days, 0.26 g (26%), 0.43 g (40%); 9 days, 0.17 g (17%), 0.46 g (43%).

2. **A Thioxanthenesulfonic Acid (IX).**—A solution of 2.0 g of thioxanthene in 250 ml of 96% sulfuric acid was made. After several experiments with aliquots of this solution the best method of isolating a sulfonic acid was found to be the following. An aliquot (50 ml) was poured onto ice and the volume of the solution was diluted to about 2 l. with water. The suspension of thioxanthene and thioxanthone was filtered off, and the filtrate was neutralized with solid barium carbonate. The precipitated barium sulfate was removed and the filtrate was evaporated to dryness. The solid residue was extracted with benzene, dried, and shaken with 150 ml of water to extract the barium salt of the sulfonic acid from barium carbonate. A solution of the barium sulfonate was passed through a Dowex 50W-X4 50–100 mesh cation-exchange column, and the effluent was neutralized with standard sodium hydroxide solution.

The neutral solution was evaporated to dryness. The residue was dissolved in water and a solution of S-benzylisothiouronium chloride was added. A solid precipitated, having mp 217° before and after crystallization from acetic acid.

Anal. Calcd for $C_{21}H_{20}N_2O_3S_3$: C, 56.73; H, 4.53; N, 6.30; S, 21.63. Found: C, 55.98; H, 4.56; N, 6.11; S, 21.55, 21.63.

3. **A Thioxanthonesulfonic Acid (XI).**—The barium sulfate which was precipitated and filtered off in the isolation of the thioxanthenesulfonic acid gave a yellow-green solution when treated with 96% sulfuric acid. Although this is only slender, circumstantial evidence, we believe that it indicates the presence of the barium salt of a thioxanthonesulfonic acid. Attempts to extract the sulfonic acid were unsuccessful.

Thioxanthone was sulfonated by heating 1.5 g of the ketone with 6 g of 30% fuming sulfuric acid for 5.5 hr at 150° (similar to the method of Kurihara and Niwa[16]). We were able to isolate 1.84 g of a mixture of barium salts of thioxanthonesulfonic acids. This mixture was yellow. We were unable to separate the monosulfonic acid[16] from this mixture. The barium salts dissolved in 96% sulfuric acid and the solution was yellow-green.

4. **Sulfur Dioxide.**—The sulfur dioxide obtained from the oxidation of weighed amounts of thioxanthene by 96% sulfuric acid was carried through Ascarite-filled tubes by a current of nitrogen. Two experiments were performed and gave 81 and 82% of the theoretical amount of sulfur dioxide based on a two-electron oxidation per molecule of thioxanthene.

Thioxanthene in Aqueous Acid.—Finely ground thioxanthene (0.200 g), mp 129–130°, was placed in 400 ml of 0.9 *N* sulfuric acid for 8 days with occasional shaking. Filtration gave 0.184 g, mp 128–130°. Thin layer chromatography showed the presence of thioxanthone.

Products from Thioxanthene 10-Oxide in 96% Sulfuric Acid.—A solution of 1.00 g of the oxide in 100 ml of 96% sulfuric acid was kept for 24 hr and poured onto crushed ice. The orange color of the aqueous solution slowly disappeared. A precipitate formed and was filtered off after standing 1 day. After being washed with water and dried, the solid weighed 0.944 g, mp 150–175°. Column chromatography with silica gel and benzene elution gave 409 mg of thioxanthene, mp 127–128°, and 496 mg of thioxanthone, mp 210°. The amounts anticipated on the basis of the reaction of the thioxanthylium ion with its hydration product (thioxanthenol) were 462 and 495 mg, respectively.

Recovery of Thioxanthone from Its Solution in 96% Sulfuric Acid.—A solution of 1.00 g of thioxanthone in 100 ml of acid was made. After 15 min, 20 ml of this solution was poured onto ice. A solid precipitated immediately. Its weight after washing and drying was 199 mg, mp 213–214°. After being kept for 48 hr, 50 ml of the acid solution was similarly treated giving 470 mg, mp 212°. Each experiment represents almost quantitative recovery of thioxanthone.

Anodic Oxidation of Thioxanthene.—A solution of thioxanthene (10^{-2} *M*) and tetrabutylammonium perchlorate (10^{-1} *M*) in nitromethane was used. Electrolysis was carried out in a Varian Associates electrolysis cell, using a platinum grid anode and changing the voltage periodically while searching continuously for an esr signal, but none was detected. The solution near the anode was colored orange, and the color did not disappear on standing after the current was stopped.

Sulfonation of Xanthene.—A solution of 1.0 g of xanthene in 100 ml of 96% sulfuric acid was kept for 2 hr and poured onto ice. The golden solution was neutalized with solid barium hydroxide. The barium sulfate was removed and the filtrate was concentrated to 100 ml. Filtration was repeated and the filtrate was converted to a solution of the acid with a cation-exchange column. The acid solution was neutralized with sodium hydroxide and evaporated to dryness. A portion (0.200 g) of the sodium salt was converted to the free acid by ion exchange and the acid was found by titration to have the equivalent weight of a xanthenedisulfonic acid.

Spectra.—Nmr spectra were obtained with a Varian Associate's A-60 instrument. The internal reference used for the sulfuric acid solutions was tetramethylammonium chloride (TMA). When the instrument had been "zeroed" for tetramethylsilane (TMS) in deuteriochloroform the single peak of TMA in 96% sulfuric acid came at −3.11 ppm. Calibration of TMA against TMS was not made in any other way. The minor changes in the displacement of a TMA signal with respect to TMS which occur when solvents are varied have been discussed by Deno.[17] The temperature of the samples in the probe was about 35°.

Ultraviolet and visible spectra were obtained with a Beckman DK-2 Instrument, using ground-glass stoppered cells.

(16) T. Kurihara and H. Niwa, *J. Pharm. Soc. Japan*, **73**, 1378 (1953); we wish to thank Dr. Pill-Soon Song for translating this paper.

(17) N. C. Deno, *et al.*, *J. Am. Chem. Soc.*, **85**, 2991 (1963).

Reactions of Phosphorus Compounds. XI. A General Synthesis of Substituted 1,2-Dihydroquinolines

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A series of acyl- and arylsulfonyl-1,2-dihydroquinolines has been prepared from substituted *o*-formyl- and *o*-ketoanilines employing vinyltriphenylphosphonium bromide as the cyclization reagent.

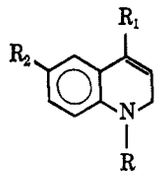
The use of vinyltriphenylphosphonium bromide (**3**) as a general reagent for the synthesis of heterocyclic and carbocyclic compounds has been demonstrated.[1-3] This reagent has also been used in preparing olefinic compounds *via* a chain-extension reaction.[4] We now wish to report the further use of salt **3** in a general synthesis of 1,2-dihydroquinolines, as shown in Scheme I.

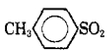
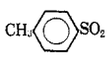
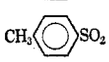
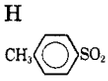
The sodium salts **2a–g** were prepared by reaction with sodium hydride in ether or benzene and were not isolated. Addition of the vinylphosphonium salt **3** and dimethylformamide to the salt **2** resulted in the formation of the highly colored ylide **4**. Stirring at room temperature and, in some cases, with heating

(1) E. E. Schweizer, *J. Am. Chem. Soc.*, **86**, 2744 (1964).
(2) E. E. Schweizer and K. Light, *J. Org. Chem.*, **31**, 870 (1966).
(3) E. E. Schweizer and G. O'Neill, *ibid.*, **30**, 2082 (1965).
(4) E. E. Schweizer, L. Smucker, and R. Votral, *ibid.*, **31**, 467 (1966).

TABLE I

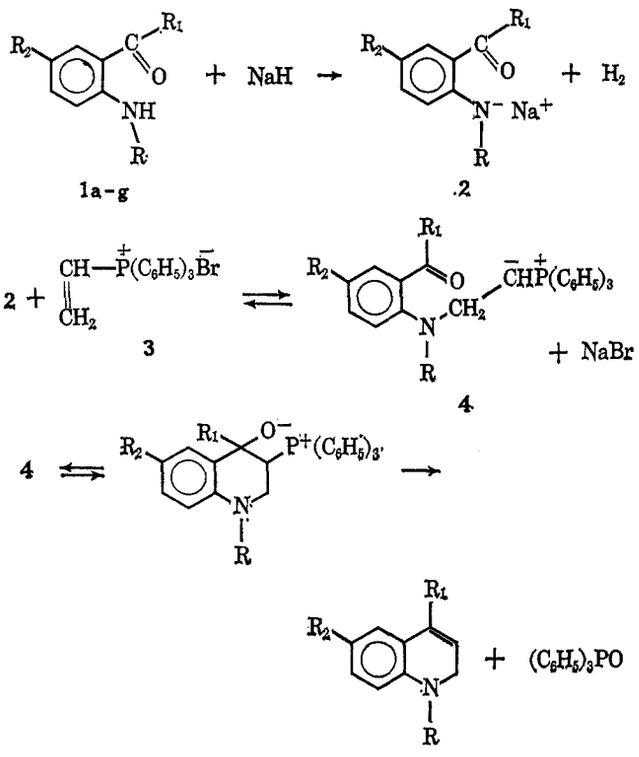
SOME PHYSICAL AND ANALYTICAL DATA OF SUBSTITUTED 1,2-DIHYDROQUINOLINES



No.	Compound R	Compound R_1	Compound R_2	Formula	Mp or bp, °C (mm)	Yield, %	Anal, % Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
5a		H	H	$C_{16}H_{15}NO_2S$	89–90	50						
5b		CH_3	H	$C_{17}H_{17}NO_2S$	105–106	9	68.2	5.7	4.7	68.3	5.7	4.5
5c		C_6H_5	H	$C_{22}H_{19}NO_2S$	166–167	48	73.1	5.3	3.9	73.1	5.3	3.8
5d	CH_3CO	H	H	$C_{11}H_{11}NO$	110–120 (0.2)	48						
5e	H	H	H	C_9H_9N	*a*	4						
5f		C_6H_5	Cl	$C_{22}H_{18}ClNO_2S$	169–170	55	66.8	4.6	3.5	66.6	4.6	3.4
5g	CH_3CO	H	NO_2	$C_{11}H_{10}N_2O_3$	105–106	36	60.5	4.6	12.8	60.4	4.4	12.6

[a] This product was not isolated; see the Experimental Section for details.

SCHEME I



5a–g

a, R = p-$SO_2C_6H_5CH_3$; R_1 = H; R_2 H
b, R = p-$SO_2C_6H_5CH_3$; R_1 = CH_3; R_2 = H
c, R = p-$SO_2C_6H_5CH_3$; R_1 = C_6H_5; R_2 = H
d, R = $COCH_3$; R_1 = H; R_2 = H
e, R = H; R_1 = H; R_2 = H
f, R = p-$SO_2C_6H_5CH_3$; R_1 = C_6H_5; R_2 = Cl
g, R = $COCH_3$; R_1 = H; R_2 = NO_2

resulted in the elimination of triphenylphosphine oxide and the formation of the 1,2-dihydroquinolines **5a–g**.

Many 1,2-dihydroquinolines that are unsubstituted on the 1 and/or 2 position are unstable. For this reason the synthesis was developed using either N-acetyl- or N-p-tolylsulfonyl-substituted starting materials. One reaction was completed using the unsubstituted compound anthranilaldehyde (**1e**). In this latter case the product, 1,2-dihydroquinoline (**5e**), was shown to be present in only 4% yield by vapor phase chromatography (vpc).

Yields of the N-substituted dihydroquinolines prepared, as shown in Table I, range from 36 to 55% (except for **1b**). Only in the case of the N-p-tolylsulfonyl-2-aminoacetophenone (**1b**) were attempts made to maximize the yield; however, the highest yield obtained was only 9%. The yield in this reaction is low when R is methyl but is substantially higher when R is H (**5a**), or when R is phenyl (**5c**).

The synthesis of 1,2-dihydroquinolines has usually been accomplished by reduction of quinoline compounds. Probably the most common reagent for carrying out this reduction is lithium aluminum hydride. Schmid and Karrer[5] first prepared dihydroquinolines by this method. Several others have extended this synthesis.[6] Dialkylaluminum hydrides have been used very successfully.[7] Sodium in liquid ammonia[8] and sodium hydrazide in hydrazine or benzene[9] are other reduction methods employed.

Johnson and Buell[10] first prepared 1,2-dihydroquinoline by elimination of β-phenylethylamine from 4-(β-phenylethylamino)-1,2,3,4-tetrahydroquinoline. Other eliminations from substituted tetrahydroquinolines have been reported.[11,12]

(5) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 960 (1949).
(6) (a) E. Braude, J. Hannah, and R. Linstead, *J. Chem. Soc.*, 3249 (1960); (b) R. Elderfield and B. Wark, *J. Org. Chem.*, **27**, 643 (1962); (c) for a review of methods before 1957, see N. Campbell, "Chemistry of Carbon Compounds," Vol. IVA, E. Rodd, Ed., Elsevier Publishing Co., Amsterdam, 1957, p 584 ff.; and R. Elderfield, "Heterocyclic Compounds," Vol. IV, R. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, pp 271–282.
(7) W. P. Neumann, *Ann.*, **618**, 90 (1958); W. P. Neumann, *Angew Chem.*, **70**, 401 (1958).
(8) W. Huckel and L. Hagedorn, *Ber.*, **90**, 752 (1957).
(9) T. Kaufmann, *et al.*, *Angew. Chem.*, **72**, 918 (1960).
(10) W. Johnson and B. Buell, *J. Am. Chem. Soc.*, **74**, 4517 (1952).
(11) R. F. Collins, *J. Chem. Soc.*, 2053 (1960).
(12) L. Zalukaev and T. Zheltukhina, *Dokl. Akad. Nauk. SSSR*, **152**, 943 (1963).

Dihydroquinoline syntheses by ring closure methods are not common. Although several of the ring closures for quinolines (*e.g.*, Skraup synthesis, Doebner–von Miller synthesis) pass through dihydroquinoline intermediates, the development of dihydroquinoline syntheses from these reactions has not been accomplished.

The value of the synthesis described herein is that it provides a convenient method of closing a ring directly to a dihydroquinoline which is not further oxidized under the reaction conditions employed. The absence of a reducing medium also allows the preparation of dihydroquinolines containing an easily reducible substituent (*e.g.*, nitro group).

Experimental Section

Infrared spectra were obtained on a Perkin-Elmer Infracord 137 and nmr spectra were obtained on a Varian A-60 analytical nmr spectrometer, using tetramethylsilane as standard. All melting points were uncorrected and obtained on a Fischer-Johns melting point apparatus. Analyses were by Micro-Analysis, Inc., Wilmington, Del.

Reagents.—The vinyltriphenylphosphonium bromide was prepared according to the procedure of Bach and Schweizer.[13] Sodium hydride was obtained as approximately 54% dispersion in mineral oil from Metal Hydrides, Inc., Beverly, Mass. The 2-aminoacetophenone, 2-nitrobenzaldehyde, and 5-chloro-2-aminobenzophenone were obtained from Aldrich Chemical Co., Inc. Preparation of all *p*-tolylsulfonylamides followed the general procedure of Vogel.[14]

Other reagents were prepared by the method indicated in the literature: anthranilaldehyde,[15] 2-aminobenzophenone,[16] N-acetylanthranilaldehyde,[17] 5-nitro-N-acetylanthranilaldehyde.[18]

Florisil, 60–200 mesh, was used for column chromatography and was obtained from Matheson Coleman and Bell. Anhydrous reagent grade solvents were used in all cases.

1,2-Dihydro-1-*p*-tolylsulfonylquinoline (5a).—In a typical procedure, sodium hydride (0.0075 mole) and N-*p*-tolylsulfonylanthranilaldehyde (0.0075 mole) in 100 ml of anhydrous ether were refluxed under a nitrogen atmosphere for 18 hr. To this mixture were added 0.0075 mole of vinyltriphenylphosphonium bromide and 100 ml of dimethylformamide; the reaction was allowed to heat at reflux temperature for 2 days. After cooling to room temperature, water and ether were added, and the ether extracts were washed with water and dried over anhydrous magnesium sulfate. Evaporation of the ether extracts gave an oil from which 0.8 g of triphenylphosphine oxide was isolated by recrystallization from ether (identified by mixture melting point and comparison of infrared spectrum with authentic sample's). The remaining oil (1.4 g) was placed on a column made up with 75 g of Florisil. Elution with a solution of 75% chloroform in benzene gave 1.0 g of the known[11] 1,2-dihydro-1-*p*-tolylsulfonylquinoline; the total yield of this product was 50%. Recrystallization from an ether–petroleum ether (bp 90–100°) mixture gave white crystals, mp 89–90° (lit.[11] mp 91°). The infrared spectrum was identical with that of an authentic infrared spectrum.[19]

1,2-Dihydro-4-methyl-1-*p*-tolylsulfonylquinoline (5b).—Sodium hydride (0.02 mole), N-*p*-tolylsulfonyl-2-aminoacetophenone (0.02 mole), and 40 ml of anhydrous benzene were stirred at room temperature under a nitrogen atmosphere for 15 min. Vinyltriphenylphosphonium bromide (0.02 mole) and 150 ml of dimethylformamide were added and the mixture was stirred at room temperature for 2 hr, then heated to 120° for 7 days. Ether extraction was carried out as described above for compound **5a**. Evaporation of the ether extracts gave an oil to which methanol was added and subsequent recrystallization gave 1.45 g of a white solid. This was placed on a 1-in. chromatographic column made up with 75 g of Florisil. Elution with benzene followed by 15% chloroform in benzene gave 0.72 g of an oil which was taken up in methanol and recrystallized to give 0.52 g of **5b**: ν^{KBr} 1590 w, 1650 w, 1340 s, 1165 s cm^{-1}; nmr (δ^{CCl_4}) 1.5 (m, three, CH_3), 2.3 (s, three, CH_3), 4.2 (m, two, CH_2), 5.1–5.4 (m, one, CH), 6.8–7.8 ppm (m, eight, aryl).

1,2-Dihydro-4-phenyl-1-*p*-tolylsulfonylquinoline (5c).—Sodium hydride (0.0116 mole), 2-amino-N-*p*-tolylsulfonylbenzophenone (0.0116 mole), and 50 ml of anhydrous benzene were stirred with warming under a nitrogen atmosphere for 15 min. Vinyltriphenylphosphonium bromide (0.0116 mole) and 100 ml of dimethylformamide were added and the mixture was stirred at room temperature for 1 hr, then at 70° for 40 hr. Ether extraction was carried out as described above for compound **5a**. The ether extracts were evaporated and methanol was added to the remaining oil. Recrystallization from methanol gave 2.0 g of **5c**, mp 128–135°. Several recrystallizations from carbon tetrachloride gave an analytical sample: mp 166–167°; ν^{KBr} 1600 w, 1340 s, 1160 s cm^{-1}; nmr (δ^{CDCl_3}) 2.3 (s, three, CH_3), 4.5 (d, two, CH_2), 5.55 (t, one, CH), 6.6–7.9 ppm (m, 13, aryl).

1-Acetyl-1,2-dihydroquinoline (5d).—Sodium hydride (0.0076 mole), N-acetylanthranilaldehyde (0.0076 mole), and 75 ml of anhydrous ether were refluxed under a nitrogen atmosphere for 30 min. After cooling the mixture, vinyltriphenylphosphonium bromide (0.0076 mole) and 100 ml of dimethylformamide were added and the mixture was heated at reflux for 24 hr. Ether extraction was carried out as described above for compound **5a**. Concentration of the ether extracts followed by a short-path distillation gave 0.9 g of **5d**: bp 110–120° (0.2 mm); $n^{25}D$ 1.6005 [lit.[20] bp 102° (0.8 mm), $n^{23}D$ 1.6028]; ν^{KBr} 1670 s, 1610 w cm^{-1}; nmr (δ^{CDCl_3}) 2.05 (s, three, CH_3), 4.3 (d, two, CH_2), 5.9 (m, one, CH_2CH=), 6.4 (d, one, C_6H_4CH=), 6.9–7.2 ppm (m, four, aryl). Ether was added to the residue from the distillation and 1.2 g of triphenylphosphine oxide (54% yield) was recrystallized.

1,2-Dihydroquinoline (5e).—Sodium hydride (0.0163 mole), anthranilaldehyde (0.0163 mole), and 75 ml of anhydrous benzene were refluxed for 10 min, then stirred at room temperature for 1 hr. Vinyltriphenylphosphonium bromide (0.0163 mole) and 100 ml of dimethylformamide were added and the mixture was refluxed for another 30 min. Ether extraction was carried out as described above for compound **5a**. The ether extracts were allowed to dry for only 2 hr over anhydrous magnesium sulfate; concentration on a steam bath was followed by a short-path distillation which gave 0.6 g of an oil which was shown by vpc analysis to contain 86% anthranilaldehyde and 14% 1,2-dihydroquinoline. Presence of the 1,2-dihydroquinoline was indicated by the nmr spectrum of the mixture, a split pair of doublets representing the methylene group appeared at 4.0 ppm, and the characteristic absorption[4] for the *cis*-cinnamyl protons appeared, two pairs of unresolved triplets, one pair centered at 5.45 and the other pair centered at 6.18 ppm. Air oxidation of 1,2-dihydroquinoline to quinoline has been shown to take place within 2 days.[10] After the mixture of anthranilaldehyde and 1,2-dihydroquinoline was allowed to stand in air for 4 days, the infrared spectrum of this mixture showed the presence of medium bands appearing at 790 and 810 cm^{-1} which were not present in the previous infrared spectra. These bands concur with the strong bands occurring at 790 and 810 cm^{-1} in an authentic quinoline sample. Further proof of the presence of quinoline was shown by peak enhancement using vapor phase chromatography.

6-Chloro-1,2-dihydro-4-phenyl-1-*p*-tolylsulfonylquinoline (5f).—Sodium hydride (0.035 mole), 5-chloro-2-N-*p*-tolylsulfonylaminobenzophenone (0.035 mole), and 50 ml of anhydrous benzene were stirred at room temperature under a nitrogen atmosphere for 10 min. Vinyltriphenylphosphonium bromide (0.035 mole) and 100 ml of dimethylformamide were added and the mixture was stirred at room temperature for 20 hr, then at 70° for 4 hr. Ether extraction was carried out as described above for compound **5a**. The ether extracts were evaporated on a steam bath to give a dark oil. Methanol was added and a solid was formed. A small amount of petroleum ether (bp 30–60°) was added to wash out the mineral oil present originally from the sodium hydride–oil dispersion. After the petroleum ether was decanted off, recrystallization from methanol gave 7.6 g (55% yield) of the crude product (**5f**), mp 155–160°. Several recrystallizations from

(13) E. E. Schweizer and R. Bach, *J. Org. Chem.*, **29**, 1746 (1964).

(14) A. Vogel, "Practical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1963, p 653.

(15) L. Smith and J. Opie, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 56.

(16) H. Scheifele and D. DeTar, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 34.

(17) P. Friedlaender, *Ber.*, **15**, 2574 (1882).

(18) P. Cohn and L. Springer, *Monatsh. Chem.*, **24**, 96 (1903).

(19) The authors wish to thank Dr. R. F. Collins for an authentic infrared spectrum of this compound.

(20) E. Braude, J. Hannah, and R. Linstead, *J. Chem. Soc.*, 3254 (1960).

an ethanol–ethyl acetate mixture gave an analytically pure sample: mp 169–170°; ν^{KBr} 1600 w, 1350 s, 1170 s cm^{-1}; nmr (δ^{CDCl_3}) 2.3 (s, three, CH_3), 4.56 (d, two, CH_2), 5.65 (t, one, CH), 6.6–7.9 ppm (m, 12, aryl).

1-Acetyl-1,2-dihydro-6-nitroquinoline (5g).—Sodium hydride (0.0255 mole), 5-nitro-N-acetylanthranilaldehyde (0.0255 mole), and 50 ml of anhydrous benzene were refluxed under a nitrogen atmosphere for 1.5 hr. After cooling the mixture to room temperature, vinyltriphenylphosphonium bromide (0.0255 mole) and 100 ml of dimethylformamide were added and the mixture was stirred at room temperature for 12 hr. Ether extraction was carried out as described above for compound **5a**. Evaporation of the ether extracts gave a yellow solid–oil mixture. Petroleum ether (bp 30–60°) was added to wash out the mineral oil and then decanted off. Methanol was then added and the mixture was heated slightly. Cooling and filtration gave 1.98 g of the crude compound **5g**, mp 95–102°. Several recrystallizations from methanol gave an analytically pure sample of yellow crystals: mp 105–106°; ν^{KBr} 1670 s, 1610 w, 1580 w cm^{-1}; nmr (δ^{CDCl_3}) 2.26 (s, three, CH_3), 4.45 (d, two, CH_2), 6.18 (m, one, $CH_2CH=$), 6.6 (d, one, $C_6H_3CH=$), 7.25–8.0 ppm (m, three, aryl).

N-p-Tolylsulfonylanthranilaldehyde.—The reaction of anthranilaldehyde with p-tolylsulfonyl chloride in pyridine, according to the general procedure of Vogel,[14] gave N-p-tolylsulfonylanthranilaldehyde which was recrystallized from ethanol to give an analytical sample: mp 135–136° (lit.[21] mp 203–205°); nmr (δ^{CDCl_3}) 2.35 (s, three, CH_3), 7.0–7.9 (m, eight, aryl), 9.8 (s, one, CHO), 10.76 ppm (s, one, NH).

Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.06; H, 4.76; N, 5.10. Found: C, 61.10; H, 4.68; N, 5.20.

2-Amino-5-chloro-N-p-tolylsulfonylbenzophenone.—The reaction of 5-chloro-2-aminobenzophenone with p-tolylsulfonyl chloride in pyridine according to the general procedure of Vogel[14] gave light brown crystals of the desired product upon recrystallization from ethanol. Several recrystallizations gave an analytical sample: mp 121–122°; nmr (δ^{CDCl_3}) 2.3 (s, three, CH_3), 6.9–7.9 (m, twelve, aryl), 9.38 ppm (broad singlets, one, NH).

Anal. Calcd for $C_{20}H_{16}ClNO_3S$: N, 3.63. Found: N, 3.65.

Acknowledgment.—This work was supported by a Public Health Service Grant (GM 12692-01). We gratefully acknowledge this support.

(21) G. Kulischer, H. Rutter, and E. Harold, U. S. Patent 1,876,955 (Sept 13, 1933).

Some Reactions of Steroidal α-Bromo Ketones[1]

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16α-Bromoandrostan-3β-ol-17-one (I) is converted by methoxide ion into the dimethyl ketal of 3β-16α-dihydroxyandrostan-17-one (II). The 16β-bromo epimer Ia and the 5,6-dehydro analog Ib undergo the same transformation. The structure of the ketal II was apparent from its hydrolysis to 16α-hydroxy-17-ketone (III), its acetylation, its reduction to the 16α,17β-diol (VI), and its nmr spectra. The reaction of bromo ketone I with ethoxide takes a different course. The stereochemical results of the reaction of methoxide with I and Ia are discussed assuming 17β-methoxy-16α,17β-epoxyandrostan-3β-ol (VIII) as an intermediate. Some ring-opening reactions of acetoxy epoxides are discussed.

Our recent studies of the rearrangement of 16-amino-17-keto steroids to 17β-hydroxy-16-keto steroids in the presence of water[2] led us to the investigation of other reactions in the D ring of these systems. A possible route to various 16-substituted 17-keto steroids could be the displacement of 16-bromo 17-ketones with amines and other bases, in particular since it is known that dehydrobromination or Favorski rearrangement of 16-bromo 17-ketones do not occur readily under basic conditions.[3]

It was of interest to establish whether the reaction of 16α-bromoandrostan-3β-ol-17-one with strong base would lead to substitution or to three-membered ring intermediates such as VIII or VIIIa. Stevens and coworkers[4] have shown that methoxy epoxides are intermediates in the reaction of α-bromo ketones with methoxide. We found that bromo ketone I reacted readily upon heating for short periods of time with potassium hydroxide in methanol to yield a product identified as 17,17-dimethoxyandrostane-3β,16α-diol (II, Scheme I). These results are analogous to those obtained in the estrone series by Mueller, *et al.*,[5] using anhydrous methoxide as a base. The structure of the dimethyl ketal II was proved by acid hydrolysis to the 16α-hydroxy 17-ketone III. The identity of the latter was apparent by conversion to its diacetate IIIa, by base isomerization of III to the more stable isomer IV, as well as by conversion of III and IV to the bisphenylhydrazone V. As expected, the ketal diol II was stable to lithium aluminum hydride, but formed a diacetate derivative IIa. The nmr spectrum of II indicates two distinct methoxy groups at τ 6.53 (H_3, singlet) and 6.65 (H_3, singlet), and a C-16 proton at 5.74 (triplet).

Stevens and co-workers[4] as well as Tchoubar, *et al.*,[6] have investigated the reaction of simpler α-bromo ketones with anhydrous methoxide and have shown it to lead to α-hydroxy ketals. The stereochemical results of the conversion of I to II require further comment.[7] Since the same product, namely II, is obtained whether one uses anhydrous methoxide or potassium hydroxide in methanol the 16α-hydroxy function could not have been derived by a displacement at C-16 but is most likely the result of ring opening of an α-epoxide such as VIII. In order to obtain a 16α,17α-epoxide, attack by methoxide ion on I must have taken place at C-17 from the β side, which is rather surprising in view of the well-established preferred attack from the α side in 17-keto steroids. The

(1) Stereochemistry. XVIII. Three Membered Ring Intermediates. For paper XVII, see A. Hassner, L. A. Levy, and R. Gault, *Tetrahedron Letters*, 3119 (1966).

(2) A. Hassner and A. W. Coulter, *Steroids*, **4**, 281 (1964).

(3) W. S. Johnson and W. F. Johns, *J. Am. Chem. Soc.*, **79**, 2005 (1957).

(4) C. L. Stevens, W. Malik, and R. Pratt, *ibid.*, **72**, 4758 (1950); C. L. Stevens, J. Beereboom, and K. Rutherford, *ibid.*, **77**, 4590 (1955).

(5) G. P. Mueller and W. F. Johns, *J. Org. Chem.*, **26**, 2403 (1961).

(6) R. Tchoubar, *Bull. Soc. Chem. France*, 1363 (1955).

(7) These results and the analogous ones discussed earlier by Mueller and Johns[5] warrant a detailed analysis because the reaction product is not the one expected from direct displacement on I, from cleavage of the logical intermediate VIIIa, or from ring opening of intermediate VIII at the less hindered C-16.