An independent synthesis of this substance (XII) was effected as follows. To a solution of 5 ml. of methanol, 45 ml. of xylene and 1.00 g. of carbinol XIII was added 0.11 g. of sodium. After the metal had reacted, the solution was concentrated at atmospheric pressure to a volume of 25 ml. By this time, the sodium salt of XIII had precipitated. The chloro compound (V, 1.09 g.) was added and the mixture was heated under reflux for 7 hr. Solid material was removed by filtration of the hot solution. Concentration of the filtrate to dryness and crystallization of the residue from benzene (cooling only to 25°) gave 0.71 g. (37%) of XII, m.p. 199–201°. This substance did not depress the melting point of that described above. Their infrared spectra were identical.

Reaction of 9-Bromomethyl-10-methylphenanthrene (VII) with Ethereal Silver Perchlorate.—This reaction was conducted in the manner described above for the chloro compound. From 2.00 g. of VII, 4.0 g. of silver perchlorate and 100 ml. of anhydrous ether, there was obtained a solid melting over the range 94–122°. Chromatography on alumina (120 g.) using benzene and petroleum ether for elution afforded 0.70 g. (48%) of 9,10-dimethylphenanthrene (XV). The unusual nature of this reaction prompted a more rigorous proof of identity than the usual mixture melting point. This substance has an ultraviolet spectrum identical with that of XV obtained as described above. The n.m.r. spectrum indicated that all non-aromatic hydrogen atoms are of the same type. Its molecular weight, obtained from the mass spectrum, was 206 (calculated 206).

Further washing of the alumina column with acetone gave 0.30 g. (17%) of material having m.p. 91–92°. This was identified as the ethyl ether XI by mixture melting point and by comparison of infrared and ultraviolet spectra with those of a sample prepared as described above. The reaction between VII and silver perchlorate in benzene under conditions similar to those used in the ether experiment gave a colorless solid (m.p. 190–210°) which appeared to be polymeric. Careful chromatography on alumina did not shorten this melting range.

Dimer of 9,10-Phenanthraquinodimethane (XVII).—One gram of the quaternary ammonium bromide XVI was dissolved in 20 ml. of a suspension of freshly prepared silver oxide in distilled water. The mixture was stirred at 30° for 4 hr. and then filtered. The colorless filtrate was concentrated to dryness at an aspirator (oil-bath, magnetic stirring). The bath temperature did not exceed 80° during this process. The insolubility of the colorless solid residue in water suggested that elimination of trimethylamine had taken place during the concentration process. The solid was boiled with several portions of ethanol and the combined extracts were then concentrated at atmospheric pressure until crystallization began. Well formed crystals of XVII obtained in this way amounted to 0.11 g. (19%), m.p. 252–253°. Recrystallization was best effected by dissolving the material in benzene, in which it is readily soluble, and evaporating on a hot-plate while replacing evaporative loss with ethanol. When crystallization started, the temperature was lowered to 0° and the product collected by suction filtration, m.p. 252–253°.

Anal. Calcd. for $C_{32}H_{24}$: C, 94.08; H, 5.92. Found: C, 93.84; H, 6.22.

This substance absorbs rather strongly in the infrared at 11.1 μ. Its ultraviolet spectrum (95% ethanol) exhibited high intensity maxima at 245, 256 and 272 mμ with extinction coefficients ($\times 10^4$) 2.75, 2.90 and 2.75, respectively. It almost instantly decolorized a dilute solution of bromine in chloroform.

A 0.290-g. sample of XVII absorbed 15.7 ml. (94% for one double bond) of hydrogen when shaken with palladium-charcoal suspended in ethanol under one atmosphere of hydrogen. The dihydro compound was obtained in an amorphous state, m.p. 140–160°, despite repeated attempts at crystallization. After several reprecipitations (heating and cooling) from ethanol it was analyzed.

Anal. Calcd. for $C_{32}H_{26}$: C, 93.62; H, 6.38; mol. wt., 410. Found: C, 93.46; H, 6.15; mol. wt., 422 (cryoscopic in benzil).

The infrared spectrum had no absorption in the 11.1 μ region. The ultraviolet spectrum (95% ethanol) exhibited high intensity absorption at 225, 256, 271, 287 and 299 mμ with ϵ-values ($\times 10^4$) 4.12, 6.56, 3.04, 1.57 and 1.47, respectively. Principal low intensity absorption[14] at 319, 327, 335, 343 and 351 mμ had ϵ-values ($\times 10^2$) of 3.59, 3.10, 5.16, 2.83 and 5.66, respectively. The corresponding low intensity absorption of 9,10-dimethylphenanthrene (XV) is found at 321, 337 and 353 mμ with ϵ-values ($\times 10^2$) of 3.57, 4.92 and 4.48, respectively. The similarity in low intensity extinction coefficients indicates XVII to have only one intact phenanthrene nucleus.

Acknowledgment.—The authors are indebted to The Robert A. Welch Foundation for the financial support of this study. We wish also to express our appreciation for the kindness shown by Dr. M. J. O'Neal and his associates at the Houston Research Laboratory of the Shell Oil Co. for n.m.r. data and mass spectra and for their interpretations.

AUSTIN 12, TEX.

[CONTRIBUTION FROM THE INSTITUTE OF SCIENTIFIC AND INDUSTRIAL RESEARCH, OSAKA UNIVERSITY]

The Effect of Conformation on Reactivity. II. Rates of Acetolysis of Isomeric Cholestanyl *p*-Toluenesulfonates

BY SHINYA NISHIDA

RECEIVED JANUARY 20, 1960

The rigid molecular structure of the isomeric cholestanols provides a valuable tool for study of the effect of conformation on reactivity. With this objective in mind, the isomeric *p*-toluenesulfonates of cholestan-2α, 2β-, 3α-, 3β- and 6α-ol were synthesized and their rates of acetolysis measured. The observed sequence of rates is $3\beta \approx 6\alpha < 2\alpha < 3\alpha \ll 2\beta$. The above rate sequence is explicable in terms of the 1,3-diaxial interactions previously utilized to account for the variation in rates in the *trans*-decalyl tosylates with related fixed conformations.

It is a problem of considerable importance to attain a quantitative understanding of the effect of conformation in cyclohexane derivatives on their reactivities.[1] Unfortunately, in simple cyclohexane derivatives the problem is complicated by the ready interconversion of axial and equatorial bonds in these molecules.[2–4]

One attempt to circumvent this difficulty is based on the use of *t*-butylcyclohexyl derivatives.[5] An alternative approach to this problem is to utilize a system with a fixed conformation, such as the *trans*-decalyl tosylates.[1] The value of this

(1) I. Moritani, S. Nishida and M. Murakami, THIS JOURNAL, **81**, 3420 (1959).

(2) K. Kojima and T. Yoshino, *ibid.*, **75**, 166 (1953).

(3) M. Larnaudie, *Compt. rend.*, **236**, 909 (1953).

(4) For a detailed discussion of this field see W. Hückel, *Ann.*, **624**, 142 (1959).

(5) S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955).

approach was indicated in our earlier study by the relative simplicity of the interpretation of the observed rate data in terms of 1,3-diaxial interactions with the tosyl group.[1]

The steroid structure provides another system with fixed conformations.[6] Accordingly, it was of interest to examine the behavior of several representative tosylates based on this system to see whether the observed reactivities could likewise be simply interpreted in terms of the steric interactions within the molecules. For this purpose the tosylates of cholestan-2α-, 2β-, 3α-, 3β- and 6α-ol were synthesized and their rates of acetolysis measured.

Results

The rates of acetolysis of the tosylates were measured at 75°, with one exception. In the case of cholestan-2β-yl tosylate, the rate at 75° was too fast for convenient measurement. Consequently the rate was measured at 60° and the rate at 75° was calculated by assuming the frequency factor for this compound to be the same as that observed for *trans-cis*-1-decalyl tosylate.[1] This assumption appears quite reasonable in view of the similarity in the rate constants at 60° for these two related molecules: 1.45×10^{-4} sec.$^{-1}$ for cholestan-2β-yl tosylate and 1.00×10^{-4} sec.$^{-1}$ for *trans-cis*-1-decalyl tosylate.

The experimental results for all of the compounds examined in this study are summarized in Table I.

TABLE I

RATE CONSTANTS FOR THE ACETOLYSIS OF THE CHOLESTANYL TOSYLATES

Cholestanyl tosylate	Temp., °C.	10^5 k_1, sec.$^{-1}$
3β	75.3	2.84 ± 0.02
	75.0	2.54 ± .05
	75.0	2.62 ± .01
3α	75.3	17.0 ± .18
	75.0	16.0 ± .9
2α	75.0	8.14 ± .27
2β	59.9	13.9 ± .4
	60.1	15.1 ± .1
	75.0	77.6[a]
6α	75.0	2.25 ± 0.02

[a] Extrapolated as described in text.

Discussion

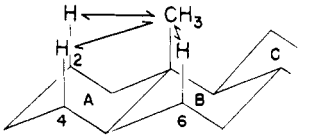
For convenience in following the discussion, the structures of the cholestanyl tosylates and the related decalyl tosylates, together with pertinent data, are summarized in Table II.

The rate constant for the solvolysis of 3β[7] at 75.0° is 2.62×10^{-5} sec.$^{-1}$. This is slightly larger than the rate constant for the solvolysis of *trans-cis*-2-decalyl tosylate,[1] 1.99×10^{-5} sec.$^{-1}$. Consequently, it appears that the two systems are quite similar, with the angular methylgroup and the C and D rings of the steroid system resulting in only a minor rate increase in the rate of solvolysis of this equatorial tosylate.

(6) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

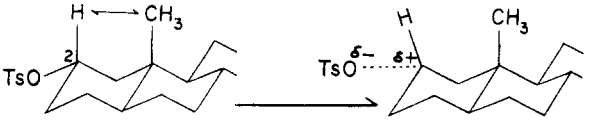
(7) For convenience, the symbol 3β will be used to refer to cholestan-3β-yl tosylate, and the related symbols, 6α, 2α, 3α and 2β, will be used to refer to the related tosylates.

The 2α-derivative is also a simple equatorial derivative, similar to the 3β-compound in having no significant interactions between the tosyl group and the 1,3-axial positions. However, it exhibits a rate of solvolysis which is larger than that of the 3β-derivative by a factor of 3.1. This increase in rate is attributed to the 1,3-diaxial interactions between the angular methyl group and the axial hydrogen atoms in the 2-, 4- and 6-positions (I).



I

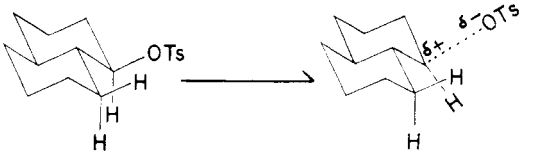
Ionization of the tosyl group in the 2-position permits the axial hydrogen in that position to move away from the strained axial conformation (II, III).



II III

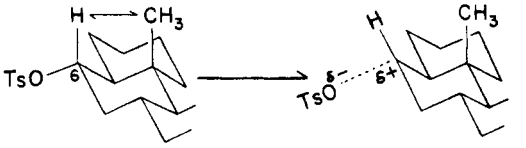
This decrease in steric strain should provide a driving force for the ionization[8] which is absent in the related 3β-derivative.

In the *trans-trans*-1-decalyl tosylate there is observed a decrease in rate over the *trans-cis*-2- of a factor of 0.5. This decrease was attributed to the energy requirement moving the 2-hydrogen atom into opposition with one carbon–hydrogen and one carbon–carbon bond (IV, V).[1]



IV V

The same situation is involved in the solvolysis of the 6α-derivative. However, the decrease in rate is smaller than that observed in the *trans-trans*-1-decalyl derivative. In the 6α-derivative there is a 1,3-methyl–hydrogen interaction which should facilitate the ionization and aid in overcoming the energy requirements of the ionization stage (VI, VII).

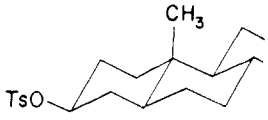
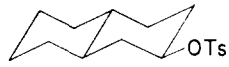
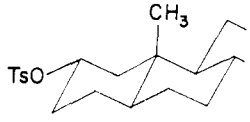
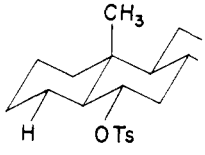
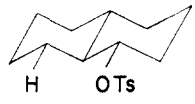
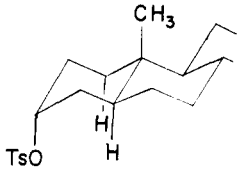
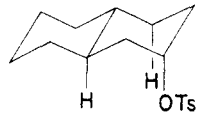
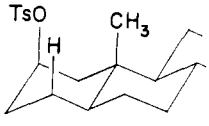


VI VII

(8) H. C. Brown, *Science*, **103**, 385 (1946); H. C. Brown and I. Moritani, THIS JOURNAL, **77**, 3623 (1955).

TABLE II

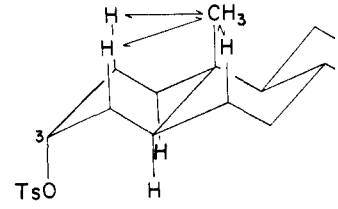
RELATIONSHIP BETWEEN THE 1,3-DIAXIAL INTERACTIONS AND THE RELATIVE REACTIVITY OF THE CHOLESTANYL AND *trans*-DECALYL TOSYLATES

Cholestanyl tosylate Conformation		1,3-Diaxial interaction X (H)	1,3-Diaxial interaction X (CH_3)	$10^5 k_1$, sec.$^{-1}$ 75.0°	Relative rate[a]	Decalyl tosylate Conformation		1,3-Diaxial interaction X (H)	$10^5 k_1$, sec.$^{-1}$ 75.0°	Relative rate[b]
	3β	0	0	2.62	1.0		*trans-cis*-2	0	1.99	1.0
	2α	0	0	8.14	3.1					
	6α	1	0	2.25	0.9		*trans-trans*-1	1	1.05	0.5
	3α	2	0	16.0	6.1		*trans-trans*-2	2	6.19	3.1
	2β	1	1	77.6	31					

[a] Based on cholestan-3β-yl tosylate. [b] Based on *trans-cis*-2-decalyl tosylate.

The behavior of the derivatives containing the tosyl groups in the axial position is of special interest. An increase in rate of 2.7 is observed for the axial tosyl derivative in 4-*t*-butylcyclohexyl tosylate, and an increase of 3.3 is observed in the related 3-*t*-butylcyclohexyl derivative.[5] In the *trans*-2-axial decalyl tosylate there was observed an increase in reactivity of 3.1 over that of the 2-equatorial derivative.[1]

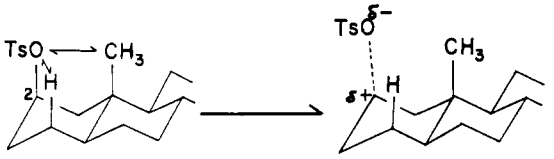
In the present study, the axial 3α-derivative undergoes solvolysis at a rate 6.1 greater than the equatorial 3β-derivative. This larger effect must be the result of steric interaction between the angular methyl group and the axial hydrogen atoms in the 2-, 4- and 6-positions. Even though this interaction is on the opposite side of the ring system from the axial tosyl groups, the steric interactions must result in a stiffening of the ring and reduce the ability of the tosyl group to reduce its strained conformation by taking advantage of the flexibility of the ring (VIII).



VIII

Finally, the 2β-derivative is stereochemically similar to the *trans-trans*-2-decalyl tosylate, with the exception that the tosyl groups is subjected to 1 carbon–hydrogen and 1 carbon–carbon 1,3-diaxial interaction in the latter. From the greater steric requirements of the methyl group, the axial tosyl group in the cholestan-2β-derivative should be subjected to much larger strains. The increase in the rate of solvolysis of 31, as compared to the

factor of 3.1 observed in the decalyl system, is in accord with this interpretation (IX, X).



IX X

From the results realized in these studies of the *trans*-decalyl and the cholestanyl systems, it appears that the reactivities of the individual isomers is readily interpretable in terms of 1,3-diaxial interactions. The fixed conformations realized in these systems greatly facilitates the analysis. It is hoped that these studies will be extended to other reactions and other derivatives to test the full utility of this approach in attaining a quantitative understanding of the influence of conformation on reactivity.

Experimental

Materials.—All carbinols were purified by utilizing the column chromatography followed by recrystallization.

Cholestan-3β-ol.—Cholestanone, prepared from cholesterol,[9,10] was reduced with metallic sodium in absolute ethanol; m.p. 139–140° (lit.[11] 140–141°). The Lieberman–Burchard test[9] proved that the compound was free from cholesterol.

Cholestan-3α-ol.—Cholestanone[9,10] was hydrogenated at 50° using platinum oxide as catalyst in acetic acid; m.p. 183–184° (lit.[12] 186–187°).

Cholestan-2-one was synthesized from cholestan-3-one by the route established by Ruzicka and co-workers[13,14]; m.p. 128–129° (lit.[15] 129–130°).

(9) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 191.

(10) *Ibid.*, p. 139.

(11) B. Heath-Brown, I. M. Heilbron and E. R. H. Jones, *J. Chem. Soc.*, 1482 (1940).

(12) L. Ruzicka, H. Brüngger, E. Eichenberger and J. Meyer, *Helv. Chim. Acta*, **17**, 1407 (1934).

Cholestan-2α- and 2β-ol were prepared according to the methods reported by Dauben and co-workers.[15] The 2α-ol melted at 177° (lit.[15] 177.1–178.9°) and the 2β-ol at 155° (lit.[15] 153–155°).

Cholestan-6-one was prepared from cholesterol by following the procedure of Shoppee and Summers[16]; m.p. 94–96° (lit.[16] 96–98°).

Cholestan-6α-ol.—The above ketone was reduced with metallic sodium in absolute ethanol; m.p. 129–130° (lit.[17] 128–129°).

Cholestanyl tosylates were prepared by the reaction of cholestanol with tosyl chloride in dry pyridine.[1] Cholestan-2α-, 3β- and 6α-ol reacted with molar equivalents of tosyl chloride for 2 days at 5°. Cholestan-3α ol reacted with two molar equivalents of tosyl chloride for 4 days at 5°. Cholestan-2β-ol was treated with three moles of tosyl chloride for 6 hours at 30°. The melting points of isomeric cholestanyl tosylates were: 3β, 135–136° (lit.[18] 136.5–137.5°); 3α, 138° (dec.); (lit.[18] dec.); 6α, 108–109° (lit.[16] 109–110°); 2α, 143.5–144; 2β, 114–115° dec.

Anal. Calcd. for $C_{34}H_{54}O_3S$: C, 75.22; H, 10.01. Found: (3α) C, 74.95; H, 10.10; 2α, C, 75.36; H, 10.17; 2β, C, 74.81; H, 9.93.

Rate Measurement.—Since the solubility of the cholestanyl tosylates was found to be low in acetic acid, the rate measurements were made at a concentration of about 0.01 mole/l. The methods of the measurement were the same as those of decalyl tosylate.[1]

Acknowledgment.—This work was partly supported by the Grant in Aid provided by the Ministry of Education for which I express my gratitude. I am also indebted to Professor Masuo Murakami, Professor Ichiro Moritani and Professor Herbert C. Brown for their valuable suggestions.

(13) L. Ruzicka, Pl. A. Plattner and R. Aeschbacher, *ibid.*, **21**, 866 (1938).

(14) L. Ruzicka, Pl. A. Plattner and M. Furrer, *ibid.*, **27**, 524 (1944).

(15) W. G. Dauben, E. J. Blanz, Jr., J. Jiu and R. A. Micheli, THIS JOURNAL, **78**, 3752 (1956).

(16) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 3361 (1952).

(17) R. Tschesche, *Ber.*, **65**, 1842 (1932).

(18) H. R. Nace, THIS JOURNAL, **74**, 5937 (1952).

SAKAI-SHI, OSAKA, JAPAN

[CONTRIBUTION FROM THE RESEARCH DIVISION OF CHAS. PFIZER AND CO., INC., GROTON, CONN.]

The Dehydrogenation of Corticosteroids with Chloranil[1]

BY E. J. AGNELLO AND G. D. LAUBACH

RECEIVED JANUARY 19, 1960

The reaction of tetrachloro-*p*-benzoquinone (chloranil) with a variety of steroid 3-ketones is described. Δ^4-3-Ketones are converted in one step to their Δ^6-dehydro or $\Delta^{1,6}$-bisdehydro derivatives depending on the reaction conditions employed. The scope, limitations and mechanism of the dehydrogenation are discussed.

In the course of a study of new methods for the dehydrogenation of steroid 3-ketones, it was found that the treatment of Δ^4-3-ketosteroids with chloranil (tetrachloro-*p*-benzoquinone) can afford Δ^6-dehydro or $\Delta^{1,6}$-bisdehydro derivatives depending on the reaction conditions employed. A preliminary report of this single step method of synthesizing dehydro derivatives of corticosteroids from Δ^4-3-ketones has been published.[2] In the present communication additional data are presented with a discussion of the scope, limitations and mechanism of the reaction.

The first dehydrogenation of a corticosteroid with chloranil was performed on Δ^4-pregnene-17α,-21-diol-3,20-dione diacetate (I). The reaction afforded a product which was identical with a sample of the Δ^6-dehydro derivative, $\Delta^{4,6}$-pregnadiene-17α,21-diol-3,20-dione diacetate (II), prepared from I by the well-known bromination–dehydrobromination sequence.[3]

(1) Presented in part before the Division of Organic Chemistry of the International Congress of Pure and Applied Chemistry, Paris, France, July, 1957, and the Division of Organic Chemistry of the American Chemical Society at the 132nd National Meeting, New York, September, 1957.

(2) E. J. Agnello and G. D. Laubach, THIS JOURNAL, **79**, 1257 (1957).