloride and picrate of this base were identical with those obtained from II.

1,2-Benzo-7,8-(1′-ethoxymethyl-2′,3′-indolo)-tetrahydroquinolizine Hydrochloride.—To a dry saturated solution of ethanolic hydrogen chloride there was added 100 mg. of 1,2-benzo-7,8-(1′-hydroxymethyl-2′,3′-indolo)-tetrahydroquinolizine and the resulting solution was warmed on a steam-bath for 10 minutes. Stout white crystals began forming during this period of heating. These were collected and recrystallized from ethanol to give white crystals, m.p. 244–246° dec.

Anal. Calcd. for $C_{22}H_{25}N_2OCl$: C, 71.64; H, 6.83. Found: C, 72.08; H, 7.21.

1,2-Benzo-6-methyl-7,8-(2′,3′-indolo)-tetrahydroquinolizine Hydrochloride.—This was prepared according to the general procedure of Hahn and Ludwig.[19] To a solution of 150 mg. of 1-skatyl-1,2,3,4-tetrahydroisoquinoline in 15 ml. of 1 *N* hydrochloric acid there were added 0.1 ml. of acetaldehyde and sufficient aqueous sodium acetate (10%) to bring the *p*H of the solution to 5.5. The clear solution was allowed to stand at room temperature for one week. The white crystals which formed during this period were collected and, on crystallization from a methanol–acetone mixture, they gave 90 mg. (64%) of white crystals, m.p. 249–250°.

Anal. Calcd. for $C_{20}H_{21}N_2Cl$: C, 73.96; H, 6.52. Found: C, 74.41; H, 6.38.

Decarboxylation of 1-(2′-Carboxyskatyl)-isoquinoline.—The 1-(2′-carboxyskatyl)-isoquinoline used in this experiment was obtained by dissolving a sample of 1-(2′-carboxyskatyl)-isoquinoline hydrochloride[2] in dilute sodium hydroxide solution and then bringing the *p*H of the solution to 6.0 by adding dilute hydrochloric acid. The precipitate, which separated, was an amorphous white powder, m.p. 158–160°. (*Anal.* Calcd. for $C_{19}H_{14}N_2O_2$: C, 75.50; H, 4.64. Found: C, 75.52; H, 4.64).

A suspension of 850 mg. of the 1-(2′-carboxyskatyl)-isoquinoline in 10 ml. of mineral oil was heated at 200–210° with 17 mg. of copper chromite catalyst under an atmosphere of nitrogen. Carbon dioxide was evolved and, after 10 minutes, the hot reaction mixture was filtered to remove the catalyst. The solution was diluted with chloroform, washed with dilute sodium hydroxide, and then extracted with dilute hydrochloric acid. When the acid extract was made basic, a yellow solid separated which, on crystallization from ethanol, gave 300 mg. (41%) of white prisms, m.p. 171–172°. On admixture of a sample of 1-skatylisoquinoline prepared by the alkylation of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline with gramine,[2] there was no depression of melting point. Likewise the picrates of the two samples of 1-skatylisoquinoline were shown to be identical by a mixed melting point determination.

1-(2′-Carbomethoxyskatyl)-isoquinoline (VII).—To a solution of 5.0 g. of 1-(2′-carbethoxyskatyl)-1-cyano-2-benzoyl-1,2-dihydroisoquinoline[2] in 100 ml. of methanol there was added 30 ml. of a 10% methanolic potassium hydroxide solution. After the solution had been boiled under reflux for three hours, the solvent was removed under reduced pressure and the residue was extracted with ether. The ethereal extract was in turn extracted with 3 *N* hydrochloric acid. When the acid extract was made basic, a white precipitate formed which was collected and recrystallized from ethanol. This gave 1.77 g. (50%) of white crystals, m.p. 199–200°. This method was found to be more satisfactory for the preparation of esters of this series than the previous method[2] of complete hydrolysis to the acid followed by re-esterification.

Anal. Calcd. for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.09. Found: C, 75.94; H, 5.34.

The picrate of 1-(2′-carbomethoxyskatyl)-isoquinoline was prepared using ethanolic picric acid and was obtained, on crystallization from ethanol, as yellow crystals, m.p. 234–235° dec.

Anal. Calcd. for $C_{26}H_{19}N_5O_9$: C, 56.85; H, 3.51. Found: C, 57.07; H, 4.03.

1,2-Benzo-7,8-(2′,3′-indolo)-6-quinolizone (VIII).—A solution of 5.0 g. of 1-(2′-carbomethoxyskatyl)-isoquinoline in 85 ml. of α-methylnaphthalene (b.p. 244°) was boiled under reflux for 20 hours. When the solution was cooled, 3.8 g. (85%) of yellow crystals separated. These were recrystallized from dioxane to yield 3.1 g. of yellow needles, m.p. 248–250°.

Anal. Calcd. for $C_{19}H_{12}N_2O$: C, 80.26; H, 4.25. Found: C, 80.16; H, 4.37.

Sodium–Butanol Reduction of 1,2-Benzo-7,8-(2′,3′-indolo)-6-quinolizone.—To a suspension of 1.0 g. of VIII in 250 ml. of boiling *n*-butanol, 4.0 g. of sodium was added in small pieces. After all of the metal had been added, the solvent was removed by steam distillation and the brown solid residue was collected. Crystallization of the residue from methanol gave 0.9 g. of white needles, m.p. 204–206°. Admixture of a sample of 1,2-benzo-7,8-(2′,3′-indolo)-tetrahydroquinolizine (II) caused no depression of melting point. Likewise the hydrochlorides of both samples had identical melting points and mixing caused no depression of melting point.

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.16; H, 6.61. Found: C, 83.22; H, 6.88.

1-(2′-Hydroxymethylskatyl)-isoquinoline (XI).—To a solution of 5.0 g. of 1-(2′-carbomethoxyskatyl)-isoquinoline in 200 ml. of benzene there was added dropwise 34 ml. of a 0.55 *M* ethereal solution of lithium aluminum hydride under a nitrogen atmosphere and with protection against moisture. After the mixture had boiled under reflux for two hours, water was added to decompose the excess lithium aluminum hydride. The precipitate of metallic hydroxides was separated and extracted with absolute acetone. Removal of the acetone gave 2.5 g. of white crystals. An additional 0.85 g. of product was obtained by concentration of the benzene filtrate. The combined residues (3.35 g., 74%) were crystallized from chloroform to give white crystals, m.p. 189–190°.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.20; H, 5.59. Found: C, 79.19; H, 5.89.

Although various attempts were made to affect cyclization of the 1-(2′-hydroxymethylskatyl)-isoquinoline by means of acidic reagents, these reactions proved to be more complex

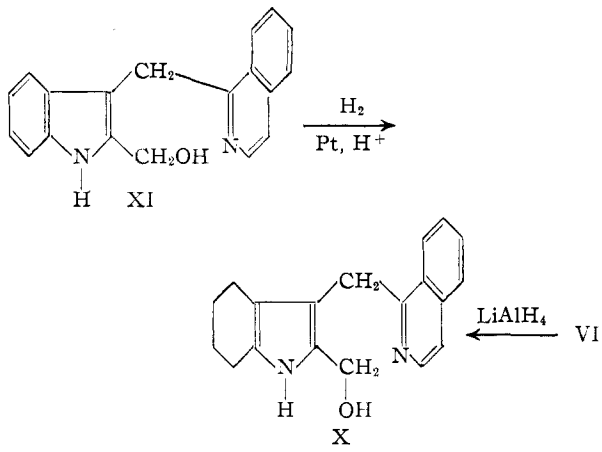
(10) G. Hahn and H. Ludwig, *Ber.*, **67**, 2031 (1934).

than anticipated and a description of these results will be reserved for a later discussion.

Catalytic Hydrogenation of 1-(2'-Hydroxymethylskatyl)-isoquinoline.—A solution of 500 mg. of 1-(2'-hydroxymethylskatyl)-isoquinoline (XI) in 20 ml. of glacial acetic acid containing 100 mg. of Adams catalyst was subjected to hydrogenation at room temperature and under atmospheric pressure of hydrogen. After two molar equivalents of hydrogen had been absorbed (3 hr.), the catalyst was removed and the solution was made basic with aqueous sodium hydroxide solution. When the resulting precipitate was recrystallized from chloroform, it yielded 400 mg. (79%) of white needles, m.p. 204–205°.

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89. Found: C, 78.17; H, 6.86.

It was shown by a mixed melting point determination that this product was identical with the lithium aluminum hydride reduction product of the tetrahydro derivative of 1-(2'-carbethoxyskatyl)-isoquinoline.[2] This product had previously been designated as 1-(2'-hydroxymethyl-3'-indolyl)-methyl-1,2,3,4-tetrahydroisoquinoline but, in view of the earlier discussion in this paper this designation must be incorrect and the compound is now assigned structure X. The two syntheses of this compound are illustrated below. The catalytic reduction product of 1-(2'-carbethoxyskatyl)-isoquinoline, which was previously designated as 1-(2'-carbethoxy-3'-indolyl)-methyl-1,2,3,4-tetrahydroisoquinoline,[2] is now assigned structure VI.



ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF SYDNEY]

β-Acylethylation with Ketonic Mannich Bases. The Synthesis of Some Diketones, Ketonic Sulfides, Nitroketones and Pyridines

BY NAIDA S. GILL,[1] KENNETH B. JAMES,[2] FRANCIS LIONS AND KEVIN T. POTTS[2]

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Decomposition of ketonic Mannich bases by controlled heating of their solutions in suitable ketones leads to β-acylethylation of the ketone and formation, primarily, of a 1,5-diketone. Certain of these diketones have been caused to react with hydroxylamine hydrochloride, or, alternatively, with hydrazine followed by hydrogen chloride, to yield pyridines not otherwise readily accessible. Thermal decomposition of ketonic Mannich bases in presence of thiols gives β-acylethyl alkyl (or aryl) sulfides in good yields, as does the interaction in solution of Mannich base methiodides with the alkali salts of thiols. Similarly, thermal decomposition of ketonic Mannich bases in primary or secondary nitroparaffins β-acylethylates them to γ-nitroketones in good yields.

Much of the usefulness of Mannich bases of the type $R{\cdot}CO{\cdot}CH(R'){\cdot}CH_2{\cdot}NR''_2$ in synthesis stems from the fact that they, or their quaternary metho salts, are readily broken down to α,β-unsaturated ketones under alkaline conditions which can further promote the interaction of these products with substances possessing activated hydrogen atoms in reactions of the Michael type. The process can be usefully described as β-acylethylation in analogy with cyanoethylation, and the earliest studies of it[3] have been greatly amplified in recent years.

The methods studied to date for such utilization of ketonic Mannich bases apparently do not include thermal decomposition of the bases in the presence of the reagent to be added, although Snyder and his co-workers[4] have shown that gramine and similar bases can be readily condensed with nitroparaffins or with acetaminomalonic ester by heating them together in presence of a small amount of alkali, dimethylamine or other secondary base being extruded; and Snyder and Brewster[5] have recorded amine exchange reactions of Mannich bases under the influence of heat.

This paper records experiments which show that ketonic Mannich bases break down smoothly when heated in presence of such reagents as reactive ketones, thiols or nitroparaffins, secondary base being extruded and the reagent being added across the olefinic bond of the resulting α,β-unsaturated ketone. Because of the volatility of the extruded secondary base it is best to work with Mannich bases derived from dimethylamine or diethylamine, but almost equally good results can be obtained with Mannich bases derived from amines such as morpholine, when, however, the method of product recovery is less simple.

Heating of a ketonic Mannich base in excess of a suitable ketone containing a keto-methylene system leads to β-acylethylation of the ketone and formation, primarily, of a 1,5-diketone. Thus, as an example, 3-dimethylamino-1-phenyl-1-propanone (A), heated in an excess of cyclohexanone at 160° for 20 minutes gave an almost quantitative yield of 1-(2'-cyclohexanonyl)-3-phenyl-propan-3-one (2-β-benzoylethylcyclohexanone (I)). Further examples are listed in Table I. The formation of 4-(2'-cyclopentanonyl)-butan-2-one (2-β-acetylethylcyclopentanone) from 4-diethylamino-butan-2-one (C) and cyclopentanone, and its failure under the

(1) Commonwealth Research Assistant, University of Sydney.

(2) Teaching Fellow, University of Sydney.

(3) *Cf.* S. M. Abdullah, *J. Indian Chem. Soc.*, **12**, 62 (1935); C. Mannich, W. Koch and F. Borkowsky, *Ber.*, **70B**, 355 (1937); E. C. du Feu, F. J. McQuillen and R. Robinson, *J. Chem. Soc.*, 53 (1937).

(4) *Cf.* H. R. Snyder and L. Katz, THIS JOURNAL, **69**, 3140 (1947); E. E. Howe, A. J. Zambito, H. R. Snyder and M. Tishler, *ibid.*, **67**, 38 (1945).

(5) H. R. Snyder and J. H. Brewster, *ibid.*, **70**, 4230 (1948).