tained best by heating cautiously over a free flame a mixture of cinnamoyl chloride with two equivalents of guanidine hydrochloride until an exothermic reaction was initiated with copious evolution of hydrogen chloride. When the violent process had subsided the reaction mixture was stirred up with acetone, which was filtered and discarded. The insoluble solid was recrystallized from methanol to give a 70–80% yield of cinnamoylguanidine hydrochloride, m.p. 269–270°. Cinnamoylguanidine base liberated from this hydrochloride and recrystallized from water melted at 141–142°.

Using guanidine carbonate instead of the hydrochloride a small yield of II·HCl was obtained by a similar procedure.

Cinnamoyl chloride with excess aqueous guanidine base gave almost entirely cinnamic acid.

Excess guanidine base reacted with cinnamoyl chloride in dry benzene to give as the chief product isolated, although in moderate yield, dicinnamoylguanidine hydrochloride. This was recrystallized from methanol to give white crystals, m.p. 225–226°.

Anal. Calcd. for $C_{19}H_{18}O_2N_3Cl$: C, 64.1; H, 5.1. Found: C, 64.4; H, 5.1.

Attempts to Cyclize Cinnamoylguanidine (II) to the Dihydropyrimidine (I).—Numerous attempts were made to cyclize the open chain cinnamoylguanidine base (II) using conditions some of which resembled those prevailing in the condensation of methyl cinnamate with guanidine. In no case was any isolable amount of I obtained. In most cases the starting compound II, methyl cinnamate, and cinnamic acid were the only substances recovered. These facts seem to indicate that II is not an intermediate in the formation of I.

Ultraviolet Absorption Spectra.—The ultraviolet spectra were obtained using a Beckman quartz spectrophotometer model DU, cell length 1 cm., and solutions were made up at a concentration of 10 mg. per liter in 95% ethyl alcohol.

Acknowledgment.—The authors are indebted to S. W. Blackman and N. Martinez, Jr., for the microanalytical results included and to Miss Dian Cameron for the ultraviolet absorption spectra.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY]

2-Vinylpyrrole and Homologs

BY WERNER HERZ AND CHARLES F. COURTNEY[1]

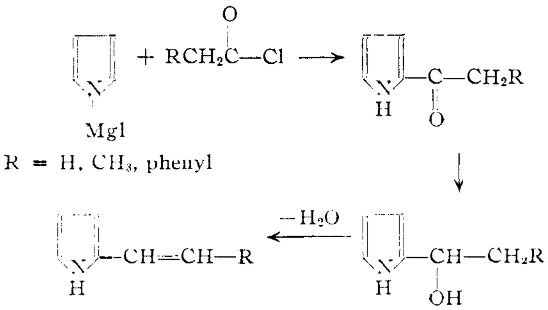
RECEIVED AUGUST 13, 1953

2-Pyrrolecarbinols are obtained in excellent yield by the inverse lithium aluminum hydride reduction of 2-pyrrole ketones. Their dehydration furnishes fair yields of homologs of 2-vinylpyrrole. 2-Vinylpyrrole itself is best prepared by vapor phase dehydration of 2-pyrroleethanol.

The recent literature contains a number of references to the preparation of five-membered heterocyclic analogs of styrene which have been carried out primarily to study the polymerizability of such substances. Thus 2-vinylfuran,[2] 2-vinylthiophene,[3] 2-vinylthiazole[4] and 2-vinylimidazole[5] are known and several homologs have been synthesized.[6] On the other hand, the properties of 2-vinylpyrrole are not recorded although there exists a patent[7] which claims that it may be made by dehydrogenation of 2-ethylpyrrole.

A priori, one might expect considerable instability in a compound of this type, in spite of the fact that polysubstituted vinylpyrroles, which are of interest because of their close relationship to naturally-occurring pigments, exhibit no tendency to decompose or to polymerize. In view of our interest in the chemistry of simple monofunctional derivatives of pyrrole we have undertaken the investigation of 2-vinylpyrrole and its homologs. The present paper describes the synthesis of 2-vinyl-, 2-propenyl- and 2-(β-styryl)-pyrrole by methods which are capable of extension to other compounds.

The scheme for the preparation of the desired substances is



The reduction of pyrrolealkyl ketones to pyrrolealkylcarbinols has so far not been accomplished satisfactorily. Dennstedt and Zimmermann[8] reduced 2-acetylpyrrole with sodium amalgam and reported the isolation of two products in unstated yield, one a solid, presumably a pinacol, the other a high-boiling liquid, probably the expected carbinol. Hess and co-workers[9] demonstrated that the pyrrole ring as well as the carbonyl group of 2-acylpyrroles was reduced by means of sodium and ethanol or by catalytic hydrogenation at low pressure. High pressure hydrogenation, on the other hand, apparently cannot be stopped at the carbinol stage, but proceeds further, through hydrogenolysis, to give an alkylpyrrole.[10]

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(1) Abstracted from the thesis of Charles F. Courtney submitted in partial fulfillment of the requirements for the degree Master of Science, 1953.

(2) M. Moureu, C. Dufraisse and J. R. Johnson, *Ann. chim.*, [10] **7**, 15 (1927).

(3) R. Kuhn and O. Dann, *Ann.* **547**, 293 (1941); D. T. Mowry, M. Renoll and W. F. Huber, THIS JOURNAL, **68**, 1105 (1946); R. T. Nazzaro and J. L. Bullock, *ibid.*, **68**, 2121 (1946).

(4) D. L. Schoene, *ibid.*, **73**, 1970 (1951).

(5) J. K. Lawson, Jr., *ibid.*, **75**, 3398 (1953).

(6) For examples, see G. B. Bachman and L. V. Heisey, *ibid.*, **70**, 2378 (1948); **71**, 1985 (1949); R. H. Wiley and N. R. Smith, *ibid.*, **72**, 5198 (1950).

(7) C. R. Wagner, U. S. Patent No. 2,393,132 (Jan. 15, 1946).

(8) M. Dennstedt and J. Zimmermann, *Ber.*, **19**, 2204 (1886).

(9) K. Hess, *ibid.*, **46**, 3113 (1913); K. Hess, F. Merck and C. Uibrig, *ibid.*, **48**, 1886 (1915).

(10) M. DeJong and J. P. Wibaut, *Rec. trav. chim.*, **49**, 237 (1930), F. K. Signaigo and H. Adkins, THIS JOURNAL, **58**, 709 (1936); J. L. Rainey and H. Adkins, *ibid.*, **61**, 1104 (1939); H. Adkins and H. L. Coonradt, *ibid.*, **63**, 1563 (1941).

Our attempts to use the Meerwein–Ponndorf–Verley method for the reduction of acylpyrroles showed little promise and we therefore investigated the action of lithium aluminum hydride. When 2-acetylpyrrole, dissolved in ether, was added to an ether solution of the hydride in the usual manner, two liquids were obtained in low yield. The lower boiling fraction was identified as 2-ethylpyrrole by comparison with an authentic sample; the second fraction was the expected carbinol on the basis of physical constants, analysis and infrared spectrum. Variation of solvent did not improve the yields of carbinol, the majority of the product being represented by resinous material. These results indicate that under the influence of lithium aluminum hydride hydrogenolysis of pyrrolecarbinols proceeds easily with the formation of alkylpyrroles. A similar instance of "overreduction" was reported by Conover and Tarbell[11] who noted that 2-amino-4-methyl-5-carbethoxythiazole was reduced to 2-amino-4,5-dimethylthiazole. Similar observations recently have been made by Treibs and Scherer[12] who were unable to prepare pyrrolecarbinols by lithium aluminum hydride reduction of polysubstituted carbethoxy- and acylpyrroles.

Further reflection suggested that "overreduction" might be avoided by inverse addition of lithium aluminum hydride to a solution of the acylpyrrole. This proved to be the case and the desired carbinols were isolated in yields ranging from 70–80% of theory. That reduction by inverse addition of lithium aluminum hydride is indeed a generally applicable procedure for the synthesis of alcohols of the pyrrole series was also demonstrated by the reduction of ethyl 2-pyrroleacetate to 2-(2-pyrrole)-ethanol in 50% yield. All of the carbinols were very unstable, discolored quickly on standing at room temperature and gradually solidified to a yellow resin. The usual procedures for the preparation of derivatives did not result in the isolation of crystalline material due to decomposition.

As the result of a considerable number of trials it appears that the best general method for the dehydration of pyrrolealkylcarbinols is vapor phase dehydration over alumina at 260–280°. Thus 2-pyrroleethylcarbinol gave a 52% yield of 2-propenylpyrrole. However, 2-pyrrolemethylcarbinol could not be dehydrated to 2-vinylpyrrole in yields of better than 1–2% by this method due to resinification on the column. Hence we resorted to vapor phase dehydration of the isomeric 2-(2-pyrrole)-ethanol which furnished 2-vinylpyrrole in 42% yield. Benzyl-2-pyrrolecarbinol, a solid, was dehydrated by distillation from hot solid potassium hydroxide.

In order to establish structures and to dismiss the possibility of rearrangement during the dehydration step the vinylpyrroles were reduced catalytically to the corresponding alkylpyrroles. Authentic samples of 2-ethylpyrrole, 2-propylpyrrole and 1-(2-pyrrole)-2-phenylethane were prepared by the Huang-Minlon modification of the Wolff–Kishner reduction. Physical properties and infrared spectra of the products obtained by the two independent procedures were identical.

The 2-vinylpyrroles assume a dark red color on standing when exposed to air, but there appears to be no indication of rapid polymerization since redistillation yields the original light yellow liquids whose odor is reminiscent of styrene. The reactions of these compounds will be the subject of future studies.

Acknowledgment.—We wish to thank Dr. H. J. Barrett of the Electrochemicals Department, E. I. du Pont de Nemours and Company, for the generous gift of chemicals.

Experimental[13]

"Normal" Reduction of 2-Acetylpyrrole with Lithium Aluminum Hydride.—A solution of 10.9 g. of 2-acetylpyrrole[14] in 125 ml. of anhydrous ether was added dropwise to a clear solution of 1.9 g. of lithium aluminum hydride in 100 ml. of ether. On working up in the usual manner there was obtained 3.3 g. of 2-ethylpyrrole, b.p. 36° (2 mm.), $n^{23}\mathrm{D}$ 1.4960 (lit. 59–60° at 15 mm.[15]; 68° at 14 mm.[18]) and 2.3 g. of 2-pyrrolemethylcarbinol, b.p. 83.5° (2 mm.), $n^{23}\mathrm{D}$ 1.5242, d^{20}_4 1.073, $(R)\mathrm{D}$ obsd., 31.4; calcd. 31.9. The infrared spectrum exhibited the broad band characteristic of bonded hydroxyl. Due to the rapid decomposition of the sample, analytical values were invariably high.

Anal. Calcd. for C_6H_9NO: N, 12.61. Found: N, 13.21.

Inverse Addition of Lithium Aluminum Hydride.—A clear solution of 5.8 g. of lithium aluminum hydride in 100 ml. of anhydrous ether was added dropwise, with stirring, to 21.8 g. of 2-acetylpyrrole in 150 ml. of dry ether. After the addition was completed, refluxing was continued for one-half hour on the steam-bath. The flask was cooled with ice and the excess hydride was decomposed with water. The solid residue was extracted with ether and the combined ether extracts were dried and distilled. The yield of 2-pyrrolemethylcarbinol, b.p. 81–82° (1–2 mm.), was 80%.

Reduction of 2-propionylpyrrole[14] gave a 74% yield of 2-pyrroleethylcarbinol, b.p. 86° (1 mm.), $n^{23}\mathrm{D}$ 1.5120.

Anal. Calcd. for $C_7H_{11}NO$: N, 11.19. Found: N, 11.03.

Reduction of benzyl 2-pyrrole ketone[14] furnished benzyl-2-pyrrolecarbinol in 73% yield, b.p. 161° (3 mm.), m.p. 54–55°.

Anal. Calcd. for $C_{12}H_{13}NO$: N, 7.48. Found: N, 7.50.

Ethyl 2-pyrroleacetate[17] gave a 54% yield of the known 2-(2-pyrrole)-ethanol, b.p. 94–95° (1.5 mm.) (lit.[9] 138-142° at 15 mm.)

2-Vinylpyrrole.—An outer 29/42 standard taper ground glass joint was fitted with openings for a thermometer and a dropping funnel. It was attached to an inner joint which was in turn connected to the top of an electrically heated column. The column was filled with 8–14 mesh alumina and the apparatus was heated to 260–270° for two hours in order to dry and activate the alumina. Five grams of 2-(2-pyrrole)-ethanol dissolved in 30 ml. of dry benzene was placed in the dropping funnel, the system was evacuated to a pressure of 1 mm. and the carbinol was added slowly to the column at 260–280° in the course of one-half hour. The product was caught in a trap cooled by a Dry Ice–acetone mixture. Several washings of the still hot tube with benzene were necessary to remove the product which was held tightly to the alumina. After separation of the water layer the benzene was dried and stripped. The residual oil was distilled *in vacuo* and gave in 42% yield a light yellow oil, b.p. 64–67° (18 mm.), $n^{25}\mathrm{D}$ 1.5562.

Anal. Calcd. for C_6H_7N: N, 15.04. Found: N, 14.73.

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(11) L. H. Conover and D. S. Tarbell, THIS JOURNAL, **72**, 5221 (1950).

(12) A. Treibs and H. Scherer, *Ann.*, **567**, 139 (1952).

(13) Melting points and boiling points are uncorrected. Infrared spectra were determined by Mr. Dean F. Keeley on a Perkin–Elmer Model 21 spectrometer.

(14) B. Oddo, *Ber.*, **43**, 1012 (1910).

(15) K. Hess and F. Wissing, *ibid.*, **47**, 1416 (1914).

(16) H. Fischer, H. Beyer and E. Zaucker, *Ann.*, **486**, 55 (1931).

(17) W. Kutscher and O. Klamerth, *Z. physiol. Chem.*, **289**, 229 (1952).

Further evidence for the assigned structure is the presence in the infrared spectrum of new bands at 1635 cm.$^{-1}$, presumably due to the exocyclic double bond, and at 985 cm.$^{-1}$ (vinyl group). The -NH region exhibited the characteristic -NH bands[18] at 3485 (unassociated) and 3405 cm.$^{-1}$ (associated, varies with concentration).

Dehydration of 2-pyrrolemethylcarbinol by distillation in the presence of hydroquinone or by flash-distillation from solid potassium hydroxide resulted in the formation of 2-vinylpyrrole in yields of less than 5%. Most of the starting material had been converted to the yellow undistillable resin which the carbinol forms on standing.

2-Propenylpyrrole.—Vapor phase dehydration of 2-pyrroleethylcarbinol in the manner described above formed 2-propenylpyrrole in 52% yield, b.p. 81–82° (9 mm.), $n^{26}\mathrm{D}$ 1.5438.

Anal. Calcd. for C_7H_9N: N, 13.07. Found: N, 12.86.

The infrared spectrum of this compound exhibited a fairly strong band at 1655 cm.$^{-1}$ (C=C). The ultraviolet spectrum in 95% ethanol had a maximum at 270 mμ, ϵ 1130.

β-(2-Pyrrole)-styrene.—A small round-bottom flask containing 10 g. of benzyl-2-pyrrolecarbinol and six pellets of potassium hydroxide was exhausted to 0.2 mm. and heated in an oil-bath to 250–260°. The carbinol melted and started to boil. After ten minutes the apparatus was cooled. The solid which had collected on the flask walls was scraped out and recrystallized from benzene–petroleum ether. The yield of light yellow crystals, m.p. 136–137°, was 22%.

Anal. Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.03; H, 6.47; N, 8.50.

The infrared spectrum contained a new band at 1640 cm.$^{-1}$ (C=C) in addition to the usual phenyl frequencies at 1600 and 1500 cm.$^{-1}$. The ultraviolet absorption spectrum in 95% ethanol had a maximum at 243 mμ, ϵ 1050.

2-Ethylpyrrole.—A solution of 2 g. of 2-vinylpyrrole in 30 ml. of 95% ethanol was reduced in a low pressure Parr hydrogenator with 10% palladium-on-charcoal catalyst until hydrogen uptake ceased. The product boiled at 67° (19 mm.), $n^{24}\mathrm{D}$ 1.4962.

An authentic sample was prepared by refluxing 10.8 g. of 2-acetylpyrrole, 12.8 g. of potassium hydroxide, 5 ml. of hydrazine hydrate and 100 ml. of triethylene glycol at 125° for one hour, distilling until the temperature had reached 205° and continuing to reflux for three hours. The product boiled at 65–68°, $n^{24}\mathrm{D}$ 1.4952. The infrared spectra of the two samples were identical.

2-Propylpyrrole.—Catalytic reduction of 2-propenylpyrrole yielded a product of b.p. 67–68° (9 mm.), $n^{23}\mathrm{D}$ 1.4980. The authentic sample, prepared by Wolff–Kishner reduction of 2-propionylpyrrole, boiled at 64–65° (9 mm.), $n^{25}\mathrm{D}$ 1.4972 (lit.[9] b.p. 70–71° at 17 mm.). The infrared spectra of the two samples were identical.

Benzyl-2-pyrrolemethane.—Catalytic hydrogenation of β-(2-pyrrole)-styrene gave a white solid which was purified by distillation, b.p. 140–147° (7 mm.), and which melted at 46–47° after recrystallization from petroleum ether. A mixed m.p. with a sample prepared by Wolff–Kishner reduction of benzyl 2-pyrrole ketone was not depressed. The infrared spectra of both products were identical.

Anal. Calcd. for $C_{12}H_{13}N$: C, 84.13; H, 7.65. Found: C, 84.36; H, 7.72.

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[18] N. Fuson, M. Josien, R. L. Powell and E. Utterback, *J. Chem. Phys.*, **20**, 145 (1952).

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

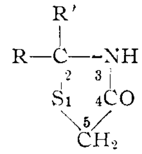
4-Thiazolidones. VI.[1] The Preparation of Some 2-Substituted Derivatives

BY ALEXANDER R. SURREY AND ROYAL A. CUTLER

RECEIVED AUGUST 10, 1953

A general procedure for the preparation of 2-substituted 4-thiazolidones is described. Oxidation of several of the 4-thiazolidones to the corresponding 1-dioxides also is reported.

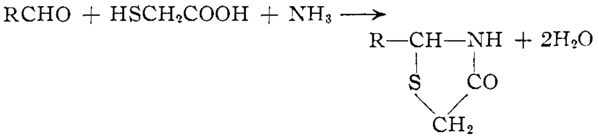
As part of our general investigation of the synthesis of 4-thiazolidones we have prepared a series of compounds unsubstituted in the 3-position (I).



I

The present communication deals mainly with the formation of some 2-(halophenyl) derivatives (I, R = XC_6H_4, $X_2C_6H_3$; R' = H or CH_3) which were then oxidized to the corresponding 1-dioxides. The latter have been found to possess significant amebacidal activity (*Endamoeba criceti*) when tested in hamsters.[2]

Our general procedure for the synthesis of the 2-substituted 4-thiazolidones consisted of heating a mixture of the appropriate aldehyde or ketone with thioglycolic acid and ammonia or an ammonium salt such as ammonium acetate or carbonate. For the most part the best results were obtained using benzene as the solvent with ammonium carbonate as the source of ammonia, and removing the water as it was formed. The use of ammonia itself rather than one of its salts, usually gave poorer yields.



Usually the reaction mixture was heated until the theoretical amount of water was collected. In most cases the time required ranged from one to eight hours. However, with 4-chlorobenzaldehyde and α-thiobutyric acid the calculated amount of water was collected in 30 minutes and a 76% yield of the 2,5-disubstituted derivative, 2-(4-chlorophenyl)-5-ethyl-4-thiazolidone was obtained. In contrast, in the condensation of the ketone, 4-chloroacetophenone, with thioglycolic acid and ammonium carbonate, the yield of 2-(4-chlorophenyl)-2-methyl-4-thiazolidone was 30% after heating for 56 hours. The use of dioxane as the solvent in the present condensations appears to be most effective with benzaldehydes having electropositive substituents on the ring. For example, with 4-acetamidobenzaldehyde, a 69% yield of the corresponding thiazolidone was obtained after heating the mixture on a steam-bath for 24 hours.

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[1] For the previous paper in this series see: A. R. Surrey, THIS JOURNAL, **74**, 3450 (1952).

[2] We are indebted to Dr. D. A. Berberian for the chemotherapeutic testing.