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

Chemistry of Ethylenimine. II. Ring-opening of 2,2-Dimethyl-1-(N-phenylthiocarbamyl)aziridine[1]

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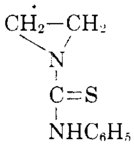
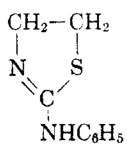
Treatment of 2,2-dimethyl-1-(N-phenylthiocarbamyl)aziridine (III) or N-(2-hydroxy-2-methylpropyl)-N′-phenylthiourea with hot, concentrated hydrochloric acid gives isobutyraldehyde, phenylthiourea, and 2-anilino-5,5-dimethyl-2-thiazoline. Reaction of III with anhydrous hydrogen chloride gives N-(2-chloro-2-methylpropyl)-N′-phenylthiourea. These reactions may be rationalized as occurring *via* a common carbonium ion intermediate.

With methanol, III gives products corresponding to both primary carbon- and tertiary carbon-nitrogen cleavage as shown by the isolation of 2-anilino-4,4-dimethyl-2-thiazoline (XIII) and N-(2-methoxy-2-methylpropyl)-N′-phenylthiourea. Authentic XIII was prepared by the cyclization of N-(1,1-dimethyl-2-hydroxyethyl)-N′-phenylthiourea.

The preparation of 1-(N-phenylthiocarbamyl)-aziridine (I) was described in one of the earliest papers in the field of ethylenimine chemistry by Gabriel and Stelzner,[3] who erroneously formulated the compound as N-phenyl-N′-vinylthiourea. They also reported that compound I was converted to 2-anilino-2-thiazoline (II) by heating with concentrated hydrochloric acid. In a repetition of their experiment, we found that this was a clean reaction which resulted in the formation of II in 90% yield. No aldehyde was formed in the reaction, and the same product was also obtained by heating N-(2-hydroxyethyl)-N′-phenylthiourea with concentrated hydrochloric acid.


I


II

An attempt to extend this reaction to 2,2-dimethyl-1-(N-phenylthiocarbamyl)azirdine (III) gave a much more complicated result. When III was heated for 1.5 hours with concentrated hydrochloric acid and the reaction mixture was distilled, a 47–52% yield of isobutyraldehyde (IV) was obtained in the distillate, and the residue was found to contain a 48% yield of phenylthiourea (V) and 30% yield of 2-anilino-5,5-dimethyl-2-thiazoline (VI).

Similar yields of the same products were obtained when N-(2-hydroxy-2-methylpropyl)-N′-phenylthiourea (VII) was heated with hydrochloric acid[4] in the same way as III.

Treatment of III with anhydrous hydrogen chloride in ether or with hot, concentrated hydrochloric acid for a short time gave N-(2-chloro-2-methylpropyl)-N′-phenylthiourea (VIII). The structure of VIII was demonstrated by prolonged treatment with concentrated hydrochloric acid, which gave the same mixture of products obtained from III or VII.

These observations may be rationalized in terms of the formation of the carbonium ion (X) as a common intermediate.[5] In the presence of chloride ion, X is converted reversibly to VIII, and on prolonged treatment with concentrated hydrochloric acid all of these compounds are unstable relative to IV, V, and VI. The latter product is an example of a highly acid-stable thiazoline,[6] since it remains unchanged on prolonged heating with concentrated hydrochloric acid. The formation of IV and V may be pictured as occurring *via* hydrolysis of XIb which is a tautomer of the vinylamine XIa formed by the loss of a proton from X without cyclization.

Prolonged refluxing of III in methanol in the absence of an acid catalyst gave products corresponding to cleavage of each of the carbon-nitrogen bonds in the ethylenimine ring. The product of the cleavage of the tertiary carbon-nitrogen bond was N-(2-methoxy-2-methylpropyl)-N′-phenylthiourea (IX), the structure of which was proved by heating with concentrated hydrochloric acid to give a mixture of IV, V, and VI. The occurrence of a cleavage between the primary carbon-nitrogen bond in the

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(2) Illinois Institute of Technology Graduate Research Fellow, 1955–1956. Inquiries regarding this article should be addressed to P. E. Fanta.

(3) Gabriel and Stelzner, *Ber.*, **28**, 2929 (1895).

(4) This reaction had previously been reported by Dersin, *Ber.*, **54**, 3158 (1921), who isolated 2-anilino-5,5-dimethyl-2-thiazoline but failed to note the formation of isobutyraldehyde and phenylthiourea.

(5) An S_N1 mechanism with an intermediate carbonium ion has been postulated for other reasons involving cleavage of the tertiary carbon-nitrogen bond of an ethylenimine ring; further references are given in footnote 7.

(6) Some acid-stable thiazolines have been discussed recently by Crawhall and Elliott, *J. Chem. Soc.*, 3094 (1952).

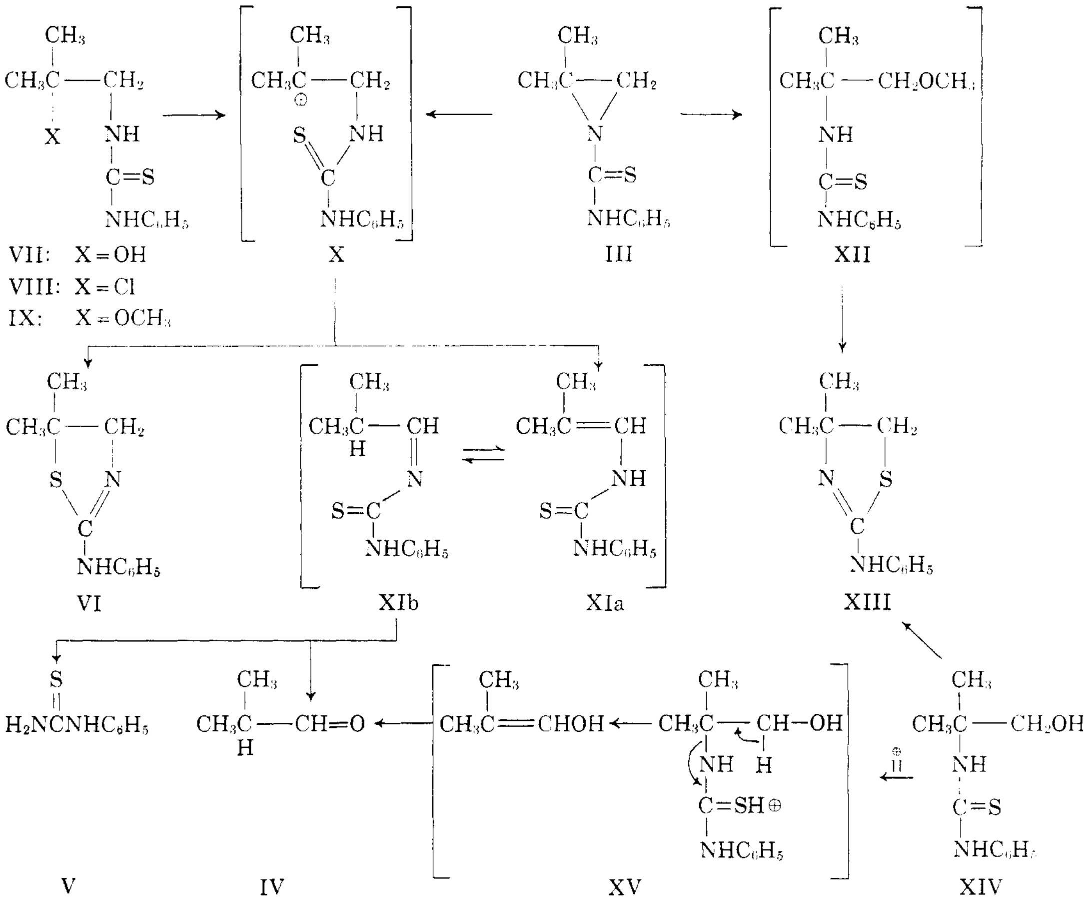

Fig. 1.—Hypothetical Intermediates Are in Brackets.

methanolysis of III was indicated by the isolation of a small amount of 2-anilino-4,4-dimethyl-2-thiazoline (XIII), which was presumably formed by way of some such intermediate as XII.

For the identification of XIII, an authentic sample was prepared by heating N-(1,1-dimethyl-2-hydroxyethyl)-N′-phenylthiourea with concentrated hydrochloric acid. In this reaction a small amount of isobutyraldehyde was also obtained, which may be pictured as arising from the reaction sequence in the bracket XV.

These data are in marked contrast to the results reported recently in a study of the hydrolysis of 2,2-dimethylethylenimine in hydrochloric acid,[7] where the product corresponding to primary carbon-nitrogen cleavage predominates. It is evident that substituents on the nitrogen atom have a profound effect on the mode of ethylenimine ring-opening reactions and further details of our investigations in this field will be presented in subsequent papers in this series.

EXPERIMENTAL[8]

1-(N-Phenylthiocarbamyl)aziridine (I). A solution of 2.6 g. (0.06 mole) of ethylenimine in 85 ml. of ether was stirred at 0° while 8.1 g. of phenyl phenyl isothiocyanate (one equivalent) was added. White crystals were formed which were allowed to stand for 15 minutes in the cold reaction mixture, and then were collected on a filter, washed with cold ether, and dried to give 7.6 g. (71%) of I, m.p. 74–77°. Two recrystallizations from ether raised the m.p. to 77–79°. The reported[3] m.p. is 80°.

2-Anilino-2-thiazoline (II). A solution of 1.025 g. (0.0575 mole) of compound I in 30 ml. of concentrated (12 *N*) hydrochloric acid was heated in a distilling flask for $1\frac{1}{2}$ hours. During this time approximately 10 ml. of distillate was collected, which gave a negative test for the presence of aldehyde with 2,4-dinitrophenylhydrazine reagent. Cooling and dilution of the residue with 25 ml. of water gave a turbid solution which was extracted with ether. The clear, aqueous solution was made basic by the addition of 10% aqueous sodium hydroxide, whereupon white crystals were formed which were extracted with ether. The ethereal solution was washed with water, dried over sodium sulfate, and evaporated, giving 931 mg. (91%) of crude, crystalline II, m.p. 145–155°. Systematic recrystallization from methanol gave a total of 772 mg. of pure II, m.p. 158–160° (literature[3] value, 160°).

N-(2-hydroxyethyl)-N′-phenylthiourea was prepared by the reaction of ethanolamine with phenyl isothiocyanate in the

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[7] Schatz and Clapp, *J. Am. Chem. Soc.*, **77**, 5113 (1955) report that 85–90% of 1-chloro-2-amino-2-methylpropane is obtained from the reaction of 2,2-dimethylethylenimine with 6 *N* hydrochloric acid at 25°, which is formulated as an S_N2 reaction.

[8] Melting points are corrected. Analyses are by Micro-Tech Laboratories, Skokie, Illinois.

usual manner.[9] The analytical sample was prepared by recrystallization from methanol, m.p. 137–138°.

Anal. Calc'd for $C_9H_{12}N_2SO$: C, 55.05; H, 6.16; N, 14.27. Found: C, 55.26; H, 6.11; N, 14.48.

When this compound was treated with concentrated hydrochloric acid in the same way as described for compound I, the distillate gave a negative test for aldehyde and a 90% yield of II was isolated from the residue.

2,2-Dimethyl-1-(N-phenylthiocarbamyl)aziridine (III). An equivalent amount (9.8 g.) of phenyl isothiocyanate was added to a solution of 5.14 g. (0.0725 mole) of 2,2-dimethylethylenimine in 85 ml. of ether at 0°. During the addition, white crystals were formed which were allowed to stand in the cold reaction mixture for 1$^1/_2$ hours, then were collected on a filter and washed with cold ether. The yield was 9.1 g. (61%), m.p. 91–92°.

Anal. Calc'd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84; N, 13.58. Found: C, 63.92; H, 6.91; N, 13.45.

Prolonged reaction of III *with hydrochloric acid.* A solution of 1.2 g. (0.0058 mole) of III in 35 ml. of 12 *N* hydrochloric acid in a small distilling flask was heated for 1$^1/_2$ hours. During the period of heating, approximately 10 ml. of distillate was collected in a solution of 780 mg. (0.0068 mole) of 2,4-dinitrophenylhydrazine in 1 liter of 2 *N* hydrochloric acid. The yellow solid which was formed was shown by melting point and mixture melting point with an authentic sample to be isobutyraldehyde 2,4-dinitrophenylhydrazone. The quantity corresponded to a 47–52% yield in two separate experiments.

The residue from the distillation was extracted with ether. The ether layer was washed with water, dried with sodium sulfate, and evaporated to yield 431 mg. of crude phenylthiourea, m.p. 140–145°. Systematic recrystallization from acetone gave 374 mg. of pure material, m.p. 153–154°. Mixture with an authentic sample of phenylthiourea[10] gave no depression of the melting point.

The combined acid residue and water washings from the preceding extraction were made basic by the addition of a 10% sodium hydroxide solution. White crystals were formed which were extracted with ether. The ether was washed with water, dried with sodium sulfate, and evaporated to yield 462 mg. of crude 2-anilino-5,5-dimethyl-2-thiazoline, VI. Systematic recrystallization from methanol gave 287 mg. of pure material, m.p. 153–154°. The previously reported[4] value is 153–154°.

By chromatography on alumina of the residues from the purification of VI, additional pure phenylthiourea (total 48%) was obtained in the 1:1 ligroin-benzene eluate and additional pure VI (total 30%) was obtained in the 20:1 benzene-ether eluate.

Prolonged reaction of VII *with hydrochloric acid.* Compound VII was prepared from 1-amino-2-methyl-2-propanol[11] and phenyl isothiocyanate as described by Dersin.[4] When treated with hydrochloric acid and worked up in the same way described for III, isobutyraldehyde was obtained in 57–58% yield, phenylthiourea in 48% yield, and VI in 31% yield.

Acid-stability of VI. A sample of VI was recovered unchanged after refluxing for three hours in 12 *N* hydrochloric acid.

Preparation of N-(2-chloro-2-methylpropyl)-N′-phenylthiourea, VIII. Hydrogen chloride gas was passed for 45 minutes at room temperature through a solution of 1.27 g. of III in anhydrous ether. The ether solution was washed with a 10% sodium hydroxide solution and water, dried with sodium sulfate, and evaporated to yield 300 mg. (20%) of nearly pure VIII, m.p. 124–127°. Three successive recrystallizations from acetone-ligroin gave an analytical sample, m.p. 130–131°.

Anal. Calc'd for $C_{11}H_{15}ClN_2S$: C. 54.41; H, 6.23; N, 11.54. Found: C, 54.67; H, 6.33; N, 11.35.

VIII was also obtained when a solution of 464 mg. of III in 20 ml. of 12 *N* hydrochloric acid was heated for eight minutes, cooled in an ice-bath, and extracted with ether. The ether extract was washed with a 10% sodium hydroxide solution and water, dried, and evaporated to yield 182 mg. of crude VIII, m.p. 113–118°. Three recrystallizations raised the m.p. to 130–131° and the infrared spectrum then was identical with the analytically pure sample.

A solution of 120 mg. of VIII in 8 ml. of 12 *N* hydrochloric acid was treated as described for III. The yield of isobutyraldehyde was 52%, phenylthiourea 52%, and VI 26%.

Reaction of III *with methanol.* A solution of 1.40 g. of III in 35 ml. of anhydrous methanol was refluxed for one week. After evaporation of the solvent, an oil remained which was taken up in ether and washed with three 25-ml. portions of 10% hydrochloric acid. The combined acid washings were reserved. The ethereal solution was washed with water, dried with sodium sulfate, and evaporated to yield 900 mg. of an oil. Crystallization from acetone-ligroin gave 518 mg. of crude N-(2-methoxy-2-methylpropyl)-N′-phenylthiourea, IX, m.p. 80–95°. Three recrystallizations from acetone-ligroin gave 118 mg. (7%) m.p. 113–115°. An analytical sample, prepared by an additional recrystallization, melted at 115–116°.

Anal. Calc'd for $C_{12}H_{18}N_2OS$: C, 60.47; H, 7.61; N, 11.75. Found: C, 60.66; H, 7.96; N, 11.50.

The acid washings mentioned above were made basic by the addition of a 15% sodium hydroxide solution. The turbid solution was extracted with ether, and the ether extract was washed with water, dried with sodium sulfate, and evaporated to give 400 mg. of an oil. Successive recrystallizations from methanol finally gave 12 mg. (1.5%) of nearly pure 2-anilino-4,4-dimethyl-2-thiazoline (XIII), m.p. 145–148°. One further recrystallization raised the melting point to 151–153°. This material was shown by mixture melting point and comparison of the infrared absorption spectrum to be identical with an authentic sample of XIII, and different from VI.

A solution of 96 mg. of IX in 8 ml. of 12 *N* hydrochloric acid was treated as described for III, and the products were shown to be isobutyraldehyde, phenylthiourea, and VI. The identity of the latter product was confirmed by mixture melting point and comparison of the infrared absorption spectrum.

N-(1,1-dimethyl-2-hydroxyethyl)-N′-phenylthiourea (XIV) was prepared from commercially available 2-amino-2-methyl-1-propanol by treatment with phenyl isothiocyanate in the usual manner.[9] Two recrystallizations from methanol gave an analytical sample, m.p. 127–128°.

Anal. Calc'd for $C_{11}H_{16}N_2OS$: C, 58.63; H, 7.60; N, 12.43. Found: C, 58.63; H, 7.24; N, 12.43.

Reaction of XIV *with hydrochloric acid.* A solution of 1.030 g. of XIV in 35 ml. of 12 *N* hydrochloric acid was heated for 1$^1/_4$ hours, while approximately 10 ml. of distillate was collected in 250 ml. of 2 *N* hydrochloric acid saturated with 2,4-dinitrophenylhydrazine. The yield of isobutyraldehyde 2,4-dinitrophenylhydrazone, whose identity was confirmed by mixture melting point, was 85 mg. (7%). The residue from the distillation was extracted with ether, then made basic, and extracted with fresh ether. Drying and evaporation of this second ether extract gave 147 mg. (44%) of crude 4,4-dimethyl-2-thiazoline, XIII, m.p. 147–150°. An analytical sample prepared by recrystallization from methanol melted at 156.5–157°.

Anal. Calc'd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.83; N, 13.58. Found: C, 63.74; H, 6.63; N, 13.58.

Infrared absorption spectra. The bands which were most

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[9] Shriner and Fuson, *The Systematic Identification of Organic Compounds*, 3rd Edition, John Wiley and Sons, Inc., New York, 1948, p. 179.

[10] Otterbacher and Whitmore, *J. Am. Chem. Soc.*, **51**, 1909 (1929).

[11] Cairns and Fletcher, *J. Am. Chem. Soc.*, **63**, 1035 (1941).

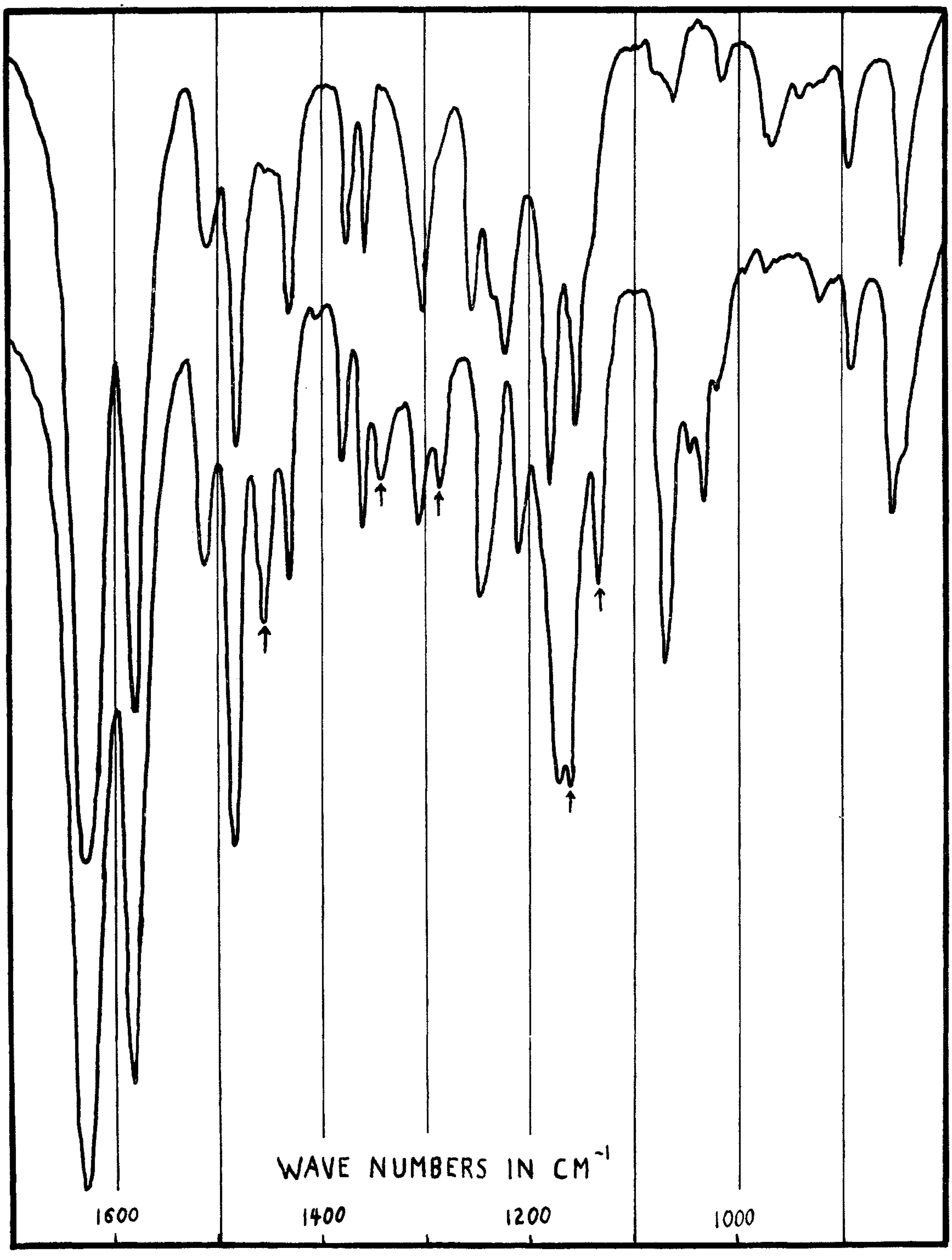

FIG. 2—INFRARED ABSORPTION SPECTRA OF 2-ANILINO-5,5-DIMETHYL-2-THIAZOLINE, VI (lower curve) AND 2-ANILINO-4,4-dimethyl-2-thiazoline, XIII (upper curve) in carbon tetrachloride solution.

useful for distinguishing the isomeric anilino-dimethylthiazolines VI and XIII are indicated by arrows in Fig. 2. The spectra were obtained with the Perkin-Elmer Model 21 Spectrophotometer using the sodium chloride optics.

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