

solution was then diluted with 50 cc. of water and acidified with 20 cc. of 3 *N* hydrochloric acid solution. There was obtained 5.0 g. of solid of indefinite melting point. This was recrystallized from 200 cc. of aqueous ethanol (1:1). Four grams (82%) of well-formed needles was obtained. Samples melted at 186–187° (uncor.) with much pre-shrinking. The melting point given by Snapper and Grunbaum¹ is 179°. The acid was readily and completely soluble in warm sodium bicarbonate solution (compare Fischer and Lipschitz⁵ for behavior of a related acid and ester) and was not appreciably soluble in chloroform. A sample of the compound failed to give a ninhydrin test. In contrast to this behavior, both diiodotyrosine and the methyl ether of tyrosine⁶ gave positive ninhydrin reactions.

Anal. Calcd. for C₁₆H₁₃O₄Nl₂ (537): N, 2.6. Found: N, 2.5; equivalent wt. by titration (methyl red), 536 ± 1.

(5) Fischer and Lipschitz, *Ber.*, **48**, 374 (1915).

(6) Behr and Clarke, *THIS JOURNAL*, **54**, 1630 (1932).

$[\alpha]_{D_{27}} + 10.9^\circ \pm 0.3^\circ$ for 0.607 g. dissolved in 0.5 *N* sodium hydroxide solution to 10.0 cc. After a second recrystallization, $[\alpha]_{D_{27}} = +10.6 \pm 0.7^\circ$ for 0.671 g. dissolved in 0.5 *N* sodium hydroxide solution to 10.0 cc.

Thanks are due Miss Velma Ladwig and Mr. Luther Eggman for Kjeldahl analyses.

Summary

The synthesis of a number of derivatives of diiodotyrosine for testing as radio-opaque pharmaceutical compounds, is described. Details are given for the conversion of diiodotyrosine to *N*-benzoyldiiodotyrosine through some of these intermediates in better than 60% over-all yield.

AMES, IOWA

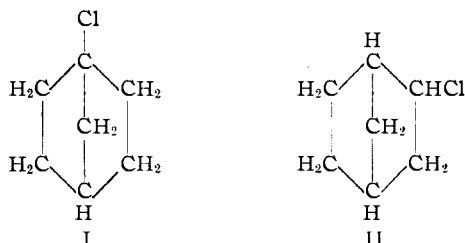
RECEIVED OCTOBER 4, 1945

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF UNIVERSAL OIL PRODUCTS COMPANY]

The Exchange of Hydrogen and Chlorine between Bicyclo(2,2,1)heptane and *t*-Butyl Chloride

BY LOUIS SCHMERLING

The hydrogen-chlorine exchange reaction¹ of bicyclo(2,2,1)heptane (also called norcamphane) with *t*-butyl chloride was investigated because it seemed to offer a convenient means for preparing the tertiary chloride, 1-chlorobicyclo(2,2,1)heptane (I), and thence (by condensation with olefins²) bicycloheptylalkyl chlorides containing quaternary carbon atoms.



Bartlett, Condon and Schneider¹ reported that poorly characterized products were obtained by the reaction of bicyclo(2,2,1)heptane with alkyl halides in the presence of aluminum chloride or aluminum bromide. Their general procedure consisted in shaking a mixture of the reactants and the catalyst at room temperature in a separatory funnel for a period of time varying from ten seconds to several minutes and then stopping the reaction either by separating the catalyst layer or by adding water. In the present investigation it was found that smooth transfer of chlorine from *t*-butyl chloride to bicycloheptane can be accomplished in the presence of aluminum chloride by using lower reaction temperatures (about 0°) and longer contact times (thirty to sixty minutes).

(1) P. D. Bartlett, F. E. Condon and A. Schneider, *THIS JOURNAL*, **66**, 1531 (1944).

(2) For a description of the condensation of alkyl halides with, for example, ethylene see L. Schmerling, *ibid.*, **67**, 1152 (1945).

Chlorobicycloheptane was obtained in 22–24% of the theoretical yield based on the bicycloheptane charged or in 74–84% yield based on unrecovered bicycloheptane. However, the chloride was not the expected tertiary compound but was instead the secondary isomer, 2-chlorobicyclo(2,2,1)heptane (II), which was also obtained by adding hydrogen chloride to bicyclo(2,2,1)-2-heptene. Its structure was further proved by hydrolyzing it to 2-hydroxybicyclo(2,2,1)heptane, better known as β -norcamphanol. β -Norcamphanol ether was obtained as a by-product of the hydrolysis.

The fact that the bicycloheptane yields a secondary chloride is significant since it indicates that this hydrocarbon differs from those previously studied¹ in that a hydrogen atom attached to a secondary carbon atom rather than one attached to a tertiary carbon atom is involved in the exchange reaction. This non-formation of the tertiary bicycloheptyl compound may be explained as being due to the impossibility in this case of forming the intermediate tertiary carbonium ion as postulated by the mechanism of Bartlett and his co-workers.¹ The tertiary bicycloheptyl carbonium ion presumably cannot exist because the central carbon atom and the three carbon atoms forming bonds with it cannot be coplanar.³

Experimental

Reaction of Bicyclo(2,2,1)heptane with *t*-Butyl Chloride.

—A solution of 52 g. (0.54 mole) of the bicycloheptane (prepared according to the directions given by Thomas),⁴ 52 g. (0.56 mole) of *t*-butyl chloride and 25 g. of *n*-pentane diluent was placed in a large test-tube of such dimensions

(3) P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3184 (1939).

(4) C. L. Thomas, *Ind. Eng. Chem.*, **36**, 310 (1944).

(50 mm. \times 350 mm.) that it could readily be cooled by immersion in a Dry Ice-acetone-bath in a quart Dewar jar. A low-temperature thermometer was suspended in the test-tube by means of a wire. The solution was cooled to about -70° and 3 g. of powdered resublimed aluminum chloride was added. The test-tube was removed from the bath and allowed to warm up while being shaken manually. Relatively little reaction occurred until the temperature reached -5° . The temperature was maintained at 0 to 15° during the next twenty minutes by occasional cooling. A test sample showed that the yield of chlorobicycloheptane was low. More catalyst (3 g.) was added and the intermittent shaking and cooling was continued for thirty minutes, the temperature being kept at -10 to $+5^\circ$. The clear yellow upper layer was then decanted from the reddish brown sludge, washed with water, dried and distilled. Besides unreacted materials and isobutane (not collected), there was obtained 16 g. (23% of the theoretical yield based on the charge) of 2-chlorobicyclo(2,2,1)-heptane or 2-chloro- β -norcamphane,⁵ b. p. $69-70^\circ$ (30 mm.) or $162-163^\circ$ (760 mm.); m. p. -8 to -7° ; n_D^{20} 1.4825. Only a trace of higher boiling product was obtained.

2-Chloro- β -norcamphane was previously prepared by Komppa and Beckmann⁶ by the action of phosphorus pentachloride on β -norcamphanol which was obtained in several steps from norcamphor. Their product boiled at $66-67^\circ$ (25 mm.) and at $160-162^\circ$ (atm. pressure) and melted at -5° .

An attempt was made to increase the yield of the chloronorcamphane by more careful control of the reaction conditions. *t*-Butyl chloride (100 g., 1.08 moles) was added during fifty minutes to a stirred mixture of 100 g. (1.04 moles) of bicyclo(2,2,1)heptane; 50 g. of *n*-pentane and 10 g. of aluminum chloride in the conventional type of three-necked flask equipped with a dropping funnel, a mercury-sealed stirrer, and a reflux condenser. The temperature was maintained at $0-2^\circ$. Stirring was continued for one hour, after which the product was worked up in the usual manner. There was obtained 30 g. (22% of the theoretical yield) of 2-chlorobicyclo(2,2,1)heptane, b. p. $61-62^\circ$ (20 mm.); m. p. -5° ; n_D^{20} 1.4832. A mixture of this material with the product obtained by adding hydrogen chloride to bicyclo(2,2,1)-2-heptene (see below) also melted at -5° .

In a third experiment, the *t*-butyl chloride (100 g.) was gradually added to the stirred mixture of 100 g. of bicycloheptane, 50 g. *n*-pentane, and 10 g. of aluminum chloride at -18 to -10° . A test sample showed that not more than 5% of chloronorcamphane was formed. The reaction temperature was therefore permitted to rise to 0° and stirring was continued at that temperature for one hour. Distillation of the washed product yielded 32 g. (24% of the theoretical yield) of 2-chlorobicyclo(2,2,1)-heptane and, as in the other experiments, very little higher-boiling material.

Addition of Hydrogen Chloride to Bicyclo(2,2,1)-2-heptene.—A stream of hydrogen chloride was bubbled through a stirred solution of 50 g. of bicycloheptene⁴ in 100 g. of technical *n*-pentane. The reaction temperature was kept at -28 to -34° during the first fifteen minutes; only 5.5 g. of hydrogen chloride was absorbed, the major portion passing through unreacted. Lowering the temperature to about -70° resulted in more rapid absorption during the next fifteen-minute period. Distillation of

the washed product yielded 52 g. (75%) of 2-chlorobicyclo(2,2,1)heptane, b. p. 52° (11 mm.); m. p. -5° ; n_D^{20} 1.4849.

Hydrolysis of 2-Chlorobicyclo(2,2,1)heptane.—A sealed tube containing 9 g. of the chlorobicycloheptane (obtained by the reaction of bicycloheptane with *t*-butyl chloride), 2 g. of magnesium oxide and 100 g. of water was heated in an Ipatieff-type rotating autoclave at 240° for four hours. Water was placed outside the sealed tube in order to prevent its bursting. The chloride was converted into a yellow crystalline solid which was taken up in ether, and distilled under reduced pressure (30 mm.). The major portion (about 4 g.) of the material sublimed to the top of the fractionating column, leaving 0.8 g. of residue in the flask. The sublimate was recovered by refluxing ethanol through the column. Water was added to the alcoholic solution, and the resulting mixture of oil and aqueous ethanol was distilled through a 14-inch total reflux fractionation column.⁷ A mixture of oil and water distilled over at 95° . The oil crystallized on cooling to room temperature. The crystals (2.5 g.) melted at $120-121^\circ$ and boiled at $178-179^\circ$ (in a test tube). They yielded a phenylurethan which melted at 145° , proving that the material was β -norcamphanol. Komppa and Beckmann⁶ report that β -norcamphanol boils at $176-177^\circ$, melts at $123-124^\circ$ or $127-128^\circ$, and yields a phenylurethan melting at $145-146^\circ$.

The residue (0.8 g.) from the vacuum distillation was also steam distilled. Crystals melting at $66-67^\circ$ were obtained. These consisted of bicyclo(2,2,1)heptyl ether which has also been obtained⁸ as a by-product of the hydration of bicyclo(2,2,1)-2-heptene with dilute sulfuric acid. The ether crystals differed physically from the norcamphanol crystals in that they were transparent, hard, and brittle while the alcohol crystals were white and fluffy.

Eighteen grams of the chlorobicycloheptane obtained by the addition of hydrogen chloride to the bicycloheptene was hydrolyzed in a similar manner. The crystalline product was taken up in methanol (in order to remove it from the tube) and the resulting solution plus the aqueous layer and the magnesium hydroxide was distilled through the 14-inch column. A mixture of water and β -norcamphanol (8 g.) distilled over at $95-97^\circ$ and of water and dinorcamphanol ether (4 g.) at 98° . The β -norcamphanol which melted at 120° was further characterized by means of its 3,5-dinitrobenzoate,⁹ m. p. 105° . The bicycloheptyl ether crystals melted at 67° and boiled at $245-250^\circ$ in a test-tube.

Summary

Exchange of hydrogen for chlorine occurs when bicyclo(2,2,1)heptane is contacted with *t*-butyl chloride at about 0° in the presence of aluminum chloride. The product is 2-chlorobicyclo(2,2,1)-heptane rather than the expected tertiary chloride, 1-chlorobicyclo(2,2,1)heptane.

Hydrolysis of the chloride yields 2-hydroxybicyclo(2,2,1)heptane (*i. e.*, β -norcamphanol) and β -norcamphanol ether.

RIVERSIDE, ILLINOIS

RECEIVED OCTOBER 26, 1945

(5) *Chemical Abstracts* nomenclature. Komppa and Beckmann⁶ state that this and the related compounds are more correctly named as derivatives of norbornylane.

(6) G. Komppa and S. Beckmann, *Ann.*, **512**, 172 (1934).

(7) C. L. Thomas, H. S. Bloch and J. Hoekstra, *Ind. Eng. Chem., Anal. Ed.*, **10**, 153 (1938).

(8) H. A. Bruson and T. W. Riener, *THIS JOURNAL*, **67**, 728 (1945).

(9) Alder and Rickert, *Ann.*, **543**, 1 (1939).