to yield 8.2 g. (88%) of the sodium salt of triphenylgermanethiol (I), m.p. 185–195°. The melting point could not be improved by recrystallization.

Anal. Calcd. for $C_{18}H_{15}GeSNa$: Na, 6.45; Found: Na, 6.34.

Typical Reaction Conditions.—A solution of the RX compound (5.8 mmoles) in 10 ml. of benzene was added slowly to a solution of 2.0 g. (5.8 mmoles) of the sodium salt (I) and the mixture stirred for 3 hr. The white precipitate of sodium halide that formed during the reaction was filtered and washed with 2 ml. of benzene. The filtrate was evaporated in vacuum and the crude product recrystallized from hexane.

Reaction of I with Carbon Disulfide.—A 2.0-g. sample (5.8 mmoles) of I was dissolved in 50 ml. of carbon disulfide. The clear solution slowly formed an orange precipitate. After 10 days the mixture was filtered. The yield was 600 mg. The orange-colored compound turned red in moist air, was insoluble in benzene and soluble in water.

Evaporation of the filtrate and recrystallization from hexane yielded 1.3 g. of long, white needles, m.p. 138°, bis(triphenylgermanium) sulfide identified by infrared spectra and mixed melting point using a known sample.

The orange compound (250 mg.) was refluxed with 0.2 ml. of methyl iodide in 30 ml. of benzene for 5 hr. during which time the benzene solution became yellow and a precipitate (400 mg.) of sodium iodide formed. The benzene was evaporated leaving a strong smelling, yellow oil (150 mg.). The mass spectral pattern indicates a molecular weight of 136. This information together with the infrared spectrum tentatively suggests this compound to be dimethyl trithiocarbonate.

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The Reaction between 2-Nitro-1-phenylpropene and Cyclohexanone

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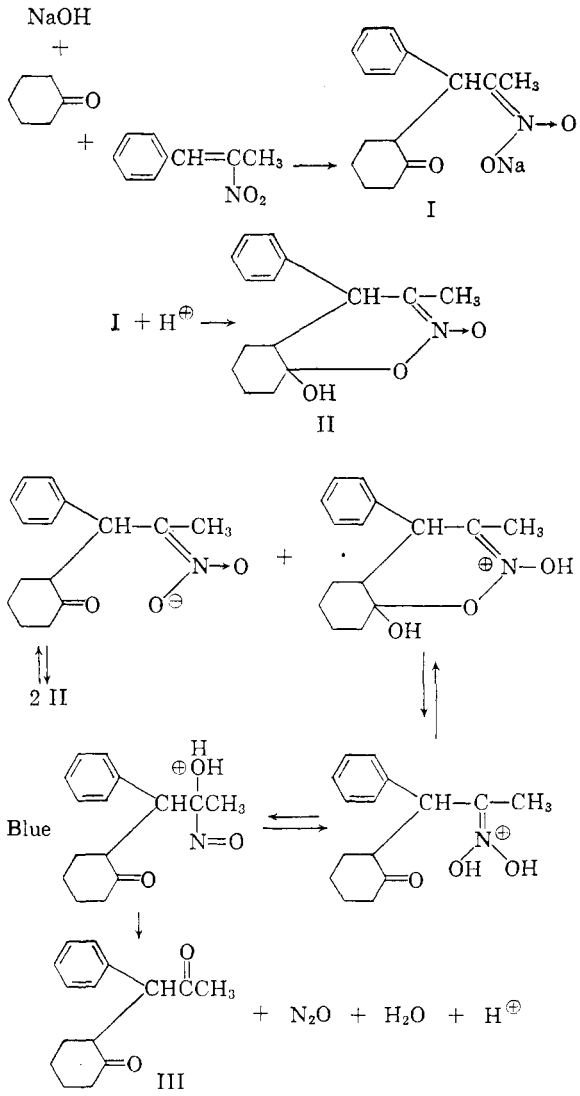
In an attempt to prepare a nitro ketone desired for synthetic work an aqueous solution of one equivalent of sodium hydroxide was added to a solution of one equivalent of 2-nitro-1-phenylpropene in excess cyclohexanone. Upon stirring, a sharp temperature rise occurred and the mixture became one phase. Addition to methanol containing an excess of acetic acid led to a crystalline precipitate which has an analysis corresponding to the expected nitro ketone, but which is now believed to be the cyclic condensation product II.

Compound II melts with decomposition, is only slightly soluble in organic solvents or water, but dissolves readily in aqueous sodium hydroxide. The infrared spectrum is complex, but strong bands are absent from the regions around 1700 cm.$^{-1}$, 1540 cm.$^{-1}$, and 1350 cm.$^{-1}$ where intense bands would be expected from a nitro ketone. Of interest are strong bands at 1615 cm.$^{-1}$ and 3145 cm.$^{-1}$, which we interpret as evidence for a ring C=N,[1] and a hydroxyl group, respectively.

Refluxing II in methanol leads to the development of a blue color, the evolution of nitrous oxide, and finally, to the formation of a crystalline product containing no nitrogen, showing strong carbonyl absorption, and giving the correct analysis for the 1,4-diketone III. Further evidence for the 1,4-diketone structure is the reaction of III with aniline which gives a compound having a nitrogen analysis corresponding to the expected 4,5,6,7-tetrahydroindole.

On dissolving compound II in aqueous sodium hydroxide and adding this solution to a large excess of acetone a crystalline sodium salt forms (as a hexahydrate) which shows strong absorption in the carbonyl region of the infrared spectrum. Reaction of this sodium salt with bromine gives a bromo nitro ketone, while reaction with benzyl chloride gives sodium chloride, a strong odor of



(1) N. E. Boyer, G. M. Czerniak, H. S. Gutowsky, and H. R. Snyder, *J. Am. Chem. Soc.*, **77**, 4238 (1955), found a band for the C=N at 1625–1600 cm.$^{-1}$ in the furoxan ring.

benzaldehyde and what appears to be a cyclic condensation product of the monoxime.[2]

The equations below are suggested as possible routes of the main reactions involved.[3]

This series of reactions might be thought of as an interrupted Nef reaction.

The addition of ketones to 2-nitro-1-phenylpropene appears to be fairly general, since both acetone and diethyl ketone give salts similar to I. Pure compounds corresponding to II have not been isolated from these salts, however.

Experimental[4]

Addition of Cyclohexanone to 2-Nitro-1-phenylpropene.—To 65.2 g. (0.4 mole) of 2-nitro-1-phenylpropene in 160 ml. of cyclohexanone was added a solution of 20 g. (0.5 mole) of sodium hydroxide in 50 ml. of water. The mixture was stirred and cooled for about 30 min. during which time it became one phase and the temperature rose to 60°, and then subsided.

Acidification of Addition Product.—The above reaction mixture was poured slowly with stirring and cooling into 300 ml. of methanol containing 60 ml. of acetic acid. After 30 min. the white, crystalline precipitate (II) was filtered and air-dried. There was 47 g. (45%); m.p. 137–139° dec.

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 68.9; H, 7.33; N, 5.36. Found: C, 69.2; H, 7.49; N, 5.22.

Preparation of 1-(2-Oxocyclohexyl)-1-phenyl-2-propanone (III).—A mixture of 100 ml. of methanol and 26 g. (0.1 mole) of compound II was refluxed for 4 hr. A blue color appeared after a few minutes, then this slowly turned to yellow toward the end of the reaction. The solid went into solution gradually, and a gas was evolved. Analysis by a mass spectrometer showed this gas to be pure nitrous oxide. After evaporation of the methanol, addition of 10 ml. of cyclohexane caused crystallization. After filtration and drying there were 16.4 g. (71%), m.p. 79–80° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.2; H, 7.88. Found: C, 78.4; H, 8.02.

Preparation of the Sodium Salt of 1-(2-Oxocyclohexyl)-2-nitro-1-phenylpropene (I).—A solution of 13 g. (0.05 mole) of II in 40 ml. of water plus 2.2 g. (0.055 mole) of sodium hydroxide was filtered into 300 ml. of acetone. A crystalline precipitate formed which weighed 18 g. (92%), m.p. 75–77°. The infrared spectrum of this had a strong band at 1700 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{18}NO_3Na\ 6H_2O$; C, 46.0; H, 7.72; N, 3 58. Found: C, 46.6; H, 7.40; N, 3.52.

Bromination of the Sodium Salt of 1-(2-Oxocyclohexyl)-2-nitro-1-phenylpropene (I).—A solution of 13 g. (0.05 mole) of II in 100 ml. of water plus 2.2 g. (0.055 mole) of sodium hydroxide was added slowly with stirring and cooling to 20–25° to 200 ml. of methanol containing 2.5 ml. (0.05 mole) of bromine. The mixture was left in the refrigerator overnight, filtered to give 14 g. of white crystals. After several recrystallizations from isopropyl alcohol the melting point was 113–115°. This compound showed strong bands at 1710 cm.,$^{-1}$ 1550 cm.,$^{-1}$ and 1330 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{18}BrNO_3$: N, 4.12; Br, 23.5. Found: N, 4.35; Br, 23.8.

Reaction of the Sodium Salt of 1-(2-Oxocyclohexyl)-2-nitro-1-phenylpropene (I) with Benzyl Chloride.—To 8.0 g. (0.02 mole) of the sodium salt of 1-(2-oxocyclohexyl)-2-nitro-1-phenylpropene in 100 ml. of ethanol was added 2.6 g. (0.021 mole) of benzyl chloride. The mixture was heated in a steam bath for 2 hr., then cooled overnight and filtered to give 1 g. of sodium chloride. The filtrate had the odor of benzaldehyde. It was concentrated to 30 ml., 10 ml. of water was added, and the mixture was cooled overnight. This gave 2.5 g. (42%) of a compound which, after two recrystallizations from isopropyl alcohol, melted at 165–166°. The infrared spectrum of this had intense bands in the regions of 3200 cm.$^{-1}$ and 1615 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{20}NO_2$: N, 5.71. Found: N, 5.47.

Preparation of 1,3-Diphenyl-2-methyl-4,5,6,7-tetrahydroindole.—A mixture of 4.0 g. (0.17 mole) of 1-(2-oxocyclohexyl)-1-phenyl-2-propanone (III), 2 g. (0.21 mole) of aniline, 2 drops of hydrochloric acid, and 25 ml. of ethanol was heated on a steam bath for 2 hr., then cooled 2 hr., and filtered to give 4.3 g. (88%) of white crystals. After recrystallization from ethanol the melting point was 77–79°.

Anal. Calcd. for $C_{21}H_{21}N$: N, 4.87. Found: N, 4.97.

Reaction of Acetone with 2-Nitro-1-phenylpropene.—To 100 ml. of acetone with 16.3 g. (0.1 mole) of 2-nitro-1-phenylpropene was added a solution of 4 g. (0.1 mole) of sodium hydroxide in 10 ml. of water. The mixture was stirred for 1.5 hr. during which a crystalline precipitate formed and the temperature rose to 38° and then dropped. Filtration gave a yellow solid which was dissolved in 50 ml. of 50% aqueous methanol. This was filtered into 300 ml. of acetone to give 11 g. (45%) of a white crystalline product, melting point 110–115° dec.

Anal. Calcd. for $C_{12}H_{14}NO_3Na\cdot 3H_2O$: N, 4.71. Found: N, 4.52.

Acidification of this by acetic acid in methanol led to a blue color, but no crystalline product was recovered.

Diethyl ketone gave a similar salt.

(2) See H. B. Hass and M. L. Bender, *J. Am. Chem. Soc.*, **71**, 3482 (1949).

(3) The mechanism of the Nef reaction is discussed by W. E. Noland, *Chem. Rev.*, **55**, 137 (1955).

(4) Melting points are uncorrected. Infrared data were taken with a Perkin-Elmer Model 21 double beam recording spectrophotometer equipped with sodium chloride optics. Potassium bromide disks were used for all determinations. Gas analysis was done with a Model 21-103-C Consolidated Engineering mass spectrometer.

Peptide Synthesis. An Application of the Esterase Activity of Chymotrypsin

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A frequently required step in peptide synthesis is the hydrolysis of an ester function used to block the terminal carboxyl group. The conventional methods for accomplishing this step may cause side reactions.[1] When we hydrolyzed the methyl ester of isoleucine-5 angiotensin octapeptide[2,3] under either acidic or basic conditions, we obtained low yields of the desired peptide. Chymotrypsin[4]

(1) R. Schwyzer, *Chimia*, **12**, 53 (1958); M. Goodman and G. W. Kenner, "Advances in Protein Chemistry," Vol. XII, Academic Press, New York, 1957, p. 474.

(2) Angiotensin is the present name for the substance formerly called angiotonin and hypertensin: E. Braun-Menendez and I. H. Page, *Science*, **127**, 242 (1958).

(3) H. Schwarz, F. M. Bumpus, and I. H. Page, *J. Am. Chem. Soc.*, **79**, 5697 (1957); R. Schwyzer, B. Iselin, H. Kappeler, B. Riniker, W. Rittel, and H. Zuber, *Chimia*, **11**, 335 (1957).

(4) M. Dixon and E. C. Webb, "Enzymes," Academic Press, Inc., New York, 1958, p. 269; and H. Neurath and G. W. Schwert, *Chem. Rev.*, **46**, 69 (1950) review the proteolytic and esterase activities of chymotrypsin.