[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

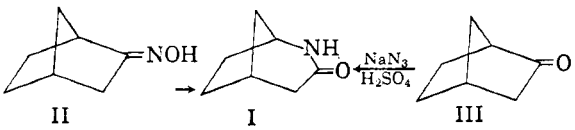
Schmidt and Beckmann Reactions of Norcamphor and Cyclopentanonorcamphor[1]

ROBERT C. ELDERFIELD AND EDWARD T. LOSIN

Received July 28, 1960

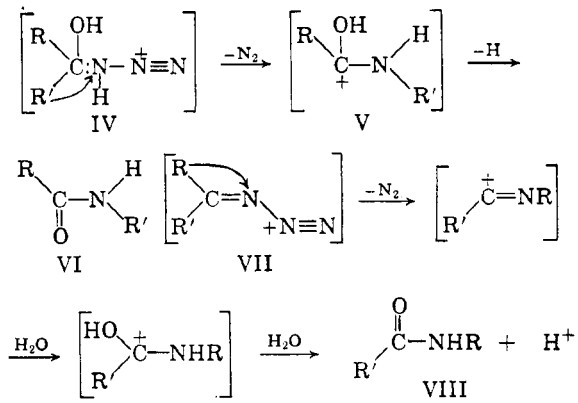
Norcamphor and cyclopentanonorcamphor furnish isomeric lactams under conditions of the Schmidt reaction and Beckmann rearrangement respectively. Evidence is presented that the structure of the product of the acid catalyzed hydration of dicyclopentadiene is best represented by 2,5-methanobicyclo[4.3.0]non-7-en-3-ol rather than by tricyclo[4.2.2.$0^{1,6}$]dec-(2 or 3)-en-8-ol.

The formation of 2-azabicyclo[3.2.1]octan-3-one (I) by Beckmann rearrangement of the oxime of norcamphor (II) has been reported in a Swiss patent[2] and polyamides are reportedly formed from I when it is heated with hydrochloric acid.

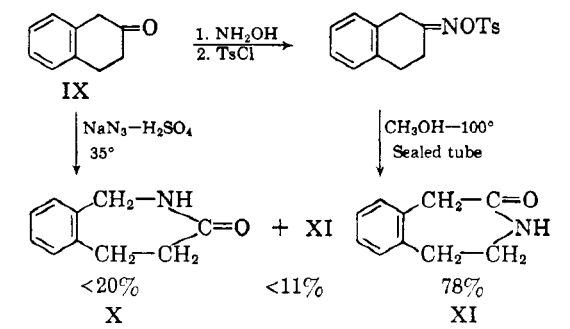


No structure proof was offered for I. It is presumed that the Swiss workers proposed the structure I on the assumption that the most heavily substituted carbon atom would migrate from carbon to nitrogen in the usual fashion.

The Schmidt reaction does not appear to have been applied to norcamphor(III). On the basis of currently held views[3,4] on the mechanism of the Beckmann rearrangement and the Schmidt reaction, it would be expected that the product would be the same from both reactions. The Smith[4] and Newman[3] suggestions for the mechanism of the Schmidt reaction differ only in the details of the step whereby the lactam is formed from the azide. According to Newman the decomposition and migration of one substituent may be represented by (IV–VI) whereas Smith pictures the change as proceeding by the sequence IV–VII–VIII. Thus the suggested intermediate (VII) is expected to show *syn-anti* configurations analogous to those of the oximes in the Beckmann rearrangement, and the Schmidt rearrangement is considered to involve a *trans* migration of R with simultaneous loss of nitrogen.



Although these considerations account fairly satisfactorily for the experimental observation with open-chain ketones, the situation becomes more complex with cyclic and bicyclic ketones. Knunyants and Fabrichnyi[5] have investigated both the Beckmann and the Schmidt reactions with β-tetralone. Their results are summarized in formulas IX–XI.



The percentages represent the yields of pure lactams isolated by fractional crystallization and may not represent actual yields. Further, a direct comparison of the two reactions is probably valid only when the derivative of the oxime that rearranges is sterically similar to the azido group and the reactions are carried out at comparable temperatures. Despite these limitations it is apparent that the two reactions with the cyclic ketone (IX) do not parallel each other exactly.

(1) The work here reported was done under a contract between Esso Research and Engineering Company and the University of Michigan.

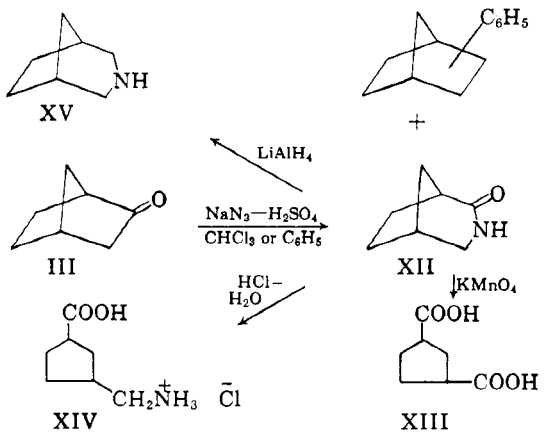
(2) Swiss Patent 270,546, January 3, 1951; *Chem. Abstr.*, 46, 780 (1952).

(3) M. L. Newman and H. L. Gildenhorn, *J. Am. Chem. Soc.*, 70, 317 (1948).

(4) P. A. S. Smith, *J. Am. Chem. Soc.*, 70, 320 (1948); P. A. S. Smith and J. P. Horwitz, *J. Am. Chem. Soc.*, 72, 3718 (1950); *cf.* P. A. S. Smith, *J. Am. Chem. Soc.*, 76, 431 (1953), and C. L. Arcus, M. M. Coombs, and J. V. Evans, *J. Chem. Soc.*, 1498 (1956); P. A. S. Smith and E. P. Antoniades, *Tetrahedron*, 9, 210 (1960).

(5) I. L. Knunyants and B. P. Fabrichnyi, *Doklady Akad. Nauk, S.S.S.R.*, 68, 523 (1949).

When norcamphor (III) is subjected to the Schmidt reaction, the major product is not 2-azabicyclo[3.2.1]octan-3-one (I) as reported for the product of the Beckmann rearrangement,[2] but rather 3-azabicyclo[3.2.1]octan-2-one (XII).



Evidence for the structure assigned to XII was provided by its oxidation by permanganate to *cis*-cyclopentane-1,3-dicarboxylic acid (XIII).

Hydrolysis of XII with concentrated hydrochloric acid gave the amino acid hydrochloride (XIV) and reduction of XII with lithium aluminum hydride gave 3-azabicyclo[3.2.1]octane (XV). All attempts at preparing polyamides from XIV failed.

When the reaction was carried out in the presence of benzene, a small amount of a hydrocarbon the infrared spectrum of which indicated a monosubstituted benzene derivative, was isolated. On the basis of analysis and oxidation to benzoic acid, this is formulated as a phenylbicyclo[3.2.1]heptane. The position of the phenyl group is uncertain. Formation of alkylbenzenes is not uncommon under Schmidt reaction conditions when benzene is present.[6] The hydrocarbon was not obtained when chloroform was the solvent.

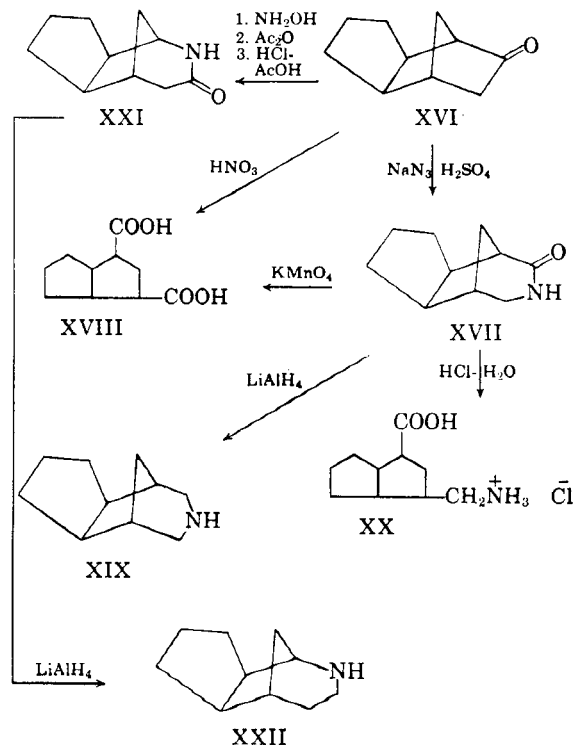
The behavior of norcamphor oxime on Beckmann rearrangement did not parallel that of norcamphor in the Schmidt reaction, nor did it agree with that reported in the patent literature.[2] After investigation of numerous procedures for accomplishing the rearrangement, the best one seemed to involve merely refluxing the *p*-toluenesulfonic acid ester in ethanol. There was thus obtained a very small amount of the usual cleavage product from such reactions, cyclopentene-3-acetonitrile along with the major product presumably the lactam (I). I and the lactam from the Schmidt reaction (XII) were not identical as shown by widely divergent infrared spectra. Unfortunately all attempts at oxidative degradation of I to cyclopentanone-3-acetic acid have failed. Likewise attempts at conversion of I to polyamides have been unsuccessful. Hydrolysis of I to an amino acid has also failed.

(6) H. D. Zook and S. C. Paviak, *J. Am. Chem. Soc.*, **77**, 2501 (1955).

Analytical data suggest that one oxygen has been lost during treatment of I with concentrated hydrochloric acid.

Reduction of I with lithium aluminum hydride gave an amine, presumably 2-azabicyclo[3.2.1]-octane, which was very difficult to purify. Its infrared spectrum was widely divergent from that of 3-azabicyclo[3.2.1]octane (XV) obtained from the product of the Schmidt reaction.

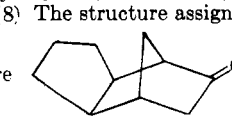
The two reactions have also been investigated with cyclopentanonorcamphor (XVI).[7] From the products of the Schmidt reaction a substance, (XVII),[8] presumably the lactam (XVII) by analogy to the formation of XII from norcamphor, was obtained.



The structure assigned to XVII was confirmed by formation of bicyclo[3.3.0]octan-2,4-dicarboxylic acid (XVIII) upon permanganate oxidation of XVII. The acid (XVIII) was identical with XVIII prepared by nitric acid oxidation of XVI as judged by identical infrared spectra, melting points, and mixture melting points.

Reduction of XVII with lithium aluminum hydride gave 2,6-methano-4-azabicyclo[5.3.0]decane (XIX).

(7) The shorter name, cyclopentanonorcamphor, rather than the cumbersome systematic name, 2,5-methanobicyclo[4.3.0]nonan-3-one, will be used to denote XVI.

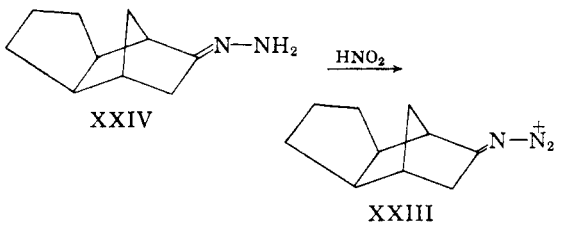
(8) The structure assigned to XVII is based on the structure  for cyclopentanonorcamphor. This point is discussed more fully in the sequel.

When the acetate of cyclopentanonorcamphor oxime was refluxed in a mixture of hydrochloric and acetic acids the expected Beckmann rearrangement occurred. Again as with norcamphor, the lactam isolated (XXI) was different from the lactam (XVII) formed in the Schmidt reaction. It is formulated as XXI by analogy with the products obtained from norcamphor by the two routes.

The two lactams differed in their behavior on acid hydrolysis. XVII on boiling with hydrochloric acid readily gave the hydrochloride of 1-aminomethylbicyclo[3.3.0]octan-3-carboxylic acid (XX). In contrast acid hydrolysis of XXI gave a product the properties of which were not consistent with those of an amino acid.

Reduction of XXI with lithium aluminum hydride gave an amine isomeric with XIX which is presumably 2,6-methano-3-azabicyclo[5.3.0]decane (XXII).

If the course of the Schmidt reaction indeed involves an intermediate (VII), then preparation of a substance of the type of VII and a study of its decomposition could conceivably throw some light on the factors which are operative in the Schmidt and Beckmann reactions. Specifically, rearrangement of the diazonium compound (XXIII) derived from cyclopentanonorcamphor would be expected to follow a course similar to that of the Beckmann rearrangement of the oxime of XVI, since both the oxime and XXIII presumably would have the same *syn-anti* steric relationship.

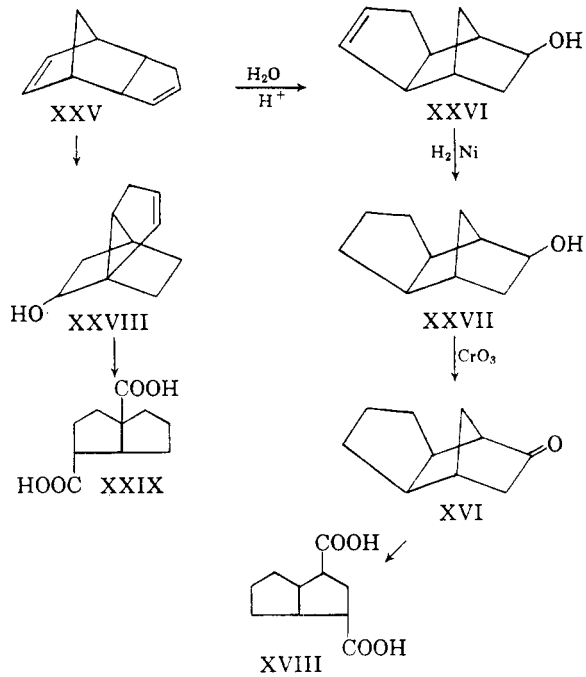


Attempts to prepare the hydrazone (XXIV) of cyclopentanonorcamphor resulted in the formation of either the azine, the acetate of the hydrazone, or of a substance which appeared to be the crude hydrazone (XXIV). However, on attempted recrystallization it reverted to the azine. Reaction of either crude XXIV or its acetate with sodium nitrite in concentrated sulfuric acid gave a very poor yield of an oil which could not be purified. These observations parallel the difficulties encountered in the preparation and rearrangement of the hydrazones of open-chain aliphatic ketones.[9]

It thus appears that under the conditions employed the Schmidt reaction with both norcamphor and cyclopentanonorcamphor takes a course different from that of the Beckmann rearrangement. But one lactam has been isolated from each reaction and the site of ring expansion would seem to be at one or the other position immediately adjacent to the carbonyl group in the ketone. Whether this divergent behavior is due to difference in reaction conditions in the two reactions or to some stereochemical feature of the bicyclic ketones remains to be determined. Although the products of the Beckmann rearrangements appeared to be lactams, their somewhat unexpected properties, particularly the divergence of the infrared spectra from those of the Schmidt lactams, may indicate a deep-seated rearrangement of the carbon skeleton. This requires further investigation.

The norcamphor required for these studies was prepared by oxidation of norborneol which was in turn prepared by hydration of norbornylene. Considerable improvements in the preparation of norborneol have been worked out.

Cyclopentanonorcamphor was prepared from dicyclopentadiene (XXV) by the following series of reactions. Hydration of dicyclopentadiene was



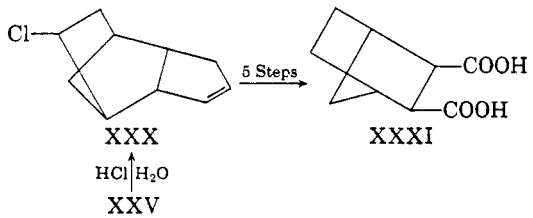
accomplished essentially according to Bruson and Reiner.[10] However, these workers proposed structure XXVIII (tricyclo[4.2.2.0^{1,5}]dec-(2 or 3)-en-8-ol) for the product of the hydration. Obviously the formation of such a compound must involve extensive rearrangement of the carbon skeleton of XXV during the course of the reaction. The bicyclooctane dicarboxylic acid derived from XXVIII on oxidation then would have the structure XXIX as described by Bruson and Reiner. We believe that the series of reactions leading to the bicyclooctane dicarboxylic acid is more correctly represented by the sequence XXV–XVIII

(9) D. E. Pearson *et al.*, *J. Am. Chem. Soc.*, **71**, 1895 (1949); **75**, 5905 (1953).

(10) H. A. Bruson and T. W. Reiner, *J. Am. Chem. Soc.*, **67**, 723 (1945).

and that the acid has the structure XVIII for the following reasons.

Structure XXVI, representing the unsaturated carbinol formed on hydration of endodicyclopentadiene (XXV), may arise by the usual Wagner-Meerwein shifts commonly encountered in such bicyclic systems.[11,12] Furthermore, Bartlett and Schneider[13] have conclusively proved that addition of hydrogen chloride to XXV occurs in such fashion as to give the *exo*-chloro derivative (XXX). The final dibasic acid formed on degradation of XXX was shown to be β-(*exo*)-*cis*-3,6-methanohexahydrophthalic acid (XXXI). Since it is to be expected that the acid-catalyzed addition of water to XXV parallels the addition of hydrogen chloride, assignment of structure XXVI to the unsaturated carbinol rather than structure XXVIII appears to be warranted.



Further confirmation for structure XVIII for the bicyclooctane dicarboxylic acid is provided by the ready formation of diesters by the Fischer method. An acid carrying a tertiary carboxyl group such as XXIX would hardly be expected to undergo such easy esterification.[14] Finally, the bicyclooctane dicarboxylic acid readily forms an anhydride on treatment with acetyl chloride in toluene. An acid of structure XXIX would be expected to give an anhydride only with difficulty since considerable strain would be involved.

EXPERIMENTAL[15,16]

Norborneol by hydration of norbornylene. The procedure described by Bruson[10] for hydration of norbornylene using 40 weight % sulfuric acid at 95–100° for 5 hr. gives poor yields of norborneol and relatively large amounts of dinorbornyl ether. Accordingly a new procedure based on that of Walborsky and Loncsini[17] has been developed which gives satisfactory yields of norborneol.

A mixture of 50 g. of norbornylene, 850 g. of concd. sulfuric acid, and 150 ml. of water was stirred in an ice bath until homogeneous (about 1.5–2.5 hr.). The mixture was diluted with 1.8 l. of water and extracted with ether. After washing the extract with water and drying over anhydrous sodium sulfate, removal of the solvent left a partially crystalline product. Recrystallization from petroleum ether (b.p. 30–60°) gave 30–35 g. of norborneol, m.p. 128–129° (reported m.p., 125–126°,[18] 126–127°[18]). The phenylurethan melted at 149–150° (reported m.p. 145–146°[18]).

Norcamphor. A solution of 36 g. of chromic oxide in 150 ml. of glacial acetic acid and 50 ml. of water was added dropwise with stirring to a solution of 33.6 g. (0.3 mole) of norborneol in 150 ml. of glacial acetic acid. After the addition was complete, the mixture was allowed to stand at room temperature for 30 min. It was partially neutralized with dilute sodium hydroxide solution and then extracted with ether. The ether extract was washed successively with water, dilute sodium hydroxide solution, and water, and dried over anhydrous sodium sulfate. Removal of the solvent left 24–26 g. (80%) of norcamphor, m.p., 96°.

Schmidt reaction with norcamphor. Procedure A. A mixture of 55 g. (0.5 mole) of norcamphor, 250 ml. of anhydrous benzene, and 250 ml. of concd. sulfuric acid was placed in a 1-l., three-necked flask equipped with a stirrer and reflux condenser and chilled in an ice bath. To this was added 33 g. of sodium azide in small portions with stirring at such a rate that the temperature was maintained at 15°. After addition of the sodium azide was complete, the reaction mixture was stirred for an additional 12 hr. during which the ice bath was allowed to come to room temperature. The mixture was again cooled, diluted with water, and made alkaline with 25% sodium hydroxide solution After extraction with several portions of chloroform, the combined chloroform extracts were washed with water and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was distilled under reduced pressure to yield 9.5 g. of liquid material, b.p., 72–73° (20 mm.), n_D^{29} 1.4671, and 6.5 g. of crude lactam (XII). The crude lactam (3-azabicyclo[3.2.1]octan-2-one) was recrystallized from petroleum ether (b.p. 30–60°) and gave a crystalline product, m.p., 93–94°.

Anal. Calcd. for $C_7H_{11}NO$: C, 67.16; H, 8.86; N, 11.18. Found: C, 67.23, 67.09; H, 8.91, 8.89; N, 11.07, 10.99.

The liquid fractions, b.p., 72–75° (20 mm.), from two such runs were combined and redistilled three times, yielding a water white liquid, b.p., 70.5–71.5° (0.65 mm.).

Anal. Calcd. for $C_{13}H_{16}$: C, 90.63; H, 9.36. Found: C, 90.39; H, 9.60.

The infrared spectrum of this material shows it to be a mono-substituted benzene derivative. It resists oxidation by permanganate under mild conditions but is oxidized by hot alkaline permanganate to benzoic acid. A mixture of 1 g. of the hydrocarbon, 4.0 g. of potassium permanganate, 30 ml. of water, and 6 drops of 25% sodium hydroxide solution was heated on the steam bath for 12 hr. After cooling and filtering, the solution was extracted with ether. After acidification with hydrochloric acid, the aqueous solution was again extracted with ether. Removal of the ether and recrystallization of the residue from water gave 0.25 g. of benzoic acid identified by mixed melting points and infrared spectra.

Procedure B. To a solution of 4.90 g. (0.04 mole) of norcamphor in 10 ml. of cold concd. sulfuric acid and 20 ml. of chloroform, 2.6 g. (0.04 mole) of sodium azide was added in small portions with stirring, during which the temperature of the mixture was held at −10° by an ice bath. After addition of the azide, the mixture was allowed to come to room temperature and made alkaline with cooling with 25% sodium hydroxide solution. The basic solution was extracted three times with chloroform. After drying, removal of the solvent left an oil which was sublimed at 90° and 18 mm., giving 1.0 g. of cyclopentene-3-acetonitrile and 1.5 g. (30%) of crystalline material, m.p., 72–79°. Resublimation of this at 100° and 18 mm. followed by recrystallization from petro-

(11) H. Meerwein and K. van Amster, *Ber.*, **53**, 1815 (1920).

(12) F. C. Whitmore, *J. Am. Chem. Soc.*, **54**, 3274 (1932).

(13) P. D. Bartlett and A. Schneider, *J. Am. Chem. Soc.*, **68**, 6 (1946).

(14) L. P. Hammett, *Physical Organic Chemistry*, McGraw Hill Book Co., New York, 1940, p. 212.

(15) All melting points are corrected and boiling points are uncorrected.

(16) Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(17) H. M. Walborsky and D. F. Loncsini, *J. Am. Chem. Soc.*, **76**, 5396 (1954).

(18) K. Alder, *Ber.*, **71**, 2451, 2458 (1938).

leum ether (b.p. 30–60°) gave the lactam (XII), m.p., 93–94°.

Procedure C. To a stirred mixture of 15.5 g. (0.14 mole) of norcamphor in 150 ml. of concd. sulfuric acid held at 7–12° with an ice bath, 9.8 g. (0.15 mole) of sodium azide was added in small portions. After stirring overnight at room temperature, the mixture was poured on to crushed ice and made alkaline with 25% sodium hydroxide solution. Extraction with chloroform and removal of the solvent from the extract gave an oil from which 3.3 g. (20%) of crude lactam, m.p., 75–79°, was obtained after sublimation at 100° and 18 mm.

Oxidation of 3-azabicyclo[3.2.1]octan-2-one. A mixture of 300 mg. of the lactam and 20 ml. of 0.1*N* potassium permanganate solution was allowed to stand at room temperature for 20 hr. After removal of the manganese dioxide by filtration, extraction of the filtrate with ether gave 20 mg. of unchanged lactam, m.p., 88–89°. The aqueous layer was acidified with hydrochloric acid and concentrated to dryness under reduced pressure. The residue was extracted with chloroform. Removal of the chloroform from the extract left 150 mg. of material, m.p., 117–117.5°, after recrystallization from benzene. This was identified as *cis*-1,3-cyclopentanedicarboxylic acid on the basis of mixed melting points and comparison of the infrared spectrum with that of a known sample.

Hydrolysis of 3-azabicyclo[3.2.1]octan-2-one. A mixture of 0.8 g. of 3-azabicyclo[3.2.1]octan-2-one and 25 ml. of concd. hydrochloric acid was refluxed for 12 hr. After removal of the solvent *in vacuo*, the crystalline residue was dried *in vacuo* at 60° for 8 hr. The crude hydrochloride of 3-aminomethylcyclopentanecarboxylic acid (XIV) melted at 119–121°. Recrystallization from ethanol-ether gave material, m.p., 122.5–123.5°. The infrared spectrum of this amino acid hydrochloride shows disappearance of the bands at 3250, 1650, and 1625 cm.$^{-1}$ which are present in the spectrum of the original lactam. Weak absorption bands at 3200, 2600, 2000, and 1601 cm.$^{-1}$ are present. These are characteristic of most amino acid hydrochlorides.

Anal. Calcd. for $C_7H_{14}ClNO_2$: C, 46.81; H, 7.86; N, 7.80. Found: C, 46.55; H, 7.57; N, 7.67.

Beckmann rearrangement of norcamphor oxime. To a solution of 16.0 g. (0.128 mole) of norcamphor oxime[19] in 400 ml. of glacial acetic acid contained in a 1-l. round bottom flask equipped with a reflux condenser was added 26.2 g. (0.256 mole) of acetic anhydride. After standing at room temperature for 12 hr., the mixture was saturated with anhydrous hydrogen chloride and heated slowly in an oil bath until gentle refluxing ensued. After refluxing for 6 hr., the mixture was resaturated with hydrogen chloride and refluxed for an additional 11 hr. After cooling, the mixture was poured into a dilute sodium hydroxide–ice mixture and partially neutralized with 25% sodium hydroxide solution. It was then extracted with four portions of chloroform. The combined chloroform extracts were washed successively with 5% sodium hydroxide solution and water and dried over anhydrous sodium sulfate. Removal of the solvent left a residue which was distilled through a 12-cm. Vigreux column at 12–14 mm., yielding the following fractions:

Fraction	B.P.	n_D^{23}	Weight, g.
I	60–61	—	0.3
II	61–61.5	1.4619	3.0
III	62–66	—	1.0
IV	66–119.5	—	1.1
V	119.5–127	1.4794	1.75
VI	Residue		

The infrared spectrum of Fraction II indicated that it was an unsaturated nitrile, presumably cyclopentene-3-acetonitrile with absorption bands at 3040 cm.$^{-1}$ (vinyl C—H stretching), 2240 cm.$^{-1}$ (C ≡ N stretching) and 1610 cm.$^{-1}$ The latter is probably due to a contaminant. The spectrum was essentially the same as that given by cyclopentene-3-acetonitrile isolated from the Schmidt reaction.

Fractions I, II, and III were combined and redistilled through a 6-cm. Vigreux column to yield Fraction VII, b.p., 62.5–63.5° (12 mm.), n_D^{24} 1.4610 (2.7 g.). The infrared spectrum of Fraction VII showed the same type of absorption as Fraction II, except that the 1610 band was shifted to 1720 cm.$^{-1}$ Analysis still indicated some contamination.

Anal. (Fraction VII) Calcd. for C_7H_9N: C, 78.43; H, 8.46; N, 13.07. Found: C, 79.92; H, 8.80; N, 11.25.

Reduction of Fraction VII with hydrogen over palladium on carbon in absolute ethanol at room temperature resulted in the uptake of 0.98 equivalent of hydrogen. The reduction product (cyclopentaneacetonitrile) was distilled, b.p., 185–186°, n_D^{26} 1.4474. In the infrared it showed disappearance of the bands at 3040 cm.$^{-1}$ and 1610 cm.$^{-1}$, but retained the typical nitrile absorption at 2240 cm.$^{-1}$ as well as the band at 1730–1740 cm.$^{-1}$ Analysis indicated that the nitrile was contaminated by a small amount of impurity which had carried through.

Anal. Calcd. for $C_7H_{11}N$: C, 77.00; H, 10.16; N, 12.83. Found: C, 76.46, 76.44; H, 9.81, 9.82; N, 11.69, 11.61.

Fraction VI was distilled through a 6-cm. Vigreux column at 0.45 mm., and gave the following fractions.

Fraction	B.P.	$n_D^{23.5}$	Weight, g.
VI-a	82.0–85.5	1.4787	0.51
VI-b	85.5–88.5	1.4740	0.97
VI-c	88.5–89.0	1.4677	2.62
VI-d	89.0–89.5	1.4673	0.3
VI-e	Residue		

The infrared spectrum of Fraction VI-d indicated that it was a mixture showing N—H or O—H absorption between 3200 and 3400 cm.$^{-1}$, nitrile absorption at 2240 cm.$^{-1}$, and two bands in the double bond region at 1725 and 1660 cm.$^{-1}$

The residue (VI-e) was transferred to a semimicro molecular still and evaporatively distilled at 74° and 0.4 mm. The temperature was gradually raised and the following fractions were collected.

Fraction	Bath Temp.	n_D^{25}	Weight, g.
VI-e-1	74	1.4937	—
VI-e-2	100–102	1.5020	0.40
VI-e-3	102–104	1.5025	0.35

The infrared spectrum of Fraction VI-e-3, taken as a thick film, showed no absorption in the triple bond stretching region, but showed two bands in the double bond stretching region at 1670 (strong) and 1730 (weak) cm.$^{-1}$ and an N—H stretching absorption at 3300–3200 cm.$^{-1}$ This spectrum differs markedly from that of the lactam obtained by the Schmidt reaction on norcamphor.

Beckmann rearrangement of norcamphor oxime tosylate. The tosylate of norcamphor oxime was prepared by a modification of the procedures of Knunyants and Fabrichnyi[5] and Vargha and Gönczy.[20] To a solution of 2.77 g. (0.022 mole) of norcamphor oxime in 40 ml. of dry pyridine at 0°, 4.23 g. (0.0223 mole) of *p*-toluenesulfonyl chloride was added. The mixture was kept at 0° in an ice bath with frequent shaking for 4 hr. It was then allowed to warm up to room temperature

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

(20) L. Vargha and F. Gönczy, *J. Am. Chem. Soc.*, **72**, 2738 (1950).

overnight. After pouring the mixture into ice and water, concentration under reduced pressure at 30° left a partially crystalline hygroscopic material which was insoluble in petroleum ether (b.p. 30–60°) and soluble in ethanol. The dried residue was refluxed in 150 ml. of absolute ethanol for 2.5 hr. Concentration under reduced pressure gave a tan crystalline residue which was taken up in 50 ml. of 10% sodium hydroxide solution. Extraction of the alkaline solution with chloroform and removal of the solvent from the dried extract left a residue which was evaporatively distilled in a molecular still at 0.5 mm. and 85–90° bath temperature. After a few drops of forerun, material which solidified on the cold finger of the still was obtained. This was boiled with a mixture of petroleum ether (b.p. 30–60°) and ether. After decanting the supernatant liquid, refrigeration of the residue gave crystalline material which melted at room temperature. The yield was 1.0 g. (35%) on the assumption that the substance was the expected lactam.

Anal. Calcd. for $C_7H_{10}NO$: N, 11.18. Found: N, 11.15.

The infrared spectrum of this material shows N—H absorption at 3220 cm.$^{-1}$ and carbonyl absorption at 1660 cm.$^{-1}$ consistent with a lactam structure. However, the spectrum is not identical with that of the lactam produced by the Schmidt reaction.

3-Azabicyclo[3.2.1]octane (XV). A solution of 0.5 g. (0.004 mole) of 3-azabicyclo[3.2.1]octan-2-one (XII) in 70 ml. of absolute ether was added dropwise to a stirred suspension of 0.2 g. (0.002 mole) of lithium aluminum hydride in 50 ml. of absolute ether. After addition of the lactam, the mixture was refluxed gently for 6 hr. and then allowed to stand at room temperature for 12 hr. Water was carefully added to destroy the excess hydride until a clear ether layer resulted. Concentration of the ether layer gave the crystalline amine, m.p., 137–138.5°. The infrared spectrum, taken as a Nujol mull, showed disappearance of the mono-substituted amide (lactam) absorption at 1625 and 1650 and 1490 cm.$^{-1}$

For characterization of the amine, the hydrochloride was prepared by saturating an ethereal solution of the amine with anhydrous hydrogen chloride. After recrystallization from absolute ethanol-ether, the amine hydrochloride darkened above 240° and decomposed above 300°.

Anal. Calcd. for $C_7H_{14}NCl$: C, 56.93; H, 9.56; N, 9.49. Found: C, 57.41; H, 9.91; N, 9.28.

2-Azabicyclo[3.2.1]octane. 2-Azabicyclo[3.2.1]octan-3-one (I) was reduced with lithiumaluminum hydride as in the above case. Evaporation of the ether layer left an oil which could not be crystallized. The amine hydrochloride was precipitated as above and purification was accomplished, not too satisfactorily, from absolute ethanol–ether, yielding a substance which softened at 220° and decomposed at 244°.

Anal. Calcd. for $C_7H_{14}NCl$: C, 56.93; H, 9.56; N, 9.49. Found: C, 58.48; H, 10.33; N, 9.93.

The infrared spectrum of this amine hydrochloride was not identical with that of the amine hydrochloride obtained by reduction of the lactam (3-azabicyclo[3.2.1]-octan-2-one) obtained by the Schmidt reaction.

Schmidt reaction with cyclopentanonorcamphor. 2,6-Methano-4-azabicyclo[5.3.0]decan-3-one (XVII). This was done according to a general procedure described by Wolff.[21] To a stirred mixture of 30.0 g. (0.2 mole) of cyclopentanonorcamphor, 200 ml. of reagent grade chloroform, and 70 ml. of concd. sulfuric acid contained in a 1-l. flask equipped with a reflux condenser and stirrer, 13 g. (0.2 mole) of sodium azide was added in small portions during which the temperature was held at 0–5° by means of an ice bath. After addition of the azide was complete, the mixture was stirred for an additional 4 hr. and then allowed to come to room temperature as the ice bath melted. The cooled mixture was poured onto ice, made alkaline with 25% sodium hydroxide solution, and extracted with three portions of chloroform. The combined chloroform extracts were washed twice with water and dried over anhydrous sodium sulfate. Removal of the solvent left a residue which was evaporatively distilled at 16–18 mm., yielding the following fractions.

Fraction	Bath Temp.	Weight, g.
I (liquid)	70–100	15.8
II (liquid)	100–125	2.5
III (solid)	100–125	0.2
IV (solid)	125+	2.1

Two recrystallizations of Fraction IV gave white crystals, m.p., 104.5–105.5°.

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.63, 72.49; H, 8.96, 9.09; N, 8.58, 8.54.

The infrared spectrum taken as a Nujol mull showed absorption bands at 3070–3200 cm.$^{-1}$ (N—H stretching) and 1665 cm.$^{-1}$ (amide carbonyl stretching).

The liquid fraction I was redistilled through a 6-cm. Vigreux column and the following fractions were collected.

Fraction	B.P./12–14 mm.	n_D^{22}	Weight, g.
1-A	101.5–102.5	1.5018	8.7
1-B	102.5–103.5	1.5015	
1-C	103.5–106.5	1.5016	6.0
1-D	106.5+	1.5013	0.4

Fraction 1-C was recovered cyclopentanonorcamphor as shown by boiling point, refractive index, and infrared spectrum. Fractions 1-A and 1-B also were largely recovered ketone.

Oxidative degradation of 2,6-methanol-4-azabicyclo-[5.3.0]-decan-3-one. A mixture of 0.5 g. of the above lactam, 2.0 g. of potassium permanganate, 0.5 ml. of 25% sodium hydroxide solution, and 40 ml. of water was refluxed for 2 hr. The cooled reaction mixture was filtered from manganese dioxide by gravity and the filtrate was extracted with ether. The aqueous solution was acidified with hydrochloric acid and extracted with ether. Concentration of the ether extract of acidic material gave 0.2 g. of crystalline material, m.p., 150–152°. Recrystallization from toluene raised the m.p. to 175–176°. Mixture melting points with an authentic sample of bicyclo[3.3.0]octan-2,4-dicarboxylic acid, m.p. 178–179°, were 177–178°. The infrared spectra of the degradation product and the authentic sample of the acid were identical, except for a weak absorption at 3425 cm.$^{-1}$ displayed by the degradation product which was absent in the authentic sample.

Hydrolysis of 2,6-methanol-4-azabicyclo[5.3.0]decan-3-one. A mixture of 200 mg. of the lactam and 10 ml. of concd. hydrochloric acid was refluxed for 5 hr. Concentration to dryness gave the hydrochloride of 4-aminomethylbicyclo-[3.3.0]octan-2-carboxylic acid, m.p., 185–186°, after recrystallization from absolute ethanol-ether.

Anal. Calcd. for $C_{10}H_{18}ClNO_2$: C, 54.67; H, 8.26; N, 6.38. Found: C, 54.33, 54.31; H, 8.11, 8.06; N, 6.26.

Cyclopentanonorcamphor oxime. A mixture of 90.0 g. (0.6 mole) of cyclopentanonorcamphor, 60 g. of hydroxylamine hydrochloride, 60 g. of hydrated sodium acetate, 120 ml. of methanol, and 60 ml. of water was allowed to stand at room temperature for 48 hr. and then heated on the steam bath for 0.5 hr. After cooling and diluting with water, the solution was extracted with ether. Removal of the solvent from the ether extract left a heavy oil which crystallized on cooling. Recrystallization from dilute ethanol gave the oxime as colorless plates, m.p., 69–70°. The yield was 61 g. (61%).

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.70; H, 9.15; N, 8.48. Found: C, 72.63; H, 9.16; N, 8.45.

(21) H. Wolff, *Org. Reactions*, **3**, 307 (1946).

Beckmann rearrangement of cyclopentanonorcamphor oxime. A solution of 14.0 g. (0.085 mole) of the oxime in 200 ml. of glacial acetic acid and 17.3 g. (0.17 mole) of acetic anhydride was allowed to stand at room temperature overnight. It was then saturated with anhydrous hydrogen chloride and refluxed for 3 hr. After resaturating with hydrogen chloride it was refluxed for an additional 7 hr. The cooled mixture was poured into a dilute sodium hydroxide–salt mixture, made alkaline with 25% sodium hydroxide solution, and extracted with chloroform. After washing with water and drying over anhydrous sodium sulfate, removal of the solvent left a heavy oil which was evaporatively distilled in a molecular still, yielding the following fractions.

Fraction	Bath Temp.	Pressure, mm. Hg	Weight, g.
I	96	16	1.03
	83	6.0	
II	96–100	14–16	2.60
III	104	0.4	1.85
IV	104+	0.4	2.20
V	Residue		2.10

Recrystallization of Fraction III from petroleum ether (b.p. 30–60°) gave colorless plates, m.p., 99–100°, which gave analytical figures agreeing with those of the expected lactam.

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.81; H, 9.12; N, 8.07, 8.10.

A mixture of equal parts of this lactam and that obtained by the Schmidt reaction on cyclopentanonorcamphor melted at 76–92°. Further, the infrared spectrum of this lactam shows bands at 3150 cm.$^{-1}$ (N—H stretching frequency) and at 1670 cm.$^{-1}$ (amide carbonyl stretching frequency). This spectrum is very different from that of the lactam obtained by the Schmidt reaction.

Fraction I appeared to be an unsaturated nitrile from its infrared spectrum. Catalytic hydrogenation of 0.77 g., n_D^{24} 1.4893, over palladium on carbon in absolute ethanol was very sluggish. After 20 hr., 145 ml. of hydrogen was absorbed. Calculated absorption for one double bond: 130 ml. After filtering from the catalyst, removal of the solvent left a residue which was distilled at 72–73° (1.0 mm.), n_D^{25} 1.4788. The calculated boiling point of the starting material is 56° at 1 mm. The infrared spectrum of the reduction product showed disappearance of the bands at 3030 and 1615 cm.$^{-1}$ which are present in the starting material. Nitrile absorption at 2210 cm.$^{-1}$ and a band at 1740 cm.$^{-1}$ are shown in the spectra of both materials.

Acid hydrolysis of 4,8-methanol-7-azabicyclo[0.3.5]decan-6-one. A solution of 0.2 g. of the above lactam in 10 ml. of concd. hydrochloric acid was boiled under reflux for 9 hr. Concentration of the mixture *in vacuo* left a crystalline residue, m.p., 177–179°. Recrystallization from absolute ethanol-ether followed by vacuum sublimation gave material, m.p., 178–180°. The analytical data did not correspond to those demanded by the expected amino acid hydrochloride. No reasonable structure could be fitted to the data.

Anal. Calcd. for $C_{10}H_{18}ClNO_2$: C, 54.67; H, 8.26; N, 6.38. Found: C, 66.78, 66.85; H, 8.44, 8.41; N, 7.62.

The infrared spectrum shows a weak absorption band at 2650 cm.$^{-1}$ and strong bands at 2120, 1800, and 1660 cm.$^{-1}$ This is radically different from the spectrum of the amino acid obtained *via* the Schmidt reaction.

2,6-Methano-4-azabicyclo[5.3.0]decane (XIX). A solution of 0.3 g. (0.0018 mole) of XVII in 50 ml. of absolute ether was reduced with 0.15 g. (0.04 mole) of lithiumaluminum hydride as in the preceding cases. After addition of the lactam, the mixture was refluxed for 8 hr. and allowed to stand at room temperature for 12 hr. After careful addition of water, the ether layer was separated and concentrated leaving an oil residue. The oil was evaporatively distilled in a microstill at 60° and 18 mm., yielding a clear liquid. Anhydrous hydrogen chloride was passed into an absolute ethereal solution of the liquid on which the hydrochloride of the amine separated. After drying *in vacuo* at 60° for 3 hr., it darkened at 260° and decomposed at 280°.

Anal. Calcd. for $C_{10}H_{18}ClN$: C, 63.99; H, 9.66; N, 7.46. Found: C, 64.00; H, 9.60; N, 7.41.

A portion of the amine hydrochloride was converted to the free amine by solution in dilute sodium hydroxide solution and extraction of the basic solution with ether. Addition of alcoholic picric acid solution to the ether extract and concentration gave a crystalline picrate of the amine, m.p., 193.5–194.5°, after two recrystallizations from 95% ethanol.

Anal. Calcd. for $C_{16}H_{20}N_4O_7$: N, 14.73. Found: N, 14.79.

A mixture of this picrate with that of 2,6-methano-3-azabicyclo[5.3.0]decane (see below) melted at 150–168°.

2,6-Methano-3-azabicyclo[5.3.0]decane (XXII). XXI (0.2 g.) was reduced with 0.2 g. of lithiumaluminum hydride in absolute ether as in the preceding case. The mixture was refluxed for 10 hr. after addition of the lactam and then allowed to stand overnight at room temperature. The oil remaining after removal of the ether was evaporatively distilled in a microstill at 48° and 12 mm. A portion of the distillate was treated with anhydrous hydrogen chloride in absolute ether. The hydrochloride which precipitated immediately redissolved. Removal of the solvent left a crystalline material, m.p. 161.5–163.5°, for the purification of which no suitable solvent could be found. It was dried *in vacuo* at 50° for 7.5 hr. for analysis.

Anal.: Calcd. for $C_{10}H_{18}ClN$: C, 63.99; H, 9.66. Found: C, 64.77; H, 10.38.

The infrared spectrum of this hydrochloride is not identical with that of the hydrochloride of the amine obtained by reduction of the lactam (2,6-methano-4-azabicyclo[5.3.0]-decan-3-one) resulting from the Schmidt reaction.

A picrate of the amine was prepared in ethanol. After recrystallization from 95% ethanol the pale yellow crystals melted at 165.5–166°. However, analysis indicated some contamination.

Anal. Calcd. for $C_{16}H_{20}N_4O_7$: C, 50.52; H, 5.30; N, 14.73. Found: C, 51.23; H, 5.68; N, 14.74.

Reaction of cyclopentanonorcamphor with hydrazine. A. *The azine.* A solution of 10 ml. of cyclopentanonorcamphor and 10 ml. of 64% aqueous hydrazine solution in 100 ml. of glacial acetic acid was heated on the steam bath for 2 hr. After cooling, the mixture was poured onto crushed ice, made alkaline with 10% sodium hydroxide solution, and extracted three times with ether. After drying the combined ether extracts over anhydrous sodium sulfate, removal of the solvent left a partially crystalline residue (2.5 g.) which was recrystallized successively from petroleum ether (b.p. 60–75°) and absolute ethanol to give the bishydrazone, m.p., 174–174.5°.

Anal. Calcd. for $C_{20}H_{28}N_2$: C, 81.08; H, 9.52; N, 9.45. Found: C, 80.89; H, 9.70; N, 9.37.

B. Acetyl derivative of cyclopentanonorcamphor hydrazone. A solution of 15 g. of cyclopentanonorcamphor in 100 ml. of glacial acetic acid was added to 10 g. of 64% aqueous hydrazine solution and the mixture was heated on the steam bath for 6 hr. After pouring onto ice, the solution was made alkaline with 25% sodium hydroxide solution and extracted with ether. After drying the ether extract over anhydrous sodium sulfate, removal of the solvent left 5.0 g. of liquid. This was taken up in petroleum ether (b.p. 30–60°). After refrigeration, the solution deposited 2.5 g. of crystalline material, m.p., 130–131.5°. Two recrystallizations from ether–petroleum ether raised the melting point to 133–133.5°.

Anal. Calcd. for $C_{12}H_{18}N_2O$: C, 69.86; H, 8.79; N, 13.58. Found: C, 69.82; H, 8.78; N, 13.74.

C. Cyclopentanonorcamphor hydrazone. The general procedure of Curtius and Pflug[22] was followed. A mixture of 15

(22) T. Curtius and L. Pflug, *J. prakt. Chem.*, [2], **44**, 535 (1891).

TABLE I

ESTERS OF BICYCLO[3.3.0]OCTANE-2,4-DICARBOXYLIC ACID

Alcohol Used	Bath Temp.	Pressure, mm.	n_D^{22}	Calcd. C	Calcd. H	Found C	Found H
oxo-C_8	165–170	1.5	1.4677	73.90	10.97	72.55	10.89
oxo-C_{10}	175–185	0.9	1.4690	75.27	11.37	75.59	11.84
oxo-C_{13}	180–190	0.9	1.4703	76.82	11.82	76.74	12.00

g. of cyclopentanonorcamphor, 7.0 g. of 64% aqueous hydrazine solution, and 2.0 g. of barium oxide was allowed to stand at room temperature for 65 hr. After addition of 250 ml. of ether, the solution was filtered and concentrated, yielding 10 g. of white crystalline material. On recrystallization of this from petroleum ether (b.p. 30–60°), 0.5 g. of crystalline material, m.p., 56–57°, was obtained. Additional amounts of hydrazone, m.p., 51.5–53°, were obtained from the mother liquors. On further recrystallization from ethanol, the hydrazone disproportionated to the azine.

Hydration of dicyclopentadiene. 2,5-Methano[4.3.0]bicyclonon-7-en-3-ol (XXVI). A mixture of 600 g. (4.55 moles) of dicyclopentadiene and 1600 g. of 30% sulfuric acid was heated with stirring under gentle reflux for 3 hr. and stirred an additional hour while cooling to room temperature. The cooled mixture was poured onto ice and extracted with ether. After washing the ether extract successively with water, twice with 10% sodium hydroxide solution, and twice with water, it was dried over anhydrous sodium sulfate. After removal of the ether, the residue was distilled under reduced pressure. Dicyclopentadiene (86.1 g.), b.p., 74–75° (22 mm.) was recovered, followed by the carbinol (486.7 g.), b.p., 93–95° (2.5 mm.), 89–91° (1.7 mm.). The yield was 80% based on dicyclopentadiene reacted, or 68.6% based on dicyclopentadiene used initially.

Reduction of 2,5-methano[4.3.0]bicyclonon-7-en-3-ol. 2,5-Methanobicyclo[4.3.0]nonan-3-ol. (XXVII). The unsaturated carbinol was reduced either over platinum oxide in ethanol at room temperature and 40 p.s.i.g. hydrogen pressure, or over Raney nickel (W-5) catalyst[23] at 110° and 1500 p.s.i.g. hydrogen pressure. The saturated carbinol boiled at 77–79° (1 mm.).

2,5-Methanobicyclo[4.3.0]nonan-3-one (cyclopentanonorcamphor) (XVI). To a stirred solution of 1096 g. (7.2 moles) of XXVII in 2 l. of glacial acetic acid, a solution of 5.80 g. (5.8 moles) of chromic acid in 400 ml. of water and 1.5 l. of acetic acid was added dropwise. After addition of the chromic acid was complete, the mixture was stirred and heated at 90–95° for 4 hr. After cooling, the mixture was poured onto ice and partially neutralized with 25% sodium hydroxide solution and extracted four times with ether. The combined ether extracts were washed successively with water, dilute sodium hydroxide solution until the washing remained alkaline to *p*H paper, and three times with water. After drying over anhydrous sodium sulfate, removal of the ether and distillation of the residue under reduced pressure gave 1000 g. (90%) of cyclopentanonorcamphor, b.p., 111–112° (14 mm.). Bruson and Reiner report a yield of 63% of the ketone.[10]

Bicyclo[3.3.0]octane-2,4-dicarboxylic acid (XVIII). To 200 g. (1.33 moles) of cyclopentanonorcamphor in a 2-l. flask fitted with a reflux condenser and heated on a steam bath, 25–30 ml. of nitric acid (sp. gr. 1.50) was added. After the formation of brown oxides of nitrogen had moderated, a second portion of nitric acid was added. This process was repeated until a total of 375 ml. of nitric acid had been added, after which the mixture was heated on the steam bath for 7 days. After cooling and dilution with water, the crude crystalline acid was collected and air dried. The yield of crude material was 107.4 g. (50%). Recrystallization from water gave material, m.p., 175–177°.

Anhydride of bicyclo[3.3.0]octane-2,4-dicarboxylic acid. A solution of 1 g. of the dicarboxylic acid and 0.5 g. of acetyl chloride in 10 ml. of toluene was heated under reflux for 2 hr. and taken to dryness. The residue was taken up in chloroform, filtered, and again concentrated to dryness. The crystalline residue was recrystallized from petroleum ether (b.p. 90–100°) to give fine, long, colorless needles of the anhydride, m.p., 64.5–65°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.7; H, 6.7. Found: C, 67.1; H. 7.1.

The infrared spectrum of the anhydride, taken as a Nujol mull, showed the typical double carbonyl absorption at 1810 and 1760 cm.$^{-1}$ with disappearance of the associated hydroxyl stretching absorption which is present in the spectrum of the dicarboxylic acid.

Esters of bicyclo[3.3.0]octane-2,4-dicarboxylic acid. Esters were prepared with commercial C_8, C_{10} and C_{13} oxo alcohols by a standard procedure. In a 50-ml. round bottom flask, 2.0 g. of the acid, 4 ml. of the alcohol, 8 ml. of toluene, and 4 drops of concd. sulfuric acid were placed. The flask was connected to a 12-cm. Vigreux column, the mixture was heated and the azeotropic distillate was collected until the temperature at the top of the column reached the b.p. of toluene (110°). The residue after removal of solvent was distilled in a molecular still. Data on the esters is given in Table I.

ANN ARBOR, MICH.

(23) H. Adkins and H. R. Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).