The product similarly obtained from the (+)-acid had m.p. 106–107°, $[\alpha]^{30}\mathrm{D}$ +75° (*c* 0.63, methanol), $[\alpha]^{30}\mathrm{D}$ +141° (*c* 0.91, benzene).

Anal. Calcd. for $C_{14}H_{12}Cl_2O_2$: C, 59.4; H, 4.3; Cl, 25.0. Found: C, 59.2; H, 4.0; Cl, 25.4.

Melting Points of Mixtures.—Weighed amounts of the component acids or alcohols were thoroughly mixed and ground. Melting points were determined by the capillary method with a Hershberg melting point apparatus; the heating rate was 1–2°/min. The initial thawing temperatures and the final melting temperatures were recorded, respectively, as points on the solidus and the liquidus curves, Figs. 1–5.

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[Contribution from the Wm. H. Nichols Chemical Laboratory, New York University]

Direct Configurational Intercorrelation of 6,6′-Dinitro-, 6,6′-Dichloro- and 6,6′-Dimethyl-2,2′-diphenic Acid. Absolute Configuration of 6,6′-Dimethyl-2,2′-biphenyldiamine[1]

By Francis A. McGinn, Allan K. Lazarus,[2] Maurice Siegel, John E. Ricci and Kurt Mislow[3]

Received July 1, 1957

6,6′-Dinitro-2,2′-bis-(bromomethyl)-biphenyl, 6,6′-dichloro-2,2′-bis-(hydroxymethyl)-biphenyl and 6,6′-dimethyl-2,2′-diphenic acid have each been related by chemical paths to 6,6′-dimethyl-2,2′-biphenyldiamine (I) and therefore to each other. The results serve as unequivocal confirmation of those obtained by the indirect method of thermal analysis and also provide an absolute configurational assignment for I which is in conflict with the results[15] of certain theoretical considerations. The optical sign of I is solvent dependent. Evidence is presented that the *monoprotonated* form in 50 wt.% dioxane has a sign opposite to that of the unprotonated diamine in the same medium. Approximate values are calculated for the ionization constants and for the specific rotations of the unprotonated and monoprotonated species.

The method of thermal analysis has served in the configurational correlation of (−)-6,6′-dinitro-, (−)-6,6′-dichloro- and (+)-6,6′-dimethyl-2,2′-diphenic acid.[4] It was felt desirable to confirm these results by independent, completely unambiguous means. In the biphenyl series, the most unequivocal method is the chemical one, for retention of optical activity in a chemical transformation involving the blocking substituents can only imply retention of configuration: the possibility of racemization is the sole alternative.

The desired chemical correlation was achieved by transformation of 6,6′-dinitro-2,2′-diphenic acid into 6,6′-dimethyl-2,2′-biphenyldiamine (I), and conversion of the latter into 6,6′-dichloro- and 6,6′-dicyano-2,2′-dimethylbiphenyl, obtained from 6,6′-dichloro- and 6,6′-dimethyl-2,2′-diphenic acid, respectively. Certain attractive alternative paths were excluded on the basis of previous information: (a) chemical reduction[5] or catalytic hydrogenation (*cf.* Experimental) of 6,6′-dinitro-2,2′-diphenic acid yields the (inactive) dilactam of 6,6′-diamino-2,2′-diphenic acid as does hydrolysis of the diacetyl derivative of the latter[5,6] and (b) it has been reported[7] that compound I cannot successfully be prepared by the Curtius and Hofmann rearrangements in attempts at conversion from 6,6′-dimethyl-2,2′-diphenic acid.

S(−)-6,6′-Dinitro-2,2′-diphenic acid has been converted[8] to *S*(−)-6,6′-dinitro-2,2′-bis-(hydroxymethyl)-biphenyl. Judging by the observation that *p*-nitrobenzyl alcohol can be smoothly hydrogenated to *p*-toluidine, it was anticipated that the dinitrodiol could be hydrogenolyzed directly to I. Contrary to expectations, reduction ceased after absorption of six moles of hydrogen, yielding *S*(−)-6,6′-bis-(hydroxymethyl)-2,2′-biphenyldiamine. The twisted geometry of the molecule apparently prevents the required orientation for adsorption on the catalytic surface of the hydroxymethyl, but not of the nitro groups; to our knowledge similar observations do not appear to have been reported previously.[9]

The route chosen, as a consequence, involved preparation[8] of *S*(−)-6,6′-dinitro-2,2′-bis-(bromomethyl)-biphenyl from the dinitrodiol, followed by reduction with $NaBH_4$–$AlCl_3$[10] to (−)-6,6′-dinitro-2,2′-dimethylbiphenyl and catalytic reduction of the latter to (−)-I,[11] which must therefore have the *S*-configuration.

S(−)-I[11] was converted, *via* the Sandmeyer reaction, to *S*(−)-6,6′-dichloro-2,2′-dimethylbiphenyl. (+)-6,6′-Dichloro-2,2′-bis-(hydroxymethyl)-biphenyl, prepared[4] from (+)-6,6′-dichloro-2,2′-diphenic acid, was converted to (+)-6,6′-dichloro-2,2′-bis-(bromomethyl)-biphenyl, reduction of which afforded *R*(+)-6,6′-dichloro-2,2′-dimethylbiphenyl. The starting acid must therefore have the *R*-configuration.

Finally, *R*(+)-I[11] was converted, *via* the Sandmeyer reaction, to *R*(+)-6,6′-dicyano-2,2′-dimethylbiphenyl. Since (+)-6,6′-dimethyl-2,2′-diphenic acid could be derivatized to *S*(−)-6,6′-dicyano-2,2′-dimethylbiphenyl, the starting acid has the *S*-configuration.

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(1) Configurational Studies in the Biphenyl Series III. Part II, preceding paper.

(2) Allied Chemical and Dye Fellow, 1956–1957.

(3) To whom correspondence regarding the article should be addressed.

(4) M. Siegel and K. Mislow, This Journal, **80**, 473 (1958).

(5) J. Kenner and W. V. Stubbings, *J. Chem. Soc.*, 593 (1921).

(6) J. Meisenheimer and M. Höring, *Ber.*, **60**, 1425 (1927).

(7) F. Bell, *J. Chem. Soc.*, 835 (1934).

(8) P. Newman, P. Rutkin and K. Mislow, This Journal, **80**, 465 (1958).

(9) For a summary of hydrogenolysis reactions, *cf.* W. H. Hartung and R. Simonoff, "Organic Reactions," Vol. VII, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 263.

(10) This reagent mixture has been successfully employed in similar reductions by H. C. Brown and B. C. S. Rao, This Journal, **78**, 2582 (1956).

(11) Sign of rotation refers to solvent ethanol; *cf.* Table I.

It may be noted that replacement of *both* amino groups in I by chloro or cyano groups proceeded with at least about 90% retention of optical purity; the same result has been obtained previously in the analogous replacement by iodine.[7]

The results of these chemical correlations constitute unequivocal evidence for the correctness of the configurational assignments made earlier[4] on the basis of an indirect method. In addition to proving the validity of the method of thermal analysis as applied to optically active biphenyls, the above synthetic scheme serves, by contrast, to illustrate the usefulness of the indirect method as a means for avoiding complex and time-consuming intercorrelations in this series.

Optical Sign and Absolute Configuration of 6,6'-Dimethyl-2,2'-biphenyldiamine.—6,6'-Dimethyl-2,2'-biphenyldiamine (I), the common relay compound in the intercorrelation described above, has now been assigned absolute configuration. It is important to refer the sign of I to the solvent for, as earlier pointed out by R. Kuhn and P. Goldfinger,[12] the sign is solvent-dependent. In Table I are listed the rotations of one of the enantiomeric forms in various solvents. It is clear that the sign is positive in aprotic solvents but negative in acidic solvents. The magnitude of the rotations does not appear to follow a simple order dependent on refractive index[13] or dielectric constant of the medium.

While these data are suggestive of the possibility that the protonated and the unprotonated forms of I have opposite signs of rotation, it was recognized that signs are not strictly comparable so long as they refer to solutions in different media. Accordingly, the dependence on *p*H of the sign and magnitude of the optical rotation of I in aqueous dioxane was studied in an attempt to correlate the effect with the distribution of ionic species in the solution and to assign, if possible, separate specific rotations to the unprotonated and protonated forms.

TABLE I

SPECIFIC ROTATIONS[a] OF 6,6'-DIMETHYL-2,2'-BIPHENYLDIAMINE

Solvent	c	$[\alpha]^{24}D$	Solvent	c	$[\alpha]^{24}D$
n-Hexane	0.21	+126°	Acetonitrile	1.64	+85°
Dioxane	1.66	+116	Ethanol	1.52	+49
Pyridine	1.19	+111	Methanol	1.91	+42
Benzene	1.86	+101	Sulfuric acid[b]	1.82	−25
Acetone	1.41	+100	Aqueous (*N*) HCl	1.60	−36
Iodobenzene	0.68	+ 86	Acetic acid	1.63	−60

[a] l 1 dm. [b] $[\alpha]^{26}_{365}$ −98° (c 1.71).

The data, obtained at a concentration c of the diamine (0.033 *M*) in 50 wt. % dioxane, are shown in Fig. 1, the rotations in the upper part[14] and the *p*H values in the lower part plotted against n, the number of moles of HCl per mole of diamine. The experimental points do not represent the actual continuous titration of one sample; each point is a measurement made on a separately prepared mixture in order to maintain the solvent composition and the diamine concentration constant throughout. The ionic strength also was kept approximately constant by addition of NaCl at a concentration such that [NaCl] + [HCl] = 2c; for these conditions the activity coefficient γ of the hydrogen ion was estimated as ~0.7 by comparison of *p*H readings (glass electrode, Beckman *p*H meter) with varying concentrations of HCl in absence of the diamine.

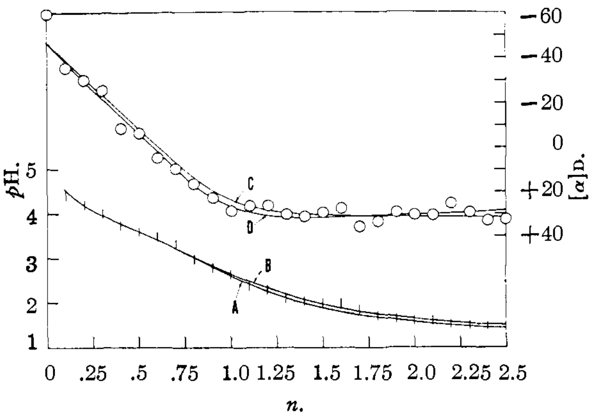

Fig. 1.—*p*H values (A and B) and specific rotations (C and D) of 6,6'-dimethyl-2,2'-biphenyldiamine in 50 wt. % dioxane *vs.* moles HCl/mole diamine (n).

The *p*H data for the titration of the first equivalent give a value of K_2 (= $a_{H^+}[I^0]/[IH^+]$) of ~2.7 × 10^{-4}, with very little dependence upon the value assumed for the activity coefficient of the hydrogen ion. For the higher acidities through the second half of the titration, however, the data show simply that K_1(= $a_{H^+}[IH^+]/[IH_2^{++}]$) is high, and not smaller than ~0.1. The curves A and B drawn through the observed points in Fig. 1 are calculated with γ = 0,7, K_2 = 2.7 × 10^{-4}, and either K_1 = ∞ (curve A) or K_1 = 0.1 (curve B). Similar results were obtained in a titration at higher concentration (c = 0.066 and [NaCl]+ [HCl] = 1.5c): $K_2 \cong 4.2 \times 10^{-4}$ and K_1 not less than ~0.2.

The species present, then, with K_1 very large, are solely or principally I^0 and IH^+. With K_1 = ∞, we have $[IH_2^{++}]$ = 0; the fraction of the diamine in the monoprotonated form is practically equal to n through n = 0.5, equals ~0.10 at n = 1, and then falls to ~0.01 at n = 2.5. From the data in the upper part of Fig. 1, the specific rotations of the species I^0 and IH^+ are thus seen to be, very roughly, about −50° and +30°, respectively. Curve C is a rotation curve calculated on the basis of −47° and +32° for the respective specific rotations, and with K_2 = 2.7 × 10^{-4} and K_1 = ∞.

On the other hand, if K_1 is assumed to be as low as 0.1, the species distribution remains practically the same, with $[IH_2^{++}] \cong 0$, through n = 1. Thereafter, however, while the monoprotonated fraction falls off, the diprotonated fraction increases to ~0.2 at n = 2.5. The data still fix the specific rotations for the species I^0 and IH^+ as roughly −50° and +30 to 35°, respectively, but very little may be

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[12] R. Kuhn and P. Goldfinger, *Ann.*, **470**, 183 (1929).

[13] By correction to "rotivity" (C. O. Beckmann and K. Cohen, *J. Chem. Phys.*, **4**, 784 (1936)).

[14] Curves C and D, Fig. 1, calculated as explained in the text, are similar to but not identical with the previously published curve (K. Mislow, *Trans. N. Y. Acad. Sci.*, [2] **19**, 298 (1957)), which was simply the "best curve" drawn by inspection. Enantiomer in Fig. 1 is opposite in configuration to that referred to in Table I.

said about the rotation of the diprotonated form. One may assign, for example, specific rotations of −47°, +37° and 0° to the species I^0, IH^+ and IH_2^{++}, respectively, and calculate curve D with $K_2 = 2.7 \times 10^{-4}$ and $K_1 = 0.1$. This means that *the very sign of the rotation of the diprotonated form is not fixed by the data.*

Although, therefore, the observations do not rule out the existence of a diprotonated form in this medium, the chief effect is clearly the change of optical sign between unprotonated and monoprotonated forms, the initial rotation of $\sim -50°$, at $n = 0$, representing that of the unprotonated, and the rotation of $\sim +30°$ (practically constant) at $n > 1$ being essentially that of the monoprotonated diamine.

The results of this study bear directly on the problem of the absolute configuration of compound I. W. Kuhn and R. Rometsch have concluded[15] from the results of explicit calculations, based on a theoretical model,[16] that *S*-I and *S*-2,2′-dichloro-6,6′-dimethyl-4,4′-biphenyldiamine (II) probably correspond to the dextrorotatory forms.[17] We are not certain to what extent this conclusion is vitiated by an error in the cited work: the sign of rotation of I in the visible and near-ultraviolet regions is reported to be the same (*levo*) for hexane and for sulfuric acid solutions.[18] This is contrary to fact (Table I). In any event, the assignment of the *S*-configuration to (+)-I[11] is at variance with our own conclusions. The configurations of I and of the absolute standard (tartaric acid) have been correlated (*via* (+)-DNDBCH-6-one and (+)-2-octanol) by a direct and unequivocal chemical route, with but a single questionable step: the partial asymmetric reduction.[8] We believe that the highest degree of confidence may be placed in the stereochemical relationships arrived at on the basis of the last-named reaction, and we accordingly assign the *R*-configuration to (+)-I.[11] With reference to solutions of I in sulfuric acid, *i.e.*, the protonated species, our results are, of course, in agreement with those of Kuhn and Rometsch.[19]

The difference in the sign of the specific rotation between the unprotonated and the monoprotonated forms of I may be explained by theoretical considerations. According to calculations based upon the polarizability theory of optical rotatory power, the specific rotations of the *cis* and *trans* conformations of I have opposite signs. In this case, *R*(+)-I is the unprotonated form and has the *trans* conformation, while *R*(−)-I is the monoprotonated form and has the *cis* conformation. The details of the application of the polarizability theory to this problem are presented as part of the following paper in this series.

The observation that the optical sign changes with change of solvent is not unique in the series of optically active biphenyls. 6,6′-Diacetamido-2,2′-diphenic acid is levorotatory in acetone, dextrorotatory in aqueous alkali[6]; 4,5,6,4′,5′,6′-hexahydroxy-2,2′-diphenic acid is levorotatory in methanol as the acid and as the disodium salt, dextrorotatory as the acid sodium salt[20]; 1,1′-bi-2-naphthylamine is dextrorotatory in benzene and pyridine, levorotatory in aqueous HCl.[12] A routine examination did not reveal similar reversal of signs in some other optically active 2,2′-diphenic acids, with the possible exception of the 6,6′-dichloro derivative (Table II).

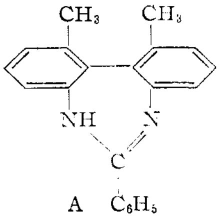
TABLE II

$[\alpha]_D$ OF SOME 2,2′-DIPHENIC ACIDS[a]

Solvent	Nitro	6,6′-Substituents Chloro	Methyl	Benzo[b]
Acetone	−128°	+ 1°	+15°	−50°
Methanol	−127	− 7	+26	−34
0.1 *N* NaOH	−256	−14	+33	−84

[a] Properties as described in ref. 4. [b] 1,1′-Binaphthalene-2,2′-dicarboxylic acid.

The absolute configuration of a number of substances related to I is now automatically established. Thus (−)-6,6′-dimethyl-2,2′-biphenyldiacetamide has been oxidized[6] to (−)-6,6′-diacetamido-2,2′-diphenic acid,[21] which therefore has the *R*-configuration. Sako's hindered diphenimidines[22]



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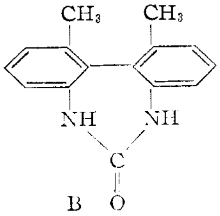

B

also have the *R*-configuration.

The enantiomeric 6,6′-dimethyl-7,7′-diisatyls (III) have proven[23] to be stereospecific dehydrogenation catalysts[24]: (−)-III is more active toward (−)-alanine, (+)-III toward (−)-asparagine. Since the enantiomeric forms were prepared from I of like sign (in 0.3 *N* HCl), (−)- and (+)-III therefore have the *R*- and *S*-configuration, respectively.

Finally, this work establishes the absolute configuration of the tetrahedral copper complex, 2,2′-bis-(salicylideneamino)-6,6′-dimethylbiphenyl-copper (II).[25] The form having $[\alpha]^{24}_D$ +75° (ethanol), prepared from (−)-I (in 0.3 *N* HCl), accordingly has the *R*-configuration, depicted in Fig. 1 of the original paper.[25]

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[15] W. Kuhn and R. Rometsch, *Helv. Chim. Acta*, **27**, (a) 1080, (b) 1346 (1944).

[16] Recently reviewed by W. Kuhn, *Z. Elektrochem.*, **56**, 506 (1952).

[17] Ref. 15b: "Die Formeln I und II stellen voraussichtlich je den im Sichtbaren rechtsdrehenden Antipoden dar."

[18] Figure 13 (ref. 15a) describes the rotatory dispersion of I in hexane. The value at 589 mμ is closely similar to ours (Table I) in magnitude. Figure 14 (ref. 15a) of which Fig. 19 (ref. 15b) is a detail, describes the rotatory dispersion of I in sulfuric acid (the graph mistakenly refers to II; *cf.* authors' correction (ref. 15b). The value at 365 mμ is closely similar to ours (Table I) in magnitude. Both Figs. 13 and 14 are labeled with the same enantiomeric formula of I; indeed, the authors state the identity explicitly (ref. 15a) when, in referring to Fig. 13 and 14, they speak of "derselben Substanz" (p. 1101).

[19] The fact that (−)-6,6′-dinitro-2,2′-diphenic acid has been assigned the *R*-configuration by W. Kuhn and K. Bein, *Z. physik. Chem.*, **24B**, 335 (1934), whereas our results clearly point to the *S*-configuration for this form, has already been remarked upon (ref. 8).

[20] O. T. Schmidt and K. Demmler, *Ann.*, **586**, 179 (1954).

[21] The sign refers to solutions in acetone.

[22] The levorotatory forms of A and B were obtained from *R*-I (S. Sako, *Mem. Coll. Eng. Kyushu Imp. Univ.*, **6**, 263 (1932); *C. A.*, **26**, 3246 (1932)).

[23] W. Dethloff and H. Mix, *Chem. Ber.*, **82**, 534 (1949).

[24] W. Langenbeck, *Ber.*, **60**, 930 (1927), *et seq.*, has demonstrated that isatins serve as synthetic models for dehydrogenase.

[25] F. Lions and K. V. Martin, This Journal, **79**, 1273 (1957).

Experimental Part[26]

Catalytic Hydrogenation of (+)-6,6'-Dinitro-2,2'-diphenic Acid.—A solution of 0.815 g. of the acid in 25 ml. of ethanol was shaken under hydrogen (50 p.s.i.) at room temperature, in the presence of 0.300 g. of 5% palladinized charcoal. Hydrogen uptake ceased after 1.5 hours. The product, obtained after filtration and removal of solvent, was a cream-colored solid, m.p. >300°, insoluble in common organic solvents, soluble in sulfuric acid with a strong blue fluorescence.[5] The material was optically inactive (*c* 0.1, *l* 2, λ 589 and 578 mμ, 10% methanolic potassium hydroxide).

(−)-6,6'-Bis-(hydroxymethyl)-2,2'-biphenyldiamine.—A mixture of 0.175 g. of (−)-6,6'-dinitro-2,2'-bis-(hydroxymethyl)-biphenyl,[8] 0.066 g. of 5% palladinized charcoal and 25 ml. of abs. ethanol was hydrogenated at 26° and 1 atm. Hydrogen was absorbed smoothly, at a rate of 10 ml./min. Uptake of gas stopped abruptly after 87 ml. had been consumed (theory 85 ml. for 6 moles of H_2 per mole of substrate). The solid obtained after filtration and removal of solvent was recrystallized from methanol–benzene to give product, m.p. 157–158°, $[\alpha]^{20}\text{D}$ −135° (*c* 0.77, methanol).

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.8; H, 6.6; N, 11.5. Found: C, 69.0; H, 6.4; N, 11.4.

In a similar experiment, *p*-nitrobenzyl alcohol yielded a product which was directly acetylated to give a solid, m.p. 148–150° after recrystallization from ethanol–ligroin, undepressed by admixture of authentic acet-*p*-toluidide, m.p. 148–150°.

(−)-6,6'-Dinitro-2,2'-dimethylbiphenyl.—A slurry of 0.83 g. of sodium borohydride in 21.5 ml. of "diglyme" (diethylene glycol dimethyl ether, purified by refluxing over sodium prior to distillation) was added to a mixture of 2.17 g. of (−)-6,6'-dinitro-2,2'-bis-(bromomethyl)-biphenyl,[8] 1.04 g. of anhydrous aluminum chloride and 6 ml. of diglyme. The mixture was stirred at 75° for one hour and then decomposed by addition of 86 ml. of 6 *N* sulfuric acid. The emulsion thus formed crystallized overnight. The solid, collected by filtration, could not be purified by repeated crystallizations from ethanol and hexane. Chromatography on alumina (Woelm, acid (anionotropic), activity grade 1), using benzene as eluent, afforded product, needles from hexane, m.p. 95–97°, $[\alpha]^{27}\text{D}$ −25° (*c* 2.5, ethanol).

Anal. Calcd. for $C_{14}H_{12}N_2O_4$: C, 61.8; H, 4.4; N, 10.3. Found: C, 62.0; H, 4.2; N, 10.3.

In a parallel experiment, (±)-6,6'-dinitro-2,2'-bis-(bromomethyl)-biphenyl[8] was reduced to racemic 6,6'-dinitro-2,2-dimethylbiphenyl, m.p. 108–110°, undepressed by admixture of authentic material,[27] m.p. 108–110°.

(−)- and (+)-6,6'-Dimethyl-2,2'-biphenyldiamine.—Resolution of (±)-6,6'-dimethyl-2,2'-biphenyldiamine *via* the tartrate salts was achieved following the excellent directions of Meisenheimer and Höring.[6] Decomposition of the insoluble tartrate afforded diamine, m.p. 156–158°, $[\alpha]^{33}\text{D}$ −35° (*c* 3.5, *N* HCl), $[\alpha]^{31}\text{D}$ +48° (*c* 2.5, abs. ethanol) (lit.[6] m.p. 156°, $[\alpha]\text{D}$ −34.8° (*N* HCl)), after recrystallization from ethanol. The derived **6,6'-dimethyl-2,2'-biphenyldiacetamide** had m.p. 232–234°, $[\alpha]^{25}\text{D}$ −126° (*c* 1.2, abs. ethanol) (lit.[6,28] m.p. 229°, $[\alpha]\text{D}$ ±133°), after recrystallization from ethanol. Decomposition of the mother liquors from the resolution yielded diamine, m.p. 156–158°, $[\alpha]^{30}\text{D}$ +34° (*c* 3.5, *N* HCl), $[\alpha]^{26}\text{D}$ −47° (*c* 3.0, abs. ethanol), after recrystallization from ethanol. The derived **6,6'-dimethyl-2,2'-biphenyldiacetamide** had m.p. 233–235°, $[\alpha]^{26}\text{D}$ +128° (*c* 1.0, abs. ethanol), after recrystallization from ethanol.

Catalytic Hydrogenation of (−)-6,6'-Dinitro-2,2'-dimethylbiphenyl.—A mixture of (−)-6,6'-dinitro-2,2'-dimethylbiphenyl (0.122 g.) and 0.024 g. of 5% palladinized charcoal in 25 ml. of abs. ethanol was hydrogenated at 26° and 1 atm. The product, obtained after filtration and removal of solvent, had $[\alpha]^{26}\text{D}$ −49° (*c* 2.9, ethanol), m.p. 153–158°, undepressed (m.p. 156–158°) by admixture of authentic (−)-6,6'-dimethyl-2,2'-biphenyldiamine.[11]

The hydrogenation product was warmed with acetic anhydride to give a derivative, $[\alpha]^{30}\text{D}$ +134° (*c* 0.94, abs. ethanol), m.p. 232–233°, undepressed by admixture of authentic (+)-6,6'-dimethyl-2,2'-biphenyldiacetamide.

In a parallel experiment, (±)-6,6'-dinitro-2,2'-dimethylbiphenyl[27] was converted to a product, m.p. 207–209.5° (lit.[5] m.p. 205° for (±)-6,6'-dimethyl-2,2'-biphenyldiacetamide).

(+)-6,6'-Dichloro-2,2'-bis-(bromomethyl)-biphenyl.—A mixture of 2.9 g. of (+)-6,6'-dichloro-2,2'-bis-(hydroxymethyl)-biphenyl[4] and 140 ml. of 48% hydrobromic acid was refluxed for one hour. The resulting emulsion was induced to crystallize and filtered. The crude solid (m.p. 50–70°, 4.1 g.) was recrystallized from methanol, yielding 3.0 g. (72%) of product, m.p. 70–71°, $[\alpha]^{29}\text{D}$ +77° (*c* 0.93, benzene).

Anal. Calcd. for $C_{14}H_{10}Br_2Cl_2$: C, 41.1; H, 2.5; Cl, 17.3; Br, 39.1. Found: C, 41.4; H, 2.1; Cl, 17.5; Br, 39.3.

(+)-6,6'-Dichloro-2,2'-dimethylbiphenyl.—A mixture of (+)-6,6'-dichloro-2,2'-bis-(bromomethyl)-biphenyl (2.0 g.), sodium borohydride (0.75 g.), diglyme (25 ml.) and anhydrous aluminum chloride (0.96 g.) was heated for one hour at 75° and then decomposed by addition of 75 ml. of 6 *N* sulfuric acid. The insoluble oil formed could not be induced to crystallize. Hydrogenation (50 p.s.i.) of the oil in the presence of 0.20 g. of 5% palladinized charcoal in 20 ml. of methanol yielded, after filtration and removal of solvent, solid, 1.2 g., m.p. 108–112°. Recrystallization from ethanol–water afforded the desired product, 0.80 g. (65%), m.p. 110–111°, $[\alpha]^{27}\text{D}$ +33° (*c* 2.8, abs. ethanol), $[\alpha]^{27}\text{D}$ +45° (*c* 1.0, hexane).

Anal. Calcd. for $C_{14}H_{12}Cl_2$: C, 67.0; H, 4.8; Cl, 28.2. Found: C, 66.8; H, 5.0; Cl, 28.3.

(−)-6,6'-Dichloro-2,2'-dimethylbiphenyl.—To a mixture prepared by addition of aqueous sodium nitrite (3.5 g./10 ml.) at −5° to a solution of (−)-6,6'-dimethyl-2,2'-biphenyldiamine (5.3 g., m.p. 156–158°, $[\alpha]^{31}\text{D}$ −47° (*c* 3.0, abs. ethanol)) in 28% hydrochloric acid (22 ml.) at −5°, was added a cold (−5°) solution of cuprous chloride (7.5 g.) in 28% hydrochloric acid (22 ml.). Considerable foaming occurred at the beginning of the reaction, and the rate of addition was adjusted accordingly. The mixture was warmed at 60° for five minutes, extracted with ether, and the extracts washed with 20% sodium hydroxide, followed by water. Ether was removed and the residue distilled with steam to give 1.4 g. of solid, m.p. 70–98°. Recrystallization from 95% ethanol gave the desired product, m.p. 109–111°, $[\alpha]^{27}\text{D}$ −30° (*c* 4.6, abs. ethanol).

Anal. Calcd. for $C_{14}H_{12}Cl_2$: C, 67.0; H, 4.8; Cl, 28.2. Found: C, 67.0; H, 5.0; Cl, 28.0.

(±)-2,2'-Dichloro-6,6'-dimethylbiphenyl was prepared in a similar manner from (±)-6,6'-dimethyl-2,2'-biphenyldiamine. The resulting white solid had m.p. 117–118° (lit.[29] m.p. 119°). The same compound, m.p. 117–119°, also was prepared by reduction with 50% hypophosphorous acid[30] of tetrazotized 2,2'-dichloro-6,6'-dimethyl-4,4'-biphenyldiamine.[31]

The infrared spectra of (±)-, (+)- and (−)-6,6'-dichloro-2,2'-dimethylbiphenyl were identical.

(+)-6,6'-Dicyano-2,2'-dimethylbiphenyl.—Aqueous sodium nitrite (3.4 g./10 ml.) at 0–5° was added to a solution of (+)-6,6'-dimethyl-2,2'-biphenyldiamine (5.0 g., $[\alpha]^{31}\text{D}$ +48° (ethanol), m.p. 156–158°) in a mixture of 10 ml. of concd. hydrochloric acid and 48 ml. of water. Aqueous sodium cyanide (7.8 g./12 ml.) was added to an aqueous (12 ml.) slurry of cuprous chloride, prepared[32] by addition

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[26] Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

[27] G. Wittig and O. Stichnoth, *Ber.*, **68**, 928 (1935).

[28] The earlier authors (ref. 6) did not state the sign relationship between diamine and diacetamide; *cf.* however ref. (12).

[29] A. Angeletti, *Atti X° congr. intern. chim.*, **3**, 26 (1939) (*C. A.*, **34**, 1008 (1940)); *cf.* also *C. A.*, **34**, 406 (1940) and *Chem. Zentr.*, **109**, **I**, 3770 (1938)), prepared the racemic compound *via* the Sandmeyer reaction from (±)-6,6'-dimethyl-2'-chloro-2-biphenylamine.

[30] Following the general procedure described by N. Kornblum, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 262.

[31] W. Kuhn and R. Rometsch, (ref. 15a); these authors did not report a characterization of the intermediate **3,3'-dichloro-5,5'-dimethylazobenzene**. We found this compound to be an orange solid, m.p. 138–139° after recrystallization from 95% ethanol. *Anal.* Calcd. for $C_{14}H_{12}Cl_2N_2$: C, 60.2; H, 4.3; N, 10.0. Found: C, 60.5; H, 4.5; N, 10.2.

[32] H. T. Clarke and R. R. Read, in Gilman and Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 514.

of a solution of sodium bisulfite (3.2 g.) and sodium hydroxide (2.1 g.) in 24 ml. of water to a hot solution of cupric sulfate hydrate (15.0 g.) and sodium chloride (3.9 g.) in 48 ml. of water, followed by washing of the precipitate. The tetrazotized solution was added to the cuprous cyanide mixture at 0–5°. The resulting precipitate was extracted with toluene, the organic solvent was removed, and the residue was distilled with steam to give an almost white solid (0.40 g.) suspended in 3 l. of distillate. Recrystallization from benzene–hexane afforded 0.10 g. (2%) of the desired product, m.p. 157-157.5°, $[\alpha]^{28}D$ +20° (*c* 1.9, tetrahydrofuran); the infrared spectrum (KBr wafer) exhibited the characteristically aciform and pronounced absorption at 2220 cm.$^{-1}$ (C≡N).

Anal. Calcd. for $C_{16}H_{12}N_2$: C, 82.7; H, 5.2; N, 12.1. Found: C, 83.0; H, 5.2; N, 12.1.

(−)-6,6′-Dicyano-2,2′-dimethylbiphenyl.[33]—Phosphorus pentachloride (6.5) was added to a mixture of (+)-6,6′-dimethyl-2,2′-diphenic acid[4] (2.1 g.) and *p*-toluenesulfonamide (2.8 g.) in a 50-ml. flask connected for distillation. The reaction started without external heating, but an oil-bath at 200–205° was now applied and heating continued until distillation was complete. Pyridine (6 ml.) and then water (28 ml.) was added to the residue. The resulting solid was collected by filtration and recrystallized from benzene–ligroin to give 0.70 g. (39%) of the desired product, m.p. 157–157.5°, $[\alpha]^{28}D$ −18° (*c* 5.6, tetrahydrofuran). The infrared spectrum was identical with that of the (+)-isomer.

Anal. Calcd. for $C_{16}H_{12}N_2$: C, 82.7; H, 5.2; N, 12.1. Found: C, 82.8; H, 5.4; N, 11.9.

Acknowledgment.—A portion of this work was supported by a grant from The Trubek Laboratories.

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[33] Patterned on the preparation of *p*-nitrobenzonitrile, C. S. Miller, in E. C. Horning, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 646. We are indebted to Dr. Alvin I. Kosak for bringing this elegant method to our attention.

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Conformation and Optical Rotation of Restricted Biphenyls. Configurational Correlation of Biaryls by Optical Displacement. The Absolute Configuration of Restricted 1,1′-Binaphthyls[1]

BY DONALD D. FITTS,[2] MAURICE SIEGEL AND KURT MISLOW

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Values for the average interplanar angle (θ) of 6,6′-dichloro-2,2′-dimethylbiphenyl (I) have been calculated using the polarizability theory of optical activity; knowledge of the optical rotation and the absolute configuration of I permits an estimate of $\theta \sim 92°$. The difference in sign of 6,6′-dimethyl-2,2′-biphenyldiamine and 1,1′-bi-2-naphthylamine in aprotic and acidic solvents may be accounted for by a change in quadrant of θ. The *S*-configuration has been assigned to (+)-9,10-dihydro-3,4,5,6-dibenzphenanthrene and to (−)-1,1′-bi-2-naphthylamine. A general Optical Displacement Rule has been proposed which allows absolute configurational assignments in the biaryl series on the basis of characteristic rotational shifts accompanying 2,2′-bridge formation. The absolute configuration of 1,1′-bianthryls is discussed in the light of this rule.

The absolute configuration of 2,2′-dichloro-6,6′-dimethylbiphenyl (I) and of 6,6′-dimethyl-2,2′-biphenyldiamine (II) has been established as the result of work reported in the previous article of this series[3]; it has been concluded that (+)-I and (+)-II have the *R*-configuration. The purpose of this article is to calculate the specific rotations of I and II and relate the rotation to the average conformation of the molecule. We shall then be in a position to offer an interpretation of the change in sign of rotation of II in passing from aprotic to acidic solvents and to suggest the theoretical basis for a new indirect method of intercorrelating the configurations of optically active biaryls.[4]

According to the electromagnetic theory of optical rotatory power, the specific rotation $[\alpha]D$ is related to the molecular rotatory parameter g by

$$[\alpha]\text{D} = 4.930 \times 10^5 \frac{n^2 + 2}{3M} g \qquad (1)$$

where n is the refractive index of the solution, M is the molecular weight of the optically active substance, and g is expressed in Å.^{4}. The parameter g is related to the molecular conformation of the asymmetric molecules and is approximated by the polarizability theory of Kirkwood[5,6] as

$$g^{(0)} = \frac{1}{6} \sum_{i<k=1}^{N} \alpha_i \alpha_k \beta_i \beta_k G_{ik} \mathbf{R}_{ik} \cdot (\mathrm{b}_i \times \mathrm{b}_k)$$
$$G_{ik} = \frac{1}{R_{ik}^3} \left[\mathrm{b}_i \cdot \mathrm{b}_k - 3 \frac{(\mathrm{b}_i \cdot \mathbf{R}_{ik})(\mathrm{b}_k \cdot \mathbf{R}_{ik})}{R_{ik}^2} \right] \qquad (2)$$
$$\mathbf{R}_{ik} = \mathbf{R}_k - \mathbf{R}_i$$

A typical asymmetric molecule is divided into N groups, each of which possesses a polarizability tensor of cylindrical symmetry. The mean polarizability of the i-th group is α_i and the anisotropy of the polarizability is β_i. The unit vector along the symmetry axis of group i is b_i. The summation in equation 2 extends over each pair of groups. The vector $\mathbf{R}_{ik}$ is the distance between groups i and k.

We now set up a right-handed Cartesian coördinate system in a molecule of 2,2′-diR-6,6′-dimethylbiphenyl as shown in Fig. 1. The phenyl ring

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[1] Configurational Studies in the Biphenyl Series. IV. Part III, preceding paper.

[2] National Science Foundation predoctoral fellow, 1954–1957.

[3] F. A. McGinn, A. K. Lazarus, M. Siegel, J. E. Ricci and K. Mislow, THIS JOURNAL, **80**, 476 (1958).

[4] The method of thermal analysis already has been successfully employed in the configurational intercorrelation of a number of optically active diphenic acids; M. Siegel and K. Mislow, THIS JOURNAL, **80**, 473 (1958).

[5] J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

[6] W. W. Wood, W. Fickett and J. G. Kirkwood, *ibid.*, **20**, 561 (1952).