Anal. Calcd. for $C_{12}H_7O_6SCl$: C, 46.0; H, 2.23. Found: 46.1; H, 2.43.

The filtrate yielded a trace of the free sulfonic acid upon evaporation before a hot air fan.

B. 9-Methoxypsoralene (1.0 g., 0.0046 mole) was dissolved in 15 ml. chloroform and cooled in an ice bath. Chlorosulfonic acid (3 ml.) was added dropwise with stirring. After standing for 5 min. in the ice bath, the temperature was allowed to rise to 20°. The chloroform solution was then poured over 75 ml. ice. After the ice had melted, more chloroform was added; whereupon the layers separated. The aqueous layer was extracted once more with chloroform. The combined chloroform extracts were taken to dryness and yielded from 0.15 to 0.25 g., 10–16%, 9-methoxypsoralene-4-sulfonyl chloride. This product was identical as judged by mixed melting point with that described in procedure *A*.

The aqueous layer upon evaporation yielded 1.3 g., 89%, of the sulfonic acid. This product was crystallized from acetic acid and dried by an azeotropic distillation of a benzene suspension. The melting point was 205° dec.

Anal. Calcd. for $C_{12}H_8O_7S \cdot H_2O$: C, 46.1; H, 3.18. Found: C, 46.7; H, 3.30.

9-Methoxypsoralene-4-sulfonic acid (XII). 9-Methoxypsoralene-4-sulfonyl chloride (0.2 g.) was suspended in 25 ml. water and refluxed 45 min. The resulting solution was evaporated before a hot air fan yielding 0.17 g., 85%, of product after crystallization from acetic acid. This material was shown by infrared data to be identical with the sulfonic acid obtained by the direct sulfonation described above.

4-Bromo-9-methoxypsoralene (XIII). 9-Methoxypsoralene-4-sulfonic acid (0.25 g., 0.00079 mole) was suspended in 50 ml. chloroform, and 0.09 ml., (0.019 mole) of bromine was added. This mixture was heated on the steam bath with stirring until solution was effected and most of the chloroform had evaporated. Petroleum ether was then added to precipitate the product. The product was dissolved in 50 ml. acetone and treated with 0.5 g. sodium iodide for 4 hr. at room temperature to remove any tribromo-derivative which might have been formed[2]. The acetone solution was filtered and diluted with water. The insoluble product was collected and crystallized from ethanol; yield 0.15 g., 64%. A mixed melting point determination and infrared comparison indicated that this material was identical to 4-bromo-9-methoxypsoralene obtained by direct bromination.[2]

9-Methoxy-4-nitropsoralene (V). 9-Methoxypsoralene-4-sulfonic acid (0.25 g.) was dissolved in 10 ml. glacial acetic acid and 10 ml. concentrated nitric acid. The resulting solution was heated 5 min. on the steam bath. It was then poured onto 50 g. ice, and the insoluble product was collected and crystallized from ethanol; yield 0.15 g., 72%. A mixed melting point determination and a comparison of infrared spectra showed that this product was identical to 9-methoxy-4-nitropsoralene obtained by direct nitration.[2]

Acknowledgment. The authors wish to thank the Paul B. Elder Co. of Bryan, Ohio, whose generous contribution of xanthotoxin made this investigation possible.

CORVALLIS, ORE.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Chemistry of Ethylenimine. VI. Pyrolysis of 7-Acetyl-7-azaspiro[5.2]octane[1]

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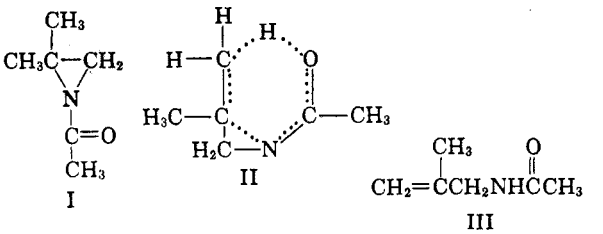
Received September 16, 1958

7-Acetyl-7-azaspiro[5.2]octane undergoes a pyrolytic rearrangement to give *N*-(1-cyclohexenylmethyl)acetamide. The structure of the latter compound was proven by hydrogenation, followed by hydrolysis to the known cyclohexanemethylamine. Hydrolysis of 7-azaspiro[5.2]octane in dilute sulfuric acid occurs with cleavage of the nitrogen–tertiary carbon bond.

In a previous paper in this series,[4] the pyrolytic rearrangement of 1-acetyl-2,2-dimethylethylenimine (I) to give *N*-(β-methallyl)acetamide (III) was described. Evidence was presented that the rearrangement occurs by an intramolecular mechanism similar to the Chugaev reaction, involving a cyclic transition state (II).

The present research was undertaken with the objective of further elucidating the structural and stereochemical requirements of this novel reaction. For this purpose, the structurally more rigid 7-azaspiro[5.2]octane system was investigated, as summarized in Fig. I.



I II III

7-Azaspiro[5.2]octane (V) was prepared from 1-aminocyclohexanemethanol (VIII) *via* the sulfate ester (IV) according to the conventional Wenker procedure.[5] The imine is a colorless liquid which was further characterized by the preparation of a crystalline *N*-phenylthiocarbamyl derivative.

(1) This research was aided by a grant from the Phillip Armour Foundation Cancer Fund and a grant from the American Cancer Society which provided a postdoctoral stipend for P.B.T.

(2) On study leave from the East India Pharmaceutical Works, Calcutta, India.

(3) To whom inquiries regarding this paper should be sent.

(4) P. E. Fanta and A. S. Deutsch, *J. Org. Chem.*, **23**, 72 (1958).

(5) J. S. Fruton in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 62.

When 7-acetyl-7-azaspiro[5.2]octane (VI), obtained by the treatment of the imine with ketene, was heated at atmospheric pressure, it was rapidly converted in high yield to *N*-(1-cyclohexenylmethyl)acetamide (VII). Catalytic hydrogenation of the unsaturated amide followed by hydrolysis of the product with hydrochloric acid gave cyclohexanemethylamine (XI), which was identified by the preparation of previously reported crystalline derivatives. In concentrated sulfuric acid at room temperature, the unsaturated amide VII was cyclized to the spiro-oxazoline, 8-methyl-7-oxa-9-azaspiro[5.4]-8-decene (X).

Further evidence for the structures of VI and VII was provided by the infrared absorption spectra. The spectrum of VII had a strong band characteristic of the NH bond at 3.03 mμ which was absent in the spectrum of VI.

A concerted mechanism of the Chugaev type is acceptable for this rearrangement, since the transition state (XII) is structurally similar to the well known cholesterol 5,6-oxides (XIIIa and b)[6] and therefore is not prohibitively strained.

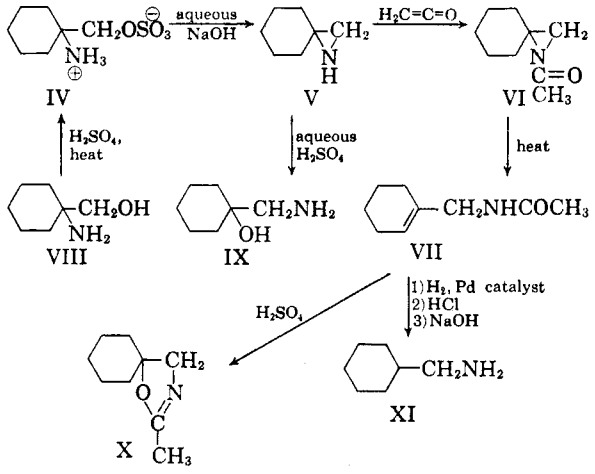
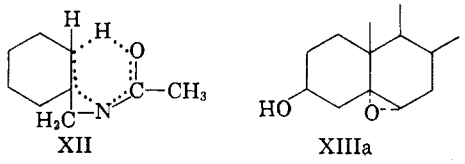
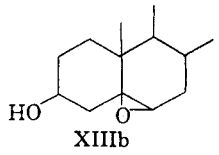


Fig. 1. Reactions in the 7-azaspiro[5.2]octane system





In view of the current interest in the application of conformational analysis to the reactions of cyclohexane derivatives, it is pertinent here to discuss the conformation of the transition state XII. The flattening of the cyclohexane ring in the spiro[5.2]octane system must be even less than in cyclohexanone,[7] therefore, the cyclohexane ring of XII may reasonably be expected to be in the chair form. The N and H atoms participating in the cyclic transition state are probably not *trans*, since this would require either an extremely strained bridging of adjacent axial substituents or the unfavorable elimination of equatorial substituents on adjacent carbon atoms. A study of the models of the two possible *cis*-conformations does not suggest which is preferred, since both conformations (axial N–equatorial H or equatorial N–axial H) would result in *cis*-elimination in accord with the well developed generalizations on the course of the Chugaev and related elimination reactions.[8]

Incidental to the main objective of this research, it was observed that hydrolysis of 7-azaspiro[5.2]-octane with dilute sulfuric acid gave 1-(aminomethyl)cyclohexanol (IX), which was isolated in the form of the crystalline *N*-phenylthiocarbamyl derivative. Under the conditions employed in the experiment, reaction was incomplete, and unreacted imine was recovered also in the form of the *N*-phenylthiocarbamyl derivative. The opening of the imine ring therefore occurred with cleavage of the nitrogen–tertiary carbon bond, as expected from the previous literature on the hydrolysis of unsymmetrical imines.[9]

EXPERIMENTAL[10]

1-Aminocyclohexanemethanol (VIII) was prepared as previously described,[11] b.p. 115–117°/25 mm., n_D^{25} 1.4963 (lit. b.p. 84°/1 mm., n_D^{25} 1.4959). Reaction of the amino alcohol with phenyl isothiocyanate gave the *N-phenylthiocarbamyl derivative*, white needles from aqueous alcohol, m.p. 141.6°.

Anal. Calcd. for $C_{14}H_{20}N_2OS$: C, 63.60; H, 7.63; N, 10.60. Found: C, 63.81; H, 7.77; N, 10.57.

1-Aminocyclohexanemethyl hydrogen sulfate (IV). A cold solution of 1.04 g. of concentrated sulfuric acid in 6 ml. of water was cautiously added to 1.29 g. of the amino alcohol, and water was slowly removed from the solution by heating it first at atmospheric pressure and finally for 15 min. at 160–170°/20 mm. A solution of the brown, solid residue in the minimum of water was treated with charcoal, filtered, and diluted with an equal volume of ethanol, giving 1.35 g. (65%) of tan solid, m.p. 256–257° dec. (uncorr.). Recrystallization from 95% ethanol gave white needles, m.p. 258–259° dec. (uncorr.).

(6) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold, New York, 1949, p. 222.

(7) W. G. Dauben and K. S. Pitzer in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, 1956, p. 39.

(8) The structural requirements for *cis* and *trans* Chugaev reactions have been discussed recently by F. G. Bordwell and P. S. Landis, *J. Am. Chem. Soc.*, **80**, 2450 (1958).

(9) V. B. Schatz and L. B. Clapp, *J. Am. Chem. Soc.*, **77**, 5113 (1955).

(10) Unless otherwise stated, melting points are corrected and boiling points are uncorrected. Analyses are by Micro-Tech Laboratories, Skokie, Ill. Infrared absorption spectra were determined in carbon tetrachloride solution between sodium chloride plates, using the Perkin-Elmer Infracord spectrophotometer.

(11) W. E. Noland, J. I. Kneller, and D. E. Rice, *J. Org. Chem.*, **22**, 695 (1957).

Anal. Calcd. for $C_7H_{15}NO_4S$: C, 40.17; H, 7.22; N, 6.69. Found: C, 40.05; H, 7.25; N, 6.60.

7-Azaspiro[5.2]octane (V).[12] A solution of sodium hydroxide (24 g.) in 30 ml. of water was added to 12 g. of the sulfate ester IV and the mixture was distilled with a small flame until the residue was nearly dry. The distillate was collected in an ice-cooled receiver containing ether and sodium hydroxide pellets. The ether solution was separated and the aqueous solution was extracted with 3 × 15 ml. portions of ether. The combined ether extracts after drying over sodium hydroxide pellets and distillation of the ether gave a pale yellow oil. Distillation of the crude product from a piece of metallic sodium gave 4.25 g. (66%) of a colorless oil with a characteristic sharp odor, b.p. 158–159°; n_D^{20} 1.4740, λ_{max} 3.07 μ (N—H band).

Anal. Calcd. for $C_7H_{13}N$: C, 75.62; H, 11.78. Found: C, 75.42; H, 11.96.

Reaction of the imine with phenyl isothiocyanate gave the *N-phenylthiocarbamyl derivative*, white lustrous plates from acetone-ligroin (30–60°) m.p. 104.7°.

Anal. Calcd. for $C_{14}H_{18}N_2S$: C, 68.25; H, 7.36; N, 11.37. Found: C, 68.36; H, 7.47; N, 11.47.

7-Acetyl-7-azaspiro[5.2]octane (VI). An excess of ketene from a modified apparatus[4] was passed through a solution of 3.7 g. of the imine V in 25 ml. of ether at room temperature. Distillation of the light yellow solution gave 3.43 g. (68%) of colorless oil, b.p. 110–112°/15 mm., $n_D^{24.5}$ 1.4760. No N—H band in the infrared absorption spectrum.

Anal. Calcd. for $C_9H_{15}NO$: C, 70.54; H, 9.87; N, 9.14. Found: C, 70.04; H, 10.13; N, 9.27.

Further distillation of the residue from this preparation gave 700 mg. (14%) of a pale yellow liquid which was identified as the rearrangement product VII by determination of the infrared absorption spectrum.

Pyrolysis of VI to form N-(1-cyclohexenylmethyl)acetamide (VII). The acetyl imine VI (2.5 g.) was gradually heated in a Claisen flask provided with a thermometer immersed in the liquid. At about 155° an exothermic reaction occurred with a concomitant rise in temperature to 230°, where it remained for a few minutes. Further heating at 210° for 15 min., followed by a vacuum distillation yielded 2.26 g. (90%) of light yellow, viscous liquid, b.p. 166–168°/16 mm., n_D^{24} 1.5000, λ_{max} 3.03 μ (N—H band).

Anal. Calcd. for $C_9H_{15}NO$: C, 70.54; H, 9.87. Found: C, 70.14; H, 9.64.

Spiro-oxazoline, X. Concentrated sulfuric acid (5 ml.) was added slowly with cooling and swirling to 3 g. of the amide VII while the temperature was kept below 40°. After 10 min. at room temperature, crushed ice was added to the red solution, followed by an excess of sodium hydroxide. An oil separated which was extracted with 3 × 10 ml. portions of ether. The ether solution was dried over sodium hydroxide pellets and distilled, giving 1.7 g. (57%) of colorless, mobile oil, b.p. 88–89°/16 ml., $n_D^{24.5}$ 1.4690. No N—H band in the infrared.

Anal. Calcd. for $C_9H_{15}NO$: C, 70.54; H, 9.87. Found: C, 70.34; H, 9.89.

The oxazoline formed a *picrate*, yellow needles from ethyl acetate, m.p. 188.8°.

Anal. Calcd. for $C_{15}H_{18}N_4O_8$: C, 47.12; H, 4.75. Found: C, 47.19; H, 4.80.

Hydrogenation of VII *and hydrolysis of the resulting product to cyclohexanemethylamine* XI. A solution of 1.0 g. of VII in 20 ml. of absolute ethanol was subjected to hydrogenation at atmospheric pressure with the aid of 200 mg. of 10% palladized charcoal catalyst. In the course of 40 min., the calculated amount of hydrogen (165 ml.) was absorbed and further treatment caused no more uptake of hydrogen. After removal of the catalyst, distillation gave an almost quantitative yield of colorless oil, b.p. 165–166°/17 mm., $n_D^{24.5}$ 1.4800, which was refluxed for 4 hr. with 10 ml. of 6*N* hydrochloric acid. The solution was evaporated to dryness and the white, solid residue was washed with dry ether, dissolved in a small amount of water, and made weakly alkaline by the addition of aqueous sodium hydroxide. The aqueous solution was used for the preparation of two previously reported[13] solid derivatives of cyclohexanemethylamine: the *N*-benzoyl derivative, white needles from aqueous ethanol, m.p. 106.4° (lit. 105–106°) and the *N*-phenylthiocarbamyl derivative, white plates from acetone-ligroin (30–60°), m.p. 128.4–129.4° (lit. 128–129°).

1-(Aminomethyl)cyclohexanol (IX) was prepared as previously described[14] and further characterized by the formation of the picrate, m.p. 168–169° (lit. 168–170°). Treatment of the amino alcohol with phenyl isothiocyanate gave an authentic sample of the *N-phenylthiocarbamyl derivative*, m.p. 134.5–135°, from acetone-ligroin (30–60°).

Anal. Calcd. for $C_{14}N_{20}N_2OS$: C, 63.60; H, 7.62; N, 10.59. Found: C, 63.80; H, 7.77; N, 10.57.

Hydrolysis of 7-azaspiro[5.2]octane with aqueous sulfuric acid. A solution of 500 mg. of the imine V in 10 ml. of 1*M* sulfuric acid was heated on a steam bath for 2 hr. The solution was neutralized with dilute aqueous sodium hydroxide and extracted with chloroform. The chloroform extract was dried and evaporated and the residue was treated with phenyl isothiocyanate. The product obtained was twice recrystallized from acetone-ligroin and shown by m.p. (103–104°) and mixed m.p. to be the *N*-phenylthiocarbamyl derivative of the imine V.

The aqueous solution after the chloroform extraction was made weakly alkaline and shaken with a few drops of phenyl isothiocyanate for a few minutes. Extraction with chloroform followed by evaporation of the chloroform and recrystallization of the residue from aqueous alcohol gave a crystalline solid, m.p. 133.1–134.1°, undepressed on mixing with the authentic *N*-phenylthiocarbamyl derivative of amino alcohol IX.

CHICAGO 16, ILL.

(12) C. Schuster, German Patent **871,149** (Feb. 23, 1951) claimed the preparation of this imine, b.p. 53–55°/8 mm. in 25% yield by passing the amino alcohol VIII over hot alumina.

(13) R. A. Benkeser, C. Arnold, R. F. Lambert, and O. H. Thomas, *J. Am. Chem. Soc.*, **77**, 6042 (1955).

(14) H. J. Dauben, H. J. Ringold, R. H. Wade, and A. G. Anderson, *J. Am. Chem. Soc.*, **73**, 2359 (9151).