of potassium cyanide, and 300 ml. of anhydrous acetonitrile was heated at reflux temperature for 16 hr., cooled, and poured into 500 ml. of water. The precipitate was collected by filtration and washed thoroughly with water, giving 12.1 g. (85%) of cruce 17α-cyano steroid, m.p. 174–178°, which was chromatographed on neutral, activity grade III alumina: $\nu_{\max}^{\mathrm{CHCl_3}}$ 2220 cm.$^{-1}$ (no bands in carbonyl region).

17β-(N-Pyrrolidinyl)-4-androsten-3-ones.—The following is a typical procedure used for the preparation of the unsaturated ketones **3a–c**. A solution of 8.0 g. (22.4 mmoles) of 3β-hydroxy-17α-methyl-17β-(N-pyrrolidinyl)-5-androstene (**3b**) in 700 ml. of toluene and 100 ml. of cyclohexanone was distilled until 200 ml. of distillate had been removed and then a solution of 8.0 g. of aluminum isopropoxide in 100 ml. of dry toluene was added quickly (5 minutes or less) to the boiling mixture. The yellow-orange mixture was heated at reflux temperature for 30 min., cooled, and extracted with three 150-ml. portions of 5% sodium hydroxide and then with saturated sodium chloride solution. The toluene solution was evaporated to dryness *in vacuo* and the residue was taken up in ether. Filtration of the ether solution and introduction of gaseous hydrogen chloride into the filtrate gave the insoluble amine hydrochloride, which was separated by filtration, dissolved in methanol, and neutralized with aqueous ammonia. Addition of water and extraction with ether gave on evaporation of the ether extract 6.90 g. of crude ketone which was purified by chromatography on basic, activity grade III alumina. **5a–c** had $\lambda_{\max}^{\mathrm{EtOH}}$ 240 mμ (ε *ca.* 16,000) and 306 mμ (ε *ca.* 85).

3β,17β-Bis(N-pyrrolidinyl)-5α-androstane (6).—A solution of 8.64 g. (30 mmoles) of 5α-androstane-3,17-dione, 18.0 ml. of pyrrolidine, and 12.5 g. (66 mmoles) of *p*-toluenesulfonic acid monohydrate in 350 ml. of diethylene glycol dimethyl ether (toluene was not satisfactory) was heated at reflux temperature in a Soxhlet extractor having calcium carbide in the thimble. After 4 hr., the Soxhlet head was replaced by a Vigreux column and 200 ml. of distillate was removed. The residue was cooled in an ice bath, and 125 ml. of ether was added and then 5.7 g. (150 mmoles) of lithium aluminum hydride was added with stirring. After the vigorous reaction had subsided, the reaction mixture was kept at room temperature for 24 hr. Excess water saturated with sodium sulfate was added, and the mixture filtered. The filter cake was washed thoroughly with ether, and the combined organic phases were washed with 5% aqueous sodium hydroxide, water, and saturated aqueous sodium chloride. The dry solution was treated with gaseous HCl, giving 11.6 g. of steroid amine hydrochloride as a buff-colored precipitate. The hydrochloride salt was dissolved in methanol and treated with excess aqueous sodium hydroxide. The crude amine that precipitated was chromatographed on 180 g. of basic, activity grade III alumina. Elution with petroleum ether-benzene (3:1 v./v.) gave the diamine **6**, which was crystallized from ethanol-water (Table I).

1- and 2-Bromo-1,3-cyclohexadiene[1]

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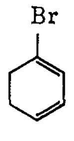
It was reported recently that treatment of 1,3-cyclohexadiene with potassium *t*-butoxide in dimethyl sulfoxide results in formation of equal amounts of benzene and cyclohexene.[2] Interestingly, we have noted that similar treatment of 1- or 2-bromo-1,3-cyclohexadiene[3] (**1** and **2**, respectively) at 75° results in formation of an equilibrium mixture consisting of 79% **1** and 21% **2**. Described here are the preparation, characterization, and equilibration of **1** and **2**.



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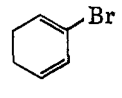

2

2,3-Dibromocyclohexene[4] (**3**) with quinoline at 125 and at 175° gave different liquid products with the same boiling point (43° at 15 mm.). The product obtained at 125° appeared to be a single compound when analyzed by gas–liquid partition chromatography (g.l.p.c.), but similar analysis of the product obtained at the higher temperature indicated that it was a mixture of two compounds in a ratio of 2:1. The major component was the same compound that was obtained pure at the lower temperature, and the minor component was obtained pure by preparative-scale g.l.p.c.

Both compounds had the empirical formula C_6H_7Br. Considering their origin, the product obtained at 125° was assigned the 2-bromo-1,3-cyclohexadiene (**2**) structure, and its isomer was assigned the 1-bromo-1,3-cyclohexadiene structure. The structural assignments seem reasonable because formation of **2** can be pictured as occurring by β elimination of the elements of hydrogen bromide from **3**, and formation of **1** can be rationalized as occurring by a slower, base-induced, prototropic rearrangement of **2**. Evidence supporting the structural assignments was obtained by carrying out an additional reaction at 175° with a reaction time of 25 instead of 18 hr.; the product obtained consisted of 46% **1** and 54% **2**.[5]

The infrared, n.m.r., and ultraviolet spectra of **1** and **2** are in accord with the bromo-1,3-cyclohexadiene structure. The infrared spectrum of **1** possesses absorptions in the 1630-cm.$^{-1}$ region characteristic of a conjugated diene without a center of symmetry,[6] *i.e.*, bands of moderate intensity at 1580 and 1640 cm.$^{-1}$. The infrared spectrum of **2** possesses similar absorptions at 1575 and 1680 cm.$^{-1}$. The n.m.r. spectrum of **1** at 60 Mc. has considerable fine structure and consists of two series of lines from 402–361 (=CH, 3H) and 196–142 (CH_2, 4H) c.p.s. downfield from the tetramethylsilane (TMS) resonance. The n.m.r. spectrum of **2** consists of a broad band from 373–348 c.p.s. with peaks at 369 and 361 c.p.s. (=CH, 3H) and a broadened band ($\omega_{1/2} \sim 4$ c.p.s.) centered at 140 c.p.s. (CH_2, 4H). The ultraviolet spectra of **1** and **2** are similar but distinguishable: **1** has $\lambda_{\max}$ 269 mμ (ε 7900), and **2** has $\lambda_{\max}$ 268 mμ (ε 7600).[7]

As prototropic rearrangements of alkenes occur at particularly favorable rates in dimethyl sulfoxide,[9]

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[1] This research was supported by Grant GM-10606 from the National Institute of General Medical Sciences of the U. S. Public Health Service.

[2] J. E. Hofmann, P. A. Argabright, and A. Schriesheim, *Tetrahedron Letters*, No. **17**, 1005 (1964).

[3] R. Cornubert, A. Rio, and P. Senechal [*Bull. soc. chim. France*, **46** (1955)] noted that a small amount of a rather impure material, which they suggested might be **1** or **2**, was obtained as a minor product from the reaction of 2,3-dibromocyclohexyl acetate with potassium acetate.

[4] J. Sonnenberg and S. Winstein, *J. Org. Chem.*, **27**, 750 (1962).

[5] The greater elution time (on octyl phthalate) of **2**, which has the higher dipole moment, is also consistent with the structural assignments.

[6] R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 59.

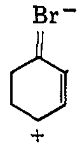
[7] *Cf.* the ultraviolet spectra of 1,3-cyclohexadiene, $\lambda_{\max}$ 256.5 mμ (ε 8000),[8] and a number of alkyl substituted 1,3-cyclohexadienes summarized by H. H. Jaffé and M. Orchin ["Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, p. 202].

[8] V. Henri and L. W. Pickett, *J. Chem. Phys.*, **7**, 439 (1939).

[9] A. Schriesheim, R. J. Muller, and C. A. Rowe, Jr., *J. Am. Chem. Soc.*, **84**, 3164 (1962).

we examined the reaction of 2 with potassium *t*-butoxide in dimethyl sulfoxide in order to determine if such reaction conditions would provide a more suitable means of preparing 1 from 2. Treatment of 2 with 0.5 *M* potassium *t*-butoxide in dimethyl sulfoxide for 8 hr. at 75° gave in 35% yield a mixture of 79% 1 and 21% 2. In order to determine if this was the equilibrium mixture, 1 was treated in a similar manner; the mixture of bromocyclohexadienes obtained was identical with that obtained from 2.[10]

The difference in free energy between 1 and 2 (0.9 kcal. at 75°) appears to be the results of greater conjugation of bromine with cyclohexadiene system in 1 (*cf.* 5).



5

Although admittedly some disproportionation to bromobenzene and bromocyclohexene could have occurred, and these products, because of further reaction with potassium *t*-butoxide, escaped detection,[11] it is clear that *t*-butoxide-catalyzed disproportionation of 1 and 2 occurs considerably more slowly than the disproportionation of 1,3-cyclohexadiene to benzene and cyclohexene under similar conditions.[2] The slow step postulated for the disproportionation of 1,3-cyclohexadiene is transfer of hydride from cyclohexadienyl anion to cyclohexadiene to form benzene and cyclohexenyl anion. Apparently, substitution of bromine on the cyclohexadiene ring results in the introduction of substantial, nonbonded interactions in the transition state for hydride transfer and thereby markedly decreases the rate of disproportionation.

Experimental

Boiling points are uncorrected. Infrared spectra were obtained with a Beckman IR-4 spectrophotometer. Ultraviolet spectra of cyclohexane solutions were obtained with a Cary Model 14 recording spectrophotometer. N.m.r. spectra were obtained with a Varian Associates HR-60 system equipped with integrator and base-line stabilizer of samples as 20% solutions in carbon tetrachloride contained in 5-mm.-o.d. tubes. Resonance frequencies in n.m.r. spectra were determined relative to internal TMS using the side-band technique with a Packard CD-200 audiooscillator. Gas–liquid partition chromatograms were obtained using a 0.25 in. × 15 ft. column packed with octyl phthalate on Chromasorb W-HMDS in an Aerograph Model A-700 (Wilkens Instrument and Research, Inc., Walnut Creek, Calif.). Microanalyses were performed by Mr. V. H. Tashinian, Berkeley, Calif.

2-Bromo-1,3-cyclohexadiene (2).—A mixture of 6.0 g. (0.025 mole) of 2,3-dibromocyclohexene[4] and 150 ml. of quinoline was heated at 125° for 16 hr. The reaction mixture was allowed to cool, 300 ml. of ether was added, and the organic solution was extracted with dilute aqueous hydrochloric acid in order to remove the quinoline. The ether solution was dried and distilled to give 2.1 g. (53%) of pale yellow liquid with b.p. 43° (15 mm.), $n^{26}\mathrm{D}$ 1.5293.

Anal. Calcd. for C_6H_7Br: C, 45.32; H, 4.44. Found: C, 44.99; H, 4.40.

1-Bromo-1,3-cyclohexadiene (1).—Following the procedure described for the preparation and isolation of 2 except that the reaction temperature was 175°, a pale yellow liquid was obtained in 40% yield. The gas–liquid partition chromatogram showed the presence of 2 and a second compound (1) in a ratio of 2:1 (assuming equal thermal conductivities). Compound 1 was obtained pure by preparative-scale g.l.p.c. It had $n^{24.5}\mathrm{D}$ 1.5365.

Anal. Calcd. for C_6H_7Br: C, 45.32; H, 4.44. Found: C, 44.84; H, 4.30.

Equilibration of 1 and 2.—A mixture of 3.0 g. (0.027 mole) of potassium *t*-butoxide, 50 ml. of dimethyl sulfoxide, and 2.0 g. (0.013 mole) of 2 was heated at 75° for 8 hr. The dark mixture was cooled, water and ether were added, and the phases were separated. The ether solution was dried with magnesium sulfate and concentrated by distillation. Analysis of the concentrate by g.l.p.c. showed the presence of 1 and 2 in a ratio of 79:21. Continued distillation gave 0.7 g. (35%) of a mixture of 1 and 2, the infrared spectrum of which was consistent with the analysis obtained by g.l.p.c.

1-Bromo-1,3-cyclohexadiene (1, 0.4 g.) was treated as described for 2. Analysis of the resulting ether concentrate by g.l.p.c. showed the presence of 1 and 2 in a ratio of 79:21.

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[10] (a) From consideration of results of base-catalyzed equilibrations of cyclohexadienes,[10b,c] equilibration of 1 and 2 is likely to occur through the intermediacy of 1-bromo-1,4-cyclohexadiene (4). Interestingly, although the equilibrium constant for the 1,3- $\rightleftharpoons$ 1,4-cyclohexadiene interconversion is ~0.5, the 1 and 2 appeared to be essentially free of 4. (b) W. v. E. Doering, G. Schroeder, K. Trautner, and S. Staley, 144th National Meeting of The American Chemical Society, Los Angeles, Calif., April 1963, Abstracts of Papers, p. 14 m. (c) R. B. Bates, R. H. Carnighan, and C. E. Staples, *J. Am. Chem. Soc.*, **85**, 3032 (1963).

[11] Treatment of bromobenzene with potassium *t*-butoxide in dimethyl sulfoxide has been reported to yield *t*-butyl phenyl ether.[12] The fate of 1-bromocyclohexene on similar treatment remains to be determined; however, likely products include *t*-butyl cyclohexenyl ethers, and cyclohexadiene and its disproportionation products. The 1 and 2 obtained from the equilibrations were essentially free (<2%) of *t*-butyl ethers and carbonyl compounds, but it is conceivable that minor amounts (<10% yield) of volatile hydrocarbons could have escaped detection.

[12] D. J. Cram, B. Rickborn, and G. R. Knox, *J. Am. Chem. Soc.*, **82**, 6412 (1960).

A Convenient Method for the Preparation of 1,3-Cyclohexanedione[1]

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In connection with some steroidal studies, it became necessary to have on hand substantial quantities of the useful intermediate,[2] 1,3-cyclohexanedione. Existing procedures[3] for obtaining this compound require rather tedious techniques, among them, high pressures (90–100 atm.) and complex nickel catalysts. Employing milder conditions result in poor yields and considerable recovery of starting materials.

It has been observed that 1,3-cyclohexanedione can be readily prepared by room-temperature, low-pressure hydrogenation of resorcinol in aqueous alkaline solution in the presence of rhodium on alumina. The yield of the diketone, after 16–18 hr., was 85%. The use of ethanol or acetic acid solvent in the absence of alkali results in the complete reduction to 1,3-cyclohexanediol. When the rhodium catalyst was first preconditioned[4] by suspension in acetic acid for 2 hr. and sub-

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[1] This study supported by the National Institutes of Health (GM-06248-06).

[2] V. I. Gunar and S. I. Zavyalov, *Vopr. Khim. Terpenov i Terpenoidov*, 213 (1960) [*Chem. Abstr.*, **55**, 14714*a* (1961)], and other references cited therein.

[3] "Organic Synthesis," Coll. Vol. III, E. C. Horning, Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p. 278. References for other methods of preparation are also cited.

[4] A. I. Meyers, W. Beverung, and G. Garcia-Munoz, *J. Org. Chem.*, **29**, 3427 (1964).