sodium hydroxide for 15 hours. At the end of this time, the mixture was cooled, and stirred with 5 g. of Raney nickel. The mixture was filtered, evaporated, and the residue was sublimed at 0.4 mm. and 150°. The sublimate was crystallized from 95% ethanol to give 0.10 g. of the morpholide of XIII, m.p. 194–200°.

Anal. Calcd. for $C_{22}H_{25}O_2N$: C, 78.80; H, 7.52. Found: C, 79.10; H, 7.45.

In a second run, the above procedure was followed except that the thiomorphilide was hydrolyzed for 3 hours in 30 ml. of 4 *N* sodium hydroxide–ethylene glycol at reflux. The resulting mixture was cooled, and shaken with water and ether. The aqueous layer was acidified and extracted three times with ether. The ether extract was washed with water, dried, and evaporated to give a brown oil. This material was distilled at 170° and 10^{-4} mm. to give 0.10 g. of white crystals of acid XIII, m.p. 210–210.2°. An additional 0.070 g. of acid of similar melting point was recovered from the ether extract of the basic ethylene glycol solution.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.08; H, 6.82.

Attempted Cyclization of 4-Carboxymethylene [2.2]paracyclophane (XIII), and Preparation of 4-Carboethoxymethylene[2.2]paracyclophane.—A solution of 0.085 g. of acid XIII in 3 ml. of thionyl chloride was held at reflux for 10 minutes, and the excess thionyl chloride was evaporated to give brownish crystals. This acid chloride was dissolved in a solution of 7 ml. of freshly-distilled *sym*-tetrachloroethane that contained 0.3 g. of anhydrous aluminum chloride. The mixture was swirled at room temperature for 5 minutes, cooled to 0° and diluted with 9 ml. of 1 *N* hydrochloric acid. The organic layer was separated, dried, and evaporated. The residue was chromatographed on 30 g. of activity II neutral alumina.[11] The column was washed with pentane to give only tetrachloroethane, and material was eluted with ether. The ether solution was evaporated, and the residue was crystallized from absolute ethanol to give crystals of ethyl ester of XIII, m.p. 79–79.8°, weight 0.020 g.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.52; H, 7.72.

Ultraviolet Spectra.—The ultraviolet spectra were all taken in 95% ethanol in a Cary recording spectrophotometer, model 11PMS.

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ZURICH, SWITZ.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

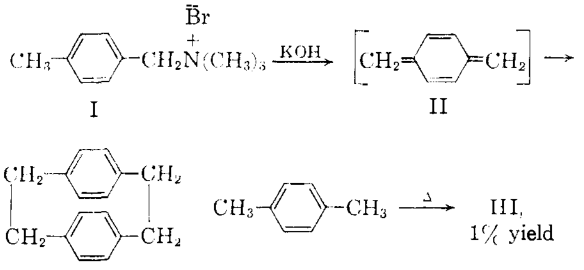
Macro Rings. XXII. Substituted Stilbenes from Attempted Dehydro[2.2]paracyclophane Synthesis[1]

BY DONALD J. CRAM AND RALPH H. BAUER

RECEIVED FEBRUARY 14, 1959

In an attempt to prepare 1,2-dehydro[2.2]paracyclophane (VI), 1,2-bis-(4-trimethylammoniummethylphenyl)-ethane dibromide (IV) was treated with base under a variety of conditions. The five stilbene derivatives VII, VIII, IX, X and XI were obtained.

When *p*-methylbenzyltrimethylammonium bromide (I) is treated with base, [2.2]paracyclophane (III) is produced.[2] The yields of III are much higher in this transformation than in the synthesis of III by the pyrolysis of *p*-xylene,[3] although both reactions presumably pass through *p*-xylylene (II)[4] as an intermediate. A similar reaction has been reported[5] in which 1,2-diphenyl[2.2]paracyclophane was prepared from *p*-benzylbenzyltrimethylammonium bromide.

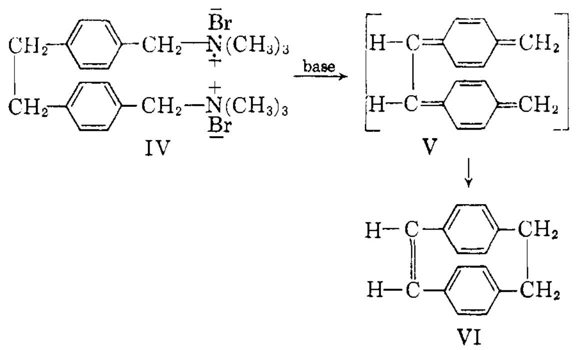


I II

III, 20% yield

III, 1% yield

These results suggested that treatment of the bis-quaternary ammonium salt IV with base could lead to V, which might cyclize to give VI. This cycle has been previously prepared,[6] but the synthetic route was long and troublesome. Although attempts to convert IV to VI failed, products were encountered which are of interest because they appear to arise from intermediates that contain conjugated systems similar to that of II.



IV V

VI

Elimination Reactions of Bis-quaternary Ammonium Salt IV.—When treated with sodium hydroxide under the Fawcett conditions[2] (aqueous solution at reflux), compound IV gave stilbene derivative VII. When the reaction was carried out in a refluxing solution of potassium hydroxide in di-

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[1] The authors wish to thank the Upjohn Co. for a generous research grant for the support of this research.

[2] [2.2]Paracyclophane has been prepared by extracting with toluene or with ethanol a polyparaxylylene obtained either by thermal decomposition of *p*-methylbenzyltrimethylammonium hydroxide (Fawcett, U. S. Patent 2,757,146, Ex. 1) or by the treatment of *p*-methylbenzyltrimethylammonium halide with concentrated aqueous alkali (British Patent 807,196, 1959). The details of these methods will shortly be published by Dr. H. E. Winberg and Dr. F. S. Fawcett of the Central Research Department, E. I. du Pont de Nemours and Co.

[3] C. J. Brown and H. C. Farthing, *Nature*, **164**, 915 (1949), and L. A. Errede, private communication.

[4] L. A. Errede and B. F. Landrum, THIS JOURNAL, **79**, 4952 (1957).

[5] H. W. Bersch, *Angew. Chem.*, **67**, 237 (1957).

[6] K. C. Dewhirst and D. J. Cram, THIS JOURNAL, **80**, 3115 (1958).

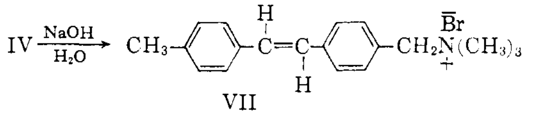
TABLE I

IMPORTANT ABSORPTION BANDS IN THE INFRARED[a] AND ULTRAVIOLET ABSORPTION SPECTRA[b] OF STILBENE DERIVATIVES

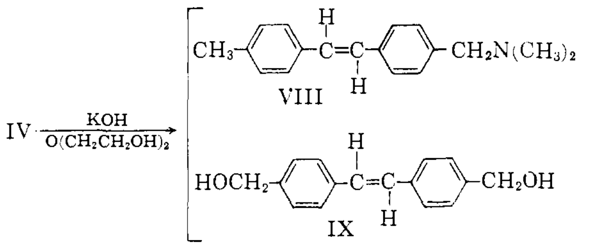
Compound	Ultraviolet band positions in mμ[c]							Infrared band positions in cm.$^{-1}$ [d]	
trans-Stilbene	224(i)	229	236(i)	285(i)	295	308	320(i)	1295(w)	958(s)
VII	228(i)	233	241(i)	294(i)	306(i)	318	331(i)	1302(w)	965(s)
VIII	226(i)	232	239(i)	292(i)	302	315	328(i)	1307(w)	967(s)
IX	227(i)	231	238(i)	294(i)	302	315	328(i)	1295(w)	969(s)
X	226(i)	231	236(i)	292(i)	301	315	328(i)	1300(w)	965(s)
XI	...	..	...	274	372(i)	386	406(i)	1302(w)	967(s)

[a] Taken on a Cary recording spectrophotometer, model 11MPS, in 95% ethanol. [b] Taken on a Perkin-Elmer recording spectrophotometer, model 21, KBr pellet. [c] λ_{max}. unless designated with (i), which stands for inflection. [d] (w) indicates a weak and (s) a strong band.

ethylene glycol, stilbene derivatives VIII and IX were produced. Treatment of IV with potassium *t*-butoxide in dimethyl sulfoxide gave compounds X and XI.

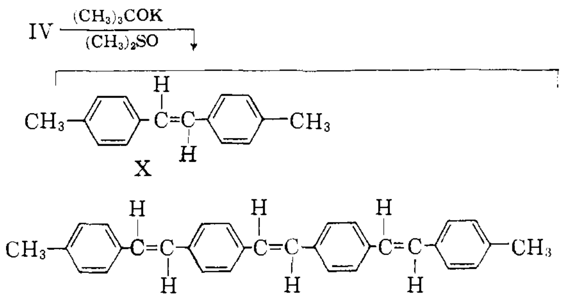


VII



VIII

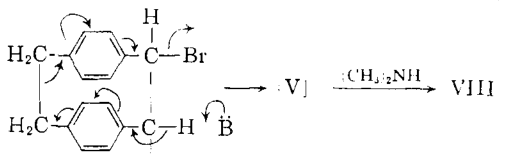
IX



X

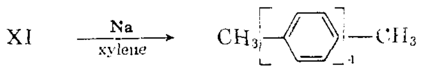
XI

The structures of compounds VII–X were inferred from their analytical and spectral properties (see next section). The structure of VIII was confirmed through its comparison with the same compound obtained previously by the treatment of 1-bromo[2.2]paracyclophane with dimethylamine.[6] The structure of X was further demonstrated by its



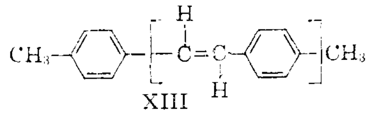
oxidation to terephthalic acid (67%) and reduction to the known[7] *p,p*-dimethylbibenzyl.

The structure of triene XI was demonstrated by the following reactions. Oxidation of XI gave a 68% yield of terephthalic acid, whereas ozonolysis of XI led to a mixture of terephthalic acid and *p*-toluic acids (60%). Although the components of this mixture were not isolated, their presence was demonstrated with infrared spectra and paper chromatography. Attempts to reduce catalytically the three double bonds of triene XI fails because of the extreme insolubility of the substance. However, XI gave XII when treated with sodium and xylene. The latter substance was identified by its molecular weight, analysis and ultraviolet absorption spectrum. When XI was treated with bromine, both hexa- and octabromo derivatives were produced. The hexabromo derivative when treated with base gave an enediyne. The possible structures of the hexabromo derivative and the enediyne were not differentiated, although analytical and spectroscopic data clearly established the presence of a *trans*-stilbene residue in both compounds, and the presence of two triple bonds in the enediyne.[8]



XII

Under the three sets of conditions employed for the elimination reactions of the bis-tetraalkylammonium salt IV, small amounts of a lustrous black polymer were obtained. This material was insoluble in any solvent, and probably possesses the general structure XIII.



XIII

Spectral Properties of Compounds VII–XI.—The positions of the important absorption bands in the ultraviolet and infrared spectra of compounds VII–XI, and of the model compound, *trans*-stilbene, are recorded in Table I. The similarity in the ultraviolet spectra of compounds VII–X and *trans*-stilbene indicates the presence in these molecules of a *trans*-stilbene unit. The shift of the absorption bands to longer wave lengths and higher intensities[9] in compound XI is compatible with the longer conjugated system in the assigned structure. The longest wave length maximum (λ 386 mμ) of XI occurs at 71 mμ longer wave length than the longest wave length maximum (λ 315 mμ) of X.

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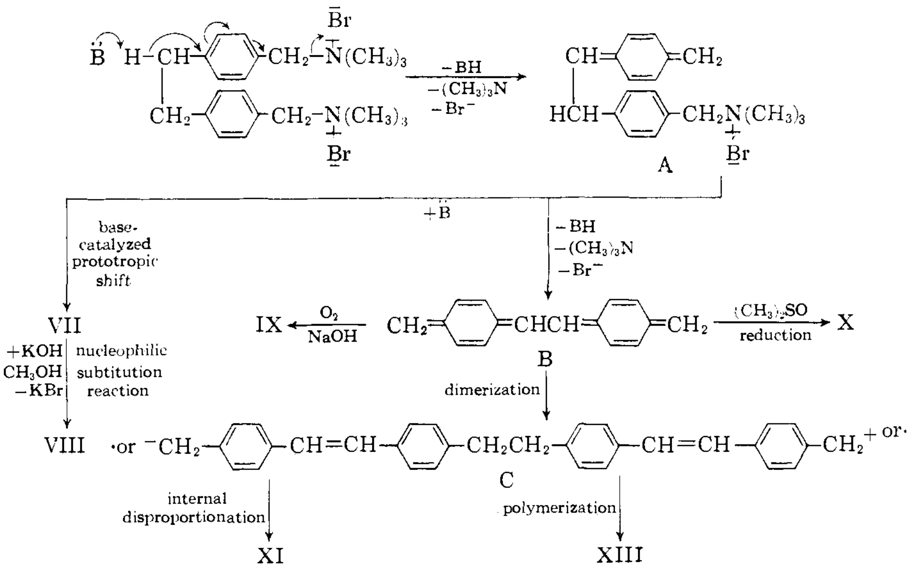
(7) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951).

(8) Compound XI was recently reported [G. Drefahl and G. Plötner, *Ber.*, **91**, 1274 (1958)], and the physical properties of our material and those of the above authors correspond to one another.

(9) The shorter wave length λ_{max} of the stilbene derivatives had extinction coefficients of approximately 18,000, and the longer wave length λ_{max} of approximately 28,000. The extreme insolubility of XI made accurate measurement of extinction coefficients impossible, but λ_{max} of the longer wave length band had ε in excess of 65,000.

A similar difference (69 mμ) is observed in the longest wave length bands for stilbene (λ_{max} 308 mμ) and *p,p'*-distyrylstilbene (λ_{max} 377 mμ).[10] Ultraviolet irradiation of an ethanol solution of XI and a trace of iodine resulted in decreased intensity of absorption of the solution at 386 mμ. This fact suggests that XI is an all *trans* isomer, and that the decrease in absorption is associated with isomerization of the substance about the carbon–carbon double bonds.

Strong evidence that compounds VII–XI contain *trans*-stilbene-like linkages is found in the similarity in the absorption of these compounds and that of *trans*-stilbene in the region of 1300 and 960–970 cm.$^{-1}$. Absorption bands in this region are associated with out-of-the-plane deformations of hydrogen attached to *trans*-carbon–carbon double bonds.[11]



Possible Intermediates in the Formation of Compounds VII–XI.—Comparison of the structures of the bis-quaternary salt IV and compounds VII–XI provides some hints as to the types of mechanisms and intermediates that were involved in the transformation. The formation of compounds VII–XI can readily be rationalized in terms of a sequence which involves a 1,6-elimination reaction as the first stage to give intermediate A. This substance in a base-catalyzed prototropic shift could readily give VII, which in turn could undergo nucleophilic substitution to provide VIII. In a second 1,6-elimination, A could give B. This quinonoid system should be subject to both oxidation and reduction, the former leading to IX and the latter to X. Either radical or polar dimerization of B could give C which in turn would be expected to undergo disproportionation to give XI, or polymerize and disproportionate to provide polymer XIII. Although other attractive reaction schemes can be visualized, they represent variants of the above general sequence.

Experimental

1,2-Bis-(4-trimethylammoniummethylphenyl)-ethane Dibromide (IV).—To a mixture of 100 ml. of 2-butanone and 75 ml. of water in a flask equipped with a gas inlet tube, stirrer, Dry Ice condenser, and drying tube was added 10 g. of 1,2-bis-(4-bromomethylphenyl)-ethane.[7] Trimethylamine was added at −10° while the mixture was stirred. The reaction was allowed to proceed 1.5 hours during which time a steady flow of the amine gas was maintained. The reaction mixture was homogeneous upon completion of the reaction. Approximately 100 ml. of ether was added to the solution, and the layers were separated after shaking in a separatory funnel. The ether layer was washed with water, and the aqueous layers were combined. Depending on whether the ditetraammonium salt was to be used in solution or as an anhydrous salt, different procedures were used at this point. If the salt was to be used in solution, the aqueous layers were purged of residual ether by warming under vacuum for a short time. This solution was then used in the reactions described below. If the salt was to be used in an anhydrous reaction, the water from the aqueous layers was removed by azeotropic distillation with benzene. Upon completion of this distillation, the benzene was removed under vacuum and the solid remaining was dried in a vacuum desiccator at 10^{-1} mm. This procedure yielded 79% of the crude salt. This solid was then used directly in the experiments described below.

***p*-Methyl-*p'*-methyl(trimethylammonium bromide)-stilbene (VIII).**—The aqueous solution of IV from the above experiment was slowly added to a refluxing solution of 50 g. of sodium hydroxide in 50 ml. of water in a flask equipped with a stirrer, condenser and addition funnel. The ammonium solution was added over a 40-minute period. After the reaction had proceeded an additional 2.5 hours, the mixture was allowed to cool to room temperature. The solution was filtered to give a rather soapy residue. This residue passed through the filter paper when washed with water or dilute acetic acid. A small amount of this residue was retained and dried. The dried solid was extracted with absolute ethanol in a Soxhlet apparatus. After extraction for 12 hours, the ethanol was evaporated. The residue was taken up in 50% benzene–methanol and filtered free of insoluble material. The solution was evaporated to half its original volume, and the crystals which appeared were separated in a Buchner funnel. This material was crystallized twice from a 3:1 mixture of benzene–methanol yielding 0.2 g. of white, fluorescent crystals (m.p. 239–241°). The ultraviolet and infrared absorption spectra indicated the presence of a *trans*-stilbene skeleton. The compound was water soluble, and an aqueous solution gave a precipitate with aqueous silver nitrate. An aqueous solution of the compound gave no precipitate with solid potassium hydroxide.

Anal. Calcd. for $C_{19}H_{24}NBr$: C, 65.89; H, 6.98. Found: C, 65.47; H, 6.98.

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[10] J. Dale, *Acta Chem. Scand.*, **11**, 971 (1957).

[11] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 31.

***p,p'*-Dihydroxymethylstilbene (IX) and *p*-Methyl-*p'*-dimethylaminomethylstilbene (VIII).**—The water solution of IV from a run similar to the one described in the first experiment was added to a solution of 80 g. of potassium hydroxide in 100 ml. of water. This mixture was heated for 1 hour at reflux. To this solution was added 30 ml. of diethylene glycol, and the water was slowly distilled over a period of three hours. The bath temperature at the end of this time was 260°. The solution was cooled to room temperature, and the residue present was collected to give a soapy, dark-colored material. The residue was washed with water and dilute acetic acid. The water was removed from this residue by azeotropic distillation with benzene. The benzene was evaporated under vacuum, and the residue was crystallized from benzene. The first crop, 0.2 g., was treated by chromatography as described below. The second crop, 3 g., was crystallized 4 times from ethanol to give 2.3 g. of white, fluorescent crystals of IX, m.p. 158–159.5°. The ultraviolet and infrared absorption spectra of this compound indicated the presence of a *trans*-stilbene skeleton.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 80.00; H, 6.71. Found: C, 79.86; H, 6.78.

All mother liquors and residues from the above isolation were combined and evaporated to dryness. The resulting solid and the solid obtained from the first crystallization above were dissolved in benzene, and chromatographed on neutral, activity II[12] alumina. All pentane and pentane–ether fractions were negative. The earlier ether fractions yielded a total of 0.5 g. of a low-melting solid. This material (0.30 g.) melted at 102–102.5° after 4 crystallizations from 95% aqueous ethanol. Treatment of a small amount of this solid with acetyl chloride gave a high-melting (267–268°), water-soluble compound. An aqueous solution of the latter compound gave a precipitate with aqueous silver nitrate. This was apparently the hydrochloride of VIII. An aqueous solution of this high-melting compound when made basic with solid potassium hydroxide regenerated starting material. Compound VIII was insoluble in warm concentrated hydrochloric acid. Further, VIII had an ultraviolet and infrared absorption spectrum, and melting point and mixed-melting point identical to the substance obtained from heating 1-bromo[2.2]paracyclophane with dimethylamine.[6] The later fractions of the chromatogram yielded additional amounts of VII.

Anal. Calcd. for $C_{18}H_{21}N$: C, 86.02; H, 8.32. Found: C, 86.26; H, 8.24.

***p,p'*-Dimethylstilbene (X) and Compound XI.**—Dry ditetraammonium salt, IV (14.1 g.), was added to a mixture of potassium *t*-butoxide (prepared in the usual manner from 3.0 g. of potassium metal) and 75 ml. of dry dimethyl sulfoxide. The reaction flask was equipped with a condenser, stirrer and drying tube. The reaction was stirred and heated at 110° for 6 hours, at 125° for 14 hours and at the reflux temperature (190°) of the mixture for 5 hours. At the end of this time trimethylamine was still being evolved. The reaction was allowed to cool to room temperature, and 200 ml. of water was added. The mixture was filtered and thoroughly washed with water. The residue was air-dried overnight, and then extracted 8 hours with benzene in a Soxhlet apparatus. The benzene extract was concentrated to 50 ml. and retained for the chromatography experiment described below. The insoluble material in the extractor cup fluoresced bright yellow under ultraviolet radiation. This material was purified by extracting it with xylene for 14 days in a Soxhlet apparatus and subsequently filtering the extract. This yielded 2.5 g. of yellow solid XI melting at 358–360°. The compound was insoluble in acetone, methanol, ethanol, water, acetic acid, ethyl acetate, cyclohexane, xylene, ether, benzene, dimethyl sulfoxide, dimethyl sulfate, pentane and dioxane. The compound was most soluble in N,N-dimethylformamide as judged from the relative intensity of an ultraviolet absorption spectrum of a saturated solution. In this solvent, however, 3.8 mg. of the compound would not dissolve in 1 liter. Chloroform, the second-best solvent, was about 2.5 times less effective than N,N-dimethylformamide. The analytical sample of XI was purified by sublimation at 330° and 10^{-4} mm.

Anal. Calcd. for $C_{32}H_{28}$: C, 93.14; H, 6.84. Found: C, 92.90; H, 6.67.

The concentrated benzene solution obtained from the first extraction experiment mentioned above was chromatographed on neutral, activity II[12] alumina. The pentane fractions were combined. The alumina was further washed with ether and methanol. These fractions were combined and have not been further investigated. The pentane fractions were dissolved in hot 95% aqueous ethanol and filtered free of polymeric material. The filtrate yielded a light-colored solid when cooled. This precipitate was separated, dissolved in a small amount of ether and chromatographed on neutral activity II[12] alumina. Pentane fractions 2, 3 and 4 (50 ml. each) were combined, filtered, and crystallized twice from benzene. The yield was 0.5 g. of fluorescent, white plates of X, m.p. 179–181°. The analytical sample of X was sublimed at 110° and 10^{-4} mm.

Anal. Calcd. for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.73; H, 7.42.

Oxidation Experiments with Compounds X and XI.—Oxidation of compound X with chromic oxide in acetic acid at 100° gave a 67% yield of terephthalic acid. Similar oxidation of compound XI gave a 69% yield of terephthalic acid. Ozonization of X with oxidative work up in the usual manner gave a 30% yield of *p*-toluic acid, m.p. 179–180°, undepressed by admixture with an authentic sample. Ozonization of XI was carried out as follows.

To 10 ml. of carbon tetrachloride was added 0.05 g. of XI. This solution was ozonized in the usual manner. The starting material disappeared after 45 minutes. After oxidative work up in the usual manner, 0.44 g. (60%) of a crude white solid was obtained. This material did not melt completely, but sublimed above 300°. Little fractionation of this material was obtained by trituration with ether or hot water. A part of the solid sublimed at 10^{-5} mm. and 110° (toluic acid sublimes easily at this point, whereas terephthalic acid does not). This sublimed material melted at 175–250° and had an infrared absorption spectrum very similar to that of a 1:1 mixture of *p*-toluic and terephthalic acids.

A small amount of ozonolysis product from above was dissolved in a 10% solution of concentrated ammonia in 1-butanol. A small part of this solution was chromatographed in the usual manner by descending paper chromatography on Whatman no. 1 filter paper. The chromatogram was run 12 hours. After drying the paper one hour, it was sprayed with a dilute solution of brom cresol green. The blue spots which appeared faded after 30 seconds. The R_f value of one of the spots of the unknown was similar to that of *p*-toluic acid (R_f toluic acid = 0.26, R_f unknown acid = 0.23) which was run on the same paper as a control. The terephthalic acid used as a control was not moved by the solvent, and corresponded to an unmoved spot in the unknown. No other spots were noted on the unknown chromatogram.

Reduction of Compounds X and XI.—Catalytic reduction of compound X in methanol with platinum and hydrogen in the usual manner gave a 79% yield of *p,p'*-dimethylbibenzyl, m.p. 79–81°, undepressed by admixture with an authentic sample.[7] An attempt to reduce compound XI by the same procedure failed due to the extreme insolubility of the substance. However, the compound was reduced when submitted to the following procedure.

To 75 ml. of xylene in which was suspended 1 g. of sodium was added 0.05 g. of XI. The mixture was heated at reflux for 3 hours. The reaction mixture was cooled and the unreacted sodium was removed from the clear solution. The xylene solution was washed with water and evaporated to 3 ml. The solution was allowed to cool. A wax-like material crystallized from the solution. The crystals were separated by filtration and washed with a small amount of benzene to give a 73% yield of XII, m.p. 177–179°. A small amount of the material was chromatographed on neutral, activity II alumina.[12] The column was eluted with a 1:1 mixture of benzene–pentane, and yielded crystals which melted at 179–180°. This substance (XII) possessed an ultraviolet absorption spectrum nearly identical in shape to that of *p*-xylene with an intensity 4 times that of *p*-xylene. A small amount of the chromatographed material was sublimed at 10^{-5} mm. and 150°.

Anal. Calcd. for $C_{32}H_{32}$: C, 91.82; H, 8.19; mol. wt., 419. Found: C, 91.95; H, 7.98; mol. wt., 432 (Rast).

An attempt to reduce X by the same procedure gave back starting material unchanged.

Hexabromide of XI and Octabromide of XI.—To 10 ml. of chloroform was added 0.10 g. of XI and a few drops of liquid bromine. The mixture was stirred 4 hours. The solution

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[12] H. Brockmann and H. Schodder, *Ber.*, **74B**, 73 (1941).

was filtered, and 0.15 g. of a white, non-fluorescent solid was collected. The solid was washed thoroughly with chloroform. This material did not melt, but slowly darkened between 300° and 450°. The infrared spectrum of this hexabromide of XI showed the presence of *trans*-hydrogens on a double bond.[11] *Anal.* Calcd. for $C_{32}H_{28}Br_6$: C, 43.08; H, 3.16. Found: C, 43.54; H, 3.17.

A similar reaction run 12 hours at reflux temperature yielded a similar material which did not melt but darkened as before. In this case the infrared absorption spectrum showed only slight absorption in the region characteristic of *trans*-hydrogens on a double bond.[11]

Anal. Calcd. for $C_{32}H_{26}Br_8$: C, 36.62; H, 2.51. Found: C, 34.64; H, 3.17.

Base-catalyzed Elimination Reaction on Hexabromide of XI.—A solution of 0.25 g. of the hexabromide and 6 g. of sodium methoxide in 20 ml. of diethylene glycol was heated at 260° for one hour. The resulting mixture was cooled, and 20 ml. of water was added. The insoluble residue was collected, and extracted 4 hours in a Soxhlet apparatus. The extract was evaporated to 5 ml., and the solid obtained from the cooled solution yielded 0.008 g. of a green-yellow solid. This solid decomposed at 276–278°. The analytical sample was purified by sublimation at 10^{-5} mm. and 250°.

Anal. Calcd. for $C_{32}H_{24}$: C, 94.08; H, 5.92. Found: C, 93.77; H, 5.66.

LOS ANGELES, CALIF.

[CONTRIBUTION FROM THE INSTITUTE OF APPLIED MICROBIOLOGY, UNIVERSITY OF TOKYO]

Steroid Studies. X.[1] Studies on the Configuration of 22-Hydroxycholesterol from *Narthecium ossifragum* Huds

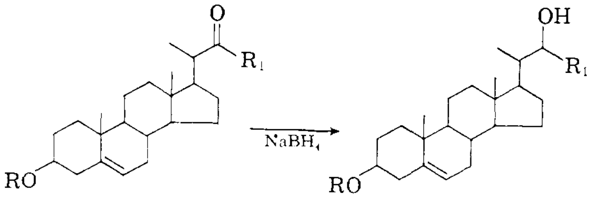
BY KYOSUKE TSUDA AND RYOICHI HAYATSU[2]

RECEIVED OCTOBER 20, 1958

Epimeric pairs of 22-hydroxycholesterol at C-22 were prepared and the absolute configuration of each group at C-22 was determined by the Prelog method. It was thereby established that the natural 22-hydroxycholesterol has the 22α-hydroxy configuration in agreement with Klyne's conclusion. Some observations were made on the conformation of these compounds.

Stabursvik[3] extracted a new sterol, together with a carotenoid pigment, from *Narthecium ossifragum* Huds (Liliaceae) in 1953 and determined it to be 22-hydroxycholesterol. Klyne and Stokes[4] have deduced from the application of Cram's rule in the reduction[5] of 22-keto-cholestanyl acetate that Stabursvik's sterol is 22-α-hydroxycholesterol. In the present paper, we furnish additional support for Klyne's conclusion. Hayatsu[6] observed the formation of both epimeric alcohols by reduction of 22-ketocholesteryl acetate and isolated the two diastereomers as benzoates. One of these was found to agree with the benzoate of the natural sterol obtained by Stabursvik.

The carbonyl group in 22-ketocholesteryl acetate[7] has a great steric hindrance and does not react with carbonyl reagents. It is also resistant to the Meerwein–Ponndorf reduction and its reduction with sodium borohydride requires over 20 hours.[6]



I, R = CH_3CO, R_1 = iso-C_5H_{11}
III, R = CH_3, R_1 = iso-C_5H_{11}
V, R = CH_3CO, R_1 = C_6H_5
VII, R = CH_3, R_1 = C_6H_5

IIa, IIb, R = H, R_1 = iso-C_5H_{11}
IVa, IVb, R = CH_3, R_1 = iso-C_5H_{11}
VIa, VIb, R = H, R_1 = C_6H_5
VIIIa, VIIIb, R = CH_3, R_1 = C_6H_5

In addition to the two diastereomers IIa and IIb reported earlier[6] as these dibenzoates, we have now carried out the reduction of several other 22-ketocholesterol derivatives and have fully characterized the original pair: isomer A (IIa), m.p. 186°, αD −39; diacetate, m.p. 103.5°, αD −37.1°; dibenzoate, m.p. 256°, αD −9.6°. Isomer B (IIb), m.p. 182°, αD −52°; diacetate, m.p. 146°, αD −51.5°; dibenzoate, m.p. 172°, αD −19.6°. The yield[4,5] of isomer B (60–65%) is always better than that of A (35–40%). The molecular rotation (M_D) of IIa and IIb, cholesterol and the corresponding 3β-methoxy derivatives (IVa, IVb and 3β-methoxy-Δ^5-cholestene) are shown in Table I.

In order to determine the absolute configuration of asymmetry at C-22 in IIa and IIb, Prelog's asymmetric synthesis[8] was employed.

It is obvious that the size of the three residual groups in IIa and IIb, other than the 22-hydroxy, increases in the order of H, –C(22)H_2– and –C(23)CH_3.H–,[8] and the asymmetric synthesis is expected to progress smoothly. In accordance with Prelog's theory, the absolute configuration of the carbon atom at 22 can be determined from the optical rotation of the optically active atrolactic acid thereby obtained.

The O-methyl ether of IIa and IIb were therefore prepared. 3β-Methoxy-bisnor-5-cholenic acid was converted to 22-ketocholesteryl methyl ether[9] (III), which was reduced with sodium borohydride to the 22-hydroxy compounds IVa, m.p. 109–111°,

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