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Optical Activity of Bis-1,1′-spiroindanes. I. Optical Resolution and Absolute Configuration

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The resolutions of 6,6′-dihydroxy-3,3,5,3′,3′,5′-hexamethyl-bis-1,1′-spiroindane (IIIa), 3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane-6,6′-dicarboxylic acid (IIIc), and 5,5′-dihydroxy-bis-1,1′-spiroindane (VIII) are reported. The circular dichroism and absorption spectra of these optically active compounds and their derivatives were measured. The spectra were analysed by means of a coupled oscillator model. The relative frequencies and signs of the rotational strengths associated with the *p*-band transition calculated for the (S)-configuration of 6,6′-disubstituted-bis-1,1′-spiroindanes agree with the positions and signs of the CD bands observed for the compounds derived from (−)-IIIc, establishing the absolute configuration of this series. The result was confirmed by the X-ray diffraction study of (−)-7,7′-dibromo-derivatives prepared from (+)-IIIa. It was found that these spiro compounds having the (S)-configuration showed a negative CD band in the longest wavelength region, except for the case in which the effect of the charge transfer between two aromatic chromophores overwhelmed that of the dipole-dipole interaction.

It is well known that, in the chiral molecules with the same two ligands at the tetragonal central atom, $X(A_2B_2)$, there are two types of structures, spiro types I and II[1] (Fig. 1). Several molecules of these types have already been resolved[2] and the absolute configuration of some of them has been determined by chemical methods.[3] It is interesting to study the relations between the structure and the CD spectrum of the molecule having C_2 symmetry like spiro type II bearing the aromatic chromophore at positions A or B, from the standpoint of the determination of the absolute configuration and the origin of the optical rotatory power.

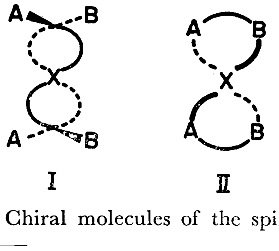

Fig. 1. Chiral molecules of the spiro type.

Curtis and his coworker[4] proved that Barnes's tetrahydroindenoindane derivatives, which were obtained from the reaction of 4-methyl-4-phenylpentane-2-one with acid,[5] had the structures of 3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane. Later the mechanisms of the above reaction were proposed by others.[6] Other bis-1,1′-spiroindane derivatives have also been prepared by Baker and his coworkers and other group[7] by the reaction of phenols and acetone in the presence of acid.

These compounds have rigidly fixed conformation and it is interesting to investigate the spectrum arising from an interaction of the transition dipoles of the same two aromatic chromophores.

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[1] R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem.*, **78**, 413 (1966).

[2] a) W. H. Mills and C. R. Nodder, *J. Chem. Soc.*, **117**, 1407 (1920). b) G. Haas and V. Prelog, *Helv. Chim. Acta*, **52**, 1202 (1969).

[3] a) G. Krow and R. K. Hill, *Chem. Commun.*, **1968**, 430. b) H. Gerlach, *Helv. Chim. Acta*, **51**, 1587 (1968). c) J. H. Brwester and R. S. Jones, Jr., *J. Org. Chem.*, **34**, 354 (1969).

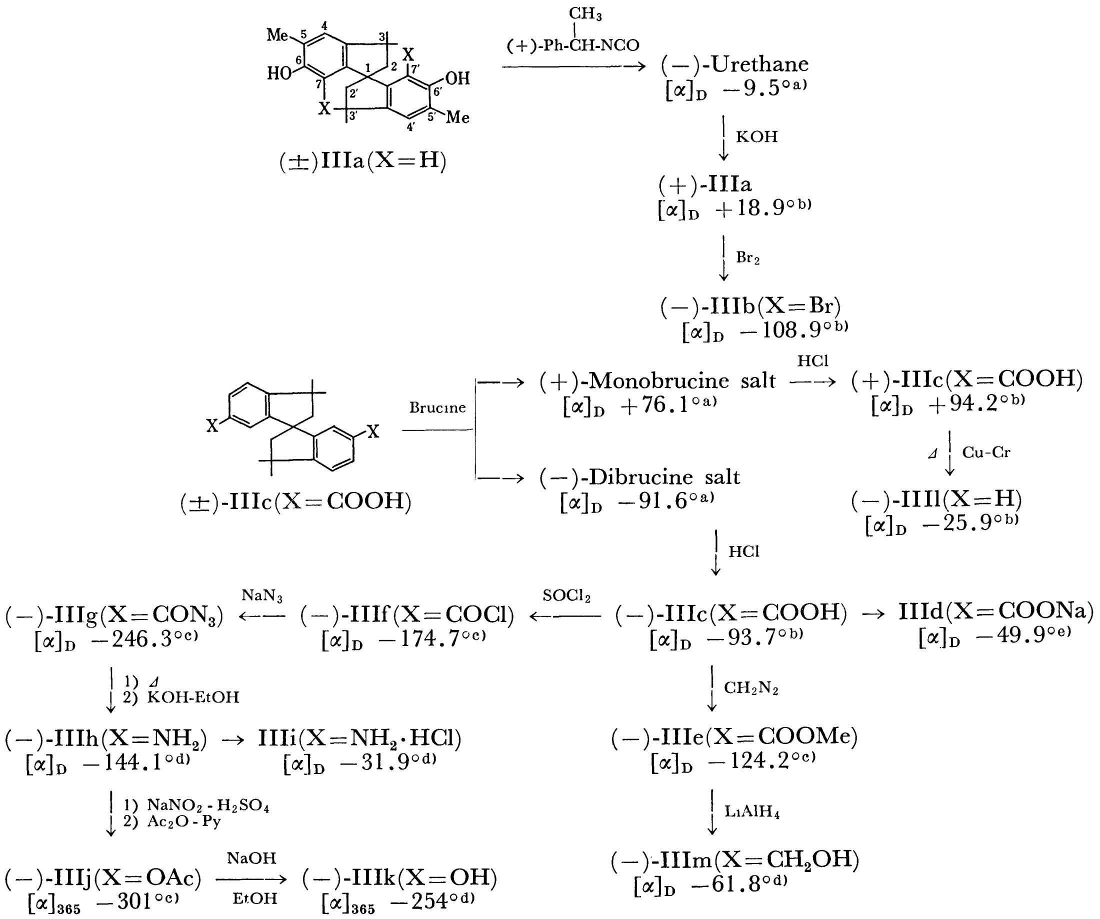
[4] a) R. F. Curtis, *Chem. Ind.* (London), **1960**, 928. b) R. F. Curtis and K. O. Lewis, *J. Chem. Soc.*, **1962**, 418.

[5] a) A. Hoffman, *J. Amer. Chem. Soc.*, **51**, 2542 (1929). b) R. A. Barnes and B. D. Beitchman, *ibid.*, **76**, 5430 (1954).

[6] L. R. C. Barclay and R. A. Chapman, *Can. J. Chem.*, **42**, 25 (1964).

[7] a) W. Baker, *J. Chem. Soc.*, **1934**, 1678. b) C. H. Fisher, R. W. Furlong, and M. Grant, *J. Amer. Chem. Soc.*, **58**, 820 (1936). c) W. Baker and J. C. McGown, *J. Chem. Soc.*, **1938**, 347. d) W. Baker and D. M. Besly, *ibid.*, **1939**, 1421. e) R. F. Curtis, *ibid.*, **1962**, 415.

Chart 1



a) $CHCl_3$ b) dioxane c) isooctane d) methanol e) H_2O

We wish to report the resolution and CD spectrum of this type of compound and the theoretical assignments of absolute configurations on some of them.

Resolution of 6,6'-dihydroxy-3,3,5,3',3',5'-hexamethyl-bis-1,1'-spiroindane, IIIa, which was prepared according to the direction of Baker and Besly,[7] was accomplished after a number of experiments[8] by using (+)-phenethylisocyanate.[9] The optically pure (−)-urethane, $[\alpha]_D$ −8.6° ($CHCl_3$), obtained by fractional recrystallization, was hydrolysed with KOH-EtOH (10%) to give (+)-IIIa, $[\alpha]_D$ +19.4° (dioxane), from which (−)-IIIb, $[\alpha]_D$ −108.9° (dioxane), was prepared by the action of bromine in chloroform.

Meanwhile, (−)-isomer of 6,6'-dicarboxylic acid derivative IIIc, $[\alpha]_D$ −93.7° (dioxane), was obtained by the decomposition of (−)-dibrucine salt, $[\alpha]_D$ −91.6° (MeOH), and also another antipode, (+)-IIIc, $[\alpha]_D$ +94.2° (dioxane), was prepared by the decomposition of (+)-monobrucine salt, $[\alpha]_D$ +76.1° (MeOH).

Optically active diamino derivative, (−)-IIIh, $[\alpha]_D$ −144.1° (MeOH), diacetoxy derivative, (−)-IIIj, $[\alpha]_{365}$ −301° (isooctane) and dihydroxy derivative, (−)-IIIk, $[\alpha]_{365}$ −254° (MeOH) were prepared from (−)-IIIc, and also non-substituted deriv-

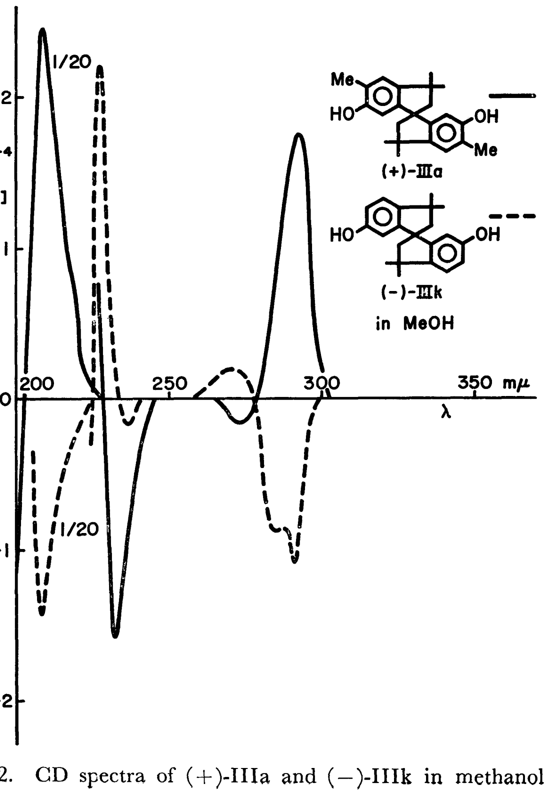


Fig. 2. CD spectra of (+)-IIIa and (−)-IIIk in methanol.

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[8] All attempts to resolve IIIa employing (+)-10-camphorsulfonic acid chloride, (−)-menthoxyacetic acid chloride and, (+)-α-phenchocomphorone-1-isocyanate failed.

[9] T. L. Cairns, *J. Amer. Chem. Soc.*, **63**, 871 (1941).

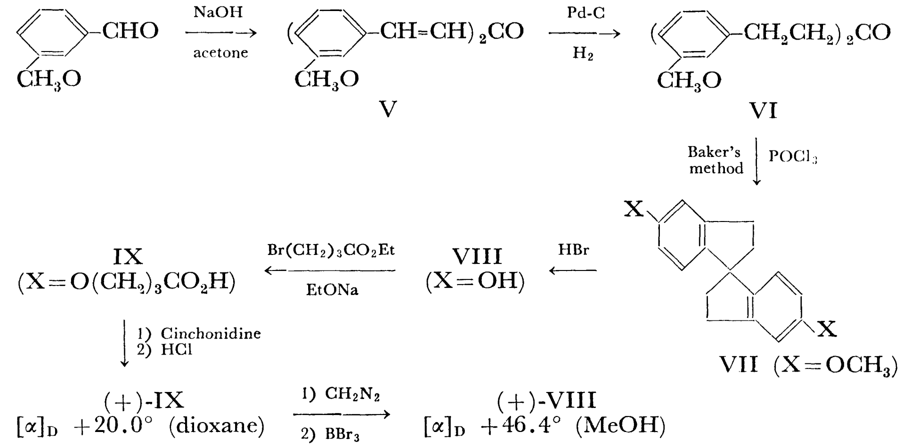

Chart 2

ative, (−)-IIIl, $[\alpha]_D$ −25.9° (dioxane) from (+)-IIIc, according to procedures similar to those used in the racemic ones described in literature.[4] We also obtained di-acid chloride, (−)-IIIf, $[\alpha]_D$ −174.7° (isooctane), and diazide, (−)-IIIg, $[\alpha]_D$ −246.3° (isooctane), stepwisely by applying the Curtius reaction to (−)-IIIc. Dicarbinol, (−)-IIIm, $[\alpha]_D$ −61.8° (MeOH), was prepared by the reduction with $LiAlH_4$ of diester, (−)-IIIe, $[\alpha]_D$ −124.2° (*n*-hexane), which was obtained by the esterification of (−)-IIIc with diazomethane. Configurational correlation among these compounds is shown in Chart 1. In connection with these 6,6′-disubstituted spiroindanes, optically active 5,5′-dihydroxy derivative IX was synthesized by the route described in Chart 2.

Comparing IIIa with IIIk, the aromatic chromophore can be regarded as the same from the viewpoint an electronic transition because the methyl group gives little perturbation effects to phenol chromophore. Thus, we considered that if optically active IIIa and IIIk had the same absolute configuration, these two derivatives would give almost the same Cotton effects. In fact, the CD spectrum of (+)-IIIa appears almost opposite to that of (−)-IIIk as shown in Fig. 2. An empirical rule can be obtained from Chart 1 and Table 1, that the compounds, (−)-IIIc—(−)-IIIm, including non-substituted spirane, (+)-IIIl, show negatively signed CD in the longest wave length [It should be noted that (−)-IIIl was derived from (+)-IIIc and hence (+)-IIIl must be correlated to the same configuration as (−)-IIIc. But even in this case, the above empirical rule was found to be valid.]. (+)-IIIa shows positively signed CD in the longest wave length. From the above observations, it was decided that the absolute configuration of (+)-IIIa and (−)-IIIb is opposite to that of the other derivatives, (−)-IIIc—(−)-IIIm, cited in Table 1.

The CD and UV spectra of these derivatives are shown in Table 1. Accessible CD spectra of these compounds consist of three bands which are termed α, *p* and β, from the longer wavelength according to the classification of Clar. From this Table it seems that the intensity and the polarization direction of the electronic transition or each aromatic chromophore have direct influence on CD spectra. For polysubstituted benzenes, a quantity called the spectroscopic monent has been assigned to each group by Platt.[10] Employing the spectroscopic moment, the absorption intensities and the transition moment directions may be calculated by the vector addition formula. The spectroscopic moment is considered to be useful for interpreting the CD of these derivatives. Following the value of the spectroscopic moment and the origin of the Cotton effect, we divided the derivatives into classes, I, II, III, and IV.

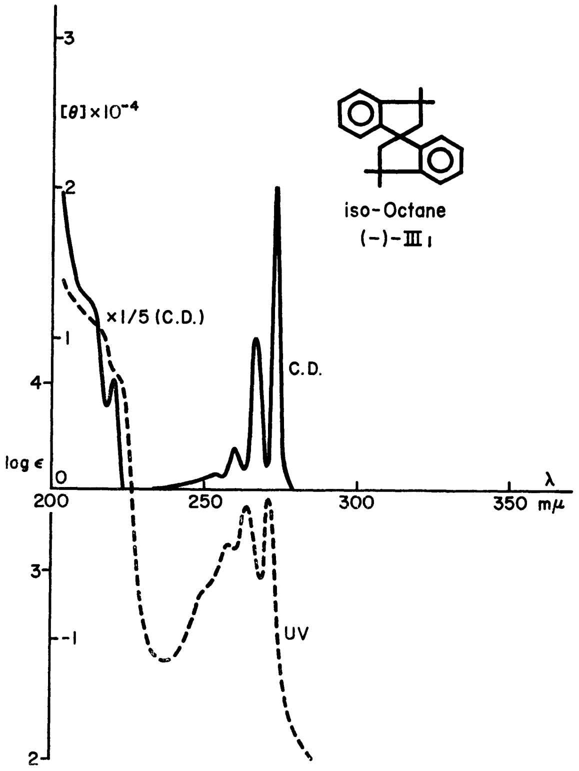

Fig. 3. CD and UV spectra of (−)-IIIl in isooctane.

In class I, the substituent groups at the position 6

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[10] J. R. Platt, *J. Chem. Phys.*, **19**, 263 (1951); J. Petruska, *ibid.*, **34**, 1111, 1120 (1961).

TABLE 1. UV AND CD SPECTRA OF THE EXAMINED SPIRO COMPOUNDS

Compd	Solv.	UV $\lambda_{m\mu}$ ($\varepsilon \times 10^3$)			CD $\lambda_{m\mu}$ ($[\theta]) \times 10^3$)		
		α	P	β	α	P	β
(+)-IIIa	MeOH	286 (8.90)	223^i (16.5)	202.3 (66.7)	292 (+17.6)	231 (−15.8)	209 (+250)
					274 (−1.65)	223^i (+14.6)	
(−)-IIIb	Dioxane	293 (8.84)			293 (−5.25)	245 (−11.2)	211 (+100)
		286 (7.77)				231 (−5.18)	
(−)-IIIc	MeOH	288 (2.43)	240 (23.4)	202.5 (55.2)	289 (−19.4)	249 (−95.0)	217 (−337)
		278 (2.78)			283 (−7.76)	232 (+65.0)	
					275 (+2.55)		
(−)-IIId	0.1 N NaOH	284 (2.01)	236 (19.4)		285 (−23.8)	245 (−66.0)	219 (−137)
		274 (2.59)			277 (−13.3)	232 (+64.7)	$208^!$ (+169)
(−)-IIIe	MeOH	288 (2.69)	241 (21.8)	216 (38.8)	290 (−23.4)	251 (−97.3)	218 (−288)
		279 (3.05)		202 (50.8)	282 (−9.14)	234 (+60.1)	209 (−336)
		270 (2.52)			275 (+3.23)		$198^!$ (+366)
(−)-IIIf	Isooctane	299 (3.83)	262^i (44.0)	222.7 (52.3)	300 (−18.2)	264 (−198)	223 (−175)
		289 (4.98)	256.5 (46.5)	206 (50.8)	291 (−10.2)	248 (+72.9)	212 (−278)
(−)-IIIg	Isooctane	298 (4.82)	263 (37.5)	223 (40.7)	299 (−25.4)	267 (−173)	222^i (−175)
		287 (6.41)	258 (37.5)	206 (41.3)	290 (−17.6)	246 (+34.3)	214 (−268)
(−)-IIIh	MeOH	296 (5.57)	236 (17.0)	207 (72.5)	299 (−14.1)	244 (−25.7)	220 (−607)
						233 (+62.7)	
(−)-IIIi	HCl - MeOH	275 (2.99)	225^i (10.2)		275 (−58.4)	227 (+39.3)	$210^!$ (−266)
		268 (2.44)	220^i (16.6)		269 (−35.3)	221^i (−82.2)	
		266 (2.47)	215^i (19.7)		261 (−10.6)		
		261 (1.77)			247 (−5.14)		
(−)-IIIj	Isooctane	276 (2.79)	217^i (17.2)		279 (−15.2)	237 (−2.71)	$208^!$ (−246)
		270 (2.69)			271 (−10.8)	226 (+28.1)	
		262^i (1.87)					
(−)-IIIk	MeOH	289 (6.24)	220^i (16.5)		290 (−10.9)	236 (−1.98)	209 (−289)
		284 (6.58)			284 (−8.05)	229 (+18.6)	
					270 (+1.98)		
(−)-IIIl	Isooctane	272 (2.59)	223 (11.0)	213^i (22.0)	273 (+20.3)	221 (+36.6)	
		265 (2.24)	218^i (18.2)		267 (+10.4)	213^i (+62.0)	$203^!$ (+99.0)
		257 (1.43)			260 (+2.97)		
					253 (+0.99)		
(−)-IIIm	MeOH	277 (2.58)	222^i (19.6)		277 (−25.7)	228 (+37.1)	$210^!$ (−383)
		268 (2.15)	217^i (22.0)		271 (−12.4)	223^i (−32.2)	
		263 (1.46)			263 (−1.90)		
(+)-VIII	MeOH	289^i (4.33)	231.8 (12.5)		289.5 (+19.2)	232.5 (−30.7)	
		282.5 (5.12)			271.5 (−0.89)		

!: last reading. i: inflection.

and 6′ of III influence the absorption spectrum of benzene to a lesser extent. (—)-IIIi, (—)-IIIl and (—)-IIIm belong to this class. They have very sharp Cotton effects in all transitions. In α-band, the Cotton effects attributable to the vibrational transition are all of negative sign, but in *p*-band, two oppositely signed Cotton effects are observed except for (—)-IIIl. In (—)-IIIl as shown in Fig. 3, the sign of all Cotton effects in the region accessible with the apparatus (205 mμ), is positive, but that of specific rotation at D-line is negative, from which it is deduced that there are very strong negatively signed Cotton effects in far-UV region.

In class II, the substituents have a comparatively large value in Platt's spectroscopic moment. In this class, (+)-IIIa, (—)-IIIc—g, and (—)-IIIj—k are included and the CD spectra seem to split into oppositely signed pair centered at each absorption region. That is, (—)-IIIk has the oppositely signed pair of Cotton effects centered at α- and *p*-bands, as shown in Fig. 2, although the rotational strengths are not the same. IIIa with the opposite absolute configuration gives negative and positive CD bands at longer and shorter wavelengths, respectively, in the region of the *p*-band.

A more typical example is observed in (—)-IIIc and (—)-IIIe (as shown in Fig. 4 on (—)-IIIc). Their Cotton effects in *p*-band are oppositely signed and almost similar in rotational strength, although in α-band they are not the same in magnitude.

(—)-IIIc was measured in a number of solvents but no remarkable solvent effect was observed. Moreover, the CD spectrum of (—)-IIId is similar to that of (—)-IIIc except for a small positively signed Cotton

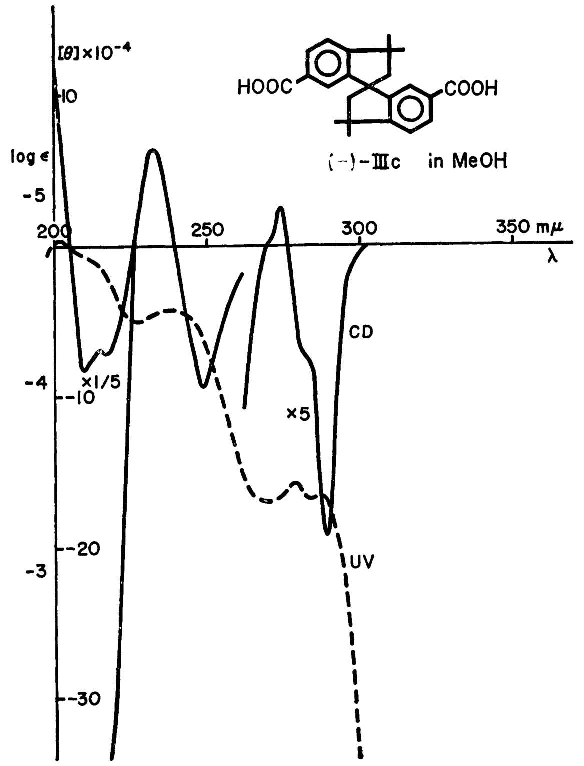

Fig. 4. CD and UV spectra of (−)-IIIc in methanol.

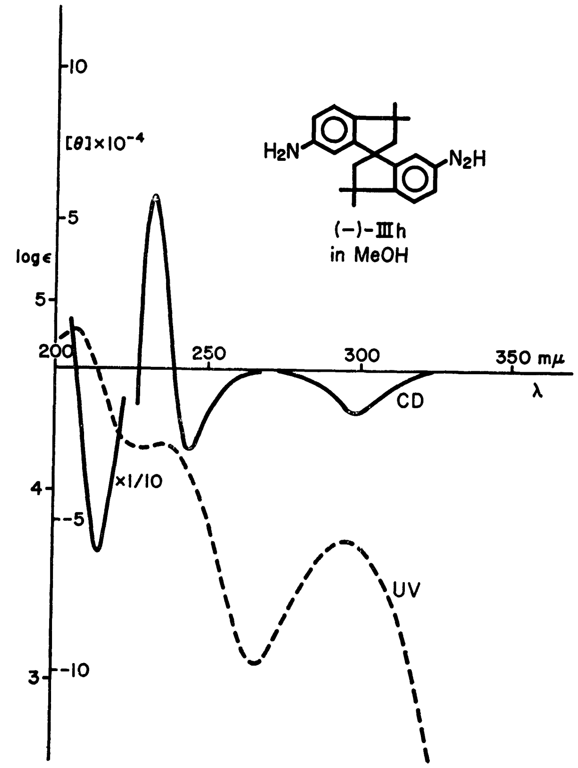

Fig. 5. CD and UV spectra of (−)-IIIh in methanol.

effect observed in α-band of (−)-IIIc.[11] (−)-IIIf and (−)-IIIg show the shift to a higher wavelength, but the curve is similar to that of (−)-IIId. From the similarlity in CD of the derivatives with COX group, it can be said that the polarization direction of the transition in the benzoyl chromophore is not affected so much, even if the group X is changed.

In class III, the substituent group interacts very strongly with the benzene ring. (−)-IIIh alone is contained in this class. Its spectrum (shown in Fig. 5) is also a typical example of splitting, as Mason and his coworkers[12] have pointed out in two-fold rotation axis molecules with aniline chromophore. But the α-band shows only negatively signed Cotton effect.

In class IV, the splitting of the CD band could not be observed, as shown in Fig. 6. (−)-IIIb is the only one example. In this molecule the bromo substituent of one aromatic chromophore is placed just over the other within the region where the exchange integral has a large value, as shown in X-ray crystallography.[13] Therefore one aromatic chromophore interacts with the other owing rather to the exchange force than the dipole-dipole interaction.

In these dissymmetrically situated dimers of aromatic chromophore, a given monomer excitation is doubly degenerated to a zero-order, but dipole-dipole interaction between the two excitation monents splits the degeneracy and gives two optically active resultant transitions, one with A and the other with B symmetry in the point group C_2.[12,14]

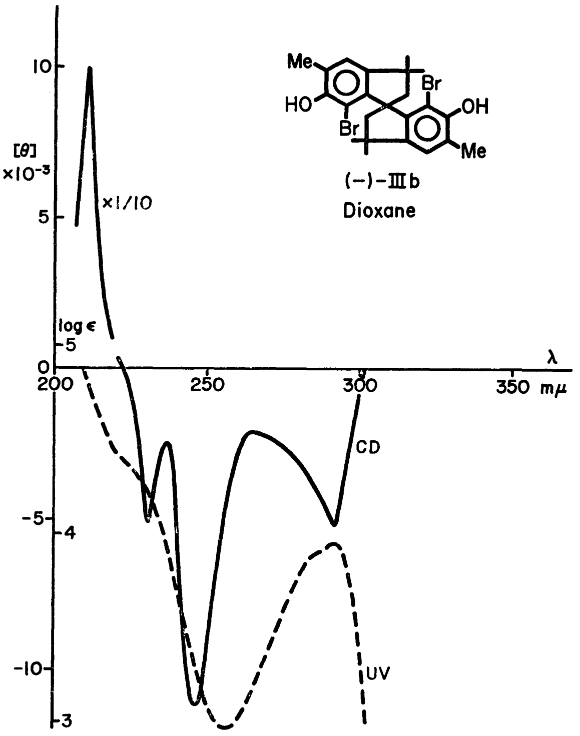

Fig. 6. CD and UV spectra of (−)-IIIb in dioxane.

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[11] We found that CD spectra of 11 (*endo*), 12 (*endo*)-dicarbomethoxy-9,10-dihydro-9,10-ethanoanthracene-1,5-dicarboxylic acid and its sodium salt show a remarkable difference at around 230 mμ. The details will be reported in the near future.

[12] a) S. F. Mason and G. W. Vane, *J. Chem. Soc.*, *B*, **1966**, 370. b) S. F. Mason, K. Schofiels, R. J. Wells, J. S. Whitehurst, and G. W. Vane, *Tetrahedron Lett.*, **1967**, 137. c) S. F. Mason, G. W. Vane, and J. S. Whitehurst, *Tetrahedron*, **23**, 4087. (1967).

[13] M. Shiro, S. Hagishita, and K. Kuriyama. Details will be published in a subsequent paper.

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

From the assumption that an excitation moment of the benzenoid chromophore is a point dipole located at the center of the benzene ring, the rotational strengths R of the two transitions are given by

$$R_{\mathrm{A}} = -R_{\mathrm{B}} = \pi\bar{\nu} d\rho^3 \cos v \;\cos t \tag{1}$$

and the separation $\Delta\bar{\nu}$ between the two resultant transition frequencies by

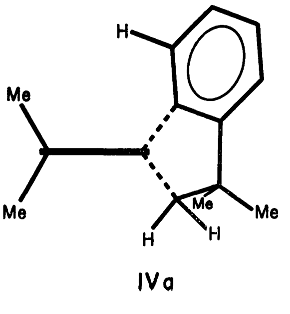
$$\Delta\bar{\nu} = \bar{\nu}_{\mathrm{A}} - \bar{\nu}_{\mathrm{B}} = 2\rho^2(\cos^2 v - \cos^2 t + 2\cos^2 r)/hcd^3 \tag{2}$$

In these expressions ρ is the transition dipole moment of the transition in the isolated chromophore which occurs at a wave number frequency of $\bar{\nu}$ and d is the distance between the centres of the two benzene rings. Each of the two excitation dipoles ρ have components directed parallel to the Cartesian axes of the dimeric system, and the magnitudes of the components are determined by the cosines of the vertical, tangential and radial angles, v, t, and r, respectively, between the excitation dipole and the local Cartesian axes, in which the x-axis is definied by the line joining the centres of the two benzene rings and z is the C_2 symmetry axis.

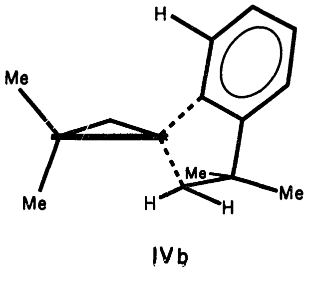
The stereochemical parameters d, v, t, and r necessary for the calculation of rotational strengths and the frequency intervals between the transitions depend upon the orientation of the excitation dipole within the benzenoid chromophore as well as the mutual stereochemical disposition of the two chromophores.

In the present case the values of the spectroscopic moments listed by Platt and an other[10)] are applicable and the direction of the transition moment of each monomer is obtained by the vector addition of the spectroscopic moments induced by each substituent. The alkyl bridge which makes up the spiro skeleton is also regarded as a substituent and the value of t-butyl group was adopted. However, NH_2 group interacts so strongly with benzene that we neglected the effect of the alkyl bridge in (−)-IIIh and used the direction of the α- and p-bands of aniline. In other cases the following values were used for calculation: COOH(−28); OH(34); t-butyl(2); CH_2OH (−7); methyl(7).

Values of the parameters, d, v, t, and r are determined not only by the transition moment directions in the benzenoid chromophore but also by the spatial relations between the two chromophores. The stereochemical parameters have unique values in the rigid dimeric systems, but they have a range of values in the case of spiro indanes, owing to the conformational lability of the molecule. Models indicate that the extreme forms of the five membered ring in indanes are the planar (IVa) and the envelope conformation (IVb), in which the carbon atom at position 2 is moved out of the plane of the other four carbon atoms by 0.285 Å and the carbon atom at the position 2' is quasiaxial.



IVa



IVb

It has been reported[15)] that the puckering of the cyclopentene ring having an atom out of the plane by an amount up to about 0.3 Å gave no change on the potential energy of the system. If we consider the 1,3-di-quasiaxial interactions between one of the gem-dimethyl group at position 3 and the methylene group at position 2', the planar conformation (IVa) would be probably more stable. In the cases of (−)-IIIh and (−)-IIIl (Table 2), the qualitative forms of the theoretical CD spectra depend only upon the configuration and are independent of the conformation. Therefore, the sets of stereochemical parameters, v, t, and r for the planar conformation of (S)-configuration are calculated from the coordinates provided by the X-ray diffraction study of 5,6-dibromoindane,[16)] and are listed in Table 2. The theoretical and experimental results indicate that for (−)-IIIl and (+)-IIIm which belong to Class I, the absolute configurations can not be predicted. The following may be one of the main reaons. We approximated the alkyl bridge to the t-butyl group, but as the value of the spectroscopic moment of the substituent at positions 6 and 6' is small, the small change is value of position 1 should exert great influence on the direction of the excitation moment. Therefore the sign of rotational strength and/or the separation of frequencies might be changed.

An amino group interacts so strongly with the benzene ring that the contribution of other substituents can be neglected as compared to that of the amino group. Therefore, the direction of the transition dipole moment in the isolated chromophore of (−)-IIIh is independent of the change in the value of the spectroscopic moment of other substituents. In the case of (−)-IIIh, the calculated rotational strengths and separation indicate that the signs of the two CD bands associated with the p-band should be negative and then positive, from longer to shorter wavelength for (S)-configuration (Table 2). Although the CD in the α-band region shows only a negative sign, the observed CD bands in the region of the absorption maximum at 236 mμ lie clearly in the expected order (Fig. 5). Thus it is deduced that (−)-IIIh has (S)-configuration. The consistency between the calculated and experimental signs of the rotational strengths associated with the p-band for the derivatives in class II supports the assignment of (S)-configuration to the compounds derived from (−)-IIIc.

In class II and III the theoretical CD spectra for (S)-configuration lie in the order positive and then negative to lower wavelength in the region of the α-band, but the sequence of signs of the observed CD bands is opposite except in (−)-IIIh which shows only negative CD spectrum.

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15) C. W. Beckett, N. K. Freeman, and K. S. Pitzer, *J. Amer. Chem. Soc.*, **70**, 4227 (1948).

16) A. Kossiakoff and H. D. Springall, *J. Amer. Chem. Soc.*, **63**, 2223 (1941).

TABLE 2. ROTATIONAL STRENGTHS AND FREQUENCY INTERVALS OF (S)-CONFIGURATION

Compd	Band	Component	Found				Theoretical				
			D (10^{-36} cgs)	λ mμ	R (10^{-40} cgs)	$\lvert\nu_A-\nu_B\rvert$ (cm^{-1})	cos r	cos t	cos v	R (10^{-40} cgs)	$\nu_A-\nu_B$ (cm^{-1})
(+)-IIIa^E	α	B A	2.70	286	−5.30 +0.41	2250	−.908	+.278	−.314	+13.2 −13.2	+340
	P	A B	5.00	223	+3.71 −1.94	1553	+.031	+.769	+.638	+178 −178	−68.6
(−)-IIIc	α	B A	1.08	278	−4.18 +0.26	1409	−.861	+.498	−.109	+3.36 −3.36	+101
	P	B A	10.0	240	−34.3 +16.9	2944	+.385	+.594	+.706	−281 +281	+334
(−)-IIIh	α	B A	2.97	296	−7.23	—	−.878	+.454	−.154	+12.3 −12.3	+305
	P	B A	8.60	236	−8.70 +14.6	1935	+.248	+.677	+.693	−274 +274	+92.7
(−)-IIIk	α	B A	2.61	285	−4.30 +0.63	2554	−.888	+.419	−.189	+11.6 −11.6	+283
	P	B A	4.20	224	−0.02 +2.38	2470	+.201	+.701	+.684	−145 +145	+18.0
(+)-IIIl^E	α	B A	0.64	270	−3.06	—	+.648	+.358	+.672	−9.16 +9.16	+56.4
	P	B A	6.38	217	−17.1	—	−.645	+.734	+.210	−73.0 +73.0	+163
(−)-IIIm	α	B A	0.83	277	−4.67	—	−.798	+.603	+.014	−0.40 +0.40	+57.0
	P	B A	5.45	220	+3.51 −1.86	3089	+.448	+.547	+.707	−153 +153	+247
(−)-IIIh*	α	B A	2.97	296	−7.23	—	−.908	+.412	−.078	+4.97 −4.93	+360
	P	B A	8.60	236	−8.70 +14.6	1935	+.198	+.584	+.787	−261 +261	+250
(+)-IIIl^{E}*	α	B A	0.64	270	−3.06	—	+.626	+.300	+.720	−8.00 +8.00	+63.3
	P	B A	6.38	217	+17.1	—	−.687	+.649	+.327	−97.7 +97.7	+328
(−)-VIII^E	α	A B	1.50	288	−6.17 +0.10	2290	+.282	−.822	−.485	+34.3 −34.3	−30.6
	P	B A	5.62	232	−9.77	—	+.866	+.016	−.500	+3.01 −3.01	+741

* Envelope conformation. E: enantiomer is measured.
Theoretical values were obtained from equations 1 and 2.

The ambiguity of the assignment of the absolute configuration due to the inconsistency between the theoretical and the experimental CD spectra in the α-band is avoided by the X-ray analysis of (−)-7,7′-dibromo-6,6′-dihydroxy-derivative, (−)-IIIb, which has the (R)-configuration. Thus, the inconsistency in α-band comes from the use of the point dipole approximation and the neglect of configurational interaction between transitions of the same symmetry. But even if the exciton theory cannot explain the CD in α-bands satisfactorily, it should be noted that all these spiro compounds having (S)-configuration except for class IV show the CD of negative sign in the longest wavelength. This means that the sign of the CD in the longest wavelength region is always determined by the configuration of spiro atom, *i.e.* the spatial arrangement of the two benzene rings.

In relation to the above consideration, it was observed that the CD of 5,5′-dihydroxyspiroindane, (+)-VIII, is similar to that of the corresponding 6,6′-derivatives, particularly in the region of α-band. The sign of the CD band was, from the longest wavelength to shorter, positive and negative in α-band, and negative in *p*-band (Fig. 7). From the feature of the CD curve (+)-VIII is considered to have (R)-configuration.

Applying the exciton theory to (R)-VIII, the calculated value of the CD should have the sign in the order negative and positive both in α-band and in *p*-band. This is contrary to the observed result. But the sign of the CD band in α-band may be reversed by a small change in the value of the parameters as in the case of spiroindane (−)-IIIl where the width of the splitting is small (−31 cm^{-1}).

The fact that the observed rotational strength in the *p*-band is greater than that calculated from exciton

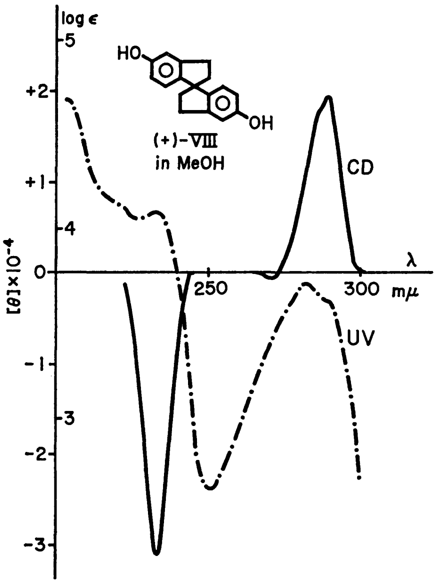

Fig. 7. CD and UV spectra of (+)-VIII in methanol.

theory may be considered to reflect the contribution from the mixing of other local transitions.

At any rate, exciton theory is not effective for deciding the absolute configuration of (+)-VIII, which should be confirmed by its correlation with other spiro compounds.

Experimental

All melting points were uncorrected. Optical rotations were measured on a Perkin Elmer polarimeter Model 141 using a 1-dm quartz cell. CD spectra were taken with a JASCO Model ORD/UV-6 and a Roussel-Jouan Dichrograph Type B. The UV spectra were run on a Hitachi Model EPS-3T spectrometer. The NMR spectra were taken at 60 Mc with a Varian A-60 spectrometer using TMS as internal standard. The IR spectra were measured on a JASCO Model DS 402G doublemonochromatic spectrophotometer in $CHCl_3$ solution. The mass spectra were measured on a Hitachi RMU-6 Single Focus Mass spectrometer.

Resolution of 6,6'-Dihydroxy-3,3,5,3',3','5-hexamethy-bis-1,1'-spiroindane (+)-IIIa. The mixture of (+)-IIIa (1.07 g), which was prepared according to the procedure of Baker and Besly,[7d] (+)-α-phenethylamine[9] (0.95 g), $[\alpha]_D$ +1.96° (*c* 1.890, benzene), and one drop of pyridine in dry toluene (10 m*l*) was heated under reflux for 25 hr. The solvent was distilled off and the residue was crystallized from toluene: *n*-hexane (405 mg). The (−)-diurethane was recrystallized from benzene three times to afford pure diastereomer (216 mg), mp 218—219°C. $[\alpha]_D$ −9.5° (*c* 0.200, $CHCl_3$). IR ν_{max} 3445, 1738 cm^{-1}.

Found: C, 78.22; H, 7.26; N, 4.17%. Calcd for $C_{41}H_{46}N_2O_4$: C, 78.06; H, 7.35; N, 4.44%.

(−)-Diurethane (216 mg) obtained above, and KOH-EtOH (10%, 5 m*l*) were heated under reflux for 6.5 hr. After cooling, the solution was acidified with 4 N HCl and crystalline product was collected, washed with H_2O and dried (100.6 mg). Recrystallization from benzene: *n*-hexane gave colorless leaflet (20.9 mg), mp 220—221°C. [α] +19.4° (*c* 0.194, dioxane). The IR spectrum in $CHCl_3$ was identical with that of racemic compound.

(−)-7,7'-Dibromo-6,6'-dihydroxy-3,3,5,3',3',5'-hexamethyl-bis-1,1'-spiroindane (−)-IIIb. Bromine (1.0 g) in $CHCl_3$ (20 m*l*) was dropped in to a solution of (+)-IIIa (150 mg) in $CHCl_3$ (5 m*l*) with stirring until the color did not fade any more. After further stirring for 20 min, EtOH was added. Crystals were filtered (138 mg), and then recrystallized from $CHCl_3$: EtOH to give prisms, mp 273—273.5°C. $[\alpha]_D$ −108.0°C (*c* 0.213, dioxane). NMR (in $CDCl_3$) τ: 8.69 (s, 6H), 8.63 (s, 6H), 7.82 (d, *J*=13.0 Hz, 2H), 7.69 (s, 6H), 7.50 (d, *J*=13.0 Hz, 2H), 4.47 (s, 2H), 3.14 (s, 2H). Mass spectrum: *m/e* 496, 492 (molecular ion). IR ν_{max} 3515 cm^{-1}.

Found: C, 55.92; H, 5.29; Br, 33.04%. Calcd for $C_{23}H_{26}Br_2O_2$: C, 55.89; H, 5.30; Br, 32.34%.

Resolution of 3,3,3',3'-Tetramethyl-bis-1,1'-spiroindane-6,6'-dicarboxylic Acid (−)-IIIc and (+)-IIIc. (±)-IIIc was prepared according to the procedure of Curtis.[7e] Mass spectrum: m/e 364 (parent peak).

Found: C, 76.40; H, 6.74%. Calcd for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64%.

(±)-IIIc (12.0 g) and brucine·$2H_2O$ (28.4 g) in 99.5% EtOH (15 m*l*) were heated under reflux for 2 hr and then left to stand overnight at room temperature. The crystals were collected, washed with EtOH, dried *in vacuo* and then recrystallized from EtOH three times (6.3 g). $[\alpha]_D$ −91.6° (*c* 0.32, $CHCl_3$).

From the mother liquor of the reaction, EtOH was distilled off under reduced pressure. The residue was crystallized from acetone. The crude diastereomer was purified by recrystallization from MeOH: $CHCl_3$ five times (1.96 g). $[\alpha]_D$ +76.1° (*c* 0.551, $CHCl_3$).

(−)-Salt (6.3 g) was shaken with 6 N HCl (50 m*l*) at 50°C for 30 min. Crystals were filtered, washed with H_2O, dried *in vacuo*, and recrystallized from dioxane: acetone (1.57 g). $[\alpha]_D$ −93.7° (*c* 0.206, dioxane). (+)-Salt (1.25 g) was treated as above to give (+)-IIIc (476 mg). $[\alpha]_D$ +94.2° (*c* 0.243, dioxane).

(−)-Dimethyl-3,3,3',3'-tetramethyl-bis-1,1'-spiroindane-6,6'-dicarboxylate (−)-IIIe. A solution of diazomethane in ether was added to a solution of (−)-IIIc (200 mg) until the yellow color still remained. Ether was distilled off. The residue was chromatographed on Al_2O_3 (6.0 g, Woelm Co., Act. II) in benzene and then crystallized from *n*-hexane to give prisms (99.8 mg), mp 170.5—171°C. $[\alpha]_D$ −124.2° (*c* 0.233, *n*-heptane). Mass spectrum: *m/e* 392 (molecular ion). IR ν_{max} 1717 cm^{-1}.

Found: C, 76.79; H, 7.44%. Calcd for $C_{25}H_{28}O_4$: C, 76.50; H, 7.19%.

(−)-3,3,3',3'-Tetramethyl-bis-1,1'-spiroindane-6,6'-dicarboxylic Acid Chloride (−)-IIIf. (−)-IIIc (1.0 g) and thionylchloride (3.3 g) in abs. THF (5.0 m*l*) were heated under reflux for 1 hr. THF and excess thionylchloride were evporated under reduced pressure. The residue was crystallized from *n*-hexane and then recrystallized further two times (773 mg), mp 175—177°C. $[\alpha]_D$ −174.7°C (*c* 0.314, isooctane). IR ν_{max} 1755 cm^{-1}. Mass spectrum: *m/e* 400, 404 (molecular ion).

Found: C, 68.70; H, 5.63; Cl, 17.86%. Calcd for $C_{23}H_{22}O_2Cl_2$: C, 68.83; H, 5.53; Cl, 17.67%.

(−)-3,3,3',3'-Tetramethyl-bis-1,1'-spiroindane-6,6'-dicarboxylic Acid Azide (−)-IIIg. Sodium azide (230 mg) in H_2O was added in one portion to a solution of (−)-IIIf (718 mg) in acetone (5 m*l*) under cooling with vigorous stirring. After stirring for 15 min, oily precipitate was extracted with CH_2Cl_2 at 0°C. CH_2Cl_2 layer was washed with ice-water and dried with Na_2SO_4. CH_2Cl_2 was distilled under reduced pressure at room temperature. The residue was crystallized from *n*-hexane (271 mg), mp 92—93°C

(dec). $[\alpha]_D$ −246.3° (*c* 0.166, isooctane). IR ν_{max} 2143, 1691 cm^{-1}.

(−)-6,6′-Diamino-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane (−)-IIIh. (1) (−)-IIIg (265 mg) in dry benzene (10 m*l*) was heated under reflux for 6 hr. Benzene was distilled off under diminished pressure. The IR spectrum showed N : C : O stretching absorption at 2270 cm^{-1}. This isocyanate was used for the next hydrolysis without further purification. The oily residue and 10% KOH-EtOH (10 m*l*) were heated under reflux for 2 hr. After cooling, H_2O (20 m*l*) was added and the mixture was extracted with benzene. The benzene solution was washed with H_2O and dried on Na_2SO_4. Benzene was distilled off. The residue was crystallized from benzene: *n*-hexane and then further sublimated at 170°C/2 mmHg (136 mg), mp 165—167°C. $[\alpha]_D$ −144.1° (*c* 0.270, MeOH). Mass spectrum: *m/e* 306 (molecular ion). IR ν_{max} 3380, 3458 cm^{-1}.

Found: C, 82.08; H, 8.56; N, 8.75%. Calcd for $C_{21}H_{26}N_2$: C, 82.30; H, 8.55; N, 9.14%.

(2) (−)-IIIc (370 mg) was treated according to the procedure of Curtis[7e] to give (−)-IIIh (236 mg), mp and the IR spectrum were identical with those of the above product.

(−)-6,6′-Diacetoxy-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane, (−)-IIIj. This was prepared according to the procedure of Curtis,[7e] and recrystallized twice from *n*-hexane, mp 152—154°C. $[\alpha]_{365}$ −301 (*c* 0.00803, isooctane).

(−)-6,6′-Dihydroxy-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane, (−)-IIIk. (−)-IIIj was hydrolyzed by the methods of Curtis,[7e] mp 96—98°C. $[\alpha]_{365}$ −254 (*c* 0.01284, MeOH). Mass spectrum: *m/e* 308 (parent peak). IR ν_{max} 3605 cm^{-1}.

Found: C, 79.07; H, 7.98%. Calcd for $C_{21}H_{24}O_2 \cdot 1/2H_2O$: C, 79.45; H, 7.94%.

(−)-3,3,3′,3′-Tetramethyl-bis-1,1′-spiroindane (−)-IIIl. Decarboxylation of (+)-IIIc was performed by using copper chromite catalyst according to literature,[7e] mp 122.0—122.5°C. $[\alpha]_D$ −25.9° (*c* 0.315, dioxane). Mass spectrum *m/e* 276 (molecular ion). IR ν_{max} 1600 cm^{-1}.

Found: C, 91.26; H, 8.79%. Calcd for $C_{21}H_{24}$: C, 91.26; H, 8.79%.

(−)-6,6′-Dihydroxymethyl-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane (−)-IIIm. $LiAlH_4$ (30 mg) in abs. ether (10 m*l*) was added to a solution of (−)-IIIe (86.2 mg) at room temperature. The reaction mixture was made to boil and then stirred for 1.5 hr. Excess $LiAlH_4$ was decomposed by dropping AcOEt and then HCl under cooling. The mixture was extracted with ether and ether layer was washed with $NaHCO_3$-H_2O and H_2O and then dried on Na_2SO_4. Solvent was distilled off and the residue was crystallized from *n*-hexane (54.1 mg). $[\alpha]_D$ −61.8° (*c* 0.647, MeOH), mp 144—145°C. Mass spectrum: *m/e* 336 (molecular ion). IR ν_{max} 3600, 3440 cm^{-1}.

Found: C, 82.02; H, 8.45%. Calcd for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39%.

Bis-(3-methoxybenzal)-acetone (V). A mixture of 50.0 g of *m*-methoxybenzaldehyde and 10.7 g of acetone in 25 m*l* of ethanol was added dropwise with stirring to the water-cooled alkaline solution (36.6 g of sodium hydroxide, 25 m*l* of ethanol and 370 m*l* of water). After stirring for 2 hr, the water layer was extracted with ether, the organic layers were combined and washed with water. Working up as usual furnished yellow oil, 60.1 g, which was chromatographed on a column of 90 g of Al_2O_3 (act. III). Benzene-petroleum ether and benzene eluate furnished 40.8 g oil, which solidified on standing. 2,4-Dinitrophenylhydrazone, mp 175.5—176.8°C.

Found: C, 62.90; H, 4.72; N, 11.77%. Calcd for $C_{25}H_{22}O_6N_4$: C, 63.28; H, 4.67; N, 11.81%.

Bis-(3-methoxybenzyl)-acetone (VI). 10 g of dienone (V) in 500 m*l* of acetone was hydrogenated on 1.0 g palladium-charcoal (10%). The uptake of hydrogen amounted to 110% of the theory in 90 min. After addition of a few drops of methanol, the catalyst was removed by filtration and the solvent was evaporated. The residual oil was taken in benzene and filtered on 20 g of Al_2O_3 (act. III).

Six runs from the total amount of 89.4 g of dienone in analogous procedure gave 85.3 g of crude oil, which was dissolved in 300 m*l* acetic acid and treated with a chromic acid solution (19.0 g of chromic trioxide, 18 m*l* of water and 150 m*l* of acetic acid). After the usual procedure the obtained oil, 72.2 g, was dissolved in benzene eluate ketone (VI) as yellow oil, 45.4 g (50%).

5,5′-Dimethoxy-bis-1,1′-spiroindane (VII). 5.2 g Bis-(3-methoxybenzyl)-acetone (VI) and 22 m*l* of freshly distilled phosphorus oxychloride dissolved in 57 m*l* of benzene were refluxed 4 hr. The reaction mixture was poured into ice-water and treated as usual. The obtained brown oil dissolved in petroleum ether was filtered on Al_2O_3 (act. III), and crystallized from petroleum ether, Yield 2.75 g (56.8%), mp 67—78°C. Recrystallisation raised the melting point to 83—85°C.

Found: C, 81.47; H, 6.61%. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81%.

5,5′-Dihydroxy-bis-1,1′-spiroindane (VIII). A mixture of 14.5 g of dimethoxy compound (VII), 120 m*l* of concentrated hydrobromic acid (d=1.48) and 120 m*l* of acetic acid was refluxed for 5 hr. After cooling, the reaction mixture was poured into 800 m*l* of water, extracted with ether and treated as usual. The obtained viscous oil was dissolved in benzene-acetone (6 : 1) and filtered on 20 g Al_2O_3 (act. III). Crystallisation from benzene yielded 7.4 g (57%) crystals, mp 175—178°C.

Found: C, 81.04; H, 6.29%. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

Bis-1,1′-spiroindane-5,5′-dioxybutyric Acid (IX). 3.00 g of dihydroxyspiroindane (VIII) in 8.3 m*l* of absolute ethanol was added under reflux into a sodium ethoxide solution (1.1 g of sodium, 20 m*l* of abs. ethanol). To the mixture was added 18.0 g of ethyl-bromobutyrate. After refluxing for 90 min, a sodium ethoxide solution (0.54 g of sodium in 5.7 m*l* of absolute ethanol) and subsequently 6.07 g of bromo ester were added again. Refluxing was continued for 6 hr and the mixture was allowed to stand overnight. 40 m*l* of 30% aqueous sodium hydroxide was added and the mixture was boiled for 1 hr. Ethanol was evaporated under reduced pressure, water was added and the solution was acidified with hydrochloric acid. After working up as usual, the viscous oil was crystallized from aqueous methanol. Yield, 2.93 g (57%), mp 208—218°C. After drying at 140°C *in vacuo* the melting point was 213—216°C.

Found: C, 70.84; H, 6.63%. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65%.

Resolution of the Dicarboxylic Acid (IX). 500 mg of the carboxylic acid (IX) dissolves in 11 m*l* of methanol was mixed with 678.8 mg of cinchonidine in 22 m*l* of methanol and allowed to stand overnight. Evaporation of the solvent gave viscous oil, which was crystallized from 47 m*l* of methanol and 59 m*l* of water. Recrystallisation from aqueous methanol was repeated 4 times. Decomposition with 1 N hydrochloric acid and recrystallisation from aqueous methanol gave optically active dicarboxylic acid, 67.5 mg, $[\alpha]_D^{20}$ +23.2° (*c* 0.25, dioxane).

872 mg of the carboxylic acid (IX) treated with cinchonidine in acetone as above gave salt, mp 91—99°C.

Found: C, 71.67; H, 7.33; N, 5.21%. Calcd for $C_{63}H_{72}O_8N_4 \cdot 2H_2O$: C, 72.10; H, 7.32; N, 5.34.

Recrystallisation of the salt six times and decomposition with hydrochloric acid gave 39 mg of dicarboxylic acid, $[\alpha]_D^{20}$ +19.2° (*c* 0.13, dioxane).

Dealkylation of the Dicarboxylic Acid. 181.5 mg of the racemic dicarboxylic acid suspended in 76 m*l* of ether was treated with excess diazomethane in ether. The obtained homogeneous solution, after evaporating, gave 200 mg of ester, which was dissolved in 25 m*l* of toluene and treated with 0.18 m*l* of boron tribromide at −10°C. After 1 hr the reaction mixture was poured into water and treated as usual. The obtained amorphous product, 71 mg, was treated with charcoal in methanol, giving 60.5 mg of dihydroxy compound. The active dicarboxylic acid, 150 mg, treated analogously gave 15 mg of active acid, mp 164—172°C.

Found: C, 78.63; H, 6.71%. Calcd for $C_{17}H_{16}O_2 \cdot 1/2H_2O$: C, 78.13; H, 6.57%.