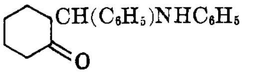
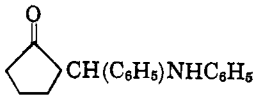
The identity of the deamination product as ethyl styryl ketone was established by adding aniline to it to furnish the adduct V. Piperidine (0.2 ml., 10 mole %) was added to a soution of 3.2 g. (0.02 mole) of the deamination product and 1.8 g. (0.02 mole) of aniline in 11 ml. of ethanol, and the yellow solution was left overnight. The first crop of the adduct V (m.p. 116–118°) was 3.2 g. (64%) and a second crop raised the yield to 76%. The melting point of this sample of the adduct was not lowered by admixture with a sample prepared from benzalaniline.

The following analogs of the adduct V, which are not deaminated efficiently by acetic acid, are deaminated by sulfuric acid.

$C_6H_5CH(NHC_6H_5)CH_2COC_5H_{11}$-*n*
(quantitative)



83%



88%

The adducts from benzalaniline and propiophenone, diethyl ketone, and cycloheptanone were destroyed on attempted deamination.

The adducts I and V are not deaminated by hydrochloric acid. When concentrated hydrochloric acid is added to hot ethanol suspensions of these adducts and the resulting solutions are cooled quickly, colorless crystalline hydrochlorides can be isolated. The hydrochlorides, which could not be crystallized, gave poor results on analysis.

*Anal.* Calcd. for $C_{21}H_{19}NO \cdot HCl$: Cl, 10.5. Found: Cl, 8.92. Calcd. for $C_{17}H_{19}NO \cdot HCl$: Cl, 12.27. Found: Cl, 11.03.

No products could be obtained when the hydrochlorides were heated alone or in solution in ethanol or acetic acid. Addition of 10% aqueous sodium carbonate to freshly prepared solutions of the hydrochlorides in ethanol or acetone regenerated the adducts.

When 1 equiv. of 1 *M* sodium methoxide in methanol was added to a suspension of the adduct I in boiling methanol, the solid dissolved after 10 min. of heating. When the hot solution was poured into ice and water, benzalacetophenone was formed in quantitative yield. When the solution was allowed to cool to room temperature and poured into water, benzalacetophenone (80%) and unchanged adduct (17%) could be isolated. The adduct V on similar treatment is unaffected, and on longer heating furnishes no definite products.

The adducts I and V formed acetyl derivatives in 90% yield when they were dissolved by heating with acetic anhydride and the solutions were left overnight, then poured into water. The acetyl derivatives were purified by crystallization from ethanol.

*Anal.* of $C_6H_5COCH_2CH(C_6H_5)N(COCH_3)C_6H_5$ (VI). Calcd. for $C_{23}H_{21}NO_2$: C, 80.46; H, 6.12. Found: C, 80.58; H, 6.38.

*Anal.* of $C_2H_5COCH_2CH(C_6H_5)N(COCH_3)C_6H_5$. Calcd. for $C_{19}H_{21}NO_2$: C, 77.29; H, 7.12. Found: C, 77.38; H, 7.52.

**Acknowledgment.**—We are appreciative of the support given this work by the Air Force Office of Scientific Research under Contract AF 49(638)-796.

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# Rotatory Dispersion Studies. IV.[1a] Substituted Cyclohexanone Oximes[1b]

Gloria G. Lyle and Renée Mestrallet Barrera

*Department of Chemistry, University of New Hampshire, Durham, New Hampshire*

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The base-catalyzed stereoselective Beckmann rearrangement of the isomeric oximes of (+)-3-methylcyclohexanone gave products permitting characterization of the α-oxime as having the *syn*-methyl configuration and the β-oxime as the *anti*-methyl isomer. A comparison of the optical rotatory dispersion curves of several cyclic ketone oximes, benzoyl derivatives of the oximes, and the lactams produced by their Beckmann rearrangements is described.

The absolute configuration of an oxime may be determined by the stereospecific Beckmann rearrangement of the oxime if only a single product (amide or lactam) is obtained from a reaction in which the configuration of the oxime is not altered. Brown and co-workers[2] found that the two isomers of isobutyrophenone oxime gave different products on treatment with benzenesulfonyl chloride in basic solution but that the use of hydrogen chloride in acetic acid produced the same amide from both oximes, the product of phenyl migration. It was apparent that the acidic medium promoted equilibration thus leading to the product resulting from the rearrangement of the group with the higher migratory aptitude.

Acid sensitivity has been observed in a number of oximes whose configuration could not be established under the usual Beckmann conditions. One such pair of oximes is that from (+)-3-methylcyclohexanone (I). (+)-Pulegone was isolated from oil of pennyroyal[3] and converted to I[4] from which the mixture of diastereomeric oximes II was prepared. The oximes II consisted of a mixture that contained approximately 65% of the α-oxime IIa, lit.[5] m.p. 60°, and 35% of the β-oxime IIb, lit.[5] m.p. 47°, the percentages being based on rotation data (*vide infra*). A partial separation of the mixture could be effected by chromatography on basic alumina. Acid-washed alumina catalyzed the Beckmann rearrangement of the oxime mixture.

The oximes were separated more satisfactorily by fractional crystallization of the O-benzoyl derivatives III as described by Hückel[5] when chromatography of the benzoates on florisil or alumina was unsuccessful. Careful hydrolysis of the benzoates gave the crystalline oximes. Heat or trace amounts of acid promoted the rapid interconversion of the oximes. The infrared absorption spectra of the isomeric benzoates III were quite similar but showed small differences in the finger-

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(1) (a) Part III: G. G. Lyle and W. Gaffield, *Tetrahedron Letters*, **No. 21**, 1371 (1963). (b) This work was supported in part by a National Science Foundation Grant, G 9489. A summary of the results was presented before the 137th National Meeting of the American Chemical Society, Cleveland, Ohio, April, 1960.

(2) (a) R. F. Brown, N. M. van Gulick, and G. H. Schmid, *J. Am. Chem. Soc.*, **77**, 1094 (1955); (b) N. H. P. Smith [*J. Chem. Soc.*, 4209 (1961)] reported that the *syn*- and *anti*-oximes of 2-bromo-5-nitroacetophenone could be stereospecifically rearranged to the corresponding amides with the use of polyphosphoric acid. These oximes are much less labile than those reported in this paper.

(3) O. Wallach, *Ann.*, **289**, 337 (1896).

(4) F. Nerdel, B. Gnauck, and G. Kresze, *ibid.*, **580**, 35 (1953).

(5) W. Hückel and M. Sachs, *ibid.*, **498**, 166 (1932).

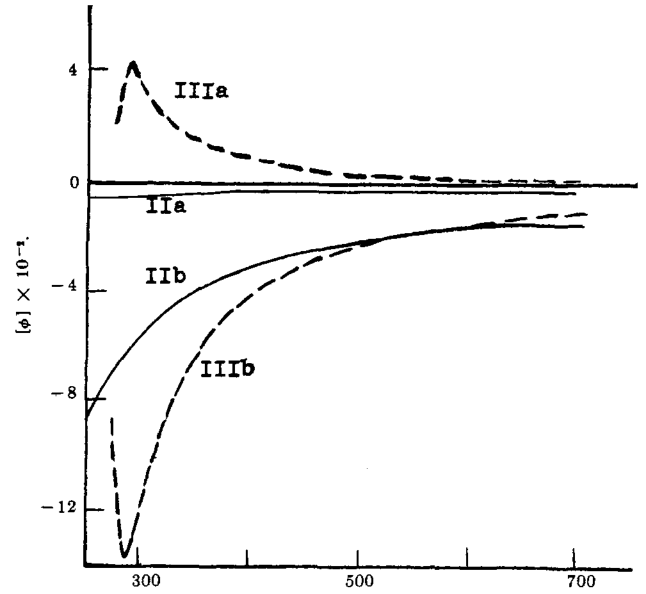


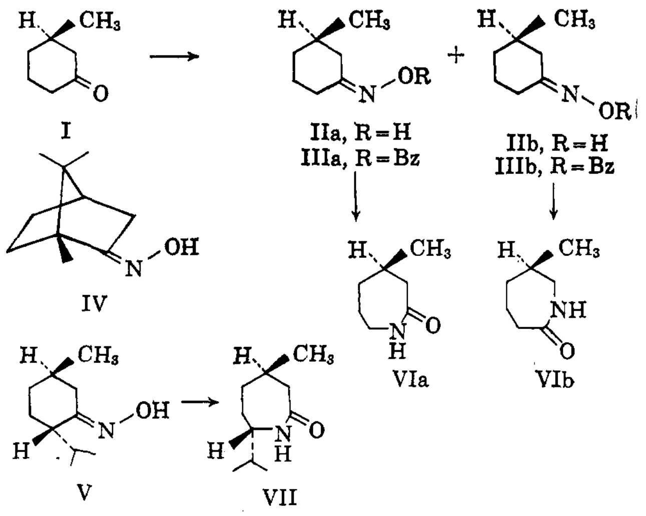
Fig. 1.—Optical rotatory dispersion curves of the α- (IIa) and β-oximes (IIb) of (+)-3-methylcyclohexanone (solid lines). The dotted lines represent the O.R.D. curves of the benzoyl derivatives (III) of the oximes.

print region, and the same situation was observed for the oximes II.

An examination of the optical rotatory dispersion curves of these compounds was undertaken in the hope that some characteristic of the curves might be consistent with configurational differences. The D-line rotations and O.R.D. curves of the isomeric oximes II and benzoates III are strikingly different (Fig. 1). The α-oxime IIa gave a negative plain curve of very low intensity, whereas the negative curve of the β-isomer IIb showed considerably stronger rotatory power. The calculation of a curve based on 65% of IIa and 35% of IIb gave a curve which was identical with that obtained from the oxime mixture isolated in the initial preparation. The oximes did not equilibrate in methanol in the time required for these measurements, and the crystalline α-oxime was isolated unchanged from the alcoholic solution.

The oximes and O-benzoyl oximino derivatives of two optically active ketonic terpenes were prepared and examined in the spectropolarimeter. The Cotton effect curves of these compounds, camphor and menthone, have been discussed and correlated with their absolute configurations *via* the Octant Rule.[6,7] In neither case was the isolation of the isomeric oxime possible[8] because of the large group adjacent to the ketonic function.

The three ketones having positive Cotton effect curves gave four oximes (II, IV, and V) with negative plain curves regardless of the configuration of the hydroxyl group. One would anticipate no Cotton effect at long wave length for the oximes of these saturated systems because the ultraviolet absorption spectra show no selective absorption above 250 mμ. The



difficulty in obtaining the β-isomer in a crystalline form and its instability required that all measurements be made immediately on isolation when the melting point and rotation were close to the reported literature values. As a result, the measurements were repeated on several samples and the O.R.D. curves provided an excellent check on the purity. Since none of the O.R.D. curves of the oximes showed a Cotton effect, correlation of the configuration of the hydroxyl group with the O.R.D. curves was not possible.

The benzoyl derivatives of the oximes apparently showed Cotton effect curves of low intensity and all were negative except for the α-isomer IIIa. Only the first extrema of these curves could be measured leaving a question as to the existence of a Cotton effect. If real, it is probably the result of the benzoyl group which shows ultraviolet absorption in the region of 280 mμ. The enantiomeric nature of the curves for IIIa and IIIb suggests that a correlation of configuration and optical rotatory dispersion might be possible by using the benzoyl derivatives of the oximes.

The Beckmann rearrangement of the oximes was effected with benzenesulfonyl chloride and sodium hydroxide.[2] The mixture of oximes II prepared from (+)-3-methylcyclohexanone (I) gave a difficultly separable mixture of lactams as had been reported previously,[9] but each pure isomeric oxime gave chiefly a single lactam under the basic conditions of the rearrangement. From the α-oxime IIa, a lactam melting at 104–106°, lit.[9] m.p. 105–106°, was obtained which was reported[9] to have the structure 4-methyl-2-oxohexamethylenimine (VIa) while the β-isomer IIb gave the isomeric 6-methyl-2-oxohexamethylenimine (VIb), m.p. 69–70°, lit.[9] m.p. 68–69°. The isolation of a relatively pure, single isomer from each rearrangement and knowledge of the *trans* rearrangement mechanism establishes the absolute configuration of IIa to be *syn*-methyl and of IIb to be *anti*-methyl. Camphor oxime (IV) produced almost exclusively cleavage products as expected[10] and no lactam could be isolated. Menthone oxime (V) gave a single lactam which has been previously identified[9] as VII.

Comparison of the O.R.D. curves of the lactams showed that the lactam VIa gave a negative, almost plain curve with fine structure at about 300 mμ, whereas

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[6] G. Jacob, G. Ourisson, and A. Rassat, *Bull. soc. chim. France*, 1374 (1959).

[7] C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp. 105–106; C. Djerassi, E. J. Warawa, J. M. Berdahl, and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **83**, 3334 (1961).

[8] E. Beckmann, *Ann.*, **250**, 322 (1888).

[9] O. Wallach, *ibid.*, **312**, 171 (1900).

[10] H. Goldschmidt, *Ber.*, **20**, 483 (1887).

the isomeric lactam VIb gave a weakly negative plain curve. The lactam VII from menthone oxime gave a strongly rotating, negative plain curve with no discontinuities of any kind. Plain curves were expected for all three compounds since there is no chromophore present that shows appreciable ultraviolet absorption above 230 mμ. The negative trend of the curves is interesting in contrast to the ketones from which they were originally derived. The configuration of the lactam VIa is identical with that of VII except for the additional isopropyl group of the latter. The much greater levorotation of VII as compared with VIa indicates the negative contribution of the isopropyl group in the seven-membered ring.

Drieding models indicate that the most stable conformation of the seven-membered lactam ring VII is the chair conformation postulated by Allinger for cycloheptanes.[11] In this conformation the isopropyl and methyl groups are both equatorial and the trigonal carbonyl carbon may be located in the position where the nonbonded interactions are most severe in a seven-membered ring. Hendrickson[12] has pointed out that these interactions in cycloheptane decrease the stability of this chair conformation to such an extent that the twist-chair is preferable. With the trigonal nature of the atoms of the amide group, however, these interactions cease to exist and should tend to stabilize the chair rather than the twist-chair conformation. The electronic transition of the amide or lactam function occurs at a shorter wave length than those reached on our spectropolarimeter, and there is insufficient evidence to permit a decision as to the conformation of the seven-membered lactam on the rotatory dispersion evidence.

## Experimental[13]

**3-Methylcyclohexanone Oxime (II).**—(+)-3-Methylcyclohexanone (I), $[\alpha]^{27}\mathrm{D}$ +15.0° (neat), lit.[14] $[\alpha]\mathrm{D}$ +13.3°, was obtained[4] from (+)-pulegone isolated from oil of pennyroyal. The most satisfactory procedure for the conversion of I to the oxime mixture II was that of Hückel.[5] Repeated extraction of the oily oximes with petroleum ether (b.p. 30–60°) to remove unreacted ketone gave crystalline oxime II, m.p. 32–39°; $\nu$ 3590, 3250 (broad, OH), and 1660 cm.$^{-1}$ (weak, C=N); $[\alpha]^{25}\mathrm{D}$ −36.5° (*c* 3.85, ethanol); lit.[14] m.p. 43–44°, $[\alpha]^{22}\mathrm{D}$ −43.8° (*c* 0.81, methanol). The oximes gave only partial separation by chromatography on basic alumina using petroleum ether (b.p. 30–60°) as eluent. Acid-washed, alumina catalyzed the Beckmann rearrangement of the oximes yielding a mixture of products.

O.R.D. of II in ethanol (*c* 0.545): $[\phi]_{695}$ −28.0°, $[\phi]_{589}$ −42.0°, and $[\phi]_{290}$ −215°. The oxime mixture appeared to give a negative Cotton effect in the region of 290 mμ although the two isomeric oximes gave negative plain curves (*vide infra*) to 250 mμ. The infrared spectra of the oxime mixture appeared to be a simple composite of the spectra of the pure oximes and, in fact, the spectra of the mixture and pure isomers were almost identical. The apparent Cotton effect of the mixture could be duplicated using different concentrations. No explanations for this anomaly can be offered at this time.

**α- and β-O-Benzoyl-3-methylcyclohexanone Oximes (III).**—Benzoylation of II (26 g.) was effected in pyridine,[5] and fractional crystallization of the benzoates (III) in petroleum ether produced 3.5 g. of the α-oxime benzoate (IIIa), m.p. 96–98°; $\nu$ 1735 and 1643 cm.$^{-1}$; $\lambda_{\max}$ 233 mμ ($\epsilon$ 14,500); $[\alpha]^{25}\mathrm{D}$ +19.1° (*c* 1.704, ether); lit.[5] m.p. 99°, $[\alpha]^{20}\mathrm{D}$ +22.9° (ether).

O.R.D. of IIIa (Fig. 1) in ethanol (*c* 1.18): $[\phi]_{695}$ +13.7°, $[\phi]_{589}$ +19.6°, $[\phi]_{290}$ +425°, and $[\phi]_{285}$ +241°.

The β-oxime benzoate (0.65 g.) melted at 82–83°; $\nu$ 1733 and 1640 cm.$^{-1}$; $\lambda_{\max}$ 233 mμ ($\epsilon$ 19,500), 271 (1060), 280 sh (738); $[\alpha]^{25}\mathrm{D}$ −87.6° (*c* 1.495, ether); lit.[5] m.p. 82–83°, $[\alpha]^{21}\mathrm{D}$ −86.2° (ether).

O.R.D. of IIIb (Fig. 1) in ethanol (*c* 0.57): $[\phi]_{695}$ −97.4°, $[\phi]_{589}$ −138°, $[\phi]_{288}$ −1350°, and $[\phi]_{285}$ −629°.

Removal of the ethanolic solvent from a sample of IIIb on a steam bath under reduced pressure resulted in decomposition of the compound yielding as the only identifiable products 3-methylcyclohexanone (I) and benzamide, m.p. 120–126°, undepressed by authentic benzamide.

**α- and β-3-Methylcyclohexanone Oximes (II).**—Saponification of IIIa was effected by adding a cold solution of 1 g. of IIIa in 10 ml. of ethanol to 10 ml. of a cold solution of 1 *N* NaOH. The mixture was allowed to stand in an ice–salt bath for 1 hr., and 15 ml. of water was added. The solution was extracted four times with 20-ml. portions of petroleum ether (b.p. 30–60°) to remove unreacted benzoate, and solid carbon dioxide was added to the aqueous solution. The solution was extracted four times with petroleum ether and the combined extracts were dried over sodium sulfate. The solvent was removed under reduced pressure at or below room temperature leaving 130 mg. of oxime IIa, m.p. 50–52°; $\nu$ 3582, 3250 (broad), and 1658 cm.$^{-1}$; $[\alpha]\mathrm{D}$ +3.07° (*c* 1.95, ethanol); lit[5] m.p. 60°, $[\alpha]\mathrm{D}$ +3.6° (alcohol). Recrystallization of IIa from petroleum ether at acetone–Dry Ice temperature raised the melting point to 58–59.5° but did not appreciably change the rotation.

O.R.D. of IIa (Fig. 1) in ethanol (*c* 0.715): $[\phi]_{695}$ −21.3°, $[\phi]_{589}$ −24.9°, and $[\phi]_{250}$ −67.6°.

The β-oxime IIb was prepared by the same procedure and melted at 43–45°; $\nu$ 3593, 3260 (broad), and 1660 cm.$^{-1}$; $[\alpha]\mathrm{D}$ −89.6° (*c* 1.35, ethanol); lit.[5] m.p. 47°, $[\alpha]\mathrm{D}$ −88.5° (alcohol).

O.R.D. of IIb (Fig. 1) in ethanol (*c* 0.64; *l*, 0.1 cm.): $[\phi]_{695}$ −140°, $[\phi]_{589}$ −160°, and $[\phi]_{250}$ −900°.

**Camphor Oxime (IV).**—(+)-Camphor was converted by standard procedures to the oxime IV, m.p. 116–117°; $[\alpha]^{25}\mathrm{D}$ −42.5° (*c* 10, ethanol); lit.[15] m.p. 115°, $[\alpha]^{25}\mathrm{D}$ −42.4° (ethanol).

O.R.D. in ethanol (*c* 0.658): $[\phi]_{695}$ −45.8°, $[\phi]_{589}$ −66.1°, and $[\phi]_{250}$ −674°.

The O-benzoyl derivative of camphor oxime was prepared from IV and melted at 90–91°; $[\alpha]\mathrm{D}$ −40° (*c* 4, ethanol); lit.[16] m.p. 88–90°, $[\alpha]^{18}\mathrm{D}$ −40.7° (ethanol).

O.R.D. in ethanol (*c* 0.336): $[\phi]_{695}$ −113°, $[\phi]_{589}$ −186°, $[\phi]_{295-290}$ −1030°, and $[\phi]_{282}$ −460°.

**Menthone Oxime (V).**—(−)-Menthone was obtained by oxidation of (−)-menthol and converted to oxime V, m.p. 54–55°; $[\alpha]\mathrm{D}$ −41.8° (*c* 3.3, ethanol); lit.[15] m.p. 58°, $[\alpha]\mathrm{D}$ −42.0° (ethanol).

O.R.D. in ethanol (*c* 0.294): $[\phi]_{695}$ −40.3°, $[\phi]_{589}$ −63.3°, and $[\phi]_{250}$ −1100°.

The O-benzoyl derivative of the oxime V melted at 53–54°; $[\alpha]\mathrm{D}$ +1.8° (*c* 2.825, ether); lit.[14] m.p. 54°, $[\alpha]\mathrm{D}$ +1.9° (*c*, 9.89, ether).

O.R.D. in ethanol (*c* 0.532): $[\phi]_{695}$ −103°, $[\phi]_{589}$ −113°, $[\phi]_{279}$ −780°, and $[\phi]_{277}$ −634°.

**Beckmann Rearrangement of Oximes.—A. Oxime Mixture II.**—A solution of 1 g. of the oxime mixture II, $[\alpha]^{25}\mathrm{D}$ −34.9° (*c* 3.585, methanol), 1.46 g. of benzenesulfonyl chloride, 0.5 g. of sodium hydroxide, 5 ml. of water, and 20 ml. of acetone was heated under reflux for 4 hr. Water (50 ml.) was added and the acetone and some of the water were removed under reduced pressure. The solution was extracted six times with chloroform and the solvent was dried over sodium sulfate and removed leaving 0.796 g. (80%) of the mixture of lactams (VI). The mixture of lactams was not successfully separated by fractional crystallization from petroleum ether. All fractions melted over a wide range, the most pure fraction (39 mg.) melting at 92–105°. Further attempts to separate the lactams were abandoned.

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[11] N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 5727 (1959).

[12] J. B. Hendrickson, *ibid.*, **83**, 4537 (1961).

[13] Infrared absorption spectra were obtained on a Perkin-Elmer Model 21 spectrophotometer in chloroform solution unless otherwise indicated. Ultraviolet absorption spectra were determined in 95% ethanol on a Perkin-Elmer Model 4000 recording spectrophotometer, which was obtained with the aid of a grant, G3901, from the National Science Foundation. The same instrument, equipped with a Perkin-Elmer attachment for rotatory dispersion, was used for some of the O.R.D. curves. The O.R.D. curves were also obtained using a Rudolph recording spectropolarimeter Model 260/655/850/810-614, which was acquired with the assistance of a grant, GM-07239, from the National Institutes of Health.

[14] O. Wallach, *Ann.*, **332**, 337 (1904).

[15] E. Beckmann, *ibid.*, **250**, 322 (1888).

[16] M. O. Forster, *J. Chem. Soc.*, **71**, 1030 (1897).

**B. α-Oxime IIa.**—The Beckmann rearrangement of 127 mg. of the α-oxime IIa, $[\alpha]_D$ +0.29° (ethanol), by the above procedure yielded 101 mg. of VIa, m.p. 99–106° (80%). Recrystallization from petroleum ether gave pure lactam VIa, m.p. 104.5–106°; ν 3418 and 1655 (strong) cm.$^{-1}$; $[\alpha]^{25}_D$ −35.7° (*c* 1.90, water); lit.[9] m.p. 105–106°, $[\alpha]_D$ −36.1° (*c* 25.6, water). None of the β-lactam VIb was isolated.

Another preparation of VI using 587 mg. of IIa, $[\alpha]^{25}_D$ −10.5° (*c* 3.17, cyclohexane), gave 71% of VIa and 4.6% of VIb, m.p. 58–69°, $[\alpha]_D$ −23.6° (*c* 0.905, water); lit.[9] m.p. 68–69°, $[\alpha]_D$ −22.2° (*c* 5.28, water).

O.R.D. of VIa in ethanol (*c* 0.26): $[\phi]_{695}$ −19.6°, $[\phi]_{589}$ −48.9°, $[\phi]_{295-285}$ −500° to −515° (fine structure), and $[\phi]_{252}$ −886°.

**C. β-Oxime IIb.**—The Beckmann rearrangement of the β-oxime IIb (441 mg., $[\alpha]_D$ −81°) was carried out as described for the oxime mixture and yielded 384 mg. (87%) of the lactams. The β-oxime was much more labile and produced a mixture of lactams which after fractional crystallization from petroleum ether yielded 82 mg. of the α-lactam, m.p. 90–103°, and 200 mg. of β-lactam, m.p. 60–77°. Purification of 104 mg. of β-lactam by chromatography on florisil and elution with 50% chloroform–petroleum ether produced 14 mg. of reasonably pure VIb, m.p. 61–66°, and 80 mg. of material melting 56–80° which was resistant to further purification.

Another rearrangement of 40 mg. of β-oxime gave 29 mg. of β-lactam, m.p. 55–72°, and 3 mg. of α-lactam, m.p. 96–105°. Recrystallization of the β-lactam gave a fraction melting 61–65°; ν 3420 and 1655 (strong) cm.$^{-1}$; $[\alpha]_D$ −22.9° (*c* 0.335, water). The infrared spectra of the α- and β-lactams have small but easily recognizable differences. The carbonyl band at 1655 cm.$^{-1}$ is evident in both compounds but the α-lactam has bands at 1340, 1170, and 1125 cm.$^{-1}$ which are much weaker or not present in the β-lactam, and absorption bands at 1385, 1312, and 1115 cm.$^{-1}$ are shown by the β- but not by the α-lactam.

O.R.D. of VIb in ethanol (*c*, 0.68): $[\phi]_{695}$ −33.7°, $[\phi]_{589}$ −48.6°, and $[\phi]_{254}$ −319°.

**D. Camphor Oxime (IV).**—The base-catalyzed rearrangement, as described in A, of camphor oxime (IV) gave a mixture of products of the cleavage reaction.[10] No solid material except unreacted oxime was recovered, and the oily nitrile ($\nu_{\text{film}}$ 2260 cm.$^{-1}$) was not investigated further.

**E. Menthone Oxime (V).**—Menthone oxime (330 mg.) was rearranged by the procedure described in A to give 300 mg. (91%) of product which was fractionally crystallized from petroleum ether yielding 95 mg. of iso-*l*-menthone oxime (VII), m.p. 120–122°; $\nu_{\text{mull}}$ 3290 and 1670 cm.$^{-1}$; $[\alpha]_D$ −51.0° (ethanol); lit.[17] m.p. 119–120°, $[\alpha]_D$ −52.25° (*c* 24, alcohol).

O.R.D. in ethanol (*c* 0.8): $[\phi]_{695}$ −78.3°, $[\phi]_{589}$ −97.3°, and $[\phi]_{250}$ −2310°.

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[17] O. Wallach and F. E. Tuttle, *Ann.*, **277**, 156 (1893).

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# The Synthesis of Some Compounds Related to 3-Amino-1-propanethiol[1]

D. S. TARBELL, DAVID A. BUCKLEY, PAULA PIMLOTT BROWNLEE, RALPH THOMAS, AND JAMES S. TODD

*Department of Chemistry, University of Rochester, Rochester, New York 14627*

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A number of aminothiols derived from 3-amino-1-propanethiol have been prepared for studies on rate of oxidation of thiols to disulfides, hydrogen bonding in thiols, and for testing for radiation-protective properties. A convenient experimental procedure for the electrolytic reduction of disulfides to thiols is described. Treatment of 4-benzylmercapto-2-methyl-2-butanol (E) with benzonitrile and boron trifluoride gives 2-phenyl-4,4-dimethyl-5,6-dihydro-1,3-thiazine (G); this is reduced by aluminum amalgam to a mixture of the tetrahydrothiazine K and the dimeric reduction product L, whose structures are established by physical and chemical evidence. The tetrahydrothiazine is readily hydrolyzed to form 3-methyl-3-amino-1-butanethiol.

The present paper describes the synthesis of a number of aminothiols derived from 3-amino-1-propanethiol (A); these were required for studies on the kinetics of

$$\underset{\text{A}}{H_2NCH_2CH_2CH_2SH}$$

oxidation of thiols to disulfides,[2] for studies on hydrogen bonding in thiols,[3] and for evaluation as radiation protective agents. The compounds prepared included primary, secondary, and tertiary amines derived from 4-amino-2-butanethiol (B) and from the higher homologs C and D.

Details on the compounds made are given in Table I. Compounds B and C were prepared by the addition of benzyl mercaptan to crotonaldehyde (for B) or to mesityl oxide (for C); the β-benzylmercaptocarbonyl compound was then converted to the oxime, and the oxime group was reduced by lithium aluminum hydride to the primary amine (B-1 or C-1).[4] The secondary amine was prepared by formylation, either by formic acid or by chloral,[5] followed by reduction of the formyl group to methyl by lithium aluminum hydride.[6] The tertiary amines were made by dimethylation of the primary amines.[7] The benzyl group was removed from the sulfur by reductive cleavage with sodium–liquid ammonia[8]; the aminothiol obtained was usually contaminated by the corresponding disulfide, formed by air oxidation during the work-up.

It was found that disulfides were conveniently converted to the corresponding thiols by electrolytic reduction in aqueous hydrochloric acid.[9]

The preparation of D-1 involved some unexpected reactions. Methyl β-benzylmercaptopropionate[10] was converted to the tertiary alcohol E, and this was sub-

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[1] Supported by Contract DA-49-193-MD-2031 of the Surgeon General's Office.

[2] (a) *Cf.* D. S. Tarbell, in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, Inc., New York, N. Y., 1961, p. 97. For leading references to recent work on this problem, see C. G. Overberger and J. J. Ferraro, *J. Org. Chem.*, **27**, 3539 (1962); T. J. Wallace and A. Schriesheim, *ibid.*, **27**, 1514 (1962); D. G. Large, H. N. Rydon, and J. A. Schofield, *J. Chem Soc.*, 1752 (1961); T. J. Wallace, J. M. Miller, H. Probner, and A. Schriesheim, *Proc. Chem. Soc.*, 384 (1962). (b) I. Pascal and D. S. Tarbell, *J. Am. Chem. Soc.*, **79**, 6015 (1957).

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