ever, should all be pushed to the side of the ring opposite the catalyst surface. As the bulk of the groups is increased, the steric strain produced during the adsorption of the nucleus will increase, and the ease of adsorption will decrease. This is observed to be the case experimentally when a methyl group is substituted for a hydrogen atom. As the number of methyl groups attached to the ring is increased, the ease of adsorption decreases. This steric strain may be divided into two distinct categories. The first category is a frontal or F type of strain which results from the mutual repulsion between the nuclear substituents and the catalyst surface. The second category embraces a back or B type of strain which results from the closer proximity of the nuclear substituents to each other. Appreciable B strain should result for substituents which are *ortho* to each other and possibly those which are *meta*. It should not result for *para* substituents.

The concept of steric strain appears incapable of explaining the relative ease of adsorption of each of the three sets of substitutional isomers studied. The relative ease of adsorption of these sets of isomers suggests that the ring may be somewhat inclined upon chemisorption with the least substituted side being closer to the catalyst surface than the more highly substituted side. The tilting of the ring may actually be a means by which the adsorbed species minimizes F strain. The ability of the ring to be inclined upon chemisorption should decrease with increasing symmetry of substitution. Thus, as the symmetry of substitution increases, the intimacy of the approach to the active surface of the least substituted side of the ring decreases. This should result in a decreased ease of adsorption as has been observed experimentally. The concept of inclined adsorption of the nucleus may also be useful in explaining the relative ease of adsorption of such homologous series as *m*-xylene, mesitylene and isodurene. The relative ease of adsorption has been rationalized on the basis of steric rather than electronic effects. The possible effect on the ease of adsorption resulting from electron release to or withdrawal from the nucleus should be ascertained by the competitive reduction of two compounds, one of which has an electron-releasing substituent and the other an electron-withdrawing substituent (*e.g.*, toluene *versus* benzoic acid).

Steric strain and inclined adsorption may be used to explain all of the relative ease of adsorption results except that of hexamethylbenzene, which appears to be slightly more strongly adsorbed than pentamethylbenzene. The most likely explanation for this apparently anomalous result is a solvent effect. Hexamethylbenzene is so slightly soluble in glacial acetic acid that it was necessary to use it as a saturated solution in the binary reductions. The amount of pentamethylbenzene in the solution was far below the saturation point. It is thus reasonable to believe that the relative chemical potentials of the two hydrocarbons are altered by the solvent to the extent that hexamethylbenzene appears to have a greater relative ease of adsorption than it would have in the absence of the solvent. This conclusion may be tested by competitively reducing these two hydrocarbons in various other solvents. The effect of the solvent upon the other series of competitive hydrogenations should be of little consequence. Jungers and Wauquier[7] have shown the absence of solvent effects in the competitive reduction of benzene, toluene and the xylenes on Raney nickel in various organic solvents.

Acknowledgment.—The authors wish to express their appreciation to the National Science Foundation for granting a Cooperative Fellowship to C. P. Rader which permitted this research to be carried out.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY, NEW YORK 53, N. Y.]

Stereochemistry of the 1,2,3,4-Dibenzcyclonona-1,3-diene System.[1] A Note on the Racemization Barrier in Bridged Biphenyls

BY KURT MISLOW, SEYMOUR HYDEN AND HANS SCHAEFER

RECEIVED OCTOBER 7, 1961

A nine-membered ring bridged biphenyl (I) has been synthesized, and optically activated by second-order asymmetric transformation. The ultraviolet spectrum reflects a large angle of torsion in the ground state. The barrier to racemization (24.0 kcal./mole) reflects directed interaction between non-bonded hydrogens in the transition state. A semi-quantitative treatment of the transition state conformations in the homologous series of seven-, eight- and nine-ring bridged biphenyls (IIb–IId) is presented.

A study of the stereochemistry of 1,2,3,4-dibenzcyclonona-1,3-diene-7-carboxylic acid (I) was prompted by several considerations. Spectroscopic investigations into the relation between conjugation and conformation of 2,2′-bridged alicyclic biphenyls without substituents in the 6,6′-positions have revealed that the position of the conjugation band suffers a monotonic hypsochromic shift and decrease in intensity as the size of the bridge and the angle of torsion (θ) increase: for derivatives of IIa, IIb and IIc, the conjugation band assumes values of 264 mμ (log ϵ 4.23–4.26),[2]

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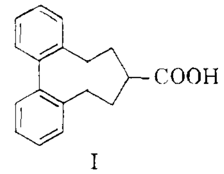
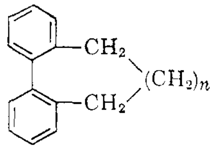
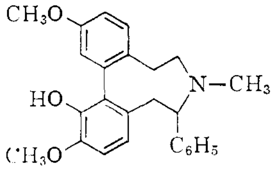
(1) Preliminary communication: *Tetrahedron Letters*, No. **12**, 410 (1961). Grateful acknowledgment is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research, and to the Alfred P. Sloan Foundation for fellowship support (K.M.).

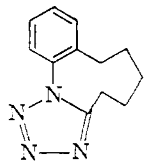
(2) F. A. Askew, *J. Chem. Soc.*, 512 (1935); R. N. Jones, *J. Am. Chem. Soc.*, **63**, 1658 (1941); G. H. Beaven, D. M. Hall, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 854 (1952).

247–249 mμ (log ε 4.18–4.23)[3–5] and 235–239 mμ (log ε 4.0–4.1),[4,5] respectively. A comparison with the next higher homolog (IId) or a simple derivative would thus be of interest; observations on somewhat related systems (III[6] and IV[7]) suggest that the conjugation band should be absent in IId. Previous attempts to synthesize appropriate derivatives of IId were abortive.[5,8]


I


II,a $n=0$ IIc, $n=2$
b, $n=1$ d, $n=3$


III

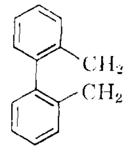

IV

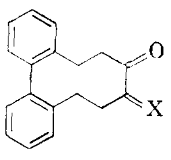
Systems II are twisted and dissymmetric; derivatives of IIb and IIc have been obtained in optically active form.[3,9] The optical stability of these systems is a reflection of the angle strain and nonbonded interaction which is introduced in the transition state conformation for racemization. One aspect of particular significance is the neat eclipsing of α-hydrogens in the transition state, as shown by Dreiding models. In IId the two α-hydrogens on C5 and C9 are almost exactly opposed.[10] A study of the optical stability of IId is thus of considerable interest.

For the purposes of our study, the choice of I was indicated by its synthetic accessibility (below) and by the fact that the carboxyl group, which may serve as a handle for resolution, does not introduce a new element of dissymmetry in its position at C7 and is far removed from the α-hydrogens whose interaction is of primary concern.

Synthesis and Spectrum.—The starting dicarboxylic acid Va[11] was converted by bishomologation to Vb *via* the Arndt–Eistert method or, for large-scale runs, by lithium aluminum hydride reduction of the diethyl ester to Vd, followed by successive conversion of Vd to Ve, Vf and Vb by standard procedures.

The possibility was tested that a direct precursor of I might be accessible by malonic ester condensation and ring closure of Ve. However, under a variety of conditions, the only product obtained was 2,2′-divinylbiphenyl. This result had not been anticipated since β-phenylethyl bromide under the same conditions gives excellent yields[12] of β-phenylethylmalonic ester, accompanied by styrene as a by-product. Exclusive elimination of a primary halide in the malonic condensation appears to be a highly unconventional result.[13]





Va, R = COOH; b, R = CH_2COOH VIa, X = O
c, R = CH_2COOCH_3; d, R = CH_2OH b, X = N_2
e, R = CH_2Br; f, R = CH_2CN;
g, R = CH_3

Acyloin ring-closure of the diester Vc (from Vb) gave a product which was directly oxidized to the diketone VIa in 25% over-all yield. The identity of VIa rests on the characteristic method of oxidation with bismuth oxide,[14] elemental analysis, molecular weight, characteristic yellow appearance, formation of a quinoxaline derivative (whose elemental analysis and molecular weight agree with calculated values) and oxidation with hydrogen peroxide to Vb. The diketone was converted to the diazoketone VIb by the method of Bamford and Stevens.[15]

The ring-contraction by the photochemical Wolff rearrangement[16] was patterned after the method of Horner and Spietschka.[17,18] Irradiation of Vb in aqueous basic dioxane gave I, completely identified by elemental analysis, neutralization equivalent, molecular weight, analysis of *p*-toluide and quinidine salt, and racemization of the optically active modification (see below).

Friedman and co-workers have shown[19] that the mono-*p*-toluenesulfonylhydrazones of medium membered cyclan-1,2-diones may be ring contracted directly to the lower ring-homologous acids by heating with base, without isolation of the intermediate diazoketone and irradiation. We were able to convert the *p*-toluenesulfonylhydrazone of

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[3] D. C. Iffland and H. Siegel, *J. Am. Chem. Soc.*, **80**, 1947 (1958).

[4] A. C. Cope and R. D. Smith, *ibid.*, **78**, 1012 (1956).

[5] G. H. Beaven, G. R. Bird, D. M. Hall, E. A. Johnson, J. E. Ladbury, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 2708 (1955).

[6] R. Robinson, *Nature*, **160**, 815 (1947), and references cited.

[7] R. Huisgen and I. Ugi, *Ann.*, **610**, 57 (1957).

[8] D. M. Hall and F. Minhaj, *J. Chem. Soc.*, 4584 (1957).

[9] L. V. Dvorken, R. B. Smyth and K. Mislow, *J. Am. Chem. Soc.*, **80**, 486 (1958).

[10] The directed non-bonded interaction of hydrogen in rigid bicyclic systems has recently been studied by L. de Vries and S. Winstein, *ibid.*, **82**, 5363 (1960); S. Winstein and R. L. Hansen, *ibid.*, **82**, 6206 (1960); L. de Vries and P. R. Ryason, *J. Org. Chem.*, **26**, 621 (1961); D. Kivelson, S. Winstein, P. Bruck and R. L. Hansen, *J. Am. Chem. Soc.*, **83**, 2938 (1961).

[11] J. Kenner and E. G. Turner, *J. Chem. Soc.*, 2101 (1911); R. Weitzenböck, *Monatsh.*, **34**, 193 (1913).

[12] A. W. Dox, *J. Am. Chem. Soc.*, **46**, 2843 (1924); M. Metayer, *Ann. Chim.*, [12] **4**, 196 (1949).

[13] It appears from molecular models that steric inhibition to nucleophilic displacement of bromide in Ve by sodiomalonic ester may greatly slow that process compared to elimination.

[14] W. Rigby, *J. Chem. Soc.*, 793 (1951).

[15] W. R. Bamford and T. S. Stevens, *ibid.*, 4735 (1952).

[16] Which can give only a single product (I). In this respect, the present reaction sequence is superior to more conventional contractions, *e.g.*, the Favorskii reaction or selenic acid–peroxide rearrangement of monoketones (G. B. Payne and C. W. Smith, *J. Org. Chem.*, **22**, 1680 (1957); H. M. Hellman and A. Rosegay, *Tetrahedron Letters*, No. **13**, 1 (1959); N. Sonoda and S. Tsutsumi, *Bull. Chem. Soc. Japan*, **32**, 505 (1959)). The corresponding precursor 1,2,3,4-dibenzcyclodeca-1,3-diene-7-one would afford a mixture of I and of 1,2,3,4-dibenzcyclonona-1,3-diene-6-carboxylic acid; the latter, which has an asymmetric carbon (C6), as a mixture of diastereomeric forms.

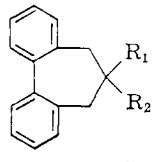
[17] L. Horner and E. Spietschka, *Chem. Ber.*, **88**, 934 (1955).

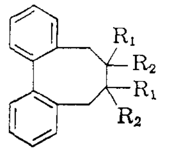
[18] W. Kirmse, *Angew. Chem.*, **69**, 106 (1957); W. Kirmse, L. Horner and K. Muth, *Chem. Ber.*, **91**, 430 (1958); M. P. Cava, R. L. Litle and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958); J. Meinwald and P. B. Gassman, *ibid.*, **82**, 2857 (1960); **82**, 5445 (1960); J. Meinwald and E. G. Miller, *Tetrahedron Letters*, No. **7**, 253 (1961).

[19] L. Friedman, A. Rosegay and R. L. Litle, private communication.

sebacil to cyclononanecarboxylic acid by that technique (heating in aqueous basic dioxane at 60°),[20] but in the case of the *p*-toluenesulfonylhydrazone of VIa difficulties were encountered in the isolation of the product due to stubborn contamination by *p*-toluenesulfinic acid. The intermediate diazoketone VIb was, however, smoothly converted to the desired acid by heating at 120° in aqueous basic dioxane–ethylene glycol. The product was identical in every respect with that obtained by the photolysis of VIb.

Comparison (Fig. 1) of the absorption spectra of I and the lower ring homologs IIa, VIIb and VIIIa discloses a pronounced hypsochromic displacement and drop in extinction of the vestigial biphenyl conjugation band (inflection at 231 mμ, ε 5550). The long wave length features are now clearly resolved, and the spectrum of I is nearly superimposable on that[21] of the open-chain analog Vg.





VIIa, $R_1 = R_2 = COOC_2H_5$ VIIIa, $R_1 = R_2 = COOC_2H_5$
b, $R_1 = COOH$, $R_2 = H$ b, $R_1 = COOH$, $R_2 = H$

It may be concluded that conjugation is more severely inhibited and that the angle of torsion is greater in I than in the lower ring homologs. The value of θ cannot be accurately estimated since, unlike IIa ($\theta = 15.3°$) and IIb ($\theta = 49.4°$), the higher homologs do not possess single conformations corresponding to minimum angle strain.[22] To a first approximation,[23] $\theta = 68°$. There is no absorption near 280 mμ, and the calculation of Braude and Forbes[24] leading to $\theta \geqslant 57°$, which is based on this band in phenyldihydrothebaine (III), is therefore devoid of significance.[25]

Optical Activation and Racemization of I.—The optical activation of I was achieved by crystallization of the quinidine salt from hot acetone. The salt was obtained in 84% yield. The acid liberated from this salt had $[\alpha]_D - 48.4°$ (C_6H_6) and was optically stable at room temperature. Heating under reflux in benzene for one hour resulted in complete racemization. The mother liquors from the crystallization of the quinidine salt did not yield the (+)-isomer on decomposition. It is thus apparent that a second order asymmetric transformation[26] rather than a resolution had taken place. The melting point of (−)-I (135–139°) was undepressed by admixture of (±)-I.

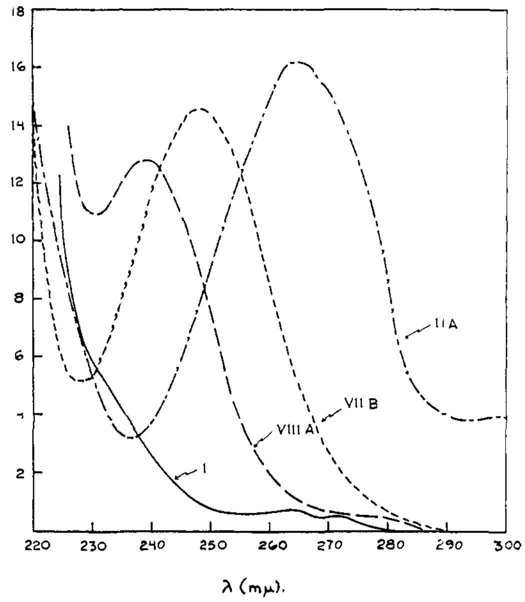


Fig. 1.—Comparison of ultraviolet spectra in the homologous series of six-(IIa), seven-(VIIb), eight-(VIIIa) and nine-(I) membered alicyclic ring 2,2′-bridged biphenyls; solvent 95% ethanol.

Racemization studies provided a quantitative basis for the above observations. The Arrhenius expression $k = 10^{12.5} \exp(-24.0/RT)$ was derived from the first-order rate constants (Experimental Part, Table I) at 50.0°, 59.6° and 70.2°. The corresponding transition state functions[27] are: $\Delta F^{\ddagger}$ 24.5 kcal./mole, $\Delta H^{\ddagger}$ 23.3 kcal./mole, and $\Delta S^{\ddagger}$ −3.3 e.u. If solvent effects are neglected, these Arrhenius parameters completely account for the qualitative information. At room temperature ($t^{25}_{0.5}$ *ca.* 24 hours) the compound is optically stable. Under conditions of the asymmetric transformation ($t^{57}_{0.5}$ *ca.* 20 min.) the interconversion of enantiomers is reasonably rapid. One hour in boiling benzene ($t^{80}_{0.5}$ *ca.* 2 min.) more than suffices to effect complete racemization (within the limits of measurement). Near the melting point ($t^{138}_{0.5}$ *ca.* 1 sec.) racemization is virtually instantaneous.

The optical rotatory dispersion of I is discussed elsewhere.[28] We note here that the extremum at 236 mμ is clearly the long-wave length trough of a

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[20] S. Hyden, Ph.D. Dissertation, New York University, 1960.

[21] P. M. Everitt, D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 2286 (1956).

[22] The conformational problem in IIb has already been discussed.[9] For the lower homologs our calculations follow in general those of Jones[8] for IIa and Beaven, *et al.*,[5] for IIb. However, we have selected 1.51 Å. rather than 1.54 Å. for C4–C5 (*i.e.*, phenylmethylene) since sp^2–sp^3 bonds are about 0.03 Å. shorter than sp^3–sp^3 bonds (*e.g.*, the C_{arom}–CH_3 bond in toluene; *cf.* F. A. Keidel and S. H. Bauer *J. Chem. Phys.*, **25**, 1218 (1956)). For the biphenyl pivot bond (sp^2–sp^2) a value of 1.49 Å. might be expected (*e.g.*, M. G. Brown, *Trans. Faraday Soc.*, **55**, 694 (1959); W. Zeil, *Angew. Chem.*, **73**, 751 (1961)). We have selected 1.50 Å., the value in planar biphenyl (A. Hargreaves, S. H. Rizvi and J. Trotter, *Proc. Chem. Soc.*, 122 (1961); J. B. Robertson, *Nature*, **191**, 593 (1961); J. Trotter, *Acta Cryst.*, **14**, 1135 (1961)) and close to the value in most non-planar biphenyls (data of O. Bastiansen, *Acta Chem. Scand.*, **3**, 408 (1949); **4**, 926 (1950); O. Bastiansen and L. Smedvik, *ibid.*, **8**, 1593 (1954); F. Fowweather and A. Hargreaves, *Acta Cryst.*, **3**, 81 (1950); F. Fowweather, *ibid.*, **5**, 820 (1952). D. L. Smare, *ibid.*, **1**, 150 (1948)). We have refrained from using the empirical relation proposed by D. Cook (*J. Chem. Phys.*, **28**, 1001 (1958)) between θ and length of sp^2–sp^2 single bond because (a) it scatters rather badly, and (b) it does not fit the parameters of cyclooctatetraene (O. Bastiansen, L. Hedberg and K. Hedberg, *J. Chem. Phys.*, **27**, 1311 (1957)).

[23] H. Suzuki, *Bull. Chem. Soc. Japan*, **27**, 597 (1954); **32**, 1340, 1350, 1357 (1959).

[24] E. A. Braude and W. F. Forbes, *J. Chem. Soc.*, 3776 (1955).

[25] As previously pointed out by D. M. Hall and F. Minhaj, *ibid.*, 4584 (1957).

[26] M. M. Harris in W. Klyne and P. B. D. de la Mare, "Progress in Stereochemistry," Vol. 2, Academic Press, Inc., New York, N. Y., 1958, p. 158.

[27] *E.g.*, D. M. Hall and M. M. Harris, *J. Chem. Soc.*, 490 (1960).

[28] K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, J. Weiss and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1455 (1962).

negative Cotton effect centered near 231 mμ. The (S)-configuration may therefore be assigned to (−)-I on the basis of the generalizations previously formulated concerning the relationship of sign and configuration of dissymmetric chromophores associated with the biphenyl conjugation band.[28]

Nature of the Barrier.—A body of experimental material is now available on the activation energies for racemization of IIb–IId (resp. derivatives thereof). In system IIb, a half-life of 80 min. at 32.5° (solvent cyclohexane) has been reported[3] for derivative VIIa. Assuming that the Arrhenius parameter A lies within the extremes of 10^{11} -10^{15} found in diverse bridged biphenyls[27] (including I), E_{act} for VIIa is 20.8–26.2 kcal./mole. In system IIc, the reported[9] E_{act} for racemization of *cis*-VIIIb is 22.8 kcal./mole (ethanol). Finally, the present work leads to E_{act} 24.0 kcal./mole (*o*-xylene) for system IId, as represented by I. If the assumption is made that E_{act} is roughly independent of solvent and (perhaps with less justification) of substitution on the bridge, the conclusion emerges that the barrier is to a first approximation independent of (or increases only very slightly with) ring size in the series IIb–IId.

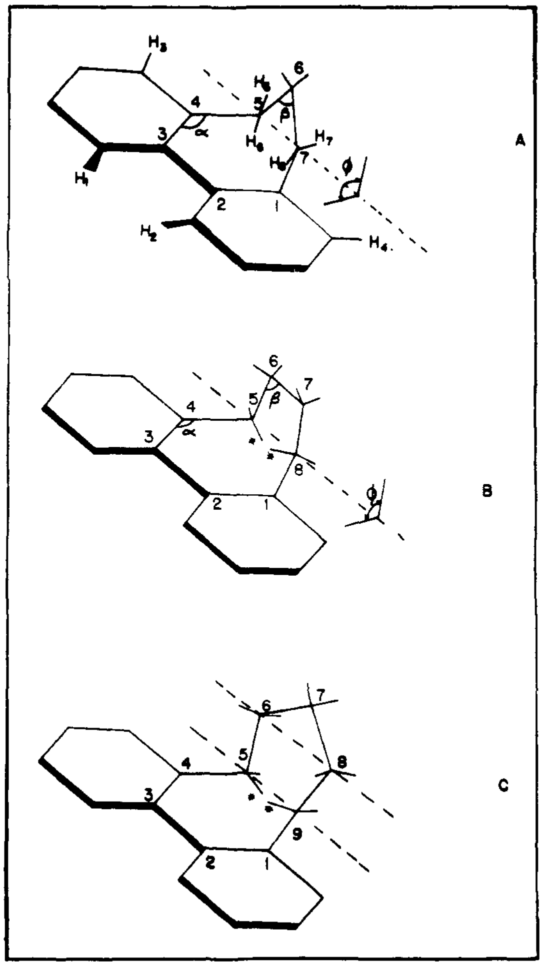

Fig. 2.—Presumed transition state conformations in the racemization of: (A), seven-(IIb); (B), eight-(IIc); and (C), nine-(IId) membered alicyclic ring 2,2′-bridged biphenyls.

The reliability of theoretical estimates of E_{act} depends on our knowledge (a) of the geometry of the transition state, and (b) of the function relating molecular deformations and intramolecular non-bonded interactions to corresponding potential energies. Despite the present unsatisfactory state of knowledge on both counts, unrefined estimates are possible and a comparative conformational analysis of the three systems is thus in order.

We follow Howlett[29] in making the assumption that bond lengths in the transition state remain invariant and that, at least to a first approximation, the biphenyl framework remains colinear and undistorted.[30] Our treatment departs from that of Howlett in explicitly recognizing the possibility of relief of angle strain by buckling of the bridge, shown for the case of IIb in Fig. 2A: the variable dihedral angle ϕ formed by the intersection of the planes containing C5–C6–C7 and C5–C4–C7 may take up any strain introduced into the CCC-angles subtended by C5 resp. C7. Employing the value 0.8×10^{-11} erg. rad^{-2} molec.$^{-1}$ for the CCC bond bending constant[31] and the usual value for bond distances,[22] the calculated[32] angle strain in IIb is 15 kcal./mole (α 79°, β 97°, ϕ 107°). The folded transition state has gained 3.5 kcal./mole resonance energy[33] but has lost 1.5 kcal./mole through non-bonded interaction of $H_1{:}H_2$[33] and 5 kcal./mole through non-bonded interaction of $H_6{:}H_8$ (which are *ca.* 1.6 Å. apart under conditions of minimum angle strain, above); the interaction of the other hydrogens ($H_3{:}H_5 + H_4{:}H_7$) which are brought to within *ca.* 1.8 Å. of each other in the transition state (from models) may be estimated at 3 kcal./mole.[34]

Although the E_{act} (21 kcal.) thus calculated comes fairly close to the above experimental estimate,[35] we are aware that this result may be fortuitous in view of the crudeness of the calculations and the neglect of higher order approxima-

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[29] K. E. Howlett, *J. Chem. Soc.*, 1250 (1955).

[30] However, minor distortions of the biphenyl framework are found not only in strained systems such as fluorene (G. M. Brown and M. H. Bartner, *Acta Cryst.*, **7**, 139 (1954)) but even in unbridged biphenyls such as the 2,2,-disubstituted benzidines (D. L. Smare, *ibid.*, **1**, 150 (1948); F. Fowweather, *et al.*, ref. 22).

[31] *E.g.*, K. S. Pitzer and W. E. Donath, *J. Am. Chem. Soc.*, **81**, 3213 (1959); A. G. Evans, *Trans. Faraday Soc.*, **42**, 719 (1946); F. H. Westheimer, in M. S. Newman "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 12; N. L. Allinger, M. A. Da Rooge and R. B. Hermann, *J. Am. Chem. Soc.*, **83**, 1974 (1961); P. v. R. Schleyer and R. D. Nicholas, *ibid.*, **83**, 2700 (1961); we note however that the legitimacy of extending the constant from C_{sp_3}–C_{sp_3}–C_{sp_3} to C_{sp_3}–C_{sp_2}–C_{sp_2} angles is questionable. Howlett[29] uses the value 0.5×10^{-11} erg. rad^{-2} molec.$^{-1}$. We have also neglected those changes in the bending constant which are expected to arise from excessive angle bending.

[32] The ground state is presumed free of angle strain.

[33] In going from the ground state (θ = 49°) to the transition state (θ = 0°); *cf.*, *e.g.*, F. J. Adrian, *J. Chem. Phys.*, **28**, 608 (1958).

[34] The $H_6{:}H_8$ interaction is taken as negligibly small in the ground state. Potential functions expressing appropriate non-bonded interactions are plentiful (for excellent recent discussions and listing of earlier references, *cf.*, *e.g.*, N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 5727 (1959); L. S. Bartell, *J. Chem. Phys.*, **32**, 827 (1960); R. Pauncz and D. Ginsberg, *Tetrahedron*, **9**, 40 (1960); K. E. Howlett, *J. Chem. Soc.*, 1055 (1960)); we have chosen the Eyring potential function $E_{H,H}$ calculated by Adrian[33] and used by him in the estimate of non-bonded interactions in biphenyl (type $H_1{:}H_2$). The approximation may be justified since the CH bonds involved (C7–H_8) and C5–H_6) happen to point toward each other at roughly the same angle (60° from models) as the CH bonds on H_1 and H_2.

tions (*i.e.*, the over-all minimization of angle (incl. CCH and HCH) and non-bonded strains, including especially molecular deformation of the biphenyl skeleton).

In IIc (Fig. 2B) similar calculations lead to a decrease in angle strain (10 kcal./mole, with α 72°, β 98° and ϕ 108°) compared to the corresponding transition state in IIb. The gain in resonance energy is slightly greater, *ca.* 4 kcal./mole,[33] since θ in the ground state is greater. This over-all lowering in energy is, however, offset by the non-bonded interaction of the hydrogens on C5 and C8 (starred) which are subtended at an angle (*ca.* 130° from models) far more obtuse than the corresponding atoms (H_6 and H_8 in Fig. 2A) in IIb. At the same time, for the calculated minimum strain conformation, C5 and C8 are now only 2.0 Å. apart, as compared to 2.3 Å. for C5 and C7 in IIb. The congestion of opposed hydrogens is almost exactly comparable, geometrically, to that of opposed pairs in the *endo–endo* fused bicycloheptane structures described by Winstein and collaborators.[10] As a result, the increase in the van der Waals forces precludes achievement of the minimum angle-strain conformation and the equilibrium conformation will adjust itself to the crowding at C5 and C8 by more acute angle deformation and molecular distortion.

In IId, angle strain in the transition state may be reduced to zero by allowing for double folding, as indicated in Fig. 2C (the new fold, through C6 and C8, would be very slight; C6 and C8 are 2.5 Å. apart). However, the overcrowding of the hydrogens (starred) on C5 and C9 has now become absurd: C5 and C9 are 1.4 Å. apart and the opposing non-bonded hydrogens are almost directly in line. Very considerable angle strain must thus in actual fact be introduced in order to accommodate the starred hydrogens.

The approximate constancy of E_{act} (for a given A-value) with bridge length in the homologous series of bridged biphenyls IIb–IId is thus recognized to be the outcome of two counterbalancing factors. As the bridge length increases from seven- to eight- to nine-ring, the angle strain in the transition state decreases only at the expense of increased non-bonded interaction of opposed α-hydrogens; the two factors roughly compensate each other. In the nine-ring, the barrier arises largely from interaction of non-bonded hydrogens oriented in direct opposition; cogwheeling (as in unbridged 2-methylbiphenyl) is precluded by the conformation of the bridge.

Work on molecules of higher symmetry now in progress[36] may cast further light on the correctness of some of the above estimates.

Experimental Part[37]

Biphenyl-2,2-diacetic acid (Va) was prepared by the hydrolysis of 2,2′-bis-(cyanomethyl)-biphenyl[11]; the product had m.p. 152–153° (lit.[2] m.p. 152°, 153–154°). On storage for several years, the m.p. changed to 174–174.5°. All preparations of this acid in our laboratory have since yielded the higher melting modification.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22; neut. equiv., 135. Found: C, 70.84; H, 5.33; neut. equiv., 142.

2,2′-Bis-(2-hydroxyethyl)-biphenyl (Vd) was prepared by reduction of the diacid Va (5.0 g.) with lithium aluminum hydride (1.75 g.) in ether in the usual manner. The compound was obtained as an oil which was crystallized from 1:1 benzene–hexane; recrystallization from this solvent mixture gave a solid, m.p. 88–89°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.11; H, 7.32.

2,2′-Bis-(2-bromomethyl)-biphenyl (Ve).—Phosphorus tribromide (112 g.) was added to a solution of diol Vd (100 g.) in benzene (300 ml.) at 10°. The solution was heated under reflux for 2 hours. The product, worked up in the usual manner, was obtained as an oil which had m.p. 48–49.5° after purification by chromatography on neutral alumina (activity III), using hexane as eluent, followed by recrystallization from methanol.

Anal. Calcd. for $C_{16}H_{16}Br_2$: C, 52.20; H, 4.38; Br, 43.42. Found: C, 52.11; H, 4.19; Br, 43.37.

A solution of dibromide Ve (6.0 g.) and sodium (0.75 g.) in 75 ml. of ethanol was heated under reflux (nitrogen atmosphere) for 16 hours. The solution was poured into water and the product (3.1 g., 94%, m.p. 73–78°) purified by chromatography on neutral alumina (activity II), using hexane as eluent. There was thus obtained 2.7 g. (82%) of **2,2′-divinylbiphenyl**, m.p. 79–81°. After recrystallization from methanol the product had m.p. 81–82° (lit.[38] m.p. 80–81°).

Anal. Calcd. for $C_{16}H_{14}$: C, 93.16; H, 6.84; mol. wt., 206. Found: C, 93.26; H, 6.85; mol. wt., 208.

The substance readily (5% Pd/C, 25°, atm. press.) absorbed 98% of the theoretical hydrogen.

A product identical in every respect (m.p., mixture m.p., infrared spectrum) with the above was obtained when dibromide Ve was treated with malonic ester and sodium ethoxide in ethanol under a variety of conditions.[39]

2,2′-Bis-(2-cyanoethyl)-biphenyl (Vf).—A mixture of dibromide Ve (59.2 g.), sodium cyanide (23.0 g.), ethanol (450 ml.) and water (70 ml.) was heated under reflux for 4 hours. The solution was concentrated, poured into water, made acid and extracted with ether. The ether extracts were washed with 6 *N* hydrochloric acid, water, 5% sodium carbonate and water. The solvent was evaporated and the residual oil purified by chromatography on acid-washed alumina (activity III), using benzene as eluent. After crystallization from ethanol, the product had m.p. 51–52°, ν_{max}^{KBr} 2410 cm.$^{-1}$ (CN).

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.20; N, 10.76. Found: C, 82.97; H, 6.19; N, 10.59.

2,2′-Bis-(2-carboxy-1-ethyl)-biphenyl (Vb) and **Dimethyl Ester** (Vc). **A.**—A suspension of dinitrile Vf (0.877 g.) in a mixture of concd. sulfuric acid (1.6 ml.), water (1.2 ml.) and acetic acid (1.4 ml.) was heated under reflux for 2 hours. The produced acid (0.986 g., 97%) was collected by filtration, washed with water and dried; it had m.p. 156–159°. Recrystallization from ethyl acetate afforded a white solid, m.p. 160–161°, ν_{max}^{KBr} 1700 cm.$^{-1}$ (CO).

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08; neut. equiv., 149. Found: C, 72.53; H, 6.20; neut. equiv., 157.

The derived **dimethyl ester Vc** was prepared from Vb and diazomethane in the usual manner (86%); crystals from methanol, m.p. 61–62°; polymorphic modification, m.p. 74.5°–75.5°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.52; H, 6.79.

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(35) The essential correctness of that estimate seems to be supported by the finding (S. R. Ahmed and D. M. Hall, *J. Chem. Soc.*, 3043 (1958)) that the related N-methylazepinium chloride having fluorine in place of H_1 and H_2 racemizes with E_{act} 27.8 kcal./mole (log A 12.7); fluorine has a somewhat larger interference radius than hydrogen (*cf.*, *e.g.*, D. M. Hall and M. M. Harris, *Proc. Chem. Soc.*, 396 1959)).

(36) K. Mislow and M. A. W. Glass, *J. Am. Chem. Soc.*, **83**, 2780 (1961).

(37) Melting points are corrected. Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

(38) D. M. Hall, J. E. Ladbury, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 3475 (1956), had obtained this material by dehydration of 2,2′-bis-(1-hydroxyethyl)-biphenyl.

(39) A. W. Dox[12]; G. B. Heisig and F. H. Stodola, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 213.

B.—Diacid Va was converted to the diacid chloride as previously described[11] and thence to the derived bis-(diazoacetyl)-2,2′-bitolyl with diazomethane according to standard procedures.[40] A sample of the product was crystallized from benzene–ligroin; fluffy yellow needles, m.p. 79–80° dec.

Anal. Calcd. for $C_{18}H_{14}O_2N_4$: N, 17.60. Found: N, 16.90.

The bis-diazoketone (29.5 g.) was refluxed with silver oxide (5.0 g.) slurried in methanol (250 ml.). After 1 hour the evolution of nitrogen had ceased. The diester obtained on workup (53%) was identical in every respect with Vc described above.

1,2,3,4-Dibenzcyclodeca-1,3-diene-7,8-dione (VIa).—A solution of dimethyl ester Vc (10.0 g.) in 250 ml. of anhydrous xylene was added over a period of 6.5 hours to a stirred (500 r.p.m., Morton flask) refluxing suspension of sodium (2.8 g., cut in air) in 750 ml. of xylene. During the entire addition, the mixture was blanketed with H.P. dry nitrogen. After the addition the orange mixture was heated under reflux for 1 hour, cooled to −3° and decomposed by the dropwise addition of methanol (30 ml.), followed by sulfuric acid (100 ml., 4 *N*) and water (100 ml.); the nitrogen atmosphere was maintained until the decomposition was completed. The xylene layer was separated, washed with water, dried and distilled. The residual oil was dissolved in glacial acetic acid (60 ml.), and bismuth oxide (4.75 g.) was added. The mixture was heated under reflux for 1 hour, cooled and filtered from the black bismuth precipitate. The filtrate was diluted with benzene and washed with saturated sodium chloride solution and water. Distillation of the benzene left an orange semi-solid which was triturated with methanol to give 2.0 g. (25% based on Vc) of a bright yellow crystalline solid, m.p. 196–201°. Recrystallization from 1:1 benzene–hexane gave yellow needles, m.p. 202–203°, $\nu_{\max}^{\text{KBr}}$ 1700 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10; mol. wt., 264. Found: C, 81.60; H, 6.09; mol. wt., 248.

Condensation of VIa (0.105 g.) with *o*-phenylenediamine (0.043 g.) in 15 ml. of glacial acetic acid gave 0.119 g. (89%) of the **quinoxaline** derivative, white needles, m.p. 151–152° after recrystallization from ethanol.

Anal. Calcd. for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33; mol. wt., 336. Found: C, 85.78; H, 5.93; N, 8.71; mol. wt., 319.

A mixture of VIa (0.155 g.), dioxane (5 ml.), 5% sodium hydroxide (20 ml.) and 30% hydrogen peroxide (5 ml.) was allowed to stand with occasional shaking for 3 days. The mixture was filtered from a small amount of insoluble material. The filtrate was partly neutralized and heated on the steam-bath for 30 minutes. The solution was concentrated to a volume of 5 ml. and made acid. There was thus obtained a precipitate (0.085 g., 48%) of diacid Vb, m.p. 159.5–161° after recrystallization from ethyl acetate, identical in every respect (mixture m.p., infrared spectrum) with authentic material.

1,2,3,4-Dibenzcyclodeca-1,3-diene-7,8-dione Mono-*p*-toluenesulfonylhydrazone.—A solution of diketone VIa (0.200 g.) and of *p*-toluenesulfonylhydrazine (0.156 g.) in 100 ml. of methanol was heated under reflux for 2 hours. The faintly yellow solution was concentrated to 10 ml. and poured into water. The precipitated solid (0.250 g., 76%) had m.p. 155–156° after several recrystallizations from methanol and featured bands in the infrared (KBr) at 3420 (NH), 1680 (C=O), 1590 (C=N), 1350 (SO_2) and 1170 cm.$^{-1}$ ($SO)_2$.

Anal. Calcd. for $C_{25}H_{24}N_2O_3S$: C, 69.42; H, 5.59; N, 6.48; S, 7.41. Found: C, 70.14; H, 5.66; N, 6.91; S, 7.59.

8-Diazo-1,2,3,4-dibenzcyclodeca-1,3-diene-7-one (VIb).—A mixture of 1.0 g. of *p*-toluenesulfonylhydrazone (previous section), 20 ml. of chloroform and 30 ml. of 0.1 *N* sodium hydroxide was stirred at room temperature for 5 hours. The chloroform layer was separated, washed with water, dried, and evaporated (30°) to give diazoketone VIb as a bright yellow, soft solid, m.p. 115–125° dec., $\nu_{\max}^{\text{KBr}}$ 2090, 1640 and 1620 cm.$^{-1}$. This product was used without purification in the next step.

(±)-1,2,3,4-Dibenzcyclonona-1,3-diene-7-carboxylic Acid (I). **A.**—A mixture of diazoketone VIb (0.77 g.), dioxane (50 ml.), water (15 ml.) and sodium carbonate (2.0 g.) contained in a quartz vessel was irradiated for 12 hours with a 100 watt G.E. S-4 lamp. During this period nitrogen gas was steadily evolved and the bright yellow color characteristic of diazoketone gradually faded. Water was added and a neutral fraction was extracted with chloroform. The aqueous layer was made acid with 6 *N* hydrochloric acid and extracted with ether. Evaporation of the ether afforded the desired product (0.47 g., 63%), m.p. 137–138.5° after recrystallization from aqueous methanol or cyclohexane. The compound was analytically free of nitrogen and sulfur. A solution of the acid in ethanol over 5% Pd/C did not absorb any hydrogen; under the same conditions, a solution of 2,2′-divinylbiphenyl smoothly absorbed the theoretical amount of hydrogen (above). The infrared spectrum featured $\nu_{\max}^{\text{KBr}}$ 1705 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81; neut. equiv., 266; mol. wt., 266. Found: C, 80.94, 81.01; H, 6.96, 6.68; neut. equiv., 280; mol. wt., 262, 258.

B.—A solution of diazoketone VIb in 1:3 dioxane–aq. ethylene glycol containing potassium hydroxide was heated at 120° for 1 hour. The mixture was poured into 6 *N* hydrochloric acid and extracted with ether. The ethereal solution was extracted with 10% potassium carbonate. The basic extracts were acidified and the precipitated product I was collected by extraction with ether, removal of the ether and recrystallization of the residual product (0.25 g., 42%) from aqueous methanol or cyclohexane. The material thus obtained had m.p. 137–138.5° and was identical in every respect (mixture m.p., infrared spectrum) with that obtained by procedure A. The neutral fraction contained the glycol ester of I, saponification of which with aqueous ethanolic potassium hydroxide afforded further quantities of I. To judge from several experiments, the yield by procedure B appears to be comparable to that by procedure A. When necessary, impure samples of I may be purified prior to recrystallization by chromatography on silica. The acid is eluted with 2% acetone in benzene.

The *p*-**toluide** of I, prepared *via* the acid chloride (from I and thionyl chloride), had m.p. 184–185° after recrystallization from aqueous methanol.

TABLE I

RACEMIZATION OF ACID I IN *o*-XYLENE

Temp., °C.	50.0	59.6	70.2
Concn., g./100 ml.	1.056	1.056	1.016
α_{435} at t_0 (l 2)[a]	−2.95°	−2.40°	−1.99°
$k_1 \times 10^4$, sec.$^{-1}$	2.18	5.92	18.4
$t_{0.5}$, min.	53	19.5	6.3

[a] t_0 is taken as the time of the first measurement, usually about 5 minutes after the sample has been dissolved.

Anal. Calcd. for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 3.94; mol. wt., 355. Found: C, 84.69; H, 7.34; N, 4.19; mol. wt., 347.

(−)-1,2,3,4-Dibenzcyclonona-1,3-diene-7-carboxylic Acid (I).—A solution of 0.500 g. of (±)-I and 0.548 g. of quinidine in 15 ml. of acetone was heated under reflux for 1 hour. **The quinidine salt** (0.842 g., 84%) which crystallized during that period and on standing overnight had m.p. 188–192°, $[\alpha]^{25}\text{D}$ + 129° (c 1.0, chf.).

Anal. Calcd. for $C_{38}H_{42}N_2O_4$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.47; H, 7.34; N, 4.75.

A solution of quinidine salt in a minimum volume of chloroform was shaken with ice-cold dil. hydrochloric acid. The mixture was extracted with ether. The combined ethereal extracts were washed with water and dried. The solvent was evaporated under reduced pressure. The residue crystallized on standing overnight at −20°. The product (88%) had m.p. 135–139°, undepressed by admixture of (±)-I. The infrared spectrum was identical with that of (±)-I; optical rotation: $[\alpha]^{28}\text{D}$ − 48.4° (c 1.0, benzene), $[\alpha]^{28}\text{D}$ − 42.3° (c 1.0, chloroform); ORD in dioxane (c 1.02–0.0045, 31°): $[\alpha]_{589}$ − 15°, $[\alpha]_{236}$ − 8840°, $[\alpha]_{226}$ − 2810° (using an automatically recording Rudolph spectropolarimeter).

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[40] W. E. Bachmann and W. S. Struve, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 38.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.44; H, 6.94.

The (+)-isomer ($[\alpha]^{25}D$ + 25° (*c* 0.9, chloroform)) was obtained by decomposition of the salt ($[\alpha]^{28}D$ − 68° (*c* 1.0, chf.)) which precipitated from (±)-I and *quinine* in acetone. The product was not further investigated.

Racemization Experiments. A.—A 1% solution of (−)-I in benzene was heated under reflux for 1 hour. The residue was crystallized from cyclohexane to give 89% of I, m.p. 139–141.5°, infrared spectrum identical with that of starting material, $[\alpha]^{25}D$ 0.0° (*c* 1.1, *l* 2, benzene).

B.—Thermostated solutions (1%) of (−)-I in redistilled *o*-xylene were examined polarimetrically (2-dm. tube) over a period of at least one half-life. Readings were taken at 435 mμ and the results were plotted as log α_t *vs.* time. Excellent straight-line relationships resulted from the minimum of fifteen readings which were obtained for each run. The values of *k* obtained from the slopes of the curves are listed in Table I.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF NEW YORK UNIVERSITY, NEW YORK 53, N. Y., AND OF STANFORD UNIVERSITY, STANFORD, CALIF.]

Configuration, Conformation and Rotatory Dispersion of Optically Active Biaryls[1,2]

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Ultraviolet and optical rotatory dispersion data have been gathered for the body of dissymmetric biaryls of known absolute configuration. The O.R.D.-curves have been found dependent on conformation and configuration. The change from open to 2,2′-bridged seven-membered ring biaryls gives rise to characteristic changes in the O.R.D. which are interpreted as reflecting changes in conformation. The absolute configuration uniquely determines the sign of the Cotton effect curves: the long-wave length Cotton effect of 2,2′-bridged biphenyls having the (*R*)-configuration is positive for the 1,1′-binaphthyls, 6,6′-dimethylbiphenyls and 6,6′-dichlorobiphenyls, and it is negative for the 6,6′-dinitrobiphenyls. The long-wave length Cotton effect of the 2,2′-bridged biaryls is generally accompanied by a Cotton effect at shorter wave lengths of opposite sign and greater amplitude, which often dominates the sign of rotation in the visible. The intense Cotton effect centered at the conjugation band of simple 2,2′-bridged biphenyls reflects the dissymmetric biphenyl chromophore, and the sign of the Cotton effect is characteristic of the absolute sense of twist of biphenyl. An amide rule has been formulated on which is based the assignment of absolute configurations to the biphenyl derivatives in the class of ellagitannins. 2,2′-Bridged seven-membered ring biaryls containing a carbonyl group in the non-conjugated position have been shown to exhibit a strengthened $n \rightarrow \pi^*$ transition akin to that of β,γ-unsaturated ketones as well as a corresponding Cotton effect curve whose amplitude is unusually high and whose sign is characteristic of the absolute sense of twist of the biaryl.

Examination of the optical rotatory power of the large body of biaryls whose absolute configuration had been secured[3–8] suggested the formulation of some generalizations. In particular, an optical displacement rule (Bridge rule) was tentatively advanced,[6] according to which the shift in optical rotation in the visible region accompanying bridging of the 2,2′-positions is diagnostic of configuration (*e.g.*, the (*R*)-configuration[9] for a negative shift). A theoretical basis for this rule was provided[6] in terms of the change in quadrant of polarizable groups attached to the biphenyl nucleus which accompanies bridging.

Subsequent work revealed[7] a counter instance (XXXIX) to the rule, and it was recognized[10] that scrutiny of the optical rotatory dispersions would be likely to furnish correlative information of greater general significance: the usefulness of O.R.D. in this connection had been established[11] in the series of classically asymmetric (asymmetric carbon[12]) compounds. Accordingly, spectral (ultraviolet and O.R.D.) information was gathered for a series of suitably substituted biaryls. The data are now presented in Tables I–VII and Figs. 1–24.

As indicated in the tables, the absolute configurations of the majority of compounds studied are known; the configurational assignments have been summarized.[10] In the case of certain compounds synthesized for the purpose of this study (Experimental part), the absolute configuration follows from that of the starting materials[10]; such cases are indicated by the double bracket (*e.g.*, ((*S*))). Of the newly reported syntheses, the conversion of (*R*)-XXII into (+)-(*R*)-VII by the Sandmeyer reaction is of interest in demonstrating that the replacement of both amino groups by bromo groups in the blocking positions proceeds without significant racemization, as had previously been observed[5] for similar replacements by cyano and

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(1) Paper XI in the series (by K. M.) "Configurational Studies in the Biphenyl Series" and paper LXVIII in the series (by C. D.) "Optical Rotatory Dispersion Studies." Communicated in preliminary form in *J. Am. Chem. Soc.*, **82**, 4740 (1960).

(2) Grants and fellowships by the Alfred P. Sloan Foundation (K. M.), The Trubek Laboratories (R. E. O., P. R.), the National Cancer Institute (C. D., grant No. CRTY-5061) and the National Science Foundation (K. M., grant No. G-15746; C. D., grant No. G-6579) are gratefully acknowledged.

(3) P. Newman, P. Rutkin and K. Mislow, *J. Am. Chem. Soc.*, **80**, 465 (1958).

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

(5) F. A. McGinn, A. K. Lazarus, M. Siegel, J. E. Ricci and K. Mislow, *ibid.*, **80**, 476 (1958).

(6) D. D. Fitts, M. Siegel and K. Mislow, *ibid.*, **80**, 480 (1958).

(7) K. Mislow and F. A. McGinn, *ibid.*, **80**, 6036 (1958); K. Mislow, V. Prelog and H. Scherrer, *Helv. Chim. Acta*, **41**, 1410 (1958).

(8) K. Mislow and P. A. Grasemann, *J. Org. Chem.*, **23**, 2027 (1958).

(9) The configurational designation proposed by R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956), will be used in this paper. The O.R.D. of constitutionally symmetrical doubly bridged biphenyls, which cannot be named by this system (K. Mislow and M. A. W. Glass, *J. Am. Chem. Soc.*, **83**, 2780 (1961)), will be discussed in another connection.

(10) K. Mislow, *Angew. Chem.*, **70**, 683 (1958).

(11) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960.

(12) Recent extentions to asymmetric sulfur (W. Klyne, J. Day and A. Kjaer, *Acta Chem. Scand.*, **14**, 215 (1960)) and asymmetric silicon (L. H. Sommer, C. L. Frye, M. C. Musolf, G. A. Parker, P. G. Rodewald, K. W. Michael, Y. Okaya and R. Pepinsky, *J. Am. Chem. Soc.*, **83**, 2210 (1961)) are noted.