ous ethanol was used. The solubility of β-dextrin in such a mixture is about equal to that in water. Enough water is present to enable adduct formation and at the same time the solubility of the lipid is slightly increased to facilitate the reaction. Oil droplets still were detectable, admixed with the crystalline adducts, even when a large excess of dextrin was used. Implying that stabilization indicates inclusion and that autoxidation indicates non-included contamination, we never could obtain pure (stabilized) adducts directly from the mixture. Such crude preparations show high rates of autoxidation for which curve I in Fig. 1 is typical. Washing with ethanol or trimethylpentane was found unreliable for removal of excess lipid. By such treatment, the rate of autoxidation is lowered but at the same time part of the included moiety also is extracted. Reproducible stabilization can be achieved by distilling off the contaminating material although the distillation does not come to a complete halt at that point. Therefore these products do not represent the maximum molar ratio host:guest. In the stable adducts the ratios are between 2.3:1 and 3.6:1 for C_{18}-derivatives, for cinnamaldehyde it is close to 1:1, when the values are calculated for the dry preparations. The heat treatment renders the products very hygroscopic.

The adducts of dextrins do not release gas when kept under dry oxygen. In the presence of water considerable amounts of gas are given off in particular from samples dehydrated by heat. Most likely this is in conjunction with a rehydration process. Sometimes hydrated products exhibit stabilities even higher than identical samples when kept dry. This, however, is not a general rule.

Unsaturated fatty acids are the most convenient material to test for inclusion protection against oxygen. Some autoxidation of the β-dextrin–cinnamaldehyde adduct (Fig. 1, IV) is to be expected since it has a demonstrable vapor tension of aldehyde. Stabilization of vitamin A palmitate is very satisfactory in deoxycholic acid (Fig. 2, III). In β-dextrin the autoxidation of vitamin A alcohol and acetate could be cut down to $^1/_{10}$ to $^1/_{20}$ of the original. These results are not yet satisfactorily reproducible and preparative conditions must still be refined.

Acknowledgment.—The authors wish to thank Distillation Products Industries for the free supply of vitamin A and its derivatives which enabled us to study the stabilization of these compounds.

AUSTIN, MINNESOTA

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

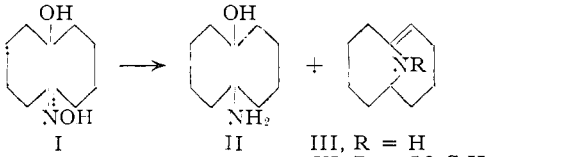
Proximity Effects. I. 6-Aminocyclodecanol and 11-Azabicyclo[4.4.1]-1-undecene from 6-Aminocyclodecanone

BY ARTHUR C. COPE, ROBERT J. COTTER[1] AND GEORGE G. ROLLER[2]

RECEIVED JANUARY 24, 1955

Reduction of 6-hydroxycyclodecanone oxime (I) with sodium and *n*-butyl alcohol has been found to yield a mixture of 6-aminocyclodecanol (II, 72%) and 11-azabicyclo[4.4.1]-1-undecene (III, 24%). Formation of the unsaturated secondary amine III is explained by the spatial proximity of the secondary alcohol and oximino groups of I. An intramolecular oxidation–reduction of the Meerwein–Ponndorf–Verley type is believed to result in partial conversion of I to 6-aminocyclodecanone (IV), which is converted to III by dehydration. The unsaturated amine III is of interest because it contains a double bond at the bridgehead of a heterocyclic [4.4.1]ring system. Evidence for the structure of III is provided by its ultraviolet and infrared spectra, by conversion to a benzenesulfonamide and phenylthiourea, by hydrolysis with hydrochloric acid to 6-aminocyclodecanone (IV, reconverted to III on heating), and by quantitative reduction to the saturated amine V. The structure of V was verified by degradation by the Hofmann exhaustive methylation procedure, and by an independent synthesis from 6-aminocyclodecanol.

This paper describes the reduction of 6-hydroxycyclodecanone oxime (I) to 6-aminocyclodecanol (II), required as an intermediate in the synthesis of *trans*-5-cyclodecen-1-ol.[3] When the oxime I was reduced with sodium and *n*-butyl alcohol, the unsaturated secondary amine 11-azabicyclo[4.4.1]-1-undecene (III) was formed as an unexpected by-product. Formation of the amine III from the oxime I and other unusual reactions described in this and the following paper are ascribed to "proximity effects," *i.e.*, to the fact that atoms located on opposite sides of medium-sized rings (ten-membered in this instance) are brought into close proximity by the geometric conformations of the rings.



I II III, R = H
VI, R = $SO_2C_6H_5$
VII, R = $C(NHC_6H_5)=S$

6-Hydroxycyclodecanone was prepared by the procedure described by Criegee,[4] as subsequently adapted to larger scale preparations,[5] with modifications in the procedure for oxidizing decalin and purifying *trans*-9-decalylhydroperoxide that are described in the Experimental part. Reaction of 6-hydroxycyclodecanone with hydroxylamine hydrochloride in pyridine and absolute ethanol formed the oxime I in 86–90% yield.

Hydrogenation of the oxime I in ethanol in the presence of W-2 Raney nickel[6] at room temperature

(1) American Cyanamid Co. Fellow, 1953–1954.

(2) Arthur D. Little Fellow, 1948–1949.

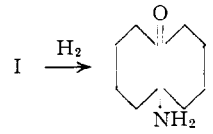
(3) A. C. Cope, R. J. Cotter and G. G. Roller, THIS JOURNAL, **77**, 3594 (1955).

(4) R. Criegee, *Ber.*, **77B**, 22, 722 (1944); R. Criegee and H. Dietrich, *Ann.*, **560**, 135 (1948); R. Criegee and W. Schnonenberg, *ibid.*, **560**, 141 (1948).

(5) A. C. Cope and G. Holzman, THIS JOURNAL, **72**, 3062 (1950).

(6) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).

and atmospheric pressure formed a mixture of 6-aminocyclodecanol (II) and a very high boiling basic compound believed to be the secondary amine, di-(6-hydroxycyclodecyl)-amine. In a hydrogenation of I in the presence of W-2 Raney nickel at 100–125 atmospheres and 85–90° in methanol saturated with ammonia (added to suppress the formation of the secondary amine), the product was a mixture of 6-aminocyclodecanol and 1,6-diaminocyclodecane. Displacement of the secondary hydroxyl group of I by an amino group to form 1,6-diaminocyclodecane at such a low temperature was unexpected, for the alkylation of ammonia or amines by alcohols in the presence of Raney nickel usually requires temperatures of 160–170°.[7] In view of the facile intramolecular hydrogen transfer in the presence of palladium resulting in partial conversion of *trans*-5-cyclodecen-1-ol into cyclodecanone that is described in the following paper,[8] a probable explanation of the formation of 1,6-diaminocyclodecane at low temperatures is the following. During hydrogenation of the oxime I, intramolecular hydrogen transfer occurs to some extent, resulting in dehydrogenation of the secondary alcohol group of I to a carbonyl group, with formation of some 6-aminocyclodecanone (IV).



IV

V, R = H
VIII, R = $SO_2C_6H_5$
IX, R = CH_3
X, R = $(CH_3)_2I$

Reductive amination of IV would be expected to occur under mild conditions, and is believed to account for the formation of 1,6-diaminocyclodecane. The intramolecular reductive alkylation product V that could be formed by reduction of IV was not isolated, but may have been present.

Catalytic hydrogenation of the oxime I in the presence of the very active W-7 Raney nickel catalyst[8] at room temperature and atmospheric pressure formed II and smaller amounts of the corresponding secondary amine than were produced with the less active catalyst. A still better procedure was the hydrogenation of I in the presence of W-7 Raney nickel at room temperature and pressures of 100–125 atmospheres, which yielded 68% of a mixture of the geometric isomers of II. 6-Aminocyclodecanol also was prepared in 66% yield by catalytic reduction of the dioxime of the dimeric peroxide of 1,6-cyclodecanedione (obtained by ozonization of 9,10-octalin).[9]

Reduction of 6-hydroxycyclodecanone oxime with sodium and *n*-butyl alcohol proved to be the most satisfactory procedure, and formed a mixture of the *cis* and *trans* isomers of II in 72% yield, together with 24% of 11-azabicyclo[4.4.1]-1-undecene (III). The mixture of 6-aminocyclodecanol isomers, m.p. 70–97°, was separated into a pure high-melting isomer, m.p. 108.2–109.6°, and an impure low-melting isomer, m.p. 68.6–74.2°, by fractional crystallization from acetonitrile.

Formation of the unsaturated secondary amine 11-azabicyclo[4.4.1]-1-undecene (III) by reduction of the oxime I was unexpected. The evidence upon which the structure assigned to this compound is based is as follows. The amine formed an alkali-insoluble benzenesulfonamide VI, and reacted with phenyl isothiocyanate to form a phenylthiourea VII. Reduction of III in the presence of a palladium catalyst resulted in absorption of 100% of one molar equivalent of hydrogen. The reduction product was shown to be 11-azabicyclo[4.4.1]undecane (V) by analysis and preparation of an alkali-insoluble benzenesulfonamide VIII, which was identical (mixed m.p.) with a sample prepared from V obtained by heating 6-aminocyclodecanol with Raney nickel in boiling decalin. The carbon ring present in V also was established by Hofmann exhaustive methylation. Decomposition of the quaternary base derived from the methiodide X resulted in formation of a mixture of the tertiary amine IX (from elimination of methanol) and 5-cyclodecen-1-yldimethylamine (XI) which was isolated as the picrate and identified by hydrogenation to cyclodecyldimethylamine. The picrate of cyclodecyldimethylamine from this source was identical with an authentic sample,[10] m.p. 145.2–146.8°.

XI

Hydrolysis of 11-azabicyclo[4.4.1]-1-undecene (III) with boiling 10% hydrochloric acid formed 6-aminocyclodecanone (IV), a viscous liquid that was partially dehydrated upon distillation under reduced pressure, reforming III. The aminoketone IV was shown to be different from III by its greater viscosity and higher boiling point, by the presence of a carbonyl band in its infrared spectrum, and by conversion into a benzenesulfonamide (different from the benzenesulfonamide of III) which reacted with semicarbazide to form a semicarbazone.

These data are consistent with the structure assigned to III or the alternate Schiff base formula XII. The observed formation of a benzenesulfon-

XII

amide and phenylthiourea from the compound would require a tautomeric shift of hydrogen to yield the derivatives VI and VII if formula XII were correct. The ultraviolet absorption spectrum of the unsaturated amine (λ_{max} 226 mμ, ϵ 5,080 in cyclohexane) is consistent with the vinylamine[11] formula III, but absorption at this long wave length also might be explained by the strain inherent in the Schiff base structure XII. Isomers with the double bond in other positions can be excluded on the basis of the observed ultraviolet maximum, because they would be expected to have the

(7) H. Adkins and C. F. Winans, THIS JOURNAL, **54**, 306 (1932).

(8) H. Adkins and H. R. Billica, *ibid.*, **70**, 695 (1948); *Org. Syntheses*, **29**, 28 (1949).

(9) R. Criegee and G. Wenner, *Ann.*, **564**, 9 (1949).

(10) A. C. Cope, D. C. McLean and N. A. Nelson, THIS JOURNAL, **77**, 1628 (1955).

(11) See K. Bowden, E. A. Braude, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 48 (1946).

absorption characteristic of an isolated double bond ($\lambda_{max} \sim 185$ mμ, ϵ 8,000). Final proof that the vinylamine structure III is correct was obtained from the infrared spectrum of the compound (Fig. 1). The spectrum shows both double bond absorption at 5.96 μ (1680 cm.$^{-1}$) (reasonable for either a strained carbon–carbon double bond[12] or a carbon–nitrogen double bond[13]), and N–H stretching absorption at 3.01 μ (3300 cm.$^{-1}$). The remote possibility that the band at 3.01 μ was an overtone of the band in the double bond region was excluded by treating the compound with deuterium oxide and sodium carbonate; the product was shown to be the 11-deutero derivative of III by the absence of N–H absorption at 3.01 μ and the presence of N–D absorption at 4.03 μ (2400 cm.$^{-1}$) in its infrared spectrum (Fig. 1). The possibility that the vinylamine III contains some of the isomer XII (which could be in tautomeric equilibrium with III) is not rigorously excluded.

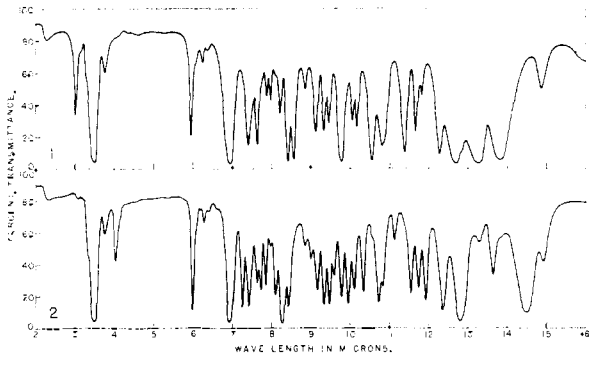
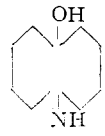


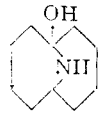
Fig. 1.—Infrared absorption spectra: curve 1, 11-azabicyclo[4.4.1]-1-undecene (III); curve 2, 11-deuterio-11-azabicyclo[4.4.1]-1-undecene, both as pure liquids in a 0.032-mm. cell.

The formation of 11-azabicyclo[4.4.1]-1-undecene (III) reported in this paper and the isolation of the corresponding compound with oxygen in place of NH in formula III (1,6-epoxy-1-cyclodecene[14]) are of interest, for they show that these heterocyclic [4.4.1]ring systems can exist with a double bond at a bridgehead position. Bredt's rule[15] excludes the location of double bonds at bridgehead positions in compounds containing rings that are too small to accommodate the strain that is produced. The double bond in III clearly is strained, as shown by the carbon–carbon double bond infrared maximum cited previously. The route by which III is formed in the reduction of I with sodium and *n*-butyl alcohol probably involves an intramolecular oxidation–reduction of I (or the corresponding imine XIII which could be formed from I as the first intermediate product of reduction) of the Meerwein–Ponndorf–Verley type. Such a process would be favored by the spatial proximity of the secondary alcohol and oximino or imino groups, and would result in formation of 6-aminocyclodecanone (IV),



XIII

which as mentioned earlier yields III by dehydration on heating. A likely intermediate in the process is the bicyclic compound XIV, which probably is a tautomer of IV, for the infrared spectrum of the compound shows weaker carbonyl absorption than would be expected on the basis of the aminoketone formula IV.



XIV

Experimental[16]

trans-9-**Decalyl Hydroperoxide.**—Decalin was oxidized by the procedure previously described,[5] with the following modifications. The temperature of the decalin was kept at 120–130° during the oxidation, in order to minimize thermal decomposition of the peroxides formed. The final portion of sodium hydroxide solution used to wash the oxidized decalin was allowed to stand in contact with it for 5–12 hours. This prolonged contact removed additional colored material and a liquid peroxide that otherwise interfered with crystallization of the product. After further washing with ethylene glycol and isolation by chromatography on silica gel and crystallization as previously described, *trans*-9-decalyl hydroperoxide was isolated in a maximum yield of 141 g. (3.5%) from 4 l. of decalin.

6-Hydroxycyclodecanone Oxime (I).—6-Hydroxycyclodecanone was prepared from *trans*-9-decalyl hydroperoxide by the method described previously[4,5] in the same yield.[5] A mixture of 27.5 g. of 6-hydroxycyclodecanone, 27.5 g. of hydroxylamine hydrochloride, 135 ml. of dry pyridine and 135 ml. of absolute ethanol was heated under reflux for 2 hours. The solvents were distilled under reduced pressure, and the residue was poured into ice-water. The 6-hydroxycyclodecanone oxime was collected on a filter, washed three times with ice-water, and air-dried. The yield was 25.7 g. (86%), m.p. 110–112° (lit.[4] m.p. 111–112°).

6-Aminocyclodecanol (II). Hydrogenation of 6-Hydroxycyclodecanone Oxime.—Of several catalytic reduction procedures that were investigated, the following was found to give the highest yield of II. 6-Hydroxycyclodecanone oxime (2.5 g.), 15 ml. of dry methanol and one-half teaspoonful of freshly prepared W-7 Raney nickel catalyst[8] were placed in a 42-ml. steel hydrogenation bomb, and the oxime was hydrogenated at room temperature and 1800 p.s.i. in a period of 2 hours. The solid product was isolated in a yield of 1.57 g. (68%) by short-path distillation at 0.5–1.0 mm. with a heating block temperature of 150–200°, after the material boiling below 126° (0.8 mm.) had been removed by distillation. The solid distillate was analytically pure 6-aminocyclodecanol (a mixture of *cis* and *trans* isomers), m.p. 72–75.5°.

In a similar reduction of the oxime I in methanol saturated with ammonia in the presence of W-2 Raney nickel at 85–90°, the product (1.93 g.) was a mixture of 6-aminocyclodecanol and 1,6-diaminocyclodecane (Calcd. for $C_{10}H_{21}NO$: N, 8.18; calcd. for $C_{10}H_{22}N_2$: N, 16.45. Found: N, 11.01). The mixture was treated with an excess of methyl iodide and sodium bicarbonate in methanol for 45 hours at room temperature and 3 hours under reflux, and gave a mixture of 6-dimethylaminocyclodecanol methiodide plus a less soluble solid that was recrystallized from methanol and identified as 1,6-bis-(dimethylamino)-cyclodecane dimethiodide by its melting point (m.p. 308–309°, lit.[17] 305–330°) and analysis.

(12) "The Infra-red Spectra of Complex Molecules," L. J. Bellamy, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 31–46.

(13) E. Bergmann, E. Zimkin and S. Pinchas, *Rec. trav. chim.*, **71**, 168 (1952).

(14) P. D. Bartlett and J. L. Kice, THIS JOURNAL, **75**, 5591 (1953).

(15) F. S. Fawcett, *Chem. Revs.*, **47**, 219 (1950).

(16) Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses. Infrared spectra were determined with a Baird double beam recording spectrometer, model B, with a sodium chloride prism.

(17) P. A. Plattner and J. Hulstkamp, *Helv. Chim. Acta*, **27**, 211, 220 (1944).

Anal. Calcd. for $C_{16}H_{36}N_2I_2$: C, 37.66; H, 7.11; N, 5.49; I, 49.74. Found: C, 37.85; H, 7.09; N, 5.77 I, 49.53.

Hydrogenation of the Dioxime of 1,6-Cyclodecanedione Dimeric Peroxide.—The dioxime[9] (1.35 g.), 15 ml. of dry methanol and one-half teaspoonful of W-7 Raney nickel[8] were placed in a 42-ml. steel bomb and shaken with hydrogen at 50° and 1950 p.s.i. until no further drop in pressure occurred (8 hours). The product was isolated by distillation through a semi-micro column, and amounted to 0.72 g. (66%) of a mixture of the *cis* and *trans* isomers of II, b.p. 116–125° (0.3 mm.), which solidified and melted at 76–82°.

Reduction of 6-Hydroxycyclodecanone Oxime with Sodium and *n*-Butyl Alcohol.—A solution of 19.2 g. of 6-hydroxycyclodecanone oxime in 450 ml. of dry *n*-butyl alcohol was stirred and heated under reflux, and small pieces of sodium totalling 25 g. were added during a period of 1.5 hours, followed by heating and stirring for an additional 0.5 hour. The mixture was cooled, poured into 300 ml. of 10% sodium hydroxide solution, and the organic material was extracted with four 250-ml. portions of ether. The combined extracts were dried over sodium sulfate, concentrated, and the *n*-butyl alcohol was distilled under reduced pressure through a Vigreux column. The residue was fractionated with a semi-micro column, and yielded as a low-boiling fraction 3.75 g. (24%) of 11-azabicyclo[4.4.1]-1-undecene (III), b.p. 79–81° (3 mm.), $n^{25}D$ 1.5139. A redistilled sample with b.p. 79–79.5° (3 mm.) was analyzed. Studies upon which the structure of III is based are described below.

Anal. Calcd. for $C_{10}H_{17}N$: C, 79.40; H, 11.33; N, 9.26. Found: C, 79.21; H, 11.33; N, 9.52.

Continuation of the distillation yielded as a higher boiling fraction 12.65 g. (72%) of 6-aminocyclodecanol (II), b.p. 120° (0.2 mm.), m.p. 70–97° (a mixture of *cis* and *trans* isomers).

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.11; H, 12.36; N; 8.18; neut. equiv., 171. Found: C, 70.19; H, 12.36, N, 8.03; neut. equiv., 173.

A 3.5-g. sample of 6-aminocyclodecanol (m.p. 70–97°) was recrystallized six times from acetonitrile. The solutions were cooled slowly to room temperature in each crystallization. Subsequent sublimation at 1 mm. with a heating block temperature of 120° yielded 0.95 g. of the high-melting isomer of II, m.p. 108.2–109.6°.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.11; H, 12.36; N, 8.18; neut. equiv., 171. Found: C, 70.25; H, 12.35; N, 8.23; neut. equiv., 170.

After removing as much of the high-melting isomer as possible from the acetonitrile mother liquors by crystallization, sublimation of the residue at 0.2 mm. with a heating block temperature of 90° yielded 0.4 g. of the impure low-melting isomer of II, m.p. 68.8–74.2°.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.11; H, 12.36; N, 8.18; neut. equiv., 171. Found: C, 70.62; H, 12.31; N, 7.92; neut. equiv., 178.

Derivatives of 11-Azabicyclo[4.4.1]-1-undecene (III).—The benzenesulfonyl derivative VI was prepared by shaking a mixture of 0.39 g. of III, 0.84 g. of benzenesulfonyl chloride and 9 ml. of 10% sodium hydroxide at room temperature for 10 minutes. The solid that precipitated was recrystallized from 50% aqueous ethanol, yielding 0.14 g. of the benzenesulfonamide VI. An analytical sample was recrystallized again from the same solvent; m.p. 144–144.6°.

Anal. Calcd. for $C_{16}H_{21}NO_2S$: C, 66.00; H, 7.27; N, 4.81. Found: C, 66.10; H, 7.57; N, 5.12.

11-Phenylthiocarbamoyl-11-azabicyclo[4.4.1]-1-undecene (VII) was prepared by heating a sample of the amine III with phenyl isothiocyanate at 100° for 10–15 minutes, and was recrystallized from aqueous ethanol to a constant melting point of 150–152°.

Anal. Calcd. for $C_{17}H_{22}N_2S$: C, 71.28; H, 7.75; N, 9.78. Found: C, 71.01; H, 7.72; N, 9.74.

11-Azabicyclo[4.4.1]undecane (V).—A solution of 2.09 g. of the unsaturated amine III in 60 ml. of dry methanol was hydrogenated in the presence of 1.0 g. of 10% palladium–on–Norit. The reduction ceased after 100% of one molar equivalent of hydrogen had been absorbed in 1 hour. After separation of the catalyst, the filtrate was acidified with hydrochloric acid, concentrated and made basic with sodium hydroxide. The saturated amine V was extracted with ether, and the extracts were dried over sodium sulfate and concentrated. Distillation of the residue through a semi-micro column yielded 0.60 g. (30%) of V, b.p. 72–73° (3.5 mm.), $n^{25}D$ 1.4999. Optimum conditions for isolating the amine were not determined.

Anal. Calcd. for $C_{10}H_{19}N$: C, 78.36; H, 12.50; N, 9.14. Found: C, 78.42; H, 12.52; N, 9.04.

Both amines III and V formed white, water-insoluble hydrates when added to water.

11-Benzenesulfonyl-11-azabicyclo[4.4.1]undecane (VIII) was prepared by shaking 0.13 g. of the amine V with an excess of benzenesulfonyl chloride and 10% aqueous sodium hydroxide in a yield of 0.18 g. The alkali-insoluble derivative was recrystallized from ethanol; m.p. 171–172.5°.

Anal. Calcd. for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.71; H, 7.75; N, 4.62.

An authentic sample of 11-azabicyclo[4.4.1]undecane (V) was prepared by heating a solution of 1.45 g. of 6-aminocyclodecanol in 6 ml. of decalin under reflux with one-half teaspoonful of Raney nickel for 4 hours. After separating the nickel, the amine was extracted with dilute hydrochloric acid, liberated with excess sodium hydroxide, and re-extracted with ether. The extracts were dried over sodium sulfate and distilled, and yielded 0.25 g. (19%) of V, b.p. 69–71° (2.7 mm.), $n^{25}D$ 1.5008. Optimum conditions for preparing V by this method were not determined. The benzenesulfonyl derivative of V from this source melted at 170.5–172°, and was identical (mixed m.p.) with the derivative prepared from V obtained by reduction of III.

11-Methyl-11-azabicyclo[4.4.1]undecane (IX).—A solution of 3.01 g. of the unsaturated amine III in 25 ml. of dry methanol was hydrogenated in the presence of 1.0 g. of 10% palladium-on-Norit. Hydrogen absorption stopped after 98% of one molar equivalent had been taken up, and the catalyst was separated and the filtrate concentrated. The residual saturated amine V was methylated by heating under gentle reflux with 5.3 g. of 87% formic acid and 5.0 g. of 37% formalin for 11.5 hours after the initial exothermic reaction ended. The solution was cooled, treated with 15 ml. of 3 *N* hydrochloric acid, and concentrated under reduced pressure. The tertiary amine IX was liberated by addition of 25 ml. of 15% sodium hydroxide, and extracted with three 25-ml. portions of ether. The extracts were dried over sodium sulfate, concentrated, and the residue was distilled through a semi-micro column, yielding 2.33 g. (71%) of IX, b.p. 78–79° (3.5 mm.), $n^{25}D$ 1.4947. The tertiary amine IX was insoluble in water and did not form a solid hydrate, but formed a carbonate upon exposure to the air.

Anal. Calcd. for $C_{11}H_{21}N$: C, 78.97; H, 12.65; N, 8.37. Found: C, 79.21; H, 12.89; N, 8.44.

11-Methyl-11-azabicyclo[4.4.1]undecane picrate was prepared from 0.11 g. of IX and picric acid in ethanol in a yield of 0.21 g. (81%). An analytical sample that was recrystallized from ethanol melted at 250–251.5° (dec., sample introduced at 246°).

Anal. Calcd. for $C_{17}H_{24}N_4O_7$: C, 51.50; H, 6.10; N, 14.14. Found: C, 51.62; H, 6.22; N, 14.27.

11-Methyl-11-azabicyclo[4.4.1]undecane methiodide (X) was prepared by heating a solution of 2.1 g. of IX and 9.2 g. of methyl iodide in 25 ml. of dry methanol under reflux for 50 hours. An additional 5.0 g. of methyl iodide was added after 19 hours. Distillation of the solvent left a quantitative yield of the methiodide X, which was purified by precipitation from methanol by addition of ethyl acetate. The yield of the pure methiodide was 3.55 g. (92%), m.p. 285–286.5° (dec., sample introduced at 270°).

Anal. Calcd. for $C_{12}H_{24}IN$: C, 46.60; H, 7.82; N, 4.53; I, 41.04. Found: C, 46.67; H, 7.91; N, 4.72; I, 41.14.

The yield of the methiodide X was reduced markedly unless the reaction time was long, and was only 12% after 3 hours.

Decomposition of 11-Methyl-11-azabicyclo[4.4.1]undecane Methohydroxide.—A solution of 2.94 g. of the methiodide X in 25 ml. of dry methanol was digested at room temperature for several hours with the silver hydroxide freshly precipitated from 8.5 g. of silver nitrate. The mixture was filtered and the filtrate, which gave a negative test

for iodide ion, was concentrated under reduced pressure. The residue was heated for 4 hours at 0.8 mm.; decomposition of the quaternary base began at 70°, and the temperature gradually was raised to 125°. The distillate and residue were combined and treated with aqueous sodium hydroxide. The product was extracted with ether and distilled; the yield was 0.63 g. (37%) of a mixture of amines, b.p. 74–82° (2.5 mm.), $n^{25}D$ 1.4914–1.4920. Analyses and the isolation of the two picrates described below showed that the mixture contained the normal product formed by Hofmann exhaustive methylation, 5-cyclodecen-1-yldimethylamine (XI). The tertiary amine IX formed by elimination of methanol from the quaternary base is believed to be the other component of the mixture, but it was not isolated.

5-Cyclodecen-1-yldimethylamine picrate was prepared from the mixture of amines described above and picric acid in ethanol and purified by recrystallization from ethanol to a constant melting point of 140–141.8°.

Anal. Calcd. for $C_{18}H_{26}N_4O_7$: C, 52.67; H, 6.39; N, 13.65. Found: C, 52.70, H, 6.59; N, 13.55.

Cyclodecyldimethylamine Picrate.—A solution of 0.326 g. of the mixture of amines described above in 5 ml. of glacial acetic acid was hydrogenated in the presence of 0.125 g. of prereduced platinum oxide. Absorption of hydrogen amounted to 67% of one molar equivalent, indicating that the mixture contained XI and IX in an approximate ratio of 2:1. Addition of picric acid in ethanol and recrystallization of the picrate to constant melting point from the same solvent gave cyclodecyldimethylamine picrate, m.p. 145.8–147.4°, which did not depress the m.p. of an authentic sample prepared from cyclodecanone.[10]

6-Aminocyclodecanone (IV).—A solution of 0.338 g. of 11-azabicyclo[4.4.1]-1-undecene in 10 ml. of 10% hydrochloric acid was heated under reflux for 1 hour, cooled, made basic with sodium hydroxide and extracted continuously with ether overnight. The extract was dried over sodium sulfate, concentrated, and purified by a short-path distillation at 0.5 mm. with a heating block temperature of 100°. The viscous distillate was a mixture of the aminoketone IV with the unsaturated amine III formed by partial dehydration during distillation. Calcd. for $C_{10}H_{19}NO$: C, 70.96; H, 11.32. Found: C, 72.95; H, 11.28. Another short-path distillation of the distillate completed the dehydration and yielded 0.14 g. of III, $n^{25}D$ 1.5153. The identity of III from this source was established by comparing its infrared spectrum with the spectrum of a sample formed as a by-product in the reduction of 6-hydroxycyclodecanone oxime with sodium and *n*-butyl alcohol.

6-Aminocyclodecanone Benzenesulfonamide.—A solution of 0.26 g. of III in 10 ml. of 10% hydrochloric acid was heated under reflux for 1 hour and then concentrated to dryness. Benzenesulfonyl chloride (0.58 g.) and 8 ml. of 10% aqueous sodium hydroxide were added to the residue, and the mixture was shaken for 15 minutes. Water was added until the solid dissolved, and the basic solution was acidified with hydrochloric acid. The semi-solid which precipitated was treated with decolorizing carbon in ethanol, and recrystallized three times from absolute ethanol to a constant melting point of 93.6–94.6°. The yield of the benzenesulfonamide was 86 mg.

Anal. Calcd. for $C_{16}H_{24}NO_3S$: C, 62.11; H, 7.49; N, 4.53. Found: C, 61.81; H, 7.53; N, 4.62.

The semicarbazone of 6-aminocyclodecanone benzenesulfonamide was prepared by heating a solution of 56 mg. of the sulfonamide, 27 mg. of semicarbazide hydrochloride and 28 mg. of sodium acetate in aqueous ethanol on a steam-bath for 15 minutes. The crystals of the semicarbazone that separated on cooling were recrystallized three times from aqueous ethanol, and melted at 171.4–173° dec.

Anal. Calcd. for $C_{17}H_{26}N_4O_3S$: C, 55.70; H, 7.15; N, 15.30. Found: C, 55.70; H, 7.22; N, 15.24.

11-Deuterio-11-azabicyclo[4.4.1]-1-undecene.—A 0.32-g. sample of III was added to 5 ml. of 99.5% deuterium oxide which had been made basic (*p*H approximately 11) with a small amount of anhydrous sodium carbonate. The mixture was shaken at room temperature for 7 hours and then the amine was extracted continuously with dry ether overnight. The extract was dried over sodium sulfate, concentrated, and the residue was purified by short-path distillation at 10 mm. The infrared spectrum of the 11-deuterio compound is shown in Fig. 1. In a control experiment, the amine III was recovered unchanged when it was subjected to the conditions described above using water in place of deuterium oxide.

CAMBRIDGE, MASSACHUSETTS

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

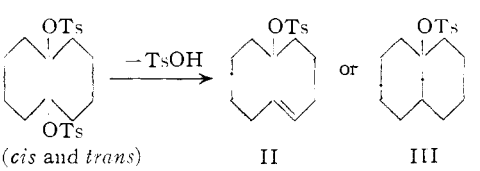
Proximity Effects. II. 1,9- and *cis*-1,2-Octalin from *trans*-5-Cyclodecen-1-yl *p*-Toluenesulfonate

BY ARTHUR C. COPE, ROBERT J. COTTER[1] AND GEORGE G. ROLLER[2]

RECEIVED JANUARY 24, 1955

trans-5-Cyclodecen-1-ol (VI) has been prepared from 6-aminocyclodecanol by the Hofmann exhaustive methylation procedure. Hydrogenation of the unsaturated alcohol VI in the presence of platinum yielded cyclodecanol, while with a palladium catalyst a mixture of cyclodecanol and cyclodecanone was produced, with hydrogen transfer from the carbinol group to the double bond of VI forming the saturated ketone. *trans*-5-Cyclodecen-1-yl *p*-toluenesulfonate (II) was heated with diethylaniline, and formed a mixture of *cis*-1,2- and 1,9-octalins, identified by their infrared spectra and by conversion to crystalline *cis*-glycols with osmium tetroxide. The occurrence of 1,6-bridging forming the octalin ring system rather than a double bond on elimination of *p*-toluenesulfonic acid from the tosylate II is explained by the spatial proximity of the double bond to the tosylate group, and is similar in some respects to the *iso*-steroid rearrangement.

Both stereoisomeric 1,6-cyclodecanediol di-*p*-toluenesulfonates have been shown to form mixtures of 1,9- and 9,10-octalin rather than cyclodecadienes on heating with diethylaniline.[3] If the elimination of *p*-toluenesulfonic acid from the ditosylates I occurs in two steps, the intermediate would be 5-cyclodecen-1-yl *p*-toluenesulfonate (II, *cis* or *trans*) or 9-decalyl *p*-toluenesulfonate (III, *cis* or *trans*), the first formed by a normal 1,2- and the second by 1,6-elimination of *p*-toluenesulfonic acid.



I (*cis* and *trans*) II III

In this investigation *trans*-5-cyclodecen-1-ol (VI) has been prepared, and the reaction of its *p*-toluenesulfonate (II) with diethylaniline has been studied. A mixture of the *cis* and *trans* isomers of 6-aminocyclodecanol, prepared by reduction of 6-hydroxycyclodecanone oxime,[4] was converted to a mixture

(1) American Cyanamid Co. Fellow, 1953–1954.

(2) Arthur D. Little Fellow, 1948–1949.

(3) A. C. Cope and G. Holzman, THIS JOURNAL, **72**, 3062 (1950).

(4) A. C. Cope, R. J. Cotter and G. G. Roller, *ibid.*, **77**, 3590 (1955).