those for the corresponding para compounds are presented. It is seen that for the nitro and methyl groups a twenty-fold change in K_0' is caused by changed position in the ring in the precipitation of anti-R serum, and only a two-fold change for anti-R′ serum. The effect of the amino group with anti-R serum is much smaller than that of the nitro group and the methyl group —only about six-fold; but the same two-fold change is shown with anti-R′ serum. The structural significance of these observations is not clear.

TABLE VIII

EFFECT OF POSITION OF SUBSTITUENTS ON HAPTEN INHIBITION CONSTANT

Substituent*	Anti-R sera			Anti-R serum, short inoculation	Anti-R′ sera		
	a	*b*	*c*	*d*	*e*	*f*	*g*
	Meta/para						
Nitro	0.46	0.31	0.22	0.25	1.23	1.15	0.81
Methyl	.44	.44	.36	.79	1.09	0.54	39
Amino	.76	.67	.69	.57	0.50	.73	.66
	Ortho/para						
Nitro	.134	.063	.043	.14	1.03	.73	.40
Methyl	.066	.044	.062	.23	1.45	.50	.37
Amino	.16	.14	.19	.36	0.35	.40	.60

* Letters *a* to *g* refer to Table VII.

The effect of the nature of the substituent group is just as pronounced for anti-R′ serum as for anti-R serum; for each antiserum an approximately fifty-fold range of values is covered by K_0' for the twenty-four haptens. The general order of effectiveness of groups is indicated by the order of the para-substituted haptens in the table.

The anti-R serum obtained after a short course of inoculations (*d* in Tables VII and VIII) shows much lower specificity of interaction with haptens than the other antisera, with respect both to the nature of the substituent group and to its position.

This investigation was carried on with the aid of a grant from The Rockefeller Foundation. We are grateful to Professor Dan H. Campbell and Dr. V. Schomaker for assistance.

Summary

A quantitative theory of the inhibition by haptens of the precipitation of heterogeneous antisera by antigens has been developed on the basis of the assumption that the heterogeneity of an antiserum can be described by a distribution function which is an error function of the free energy of interaction of antibody and hapten in competition with the precipitating antigen. The theory has been found to be in satisfactory agreement with experiment. It has been applied to data obtained in previous investigations and to data from new experiments on the inhibition by each of twenty-four haptens of the precipitation of anti-R serum and of anti-R′ serum with a dihaptenic simple antigen and with R′-ovalbumin, yielding values of the average effective inhibition constant of the haptens and of the heterogeneity index of the antisera. A discussion of the structural significance of these quantities is presented.

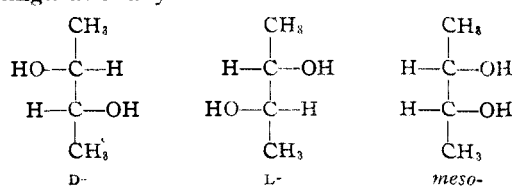
PASADENA, CALIFORNIA RECEIVED FEBRUARY 1, 1944

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

Configuration of the 2,3-Butylene Glycols[1]

BY S. A. MORELL AND A. H. AUERNHEIMER[2]

2,3-Butylene glycol is a symmetrical molecule containing two asymmetric carbon atoms. Like tartaric acid, it can occur in only three stereoisomeric forms, D-, L- and *meso*-, which are formulated configurationally as follows



2,3-Butylene glycols

Previous investigations[3,4,5] on the configuration of the 2,3-butylene glycols have been limited to the distinction between the optically inactive *meso*- and D, L- forms, rather than with relating the active forms to their respective configurational series. In order to accomplish the latter, one of the enantiomorphs must be converted to a compound whose configuration is known.

In studying the conversion of optically active 2,3-butylene glycols to butadiene, by pyrolysis of their diacetates according to the method of Hill and Isaacs,[6] the isolation of several optically active intermediates has made it possible to establish the configuration of the glycols. Both the dextro- and levorotatory glycols were used in the present investigation. From the former, a levorotatory methylvinylcarbinol acetate was obtained which yielded a dextrorotatory methylvinylcarbinol on hydrolysis. From the latter, a levorotatory methylvinylcarbinol was obtained, without isolating its intermediate acetate. The optical purity of the glycols used differed con-

(1) This is one of four regional research laboratories operated by the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Not copyrighted.

(2) Chemist and Junior Chemist, respectively, Industrial Chemical Section, Agricultural Residues Division.

(3) J. Böeseken and R. Cohen, *Rec. trav. chim.*, **47**, 839 (1928).

(4) C. E. Wilson and H. J. Lucas, THIS JOURNAL, **58**, 2396 (1936).

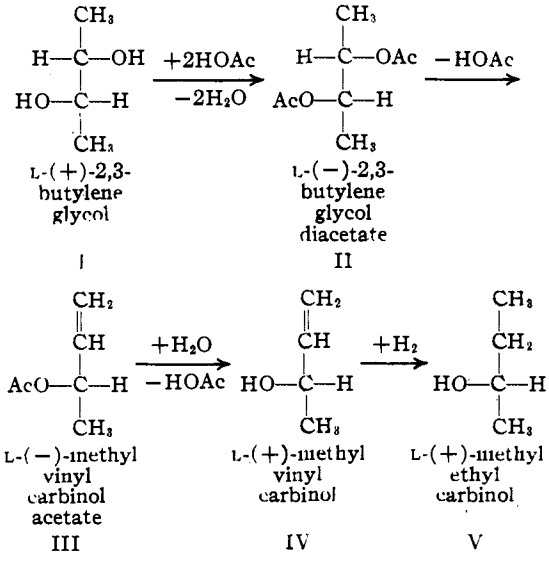
(5) S. Winstein and H. J. Lucas, *ibid.*, **61**, 1581 (1939).

(6) R. Hill and E. Isaacs, U. S. Patent 2,224,912, Dec. 17, 1940.

siderably, but it will be evident from the following discussion that the sign of rotation alone, rather than the magnitude of rotation, was sufficient to establish the necessary configurational relationships.

Winstein and Lucas[5] have found that the acetylation of an optically active, 2,3-butylene glycol proceeds with an inversion in the sign of rotation. In confirming this observation, it was found that extensive racemization occurred when the acetylating medium was acetic acid catalyzed by sulfuric acid, whereas with acetic anhydride (uncatalyzed) this reaction proceeded without racemization. Kenyon and Snellgrove[7] also noted an inversion in sign when alkyl vinyl or alkyl ethyl carbinols were converted to their acetates. On the basis of rotatory data, the latter investigators showed that the methyl vinyl and methyl ethyl carbinols of the same sign of rotation are probably related configurationally. In agreement with Kenyon and Snellgrove's[7] rotatory data, hydrogenation of our dextrorotatory methyl vinyl carbinol yielded dextrorotatory methylethylcarbinol.

Levene, Walti and Haller[8] have shown that dextrorotatory methylethylcarbinol possesses the same configuration as dextrorotatory lactic acid, which belongs to the L-series. L-(+)-Methylethylcarbinol is thus related to dextrorotatory 2,3-butylene glycol and the enantiomorphs of the latter are, therefore, L-(+)- and D-(−)- for the dextro- and levorotatory forms, respectively. The following configurational formulas show the reactions which were conducted starting with the L-(+)-glycol



From the above stereochemical formulas, it is evident that L-(−)- methyl vinyl carbinol acetate (III) is the only optically active product possible when one molecule of acetic acid is removed from L-(−)-2,3-butylene glycol diacetate (II). Deacetylation from the 2,3 position produces the isomeric acetate of the 2–3 enol of methyl ethyl ketone, CH_3—C(OAc)=CH—CH_3 which contains no asymmetric carbon atom. All of the compounds formulated above can exist in only two optically active forms, D- and L-. For any of them, therefore, the sign of rotation is sufficient to determine which active form is present. In the case of the glycols, or their diacetates, the inactive forms which can also be present are D,L-, *meso-* and a mixture of both. In the deacetylation reaction, the optically active methyl vinyl carbinol acetate formed must have the same configuration as the active glycol originally present, for any D-, L- or *meso*-glycol also present could form only D-, L-methylvinylcarbinol acetate.

Experimental

The glycols were obtained from glucose by the Fermentation Division of this Laboratory. Their isolation from the beers was conducted by the Engineering and Development Division. A complete description of the preparation of the glycols, the acetylation and pyrolysis reactions, and the separation of the bulk of the acetic acid in the pyrolysis liquors, will be included in future communications from this Laboratory on the conversion of 2,3-butylene glycol to butadiene, of which the present investigation is an incidental part.

The physical and analytical values observed for the compounds described below are given in the accompanying table. For convenience in referring to the table, each compound has been assigned a number, starting with the five compounds formulated in the reactions given above for the conversion of dextrorotatory 2,3-butylene glycol (I) to dextrorotatory methyl ethyl carbinol (V). The experiments on racemization, conducted in connection with the possibility of Walden inversion during the acetylation reaction, are treated separately and are not included in the table.

All specific rotations reported refer to the homogeneous liquids, no corrections being made for their densities. In reporting the rotations below, reference to concentration is omitted since this is 100%, unless specified otherwise. A Schmidt and Haensch polarimeter was used, readings reproducible to ±0.01° being readily obtained.

I. **Dextrorotatory 2,3-Butylene Glycol.**—The glycol was obtained from glucose by the fermentative action of *Aerobacter aerogenes*, as described by Ward, Pettijohn, Lockwood and Coghill,[9] and exhibited a rotation of $[\alpha]^{25}D$ +1.06°. This low value is due to the fact that the organism produces the *meso-* form predominantly, as shown by Fulmer, Underkofler and Bantz.[10] Several attempts to isolate the active enantiomorph, by resolution, have been reported, the highest specific rotations obtained being +5.0° (Böeseken and Cohen[3]) and +6.9° (Chappel[11]). Fulmer, Underkofler and Bantz[10] fermented the dextrorotary glycol ($[\alpha]^{25}D$ +1.0°, produced by the action of *Aerobacter aerogenes*) to acetyl methyl carbinol by means of *Aerobacter suboxydans;* the *meso-* form was preferentially attacked and the unfermented glycol exhibited a specific rotation of +10.15°. Their results indicated that little or none of the levorotatory glycol was produced by *Aerobacter aerogenes*. Since an optically pure isomer of 2,3-butylene glycol has not yet been conclusively obtained, it

(7) J. Kenyon and D. R. Snellgrove, *J. Chem. Soc.*, **127**, 1169 (1925).

(8) P. A. Levene, A. Walti and H. L. Haller, *J. Biol. Chem.*, **71**, 465 (1936).

(9) G. E. Ward, O. G. Pettijohn, L. B. Lockwood and R. D. Coghill, THIS JOURNAL, **66**, 541 (1944).

(10) E. I. Fulmer, L. A. Underkofler and A. C. Bantz, *ibid.*, **65** 1425 (1943).

(11) C. H. Chappel, "A Study of 2,3-Butylene Glycol and its Derivatives," Thesis, Iowa State College, 1935.

is not possible to calculate the concentration of the active form present in the sample used.

II. **Levorotatory 2,3-Butylene Glycol Diacetate.**—A 10 molar acetylation of I was conducted as described by Hill and Isaacs,[6] using 25 moles of acetic acid, 16.2 g. of sulfuric acid, and benzene as the water entraining agent. In five hours, water removal from the gravity separator had ceased. To the hot solution 45 g. of $NaOAc \cdot 3H_2O$ was added and after cooling, filtering and distilling, the fraction b. r. 190–192° was obtained.

III. **Levorotatory Methylvinylcarbinol Acetate.**—One hundred and seventy-five grams of II was pyrolyzed at 410° in a 2″ × 36″ Pyrex tube, packed with stainless steel shavings, at the rate of 0.73 g. per minute. The vapors from the tube entered a column where the butadiene gas was stripped from the condensed pyrolysis liquor, 162 g. of the latter, containing 35.5% acetic acid, being obtained. To 121 g. of the liquor was added 300 ml. of ether, and dry ammonia gas was passed into the solution with cooling, until it was neutral to litmus. After filtering, washing with ether and distilling, the main fraction, b. r. 111.5°–113.5°, weighing 15.7 g., was obtained. After saponification, it gave only a trace of a precipitate with 2,4-dinitrophenylhydrazine, thus indicating the absence of the isomeric acetate of 2-butene-2-ol. A determination of its iodine no. (3 min. Wijs method using mercuric acetate) gave a value of 217; theory, 222.

IV. **Dextrorotatory Methylvinylcarbinol.**—The diacetate of I (2 lb. moles) was prepared by a method similar to that described above for II. The pyrolysis was conducted at 595° in a stainless steel coil and the intermediate unsaturated acetate fraction, mixed with some by-products, was separated from the bulk of the acetic acid in the pyrolysis liquor. The mixture contained 7.2% acetic acid and 21.0% unsaturated acetates as measured by saponification. Two hundred and ninety-four grams of the mixture was saponified with a 10% calculated excess of aqueous sodium hydroxide by stirring (2 layers) under reflux on a steam-bath for eight hours. On distillation, the fraction b. r. 77–100° was collected, which separated into two layers. The upper layer was exhaustively extracted with water and the combined aqueous fractions were redistilled, the fraction b. r. 80–100° being collected. The latter was saturated with sodium chloride and the upper layer so formed was dried over sodium sulfate. On distillation, the fraction b. r. 96.2–96.5°, weighing 19.4 g., was obtained. It exhibited a rotation of +1.36° in a 2-dcm. tube at 23°. Based on Kenyon and Snellgrove's[7] value of $[\alpha]^{25}D$ +33.7° for the pure enantiomorph of methylvinylcarbinol, it contained 2.0% of the active form.

V. **Dextrorotatory Methylethylcarbinol.**—To 14.6 g. of IV was added 0.2 g. of freshly prepared PtO_2[12] and hydrogenation was conducted in a Parr apparatus[13] at an initial gage pressure of 45 lb. In one hour absorption had ceased, the theoretical quantity of hydrogen being consumed. The catalyst was filtered and washed with 20 ml. of benzyl alcohol, which facilitated the subsequent distillation of the lower boiling methylethylcarbinol, the main fraction having a b. r. of 99–100°. The carbinol weighed 9.3 g. It exhibited a rotation of +0.48° in a 2-dcm. tube at 23°. Based on Kenyon and Snellgrove's[7] value of $[\alpha]^{20}D$ +13.9° for the pure enantiomorph of methylethylcarbinol, it contained 1.7% of the active form, which is in good agreement with the 2.0% concentration of active methylvinylcarbinol in the sample, IV, hydrogenated.

VI. **Inactive Methylvinylcarbinol.**—In order to compare the physical constants of IV and X (below) under identical conditions, a sample of Shell Development Company methylvinylcarbinol was redistilled, the fraction of b. r. 96.0–96.5° being used.

VII. **Inactive Methylethylcarbinol.**—In order to compare the physical constants of V under identical conditions, sample VI was hydrogenated and the inactive methylethylcarbinol was isolated exactly as described above for V.

VIII. **Levorotatory 2,3-Butylene Glycol.**—The glycol was obtained by the fermentative action of *Bacillus polymyxa*, as described by Ward, Pettijohn, Lockwood and Coghill.[9] It exhibited a specific rotation of $[\alpha]^{22}D$ −12.85° and a b. r. of 179–180°. Levorotatory 2,3-butylene glycol, $[\alpha]^{23}D$ −2.4°, had been obtained previously by Neuberg and Nord[14] by the action of fermenting yeast on diacetyl. By a similar biochemical reduction of acetylmethylcarbinol, Neuberg and Kobel[15] obtained the levorotatory glycol $[\alpha]^{25}D$ −5.51°, b. r. 178–181°. As in the case of I, it is not possible to calculate the concentration of the active form present in the sample used.

IX. **Dextrorotatory 2,3-Butylene Glycol Diacetate.**—The glycol VIII (2 lb. moles) was acetylated as described above for II, except that acetic anhydride was used to complete the esterification. As may be seen from the saponification equivalents in the table, the anhydride readily converted the glycol monoacetate[5,16] to the diacetate.

X. **Levorotatory Methylvinylcarbinol.**—From the pyrolysis liquor of IX, the levorotatory methylvinylcarbinol was isolated as described above for IV. It exhibited a rotation of −1.28° in a 1-dcm. tube at 23°. Based on Kenyon and Snellgrove's[7] value of $[\alpha]^{25}D$ −33.7° for the pure enantiomorph, it contained 3.8% of the active form.

Effect of Method of Acetylation on the Racemization.—In considering the possibility of Walden inversion, it was of interest to acetylate one of the glycols and saponify the resulting diacetate, in order to learn whether the original glycol would be regenerated.

A. **Acetylation with Acetic Anhydride (Uncatalyzed).**—To 90 g. (1 mole) of a sample of 2,3-butylene glycol, which exhibited a rotation of −25.98° in a 2-dcm. tube at 23° ($n^{18}D$ 1.4340; d^{25}_4 0.990) was added 225 g. (2.2 moles) of acetic anhydride. The mixture was heated for one hour at 100° and then distilled, the fraction b. r. 193°–193.5°, 156.9 g., being obtained. It exhibited a rotation of +27.46° in a 2-dcm. tube at 23°, sap. equiv., 87.1, calcd. 87.1; $n^{18}D$ 1.4163; D^{30}_4 1.016.

B. **Acetylation with Acetic Acid in Presence of Sulfuric Acid.**—Ninety grams of the same sample of glycol described in A was acetylated as described above for II, three hours being required before water removal from the gravity separator had ceased. After neutralization with sodium acetate and distillation, the fraction b. r. 190–191°, 85.6 g., was obtained. It exhibited a rotation of +9.96° in a 2 dcm. tube at 23°; sap. equiv. 86.0, calcd. 87.1; $n^{18}D$ 1.4163; d^{30}_4 1.016.

C. **Saponification of the Diacetate Prepared with Acetic Anhydride.**—To 17.0 g. of the diacetate described in A was added a solution of 13 ml. of 1:1 sodium hydroxide diluted to 50 ml. with methanol. Approximately 30 ml. of water was added and after cooling to room temperature (fifteen minutes), the solution was diluted with water to 100 ml. It exhibited a rotation of −2.28° in a 2 dcm. tube at 23°. The concentration of glycol liberated on saponification was 8.80% and the specific rotation, therefore, was −12.95°, agreeing with that of the original glycol used, −12.98°. Previous analytical studies showed that under the above conditions the saponification was complete.

D. **Saponification of the Diacetate Prepared with Acetic Acid and Sulfuric Acid.**—Seventeen grams of the diacetate described in B was treated exactly as described above in C. The solution obtained on saponification exhibited a specific rotation of −4.77° for the regenerated glycol. The extent of racemization during the three-hour $HOAc$–H_2SO_4 acetylation was, therefore, 63.2%, whereas no racemization had occurred during the uncatalyzed acetic anhydride acetylation.

Discussion

In relating the configuration of the active 2,3-butylene glycols to the methyl ethyl carbinols

(12) R. Adams, V. Voorhees and R. L. Shriner, "Org. Syntheses," Coll. Vol. I, 452 (1932).

(13) R. Adams and V. Voorhees, *ibid.*, 53.

(14) C. Neuberg and F. F. Nord, *Ber.*, **52**, 2248 (1919).

(15) C. Neuberg and M. Kobel, *Biochem. Z.*, **160**, 253 (1925).

(16) S. Winstein and R. E. Buckles, THIS JOURNAL, **64**, 2790 (1942).

TABLE I

TABLE OF PHYSICAL AND ANALYTICAL DATA FOR COMPOUNDS I TO X

Compound Name	No.	$[\alpha]^{23}D$ observed	Boiling range, °C. Observed (745 mm., uncor.)	Lit.	Refractive index, n_D^{20} Observed	Lit.
2,3-Butylene glycols	I	+ 1.06	180 -182	[b]179-182[10]	1.4387 at 18°	[c]
	VIII	−12.85	179 -180	[b]178-181[14]	1.4340 at 18°	[c]
2,3-Butylene glycol diacetates	II	− 0.60	190 -192	[e]	1.4140 at 25°	[f]
	IX	+ 1.35	192 -194	[e]	1.4158 at 18°	[f]
Methylvinylcarbinol acetate	III	− 1.71	111.5-113.5	111-112[18]	1.4020 at 30°	1.4039 at 20°[18]
Methylvinylcarbinols	IV	+ 0.68	96.2- 96.5	96- 98[7]	1.4106 at 30°	1.4120 at 20°[7]
	VI	[g]0.00	96.0- 96.5	96- 97[19]	1.4106 at 30°	1.4127 at 20°[18]
	X	− 1.28	96.0- 97.0	96- 98[7]	1.4100 at 30°	1.4120 at 20°[7]
Methylethylcarbinols	V	+ 0.24	99 -100	99[20]	1.3937 at 27°	1.3954 at 20°[7]
	VII	[h]0.00	99 -100	99.5[17]	1.3935 at 27°	1.3950 at 25°[17]

Compound Name	No.	Density, $(D T_4)$ Observed	Lit.	Saponification equivalent Observed	Calcd.	[a]Micro-combustion %, C Observed	%, C Theory	%, H Observed	%, H Theory
2,3-Butylene glycols	I	0.996 at 30°	[d]	...	...	53.34	53.31	11.33	11.19
	VIII	0.990 at 25°	[d]	...	...	53.38	53.31	11.15	11.19
2,3-B. G. Diacetates	II	1.016 at 30°	[f]	85.9	87.1	55.18	55.16	8.14	8.10
	IX	1.017 at 30°	[f]	86.8	87.1	55.20	55.16	7.96	8.10
M. V. C. Acetate	III	...	...	116	114	63.29	63.18	8.80	8.84
Methylvinylcarbinols	IV	0.832 at 26°	0.836 at 15°[7]	...	...	66.58	66.63	11.10	11.18
	VI	0.831 at 26°	0.832 at 20°[18]	...	...	...	...	...	...
	X	0.830 at 28°	0.816 at 39°[7]	...	...	66.44	66.63	11.21	11.18
Methylethylcarbinols	V	...	...	...	...	64.50	64.82	13.74	13.61
	VII	...	...	...	...	...	...	...	...

[a] Conducted by the Analytical and Physical Chemical Division of this Laboratory. [b] Wilson and Lucas[4] report 176.7°$_{743}$ for the D-, L- and 181.7°$_{743}$ for the *meso*- forms. [c] Huntress and Mulliken[17] report $n^{25}D$ 1.4364 for the D-, L- form. [d] Huntress and Mulliken[17] report D^{20}_4 1.0433 for the D-, L- form. [e] Wilson and Lucas[4] report $70_{5.5}$ for the D-, L- and $66_{5.5}$ for the *meso*- forms. [f] Not reported in the literature. [g] Redistilled Shell Development Company methylvinylcarbinol, inactive. [h] From hydrogenation of VI, inactive.

(see reactions I to V above), the possibility of Walden inversion must be considered. Winstein and Lucas[5] observed that in the stepwise transformation of 2,3-butylene glycol to 2,3-dibromobutane, via 3-acetoxy-2-butanol, 2-acetoxy-3-bromobutane and 3-bromo-2-butanol, Walden inversion does not occur in the acetylation and hydrolysis reactions. Since two asymmetric carbon atoms are involved, in order that the configurations formulated above could be vitiated by Walden inversion, the inversion would have had to occur at both asymmetric centers; for inversion at only one center would produce the inactive *meso*-glycol. The regeneration of levorotatory glycol by successive acetylation and hydrolysis (as in racemization experiments above) shows that in *both* of these reactions there was either *no* inversion or *complete double* Walden inversion. The probability of the latter must be extremely small, and in view of the observations of Winstein and Lucas,[5] it is evident that the configurations assigned above to the active 2,3-butylene glycols are not in error due to Walden inversion.

The methylvinylcarbinols isolated from the pyrolysis liquors exhibited $[\alpha]^{23}D$ +0.68° and −1.28°, as obtained from the dextro- and levorotatory glycols, respectively, whereas the pure enantiomorphs of Kenyon and Snellgrove[7] showed $[\alpha]^{25}D$ ±33.7°. Hydrogenation of the dextrorotatory methylvinylcarbinol yielded methylethylcarbinol, $[\alpha]^{23}D$ +0.24°, whereas Kenyon and Snellgrove[7] report $[\alpha]^{25}D$ ±13.9° for the pure enantiomorphs. Since the values of our specific rotations were relatively low (2-dcm. polarimeter tubes were generally used, so that the observed rotations were actually twice as great as reported), the possibility of optically active impurities being present in the original fermentation glycol preparations must also be considered. If present, however, they would have been carried through the acetylation, pyrolysis, hydrolysis, and hydrogenation reactions, and at each step would have contaminated the product isolated. The analytical and physical data for each of the five compounds involved in this series of reactions agreed well with both the literature and theory. The fact that the methylvinylcarbinols isolated exhibited the same sign of rotation as the glycols from which they were prepared would require, furthermore, that any such impurity be dextrorotatory in one case and levorotatory in the other. The probability that the observed rotations were due to impuritities must, therefore, be extremely small.

The proof of the configuration of the 2,3-

(17) E. H. Huntress and S. P. Mulliken, "Identification of Pure Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1941, pp. 432, 467.

(18) J. Baudrenghien, *Bull. soc. chim. Belg.*, **31**, 160 (1922).

(19) A. Wohl and M. S. Losanitsch, *Ber.*, **41**, 3621 (1908).

(20) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **103**, 1923 (1913).

butylene glycols herein presented is somewhat unique in that reactions involving extensive racemization, namely, esterification and pyrolysis, were employed and, furthermore, the sign of rotation always indicated which active form was present. The symmetry of the glycol molecule containing two asymmetric centers permits the existence of only two active forms, the D- and L-, and on removing one of these centers by dehydration (or deacetylation of the diacetate), the methylvinylcarbinol (or its acetate) so produced also exists in only two active forms, D- or L-. As pointed out above, the active methylvinylcarbinol (or its acetate) must have the same configuration as the active glycol from which it was prepared.

Summary

In studying the conversion of optically active 2,3-butylene glycols to butadiene, the intermediate methylvinylcarbinols were isolated, each exhibiting the same sign of rotation as the glycol from which it was prepared. Hydrogenation to methylethylcarbinol also proceeded without change in sign. Since the configuration of dextrorotatory methylethylcarbinol had already been related to that of dextrorotatory lactic acid, which belongs to the L-series, the configuration of the active 2,3-butylene glycols was, therefore, established as D-(−)- and L-(+)−.

PEORIA, ILLINOIS RECEIVED FEBRUARY 17, 1944

[CONTRIBUTION FROM THE RESEARCH DIVISION OF THE GENERAL PRINTING INK CORPORATION]

Orientation in the Biphenyl System. The Preparation of 2- and 4-Aminobiphenyl-4′-sulfonamides[1]

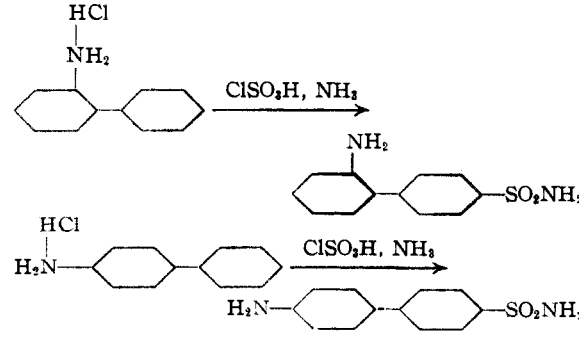
BY A. H. POPKIN AND G. B. MCVEA

Detailed studies[2] on orientation in the biphenyl system have been made in the past and several hypotheses have been proposed to explain the data obtained. These may be summarized as follows: (1) the usual directive influences ascribed to all simple groups when present in the benzene nucleus occur also in the biphenyl group; (2) those groups which normally orient ortho–para usually direct other groups into the same nucleus; conversely, meta-orienting groups direct further substitution into the adjacent ring; (3) the two nuclei of biphenyl act independently of each other.

Certain anomalous behaviors of the acetamido group which normally exhibits an ortho–para-orienting influence have been noted. The nitration of 2-acetamidobiphenyl[3] gave a 50% yield of 2-acetamido-4′-nitrobiphenyl instead of substitution into the five position of the same ring. Also the mononitration of diacetylbenzidine in concentrated sulfuric acid as solvent gave 2-nitrobenzidine instead of the expected 3-nitro-substitution.[4] More recently it was noted that the reaction of 2-acetamidobiphenyl with chlorosulfonic acid also gave substitution in the 4′-position.[5]

Bell[6] explained the anomalous behavior of the acetamido group stating that "this group enters into salt formation with a strong acid thereby being converted into a weakly orienting positive group so that further substitution naturally resembles that of 2-nitrodiphenyl."[7] This conclusion was substantiated by the work of Orton and Bradfield,[8] who showed that the velocity of chlorination of acetanilide was decreased with an increase of the concentration of hydrochloric acid which indicated a gradual shift of the acetamido group from ortho–para-orienting to a meta-orienting characteristic.

The present work confirms further the conclusions arrived at by Bell. The hydrochlorides of 2-aminobiphenyl and 4-aminobiphenyl were each treated with chlorosulfonic acid and ammonia. In each case, substitution was obtained in the 4′-position of the second ring, the products being 2-aminobiphenyl-4′-sulfonamide, 66% yield, and 4-aminobiphenyl-4′-sulfonamide, 88% yield.



The purity of the materials isolated indicated strongly the absence of isomers which might arise from substitution in the five position of the first ring. This proves that the amino group, and by

(1) Presented before the Division of Organic Chemistry, Cleveland meeting of the American Chemical Society, April, 1944.
(2) *J. Chem. Soc.*, 1926–1931.
(3) Scarborough and Waters, *ibid.*, 89 (1927).
(4) Le Fèvre and Turner, *ibid.*, 2041 (1926).
(5) Popkin, THIS JOURNAL, **65**, 2043 (1943).
(6) Bell, *J. Chem. Soc.*, 2770 (1928).
(7) Dadwell and Kenner, *ibid.*, 1102 (1927); Le Fèvre and Turner, *ibid.*, 2043 (1926); Bell and Kenyon, *ibid.*, 2707 (1926).
(8) Orton and Bradfield, 986 (1927).