2), 1.13 (m, 9). Vpc analysis indicated the sample to be 98% pure.

A crystalline hydrochloride derivative of **6** was prepared and recrystallized from absolute ethanol–ether: mp 110–112° (lit.[17,18] mp 113°, 111–112°); ir (KBr), 5.76 μ (ester C=O).

The residue which remained from the distillation of the amino ester **6** was treated with 6 *N* hydrochloric acid and resulted in gas evolution. After cessation of gas evolution the mixture was made alkaline with 40% (w/w) aqueous potassium hydroxide, extracted with ether, and dried ($MgSO_4$). After removal of the ether, the residue was distilled giving 0.53 g (7.3%) of **7**: bp 117–120° (24 mm); ir (film), 2.92 μ (associated OH). The infrared spectrum was identical with that of an authentic sample prepared by the lithium aluminum hydride reduction of ethyl N,N-diethylsuccinamate according to the procedure of Avison.[10]

Reduction of Methyl Hippurate (8) by Diborane.—Reaction of **8** (4.83 g, 0.025 mol) in THF (50 ml) with 1.0 *M* borane in THF (45 ml) gave 3.0 g of a colorless liquid, bp 91–95° (0.30 mm). Vpc analysis indicated the sample to be a mixture of three components (4, 85, and 11%) in order of increasing retention times. The infrared spectrum showed strong absorption at 3.02 (OH) and a weak band at 5.74 μ (ester C=O). Preparative vpc was employed in the separation of the major component.

The major product was identified as **9**: $n^{25}D$ 1.5411 (lit.[19] $n^{25}D$ 1.5395); ir (film), 3.02 μ (OH); nmr ($CDCl_3$), δ 7.33 (s, 5, C_6H_5), 3.79 (s, 2, NCH_2), 3.63 (t, 2, OCH_2), 2.76 (t, 2, NCH_2), 2.53 (s, 2, NH, OH). The infrared and nmr spectra were identical in all respects with the spectra of an authentic sample prepared by the reaction of ethanolamine and benzyl chloride according to the published procedure.[20]

The second major component could not be obtained in a pure state by preparative vpc, but was shown to be methyl 2-benzylaminoacetate (**10**) by a mixed vapor phase chromatograph with an authentic sample.[21] The minor component was not identified.

Reduction of Methyl *p*-Acetamidobenzoate (12) by Diborane.—Treatment of **12**[22] (5.79 g, 0.030 mol) in THF (50 ml) with 1.0 *M* borane in THF (54 ml) gave white crystals. Recrystallization from absolute methanol afforded 2.84 g of **13**, mp 135.5–138.5° (lit.[11] mp 138–139°). Concentration of the mother liquor yielded a second crop (0.56 g, mp 132–137.5°) and a third crop which was recrystallized and amounted to an additional 0.14 g, mp 137–140°, giving a total yield of 65.9%. A portion of the first crop was recrystallized again to give the pure compound: mp 138–140°; mmp 139–141° with an authentic sample;[11] ir (KBr), 2.96 (NH), 5.95 μ (ester C=O); nmr ($CDCl_3$), δ 7.90 (d, 2), 6.57 (d, 2), 3.86 (s, 4, NH, OCH_3), 3.21 (q, 2, NCH_2), 1.25 (t, 3, $C-CH_3$). The infrared spectrum of the product was identical with that of an authentic sample obtained from the ethylation of methyl *p*-aminobenzoate with ethyl sulfate according to the published procedure.[11]

Reduction of Ethyl N,N-Diethyloxamate (14) by Diborane.—Treatment of **14**[23] (6.93 g, 0.040 mol) in THF (50 ml) with 1.0 *M* borane in THF (60 ml) gave 3.97 g of an oil, bp 76–80° (27 mm). The infrared spectrum revealed strong absorption at 5.8 (ester C=O), a weak broad band at 2.9 (associated OH), and the absence of absorption at 6.06 μ (amide C=O). Vpc analysis indicated three components (5, 1, and 94%) in order of increasing retention times. Separation of the major component was achieved by preparative vpc.

The major component was identified as ethyl N,N-diethylaminoacetate (**15**): $n^{24}D$ 1.4211 (lit.[24] $n^{21.5}D$ 1.4230); ir (film), 5.80 μ (ester C=O); nmr ($CDCl_3$), δ 4.20 (q, 2, OCH_2), 3.32 (s, 2, $NCH_2C=O$), 2.68 (q, 4, NCH_2C), 1.18 (m, 9).

The component corresponding to 5% of the reaction mixture was shown to be N,N-diethylaminoethanol (**16**) by a mixed vapor phase chromatograph with an authentic sample. The third component was not identified.

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(22) G. W. K. Cavill and J. M. Vincent, *J. Soc. Chem. Ind.* (London), **67**, 25 (1948).

(23) R. Barre and L. Favreau, *Compt. Rend.*, **230**, 848 (1950).

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Registry No.—**2a**, 17012-19-0; **2b**, 17012-20-3; **4**, 17012-21-4; **5**, 7497-63-4; **8**, 1205-08-9; **12**, 17012-22-5; **14**, 5411-58-5; borane, 13283-31-3.

The Beckmann Rearrangement of Norcamphor Oxime[1]

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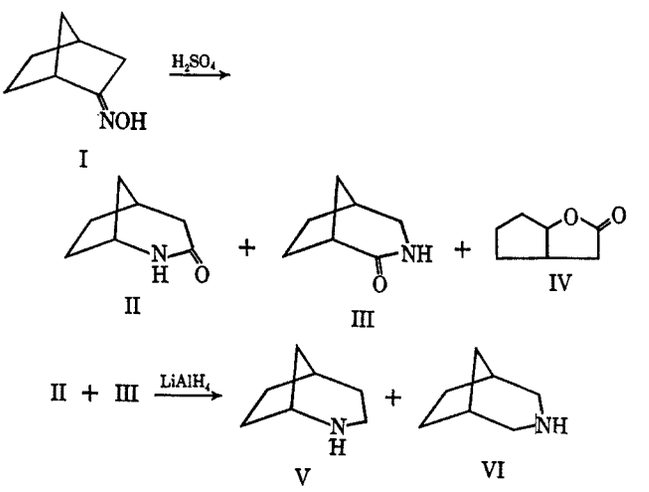
The Beckmann rearrangement of norcamphor oxime (I) in 85% sulfuric acid has been reported to yield 2-azabicyclo[3.2.1]octan-3-one (II).[2,3] Other workers[4,5] have had difficulty duplicating these results, but have failed to report the structures of the other products obtained in the reaction. Our interest in bicyclic amines prompted us to repeat this work, and we wish to report our results.

A solution of I in 85% sulfuric acid was slowly added to a flask heated to 110°.[6] Subsequent work-up produced a crude product having a wide boiling point range.

The lower boiling fractions were clear colorless liquids, composed chiefly of the lactone of *cis*-2-hydroxycyclopentane acetic acid (IV),[7] along with small amounts of II and 3-azabicyclo[3.2.1]octan-2-one (III). The structure of the lactone was established by comparison of this material with an authentic sample of IV prepared from cyclopentadiene following a known procedure.[8]



(1) Taken in part from the senior research problem of J. E. Reboulet.

(2) Swiss Patent 287,863 (1953) (to Inventa AG, Lucerne).

(3) R. Griot, *Helv. Chim. Acta*, **42**, 67 (1959).

(4) H. K. Hall, *J. Amer. Chem. Soc.*, **82**, 1209 (1960).

(5) R. C. Elderfield and E. T. Losin, *J. Org. Chem.*, **26**, 1703 (1961). These authors report an alternate rearrangement procedure. We find that the alternate procedure, followed by hydride reduction, also yields a mixture of the same two amines (V and VI) obtained above.

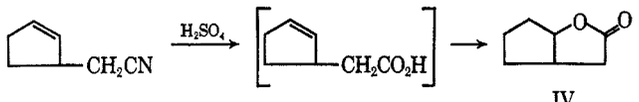
(6) For an explanation of this modification of the published procedure, see the Experimental Section.

(7) This lactone is also produced when norcamphor oxime is heated in polyphosphoric acid. We wish to thank Professor R. T. Conley of Wright State University for informing us of this result prior to publication, since this simplified our identification of IV.

(8) R. P. Linstead and E. M. Meade, *J. Chem. Soc.*, 935 (1934).

The higher boiling fractions were semisolids. Lithium aluminum hydride reduction of these fractions afforded a mixture of two amines which could be separated by preparative glpc. Yields of the amines were determined by quantitative glpc. The physical constants of these amines and their derivatives[3,5] as well as the nmr spectra of their hydrochlorides indicated the more abundant amine to be 3-azabicyclo[3.2.1]octane (VI) and the minor component to be 2-azabicyclo [3.2.1]octane (V). In addition, repeated recrystallization of the higher boiling fractions from above yielded a pure sample of III having a melting point in agreement with the reported value.[5] Lithium aluminum hydride reduction of this pure sample of III yielded VI, the principal component in the amine mixture from reduction of the Beckmann lactams. Finally, an independent synthesis of VI[3] produced material identical with the more abundant amine obtained above, as shown by glpc retention times, comparison of nmr spectra of the amine hydrochlorides, and picrate melting points.

Rearrangement of norcamphor oxime tosylate in refluxing ethanol has been reported[5] to yield Δ^2-cyclopentenylacetonitrile (VII). While the production of nitriles from ketoximes *via* the so called "second-order" Beckmann rearrangement is well documented,[9,10] none of the previous workers had reported the formation of the lactone IV in the rearrangement of norcamphor oxime. We therefore became interested in the possible intermediacy of VII as the precursor of IV. Preliminary experiments substantiated this hypothesis. Under rearrangement conditions VII was converted into IV, possibly *via* the unsaturated acid VIII which is known to undergo the lactonization as shown.[8] Further examination of this reaction was abandoned when we learned of similar work being done in another laboratory.[11]



VII VIII IV

Experimental Section

Norcamphor Oxime.—Norcamphor oxime was purchased from the Aldrich Chemical Co. and was distilled prior to use. Similar results were obtained from the oxime prepared from norcamphor following a known procedure.[12]

Beckmann rearrangement was carried out as previously described[3] except that the temperature for the reaction was increased to 110°. This change was prompted by the observation of one rearrangement which did not initiate immediately at 95° and subsequently exploded when the temperature was raised slowly to 100°. We have carried out the rearrangement on as much as 15 g of oxime at the higher temperature without incident.

In a typical rearrangement, 14.8 g (0.118 mol) norcamphor oxime in 40 ml of 85% sulfuric acid was added dropwise over 45 min to a flask heated to 110°. Heating was continued for 10 min after completion of addition. The black solution was cooled to 45° and neutralized with saturated potassium bicarbonate solution. The resultant salts and black solids were removed by filtration, and the filtrate was extracted with six 100-ml portions of chloroform. After drying over anhydrous magnesium sulfate, the combined chloroform extracts were concentrated on a rotary evaporator. Vacuum distillation of the brown residual liquid afforded 4.74 g of clear colorless liquid, bp 55–87° (0.2 mm), and 2.57 g of a colorless semisolid, bp 87–90° (0.2 mm). A similar experiment, starting with 15 g of oxime, yielded 5.46 g of the lower boiling material and 2.93 g of the partially solid material.

After four recrystallizations of 2.57 g of the lactam mixture from petroleum ether (65–70°) there was obtained 0.33 g of 3-azabicyclo[3.2.1]octan-2-one (III) as fine white needles, mp 89–93°. Four additional recrystallizations afforded an analytical sample, mp 92–93.5° (lit.[5] mp 93–94°).

Anal. Calcd for $C_7H_{11}NO$: C, 67.16; H, 8.86; N, 11.19. Found: C, 66.91; H, 9.05; N, 11.43.

Synthesis of 3-Azabicyclo[3.2.1]octane (VI). A.—Reduction of 111.7 mg (0.894 mmol) of the 3-azabicyclo[3.2.1]octan-2-one from above (mp 89–93°) with lithium aluminum hydride afforded nearly pure VI (the more rapidly eluted amine) that was contaminated with only a trace of V, as shown by glpc using a 10 ft × 1/8 in. column of 10% (4:1) Carbowax 20M–KOH on 60/80 Chromosorb W at 100°. Treatment of the product with a saturated solution of picric acid in 95% ethanol gave 96.4 mg of picrate, mp 203–206°. After two recrystallizations from 95% ethanol, a melting point of 211.5–212.5° (lit.[1] mp 209–210°) was obtained.

B.—Dry distillation of 1.0 g (5.81 mmol) of the half amide–half ammonium salt of norcamphoric acid, prepared in 81% yield by passing ammonia through a benzene solution of the corresponding anhydride,[13] afforded 0.648 g (80%) of norcamphoric acid imide after one recrystallization from ethanol–cyclohexane, mp 152–155° (lit.[3] mp 154–155°). Reduction of 0.1586 g of this material with lithium aluminum hydride in tetrahydrofuran for 24 hr at room temperature gave, after the usual work-up, a solution of VI in tetrahydrofuran. The glpc retention time of this amine was identical with that of the principal amine obtained from reduction of the mixture of Beckmann lactams. Likewise, the nmr spectra of the two amine hydrochlorides, prepared by passing gaseous hydrogen chloride through a solution of the amine in ether or tetrahydrofuran, were identical and displayed the following integrated intensities and multiplicities (solvent, D_2O): τ 4.73, 2 H (singlet); 6.20, 4 H (poorly resolved doublet, J = 1.5 cps); 6.94, 2 H (broad envelope); 7.61, 6 H (center of complex envelope). The first peak is due to HOD from exchange between solvent and the amine hydrochloride. The melting point of the picrate of the independently synthesized amine (mp 209.5–210.5°) agreed with the literature value.[3]

Isolation of 2- and 3-Azabicyclo[3.2.1]octane (V and VI).—Reduction of the mixture of lactams from a typical rearrangement was carried out with lithium aluminum hydride in refluxing ether for 12 hr. The resultant amine mixture was separated by preparative glpc using a 10 ft × 3/8 in. column of 20% (4:1) Apiezon L–KOH on 60/80 firebrick at 65°. The most rapidly eluted material was 3-azabicyclo[3.2.1]octane, a white volatile solid: mp 140.5–142.5° (sealed tube) (lit. mp 134–137°,[3] 137–138.5°[5]); picrate mp 211.5–212.5° (lit.[3] mp 209–210°). The second amine, also a white volatile solid, was 2-azabicyclo[3.2.1]octane: mp 123–125° (sealed tube) (lit. liquid,[5] semisolid[3]); picrate mp 203–205°. The nmr spectrum of the hydrochloride of V displayed the following integrated intensities and multiplicities (solvent, D_2O): τ 4.69, 2 H (singlet HOD); 5.53, 1 H (broad singlet); 6.29, 2 H (complex envelope); 6.99, 1 H (singlet); 7.64, 8 H (broad singlet).

Quantitative Analysis of Amine Mixture (V and VI).—The crude reaction mixture from a typical rearrangement of 4.1 g (0.0331 mol) of norcamphor oxime (after standard work-up) was stirred for 18 hr with 1.5 g (0.0395 mol) of lithium aluminum hydride in 100 ml of ether. The excess hydride was decomposed with 6.0 ml of water, and the salts were removed by filtration. To the filtrate was added 0.5202 g of *m*-methylanisole as an internal glpc standard. The integrated intensities (planimeter) of the peaks obtained, using a 10 ft × 1/8 in. column of 10% (4:1) Carbowax 20M–KOH on 60/80 Chromosorb W at 100°, indicated (by comparison with standards) the presence of 0.247 g (6.7%) of V and 0.272 g (8.2%) of VI. There was also a peak due to the reduction product of IV, but this did not interfere.

(9) For examples, see P. A. S. Smith in "Molecular Rearrangements," part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 501.

(10) A. Hassner and E. G. Nash, *Tetrahedron Lett.*, **9**, 525 (1965), and references cited therein.

(11) R. T. Conley, Wright State University, private communication, 1968.

(12) K. Alder and G. Stein, *Ann.*, **525**, 218 (1936).

(13) D. C. Heckert, Ph.D. Dissertation, The Ohio State University, Columbus, Ohio, 1965.

cis-2-Hydroxycyclopentylacetic Acid Lactone (IV).—Rearrangement of 5 g (0.040 mol) of norcamphor oxime yielded (after the usual work-up) 1.40 g (28%) of low boiling [85–87° (2 mm)] material. Judging from the infrared spectrum, this material is nearly pure IV (n^{23}D 1.4747). Further purification by preparative glpc gave a clear colorless liquid, n^{23}D 1.4742 [lit. bp 120–121° (12 mm),[8] n^{25}D 1.4727[14]]. Comparison of the infrared spectrum of the above material with that of an authentic sample[8] showed the materials to be identical.

Registry No.—I, 4576-48-1; III, 16994-00-6; V HCl, 16994-01-7; VI, 279-82-3.

Acknowledgment.—The authors wish to thank the Research Council and the Department of Chemistry of the University of Dayton for partial support of this investigation. The authors are also indebted to Professor P. G. Gassman of The Ohio State University, under whose direction the early part of this study was carried out.

(14) W. E. Noland, J. H. Cooley, and P. A. McVeigh, *J. Amer. Chem. Soc.*, **79**, 2976 (1957).

The Behavior of Thioxanthenol Sulfoxides in Trifluoroacetic Acid and Its Anhydride

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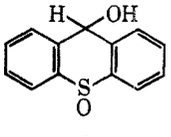
A great deal of interest has been generated in the chemistry of organosulfur compounds and, particularly, in their behavior in strongly acidic media.[2] As part of our study of the chemistry of the thioxanthene ring system,[3,4] we have examined the reactions of the isomeric thioxanthen-9-ol 10-oxides (1)[3,4] and related compounds in acidic media. We would now like to present a brief account of the reactions of these compounds in trifluoroacetic acid (TFA) and in the corresponding anhydride (TFAA).



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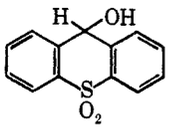

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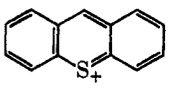
cis and *trans* **1** produce identical nmr spectra in TFA. These spectra consist of singlets at 404 and 396 Hz (relative intensities *ca.* 4:1) and a complex aromatic region. Comparison of these spectra with those of the isomeric acetates of 1[4] ($CDCl_3$ solvent) indicates that these signals represent the *trans* and *cis* trifluoroacetates of **1**, the *trans* isomer being present to a larger extent. (The *cis* and *trans* acetates of **1** exhibit methine resonances ($CDCl_3$) at 396 and 412 Hz, respectively.[5]) Thus far we have not been able to isolate and directly characterize any of the trifluoroacetates that will be discussed, apparently because of their rapid hydrolysis. The nmr spectrum of thioxanthen-9-ol 10,10-dioxide (**2**) in TFA, in addition to a complex aryl multiplet, contains a group of resonances which constitute an "AB quartet" centered at 232 Hz. In deuteriochloroform **5** exhibits an "AB quartet" centered at 238 Hz.

The nmr spectrum of the thioxanthylium ion (**3**) (perchlorate counterion) in TFA is similar to that of **3** in 96% sulfuric acid.[6] The nmr spectrum of a dilute solution of thioxanthenol (**4**) in TFA is virtually identical with that of **3**. However, more concentrated (*i.e.* near saturation) solutions of **4** in TFA result in a spectrum exhibiting two distinct singlets. One of these (572 Hz) represents the C-9 proton of the thioxanthylium ion while the other signal (395 Hz) is ascribed to the trifluoroacetate of **4**.



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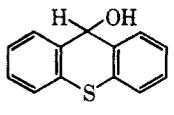

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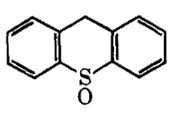

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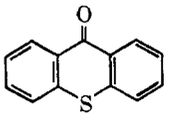

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Unlike its behavior in 96% sulfuric acid,[7] thioxanthene sulfoxide (**5**) does not form the thioxanthylium cation (**3**) in TFA. In this medium the spectrum of **5** contains a group of resonances which constitute an "AB quartet" centered at 238 Hz. In deuteriochloroform **5** exhibits an "AB quartet" centered at 238 Hz.

The behavior of **2** in TFAA is similar to its behavior in TFA. Thus, the spectrum consists of a single resonance at 403 Hz in addition to the signals resulting from the aryl protons. Unlike their behavior in TFA, the stereoisomers of **1** were "dehydrated" to thioxanthone (**6**) in TFAA. (The base-induced dehydration of **1** to **6** has already been reported.[3b]) This reaction is preceded, however, by the formation of a signal (singlet, 393 Hz) ascribed to the methine proton of one of the corresponding trifluoroacetates (integrated intensity ratio of C-9 H/aryl H 1:8). Both isomers of **1** afforded the same spectrum. Thioxanthene sulfoxide (**5**) reacts immediately with TFAA to form a red oil which possessed an nmr spectrum (acetonitrile solvent) virtually identical with that of **3**. This reaction is similar to that of **5** in 96% sulfuric acid[7] and is presumed to proceed by way of **7**.

The nmr spectrum of thioxanthenol (**4**) in TFAA consists of a singlet (563 Hz) and two regions of complex multiplet absorption (*ca.* 440–490 Hz and *ca.* 400–430

(1) To whom inquiries should be directed. Support of this research by Public Health Service Grant No. CA-10139 from the National Cancer Institute is gratefully acknowledged.

(2) For a recent review, see H. J. Shine in "Organosulfur Chemistry," M. J. Janssen, Ed., Interscience Publishers, New York, N. Y., 1967, Chapter 6.

(3) (a) A. L. Ternay, Jr., D. W. Chasar, and M. Sax, *J. Org. Chem.*, **32**, 2465 (1967); (b) A. L. Ternay, Jr., and D. W. Chasar, *ibid.*, **32**, 3814 (1967).

(4) A. L. Ternay, Jr., and D. W. Chasar, *ibid.*, **33**, 2237 (1968).

(5) A referee has suggested that the species observed in solutions of **1** in TFA may actually be the trifluoroacetylsulfoxonium salts of the trifluoroacetates of **1**. However, the similarity in the chemical shifts of the methine protons of the isomeric acetates of **1** and the observed resonances in TFA make this unlikely.

(6) H. J. Shine and L. Hughes, *J. Org. Chem.*, **31**, 3142 (1966).

(7) Thioxanthene sulfoxide is converted into the thioxanthylium ion in 96% sulfuric acid.[6]