The keto acids V could be secured by dissolving the lactones in sodium hydroxide, and acidifying, care being taken to keep the temperature low.

Upon chromic acid oxidation, the lactones gave benzoic and an *o*-benzoylbenzoic acid; the same products resulted if the lactone was first dissolved in sodium hydroxide, and then oxidized with permanganate.

When treated in the Grignard machine, the lactone showed no active hydrogen but two additions as expected. The product, worked up in the usual way, gave the ketone VIII (R = C_6H_5), the carbinol group having been dehydrated. With phenylmagnesium bromide, a carbinol VII (R = C_5H_5) was secured without any difficulty.

The bromohydrin XXII resulted when the epoxide from 2-ethyl-3-phenylindenone was allowed to stand at 10–15° for one-half hour with five times its weight of 30–32% hydrogen bromide in acetic acid. The yield was 80%. It gave an oily carbinol with methylmagnesium iodide that still retained the halogen.

2-Phenyl-2-benzoyl-(*Bz*-4,5-diphenyl)-cyclobutenone-1, XXIII.—Five grams of the epoxide from 2,3,5,6-tetraphenylindenone was added to 40 cc. of 15% hydrogen bromide in acetic acid, the whole mixture boiled for ten minutes, cooled, and crystallization initiated by scratching the side of the flask. The red ketone that separated was filtered and recrystallized from benzene–ligroin. The yield was 4 g. The ketone crystallizes in brick-red prisms, often diamond-shaped, m. p. 219–220°.

Anal. Calcd. for $C_{33}H_{22}O_2$: C, 88.0; H, 4.9. Found: C, 88.4; H, 4.9.

The same substance was formed when a 25% solution of sulfuric acid in acetic acid was used, and even by six hours of refluxing in acetic acid alone.

In the Grignard machine, the red ketone shows no active hydrogen and two additions. With the Grignard reagent, it gave the same product (VIII) as the lactone. Upon chromic acid oxidation, it gave benzoic and 4,5-diphenyl-2-benzoylbenzoic acids.

When 1.5 g. of the red ketone was added to 50 cc. of alcohol containing 2 g. of potassium hydroxide, refluxed for three hours, poured into water, and acidified cold, the acid V (R = C_6H_5) resulted. Attempts to reduce the red ketone by zinc dust and acetic acid gave the lactone—this apparent anomaly was traced to the zinc acetate formed. In acetic acid solution, in less than five minutes, zinc acetate caused the red color to disappear; the lactone separated on cooling. The same change is brought about by potassium acetate in eight hours, and by hydroxylamine hydrochloride in two hours.

The 2,4-dinitrophenylhydrazone of benzalacetophenone oxide was prepared in the usual manner; it separated from methanol in orange needles, m. p. 205°.

Anal. Calcd. for $C_{21}H_{18}O_5N_4$: C, 62.6; H, 4.0. Found: C, 62.4; H, 4.0.

Summary

A number of oxidoketones have been prepared in the indene series; the reaction appears to be fairly general.

With mineral acid, most of them give isomeric glycols in the cold, and lactones when heated; the glycols are isomerized to the same lactones by warm mineral acids.

The epoxides from 2,3-diphenyl- and 2-ethyl-3-phenylindenones give bromohydrins with cold hydrogen bromide in acetic acid.

The epoxide from 2,3,5,6-tetraphenylindenone gives an isomer for which a benzcyclobutenone structure has been proposed.

The glycols are isomerized by alkaline reagents to isobenzofurans.

A mechanism has been proposed to account for certain reactions previously termed rearrangements.

The carbonyl group is still present in oxidoketones.

ROCHESTER, N. Y. RECEIVED JANUARY 13, 1943

NOTES

Conversion of 2,7-Dibromofluorene to 2,7-Dibromophenanthrene

BY WELDON G. BROWN AND BEN A. BLUESTEIN

We have previously reported[1] a synthesis of phenanthrene, starting from fluorene, in which the ring enlargement is accomplished by a Wagner rearrangement of 9-fluorenylcarbinol. A similar series of reactions, resulting in the conversion of 2,7-dibromofluorene into 2,7-dibromophenanthrene, has been carried through which it seems desirable to record as the work has been discontinued.

Experimental

2,7-Dibromo-9-formylfluorene.—Potassium ethoxide was formed from 3.9 g. (0.1 mole) of potassium and 4.6 g. (0.1 mole) of absolute alcohol in 250 cc. of dry ether. To this mixture was added 33 g. (0.1 mole) of 2,7-dibromofluorene resulting, after a few minutes refluxing, in a dark brown solution. The slow addition of 7.4 g. (0.1 mole) of ethyl formate caused the solution to become first green,

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[1] Brown and Bluestein, THIS JOURNAL, **62**, 3256 (1940).

then brown again. After refluxing for one hour, water was added, and the aqueous layer, after washing with ether, was acidified with dilute sulfuric acid. The pale yellow solid obtained in 85% yield was twice recrystallized from glacial acetic acid, m. p. 171°.

On standing the aldehyde deepens in color and becomes diminishingly soluble in aqueous alkali.

For the purposes of characterization, the acetate was prepared by the addition of acetic anhydride to a solution of the aldehyde in aqueous potassium hydroxide. It was recrystallized from a benzene–ligroin mixture, m. p. 219°.

Anal. Calcd. for $C_{16}H_{10}O_2Br_2$: C, 48.76; H, 2.56. Found: C, 49.69; H, 2.69.

2,7-Dibromo-9-fluorenylcarbinol.—To aluminum isopropoxide, prepared from 1 g. of aluminum, was added 9.5 g. of 2,7-dibromo-9-formylfluorene in 25 cc. of isopropanol. The mixture was distilled through a Vigreux column, holding the vapor temperature at 60° for about five hours, after which the remaining alcohol was removed under reduced pressure. The residue was treated with 6 *N* sulfuric acid, and the solid product was then separated by filtration. Extraction of the solid with hot alcohol, followed by precipitation from the alcoholic extract on the addition of water, yielded 5.5 g. (58%) of material which, after three recrystallizations from ligroin, melted at 154°.

Anal. Calcd. for $C_{14}H_{10}OBr_2$: C, 47.50; H, 2.85. Found: C, 47.61, H, 3.37.

The carbinol formed an acetate readily on boiling with acetic anhydride and sodium acetate, m. p. 190° (from alcohol).

2,7-Dibromophenanthrene.—One gram of 2,7-dibromo-9-fluorenylcarbinol was refluxed for thirty minutes with 1 g. of phosphorus pentoxide and 25 cc. of xylene. The xylene layer was decanted and the xylene was removed by distillation. Recrystallization of the residual solid from a xylene–ligroin mixture yielded 0.1 g. of colorless crystals, m. p. 205° (lit.[2] m. p. 2,7-dibromophenanthrene, 202°). Oxidation of the product with chromic acid in glacial acetic acid yielded 2,7-dibromophenanthraquinone, m. p. 321° (lit.[2] m. p. 323°).

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(2) Schmidt and Mezger, *Ber.*, **40**, 4560 (1907).

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RECEIVED MARCH 10, 1943

Amide-Substituted Phenylarsine Oxides and Their Derivatives: A Group of Compounds of Possible Utility in the Treatment of Syphilis

BY HARRY EAGLE, RALPH B. HOGAN, GEORGE O. DOAK AND HARRY G. STEINMAN

We have previously found[1] that strongly acidic substituent groups introduced into phenylarsine oxide regularly caused a striking decrease in direct treponemicidal activity against *T. pallidum*, without a commensurate decrease in toxicity. The potential therapeutic utility of these compounds was therefore even less than that of the simple unsubstituted phenylarsine oxide. However, when the acidic group was blocked, as in ethyl or methyl esters, or as in the sulfone and phenone compounds, the treponemicidal activity was largely restored, and the ratio of treponemicidal activity: toxicity was increased as much as fourteen-fold, in several cases significantly exceeding that of the parent compound.

In the light of that finding, a series of phenylarsine oxides was prepared in which an acidic substituent group had been blocked by amide formation.[2,3] The majority of these amides have proved to be actively treponemicidal and relatively low in toxicity (first section of Table I). The ratio of treponemicidal activity: toxicity, which may be taken as a rough measure of potential therapeutic utility, was usually 2 to 6 times as favorable as that of the parent phenylarsine oxide, due primarily to the uniformly low toxicity of these compounds. As will be discussed in a following paper, some of these compounds have shown a chemotherapeutic index in the treatment of rabbit syphilis equal to or exceeding that of mapharsen, and on that basis are of potential value in the treatment and prophylaxis of syphilis. The favorable effect of amide-substitution has been so regular as to suggest that further study may disclose other related compounds of greater therapeutic utility than any of those here described.

The favorable effect of amide substituents on the toxicity of phenylarsine oxide was observed whether that amide group was attached directly to the benzene ring, as in the case of 3- and 4-$CONH_2$ and -SO_2NH_2 compounds, or through some intermediate linkages (*cf.* first section, Table I). Moreover, the integrity of the amide group was usually essential for the favorable activity: toxicity ratio: When either or both of the amide hydrogens were substituted, the compound usually developed properties apparently determined by the new terminal substituent (*cf.* 2nd and 3rd sections, Table I). Although treponemicidal activity was usually increased by such substitution, toxicity was increased to an even greater degree, giving a less favorable ratio. In this group of compounds, the activity and toxicity of the compound had thus reverted toward that of the simple unsubstituted phenylarsine oxide, or of phenylarsine oxides with such indifferent sub-

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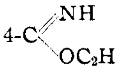
(1) H. Eagle, R. B. Hogan, G. O. Doak and H. G. Steinman, *J. Pharmacol.*, **70**, 221 (1940).

(2) G. O. Doak, H. G. Steinman and H. Eagle, THIS JOURNAL, **62**, 3012 (1940).

(3) G. O. Doak, H. G. Steinman and H. Eagle, in preparation.

TABLE I

THE TOXICITY AND TREPONEMICIDAL ACTIVITY OF AMIDE-SUBSTITUTED PHENYLARSINE OXIDES AND THEIR DERIVATIVES

$R\text{-}C_6H_4AsO$ or $R\text{-}C_6H_4As(OH)_2$	Ref.	Relative treponemicidal activity per mole	Relative toxicity per mole	Ratio of treponemicidal activity to toxicity
Phenylarsine oxide (reference compound)		100	100	1
$3\text{-}NH_2\text{-}4\text{-}OH$ (mapharsen)		38	6.94	5.5
$3\text{-}CONH_2$	*a*	41	9.8	4.1
$4\text{-}CONH_2$	*a*	45	9.6	4.6
$3\text{-}SO_2NH_2$	*b*	21	6.1	3.5
$4\text{-}SO_2NH_2$	*b*	29	4.8	6.1
$4\text{-}NHCONH_2$	*b*	38	8.1	4.7
$4\text{-}NHCH_2CONH_2$	*c*	22	4.5	4.8
$4\text{-}OCH_2CONH_2$	*b*	52	9.0	5.7
$4\text{-}CH{=}CHCONH_2$	*b*	43	9.7	4.4
$4\text{-}CH_2CONH_2$	*b*	20	8.6	2.3
$4\text{-}(CH_2)_3CONH_2$	*b*	33	13.5	2.4
$4\text{-}NHCO(CH)_2CONH_2$	*b*	25	9.0	2.7
$4\text{-}CONHCH_2CONH_2$	*d*	24	3.9	6.1
$4\text{-}CONHCONH_2$	*d*	34	6.4	5.2
$4\text{-}CH_2CONHCH_2CONH_2$	*d*	11	3.4	3.2
$4\text{-}SO_2NHCH_2CONH_2$	*d*	17	3.5	5.1
$4\text{-}CONHCH_2CH_2CONH_2$	*d*	13	3.2	4.1
$4\text{-}SO_2NHCH_3$	*b*	72	18.0	4.0
$4\text{-}SO_2N(CH_3)_2$	*b*	112	93	1.2
$4\text{-}SO_2NHC_2H_5$	*b*	72	32	2.3
$4\text{-}SO_2N(C_2H_5)_2$	*b*	101	134	0.74
$4\text{-}SO_2NHC_2H_4OH$	*b*	23	4.3	5.3
$4\text{-}CONHCH_3$	*a*	54	15	3.6
$4\text{-}CON(CH_3)_2$	*b*	48	19	2.5
$4\text{-}CONHC_2H_5$	*a*	59	26	2.3
$4\text{-}CON(C_2H_5)_2$	*b*	53	64	0.84
$4\text{-}CONHC_6H_5$	*b*	97	101	.96
$4\text{-}CONHCH_2C_6H_5$	*b*	79	80	.98
$4\text{-}CONHC_5H_4N$	*b*	74	116	.64
 $4\text{-}C(=NH)OC_2H_5$	*e*	68	87	.78
$4\text{-}CONHCH_2COOH$	*b*	0.7	15.7	.44
$4\text{-}CONHC_6H_4NHCOCH_3\text{-}(4')$	*b*	9	2.0	4.5
$4\text{-}CONHC_2H_4OH$	*a*	25	4.8	5.2
$4\text{-}CONHCONHC_2H_4OH$	*d*	30	5.0	6.5
$4\text{-}CONHCH_2CHOHCH_2OH$	*f*	14	3.7	3.72
$3\text{-}NHCONH\text{-}(4)$	*g*	20	6.9	2.93
$4\text{-}CONHCH_2CN$	*h*	27	4.5	6

[a] Gough and King, *J. Chem. Soc.*, 669 (1930). [b] Doak, Eagle and Steinman, THIS JOURNAL, **62**, 3012 (1940). [c] Cohen, King and Strangways, *J. Chem. Soc.*, 2505 (1932). [d] Doak, Steinman and Eagle, Abstracts, 105th Meeting, American Chemical Society, Detroit, Michigan, 1943. Experimental details for the preparation of these compounds will be published in a separate paper. [e] *Anal.* Calcd. for $C_9H_{12}O_3NAs$: As, 29.2; N, 5.45. Found: As, 29.8; N, 5.61. Experimental details for the preparation of this compound will be published in a separate paper. [f] *Anal.* Calcd. for $C_{10}H_{12}O_4NAs$: As, 26.3; N, 4.92. Found: As, 26.6; N, 4.56. Experimental details of this compound will be published in a separate paper. [g] Doak, Steinman and Eagle, THIS JOURNAL, **63**, 99 (1941). [h] *Anal.* Calcd. for $C_9H_7O_2N_2As$: As, 30.0; N, 11.2. Found: As, 30.0; N, 11.1. Experimental details of this compound will be published in a separate paper.

stituents as $-CH_3$, $-Cl$, or $-OCH_3$ groups.[4]

Exceptions to this unfavorable effect of blocking the amide group were the acetanilide (*p*-$CONHC_6H_4NHCOCH_3$), nitrile (*p*-$CONHCH_2CN$), and alcohol (*p*-$CONHCONHC_2H_4OH$, *p*-$CONHCH_2CHOHCH_2OH$, *p*-$CONHC_2H_4OH$, and *p*-$SO_2NHC_2H_4OH$) derivatives, with indices essentially the same as that of the parent amides.

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(4) H. Eagle, G. O. Doak, R. B. Hogan and H. G. Steinman, *J. Pharmacol.*, **70**, 211 (1940).

Molecular Weight of the Adrenocorticotropic Hormone

BY ELLEN BURTNER

Diffusion and sedimentation experiments have been performed with dilute solutions of the adrenocorticotropic hormone which has been prepared and described by Li, Simpson and Evans of the Institute of Experimental Biology, Berkeley, California.[1] In making up the solutions 20 mg. of the purified preparation was dissolved in 3 cc. of phosphate buffer of *p*H 7.0 and containing sodium chloride to give ionic strength 0.28, and dialyzed against the buffer salt system. Two sedimentation velocity experiments were performed in the standard Svedberg oil-turbine high velocity ultracentrifuge, and one diffusion experiment was carried out in a Lamm cell. The position of the peak in the former, and the spreading of the peak in the latter, at the end of successive time intervals, were observed by the Lamm scale line displacement method.

The sedimentation constant, s_{20}, was calculated by using the procedure described by Svedberg and Pedersen.[2] While the individual values of s_{20} calculated at half-hour intervals during each experiment vary somewhat, the two averaged values agree to within 5%. Variations between the results in individual experiments may be due to the fact that the material is light and thus travels only a short distance in each time interval, making the error in the determination of the change of position of the boundary an appreciable fraction of the total distance traveled. In the scale line displacement *vs.* distance in cell diagrams, the curves obtained were not unlike those characteristic of a single substance.

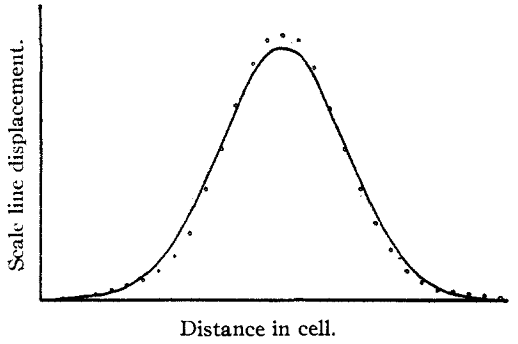

Fig. 1.

The diffusion constant was calculated from the equation $D = \sigma^2/2t$, where σ is the standard deviation of the curve obtained by plotting the scale line displacement against position in the cell. The value was then adjusted to give the diffusion constant for a hypothetical process taking place in pure water at 20°. Comparison of the experimental curve, when reduced to normal coordinates, with the Gaussian error curve, gave evidence of some inhomogeneity. In the figure the solid line represents the ideal diffusion curve of a single substance, and the circles are the experimental points.

The molecular weight was calculated by using the familiar equation $M = RTs/D(1-V\rho)$. The partial specific volume was not determined because a sufficient amount of the hormone was not available. In the absence of information to the contrary, it was assumed to be 0.75. The frictional ratio, f/f_0, was obtained by using the equations $f = M(1 - V\rho)/s$ and $f_0 = 6\pi\eta N(3MV)^{1/3}/(4\pi N)^{1/3}$. It gives as an approximate value 3:1 for the ratio of major to minor axis of the assumed unhydrated ellipsoidal molecule.

Experimental data, with calculations, are summarized to form Table I. For reasons given above the magnitude of the uncertainty involved in these figures is relatively high. (Probable error in molecular weight is ± 10%.)

TABLE I

MOLECULAR KINETIC DATA FOR THE ADRENOCORTICOTROPIC HORMONE (FRICTIONAL AND AXIAL RATIOS COMPUTED FOR UNHYDRATED ELLIPSOIDAL MOLECULE)

s_{20} (in S)	D_{20} (in 10^{-7} sq. cm./sec.)	M	f/f_0	a/b
2.08	10.4	20,000	1.1	3

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
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RECEIVED FEBRUARY 25, 1943

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[1] C. H. Li, M. E. Simpson and H. M. Evans, *Science*, **96**, 450 (1942).

[2] T. Svedberg and K. O. Pedersen, "The Ultracentrifuge," Oxford University Press, Oxford, 1940.

Tribenzylsulfonium Hydrogen Sulfate and Hydroxide

BY OTTO HAAS AND GREGG DOUGHERTY

It has been found that concentrated sulfuric acid brings about the cleavage of dibenzyl sulfide at moderate temperatures. Unlike the well known reaction of ethers and sulfuric acid, however, the products isolated are not benzyl mercaptan and benzyl hydrogen sulfate, although they are likely intermediates in the reaction. The principal product obtained is tribenzylsulfonium hydrogen sulfate and the most probable course of the reaction is

$$C_6H_5CH_2\text{—}S\text{—}CH_2C_6H_5 + H_2SO_4 \longrightarrow C_6H_5CH_2\text{—}S\text{—}H + C_6H_5CH_2\text{—}O\text{—}SO_2\text{—}O\text{—}H \quad (1)$$

$$2C_6H_5CH_2\text{—}S\text{—}H + O[\text{from } H_2SO_4] \longrightarrow C_6H_5CH_2\text{—}S\text{—}S\text{—}CH_2C_6H_5 + H_2O \quad (2)$$

and more complex products.

$$C_6H_5CH_2\text{—}S\text{—}CH_2C_6H_5 + C_6H_5CH_2\text{—}O\text{—}SO_2\text{—}O\text{—}H \longrightarrow (C_6H_5CH_2)_3S\text{—}OSO_2OH \quad (3)$$

Based on this explanation of the process the yields are nearly quantitative.

The tribenzylsulfonium hydrogen sulfate like the chloride and iodide was found to be fairly stable in water but decomposed on heating in water solution in the usual way to the sulfide and benzyl alcohol. Attempts to prepare the nitrate from the sulfate by treating the latter with silver nitrate in 95% alcohol resulted unexpectedly in the formation of tribenzylsulfonium hydroxide. Apparently, the nitrate was easily hydrolyzed to the hydroxide and since this behavior is unusual in the case of sulfonium salts, the point was investigated further. Tribenzylsulfonium nitrate was prepared by the method of Renshaw and Searle[1] and it was found that it was in fact very readily converted to the hydroxide when heated with water. By a slight modification of the procedure of Renshaw and Searle the tribenzylsulfonium hydroxide was formed directly in nearly quantitative yields from tribenzylsulfonium iodide–mercuric iodide. This constitutes a convenient and very efficient preparation method for the hydroxide.

Tribenzylsulfonium Sulfate.—Three grams of dibenzyl sulfide was added to 6 g. of concentrated sulfuric acid. Little solution occurred at room temperature, but on warming to 70–80° and shaking vigorously, solution of the sulfide was complete in about ten minutes. This dissolving was accompanied by the evolution of sulfur dioxide. After the reaction mixture had cooled, it was poured into 25 cc. of cold water. This caused the precipitation of a white crystalline product, which was washed by decantation with two 25-cc. portions of water. A crude yield of 3 g. of tribenzylsulfonium sulfate, melting at 130–135°, was obtained. Crystallization from alcohol gave pure tribenzylsulfoniumsulfate, m. p. 171°. (The reported melting points of this salt vary from 170 to 175°.)[2]

Anal. Calcd. for $C_{21}H_{22}O_4S_2$: SO_4^{--}, 24. Found: (by addition of barium chloride solution to the water solution of the sulfonium sulfate), 21. This sulfonium salt forms a trinitrophenoxide (m. p., 140°) which is identical with that prepared from known tribenzylsulfonium salts and picric acid. These are easily formed by mixing hot alcohol or water solutions of the reactants. Tribenzylsulfonium sulfate may be changed into the hydroxide by silver nitrate, if the reaction is carried out in 95% alcohol.

Tribenzylsulfonium Hydroxide.—Tribenzylsulfonium hydroxide was prepared in almost quantitative yields by the action of dilute aqueous silver nitrate (0.05 *N*) on an acetone solution of tribenzylsulfonium iodide–mercuric iodide. This addition complex was prepared by the general method of Smiles,[3] and was obtained in the form of glistening yellow plates, m. p. 137–138°.

Anal. Calcd. for $C_{21}H_{21}SI_3Hg$: S, 3.61; I, 43.0. Found: S, 3.58; I, 42.5.

After the addition of the silver nitrate, the solution was warmed to coagulate the silver iodide, which was then removed by filtration. The excess acetone was evaporated, and on cooling the residual solution, tribenzylsulfonium hydroxide separated as a white solid. When this was recrystallized from water, the hydroxide was obtained in the form of thick, white needles, which were stable and nonhygroscopic, and which melted at 133°.

Anal. Calcd. for $C_{21}H_{22}OS$: S, 9.94. Found: S, 9.84.

This sulfonium hydroxide was also prepared from tribenzylsulfonium chloride[4] and moist silver oxide. It may be converted into the trinitrophenoxide, sulfate, iodide (m. p. 78°), chloride, etc., by metathesis with the acids (or salts) in water solutions. On heating, the hydroxide decomposed into dibenzyl sulfide and benzyl alcohol.

Tribenzylsulfonium nitrate was prepared according to the method of Renshaw. The oily product obtained was converted into the sulfonium hydroxide by heating it with water.

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(1) Renshaw and Searle, This Journal, **55**, 4951 (1933).

(2) Fichter and Sjöstedt, *Ber.*, **43**, 3428 (1910).

(3) Smiles, *J. Chem. Soc.*, **77**, 160 (1900).

(4) Lee and Dougherty, *J. Org. Chem.*, **4**, 48 (1939).

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Contribution to the Theory of Racemism

By C. S. Hudson

Let the enantiomorphic forms of an optically active substance S be designated *d*-S and *l*-S. Assume that a solution containing equal quantities of *d*-S and *l*-S deposits crystals of S.

Case 1.—If these crystals are found by suitable measurements to be different from the separately and similarly prepared crystals of the single *d*-S and *l*-S components, the S crystals are a racemate, which may be designated *rac.* S. If the crystals prove to be the same as those of *d*-S and *l*-S, the racemate has not been found in the test.

Case 2.—Suppose now that the substance S is tautomeric in addition to being optically active, and assume two tautomers (S_1 and S_2) for simplicity; in this case there are two racemates possible, namely, *rac.* S_1 and *rac.* S_2. The number of possible racemates equals the number of possible tautomers.

Most racemates belong under Case 1; the designation of them as *rac.* S is quite definitive if they belong under this case. The experimental methods for the detection of such as fall under Case 1 are well known and are relatively simple. In the case of racemates which belong under Case 2, the designation *rac.* S is not definitive; obviously it must be determined experimentally whether the particular racemate is *rac.* S_1 or *rac.* S_2. The considerable number of racemic crystalline substances that have been recognized in the sugar group have always been regarded tacitly as under Case 1; it is obvious, however, as will now be shown by an example, that many of them really belong under Case 2 and that for these racemates new experimental study is required in order to classify them according to tautomeric forms. The first racemic crystals of a sugar were recognized by Ruff[1]; from a hot alcoholic solution containing equal quantities of *d*- and *l*-arabinose, well formed crystals separated on cooling; these crystals melted higher than the components and showed a much smaller solubility, which proves that they are a racemate. Ruff designated the substance "*rac.* arabinose," a name which must have appeared definitive at that time because the tautomerism of arabinose and other reducing sugars was not well recognized until later. It is now known that the mutarotation of arabinose definitely proves its tautomeric character and it is necessary to assume in the most general case that it may crystallize, under suitable conditions, as an alpha or beta form of a pyranose or of a furanose modification, or as an *aldehydo* form. There are thus five possible racemates comprised under the name "*rac.* arabinose": namely, *rac.* α-arabinopyranose, *rac.* β-arabinopyranose, *rac.* α-arabinofuranose, *rac.* β-arabinofuranose, *rac.* aldehydo-arabinose. The problem of determining which of these five racemates is represented by Ruff's "*rac.* arabinose" will require the devising of some new experimental procedure because no past observations bear upon it. Similar considerations apply to some other substances of the sugar group which have been reported as forming racemic crystals, for example some hydrazones and osazones; the mutarotation of the optically-active forms of these substances indicates tautomerism. On the other hand, the well-recognized racemate of α-methyl-mannoside[2] belongs under Case 1, since the glycosides are not tautomeric; it is definitely *rac.*-α-methyl-mannopyranoside. Likewise *rac.*-mannitol[3] and *rac.*-perseitol[4] are precise designations. An experimental study of "*rac.* arabinose" for the purpose of learning its real composition is in progress. Although the substance naturally does not exhibit "mutarotation" in the precise derivation of this term, the tautomeric change which it must undergo in solution (a sort of "masked mutarotation") should be observable through physical measurements of change of volume, refraction or solubility, or of heat of reaction, or of change of conductivity of added boric acid, to mention some of the more obvious ways. Acetylation of the racemic sugar at low temperature to yield non-tautomeric tetraacetates, which may be identifiable, seems a promising chemical method for a conclusive determination.

Drs. M. L. Wolfrom and E. F. Evans join me in expressing the opinion that the crystals of *rac.*-perseulose, which they have described recently[5] and for which they have proved the racemic nature, very probably fall under Case 2 for the reason that the *d*- and *l*-forms of perseulose exhibit mutarotation prominently.

(1) Ruff, *Ber.*, **32**, 550 (1899).

(2) E. Fischer and Beensch, *ibid.*, **29**, 2927 (1896)

(3) E. Fischer, *ibid.*, **23**, 370 (1890).

(4) W. Stanley Smith, *Ann.*, **272**, 182 (1892).

(5) Wolfrom and Brown, THIS JOURNAL, **65**, 1021 (1943).

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RECEIVED APRIL 16, 1943

Model Experiments on the Use of Cyclopentadiene in the Synthesis of Sterol-like Compounds[1]

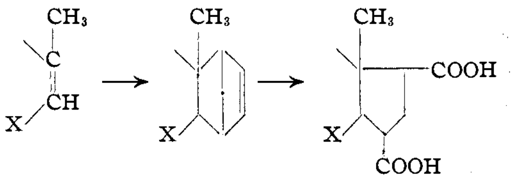
BY C. F. KOELSCH AND F. J. LUCHT

The synthesis of sterol-like compounds involves the fusion of a six-membered ring with a five-membered ring; the latter must contain a functional group, and one of the angular carbon atoms must bear a methyl group. The diene synthesis appears applicable to the formation of such substances, and attempts to use it have been made.[2] In these attempts, the six-membered ring has been formed from a diene, and the five-membered ring from a methylated cyclopentene bearing an activating group.

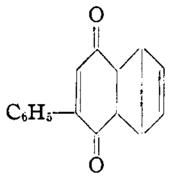
(1) This paper is from the incomplete Ph.D. Thesis of Lt. F. J. Lucht. The work is being published in its present form because military duties have necessitated postponement of the investigation by the junior author.

(2) For a discussion and references, see Woodward, THIS JOURNAL, **62**, 1478 (1940).

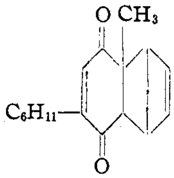
In the present investigation some experiments were carried out using methylated six-membered ring compounds containing activating groups; the five-membered ring was furnished by cyclopentadiene. It was intended to degrade the resulting bicycloheptene to a cyclopentane by oxidation, thus



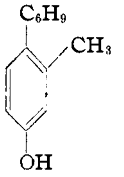
Under none of the conditions tried (seventy-two hours at room temperature, three hours at 135°, or twelve hours at 195°) did 3-methylcyclohexenone react with cyclopentadiene. But no difficulty was experienced in adding cyclopentadiene to phenylquinone or to 2-cyclohexyl-5-methylquinone. In both cases only 1:1 addition products were obtained, and it is considered that the structures indicated (I, II) are more probable than those which would result by addition to the opposite side of the quinone involved.



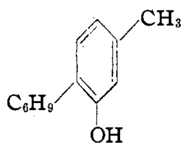
I



II



III



IV

The conjugated carbon–carbon double bond in I was reduced successfully; attempts to remove the oxygen by Clemmensen reduction gave liquid products which could not be completely purified.

The preparation of the quinone used in the synthesis of II is of interest since it establishes the structure of the product obtained by the condensation of cyclohexanone with *m*-cresol. The product was reported by Niederl and Niederl[3] to be III, but no evidence was brought forward in support of this structure. The fact that the phenol can be converted into a *p*-quinone now establishes its most probable structure as IV.

Experimental

Phenylquinone and its Addition Product (I).—Diazotized sulfanilic acid was found to be preferable to diazotized aniline in the preparation of phenylquinone, and 5-amino-2-hydroxybiphenyl was purified by crystallization of its hydrochloride from water. In other details the procedure was similar to the one described by Borsche and Scholten.[4]

A suspension of 5 g. of phenylquinone in 10 ml. of methanol and 1.8 g. of cyclopentadiene was warmed for a short time; after the quinone had dissolved, the solution was cooled and filtered. Recrystallized from methanol, the resulting **5,8-methano-2-phenyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone** (I) formed pale yellow prisms (6 g., 88%) that melted at 70.5–71°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.6; H, 5.6. Found: C, 81.7; H, 5.7.

Reduction of I (6 g.) in water (120 ml.) and acetic acid (10 g. added in portions) by stirring with zinc dust at 70° for two hours gave **2,3,4a,5,8,8a-hexahydro-5,8-methano-2-phenyl-1,4-naphthoquinone,** which formed colorless stout needles (4.5 g., 75%) that melted at 149.5–152° after crystallization from methanol.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.4. Found: C, 80.9; H, 6.3.

Clemmensen reduction of the hexahydro compound (10 g. in each of three experiments) gave an oily substance which contained starting material even when the reduction was continued for two days. Distillation gave a 50% yield of product, b. p. 200–215° at 23 mm., together with some higher boiling material. The product was redistilled, and the main part, which boiled at 136–138° at 4 mm., was analyzed.

Anal. Calcd. for $C_{17}H_{20}$: C, 91.0; H, 9.0. Found: C, 89.2; H, 9.3.

2-Cyclohexenyl-5-methylphenol (IV).—Prepared by the condensation of cyclohexanone with *m*-cresol according to the procedure of Niederl and Niederl,[3] this phenol (b. p. 180–190° at 25 mm.) was obtained in yields averaging 14%. An equal weight of material that boiled at 200–240° at 20 mm. was also isolated. The properties of this higher boiling material indicated that it was a dimer of cyclohexenylcresol, perhaps analogous to the one formed from 2-isopropenyl-5-methylphenol by the action of hydrochloric acid.[5]

The dimer crystallized from acetone in the form of large colorless prisms that softened at 106° and melted with effervescence at 111–113°.

Anal. Calcd. for $C_{26}H_{32}O_2 + C_3H_6O$: C, 80.0; H, 8.8; $(CH_3)_2CO$, 13.3. Found: C, 79.6; H, 8.8; $(CH_3)_2CO$, 12.1.

When the acetone-containing compound was heated to 130° and then crystallized from ethanol, the solvent-free dimer was obtained; it melted at 142–143° without effervescence.

Anal. Calcd. for $C_{26}H_{32}O_2$: C, 83.0; H, 8.6. Found: C, 83.2; H, 8.4.

2-Cyclohexyl-5-methylphenol.—2-Cyclohexenyl-5-methylphenol (10 g.) in acetic acid (40 ml.) containing platinum

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[3] Niederl and Niederl, THIS JOURNAL, **61**, 1785 (1939).

[4] Borsche and Scholten, *Ber.*, **50**, 596 (1917).

[5] Fries and Fickewirth, *ibid.*, **41**, 367 (1908).

oxide (0.15 g.) rapidly took up one equivalent of hydrogen. The product boiled at 166–169° at 19 mm., and crystallized on cooling; m. p. 69–70°.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.0; H, 9.5. Found: C, 82.0; H, 9.2.

4-Amino-2-cyclohexyl-5-methylphenol.—A cold suspension of cyclohexylcresol (5.7 g.) in aqueous sodium hydroxide was mixed with a solution prepared by diazotizing 6.3 g. of sulfanilic acid. After it had stood for one hour, the mixture was treated with a solution of 14 g. of sodium hydrosulfite and then warmed until reduction was complete. The product was removed by filtration and crystallized from benzene. It formed colorless nodules (4.8 g. 78%) that became pink at 170° and melted to a brown liquid at 182°.

Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.0; H, 9.3. Found: C, 76.3; H, 9.3.

2-Cyclohexyl-5-methylquinone.—A solution of the aminophenol in hot dilute sulfuric acid was poured into a solution of potassium dichromate in water. The mixture was cooled, and the product was separated by filtration (yield nearly quantitative). Crystallized from ethanol, the quinone formed bright yellow plates that melted at 60–61°.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.4; H, 7.9. Found: C, 76.3; H, 7.9.

Reduced with granulated zinc in acetic acid, the quinone yielded **2-methyl-5-cyclohexylhydroquinone,** which formed colorless plates that melted at 146–148°; yield, 95%.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.7; H, 8.8. Found: C, 75.7; H, 8.7.

2-Cyclohexyl-5,8-methano-4a-methyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (II).—A solution of 2.6 g. of 2-cyclohexyl-5-methylquinone and 2 g. of cyclopentadiene in 10 ml. of methanol was boiled for one hour and then cooled. The product was separated by filtration and recrystallized from methanol. It formed light yellow needles (3.3 g., 96%) that melted at 75–77°.

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 80.0; H, 8.2. Found: C, 80.1; H, 8.2.

No trimolecular product was formed in the addition; when 1.5 g. of the product and 5 g. of cyclopentadiene were boiled for one hour in xylene, and the solvent was then distilled, there was obtained 0.9 g. of cyclohexylmethylquinone.

Reduction of the addition product with zinc and acetic acid gave a colorless product which separated from methanol in the form of nodules that melted at 71–78°. This substance has not been investigated further.

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MINNEAPOLIS, MINN.
RECEIVED MARCH 22, 1943

[CONTRIBUTION FROM THE WESTERN REGIONAL RESEARCH LABORATORY, BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY, AGRICULTURAL RESEARCH ADMINISTRATION, U. S. DEPARTMENT OF AGRICULTURE]

Preparation of D-Galacturonic Acid from Pectin*

BY E. RIETZ AND W. D. MACLAY

Pectin is composed principally of polymers of D-galacturonic acid and at present constitutes the most readily available source material for the preparation of this compound. Members of the medical profession are displaying considerable interest in the biological properties of not only galacturonic acid but certain of its derivatives. Due to the instability of uronic acids in hot mineral acid, enzymic hydrolysis of pectic acid has proved the most satisfactory method of preparation for galacturonic acid. Ehrlich[1] reported an enzymic method giving high yields. Mottern and Cole,[2] employing the domestically-available materials, pectic acid and "Pectinol 46 AP,"[3] obtained the uronic acid in a yield of approximately 25 per cent. Manville, Reithel and Yamada[4] modified the method of Mottern and Cole to give a maximum yield of 36%. Pigman[5] further modified this method by using methanol in place of ethanol as an extracting solvent and obtained yields in excess of 67% of the weight of the uronic anhydride content of the pectic acid employed as a source material.

The preparation of D-galacturonic acid directly from pectin instead of from pectic acid was undertaken because of the somewhat laborious intermediate preparation of the pectic acid when carried out in the laboratory and the non-uniformity of commercially-available pectic acid. A number of commercial pectins have been used and yields of D-galacturonic acid ranging from 74 to 80%, based on the uronic anhydride content of the pectin, are readily obtainable. Included in these were 285- and 300-grade apple pectins and 170-, 185- and 200-grade citrus pectins with average yields of 78, 78, 80, 78, and 74%, respectively, of the uronic acid.

Experimental

Four 100-g. lots of a 300-grade apple pectin (uronic anhydride content 76.6%) were each dispersed in 2000 ml. of water by means of a Waring Blendor and adjusted to a *p*H of 3.7 by the addition of 20 ml. of 3 *N* sodium hydroxide. The pectin solutions were transferred to 3-liter Erlenmeyer flasks, 10 g. of Pectinol 46 AP was added to each, and the surfaces were covered with toluene. The reaction mixtures were placed in a 30° room for ten days, the course of the hydrolysis being observed by hypoiodite oxidations. Normally, over 50% of the hydrolysis occurs during the first twenty-four hours, and 75 and 95% within three and

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* Not copyrighted.

(1) F. Ehrlich, "Abderhaldens Handbuch der biologischen Arbeitsmethoden," Abt. 1, Teil 11, 1617 (1936).

(2) H. H. Mottern and H. L. Cole, THIS JOURNAL, **61**, 2701 (1939).

(3) Röhm and Haas Pectinol 46 AP, standardized with diatomaceous earth.

(4) I. Manville, F. Reithel and P. Yamada, THIS JOURNAL, **61**, 2973 (1939).

(5) W. W. Pigman, *J. Research Natl. Bur. Standards*, **25**, 301 (1940).

five days, respectively. The alkali originally added was neutralized with equivalent amounts of sulfuric acid, and the reaction mixtures were filtered, combined, and concentrated *in vacuo* in a water-bath at 50° to a thick sirup. Extraction of the sirup with methanol was carried out according to the directions of Pigman,[5] the extracts being combined and treated with 30 g. of decolorizing carbon. The colorless filtrate was concentrated *in vacuo* on a water-bath at 40° to a thick sirup. Ethanol (25 ml.) was added and the solution was seeded and reconcentrated *in vacuo* at room temperature for eighteen hours or until the mass had become crystallized. The crystalline mass was then triturated with 150 ml. of methanol–ethanol (60/40) and allowed to stand at −30° for twenty-four hours, yielding 248 g. (74%) of the uronic acid monohydrate. The galacturonic acid was of good purity, sintering at 108–110° and exhibiting a specific rotation $[\alpha]^{20}_{\mathrm{D}}$ +50.3° (*c*, 4) in water.

ALBANY, CALIFORNIA RECEIVED MARCH 22, 1943

The Formation of Ergostatetraene-B During the Acetylation of Ergosterol

By Harry A. Stansbury, Jr.

It has been frequently observed in this Laboratory that the acetylation of ergosterol by means of boiling acetic anhydride gives an unsatisfactory yield of ergosteryl acetate, and that the physical properties of the crude product indicate the presence of low melting by-product of positive optical rotation. This by-product has now been shown to be a hydrocarbon formed by the dehydration of ergosterol. It is identical with ergostatetraene-B, which had previously been prepared by the action of acetic anhydride[1] or maleic anhydride[2] on ergostatetraene-A, and by the dehydration of ergosterol with *p*-toluenesulfonyl chloride in pyridine.[2]

Experimental

In a typical experiment 200 g. of ergosterol was refluxed for thirty minutes with 2 liters of acetic anhydride. After cooling the crude acetate was filtered, washed with glacial acetic acid and methanol, and recrystallized from ethyl acetate. A total of 160 g. of ergosteryl acetate of m. p. 171° was thus obtained. The mother liquor from this crystallization was concentrated to a small volume, and then diluted with ethanol. Upon cooling, 3.5 g. of fine, colorless needles was obtained which after recrystallization from ether–alcohol showed m. p. 101.5° and $[\alpha]^{25}_{\mathrm{D}}$ +97°. *Anal.* Calcd. for $C_{28}H_{42}$: C, 88.8; H, 11.2. Found: C, 88.7; H, 11.0. When mixed with an authentic sample of ergostatetraene-B, m. p. 101–101.5°; $[\alpha]^{23}_{\mathrm{D}}$ +100°, prepared according to the directions of Stoll,[2] the hydrocarbon showed no depression of the melting point. Fractional recrystallization of the ergosterol used in the present experiments failed to reveal the presence of this hydrocarbon.

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RECEIVED MARCH 2, 1942

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[1] Rhyg, *Z. physiol. Chem.*, **185**, 99 (1929).

[2] Stoll, *ibid.*, **202**, 235 (1931).

Catalytic Degradation of Heptaldehyde in Vapor Phase

By T. J. Suen and Simone Fan

In a previous paper[1] the authors reported that when heptaldehyde was hydrogenated with a nickel catalyst at 250° under atmospheric pressure, *n*-hexane was obtained, together with some *n*-heptyl alcohol. In order to ascertain whether the presence of hydrogen is essential for the degradation reaction, heptaldehyde was pyrolyzed over the nickel catalyst without the admixture of hydrogen. The experimental procedure and operating conditions were the same as described previously, except that an additional trap filled with active carbon was inserted between the first trap and the wet gas meter to retain the hydrocarbon vapor uncondensed. It was subsequently stripped with live steam and combined with the other portions of the liquid products.

When analyzing the liquid products, it was found that a considerable amount of unsaturated hydrocarbons was present, and their content was determined in the following manner. Ten ml. of the liquid product fractionated over between 66–70° was shaken with 30 ml. of 96% sulfuric acid for about five minutes in a glass-stoppered buret. After standing, the volume of the oil layer was read. The decrease in volume was considered as the content of the unsaturated hydrocarbons. It was noted that the refractive index of the liquid was lowered by the acid treatment, and this agrees with the assumption that unsaturates were present.[2] The treated and redistilled product gave physical constants essentially the same as those of *n*-hexane.

It was also observed that when no hydrogen was used during the reaction, the catalyst deteriorated quite rapidly. The yield of the degradation products became lower and lower. Unreacted heptaldehyde was also found present in the products, as determined by the bisulfite method.[3]

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[1] Suen and Fan, This Journal, **64**, 1460 (1942).

[2] For *n*-hexane, n^{20}_{D} 1.37506; hexene-1, n^{20}_{D} 1.3886; hexene-2, n^{20}_{D} 1.3958; hexene-3, n^{20}_{D} 1.3942. See Egloff, "Physical Constants of Hydrocarbons," Vol. 1, Reinhold Publishing Corp., New York, N. Y., 1939.

[3] Parkinson and Wagner, *Ind. Eng. Chem.*, *Anal. Ed.*, **6**, 433 (1934).

TABLE I

RESULTS OF CATALYTIC PYROLYSIS AT 250°

Expt. no.		A	B	C
Catalyst condition, after hrs. use		fresh	1.5	7
Heptaldehyde used, ml.		42.5	47.0	44.2
Org. liq. product, ml.		33.8	41.3	38.5
Liq. b. p. 66–70°, vol. % of liq. prod.		67	62	43
Unreacted aldehyde, wt. % of liq. prod.		..	1.9	15.0
% Unsatd. in 66–70° portion		..	24	30
Gas analysis, %	CO_2	0.8	1.4	0.4
	O_2	5.4	1.6	3.2
	Unsaturates	0.6	1.2	1.8
	CO	48.2	57.4	50.2
	H_2	12.0	..	18.9
	CH_4	13.1	..	14.4
	N_2 (by diff.)	19.9	..	11.1

The results of three typical experiments are given in Table I. The fractionation curves of the liquid products are shown in Fig. 1.

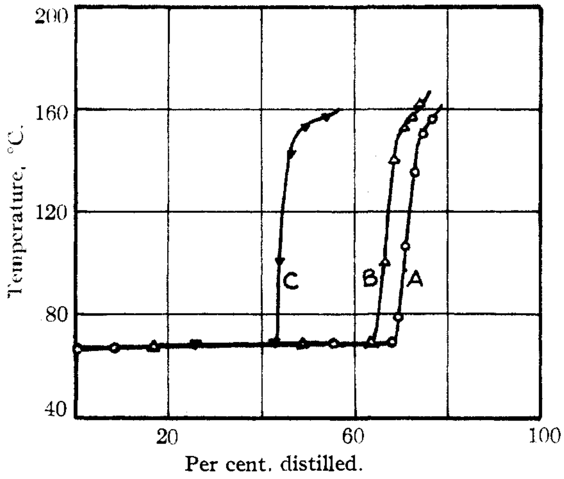

Fig. 1.

The higher-boiling portion of the liquid products was not analyzed in detail, but a rough examination of its boiling range, refractive index, and smell showed that some other compounds were present in addition to *n*-heptyl alcohol.

Experiments at 200° also have been carried out. The reaction did not go very far. Average of two experiments showed that the degradation products *i. e.*, the portion boiling between 66–70°, only amounted to 20% of the liquid products.

The results given above throw some light on the mechanism of the reaction. As indicated in Table I, free hydrogen and methane both were present in the gaseous products, although no hydrogen was primarily added. Furthermore, unsaturated hydrocarbons also were found in the degradation products. Evidently the following reaction takes place during the decomposition

$$C_6H_{13}CHO \longrightarrow C_6H_{12} + CO + H_2 \qquad (1)$$

However, this reaction does not fully account for the large amount of hydrogen and methane obtained, in comparison with hexene. In all the experiments the amount of liquid products collected was always smaller than expected. In other words, a part of the heptaldehyde used, or liquid products obtained therefrom, was decomposed into gases.

With free hydrogen present, as indicated in Equation (1), a part of the hexene formed is reduced to hexane.

$$C_6H_{12} + H_2 \longrightarrow C_6H_{14} \qquad (2)$$

It is of course also possible that hexane is the primary decomposition product, and the hexene is formed through dehydrogenation of hexane

$$C_6H_{14} \longrightarrow C_6H_{12} + H_2 \qquad (3)$$

But reaction (3) is not probable. A perusal of the literature shows that palladium black has a slight dehydrogenation action on *n*-hexane at 300° and, in the presence of nickel and added hydrogen, *n*-hexane decomposes to methane at 400°.[4,5] In the present case, the temperature seems to be too low to cause the dehydrogenation reaction. Furthermore, analysis of the degradation products obtained by decomposing heptaldehyde alone at 200° showed that it contained about 35% of unsaturated hydrocarbons while that obtained at 250° contained about 24–30% as given in Table I. This also indicates the improbableness of the above reaction.

The identity of the unsaturated portion in the degradation products, though not determined, could more or less be inferred from the available data. As its boiling range is within 66–70° (almost nothing in the liquid products was fractionated over below 66°), it is not hexene-1, which has a b. p. of 63.5°.[2] A few degrees difference in boiling temperature could be detected with the fractionating column employed. Hexene-2 and hexene-3, with their respective *cis* and *trans* forms and mixtures, all boil within the range 66–70°. During the decomposition of heptaldehyde, it is more probable that hexene-1 is first formed. However, it is known that α-olefins, if originally formed in pyrogenetic processes, tend to rearrange

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(4) Egloff, "The Reactions of Pure Hydrocarbons," Reinhold Publishing Corp., New York, N. Y., 1937, pp. 193–194.

(5) Tausz, *Chem. Z.*, **37**, 334 (1913); Tausz and von Putnoky, *Ber.*, **52B**, 1573 (1919).

mostly to β-olefins.[6] Hence, the following reaction seems to take place during the decomposition process

$$C_6H_{12}\text{ (Hexene-1)} \longrightarrow C_6H_{12}\text{ (Hexene-2)} \quad (4)$$

The formation of hexene-3 is also possible, but less likely.

The readings of refractive index of the products also check with the above assumption. A mixture of 70% of n-hexane and 30% of hexene-2 (or hexene-3) would have $n^{20}\text{D}$ about 1.382, while the value of the portion boiling between 66–70° before sulfuric acid treatment was 1.384. A mixture of hexene-1, which possesses a much lower $n^{20}\text{D}$, and n-hexane would give a far smaller value.[2]

The elucidation of the exact mechanism of the decomposition process requires further study. Owing to the present wartime pressure and difficulties, the investigation on this subject had to be discontinued.

[6] Brooks and Humphrey, THIS JOURNAL, **40**, 832 (1918).

THE RESEARCH LABORATORIES
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CHUNGKING, CHINA
RECEIVED JANUARY 2, 1943

Investigations on the Stereoisomerism of Unsaturated Compounds. VI. The Composition of Divinyl Glycol from Acrolein. The System *meso-dl*-Diethyl Glycol

BY WILLIAM G. YOUNG, STANLEY J. CRISTOL AND FRED T. WEISS

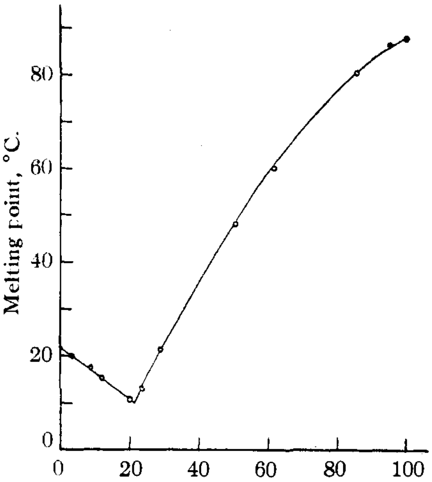
It has been demonstrated conclusively that diastereomeric unsaturated glycols are formed in the pinacolic reduction of α,β-unsaturated aldehydes.[1,2,3,4] Young, Levanas and Jasaitis[3] have shown that, in the reduction of crotonaldehyde, *meso-* and *dl*-dipropenyl glycols, which may be hydrogenated to the corresponding dipropyl glycols, are formed in equal amounts as predicted on purely geometric grounds, but not found, by Kuhn and Rebel.[5] van Risseghem has prepared the diastereomeric diethyl glycols from acrolein by the similar reaction path

$$CH_2{=}CHCHO \xrightarrow[\text{HOAc}]{\text{Zn-Cu}}$$

$$\underset{meso\text{- and }dl\text{-divinyl glycol}}{CH_2{=}CHCHOHCHOHCH{=}CH_2} \xrightarrow{H_2(Pt)} \underset{meso\text{- and }dl\text{-diethyl glycol}}{CH_3CH_2CHOHCHOHCH_2CH_3}$$

and has identified the individual isomers.

In the course of a study on the preparation of a number of pure stereoisomeric dibromides, we have prepared and separated the *dl-* and *meso*-diethyl glycols and have shown that the divinyl glycols are formed in equal quantities during the reduction of acrolein alone or in a mixture of acrolein and crotonaldehyde, contrary to the observations of Kuhn and Rebel.[5] This was accomplished by a determination of the melting point–composition diagram (Fig. 1) obtained by mixing the pure diastereomers, and by the use of this curve in a comparison with the melting point of the product mixture.



Mole per cent. of *meso*-diethyl glycol.

Fig. 1.—The melting point diagram of the system *meso-*, *dl*-diethyl glycol.

Experimental

Preparation and Separation of the Diethyl Glycols.—Divinyl glycol was prepared from acrolein by the method described previously[3] in the reduction of crotonaldehyde. The unsaturated glycol was hydrogenated with Adams platinum oxide catalyst[6] in 95% ethanol. After the catalyst was removed by centrifuging and the solvent removed by distillation, the melting point of the semi-solid residue was 50.4°. The solid was removed by filtration. Recrystallization from ligroin gave pure *meso*-diethyl glycol, m. p. 88.0–88.2°, m. p. of the bi-3,5-dinitrobenzoate, 190°.

The filtrate was fractionally distilled several times in a 3-foot long, adiabatic, metal spiral column at high reflux, until the lower boiling *dl*-isomer (b. p. 90.5–90.7° (8 mm.)) was obtained pure, m. p. 21.7°, m. p. of the bi-3,5-dinitrobenzoate, 167–168°. The melting point of this glycol did not increase upon redistillation or upon recrystallization from ligroin.

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(1) Farmer, Laroia, Switz and Thorpe, *J. Chem. Soc.*, 2937 (1927).

(2) Lespieau and Weimann, *Compt. rend.*, **194**, 1946 (1932); **196**, 886 (1933).

(3) Young, Levanas and Jasaitis, THIS JOURNAL, **58**, 2274 (1936).

(4) van Risseghem, *Bull. soc. chim. Belg.*, **47**, 194 (1938).

(5) Kuhn and Rebel, *Ber.*, **60B**, 1565 (1927).

(6) Adams, Voorhees and Shriner, "Organic Syntheses," Vol. VIII, John Wiley and Sons, New York City, 1928, p. 92.

The Melting Point Diagram for the System *meso-dl*-Diethyl Glycol.—Known mixtures of pure *dl* and *meso* glycols sealed in small melting point tubes were heated slowly under constant agitation in a water-bath, the temperature of which was raised at the rate of 1° per five minutes. The temperatures at which the last particle of solid disappeared were recorded as the melting points and are plotted in Fig. 1. The composition of the eutectic mixture is 21.5% *meso*- and 78.5% *dl*-glycol and that of the glycol mixture (m. p. 50.4°) obtained from the hydrogenation of divinyl glycol 52% *meso* and 48% *dl*.

The divinyl glycol separated from the glycol mixture formed during the reduction of a mixture of acrolein and crotonaldehyde according to the method of Lespieau and Weimann[2] gave the same mixture of diethyl glycols as that from acrolein alone.

It may therefore be concluded that the pinacolic reduction of acrolein gives equal quantities of *meso*- and *dl*-divinyl glycol.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA AT LOS ANGELES
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COMMUNICATIONS TO THE EDITOR

THE THERMODYNAMICS OF STYRENE (PHENYLETHYLENE), INCLUDING EQUILIBRIUM OF FORMATION FROM ETHYLBENZENE

Sir:

We have measured the heat capacity of styrene from 15 to 300°K., the heat of fusion, and the vapor pressure. The latter is represented between 0 and 60° by the equation

$$\log_{10} p_{\text{mm. Hg}} = -2604.67T^{-1} - 2.57692 \log_{10} T + 15.90485$$

The calculation of the entropy is summarized in Table I.

TABLE I

ENTROPY OF STYRENE

0–15°, 2 × $D(123/T)$	0.56	
15–242.47°, solid	36.82	
Fusion, 2617/242.47	10.79	
242.47–298.16°, liquid	8.61	
Liquid at 298.16°		56.78 ± 0.3 cal./deg. mole
Vaporization, 10390/298.16	34.85	
Compression, $R \ln 6.19/760$	−9.56	
Ideal gas at 1 atm.		82.07 cal./deg. mole

Since the reaction forming styrene from ethylbenzene is of considerable interest, we have calculated the equilibrium constant at various temperatures by thermodynamic methods. Measurements of the vapor pressure of ethylbenzene from 0 to 60° lead to the equation

$$\log_{10} p_{\text{mm. Hg}} = -2959.08T^{-1} - 5.8 \log_{10} T + 25.25883$$

and hence to a heat of vaporization of 10,100 cal./mole at 298.16°K. Combining this value with the observed pressure, 9.58 mm., and with the entropy of liquid ethylbenzene[1] we find for S^0_{298} 86.39 cal./deg. mole in the gas.

The heat of the reaction

$$C_6H_5CH_2CH_3 = C_6H_5CH{=}CH_2 + H_2$$

is calculable from the heats of hydrogenation of styrene and ethylbenzene.[2] Making reasonable assumptions regarding ΔC_p, we find for the temperature range 381–1000°K.

$$\log_{10} K = -5657.9T^{-1} - 6.3779 - 0.000804T + 4.3687 \log_{10} T$$

Values of the equilibrium constants calculated from this equation are tabulated in Table II.

TABLE II

DEHYDROGENATION OF ETHYLBENZENE TO FORM STYRENE

T, °K.	$-\log_{10} K$
381	10.26
400	9.48
500	6.30
600	4.15
800	1.41
1000	−0.27
(1500)	(−2.52)

Available data on the pyrolysis of ethylbenzene indicate that near-equilibrium yields were obtained at 425–550°,[3] but not at higher temperatures[4] where, however, the situation is obscured by numerous side reactions.

The details of the calorimetric work will be

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(1) Huffman, Parks and Daniels, THIS JOURNAL, **52**, 1547 (1930).

(2) Dolliver, Gresham, Kistiakowsky and Vaughan, *ibid.*, **59**, 831 (1937).

(3) Sergienko, *Compt. rend. acad. Sci.* (U. R. S. S.), **26**, 69–72 (1940); Oblad, Marschner and Hurd, THIS JOURNAL, **62**, 2066 (1940).

(4) Dobryanskiĭ, Uchenyi, Zapiski, Leningrad, Gosudarst. Univ. im. A. S. Bubnova, Ser. Khem. Nauk I, No. 1, 105 (1935); Dobryanskiĭ, *et al.*, Trans. Exptl. Research Lab. "Khimgas," Materials on Cracking and Chem. Treatment of Cracking Products (U. S. S. R.), **3**, 1 (1936); Zal'kind and Bulavskiĭ. *Plasticheskie Massui*, No. 3, 9 (1935).