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THE CONFORMATIONAL MOBILITY OF BRIDGED BIPHENYLS

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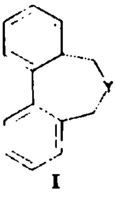
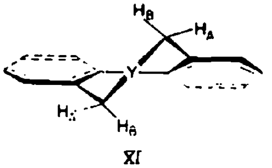
Abstract—The energy barriers to conformational inversion of a number of bridged biphenyls have been measured by the NMR method and the effects of different bridging groups examined.

CONSIDERABLE interest has been shown recently in the conformations and the energy barriers to conformational inversion of bridged biphenyls.[1-5] These energy barriers have usually been measured by polarimetry but NMR spectroscopy has also been used.[4,5] We now report the examination of conformational mobility in a series of closely related bridged biphenyls using the NMR method.

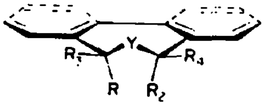
The protons of the benzylic methylene groups of the bridged biphenyls of the general structure I are expected to be magnetically non-equivalent in the normal conformation of these compounds (XI) due to their differing geometrical relationship to the aromatic rings.[6] A detailed examination of the NMR spectra of bridged biphenyls of this type by Mislow *et al.*[2] has shown that the expected non-equivalence of protons A and B (see XI) does not always occur and that the separation of the A and B proton resonance positions $\nu_0\delta_{AB}$ is dependent upon the solvent as well as the nature of Y and therefore the exact geometry of conformation (XI) for individual compounds. Conformational inversion of XI, via the transition state XII results in exchange of the positions of protons A and B and if this exchange is fast the observed NMR spectrum of the benzylic protons is a singlet whereas slow conformational



I



XI



XII

II, $Y = >SO_2$[7]
III, $Y = >S$[7]
IV, $Y = >C=NOH$[8]
V, $Y = >C(CO_2Et)_2$[9]
VI, $Y = >\overset{+}{N}Me_2Br^-$[10]
VII, $Y = >C=O$[11]
VIII, $Y = >NH$[10]
IX, $Y = >O$[11]
X, $Y = >CH_2$

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[1] K. Mislow, S. Hyden and H. Schaefer, *J. Amer. Chem. Soc.* **84**, 1449 (1962).

[2] K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon and G. H. Wahl, *J. Amer. Chem. Soc.* **86**, 1710 (1964).

[3] D. M. Hall and J. M. Insole, *J. Chem. Soc.* 2326 (1964).

[4] M. Oki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc. Japan* **36**, 1542 (1963); **37**, 1685 (1964).

[5] R. J. Kurland, M. B. Rubin and W. B. Wise, *J. Chem. Phys.* **40**, 2426 (1964).

[6] C. E. Johnson and F. A. Bovey, *J. Chem. Phys.* **29**, 1012 (1958); J. A. Pople, *Ibid.* **24**, 1111 (1956).

inversion results in the observation of the separate A and B proton signals mutually coupled as an AB system.[13] The effects of proton exchange in both coupled[14] and uncoupled systems[13,15] has been analysed in terms of the variation of line shape with exchange rate and the NMR method has frequently been applied for the determination of conformational inversion rates.[16]

The results of the study of the temperature dependence of the NMR spectra of a series of bridged biphenyls, differing only in the nature of group Y, are summarized in Table 1. All of the compounds listed in this Table show an AB system for the benzylic protons at low temperature and a singlet at high temperature. The free energy barrier to conformational inversion, $\Delta F^\ddagger$, at the temperature, T_c, at which the low temperature AB system just coalesces to a single broad line has been derived by first calculating the exchange rate, k_c, at T_c using the formula:—[4,5]

$$k_c = (\nu_0\delta_{AB}^2 + 6J_{AB}^2)^{1/2}/\sqrt{2}$$

and applying the Eyring equation to the observed values of k_c and T_c.

TABLE 1

Compound	Y	Solvent	$\nu_0\delta_{AB}$ c/s	J_{AB} c/s	T_c	$\Delta F^\ddagger$[a] Kcal/mole
II	SO_2	Pyridine[b]	12·2	13·4	87·5	18·2 (18·9)
III	S	Pyridine	9·2	12·6	34	15·5 (16·2)
		$CDCl_3$	12·7	12·6	45	16·0 (16·7)
IV	C=NOH	Pyridine (*syn* CH_2)	77	18	10·5	13·7 (13·7)
		(*anti* CH_2)	12·6	13·5	−8·5	13·2 (13·7)
V	$C(CO_2Et)_2$	Pyridine	19·9	13·8	9	14·0 (14·4)
		Pentachloroethane	21·6	13·5	17·5	14·5 (14·8)
VI	$\overset{+}{N}Me_2,Br^-$	D_2O-Pyridine (1:1)	ca52[c]		−1	(13·4)

[a] The values of $\Delta F^\ddagger$ in parentheses are calculated using the formula $k_c = \pi\nu_0\delta_{AB}/\sqrt{2}$ which is strictly applicable only for $J_{AB} = 0$.

[b] $\nu_0\delta_{AB} = 0$ in $CDCl_3$ (cf.[3]).

[c] The AB system below T_c is resolved only into two broad lines, $\nu_0\delta_{AB}$ refers to the separation of these two lines.

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[7] W. E. Truce and D. D. Emrick, *J. Amer. Chem. Soc.* **78**, 6130 (1956).

[8] J. Kenner and E. G. Turner, *J. Chem. Soc.* **2101** (1911).

[9] J. Kenner, *J. Chem. Soc.* **613** (1913).

[10] W. Wenner, *J. Org. Chem.* **16**, 1475 (1951).

[11] A. C. Cope and R. D. Smith, *J. Amer. Chem. Soc.* **78**, 1012 (1956).

[12] G. Wittig, P. Davis and G. Koenig, *Chem. Ber.* **84**, 627 (1951).

[13] J. A. Pople, W. G. Schneider and H. J. Bernstein, *High Resolution Nuclear Magnetic Resonance*. McGraw-Hill, New York (1959).

[14] S. Alexander, *J. Chem. Phys.* **37**, 967 (1962).

[15] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.* **25**, 1228 (1956); L. H. Piette and W. A. Anderson *Ibid.* **30**, 899 (1959).

[16] Recent examples, apart from those quoted elsewhere in this paper, include: F. A. Bovey, F. P. Hood, E. W. Anderson and R. L. Kornegay, *J. Chem. Phys.* **41**, 2041 (1964); P. F. Lansbury and J. F. Bieron, *J. Amer. Chem. Soc.* **86**, 2524 (1964); F. A. L. Anet and J. S. Hartman, *Ibid.* **85**, 1204 (1964); H. Friebolin, R. Mecke, S. Kabuss and A. Luttringhaus, *Tetrahedron Letters* 1929 (1964); D. Y. Curtin, C. G. Garlson and C. G. McCarthy, *Canad. J. Chem.* **42**, 565 (1964); K. G. Untch and R. J. Kurland, *J. Amer. Chem. Soc.* **85**, 346 (1963); W. L. Meyer and R. B. Meyer, *Ibid.* **85**, 2170 (1963).

The benzylic protons of VII and VIII are observed as sharp singlets down to the lowest attainable temperature (−60°), this result indicates either rapid conformational inversion down to −60° or, more probably, accidental magnetic equivalence of the benzylic protons for these compounds (cf.[2]). As expected the geminal coupling constants vary with the nature of the attached Y group presumably for both electronic and steric reasons.[17] The difference between the two AB systems corresponding to the *syn* and *anti* protons of the oxime (IV) is particularly striking and the details of this spectrum are recorded in the Experimental of this paper. The results of these measurements are at present limited to the calculation of free energy barriers to conformational inversion at the coalescence temperature and a comparison of the results for different compounds is only valid for zero entropies of activation. Clearly conformational mobility varies considerably with the nature of Y and our results agree quite well with the calculated potential energy barriers, $\Delta E\ddagger$, recently reported by Mislow *et al.*[2] for III and X. The thiepin (III) has also been examined by Kurland *et al.*[6] who found $E_a = 16\cdot1$ Kcals/mole, $\Delta S\ddagger < 2\cdot0$ e.u. The synthesis of the diester (V) in optically active form has been reported,[18] but it is clear from the results in Table 1 that the racemization rate of this compound (twice the rate of conformational inversion[19]) would be much too rapid to permit the isolation of an enantiomer at room temperature. Examination of the line width, W, of the high temperature singlet from the benzylic protons of V permits the approximation inversion rates, k, to be obtained using the formula:

$$k = \pi\nu_0\delta_{AB}{}^2/2(W - W_0)$$[13,20]

where W_0 is the extrapolated line width for $k = \infty$. This formula is restricted to fast exchange rates where the error in measuring $(W - W_0)$ is greatest leading to potentially rather large errors in calculated inversion rates, but the values of k so obtained for compound V give $E_a = 13\cdot7$ Kcals/mole, $\log_{10} A = 11\cdot9$ in good agreement with the calculated[2] potential energy of activation of 13 Kcals/mole for the compound X lacking the ester substituents. None of the compounds examined in Table 1 would be isolable in optically active form at room temperature, but the sulphone (II) in pyridine would have $t_{1/2} = 38$ secs at 0° assuming zero entropy of activation (or $t^{a}_{1/2} = 1\cdot5$ min for $\Delta S\ddagger = -6$ e.u. and $t_{1/2} = 15$ sec for $\Delta S\ddagger = +6$ e.u.) cf.[7,19]

The difference of only 0·5 Kcals between the values of $\Delta F\ddagger$ in pyridine and halogenated hydrocarbon solvents observed for compounds III and V suggested that solvent effects were quite small, and the inversion of the tetramethyloxepin (XIII)[29] was studied in order to examine solvent effects and relate them to enthalpies and entropies of activation. This compound is particularly suitable for this purpose as the low temperature NMR spectrum includes two rather widely separated methyl signals which coalesce to a single line over a convenient temperature range. The solvents used were pentachloroethane, pyridine and deuterochloroform as these have been found suitable for the study of a wide range of bridged biphenyls, both from the point of view of solubility and the temperature range that can be used. The results of

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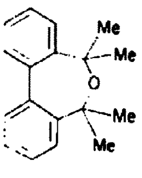
[17] H. S. Gutowsky, M. Karplus and D. M. Grant, *J. Chem. Phys.* **31**, 1278 (1959); H. J. Bernstein and N. Sheppard, *Ibid.* **37**, 3012 (1962); M. Barfield and D. M. Grant, *Ibid.* **36**, 2054 (1962).

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

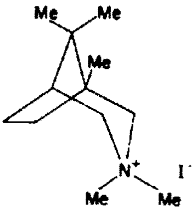
[19] D. M. Hall and M. M. Harris, *J. Chem. Soc.* 490 (1960).

[20] F. A. L. Anet, *J. Amer. Chem. Soc.* **86**, 458 (1964).

this study are recorded in Table 2. Exchange rates below the coalescence temperature were calculated by the method of Gutowsky and Holm[15] making allowance for the observed relaxation times at low temperature, fast exchange rates were calculated from line widths using the formula given above, and the exchange rate at the coalescence temperature from the usual expression (see footnote *a* to Table 1). The values for the Arrhenius parameters E_a and $\log_{10} A$ were obtained in the usual way.



XIII



XIV

The separation of the low temperature methyl signals of XIII decreased slightly with increasing temperature outside the range where the variation of signal separation was associated with the slowing down of the exchange process, and in order to calculate exchange rates by the method of Gutowsky and Holm allowance had to be made for this effect. Thus in pyridine the separation of the methyl signals of XIII varied from 36·8c/s at −30° to 35·6 c/sec at −15° (the temperature at which the separation begins to be affected by exchange). This observation suggests that the coalescence of NMR signals with increasing temperature does not necessarily mean that an exchange process is involved, and the temperature dependence of the >CMe$_2$ signals of N-methylcamphidine methiodide XIV confirms this. The separation of both the >CMe$_2$ and >$\overset{+}{\mathrm{N}}$Me$_2$ doublets for XIV at several different temperatures are recorded in Table 3.

TABLE 2. ARRHENIUS PARAMETERS FOR THE CONFORMATIONAL INVERSION OF XIII

Solvent	$\nu_0\delta_{AB}$ c/s at − 30°	T_C	E_a Kcal/mole	$\log_{10} A$
Pyridine	36·5	9	13·3	12·1
Pentachloroethane	38·2	16	13·2	11·8
CDCl$_3$	38·4	18	13·2	11·8

The changes recorded in Table 3 depend upon temperature and solvent and are accompanied by additional changes in τ values, a more detailed study of these effects is being made.

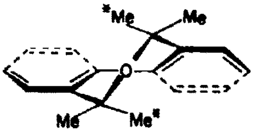
The energy barrier to the conformational inversion of the tetramethyl oxepin (XIII) (E_a = 13·2, 13·3 Kcal/mole) is considerably greater than that reported for the unsubstituted compound IX (E_a = 9·2 Kcal/mole)[6]; this result was expected in view of the obviously greater interaction between the groups R_1 and R_2 in the transition state (XII) when these are methyl as compared with hydrogen (the C—C distance between these methyl groups in undistorted Dreiding models of XII is only 1·5 A). A less obvious source of strain resulting in an increase in the energy of the ground state conformation (XV) of XIII is the unfavourable location of the starred methyl groups.

TABLE 3. TEMPERATURE DEPENDENCE OF THE $>\overset{+}{N}Me_2$ AND $>CMe_2$ DOUBLET SEPARATIONS FOR N-METHYL CAMPHIDINE METHIODIDE[21]

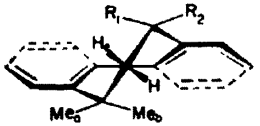
Solvent	Temperature	$\nu_0\delta_{\overset{+}{N}Me_2}$ c/s	$\nu_0\delta_{CMe_2}$ c/s
Pyridine	95	10·9	$< 0·6$[a]
	35	10·3	ca 1·0
	− 20	8·6	2·7
Pyridine-D_2O (1:1)	95	8·4	$< 0·6$
	35	7·9	$< 0·6$
	− 10	7·5	2·7

[a] The observation of a singlet implies a separation of $< 0·6$ c/s.

That these methyl groups are in energetically unfavourable positions is demonstrated by the NMR spectrum of the trimethyl-dibenzocycloheptadiene (XVI)[20] (Table 4) which appears to exist in solution almost exclusively in the conformation XVI.



XV



XVI, $R_1 = H_d$, $R_2 = Me_c$
XVII, $R_1 = Me_c$, $R_2 = H_d$

TABLE 4. THE NMR SPECTRUM OF XVI IN CCl_4 AT 60°

Proton (s)	τ value	Coupling Constants[a] c/s
a	8·67	
b	9·33	$J_{cd} = 7·0$
c	8·79	$J_{de} = 5·2$
d	7·19	
e	7·87	$J_{d_f} = 11·8$
f	8·33	$J_{e_f} = 13·2$

[a] Multiplets from H_e and H_f were analysed as the AB protons of an ABX system.[13]

At low temperatures (well below the expected NMR coalescence temperature) no sign is seen of the spectrum of the alternative conformation (XVII) which would have two low field and one high field methyl groups,[6] and vicinal coupling constants J_{de} and J_{df} in accord with dihedral angles of approximately 80° and 40° between the C—H bonds. The values of J_{de} and J_{df} recorded in Table 4 are in accord with the dihedral angles of approximately 40° and 160° measured from Dreiding models of XVI.[22]

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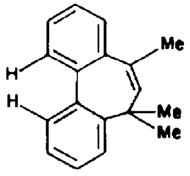
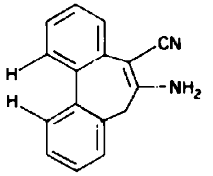
[21] We thank Dr. J. McKenna for making available a sample of this compound.

[22] M. Karplus *J. Chem. Phys.* **30**, 11 (1959); *J. Amer. Chem. Soc.* **85**, 2870 (1963); M. B. Rubin, *J. Org. Chem.* **29**, 3333 (1964).

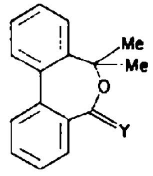
The conformational inversion of four other bridged biphenyls has been examined and the results are reported in Table 5.



XVIII



XIX



XX, Y=H$_2$
XXI, Y=O

Table 5[a]

Compound	Solvent	$\nu_0\delta_{AB}$ c/s	J_{AB} c/s	T_C	$\Delta F‡$ Kcal/mole
XVIII	Pentachloroethane	45·5		102	18·8
XIX	Pyridine	16·5	13·0	78·5	17·9 (18·3)
XX	Deuterochloroform	ca 38[b]		< -60	$< 11·5$
XXI	Pyridine	32		$-27·5$	12·3
	Deuterochloroform	31·5		-19	12·7

[a] ΔF‡ calculated as in Table 1 for XIX and from $k = \pi\nu_0\delta_{AB}/\sqrt{2}$ for XVIII, XX and XXI.

[b] The coalescence temperature was well below the lowest attainable temperature, the value of $\nu_0\delta_{AB}$ is assumed to be similar to that for XIII.

The dimethyl-oxepin (XX) shows no sign of broadening of the singlet methyl signal even at −60°, in this case a singlet signal almost certainly indicates rapid conformational inversion as germinal methyl groups of this type are consistently separated by ca. 40 c/s (e.g. compounds XIII, XVIII and XXI). The lactone (XXI) is much less mobile than XX apparently due to the loss of —O—CO— conjugation in the transition state, this is accompanied by an increase in Ar–CO– conjugation.

The 1,2,3,4-dibenzocycloheptatrienes XVIII and XIX are of some interest since the conformational mobilities of cycloheptatrienes[20,24,25] 1,2,5,6-dibenzocycloheptatrienes and tribenzocycloheptratienes[26] have previously been investigated. The planar transition state for cycloheptatriene ring inversion is destablized by bond angle strain, but stabilized by an increase in resonance energy of a planar cycloheptratiene system. (Calculated DE for hexatriene 7·7 Kcal/mole,[27] measured DE for non-planar cycloheptatriene 6·7 Kcal/mole[28].) The energy barrier to conformational inversion of cycloheptatriene is rather low ($\Delta F‡ = 5·7 \mp 0·1$,[24] 6·1[20] Kcal/mole for cycloheptatriene and $\Delta F‡ = 9·2$ Kcal/mole for 3,7,7-trimethyl-2-t-butyl cycloheptatriene[25]) but 1,2,5,6-dibenzocycloheptatriene is a rather more rigid molecule ($\Delta F‡ = 15$ Kcal/mole for

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[23] A. Carbellini and M. Angeletti, *Atti. R. Acad. Lincei* **15**, 968 (1932).

[24] F. R. Jensen and L. A. Smith, *J. Amer. Chem. Soc.* **86**, 956 (1964).

[25] K. Conrow, M. E. H. Howden and D. Davis, *J. Amer. Chem. Soc.* **85**, 1929 (1963).

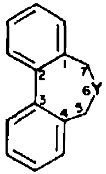
[26] W. Tochterman, U. Walter and A. Mannschreck, *Tetrahedron Letters* 2981 (1964).

[27] K. B. Wiberg, *Physical Organic Chemistry* p. 75. J. Wiley, New York (1964).

[28] G. H. Wheland, *Resonance in Organic Chemistry* p. 80. J. Wiley, New York (1955).

[29] D. M. Hall, J. E. Ladbury, M. J. Leslie and E. E. Turner, *J. Chem. Soc.* 3475 (1956).

TABLE 6. NMR SPECTRA OF BRIDGED BIPHENYLS AT 35°

A


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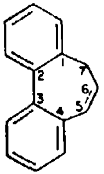

			Chemical shifts (τ-scale)		
Compound	Solvent	Aromatic H	5 H/substituents	6 group/substituents	7H/substituents
II (A, Y = $>\mathrm{SO_2}$)	Pyridine		5·74 (d) [2] 5·94 (d) [2]	$>\mathrm{SO_2}$	as 5
	PCE	2·53 (s) [8]	6·06 (s) [4]	$>\mathrm{SO_2}$	as 5
IV (A, Y = $>\mathrm{C{=}NOH}$)	Pyridine		(syn 6·03 (broad s) [2]	$>\mathrm{C{=}NOH}$	(anti) 6·42 (s) [2]
	Pyridine (−40°)		(syn) 5·33 (d) [1] 6·62 (d) [1]	$>\mathrm{C{=}NOH}$	(anti) 6·27 (d) [1] 6·48 (d) [1]
V [A, Y = $>\mathrm{C(CO_2Et)_2}$]	$\mathrm{CCl_4}$	2·73 (s) [8]	7·00 (broad s) [4]	5·85 (q) [4] 8·77(t) [6]	as 5
	Pyridine		6·73 (s) [4]	5·80 (q) [4] 8·86 (t) [6]	as 5
VI (A, Y = $>\overset{+}{\mathrm{N}}\mathrm{Me_2Br^-}$)	Pyridine-$\mathrm{D_2O}$		5·83 (s) [4]	6·37(s) [6]	as 5
VIII (A, Y = $>\mathrm{NH}$)	Pyridine		6·52 (s) [4]	$>\mathrm{NH}$	as 5
	$\mathrm{CCl_4}$	2·5 − 2·8 (m) [8]	6·70 (s) [4]	$>\mathrm{NH}$	as 5
XIII (A, Y = $>\mathrm{O}$)	PCE	2·63 (s) [8]	8·69 (broad s) [12]	$>\mathrm{O}$	as 5
	Pyridine		8·57 (s) [12]	$>\mathrm{O}$	as 5
XX (A, Y = $>\mathrm{O}$)	$\mathrm{CDCl_3}$	2·3 − 2·8 (m) [8]	8·63 (s) [6]	O	5·57 (s) [2]
XXI (A, Y = $>\mathrm{O}$)	Pyridine		8·41 (s) [6]	O	C=O
XVIII (B)	Pyridine		− CN	$-\mathrm{NH_2}$	6·76 (d) [1] 6·49 (d) [1]
XIX (B)	PCE	2·3 − 2.9 (m) [8]	4·22(q, J = 1·4) [1]	7·92(d, J = 1·4) [3]	8·42 (s) [3] 9·20 (s) [3]

s = singlet, d = doublet, t = triplet, q = quartet. The figures in brackets [ ] refer to the integrated proton count. The NMR spectra of III, VII and IX have been described by Mislow *et al.*[2] PCE refers to pentachloroethane.

7,7-dimethoxy-1,2,5,6-dibenzocycloheptatriene and $\Delta F\ddagger = 16$ Kcal/mole for 7,7-dimethoxy-3-bromo-1,2,5,6-dibenzocycloheptatriene[26]). The 1,2,3,4-dibenzocycloheptatrienes are still more rigid ($\Delta F\ddagger = 18{\cdot}8$ Kcal/mole for XVIII and $\Delta F\ddagger = 17{\cdot}9$ Kcal/mole for XIX) and this further increase in the energy barrier to ring inversion is presumably due to the interaction between the hydrogen atoms on the aromatic rings indicated in XVIII and XIX. The increased rigidity of the tribenzocycloheptatriene ring ($\Delta F\ddagger > 23$ Kcal/mole for 7,7-dimethoxytribenzocycloheptatriene[26]) is also a result of this interaction.

EXPERIMENTAL

All NMR spectra were recorded using a Varian A 60 spectrometer equipped with a V 6057 variable temp probe providing probe temp from —60° to +200°. Temps were measured with MeOH or ethylene glycol samples and temp measurements are probably accurate to ∓1°.

The compounds II to IX, XIII, XVI, XVIII, XIX and XXI were prepared according to established methods and had physical properties in agreement with those previously recorded and NMR spectra compatible with the assigned structures (Table 6).

α,α-Dimethyl-2,2′-biphenyldimethanol. A solution of XX[22] (2g) in dry ether (30 ml) was added slowly to a well stirred suspension of LAH (0·2 g) in ether (30 ml). The mixture was heated under reflux overnight then excess hydride was destroyed with ethyl acetate and the ether solution treated with dil H_2SO_4. The ether layer was dried (K_2CO_3) and evaporated to give the crude product which was recrystallized from pet. ether (b.p. 60–80°) to give pure *α,α-dimethyl-2,2′-biphenyl-dimethanol* (1·7 g, 85%) m.p. 101°; λ_{max} (in EtOH) 212 mμ (ε 19,600). (Found: C, 79·2; H, 7·4; $C_{16}H_{18}O_2$ requires: C, 79·3; H, 7·5%.)

5,7-Dihydro-5,5-dimethyl-dibenz [*c,e*] *oxepin* (XX). A suspension of the above diol (1 g) in 4N H_2SO_4 (30 ml) was boiled under reflux for 1 hr, cooled and extracted with ether. The ether solution was dried (K_2CO_3) and evaporated to give an oil (0·8 g) which was chromatographed on silica (16 g). Elution with pet. ether (b.p. 60–80°) gave an oil (0·1 g) followed by the crystalline product (0·66 g, 71%) which was recrystallized from n-pentane to give *5,7-dihydro-5,5-dimethyl-dibenz* [*c,e*] *oxepin* m.p. 68–69°; λ_{max} (in EtOH) 215 (ε 18,700), 254 mμ (ε 14,200). (Found: C, 85·4; H, 7·2; $C_{16}H_{16}O$ requires: C, 85·7; H, 7·2%.)