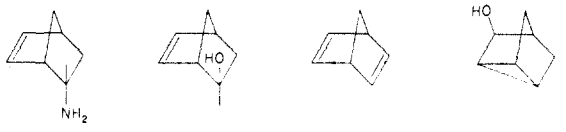
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

endo-5-Aminobicyclo[2,2,1]heptene-2

BY WILLIAM E. PARHAM, WILLIAM T. HUNTER[1] AND ROBERTA HANSON

endo-5-Aminobicyclo[2,2,1]heptene-2 has been synthesized by two methods and the reaction of this amine with nitrous acid has been investigated. Some reactions of 2-phenyl-3-nitrobicyclo-[2,2,1]-heptene-5 are also described.

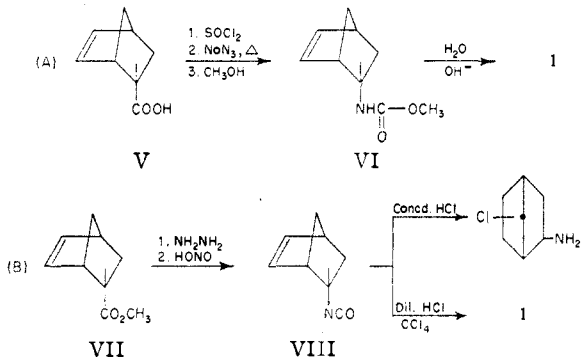
This work was directed primarily to a study of the reaction of nitrous acid with the hitherto unknown *endo*-5-aminobicyclo[2,2,1]heptene-2 (I). At the time this work was initiated little was known relative to reactions of compounds containing this bicycloheptene structure, and the expected prod-



I II III IV

uct(s) of this reaction were *exo*-dehydronorborneol (II), bicyclo-[2,2,1]heptadiene-2,5 (III) or 3-hydroxynortricyclene[2] (IV).

The amine (I) was prepared by two different procedures. Procedure A, a modification of the Curtius reaction involving the alkaline hydrolysis



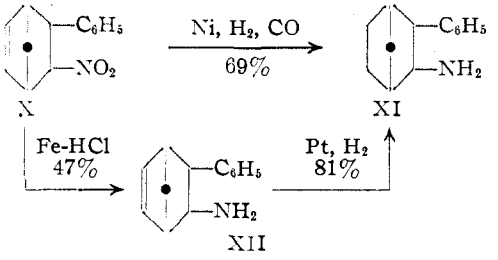
V VI VII VIII

of the corresponding carbamate, was employed in order to avoid contact of the intermediates with mineral acid, for initial attempts to hydrolyze VIII to I with hydrochloric acid resulted only in a chloramine (IX). A shorter synthesis (procedure B), resulting in a better yield of the desired amine, was developed when it was learned that the isocyanate (VIII) could be hydrolyzed to I without the formation of the chloroamine (IX), when a two-phase system involving carbon tetrachloride and water containing a molar equivalent of hydrochloric acid was employed for its hydrolysis.

endo-5-Aminobicyclo[2,2,1]heptene-2 was obtained as a colorless liquid which solidified as it distilled. The compound was quite volatile, hydroscopic, and carbodioxiphilic; consequently, entirely satisfactory analytical values for carbon and hydrogen were not obtained on the free base. The amine was characterized as its acetyl and phenylthiourea derivatives, and its structure established by its conversion into the known *endo*-5-acetylaminobicyclo[2,2,1]heptane.[3]

The action of cold nitrous acid on *endo*-5-aminobicyclo[2,2,1]heptene-2 (I) resulted in a white solid alcohol (60% yield), which melted at 99–102° after sublimation. This alcohol was identified as 3-hydroxynortricyclene by a comparison of its phenylurethan and *p*-phenylazobenzoate derivatives with those obtained from an authentic sample of 3-hydroxynortricyclene.[2a] Although it has not been established with certainty whether the decomposition of the nitrous acid salts of primary aliphatic amines occurs by an ionic or free radical mechanism, the ionic mechanism is favored and the rearranged products accompanying this reaction can be accounted for by assuming that the first step involves formation of a carbonium ion. Thus, the mechanism postulated by Roberts[2a] for the hydrolysis of 5-chlorobicyclo[2,2,1]heptene-2 can be extended to this reaction to give a satisfactory explanation of the rearrangement involved.

Incidental to this work some reactions of 2-phenyl-3-nitrobicyclo[2,2,1]heptene-5 (X) were investigated. Several unsuccessful attempts were made to hydrolyze this nitro compound to 2-phenyldehydronorcamphor by the action of cold acid on the sodium salt of X; however, no ketonic material was isolated. The reduction of X was studied, and the results are summarized by the following equations. 2-Phenyl-3-amino[2,2,1]-heptane (XI) formed a benzenesulfonamide, which



was insoluble in alkali. That no rearrangement to a secondary amine occurred during the reduction of X was established by subjecting XI to a Hofmann degradation, from which trimethylamine was isolated.

Experimental

***endo*-5-Carboxybicyclo[2,2,1]heptene-2 (V).**—The *p*-bromophenacyl ester of V[4] was prepared and recrystallized from ethanol, m.p. 88.5–90°.

Anal. Calcd. for $C_{16}H_{15}O_3Br$: C, 57.33; H, 4.51. Found: C, 57.54; H, 4.74.

The Acid Chloride of *endo*-5-Carboxybicyclo[2,2,1]-heptene-2. A.—The acid chloride (b.p. 80–82° (15–17 mm.), 123 g., 90% yield) was prepared from the acid (122 g.) in chloroform (400 ml.) by dropwise action of thionyl chloride (116 g.) at 45°. The amide, prepared from the

(1) From the Ph.D. Thesis of William T. Hunter, 1951.

(2) *Cf.* (a) J. D. Roberts, E. R. Trumbull, W. Bennett and R. Armstrong, THIS JOURNAL, **72**, 3116 (1950), and (b) J. D. Roberts, W. Bennett and R. Armstrong, *ibid.*, **72**, 3329 (1950), for a detailed discussion of the relationship between the functional groups in this system to those in the *i*-steroids.

(3) K. Alder and G. Stein, *Ann.*, **514**, 224 (1934).

(4) O. Diels and K. Alder, *Ann.*, **460**, 98 (1928).

chloride in the usual way and crystallized from water, melted at 181–183°.

Anal. Calcd. for $C_8H_{11}ON$: C, 70.04; H, 8.08. Found: C, 69.89; H, 8.10.

B.—When the reaction was carried out in benzene, using slightly more than one equivalent of pyridine, the chloride was obtained in 55% yield.

***endo*-Bicyclo[2,2,1]heptene-2 Methyl Carbamate-5 (VI).**—The carbamate (b.p. 98–100° (45 mm.), 45 g., 42% yield) was obtained from a solution of sodium azide (52 g., 0.80 mole), dry acetone (1 l.) and the acid chloride of V, which had been maintained at 45–55° with constant stirring for 16 hours. Vigorous heating was required toward the end of the distillation to distil the isocyanate from the polymeric material which formed the major part of the reaction product. The isocyanate (45 g.) was treated immediately with 100 ml. of dry methanol and the mixture heated at the reflux temperature for 24 hours. The solution was concentrated and the white solid carbamate (m.p. 67–75°, 53.5 g., 96% yield) was collected. A portion of the carbamate was purified by crystallization from aqueous methanol, m.p. 90–92°.

Anal. Calcd. for $C_9H_{13}O_2N$: C, 64.65; H, 7.84. Found: C, 64.89; H, 7.73.

***endo*-5-Aminobicyclo[2,2,1]heptene-2 (I) (Procedure A).**—Twenty grams (0.12 mole) of crude VI (m.p. 68–76°) was added to 100 ml. of 20% aqueous sodium hydroxide containing 10 ml. of methanol, and the resulting mixture was heated on a steam-bath for 27 hours. The white solid (5.8 g.) which precipitated from the solution during the course of the reaction was collected and recrystallized from aqueous methanol and then from methanol. This material (40% yield) melted at 235–236° with decomposition, and had the composition calculated for *sym*-5-bicyclo[2,2,1]heptene-2-urea.

Anal. Calcd. for $C_{15}H_{20}ON_2$: C, 73.73; H, 8.25. Found: C, 73.78; H, 8.34.

The filtrate from which the symmetrical urea was removed was extracted with ether for 24 hours using a continuous extractor. The ethereal solution was dried and the ether was removed. The amine (I) (4.4 g., 30%) was collected at 150–160° and solidified in the water condenser.

Anal. Calcd. for $C_7H_{11}N$: C, 77.01; H, 10.16. Found: C, 76.20; H, 11.10.

The white solid amine was quite volatile and reacted rapidly with carbon dioxide and water in the atmosphere; consequently, entirely satisfactory analytical values for carbon and hydrogen could not be obtained on the free base.

The acetyl derivative of I was prepared in the usual way using benzene as a solvent. The product was water soluble, and most of the amide was recovered by extraction of the alkaline wash solution with chloroform. The crude product (m.p. 88–92°, 100% yield) was decolorized with charcoal and recrystallized from petroleum ether, m.p. 93.5–95°.

Anal. Calcd. for $C_9H_{13}ON$: C, 71.49; H, 8.66. Found: C, 71.63; H, 8.65.

The Phenylthiourea Derivative of I.—The crude derivative (m.p. 160–162°) was recrystallized from aqueous ethanol to give white crystals melting at 162–163°.

Anal. Calcd. for $C_{14}H_{16}N_2S$: C, 68.81; H, 6.60. Found: C, 68.63; H, 6.99.

Evidence for the configuration of *endo*-5-aminobicyclo-[2,2,1]heptene-2 was obtained by a study of the hydrogenation of its acetyl derivative using platinum oxide catalyst in ethanol solvent. The hydrogenation was effected at room temperature and atmospheric pressure, and the hydrogen consumed corresponded to the utilization of one mole of hydrogen per mole of amide. The pale yellow product was dissolved in petroleum ether (b.p. 90–100°), decolorized with charcoal, and crystallized from petroleum ether to give a white crystalline product melting at 123–124°. Alder and Stein[3] report a melting point of 124° for *endo*-5-acetylaminobicyclo[2,2,1]heptene and a melting point of 139° for the *exo* isomer.

The Hydrazide of *endo*-5-Carboxybicyclo[2,2,1]heptene-2.—The crude hydrazide (m.p. 60–84°, 60–99% yield) was obtained by heating a solution of *endo*-5-carbomethoxy-[2,2,1]heptene-2 (VII)[5] (112 g., 0.74 mole), hydrazine hydrate (113 ml.) and ethanol (180 ml.) at the reflux temperature for six to twelve hours. The hydrazide precipitated from the cooled reaction mixture upon the addition of cold water. An analytical sample was prepared in the following manner: A sample of the hydrazide was dissolved in water containing an equivalent amount of hydrochloric acid, and the resulting solution was extracted with chloroform. The aqueous solution was then made just neutral by the addition of aqueous potassium hydroxide and the precipitated hydrazide was recrystallized three times from water. The product melted at 68–76° when allowed to dry in air, and at 82–87° when dried *in vacuo* over phosphorus pentoxide.

Anal. Calcd. for $C_8H_{12}N_2O$: C, 63.15; H, 7.95. Found: C, 63.08; H, 8.27.

The benzenesulfonyl derivative of the hydrazide was recrystallized from ethanol to give white crystals melting at 170–171°.

Anal. Calcd. for $C_{14}H_{16}O_3N_2S$: C, 57.53; H, 5.52. Found: C, 57.08; H, 6.06.

***Endo*-5-Aminobicyclo[2,2,1]heptene-2 (Procedure B).**—Seventy-five grams (0.49 mole) of the crude hydrazide (prepared as described above) was dissolved in 500 ml. of water containing 42.0 ml. (0.50 mole) of concentrated hydrochloric acid. The solution was cooled to 0° in an ice-bath, and 250 ml. of cold carbon tetrachloride was added. A solution of 33.8 g. (0.49 mole) of sodium nitrite in 100 ml. of water was cooled to 0° and added slowly (about 10 ml. every five minutes) with occasional stirring to the solution of hydrazide hydrochloride. The carbon tetrachloride containing the azide was separated from the aqueous layer and placed in a three-liter flask fitted with a stirrer and reflux condenser. Dilute hydrochloric acid (42 ml. of concentrated hydrochloric acid in 150 ml. of water) was added to the carbon tetrachloride solution and the resulting mixture was cautiously heated on a steam-bath until decomposition of the azide (as evidenced by the evolution of nitrogen) commenced. The steam-bath was shut off and the decomposition of the azide was allowed to take place spontaneously for about two hours with no further heating. At the end of this time heat was again applied, and the stirrer was started and arranged to stir at the interface of the two phases. The reaction was allowed to proceed at the reflux temperature for 72 hours. The acidic solution was then separated from the carbon tetrachloride and made strongly basic by the addition of potassium hydroxide pellets. The amine (25 g., 51%) was collected at 150–160° and solidified to a white crystalline solid in the cold receiver. The amine was shown to be identical to that prepared by Procedure A by a mixed melting point determination of the phenylthiourea derivative (m.p. and mixed m.p. 162–163°).

Bicyclo-[2,2,1](2 or 3 ?)chloro-5-aminoheptane (IX).—Initial attempts to prepare I by the acid hydrolysis of the azide (Procedure B) resulted in the formation of a chloroamine (IX). The essential difference in this procedure was that the hydrolysis of the azide was effected by heating a benzene solution containing the azide with concentrated hydrochloric acid. The chloroamine was obtained as a colorless liquid in 48% yield; b.p. 85–87° (10 mm.), $n^{20}D$ 1.5122.

Anal. Calcd. for $C_7H_{12}NCl$: C, 57.74; H, 8.31. Found: C, 57.79; H, 8.35.

The *p*-toluenesulfonyl derivative of IX was recrystallized from aqueous alcohol, m.p. 126–127°.

Anal. Calcd. for $C_{14}H_{18}NSO_2Cl$: C, 56.07; H, 6.05. Found: C, 56.52; H, 6.37.

The phenylisothiourea of IX was recrystallized from aqueous ethanol, m.p. 148–149°.

Anal. Calcd. for $C_{14}H_{17}N_2SCl$: C, 59.87; H, 6.10. Found: C, 59.81; H, 6.12.

The Reaction of *endo*-5-Aminobicyclo[2,2,1]heptene-2 with Nitrous Acid.—Five grams (0.046 mole) of I was dissolved in 15 ml. of cold (0°) water containing 4 ml. of concentrated hydrochloric acid (0.046 mole). The solution was maintained at 0° while a solution of 3.2 g. (0.046 mole) of sodium nitrite in 10 ml. of water was added. The solution was then heated on a steam-bath for 18 hours. The reaction product was then distilled with steam and the aqueous distillate, which contained solid alcohol, was saturated with sodium carbonate and extracted with ether. The ethereal solution was dried and the ether removed to give a residual white solid which weighed 3.0 g. (60% calculated as 3-hydroxynortricyclene). The crude alcohol was sublimed at 60°

(5) H. Bruson, THIS JOURNAL, **64**, 2457 (1942).

at 2 mm. and melted at 99–102°. The alcohol was not further purified but was characterized by the preparation of the following derivatives.

The phenylurethan was prepared by the reaction of the alcohol with phenyl isocyanate. The crude product (m.p. 141–144°) was recrystallized from benzene–petroleum ether (90–100°), m.p. 145–146°. An authentic sample of the phenylurethan of 3-hydroxynortricyclene was prepared according to the procedure of Roberts[2a] and co-workers, m.p. 146.5–147.5°. A mixture of the two samples melted at 145–146°.

The *p*-phenylazobenzoate was prepared by the reaction of the alcohol (0.2 g.) with *p*-phenylazobenzoyl chloride (0.4 g.) in pyridine. The crude product (0.6 g.) was dissolved in anhydrous ether and the solution was passed through a column of alumina. The ester was eluted by the ether very rapidly and was recovered by the evaporation of the ether solvent. The orange *p*-phenylazobenzoate obtained from the chromatogram melted at 115–117°. The product melted at 119.5–120.5° after recrystallization from aqueous ethanol and did not depress the melting point of an authentic sample obtained from 3-hydroxynortricyclene.[2a]

2-Phenyl-3-nitrobicyclo[2,2,1]heptene-5 (X) was prepared in 88% yield by allowing two moles of freshly distilled cyclopentadiene to react with ω-nitrostyrene for four hours at the reflux temperature of the mixture; b.p. 136–138° (1–2 mm.), $n^{20}D$ 1.5641 (reported[6] b.p. 145° (1 mm.)).

2-Phenyl-3-amino[2,2,1]heptene-5 (XII).—The amine (b.p. 124–128° (7 mm.), $n^{25}D$ 1.5694, 12 g., 40% yield) was obtained from X (36 g.) by reduction[7] with iron filings (35 g.) in hydrochloric acid (10 ml.). A sample boiling at 90° (1 mm.) had the following composition.

Anal. Calcd. for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: C, 84.00; H, 8.18.

The benzenesulfonamide of XII was recrystallized from aqueous ethanol and melted at 165–166°.

Anal. Calcd. for $C_{19}H_{19}O_2SN$: C, 70.13; H, 5.89. Found: C, 70.13; H, 6.03.

2-Phenyl-3-aminobicyclo[2,2,1]heptane (XI). 1. **From XII.**—The reduction of 7.4 g. of XII was effected in 200 ml. of 95% ethanol using platinum oxide catalyst and hydrogen at atmospheric pressure. The saturated amine was distilled to give 6 g. (81%) of product as a colorless oil; b.p. 96–97° (1 mm.), $n^{30}D$ 1.5560.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15. Found: C, 83.30; H, 9.24.

The benzenesulfonyl derivative of XI melted at 136–137.5° after two crystallizations from aqueous ethanol.

Anal. Calcd. for $C_{19}H_{21}O_2SN$: C, 69.69; H, 6.47. Found: C, 69.41; H, 6.60.

2. **From X.**—The catalytic hydrogenation of X (0.049 mole) to XI using Raney nickel catalyst (2 g.) in 95% ethanol solvent (120 ml.) was complete after three hours at 100–110°. The initial pressure was established by admitting carbon dioxide until the pressure was 500 p.s.i. and then hydrogen until the pressure was 2500 p.s.i. The amine was distilled at reduced pressure to yield 6.3 g. (69%) of product; b.p 138–142° (11–12 mm.), $n^{25}D$ 1.5558. The identity of this amine to that prepared by the reduction of XII was established by a comparison of their benzenesulfonamide derivatives; m.p. and mixed m.p. 136–137.5°.

2-Phenyl-3-dimethylaminobicyclo[2,2,1]heptane.—The methylation of XII (12 g.) was effected using formaldehyde and formic acid according to the general procedure described by Clarke.[8] The tertiary amine (9.5 g.) was obtained as a colorless oil; b.p. 107–113° (3–4 mm.), $n^{29}D$ 1.5398. Redistillation of this amine through a six-inch Vigreux column gave 8.0 g. (57%) of product boiling at 120–124° (3–4 mm.), $n^{25}D$ 1.5412–1.5427.

For analytical analysis a sample of the amine was converted into its picrate. The picrate was crystallized from 95% ethanol and melted at 159–162°, with softening at 150°.

Anal. Calcd. for $C_{21}H_{24}N_4O_7$: C, 56.75; H, 5.44. Found: C, 56.86; H, 5.68.

The Hoffman Degradation of 2-Phenyl-3-dimethylamino-[2,2,1]heptane.—The Hoffmann methylation and degradation was carried out in the usual way, and two products were obtained: (1) trimethylamine (identified as its picrate) and (2) a neutral substance, presumably 2-phenylbicyclo[2,2,1]heptene-2, which decomposed upon attempted distillation at atmosphereic pressure.

Attempts to hydrolyze X by the addition of an aqueous solution of its sodium salt to cold dilute sulfuric acid resulted in an oil, b.p. 130–149° (10–11 mm.), which failed to react with sodium bisulfite and which did not form a phenylhydrazone. The product appeared to be principally unchanged X; whether an inversion in configuration of the nitro group occurred was not established.

(6) C. F. H. Allen, A. Bell and J. W. Gates, *J. Org. Chem.*, **8**, 373 (1948).

(7) *Cf.* K. Johnson and Ed. F. Degering, THIS JOURNAL, **61**, 3194 (1939), for a more complete description of the method.

(8) H. T. Clark, H. B. Gillespie and S. Z. Weisshaus, THIS JOURNAL, **55**, 4571 (1933).

MINNEAPOLIS 14, MINNESOTA RECEIVED MARCH 9, 1951

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE VIRGINIA POLYTECHNIC INSTITUTE]

The Synthesis and Cyclization of Some 2-(Substituted Benzyl)-benzophenones[1,2]

BY FRANK A. VINGIELLO AND JAMES G. VAN OOT[3]

It has been shown that one of the important factors concerning the rate of cyclization of 2-benzylbenzophenones is the electron density at the ortho position of the benzene ring into which cyclization occurs.

The mechanism of the cyclization of *o*-benzylbenzophenones is pictured by Bradsher and Vingiello[4] as proceeding through the following steps: (1) the reversible addition of a proton to the carbonyl oxygen; (2) reaction between the positive central carbon atom and the ortho position of the benzene ring into which cyclization is to occur; (3) shedding of a proton; and finally (4) transannullar elimination of water. In conclusion these authors stated that the rate of cyclization, for similar experimental conditions, depends on several factors, one of these being the electron density at the ortho position of the benzene ring into which cyclization takes place. We now have experimental evidence to substantiate this statement since we have synthesized and measured the rates of cyclization of several 2-benzylbenzophenones substituted in the benzyl ring. The syntheses and cyclizations are shown below.

The procedure used in our rate studies is the same as that used by Bradsher and Vingiello[4]; and indeed, we repeated two of their rate measure-

(1) Presented before the Division of Organic Chemistry at the 119th Meeting of the American Chemical Society, Boston, Massachusetts, April, 1951.

(2) This paper has been abstracted from the Doctorate thesis presented by James G. Van Oot to the Virginia Polytechnic Institute in December, 1950.

(3) E. I. du Pont de Nemours and Company, Wilmington, Delaware.

(4) C. K. Bradsher and F. A. Vingiello, THIS JOURNAL, **71**, 1134 (1949).