[(hexahydro-4-indol-3-yl-1-methyl-2-oxo-3-azepinyl)carbonyl]indole, mp 266–269°. The analytical sample, mp 269–270°, was prepared by recrystallizing some of this material from methanol–ethyl acetate. The ultraviolet spectrum had end absorption, λ_{max} 221, 241, 283, and 291 mμ (ε 43,500, 25,750, 10,410, and 11,480, respectively) with inflections at 263, 269, and 299 mμ (ε 13,200, 12,300, and 8350, respectively). The infrared spectrum showed NH 3410 and C=O 1720, 1640, and 1630 cm^{-1}.

Anal. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.78; H, 6.01; N, 10.90. Found: C, 74.63; H, 5.85; N, 11.11.

The third compound eluted from the column was crystallized from methanol–ethyl acetate to give 41.8 g (13.3%) of *trans*-3-carboethoxy-4-indol-3-yl-1-methylhexahydroazepin-2-one, mp 198–202°. The analytical sample, mp 196.5–198°, was prepared by recrystallizing some of this material from methanol–ethyl acetate. The ultraviolet spectrum had λ_{max} 220, 281.5, and 290 mμ (ε 35,750, 5950, and 5150, respectively) with an inflection at 275 mμ (ε 5550). The infrared spectrum showed NH 3290 and C=O 1740 and 1627 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 68.36; H, 7.13; N, 8.98.

Hydrolysis of *trans*-1-[(Hexahydro-4-indol-3-yl-1-methyl-2-oxo-3-azepinyl)carbonyl]indole (3).—A mixture of *trans*-1-[(hexahydro-4-indol-3-yl-1-methyl-2-oxo-3-azepinyl)carbonyl]indole (1.00 g, 2.60 mmoles), 8% aqueous sodium hydroxide (15 ml), and ethanol (15 ml) was refluxed for 2 hr, cooled in an ice bath, diluted with water, and extracted with ether. The ether extract was washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. A benzene solution of the residue was filtered through a little alumina and the filtrate was crystallized from benzene–Skellysolve B to give 0.187 g of indole, mp 52–53°. The infrared spectrum (chloroform) of this material was identical with that of authentic indole.

The combined aqueous layers from the above extraction were cooled in an ice bath and acidified with hydrochloric acid. The resulting solid was collected by filtration, washed with water, and dried to give 0.474 g of crude acid. This was heated in an evacuated (18 mm) flask at 172–177° for 1 min. An ethyl acetate solution of the cooled product was decolorized with Darco G-60 and crystallized to give 0.330 g (52.4%) of 4-indol-3-yl-1-methylhexahydroazepin-2-one, mp and mmp 149–150.5°, with **4** prepared as below.

Ethanolysis of *trans*-1-[(Hexahydro-4-indol-3-yl-1-methyl-2-oxo-3-azepinyl)carbonyl]indole (3).—*trans*-1-[(Hexahydro-4-indol-3-yl-1-methyl-2-oxo-3-azepinyl)carbonyl]indole (1.00 g, 2.60 mmoles) was added to a solution of sodium (64 mg) in dry ethanol (50 ml) and the resulting mixture was refluxed under nitrogen for 6 hr and allowed to stand at ambient temperature for 18 hr. It was then poured into ice water. The crystalline product was collected by filtration, washed with water, dried, and crystallized from methanol to give 0.511 g of **2**, mp and mmp 200–201.5°, and 0.047 g of **2**, mp 199.5–200.5°.

4-Indol-3-yl-1-methylhexahydroazepin-2-one (4). A.—A solution of 1.00 g (3.18 mmoles) of *trans*-3-carbethoxy-4-indol-3-yl-1-methylhexahydroazepin-2-one in 50 ml of warm, absolute ethanol was treated with 7.33 ml of 0.433 *N* aqueous potassium hydroxide and refluxed, under nitrogen, for 7 hr. The mixture was concentrated under reduced pressure and the residue was suspended in water and filtered. The solid obtained in this manner was washed with water and dried *in vacuo* to yield 64 mg of starting material, mp 187–189°. The aqueous filtrate was cooled in an ice bath and acidified with concentrated hydrochloric acid. The solid which precipitated was collected by filtration, washed with water, and dried *in vacuo* to yield 753 mg (82.9%) of the acid, mp 151.5–154° dec. This material was insoluble in most organic solvents and was therefore not characterized. The infrared spectrum showed NH 3346 and C=O 1714 and 1589 cm^{-1}.

B.—The acid (0.589 g, 2.05 mmoles) was heated in a small evacuated (14 mm) flask at 178° for 5 min. Decarboxylation occurred rapidly as the compound melted. The cooled, colorless glass that resulted was dissolved in ethyl acetate and crystallized to yield 443 mg (89.5%) of 4-indol-3-yl-1-methylhexahydroazepin-1-one, mp 147–149°. An analytical sample, mp 148–150°, was prepared by recrystallizing this material three times from ethyl acetate. The ultraviolet spectrum had λ_{max} 221.5, 281.5, and 290 mμ (ε 38,300, 6000, and 5250, respectively) with an inflection at 275 mμ (ε 5550). The infrared spectrum showed NH 3240 and C=O 1625 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.34; H, 7.37; N, 11.22.

4-Indol-3-yl-1-methylhexahydroazepine (5).—4-Indol-3-yl-1-methylhexahydroazepin-2-one (6.0 g, 24.7 mmoles) was added, under nitrogen, to an ice-cold stirred suspension of 6.0 g of lithium aluminum hydride in 600 ml of dry tetrahydrofuran and the resulting mixture was refluxed for 6.7 hr and allowed to stand at room temperature for 18 hr. It was then cooled in an ice bath and treated successively with 6 ml of water, 6 ml of 15% aqueous sodium hydroxide, and 18 ml of water. The inorganic salts were collected by vacuum filtration and washed with ether. Concentration of the combined filtrates yielded a colorless oil which was dissolved in ether, filtered, and crystallized from ether–Skellysolve B to yield 5.07 g, mp 81–85° (89.8%), of 4-indol-3-yl-1-methylhexahydroazepine. The analytical sample, mp 81–85°, was prepared by recrystallizing a portion of this material twice from ether–Skellysolve B. The ultraviolet spectrum had λ_{max} 222, 282, and 292 mμ (ε 35,200, 5850, and 5100, respectively) with an inflection at 275 mμ (ε 5400).

Anal. Calcd for $C_{15}H_{20}N_2$: C, 78.90; H, 8.83; N, 12.27. Found: C, 78.78; H, 9.10; N, 11.91.

Registry No.—**2**, 14319-54-1; **3**, 14319-55-2; **4**, 14255-42-6; **5**, 14255-43-7.

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A Convenient Synthesis of 5-Iodoindole

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Our interest in 5-iodo-DL-tryptophan led us to investigate various routes to a key intermediate in its synthesis, 5-iodoindole (**1b**).

One method of preparation of **1b** began with the nitration[1,2] of *m*-toluidine to form 5-amino-2-nitrotoluene[3] by diazotization. Treatment of the iodo compound with ethyl oxalate by the Reissert method,[4] followed by reductive cyclization of the intermediate pyruvate with alkaline ferrous hydroxide, gave 5-iodoindole-2-carboxylic acid. Decarboxylation of the acid in quinoline with copper chromite catalyst then gave 5-iodoindole (**1b**).[5,6] Although the preparation of **1b** by this method was successful, the yield was low (4%) and the procedure was laborious.

Accordingly, we hoped to make use of a facile method of preparing 5- and 7-substituted indoles published recently by Thesing, Semler, and Mohr.[7] This method involved treatment of indole with sodium hydrogen sulfite to yield indoline-2-sulfonic acid sodium salt, which on acetylation gave N-acetylindoline-2-sulfonic acid sodium salt. Treatment of this compound with

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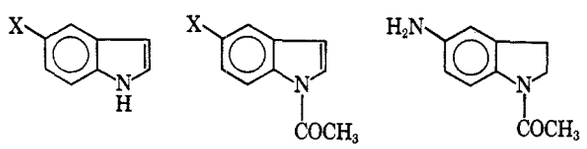
(6) H. N. Rydon and J. C. Tweddle, *ibid.*, 3499 (1955); F. L. Allen, J. C. Brunton, and H. Suschitzky, *ibid.*, 1283 (1955).

(7) D. Thesing, G. Semler, and G. Mohr, *Chem. Ber.*, **95**, 2205 (1962); British Patent 919,864 (1963); German Patent 1,123,668 (1962).

iodine monochloride should have provided 5-iodoindole, but in our hands it regenerated indole.

Attempted conversion of 5-aminoindole[8] to **1b** *via* a Sandmeyer reaction gave a tar from which no 5-iodoindole could be isolated. Consequently, 5-nitroindole (**1a**)[8] was acetylated to give N-acetyl-5-nitroindole (**2a**).[9] Catalytic reduction of the nitro group of **2a** using a 5% palladium on barium sulfate catalyst at 10 psig of hydrogen gave N-acetyl-5-aminoindole (**2b**) along with a small amount of N-acetyl-5-aminoindoline (**3**). (Catalytic reduction of **2a** with 5% palladium on carbon catalyst at 35 psig of hydrogen gave predominantly **3**.) Treatment of **2b** in hydrochloric acid with sodium nitrite and potassium iodide gave N-acetyl-5-iodoindole (**2c**), which on hydrolysis of the acetate function with Claisen's caustic then produced 5-indoindole (**1b**) by a relatively simple series of chemical steps in about 20% over-all yield.



1a, X = NO_2
b, X = I

2a, X = NO_2
b, X = NH_2
c, X = I

3

Experimental Section[10]

N-Acetyl-5-nitroindole (**2a**).—A mixture of 50 g (0.31 mole) of 5-nitroindole, 40 g of potassium acetate, and 300 ml of acetic anhydride was heated under nitrogen for 2 hr at 95°. After cooling to 5°, the mixture was filtered, the cake was washed with 30 ml of acetic anhydride, and reslurried in 200 ml of water at 55° for 5 min. Filtration and drying at 55° for 20 hr gave 53.6 g (85%) of yellow **2a**: mp 178–180° (lit.[10] mp 179.5–180°); λ_{max}^{Nujol} 5.85 μ; λ_{max}^{MeOH} 297 mμ (ε 9000), sh, 275 (12,750), 263 (23,300) 254 (23,000).

Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.8; H, 3.94; N, 13.7. Found: C, 59.0; H, 4.21; N, 13.5.

N-Acetyl-5-aminoindole (**2b**).—A mixture of 55 g (0.27 mole) of N-acetyl-5-nitroindole (**2a**), 5.5 g of 5% palladium on barium sulfate catalyst, and 1400 ml of absolute ethanol was hydrogenated at 10 psig for 1 hr. The mixture was filtered and the catalyst cake was washed with 50 ml of absolute ethanol. Concentration of the ethanol solution to about 200 ml and cooling gave 42 g (89%) of **2b**: mp 126–128°; λ_{max}^{Nujol} 2.93, 3.0, 5.94 μ; λ_{max}^{MeOH} 259 mμ (ε 20,000).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 69.0; H, 5.79; N, 16.1. Found: C, 68.8; H, 5.89; N, 16.0.

N-Acetyl-5-iodoindole (**2c**).—A mixture of 42 g (0.24 mole) of N-acetyl-5-aminoindole (**2b**), 62.4 ml of concentrated hydrochloric acid, and 124.8 ml of water at −5° was treated dropwise with a solution of 17.4 g of sodium nitrite in 36 ml of water to a positive starch–iodide test. Then a solution of 42 g of potassium iodide in 42 ml of water was added at −5°, after which the mixture was allowed to warm slowly to room temperature. The orange mixture was heated to 40°, treated with 500 ml of water and 500 ml of chloroform, and the phases were allowed to separate. The chloroform phase was washed with 500 ml each of water, 5% sodium bisulfite, 0.1 *N* hydrochloric acid, 5% sodium bicarbonate, and water in the order given. Concentration of the chloroform solution gave a 50 g residue. This was taken up in 150 ml of benzene and diluted with 150 ml of hexane to separate a tar. Further dilution with 300 ml of hexane effected complete tar removal. Concentration of the hexane solution then gave 39 g (57%) of **2c**: mp 106–107°; λ_{max}^{Nujol} 5.87 μ; λ_{max}^{MeOH} 246 mμ (ε 30,100).

Anal. Calcd for $C_{10}H_8INO$: C, 42.2; H, 2.83; N, 4.92. Found: C, 42.5; H, 3.00; I, 42.4; N, 4.58.

5-Iodoindole (**1b**).—A solution of 39 g (0.137 mole) of N-acetyl-5-iodoindole in 400 ml of Claisen's caustic (prepared by diluting a solution of 141 g of potassium hydroxide in 101 ml of water to 400 ml with methanol) was heated at 75–80° for 30 min. After cooling, the solution was diluted with 1000 ml of water and extracted with 1000-ml and 200 portions of benzene. The combined benzene extracts were washed with 500 ml each of water, 1% sodium bisulfite, 5% sodium bicarbonate, and water in the order given. The benzene solution was concentrated to about 40 ml, then diluted with 320 ml of hexane to effect separation of an oil. Decantation of the hexane solution from the oil and concentration gave 16 g (48%) of the typical silvery plates of **1b**: mp 99–102° (lit.[5] mp 99°); λ_{max}^{Nujol} 2.93, 6.40 μ; λ_{max}^{MeOH} sh 298 mμ (ε 3,210), 288 (5050), 80 (5500), 230 (44,000), 226 (46,300).

Anal. Calcd for C_8H_6IN: C, 39.5; H, 2.49; I, 52.3; N, 5.77. Found: C, 39.4; H, 2.74; I, 51.8; N, 5.70.

N-Acetyl-5-aminoindoline (**3**).—A mixture of 1.0 g (0.0049 mole) of N-acetyl-5-nitroindole (**2a**), 0.5 g of 5% palladium on carbon catalyst, and 100 ml of absolute ethanol was hydrogenated at 35 psig for 1 hr. The mixture was filtered and the catalyst cake was washed with 10 ml of absolute ethanol. Concentration of the ethanol solution gave 0.8 g (93%) of white **3**: mp 181–183°; λ_{max}^{Nujol} 6.10.

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.2; H, 6.87; N, 15.9. Found: C, 67.9; H, 6.69; N, 16.1.

(8) Available from Aldrich Chemical Co.

(9) W. E. Noland and K. R. Rush, *J. Org. Chem.*, **31**, 70 (1966).

(10) All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are corrected. The infrared and ultraviolet spectra were obtained using Perkin-Elmer 621 and Cary 15 spectrophotometers. Microanalyses were determined by the Microanalytical Laboratory of the Squibb Institute for Medical Research.

The Formation and Structure of Certain Oxazolonium Compounds

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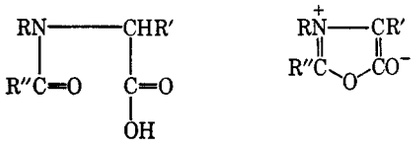
Huisgen and his co-workers[2] reported that N-substituted N-acylamino acids (**1**) readily lose a molecule of water when treated with acetic anhydride at 55° to give anhydro compounds **2**. They isolated only one compound, namely, anhydro-3-methyl-2,4-diphenyl-5-hydroxy-1,3-oxazolonium hydroxide (**2a**).



1a, R = CH_3; R′ = R″ = C_6H_5
b, R = R″ = CH_3; R′ = H
c, R = C_6H_5; R″ = CH_3; R′ = H
d, R = R″ = C_6H_5; R′ = H
e, R = CH_3; R″ = C_6H_5; R′ = H

2a, R = CH_3; R′ = R″ = C_6H_5
b, R = R″ = CH_3; R′ = $COCF_3$
c, R = C_6H_5; R″ = CH_3; R′ = $COCF_3$
d, R = R″ = C_6H_5; R′ = $COCF_3$
e, R = CH_3; R″ = C_6H_5; R′ = $COCF_3$

A short time after Huisgen's publications, we initiated a program to prepare and isolate additional derivatives of **2**, but with R′ = H, by dehydrative cyclization of

(1) To whom all inquiries should be addressed.

(2) (a) R. Huisgen, H. Gotthardt, and H. O. Bayer, *Tetrahedron Letters*, 481 (1964); (b) H. Gotthardt, R. Huisgen, and F. C. Schaeffer, *ibid.*, 487 (1964); (c) R. Huisgen, H. Gotthardt, and H. O. Bayer, *Angew. Chem. Intern. Ed. Engl.*, **3**, 135 (1964); (d) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Schaeffer, *ibid.*, **3**, 136 (1964).