hydrochloride, 844-41-7; N-cyclohexylbenzhydrylamine picrate, 989-12-8; *p*-aminobenzene-N-N-dimethylsulfonamide, 1709-59-7; N-(benzhydryl)-N′-dimethylsulfanylamide, 23511-18-4; cyclohexylurea, 698-90-8; N-(*p*-anisyl)benzhydrylamine hydrochloride, 23511-20-8; 3,3-diphenyl-5-methoxyoxindole, 20367-84-4; Ia, 722-96-3; Ib, 797-73-9; Ic, 741-36-6; Id, 23522-81-8; Ie, 23522-82-9; Va, 15427-81-3; Vb, 23522-84-1; Vc, 741-37-7; Vd, 23522-86-3; Ve, 23522-87-4; VIb, 15779-18-7; VIc, 741-38-8; VId, 23522-90-9; VIe, 23522-91-0; VIIa, 724-18-5; VIIb, 741-68-4; VIIc, 741-69-5; VIId, 23568-88-9; VIIe, 23568-89-0; XXa, 4746-87-6; XXb, 17003-65-5; XXc, 5554-37-0; XXd, 20594-45-0; XXe, 23568-86-7.

The Mechanism of Tetralone Formation from the Acid-Catalyzed Reaction of 2-(N,N-Dimethylamino)-1,4-diphenyl-1,4-butanediol

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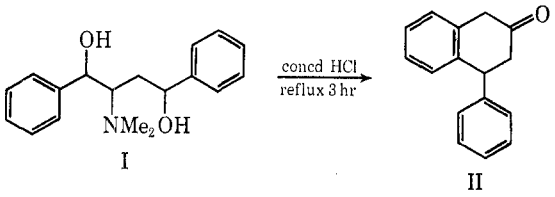
The mechanism of formation of 4-phenyl-2-tetralone from the reaction of 2-(N,N-dimethylamino)-1,4-diphenyl-1,4-butanediol with acid was investigated. A number of potential reaction intermediates were synthesized. These included 1,4-diphenyl-3-buten-2-one, 1,4-diphenyl-3-butene-1,2-diol, and 1,4-diphenyl-1,2,4-butanetriol. The first two of these compounds failed to give 4-phenyl-2-tetralone on treatment with hydrochloric acid. The triol did furnish 4-phenyl-2-tetralone in acid, but it was indirectly shown that the triol was not an intermediate in the reaction. A cyclic amino alcohol, 2-(N,N-dimethylamino)-4-phenyl-1-tetralol, afforded 4-phenyl-2-tetralone in high yield upon treatment with acid. Results of kinetic studies were consistent with intermediacy of the cyclic amino alcohol. Experimental data suggests a mechanism in which the cyclic amino alcohol undergoes dehydration to an enamine with subsequent hydrolysis to 4-phenyl-2-tetralone.

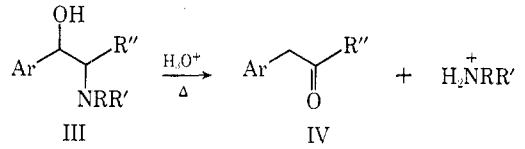
In a previous communication[2] we reported the acid-catalyzed conversion of 2-(N,N-dimethylamino)-1,4-diphenyl-1,4-butanediol (I) into 4-phenyl-2-tetralone (II). We now wish to report the results of



I II

experiments aimed at elucidating the mechanism of tetralone formation.

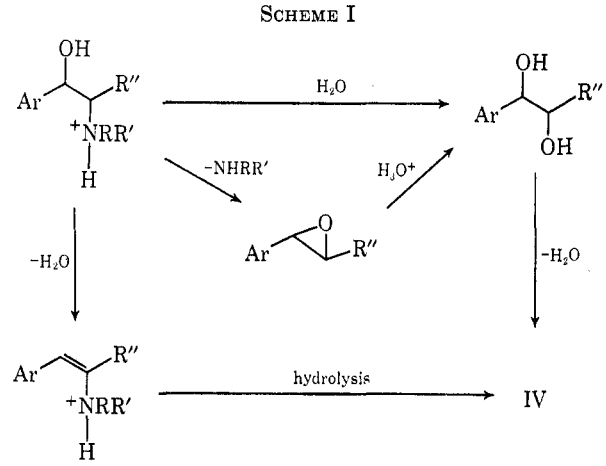
α-Aryl-β-amino alcohols are known to undergo cleavage to β-keto compounds upon treatment with strong mineral acids.[3-6] In these reactions R and R′



III IV

may be either hydrogen or alkyl, while R″ may be hydrogen, alkyl, or aryl. Because of their pharmaceutical activity, many amino alcohols related to III have been prepared; however, there are few studies dealing with the acid-catalyzed cleavage of these compounds. Among the mechanisms[3-5,7] which have been suggested to account for the cleavage, two proposals merit attention. These are outlined in Scheme I. One proposal involves conversion of the amino

SCHEME I



alcohol into a glycol, either *via* displacement of amine by neighboring hydroxyl and hydrolytic cleavage of the resulting epoxide or *via* direct displacement of amine by water.[3,4] The intermediate glycols are known to undergo acid-catalyzed dehydration to β-aryl ketones or aldehydes. In the cleavage of ephedrine derivatives with concentrated phosphoric acid the intermediate glycols were, indeed, isolated, but the mechanism of glycol formation has not been convincingly resolved.[8]

(1) To whom inquiries should be addressed.

(2) (a) S. A. Fine and R. L. Stern, *J. Org. Chem.*, **32**, 4132 (1967). (b) In ref 2a 4-phenyl-2-tetralone was synthesized independently *via* intramolecular Friedel–Crafts reaction of 1,4-diphenyl-3-buten-2-one. An unexpected by-product, not reported previously in this synthesis, was 2-naphthol, isolated by extracting the crude product with sodium hydroxide followed by acidification.

(3) F. Kröhnke and A. Schulze, *Chem. Ber.*, **75**, 1154 (1942).

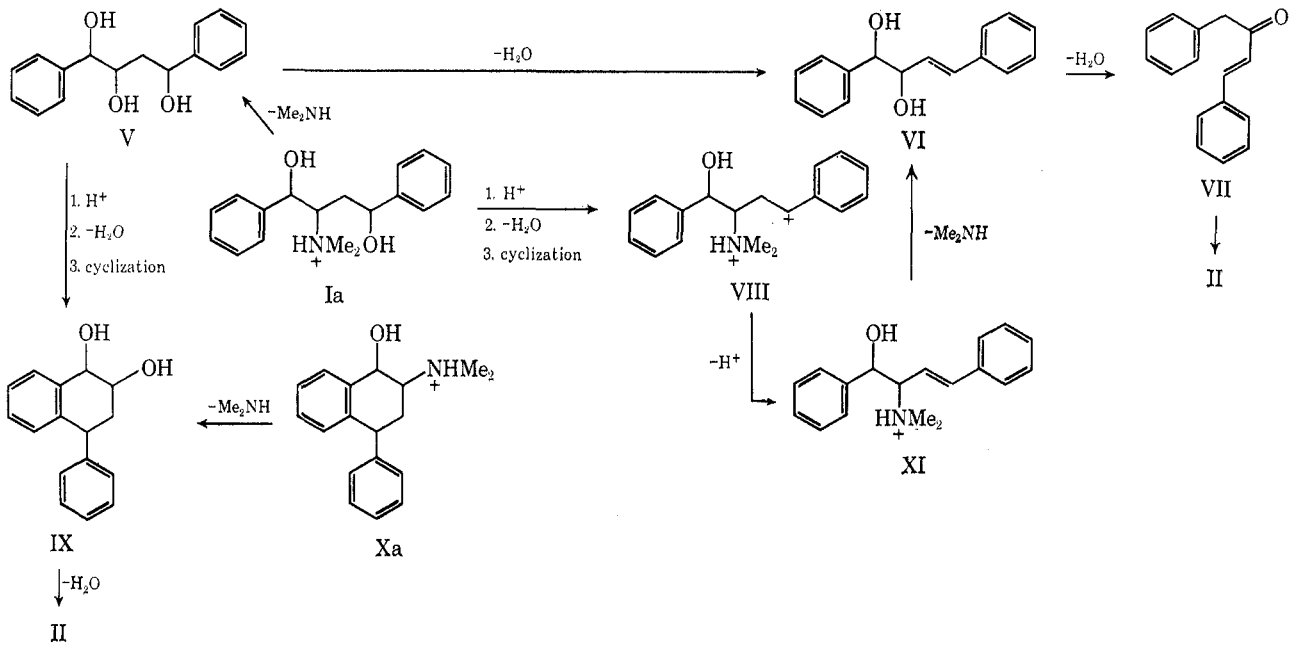
(4) H. Auterhoff and H. J. Roth, *Arch. Pharm.* (Weinheim), **289**, 470 (1956).

(5) P. T. Sou, *Bull. Fac. Sci. Univ. Franco-Chinoise*, **5**, 1 (1935); *Chem. Abstr.*, **30**, 4463 (1936).

(6) In ref 5 enamines were isolated when β-amino alcohols were treated with PCl_5.

(7) J. H. Fellman, *Nature*, **182**, 311 (1958).

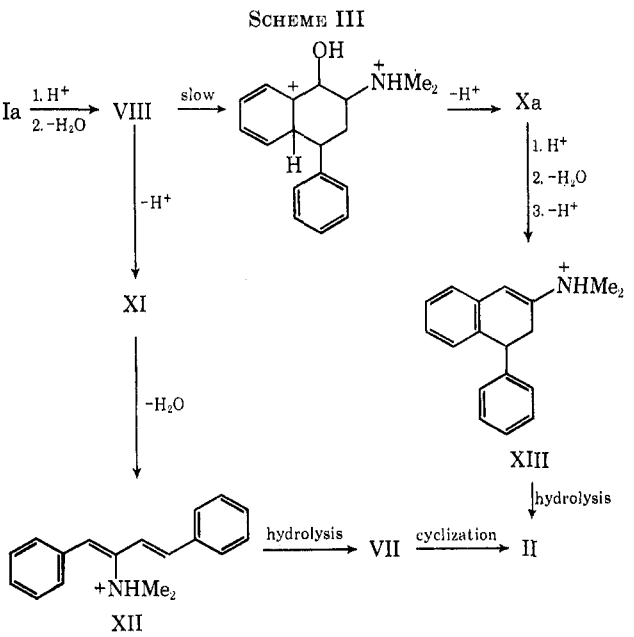
SCHEME II



An alternate mechanism involves dehydration of the amino alcohol to an enamine, which is subsequently hydrolyzed to an aldehyde or ketone.[3,5] However, convincing experimental evidence for the intermediacy of enamines is lacking.[6]

A priori, several pathways seem plausible for the acid-catalyzed conversion of aminodiol I into tetralone II. These may be conveniently arranged in sequences involving nucleophilic displacements at the carbon atom bearing the dimethylammonium moiety (Scheme II) or dehydration to enamines and subsequent hydrolysis to ketones (Scheme III). The diols VI and

SCHEME III



IX and triol V could be generated from the corresponding protonated amino alcohols *via* epoxidation and subsequent hydrolytic ring opening of the epoxides or by direct solvolytic displacement of the C-2 dimethylammonium group. The other reactions in Schemes II and III involve straightforward dehydrations and cyclizations. In order to reduce the number of mechanistic possibilities, synthesis of various intermediates was undertaken.

Results

The triol V was obtained as a mixture of stereoisomers upon borohydride reduction of the known hydroxydione XIV.[8] Likewise, the unsaturated diol VI was prepared from 1,4-diphenyl-3-butene-1,2-dione (XV); the latter was generated *via* selenium dioxide oxidation of 1,4-diphenyl-3-buten-2-one. The cyclic amino alcohol X was synthesized by reduction of the known amino ketone XVI[9] with lithium aluminum hydride. For comparison purposes the quaternary ammonium salt XVII was prepared by treatment of I with methyl iodide.

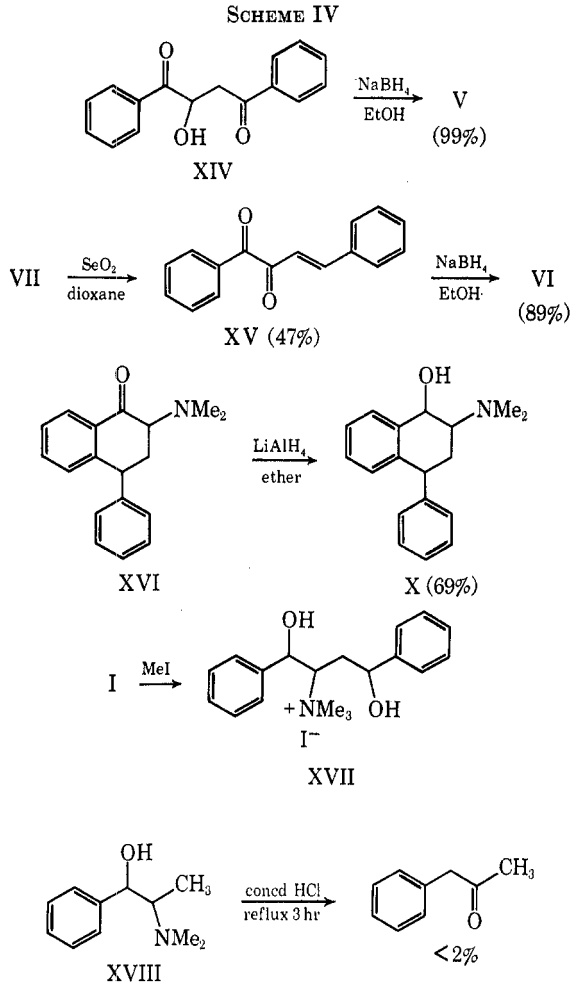
The intermediates were characterized by their elemental analyses, infrared spectra, and, in the case of VI, diagnostic chemical tests. The syntheses are summarized in Scheme IV.

Ketone VII was inert to refluxing concentrated hydrochloric acid; the unsaturated diol VI furnished a gum which, although unidentified, was shown *via* ir *not* to contain 4-phenyl-2-tetralone. The quaternary ammonium salt XVII afforded no 4-phenyl-2-tetralone. Both the triol V and the cyclic amino alcohol X afforded 4-phenyl-2-tetralone on treatment with hydrochloric acid. Infrared examination of the crude reaction product from V revealed the presence of a contaminant absorbing at 5.95 μ; no such contaminant was observed in the crude products from X and I.

In addition a model compound (XVIII), embodying the structural features of carbon atoms 1 and 2 in the aminodiol I, was subjected to concentrated hydrochloric acid and was found to be relatively unreactive.

(8) H. W. Dudley and S. Ochoa, *J. Chem. Soc.*, 625 (1933).
(9) S. Wawzonek and J. Kozikowski, *J. Amer. Chem. Soc.*, **76**, 1641 (1954).

SCHEME IV



In excess 6 *M* sulfuric acid at 110° the overall pseudo-first-order rate constant of tetralone formation from amino diol I was found to be $k_I = 8.56 \times 10^{-5}$ sec^{-1}. The activation energy for the reaction was determined by measuring the rates of the reaction at varying temperatures: $E_a = 26$ kcal/mol. The corresponding value determined for the entropy of activation was $\Delta S_0^{\pm} = -11$ eu. The rate constant of tetralone formation at 110° from the cyclic amino alcohol X is $k_X = 1.74 \times 10^{-4}$ sec^{-1}. Excellent straight-line plots were obtained in all runs except for slight convex curvature in the initial stages of the reactions.

Discussion

A priori, the unknown stereoisomeric composition of aminodiol I and of compounds V, VI, X, XVII, and XVIII would appear to curtail meaningful mechanistic conclusions. Fortunately, there is well-established evidence that optically active alcohols and β-amino alcohols in which the hydroxyl groups are benzylic undergo rapid acid-catalyzed racemization.[10-12] In these alcohols and, indeed, even in some simple *sec*-alkyl alcohols,[13] complete racemization was observed to occur prior to any detectable elimination. Hence the possible stereochemistry of the amino alcohols and polyols in the present case is unimportant, since *all* of their subsequent reactions occur in strongly acidic media.

The formation of tetralone from triol V necessitated a more definitive experiment in order to establish whether V was actually generated from I under the reaction conditions. Since trimethylamine is a weaker base than dimethylamine, the former should be a more effective leaving group than the latter. Hence, if nucleophilic displacement of the dimethylammonium group in aminodiol Ia can occur, the trimethylammonium substituent in XVII should be displaced with even greater facility. Because XVII is free to cyclize at C-4, the possibility of nucleophilic displacement at C-2 in Ia either before or after cyclization may be ruled out, thus excluding the intermediacy of V and IX.

The high-yield acid-catalyzed conversion of cyclic amino alcohol X into 4-phenyl-2-tetralone and the rates of tetralone formation from X and from I ($k_X/k_I \cong 2$ at 110°) are consistent with a mechanism of tetralone formation from I involving the intermediacy of X, although the data cannot be considered positive proof of such intermediacy. The fairly large negative entropy of activation in the sequence I → II suggests the formation of a cyclic transition state in the slow step. Hence, it seems likely that the rate-determining step involves intramolecular cyclization of the carbonium ion resulting from elimination of the protonated C-4 hydroxyl group in I (Scheme III).

The high reactivity of cyclic amino alcohol X toward acid is somewhat surprising in view of the much lower reactivity of XVIII. One factor which may contribute to this difference is that the fused aromatic ring of X has, in effect, an alkyl group *ortho* to the side chain bearing the benzylic hydroxyl group. The presence of this *ortho* substituent could inductively lower the activation energy for removal of the protonated hydroxyl group by providing added stabilization for the resulting carbonium ion. In addition, steric factors may contribute to the high reactivity of X toward acid. The formation of a stabilized benzylic carbonium ion demands coplanarity of the aromatic ring with the positively charged carbon atom and the two atoms directly attached to the latter. Examination of a molecular model of the carbonium ion derived from XVIII reveals serious steric repulsion between the large alkyl substituent and adjacent *ortho* hydrogen atom of the ring, thus rendering coplanarity difficult. Experimental support for this behavior is found in the solvolysis of α-phenylethyl chlorides, C_6H_5CHClR, in 80% aqueous ethanol, the relative rates of solvolysis decreasing rapidly with increasing size of R.[14] The geometry of the half-chair conformation of X is such that coplanarity of the aromatic ring and a developing benzylic carbonium ion is more easily achieved than in XVIII. Precedent for this hypothesis is found in the fact that 1-chlorotetralin undergoes ethanolysis at 25° more than 239 times faster than does 1-phenylethyl chloride.[15]

(10) H. Bretschneider, K. Biemann, W. Koller, and H. Sachsenmaier, *Monatsh. Chem.*, **81**, 31 (1950).
(11) L. G. Schroeter and T. Higuchi, *J. Amer. Pharm. Assoc.*, **47**, 426 (1958).
(12) E. Grunwald, A. Heller, and F. S. Klein, *J. Chem. Soc.*, 2604 (1957).
(13) D. V. Banthorpe, "Reaction Mechanisms in Organic Chemistry," Vol. II, Elsevier Publishing Co., New York, N. Y., 1963, p 145.
(14) G. Baddeley, J. Chadwick, and H. T. Taylor, *J. Chem. Soc.*, 2405 (1954).
(15) B. Baddeley and J. Chadwick, *ibid.*, 368 (1951).

Experimental Section[16]

1,4-Diphenyl-1,2,4-butanetriol (V).—A rapidly stirred suspension of 2-hydroxy-1,4-diphenyl-1,4-butanedione[8] (2.54 g, 10.0 mmol) in 95% ethanol (25 ml) was treated with sodium borohydride (378 mg, 10.0 mmol). The mixture became warm. After stirring for 0.5 hr the mixture was diluted with water and the ethanol was evaporated under reduced pressure, causing formation of a white, semisolid precipitate. The aqueous mixture was extracted four times with ether and the combined ether extracts were washed with water. Evaporation of solvent from the dried ether extract left a nearly colorless gum (2.56 g). Upon cooling overnight the gum became partially crystalline. Trituration with benzene containing a small amount of hexane followed by filtration gave a white, crystalline solid (858 mg). Recrystallization from benzene–cyclohexane (1:1) gave small, white plates (734 mg): mp 122–124°; ir 2.95 μ (s, broad, OH) and no carbonyl absorption.

Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.16; H, 7.07.

Evaporation of solvent from the benzene–hexane filtrate gave a colorless gum (1.58 g). Attempts to crystallize or distil the gum were unsuccessful: ir 2.95 μ and no carbonyl absorption.

Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.69; H, 7.22.

1,4-Diphenyl-3-butene-1,2-dione (XV).—A mixture of selenium dioxide (11.1 g, 0.100 mol), water (2 ml), and dioxane (70 ml) was warmed until homogeneous. 1,4-Diphenyl-3-buten-2-one (22 g, 0.10 mol) was added and the mixture was refluxed with stirring for 4 hr. The supernatant liquid was decanted from precipitated selenium and solvent was evaporated from the filtered solution under reduced pressure. The residual oil was distilled under vacuum, affording an orange oil, bp 150° (0.1 mm). Cooling the product for 2 days in a refrigerator caused it to solidify. Recrystallization from petroleum ether (bp 30–60°) gave 1,4-diphenyl-3-butene-1,2-dione (11 g, 47%) as yellow needles: mp 58.5–60° (lit.[17] mp 54–55°); ir 3.32 (aryl CH) and 6.05 μ (C=O) and no aliphatic CH.

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.39; H, 5.12. Found: C, 81.30; H, 5.18.

1,4-Diphenyl-3-butene-1,2-diol (VI).—A stirred mixture of 1,4-diphenyl-3-butene-1,2-dione (2.23 g, 9.45 mmol) and 95% ethanol (25 ml) was treated with sodium borohydride (360 mg, 9.52 mmol). An exothermic reaction occurred; stirring was continued for 0.5 hr. After the addition of water (75 ml) the solution was made slightly acidic by dropwise addition of 5% sulfuric acid and extracted three times with ether. Solvent was evaporated from the dried extract under reduced pressure, leaving a colorless gum (2.01 g). Recrystallization from benzene–petroleum ether (bp 60–110°) gave a white, crystalline solid, mp 60–90°. The compound decolorized a solution of bromine in carbon tetrachloride. Upon treatment with periodic acid followed by silver nitrate, the compound gave a white precipitate of silver iodate: ir 2.80 (sharp, OH), 2.95 (broad, OH), 3.34, and 3.48 μ (CH) and no carbonyl absorption.

Anal. Calcd for $C_{16}H_{16}O_2$: C, 80.01; H, 6.72. Found: C, 79.81; H, 6.55.

1,4-Diphenyl-1,4-butanediol-2-(N,N,N-trimethylammonium) Iodide (XVII).—A mixture of 2-(N,N-dimethylamino)-1,4-diphenyl-1,4-butanediol[2a] (2.0 g, 0.70 mmol) and methyl iodide (2.0 ml, 3.2 mmol) was heated gently on a steam bath for 10 min. After cooling to room temperature the mixture was triturated with acetone (15 ml) and filtered by suction, affording a white solid (1.43 g, 49%), mp 214–216°.

Anal. Calcd for $C_{19}H_{26}NO_2I$: C, 53.40; H, 6.13; N, 3.28; I, 29.69. Found: C, 53.22; H, 6.11; N, 3.03; I, 29.64.

4,4-Diphenyl-3-butenoic Acid.—The procedure of Borsche[18] was employed with a modified work-up. Diphenylacetaldehyde (50 g, 0.25 mol) was heated with malonic acid (30 g, 0.29 mol) and pyridine (50 g) for 3 hr on a steam bath with occasional swirling. The cooled reaction mixture was diluted with ice–water and acidified with 2 *N* sulfuric acid. The resulting mixture was extracted three times with ether. The combined ether extracts were washed twice with water and extracted three times with 10% sodium carbonate. Evaporation of solvent from the dried ether layer gave 17 g of recovered diphenylacetaldehyde (which could be recycled without purification in subsequent reactions with no reduction in yield).

The stirred basic layer was carefully acidified with 2 *N* sulfuric acid and the resulting white precipitate was collected, washed thoroughly with water, and dried. Recrystallization from petroleum ether (bp 60–110°) gave white crystals (25.1 g, 44%), mp 112–115° (lit.[18] mp 114–115°).

4,4-Diphenylbutyric Acid.—A solution of 4,4-diphenyl-3-butenoic acid (31.6 g, 0.133 mol) in absolute ethanol (200 ml) was hydrogenated over 10% palladium-on-charcoal catalyst (1 g) for 0.5 hr in a Parr apparatus. Filtration followed by evaporation of solvent under reduced pressure left a colorless oil which crystallized on standing. Recrystallization from petroleum ether (bp 60–110°)–benzene (10:1) gave white crystals (30.3 g, 0.126 mol, 95%), mp 103–106° (lit.[9] mp 103–106°).

2-(N,N-Dimethylamino)-4-phenyl-1-tetralol (X).—A solution of 2-(N,N-dimethylamino)-4-phenyl-1-tetralone (prepared *via* a sequence[9] starting with 4,4-diphenylbutyric acid) (8.6 g, 0.032 mol) was placed in the thimble of a Soxhlet extractor. A suspension of $LiAlH_4$ (1.00 g, 0.0264 mol) in anhydrous ether (100 ml) was refluxed so that the amino ketone was extracted into the mixture. After 19 hr the mixture was cooled to room temperature and excess $LiAlH_4$ was decomposed by dropwise addition of ethyl acetate (3 ml) in ether (5 ml) followed by slow, cautious addition of water (5 ml). The mixture was filtered with suction and solid material was washed thoroughly with ether. The organic filtrate was washed twice with water, twice with 10% Na_2CO_3, and again with water followed by drying ($MgSO_4$) and evaporation of solvent under reduced pressure, leaving a yellow-white solid (5.9 g, 69%). An analytical sample was prepared by two recrystallizations from *n*-butyl ether, giving white crystals: mp 130–146°; ir 2.87 μ (OH) and no carbonyl absorption.

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.85; H, 7.92; N, 5.24. Found: C, 81.06; H, 8.10; N, 5.17.

Attempted Reaction of 1,4-Diphenyl-3-buten-2-one (VII)[2a] with Hydrochloric Acid.—A mixture of the ketone (2 g, 9 mmol) and concentrated hydrochloric acid (50 ml) was refluxed for 18 hr with vigorous stirring. The cooled mixture was extracted with ether. Removal of solvent from the dried ether extract left a light yellow solid which had an ir spectrum identical with that of starting material.

Reaction of 1,4-Diphenyl-3-butene-1,2-diol (VI) with Hydrochloric Acid.—A mixture of the diol (524 mg, 2.18 mmol) and concentrated hydrochloric acid (25 ml) was refluxed for 3 hr. The cooled mixture was extracted three times with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and evaporated under reduced pressure, leaving an orange-brown oil (425 mg), ir 5.95 μ (conjugated C=O). There was no significant OH absorption and no absorption at 5.85 μ, the C=O wavelength in 4-phenyl-2-tetralone.[2a]

Reaction of 1,4-Diphenyl-1,2,4-butanetriol (V) with Hydrochloric Acid.—A mixture of the triol (11.2 g, 0.0433 mol, mixture of stereoisomers) and concentrated hydrochloric acid (300 ml) was refluxed for 3 hr. The cooled mixture was extracted three times with ether. The ether extract was washed with water, dried, and evaporated under reduced pressure, leaving an orange oil (11.0 g). Distillation under vacuum afforded a colorless oil (6.09 g): bp 124–130° (0.02 mm); ir 5.83 (C=O) and 5.95 μ (shoulder).

A portion of the product was reduced with sodium borohydride to a crystalline substance, mp 110–118°, which, after recrystallization from ethanol–water, was identified as 4-phenyl-2-tetralol by melting point (118–121°) and mixture melting point (119–122°) with an authentic sample.

Similar experimental results were obtained when either the crystalline isomer of the triol or the gum was employed separately.

Reaction of 1,4-Diphenyl-1,4-butanediol-2-(N,N,N-trimethylammonium) Iodide with Hydrochloric Acid.—A solution of the methiodide (1.43 g, 3.36 mmol) in concentrated hydrochloric acid (25 ml) was refluxed for 2 hr. The reaction mixture was cooled to room temperature and extracted with three portions of ether. The ether extract was washed with water, dried, and evaporated under reduced pressure, leaving a trace of tarry material.

(16) Melting points were taken on a Thomas–Hoover Unimelt apparatus and are uncorrected. Infrared spectra were determined in CCl_4 on a Beckman IR-8 instrument and were calibrated against the 6.23-μ peak of polystyrene. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(17) P. Ruggli, P. Weis, and H. Rupe, *Helv. Chim. Acta*, **29**, 1788 (1946).

(18) W. Borsche, *Justus Liebigs Ann. Chem.*, **526**, 1 (1936).

Benzene was added to the aqueous layer and water was removed by azeotropic distillation. A suspension of saltlike, white crystals, mp 163–178°, remained in the benzene.

Reaction of 2-(N,N-Dimethylamino)-1-phenylpropanol (XVIII)[19] with Hydrochloric Acid.—A solution of the amino alcohol (1.02 g, 5.69 mmol) in concentrated hydrochloric acid (30 ml) was refluxed 3 hr, cooled, diluted with water, and extracted three times with ether. The ether extract was washed with water and saturated sodium chloride solution and then dried, and the solvent was evaporated. The crude product (15 mg, 1.8%), a nearly colorless liquid, was identified as phenyl-2-propanone by comparison of ir spectra and by literature analogies[4,20] in which reaction of the same amino alcohol with phosphoric acid or sulfuric acid gave phenyl-2-propanone.

Reaction of 2-(N,N-Dimethylamino)-4-phenyl-1-tetralol with Hydrochloric Acid.—A solution of the cyclic amino alcohol (500 mg, 1.87 mmol) in concentrated hydrochloric acid was refluxed for 2 hr and then cooled on ice. The oil-containing mixture was extracted three times with ether and the combined ether extracts were washed twice with water. Drying followed by evaporation of ether under reduced pressure left a light yellow oil (365 mg, 88%). The ir spectrum of the crude product was superimposable with a spectrum of authentic 4-phenyl-2-tetralone.[2a] A portion of the product was reduced with sodium borohydride to 4-phenyl-2-tetralol, identical in every respect with an authentic sample.[2a]

Determination of Rates of Reaction of Amino Alcohols I and X with 6 *M* Sulfuric Acid.—A series of 50-ml flasks, each containing 6 *M* sulfuric acid (25.0 ml), were placed in an oil bath and the bath was heated slowly to the desired temperature. After 1 hr the amino alcohol was introduced into each flask and timing was begun with a stopwatch. During the reaction the flasks were swirled occasionally and the temperature of the oil bath was maintained within 0.5° of the desired value. At the end of the reaction, ice–water (15 ml) was added and the flask was immersed in ice–water immediately. The cooled reaction mixture was poured into a 60-ml separatory funnel and extracted with ether (two 20-ml portions followed by a 10-ml portion). The combined ether extracts were washed with water (10 ml) and saturated sodium chloride solution (10 ml) and dried ($MgSO_4$). The ether solution was filtered into a tared flask (filter paper and $MgSO_4$ were washed thoroughly with ether) and evaporated under reduced pressure, ultimately at 60–70°, until the weight of the flask remained constant. The results of the experiments and a representative run are tabulated in Tables I and II.

TABLE I

REPRESENTATIVE RUN. RAW KINETIC DATA FROM THE REACTION OF 2-(N,N-DIMETHYLAMINO)-4-PHENYL-1-TETRALOL (X) WITH 6 *M* H_2SO_4

Amino alcohol, mg	Temp, °C ± 0.5°	Reaction time, min	Isolated 4-phenyl-2-tetralone, mg
350	110	15	16.4
350	110	30	36.9
350	110	60	105.9
350	110	90	152.4
350	110	120	191.1

TABLE II

GRAPHICALLY DETERMINED PSEUDO-FIRST-ORDER RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE REACTIONS OF AMINO ALCOHOLS I AND X WITH 6 *M* H_2SO_4

Amino alcohol	Temp, °C	k, sec^{-1}
I	118	1.65×10^{-4}
I	110	8.56×10^{-5}
I	105	5.38×10^{-5}
X	110	1.74×10^{-4}

It follows that $(k_X/k_I)_{110°} = 2.03$. These data allow the graphical calculation[21] of activation parameters: $E_a = 26$ kcal/mol; $\Delta S^{\ddagger}_{\circ} = -11$ eu.

Registry No.—I, 14195-36-9; II, 14195-35-8; V, 19236-31-8; VI, 23885-33-8; X, 23885-34-9; XV, 23885-00-9; XVII, 23885-01-0.

(19) S. Sugasawa, T. Yamazaki, M. Kawanishi, and J. Iwao, *J. Pharm. Soc. Jap.*, **71**, 530 (1951).

(20) H. Takamatsu, *ibid.*, **76**, 1244 (1956).

(21) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1953, p 98 ff.

Titanium Chloride Catalyzed Addition of Aziridine to Ketones. A Route to N-Aziridinylenamines[1]

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Addition of aziridine to a series of cyclic ketones from C_5–C_8 in the presence of $TiCl_4$ and triethylamine produced 1,1-bis(aziridinyl)cycloalkanes, 1-N-aziridinylcycloalkenes, 1-N-(β-chloroethyl)cycloalkylimine, and 1-N-(β-aziridinylethyl)cycloalkylimine. The product ratio was dependent upon the ketone ring size and the ketone/$TiCl_4$ mole ratio. 1-N-Aziridinyl-1-cycloheptene (**10**) and 1-N-aziridinyl-1-cyclooctene were prepared in ~20% yield but no enamine could be isolated from cyclopentanone or cyclohexanone. 1,1-Bis(aziridinyl)cyclopentane (**2**) and cyclohexane (**3**) were synthesized for the first time; previously reported bisaziridinyl derivatives were shown to be 1-N-(β-aziridinylethyl)cycloalkylimines. 3-N-Aziridinyl-1-cyclohexene (**17**) was prepared by the addition of aziridine to 3-bromo-1-cyclohexene in the presence of potassium hydroxide; treatment of this derivative with strong bases at temperatures up to 150° failed to effect an isomerization to 1-N-aziridinyl-1-cyclohexene. All of the aziridine compounds decomposed at room temperature to yield low molecular weight polyaziridines. The structures of the derivatives were assigned on the basis of infrared, nmr, and mass spectral data.

Enamines are generally prepared by condensing aldehydes or ketones with secondary amines in aromatic solvents and removing the water evolved by azeotropic distillation. An alternate technique, which is more applicable to reaction mixtures containing low-boiling components, is to remove the water with an inorganic drying agent such as $CaCl_2$ or $MgSO_4$.[2] Recently White and Weingarten reported that titanium tetrachloride is a more effective drying agent for this reaction; it appears to enhance the reactivity of the carbonyl as well as scavenge the water.[3] We have utilized the activating influence of $TiCl_4$ to prepare enamines derived from aziridine; *i.e.*, we have prepared

(1) Presented in part at the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969.

(2) L. W. Haynes, "Enamines," A. G. Cook, Ed., Marcel Dekker, Inc., New York, N. Y., 1969, Chapter 2.

(3) R. A. White and H. Weingarten, *J. Org. Chem.*, **32**, 213 (1967).