solution was evaporated under vacuum, benzene was added to the residue and the solution taken to dryness once again. Sublimation of the residue gave 225 mg of crystalline **3c**: mp 162–163° (lit.[3] mp 163–164°,[3] 161–162° [4]); ir (CCl_4) C=O 5.79 μ (s).

Anal. Calcd for $C_7H_3ONSCl_2$: C, 38.20; H, 1.37; Cl, 32.11. Found: C, 38.02; H, 1.47; Cl, 32.06.

Thioanhydride 3d.—Exposure of the benzene solution of **3c** to atmospheric moisture some time prior to the above work-up gave **3d**: mp 92–93°; ir (CCl_4) C=O 5.81 μ (s); pmr ($CDCl_3$) δ 7.84, 9.09 (d, 1, J = 8.0 cps, pyridyl Hs), and 9.25 [s, 1, C_2–H]; (mass) mol wt, 165.

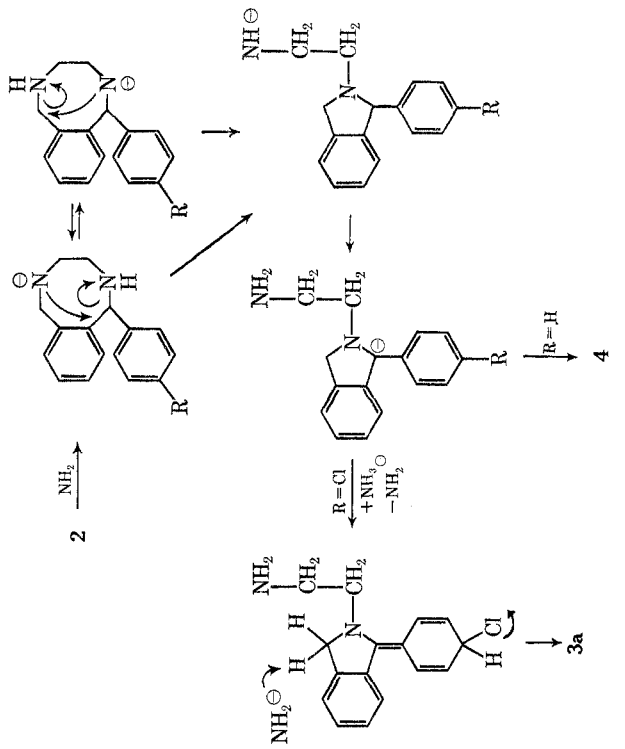
Anal. Calcd for $C_7H_3O_2NS$: C, 50.90; H, 1.83. Found: C, 50.84; H, 2.00.

A mixture of 3 g of cinchomeronic acid (**4b**) and 5 ml of thionyl chloride in 25 ml of benzene was refluxed for 1 hr. The solution was evaporated to dryness and the dark residue taken up in 15 ml of pyridine under cooling in an ice bath. A slow stream of hydrogen sulfide was passed through the solution over a period of 2 hr. The solvent was evaporated under vacuum and the residue shaken with a mixture of benzene and sodium bicarbonate solutions. The organic extract was evaporated and the residue crystallized from cyclohexane. Sublimation of the product, 1 g, yielded **3d**: mp, mmp 92–93°; spectra identical with those above.

Registry No.—**1c**, 18181-21-0; **2**, 18181-22-1; **3b**, 18181-23-2; **3d**, 18181-24-3.

Acknowledgment.—Support of this work by the U. S. Department of Health, Education and Welfare (Grant GM-11571) is acknowledged gratefully.

SCHEME II



Rearrangements of Benzodiazocines to Isoindoles and Isoindolines

M. WINN AND H. E. ZAUGG

Organic Chemistry Department, Research Division, Abbott Laboratories, North Chicago, Illinois

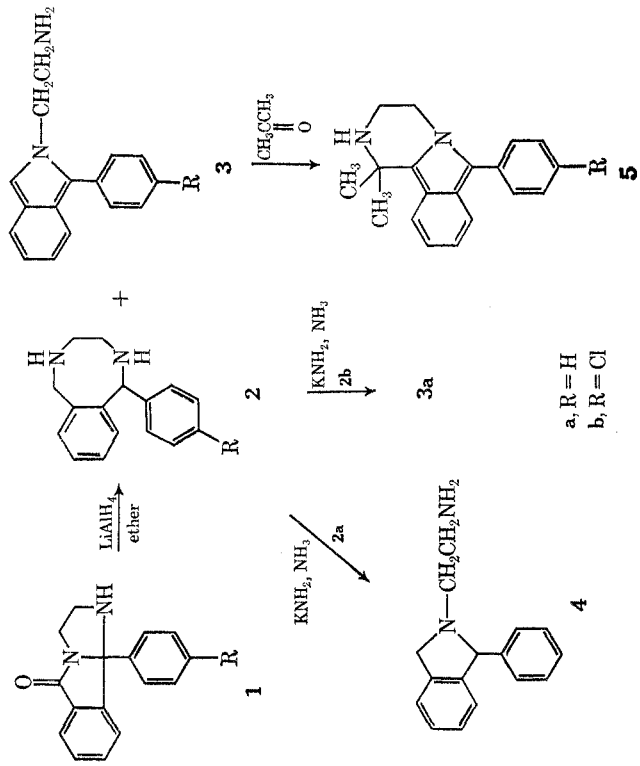
Received July 12, 1968

The syntheses of 2,5-benzodiazocines **2a** and **2b** have recently been reported.[1] In the course of studying the alkylation of **2a** in liquid ammonia containing potassium amide, we have discovered a novel ring contraction in which **2a** is converted into the known isoindoline **4**.[2] Surprisingly, when the chlorophenyl analog **2b** was treated with potassium amide in liquid ammonia, the chloro analog of **4** was not obtained, but dehydrochlorination occurred giving the isoindole **3a** in good yield (Scheme I). This is unusual in that the leaving group is on an aromatic ring.

It was also found that the isoindoles **3a** and **b** are byproducts in the synthesis of the 2,5-benzodiazocines themselves. These isoindoles could not be crystallized but underwent a novel reaction with acetone leading to the pyrazino[2,1-*a*]isoindoles **5a** and **b**, which were crystalline. They presumably arise through an attack of the electron-rich α position on the imine formed from acetone and the primary amine. The isoindole ring is so reactive that no catalyst was necessary. Merely dissolving **3** in excess acetone yields **5**.

The structure of **3a** was evident from its nmr spectrum and positive Ehrlich test[3] which indicates a

SCHEME I



(1) J. S. Sulkowski, M. A. Wille, A. Mascitti, and J. L. Diebold, *J. Org. Chem.*, **32**, 2180 (1967).

(2) W. Metlesics, T. Anton, and L. H. Sternbach, *ibid.*, **32**, 2185 (1967).

(3) D. F. Veber and W. Lwowski, *J. Amer. Chem. Soc.*, **86**, 4152 (1964).

highly reactive aromatic ring. The isoindole **3b** could only be obtained as a by-product in the synthesis of **2b**. It showed an nmr spectrum similar to **3a** but was contaminated with about 10% **2b**. When **3a** was prepared by the reduction of **1a** it too was contaminated with **2a**. However, both crude samples gave pure pyrazino[2,1-*a*]isoindoles (**5**) with acetone.

The structures of **5a** and **b** were evident from the nmr spectrum in that a one-proton singlet in the aromatic region was absent. Their ultraviolet spectrum was similar to that of 1-phenylisoindole[3] and their infrared spectra were consistent with an isoindole structure.[4] These rearrangements may be rationalized by the mechanism outlined in Scheme II (p. 249).

Experimental Section

Lithium Aluminum Hydride Reductions. 1-(*p*-Chlorophenyl)-2,2,3,4,5,6-hexahydro-2,5-benzodiazocine (2b) and 2-(2-Aminoethyl)-1-(*p*-chlorophenyl)isoindole (3b).—Reduction of **1b** (100 g) was carried out with lithium aluminum hydride in ether according to the literature procedure.[1] There was obtained 43.9 g of **2b**, mp 106–108°, and 7.0 g of solid, mp 95–105°. The mother liquors were then distilled to give 30.2 g (32%) of an oil, bp 185–190° (0.1 mm). The nmr spectrum indicated that this was mostly **3b** contaminated by about 10% of **2a**. It was used directly to prepare **5b**.

1-Phenyl-1,2,3,4,5,6-hexahydro-2,5-benzodiazocine (2a) and 2-(2-Aminoethyl)-1-phenylisoindole (3a).—The above procedure was repeated with **1a** and there was obtained 44.3 g of **2a**, mp 126–128°, and 25.5 g of crude **3a**, bp 145–150° (0.2 mm). It could not be crystallized and was used directly to prepare **5a**.

Potassium Amide Ring Contractions. 2-(2-Aminoethyl)-1,3-dihydro-1-phenylisoindole (4).—The benzodiazocine **2a** (30.0 g) was added to a 500-ml solution of potassium amide in liquid ammonia prepared from 12.0 g of potassium metal and 0.1 g of ferric nitrate. The red solution was stirred for 4 hr at reflux temperature, the ammonia was evaporated, and ether was added. The ether layer was distilled after drying to give 24.0 g (80%) of a liquid, bp 148–151° (0.2 mm), mp 47–51° (lit.[2] mp 53°); dihydrochloride mp 213–216° (*i*-PrOH), lit.[2] mp 215–220°). The nmr spectrum matched that given in the literature[2] and showed the absence of starting material.

2-(2-Aminoethyl)-1-phenylisoindole (3a).—The benzodiazocine **2b** (22.6 g) was treated with potassium amide in liquid ammonia as in the foregoing procedure. There was obtained 14.4 g (64%) of an oil, bp 180–185° (0.2 mm), which did not crystallize. It gave a positive Ehrlich test[3] (*p*-dimethylaminobenzaldehyde and acetic acid) and was converted into a tar with hydrochloric acid: nmr spectrum ($CDCl_3$), δ 0.86 (s, 2, NH_2), 3.49 (t, 2, J = 6 Hz, CH_2), 4.21 (t, 2, J = 6 Hz, CH_2), 6.8–7.1 (m, 2), 7.22 (s, 1), and 7.3–7.9 ppm (m, 7).

Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32, H, 6.82; N, 11.85. Found: C, 81.37; H, 6.70; N, 11.82; Cl, 0.00.

Cyclizations with Acetone. 1,1-Dimethyl-6-phenyl-1,2,3,4-tetrahydropyrazino[2,1-*a*]isoindole (5a).—2-(2-Aminoethyl)-1-phenylisoindole (6.20 g) was dissolved in 25 ml of acetone. Heat was evolved and crystals formed. The mixture was cooled and filtered to give 4.70 g (65%) of **5a**: mp 146–148°; nmr ($CDCl_3$), δ 1.52 (s, 1, NH), 1.85 (s, 6, $(CH_3)_2$), 3.15 (m, 2, CH_2), 4.11 (m, 2, CH_2), 6.8–7.1 (m, 2) and 7.3–7.9 ppm (m, 7); uv_{max} (dioxane) 365 mμ (log ϵ 3.59), 335 (3.44). The reported[3] ultraviolet maxima for 1-phenylisoindole are 357 mμ (log ϵ 3.10), 325 (2.99).

Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.64; H, 7.24; N, 10.12. Found: C, 82.70; H, 7.20; N, 10.05.

1,1-Dimethyl-6-(*p*-chlorophenyl)-1,2,3,4-tetrahydropyrazino-[2.1-*a*]isoindole (5b).—The crude chloro analog **3b** (6.70 g) was treated as above giving 5.10 g (66%) of **5b**, mp 169–173°. Spectral properties were similar to **5a**.

Anal. Calcd for $C_{19}H_{19}ClN_2$; C, 73.45; H, 6.12; N, 9.02. Found: C, 73.52; H, 6.22; N, 9.09.

(4) We are indebted to Dr. Lwowski for sending us examples of infrared spectra of isoindoles. Both his and our isoindoles showed broad bands of medium intensity at 1680 cm^{-1}.

Registry No.—**2a**, 3045-09-8; **2b**, 13827-78-6; **3a**, 18039-62-8; **3b**, 18039-63-9; **5a**, 18039-64-0; **5b**, 18039-65-1.

Acknowledgment.—The authors wish to thank Mr. Victor Rauschel for the microanalyses, Mrs. Ruth Stanaszek for the nmr spectroscopy, and Mrs. Brigitte Fruehwirth for the infrared spectroscopy.

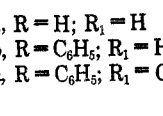
Nuclear Magnetic Resonance Spectra of Some 1,4-Thiazine 1,1-Dioxides and Their Anions

ISHAI SATATY

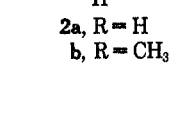
Department of Chemistry, Southern Illinois University, Carbondale, Illinois 62901

Received June 18, 1968

In contrast to extensive investigations of 1,4-benzothiazines, and particularly phenothiazines, very little work has been done on the simple derivatives of the 1,4-thiazine ring system. The parent compound of this series was described by Barkenbus and Landis.[1] In view of its failure to yield a sulfonamide by the Hinsberg method, it was assigned structure **1a**. Fujii[2] reported the synthesis of 3,5-diphenyl-1,4-thiazine by the condensation of phenacyl sulfide with ammonia. We have shown[3] that this derivative is correctly represented by structure **1b**, in conformity with the structure proposed for the parent compound. Cyclization of substituted β,β'-diketo sulfides with ammonia afforded analogous 1,4-thiazine derivatives, including compound **1c**.[4] By contrast, the condensation of phenacyl sulfone and its symmetrical dimethyl derivative with ammonia was reported to give thiazines **2a** and **2b**, respectively.[3,5] The change in position of the double bond with the state of oxidation of the sulfur has been proposed in view of the appearance of an N–H absorption band in the infrared spectrum of **2a**.[3] The structure assignments of **2a** and **2b** have now been confirmed and their anions have been studied by nmr.



1a, R = H; R_1 = H
b, R = C_6H_5; R_1 = H
c, R = C_6H_5; R_1 = CH_3



2a, R = H
b, R = CH_3

Measured in dimethyl sulfoxide-d_6, the nmr spectrum of **2a** showed a multiplet at δ 7.47–7.88 (aromatic protons) and a singlet at 6.36 (α-sulfonyl protons) in the ratio of 5:1. The downfield shift of the aromatic protons relative to benzene (which appears at δ 7.38 in DMSO-d_6) is probably due to the strong inductive effect

(1) C. Barkenbus and P. S. Landis, *J. Amer. Chem. Soc.*, **70**, 684 (1948).
(2) K. Fujii, *J. Pharm. Soc. Jap.*, **77**, 359 (1957).
(3) C. R. Johnson and I. Sataty, *J. Med. Chem.*, **10**, 501 (1967).
(4) D. Sica, C. Santacroce, and R. A. Nicolaus, *Gazz. Chim. Ital.*, **98**, 17 (1968).
(5) (a) V. Baliah and T. Rangarajan, *J. Org. Chem.*, **26**, 970 (1961); (b) G. Pagani and S. Maiorana, *Chim. Ind.* (Milan), **49**, 1194 (1967).