and gave 1.0 g. of benzophenone, 2,4-dinitrophenylhydrazone, m.p. 238° (reported[10] 239°) and 0.98 g. of *p*-benzoylbenzoic acid, m.p. 193–194° (reported[13] 194°).

F. **α-(*m*-Tolyl)-benzoin.**—A 5.0-g. sample of α-(*m*-tolyl)-benzoin, b.p. 200–204° at 0.65 mm. (reported[4] 210–240° at high vacuum), was cleaved by the procedure described above. A 2.0-g. portion of the neutral fraction (3.42 g.) was oxidized with chromic acid and gave 1.3 g. of benzophenone, 2,4-dinitrophenylhydrazone, m.p. 225–226° alone or mixed with authentic derivative (reported[10] 239°), and 0.93 g. of *m*-benzoylbenzoic acid, m.p. 163–164° (reported[14] 161–162°). The ether-extracted cleavage solution was acidified and the acid fraction was extracted with ether. Oxidation with chromic acid gave 1.1 g. of isophthalic acid, m.p. 300° (reported[10] 300°), and 0.7 g. of benzoic acid, m.p. 120–121° alone or mixed with authentic benzoic acid.

G. **α-(*o*-Tolyl)-benzoin.**—A 1.28-g. sample of α-(*o*-tolyl)-benzoin, m.p. 116.5–117° (reported[4] 116–117°), was cleaved in the usual manner. The neutral fraction (0.73 g.) proved to be benzhydrol, m.p. 65–66° alone or mixed with authentic benzhydrol (reported[10] 68°). The acid fraction (0.50 g.) proved to be *o*-toluic acid, m.p. 102–103° (reported[10] 102°). A second cleavage of 2.0 g. of α-(*o*-tolyl)-benzoin gave a neutral fraction which was oxidized with chromic acid and gave 1.1 g. of benzophenone, 2,4-dinitrophenylhydrazone, m.p. 234–240° alone or mixed with authentic derivative (reported[10] 239°). No acid compound was found as an oxidation product. The acid fraction (0.82 g.) from the cleavage was *o*-toluic acid, m.p. 100–101° (reported[10] 102°).

MANHATTAN, KANSAS

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(14) P. Senff, *Ann.*, **220**, 225 (1883).

[Contribution from the School of Chemistry of the University of Minnesota]

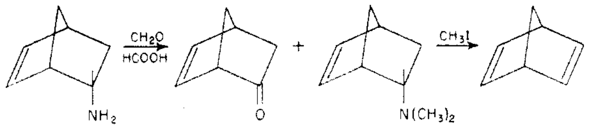
Studies of the Bicyclo[2,2,1]heptene-2 Ring System. II

By William E. Parham, William T. Hunter, Roberta Hanson and Thomas Lahr

Received April 16, 1952

The reaction of *endo*-5-aminobicyclo[2,2,1]heptene-2 with formaldehyde and formic acid gives the corresponding ketone (24%) as well as the expected tertiary amine (30%) and trimethylamine. The formation of the ketone has been attributed to steric factors and not participation of the double bond, since the saturated amine, *endo*-5-aminobicyclo[2,2,1]heptane, behaves similarly. Methylation of *d*-(β-phenylisopropyl)-amine by the Clarke procedure resulted in no racemization, thus intermediates of the type $R_2C{=}N{-}CH_3$ are not involved. When the quaternary base of *endo*-5-dimethylamino[2,2,1]-heptene-2 was pyrolyzed, the amine was regenerated. Other reactions are cited which indicate that bicyclo[2,2,1]2,5, heptadiene is not easily formed by elimination reactions involving the bicyclo[2,2,1]heptene-2 ring system.

During a previous study of compounds[1] containing the bicyclo-(2,2,1)-heptene-2 ring system, one of us observed that the action of formaldehyde and formic acid on *endo*-5-aminobicyclo-(2,2,1)-heptene-2 (I) resulted in 24% yield of ketonic material, a 30% yield of a tertiary amine and an undetermined quantity of trimethylamine. The quaternary hydroxide derived from the tertiary amine (III) did not give the expected products when subjected to the Hofmann degradation (trimethylamine and IV), but decomposed to give the original amine III and a volatile alcohol (presumably methanol). The results of the methylation reaction and the Hofmann degradation reaction were both unexpected; therefore, these reactions have been reinvestigated and additional evidence concerning the structures of the resulting compounds has been obtained.

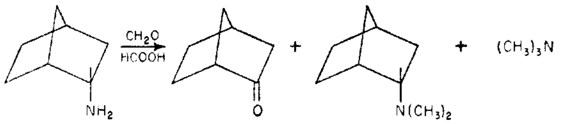


I II III IV

The unstable ketonic product II gave a 2,4-dinitrophenylhydrazone and a semicarbazone which were difficult to purify by crystallization. The ketonic product was shown to be principally 5-ketobicyclo-(2,2,1)-heptene-2 (II) by reduction (0.925 double bond) to the known 2-ketobicyclo-(2,2,1)-heptane (VI). The reduced ketone (VI) was isolated as its 2,4-dinitrophenylhydrazone and its semicarbazone. These derivatives did not depress the melting points of the corresponding derivatives prepared from an authentic sample of VI. The reduction of nortricyclanone under conditions used for the reduction of II did not result in the formation of VI by hydrogenolysis; consequently, nortricyclanone cannot be present in large amounts as an impurity in II.

The infrared spectrum of III revealed no broad absorption band near 800 cm.$^{-1}$, indicating[2] the absence of the nortricyclane ring structure. When III was reduced (Pt, H_2), 90% of one mole of hydrogen was absorbed and the product was *endo*-2-dimethylamino-(2,2,1)-heptane (VII).

The reaction of *endo*-2-aminobicyclo-(2,2,1)-heptane (V) with formaldehyde and formic acid was investigated in order to ascertain whether or not the formation of ketones during the methylation of I could be attributed to participation of the carbon–carbon double bond. The products of the reaction were: 2-ketobicyclo-(2,2,1)-heptane (VI, 40% yield), *endo*-2-dimethylaminobicyclo(2,2,1)-heptane (VII, 27% yield) and trimethylamine.



V VI VII

The formation of carbonyl compounds during the methylation of amines with formaldehyde and formic acid has been explained as outlined in the following equation.[3]

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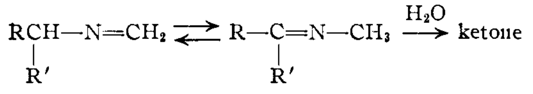
(1) W. E. Parham, W. T. Hunter and R. Hanson, This Journal, **73**, 5068 (1951).

(2) J. D. Roberts, E. R. Trumbull, W. Bennett and R. Armstrong, *ibid.*, **72**, 3117 (1950).

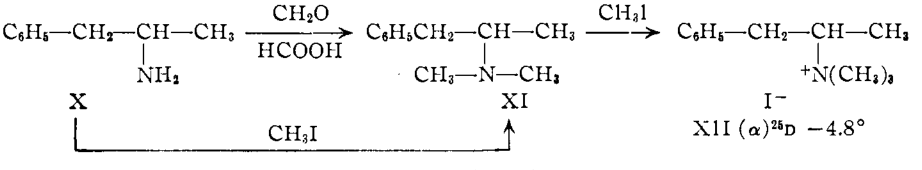
(3) H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, *ibid.*, **55**, 4571 (1933).



$$\underset{R'}{RCH}-N{=}CH_2 \rightleftarrows \underset{R'}{R-C}{=}N-CH_3 \xrightarrow{H_2O} \text{ketone}$$

VIII IX

A study employing *d*-(β-phenylisopropyl)-amine (X) showed that no racemization occurred during methylation, thus establishing that intermediates of type IX are not involved during the normal Clarke methylation reaction.

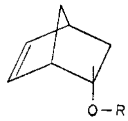


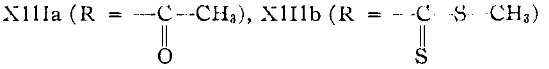
$$C_6H_5-CH_2-\underset{NH_2}{CH}-CH_3 \xrightarrow[HCOOH]{CH_2O} C_6H_5CH_2-\underset{CH_3-N-CH_3}{CH}-CH_3 \xrightarrow{CH_3I} C_6H_5-CH_2-\underset{^{+}N(CH_3)_3}{CH}-CH_3 \quad I^-$$

X XI XII $(\alpha)^{25}_D$ −4.8°

CH₃I

The failure of III to give bicyclo-(2,2,1)-2,5-heptadiene (IV) under the conditions of the Hofmann reaction is evidence that this olefin is not formed easily. Other evidence has been accumulated to substantiate this conclusion. The Kraft pyrolysis of bicyclo-(2,2,1)-2-heptene-5-acetate (XIIIa) gave cyclopentadiene, acetylene and acetic acid. The Tschugaeff degradation of bicyclo-(2,2,1)-2-heptene-5-ol (XIIIb) gave a small amount (5%) of low boiling material which reacted with phenylazide to give a product having the composition of one mole of IV plus two of phenylazide.





XIIIa (R = $-\underset{\underset{O}{\|}}{C}-CH_3$), XIIIb (R = $-\underset{\underset{S}{\|}}{C}-S-CH_3$)

Experimental

Reaction of I with Formaldehyde and Formic Acid.—A mixture of amine (20 g., 0.2 mole), 87% formic acid (53 g., 1 mole) and 40% formalin (32 g., 0.4 mole) was heated at the reflux temperature for seven hours. The resulting solution was treated with concentrated hydrochloric acid (16 ml., 0.2 mole) and distilled with steam. The distillate (100 ml.) was neutralized with sodium carbonate, saturated with sodium chloride, and extracted with ether. The ketonic material II (5.2 g., 24%) was obtained from the ethereal solution as a colorless oil.

The acidic residue from the steam distillate was made strongly alkaline with sodium hydroxide and the amine was extracted with ether. During the neutralization a gaseous amine separated which was identified as trimethylamine by the conversion of this compound to the picrate (m.p. and mixed m.p. 215–219° dec.). The tertiary amine III (7.4 g., 30%) was obtained from the ether extract by distillation (b.p. 167–175°).

Product II. 1.—The 2,4-dinitrophenylhydrazone (m.p. 133–137°) could not be obtained pure by crystallization.

A sample melting at 149–154° after repeated crystallization from ethanol had the following composition.

Anal. Calcd. for $C_{13}H_{12}O_4N_4$: C, 54.16; H, 4.03; N, 19.44. Found: C, 54.04; H, 4.62; N, 19.46.

2. **The semicarbazone** (m.p. 197–203° dec.) could not be obtained pure by crystallization. A sample melting at 197–203° dec. had the following composition.

Anal. Calcd. for $C_8H_{11}ON_3$: C, 58.16; H, 6.71; N, 25.44. Found: C, 58.28; H, 7.33; N, 25.00.

3. **Hydrogenation** of II was effected in alcohol using prereduced platinum as a catalyst. The hydrogen absorbed corresponded to 92.7% of that calculated to saturate one double bond. The product was identified as 2-ketobicyclo-[2,2,1]heptane (VI) by its conversion into the 2,4-dinitrophenylhydrazone and semicarbazone of VI.

2,4-Dinitrophenylhydrazone of VI was prepared from the reduction product of II and recrystallized from ethanol, m.p. 130–131°.

Anal. Calcd. for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.86. Found: C, 53.89; H, 5.19.

The m.p. and mixed m.p. of the 2,4-dinitrophenylhydrazone prepared from an authentic sample of VI[4] was 130–131°.

Semicarbazone of VI was prepared from the reduction product of II and recrystallized from methanol and toluene. This product decomposed when heated to 189–192° with preliminary softening at 182° (reported[4] m.p. 196.5–197.5°).

Anal. Calcd. for $C_8H_{13}ON_3$: C, 57.46; H, 7.83. Found: C, 57.46; H, 7.74.

A sample of the semicarbazone prepared from an authentic sample of VI melted at 189–192° with decomposition and preliminary softening. A mixed melting point of the two derivatives melted at 189–192° (dec.).

Nortricyclanone.[2]—The semicarbazone of nortricyclanone was recrystallized from aqueous ethanol; m.p. 214–217° (dec.).

Anal. Calcd. for $C_8H_{11}ON_3$: C, 58.23; H, 6.67. Found: C, 58.50; H, 7.13.

Reduction of Nortricyclanone.—A sample of the ketone, obtained by hydrolysis of its semicarbazone, was reduced using prereduced platinum oxide catalyst. The hydrogen absorbed amounted to 119% of that calculated to reduce one double bond. Reduction of the carbonyl group must have occurred for the product gave a single 2,4-dinitrophenylhydrazone (m.p. 187.5–188.5°) which was identified by mixed melting point determination to be that derived from the starting ketone.[2]

The Amine III.—A sample, b.p. 47° (5 mm.) had the following composition. Calcd. for $C_9H_{15}N$: C, 78.80; H, 10.9. Found: C, 78.50; H, 11.3.

1. **The picrate of III** was recrystallized from ethanol; m.p. 190–195° (dec.) with preliminary darkening at 164°.

Anal. Calcd. for $C_{15}H_{18}N_4O_7$: C, 49.18; H, 4.95. Found: C, 49.31; H, 5.10.

2. **The methiodide of III** was recrystallized from ethanol–petroleum ether (b.p. 90–100°); m.p. 160° (dec.).

Anal. Calcd. for $C_{10}H_{18}NI$: C, 43.02; H, 6.50. Found: C, 43.07; H, 6.37.

3. **Hydrogenation of III** was effected in ethanol using prereduced platinum oxide catalyst. The hydrogen absorbed amounted to 90% of that required to reduce one double bond. The ethanol solution was concentrated and used to prepare the following derivatives.

The picrate of *endo*-2-dimethylaminobicyclo-(2,2,1)-heptane (VII) was crystallized from ethanol; m.p. 213–216° (dec.).

Anal. Calcd. for $C_{15}H_{20}O_7N_4$: C, 48.91; H, 5.44. Found: C, 49.21; H, 5.63.

A mixture of this picrate and that obtained from VII, which was prepared from V (see below), melted at 213–216° (dec.).

The methiodide of *endo*-2-dimethylaminobicyclo(2,2,1)-heptane (VII) was recrystallized from ethanol; m.p. 291–293°.

Anal. Calcd. for $C_{10}H_{20}NI$: C, 42.70; H, 7.12. Found: C, 42.62; H, 7.26.

A mixture of this methiodide and that obtained from *endo*-dimethylaminobicyclo-(2,2,1)-heptane which was derived from V (see below) melted at 292° dec. The X-ray diffraction pattern of these two methiodides were identical.[5]

Reaction of V with Formaldehyde and Formic Acid.—The amine V[6] (7.2 g.) was treated with formaldehyde and formic acid by a procedure similar to that described for I.

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[4] O. Diels and K. Alder, *Ann.*, **470**, 76 (1929).

[5] The authors would like to thank Dr. W. N. Lipscomb, University of Minnesota, for the X-ray diffraction analysis. The samples were run as powders using a General Electric XRD-3 unit with Geiger counter recording.

[6] K. Alder and G. Stein, *Ann.*, **514**, 224 (1934).

The ketonic fraction (4 g., 40%) was shown to be 2-ketobicyclo-(2,2,1)-heptane (VI) by its conversion into the 2,4-dinitrophenylhydrazone of VI; m.p. and mixed m.p. with an authentic sample was 130–131°.

The tertiary amine VII (3 g., 27% yield) was distilled; b.p. 165–180°.

Anal. Calcd. for $C_9H_{17}N$: C, 77.71; H, 12.2. Found: C, 78.21; H, 12.3.

The methiodide of this amine melted at 292° with decomposition. The identity of this product to that obtained by the reduction of III has already been noted.

The Hofmann Degradation of the Methiodide of *endo*-5-Dimethylaminobicyclo-(2,2,1)-heptene-2 (III).—A solution of the methiodide (5.4 g.) in 100 ml. of 15% potassium hydroxide was distilled in an atmosphere of nitrogen. The exhaust gases were passed through a solution of picric acid. Decomposition occurred when about 85 ml. of water had distilled; however, no trimethylamine was formed. The picrate of the product melted at 190–194° (dec.) and a mixed melting point of this picrate with an authentic sample of the picrate of *endo*-5-dimethylaminobicyclo-(2,2,1)-heptene-2 (III), m.p. 190–195° (dec.), was 190–194°.

A solution of the methiodide (21 g.) in methanol (300 ml.) was treated with silver oxide (9.25 g.), and the solution of methohydroxide was distilled at atmospheric pressure. The residue decomposed at 100–180°; however, no trimethylamine was observed. The product was III.

Methylation of *d*-dimethyl-(β-phenylisopropyl)-amine (X) with formaldehyde and formic acid gave *d*-dimethyl-(β-phenylisopropyl)-amine (XI), b.p. 68–72° (2.5 mm.), 66% yield, $[\alpha]^{25}_{D}$ +5.11° (absolute ethanol).

Anal. Calcd. for $C_{11}H_{17}N$: C, 80.92; H, 10.50; N, 8.58. Found: C, 81.06; H, 10.59; N, 8.78.

Conversion of XI to XII was effected by reaction of XI with methyl iodide in ether. The product was recrystallized from ethanol; m.p. 196–197°, $[\alpha]^{25}_{D}$ −4.81° (distilled H_2O).

Anal. Calcd. for $C_{12}H_{20}NI$: C, 47.2; H, 6.56. Found: C, 47.6; H, 6.98.

Methylation of *d*-(β-Phenylisopropyl)-amine with Methyl Iodide.—A mixture of 250 ml. of water, 25 g. of sodium carbonate, 11.2 g. of X and 30 g. of methyl iodide was heated at the reflux temperature for nine hours. The reaction mixture was cooled and the crystals filtered, washed with ether, and dried. The product weighed 18.2 g. (72% yield) and was the methiodide of XI. A sample of the product was recrystallized from ethanol. The m.p. and mixed m.p. with the product described in the preceding experiment was 196–197°; $[\alpha]^{25}_{D}$ −4.83° (distilled H_2O).

The decomposition of bicyclo-(2,2,1)-2-heptene-5 acetate[7] was carried out by allowing the ester to pass (25 g./hr.) through a hot tube (580°) in an atmosphere of nitrogen. A material balance was not obtained; however, the following products were isolated: (a) acetylene (in exhaust gas), (b) acetic acid, (c) cyclopentadiene (m.p. and mixed m.p. of dibromo derivative[8] was 45–46°) and (d) vinyl acetate.

The Decomposition of the Methyl Xanthogenate of *endo*-5-Hydroxybicyclo-(2,2,1)-heptene-2 (XIIb).—The crude xanthogenate[9] (b.p. 120–126° (10 mm.)) was decomposed at 250° in an atmosphere of nitrogen. A small amount of volatile oil (*ca.* 5%) boiling at 40–70° was obtained. This product reacted with phenylazide in ether to give a crystalline product (dec. 200°) which was insoluble in ether, benzene, alcohol and chloroform. The light tan needles were washed with alcohol and ether.

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 69.08; H, 5.49. Found: C, 69.03; H, 5.81.

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[7] K. Alder and H. Rickert, *ibid.*, **543**, 15 (1939).

[8] E. Farmer and W. Scott, *J. Chem. Soc.*, 177 (1929).

[9] Whitmore and Simpson, THIS JOURNAL, **55**, 3809 (1933).

MINNEAPOLIS 14, MINNESOTA

[CONTRIBUTION FROM THE DIVISION OF PURE CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL OF CANADA]

The Characterization of Methyl and Methylene Groups in Steroids by Infrared Spectrometry. I. Correlations of Bending Frequencies with Molecular Structure[1]

BY R. NORMAN JONES AND A. R. H. COLE[2]

RECEIVED APRIL 11, 1952

The major absorption bands between 1350 and 1500 cm.$^{-1}$ in the spectra of steroids can be assigned to vibrations of methyl and methylene groups in the molecule. These vibrations appear to be localized in individual methyl and methylene groups, and the following correlations between molecular structure and infrared spectra have been established for this region of the spectrum. (a) The cyclic methylene groups of the steroid ring system absorb at a different frequency from the linear methylene groups in the side chain. (b) Methylene groups adjacent to carbonyl groups and to ethylenic linkages absorb at characteristic positions. In steroids containing the group $-CH_2-CO-$ the frequency of the α-methylene bending vibrations is determined by the location of the carbonyl group and serves to supplement the C=O stretching frequency for the characterization of the carbonyl position. (c) The angular methyl groups, the terminal side chain methyl groups, and the methyl group in the acetoxy radical of steroid acetates, absorb at different positions and can be distinguished. The band positions associated with these various types of methyl and methylene groups are listed in tables, and examples are given to illustrate the application of these correlations to the elucidation of molecular structure.

The infrared absorption bands of large organic molecules may be classified into three principal types; (i) a relatively small number of bands due to *stretching* vibrations of specific groups, notably O–H, C–H, C=O, and C=C in the higher frequency region (1575–3650 cm.$^{-1}$); (ii) C–H *bending* bands of methyl and methylene groups between 1350 and 1500 cm.$^{-1}$; (iii) a complicated pattern of overlapping bands due to skeletal stretching vibrations and C–H deformation vibrations below 1350 cm.$^{-1}$. The latter absorption is most sensible to small changes in molecular structure and has been aptly described as the "fingerprint" region.

An extensive study of the bands due to specific O–H, C=O and C=C stretching vibrations in steroids has enabled a set of correlations to be established between band position and molecular structure,[3–6] and these correlations have proved useful in determining the structure of newly isolated steroids.

From studies of the infrared spectra of simple ali-

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[1] Presented, in part, at a Symposium on Molecular Spectroscopy held at the Ohio State University, Columbus, Ohio, June, 1950, and published as Contribution No. 2857 from the Laboratories of The National Research Council of Canada.

[2] National Research Council Postdoctorate Fellow.

[3] R. N. Jones and K. Dobriner, *Vitamins and Hormones*, **7**, 293 (1949).

[4] R. N. Jones, P. Humphries, E. Packard and K. Dobriner, THIS JOURNAL, **71**, 241 (1949).

[5] R. N. Jones, P. Humphries and K. Dobriner, *ibid.*, **72**, 956 (1950).

[6] P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch and G. W. Wood, *J. Chem. Soc.*, 2402 (1951).