Optical Activity of Bis-1,1′-spiroindanes. II. Absolute Configuration of Optically Active 5,5′- and 6,6′-Disubstituted-bis-1,1′-spiroindanes and Their Circular Dichroism Spectra

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An unequivocal determination of the absolute configuration of 5,5′- and 6,6′-disubstituted bis-1,1′-spiroindane and the behavior of the CD spectra of some 5,5′-disubstituted ones are described.

In the preceding paper,[1] the absolute configuration of (−)-6,6′-disubstituted-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindanes was deduced to be (S)-configuration on the basis of the enantiomeric aspect of the CD spectra between (−)-6,6′-dihydroxy-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane, (−)-I and (+)-6,6′-dihydroxy-3,3,-5,3′,3′,5′-hexamethyl-bis-1,1′-spiroindane, (+)-II. The latter was determined to have (R)-configuration by an X-ray study of its 7,7′-dibromo derivative, (−)-III.[2] Also, the assignment of the absolute configuration was supported by the analysis of their CD spectra associated with the *p*-band transition by means of a coupled oscillator theory. However, there remains some ambiguity in the assignment of the absolute configuration, since a discrepancy is observed in the sign of the CD spectra of (−)-I and (+)-II associated with the *p*-band; also, the experimental CD spectrum in the α-band region is found to be inconsistent with the theoretical spectrum. Thus, it appeared to be important to establish the chemical correlation between the absolute configuration of (−)-I and that of (+)-II. Furthermore, as was pointed out in the previous paper, (+)-5,5′-dihydroxy-bis-1,1′-spiroindane, (+)-IX was considered to have (R)-configuration from the positively-signed Cotton effect associated with the α-band; this was done on the basis of an empirical observation that the sign of the CD spectra in the longest wavelength region was determined by the configuration of the spiro atom in bis-1,1′-spiroindanes. However, the empirical rule obtained previously could not be applied to (−)-III. Therefore, it is worthwhile to examine whether or not this rule can be applied to 5,5′-disubstituted derivatives.

In the present paper, an unequivocal determination of the absolute configuration of 5,5′- and 6,6′-disubstitutes bis-1,1′-spiroindane and the behavior of the CD spectra of some 5,5′-disubstituted ones will be described.

Chemical Correlation. 6,6′-Disubstituted bis-1,1′-spiroindane was easily prepared by the acid-catalysed cyclization of acetone with mono-substituted benzenes, such as phenols or toluene.[1,3] However, this method can not be applied to the preparation of 5,5′-disubstituted derivatives because of the orientation of the cyclization. As another route of preparing 5,5′-dimethoxy-bis-1,1′-spiroindane, we have adopted the cyclization of bis(3-methoxybenzyl)acetone with phosphorus oxychloride. However, the correlation of the absolute configurations of 6,6′-disubstituted derivatives with those of 5,5′-disubstituted derivatives has not yet been achieved by a chemical method.

The absolute configuration of (+)-6,6′-dihydroxy-3,3,5,3′,3′,5′-hexamethyl-bis-1,1′-spiroindane, (+)-II has already been established to be (R). Therefore, if the hydroxy group in (R)-(+)-II can be replaced by hydrogen, we can obtain the (R)-5,5′-dimethyl derivative VI. The conversion of the methyl groups of VI to other substituents or the replacement by hydrogen atoms will establish the configurational correlation among the 5,5′-, the 6,6′-disubstituted and the non-substituted spirobisindanes.

As is illustrated in the following scheme, the conversion has been realized. The treatment of the methanesulfonate of (R)-(+)-II with sodium in liquid ammonia afforded the desired deoxygenated product, the 5,5′-dimethyl derivative (R)-(+)-VI. (R)-(−)-3,3,3′,3′-Tetramethyl-bis-1,1′-spiroindane-5,5′-dicarboxylic acid (R)-(−)-VII was obtained by the chromium trioxide oxidation of (R)-(+)-VI. (R)-(−)-VII afforded (R)-(+)-5,5′-diamino-3,3,3′,3′-tetramethyl-bis-1,1′-spiroindane, (R)-(+)-VIII by the Schmidt reaction, as well as the nonsubstituted derivative (R)-(−)-V by the decarboxydation, according to the procedure[1] used for the 6,6′-dicarbohydroxy derivative (+)-IV.

As V obtained from (R)-(−)-VII had the same specific rotation at D-line and showed the same CD spectrum as that derived from (+)-IV, it is established, by the chemical correlation, that (S)-configuration must be assigned to (−)-6,6′-disubstituted bis-1,1′-spiroindanes; this assignment is in agreement with an inference based on the comparison of the CD spectra between (−)-I and (R)-(+)-II.

UV and CD Spectra. The UV and the CD spectra of these 5,5′-disubstituted derivatives are shown in Table 1 and in Figs. 1—4. The accessible UV and CD spectra of these compounds consist of three bands, which are termed α, *p*, and β from the longer wavelength, according to the classification by Clar. The analysis based upon the exciton theory was carried out for both the α- and the *p*-band systems of (R)-(+)-VI, (R)-(−)-VII, and (R)-(+)-VIII, the results are summarized in Table 2.

In dimeric systems with a C_2 symmetry axis, there are two coupling modes for each electronic transition

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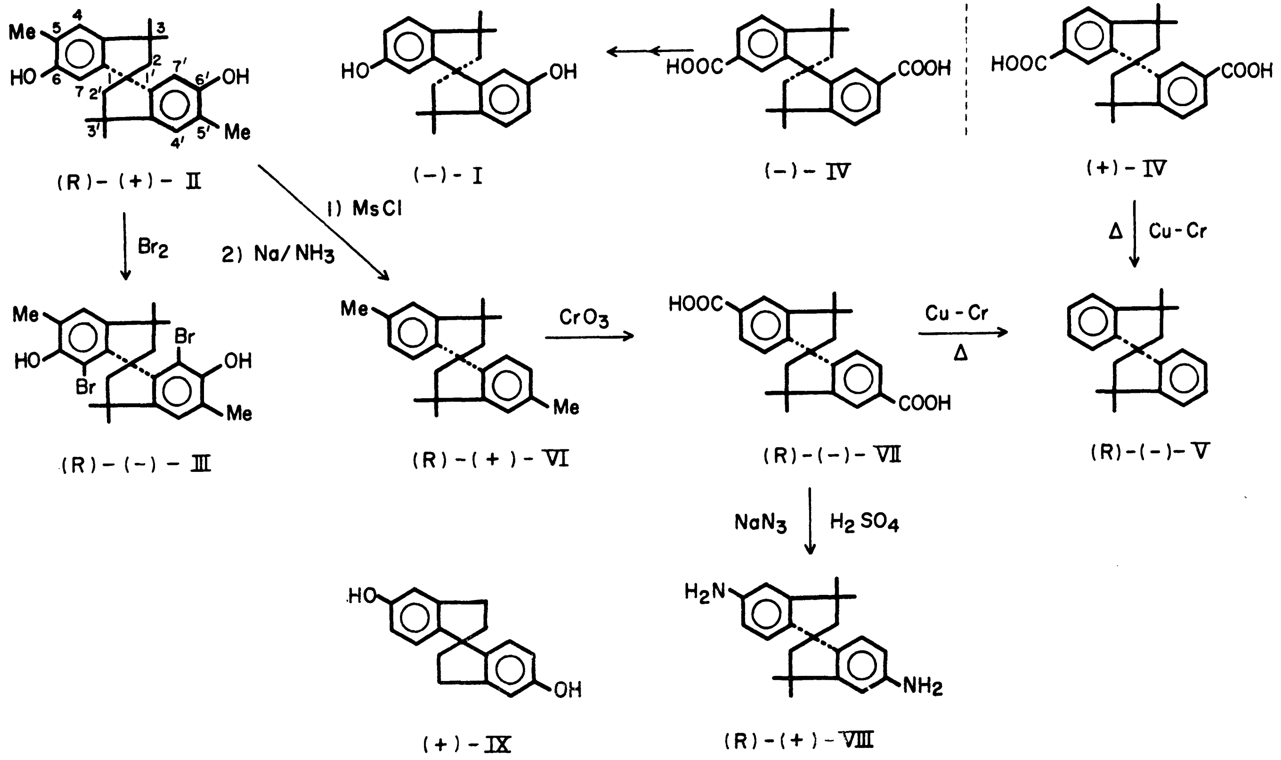
[1] S. Hagishita, K. Kuriyama, M. Hayashi, Y. Nakano, K. Shingu, and M. Nakagawa, This Bulletin, **44**, 496 (1971).

[2] To be published.

[3] L. Taimr and J. Pospišil, *Chem. Ind.* (London), **1969**, 456, and the literature cited therein.



Scheme

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

Compd	Solvent	UV $\lambda_{m\mu}^{max}$ ($\varepsilon\times10^3$)			CD $\lambda_{m\mu}^{max}$ ($\Delta\varepsilon$)		
		α	p	β	α	p	β
(R)-V	Isooctane	272 (2.59)	223 (11.0)	213^{s} (22.0)	273 (+5.54)	226$^{a)}$(−0.94)	205! (+14.8)
		265 (2.24)	218^{s} (18.2)		267 (+3.11)	221 (+10.2)	
		257 (1.43)			260 (+0.71)		
					253 (+0.40)		
(R)-VI	Isooctane	279 (3.04)	229 (14.5)	204! (60.1)	279 (+6.13)	231 (−4.02)	216 (+13.8)
		273 (2.22)	218 (20.0)		273 (+3.16)	223 (+7.11)	
		270 (2.27)			265 (+0.94)		
		265 (1.57)					
(R)-VII	MeOH	286 (4.74)	248 (24.7)	205 (68.5)	286 (−1.20)	250 (−10.0)	215 (+100.)
		278 (5.71)			278 (−1.39)	230^{s} (+10.6)	205 (−114.)
(R)-VII	0.1 N-NaOH	284 (3.45)	247 (30.7)	205 (85.2)	284 (−0.98)	248 (−9.28)	213 (+51.6)
		276 (3.95)			276 (−0.59)	230^{s} (+8.51)	
(R)-VIII	MeOH	288 (5.63)	243 (22.0)	203 (57.7)	297 (+4.73)	247 (−5.96)	213 (−20.8)
						230 (+2.76)	204 (+37.9)
(R)-VIII	HCl MeOH	290^{s} (1.46)	225^{s} (16.2)	200! (68.4)	285 (−0.16)	236 (+0.32)	200! (+56.8)
		275 (4.60)	215^{s} (24.2)		275 (+2.71)	227 (−7.09)	
		267 (4.06)			268 (+2.05)		
		262^{s} (3.79)			261 (+1.04)		

s: shoulder. !: lowest recorded values, not an extremum. a) As the result of re-examination, this weak CD band was found in (+)-(V) reported previously.

of the constituent monomer, one with *A*, and the other with *B* symmetry. The two coupling modes give rise to two CD bands with opposite signs, but the same in magnitude. Experimentally, the Cotton effects in the *p*-bands of these compounds are negative and then positive from the longer wavelength, and are almost identical in the magnitude of rotational strength, but in the α-band all the derivatives show mainly a single Cotton effect, as was observed in 6,6′-disubstituted derivatives.

In this method, we could obtain good results in the *p*-band region of the 6,6′-disubstituted derivatives, in

Table 2. Rotational strengths and frequency intervals of *R*-configuration

The values R and $\tilde{\nu}_A - \tilde{\nu}_B$ were calculated by the following equations:

$$R_A = -R_B = \pi \tilde{\nu} d \rho^2 \cos v \cdot \cos t$$

$$\tilde{\nu}_A - \tilde{\nu}_B = 2\rho^2(\cos^2 v - \cos^2 t + 2\cos^2 r)/hcd^3$$

where d: the distance between the center of the two benzene rings; ρ: the transition dipole moment in the isolated chromophore; $\tilde{\nu}$: the wave number of the transition. The following value of the spectroscopic moment were used: COOH(−28), *t*-Butyl (2) and Methyl (7). The alkyl bridge which made up the spiro skeleton is regarded as a substituent except for (R)-(+)-VIII and the value of the *t*-Butyl was used. The angles r, t and v and d were calculated on the same geometry cited in the previous paper.[1)]

Compd	Band	Found			Calculated				
		ν ($\times 10^2$ cm^{-1})	D (10^{-36} cgs)	R (10^{-40} cgs)	cos r	cos t	cos v	R (10^{-4} cgs)	$R\nu_A - \nu_B$ (cm^{-1})
(R)-(+)-VI	α A B	363	2.34	+4.79	0.061	−0.811	0.582	−28.6 +28.6	−39.1
	p B A	444	1.40	−2.84 +4.54	−0.890	0.233	−0.392	+ 4.01 − 4.01	+67.0
(R)-(−)-VII	α A B	355	4.54	−1.90	−0.290	0.840	−0.458	−43.5 +43.5	−80.1
	p B A	403	24.3	−17.1 +14.0	−0.842[a)]	0.0[a)]	0.540[a)]	0.0 0.0	+1470.
(R)-(+)-VIII	α A B	347	6.38	+9.07	−0.236	0.838	−0.491	−65.0 +65.0	− 120.
	p B A	412	22.9	−9.81 +2.93	−0.859	0.056	0.508	−19.2 +19.2	+2130.

a) The values cos r, cos t and cos v amount to −0.866, 0.019 and 0.500, respectively, by the calculation on the envelope conformation described previously.[1)] Employing them, the calculated sign of CD is consistent with that observed.

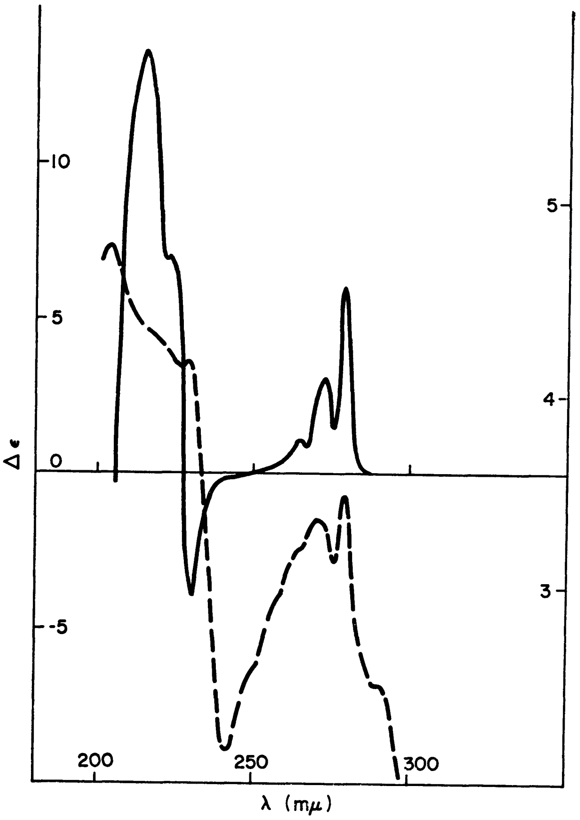


Fig. 1. CD (——) and UV (----) spectra of (R)-(+)-(VI) in isooctane.

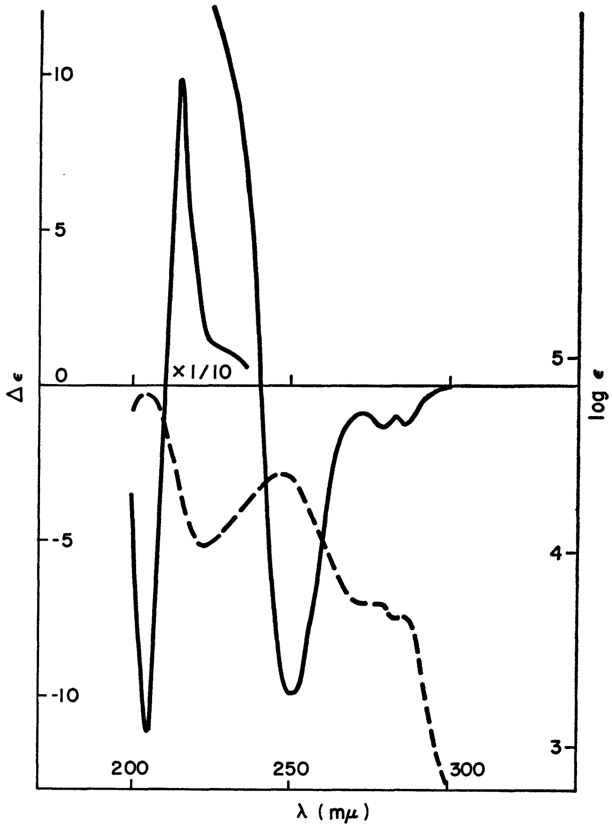


Fig. 2. CD (——) and UV (----) spectra of (R)-(−)-(VII) in methanol.

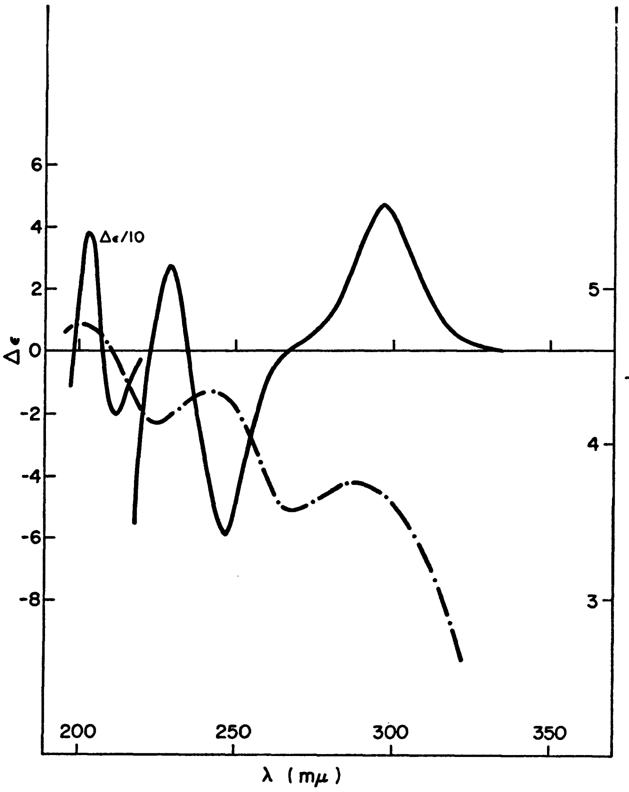


Fig. 3. CD (——) and UV (—·—·) spectra of (R)-(+)-(VIII) in methanol.

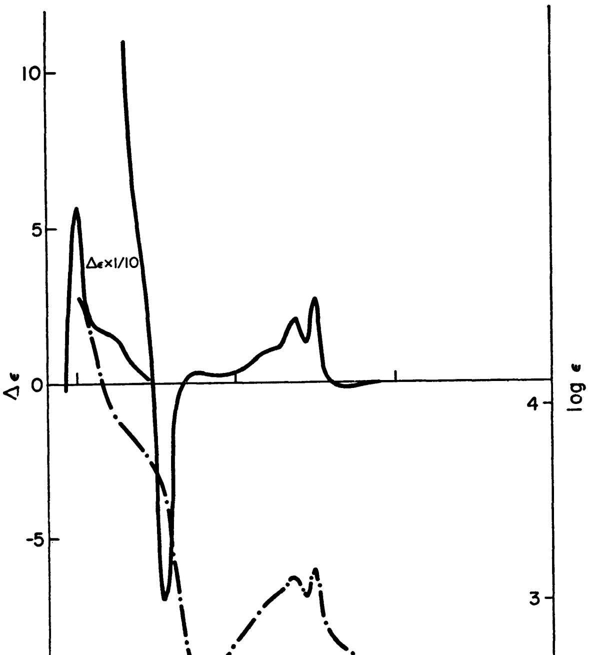


Fig. 4. CD (——) and UV (—·—·) spectra of (R)-(+)-(VIII)·HCl.

which substituents on benzene rings had a large value in the spectroscopic moment, as listed by Platt (Table 2). It can be said that the same results are observed in this series from the value in (R)-(+)-VIII, but the value of the cosine of the tangential angles, *t*, between the long-axis excitation dipole and the local Cartesian axis is small. Especially in (R)-(−)-VII, the excitation dipoles of the *p*-band of two chromophores are situated almost entirely on one plane. Therefore, the calculated value depends on the selection of the geometry of the molecule, the value of the spectroscopic moment for the alkyl bridge, and other factors. In such cases, extreme care must be taken in applying the coupled oscillator theory to the determination of the absolute configuration.

As is observed in 6,6′-disubstituted derivatives,[1] the values calculated by the coupled oscillator theory are not in accordance with those observed in the α-band region. The empirical rule obtained with 6,6′-disubstituted derivatives, that the spatial arrangement of the two benzene rings determines the sign of the CD in the longest-wavelength region, can be applied to (R)-(+)-VI and (R)-(+)-VIII, although the pattern of (R)-(−)-VII and (R)-(+)-VIII·HCl in the α-band does not agree with the above rule. The negative Cotton effect at the longest wavelength of (R)-(+)-VIII·HCl may not be correlated with the transition responsible for that of (R)-(+)-VIII. Therefore, the sign which corresponds to the same transition is positive in (R)-(+)-VIII·HCl (Figs. 1 and 4). The reason for the departure from the empirical rule of (R)-(−)-VII cannot, at present, be understood.

The CD of previously-prepared (+)-5,5′-dihydroxy-bis-1,1′-spiroindane, (+)-IX is similar to that of (R)-(+)-VIII in the pattern associated with the α- and *p*-bands. Since a hydroxy group has a large, positively-signed value in the spectroscopic moment, like an amino group, we can expect a similar CD pattern between VIII and IX with the same absolute configuration. Thus, we assign (R)-configuration to (+)-IX; this assignment is in agreement with that predicted previously.

Experimental

Melting points are uncorrected. Circular dichroism spectra were measured using a JASCO Model ORD/UV-6 apparatus. Optical rotations were measured on a Perkin-Elmer polarimeter Model 141 using a 1-dm quartz cell. Infrared spectra were taken with a JASCO Model 402G doublemonochromatic spectrophotometer. NMR spectra were measured in a solution of deuterio chloroform with a Varian A-60 spectrometer, using tetramethylsilane as the internal standard. Ultraviolet spectra were measured with a Hitachi Model EPS-3T spectrometer.

(R)-(+)-6,6′-Dihydroxy-3,3,5,3′,3′,5′-hexamethyl-bis-1,1′-spiroindanedimethanesulfonate. A solution of (R)-(+)-6,6′-dihydroxy-3,3,5,3′,3′,5′-hexamethyl-bis-1,1′-spiroindane ((R)-(+)-II, 2.2 g, $[\alpha]_D$ +18.9° (*c* 0.456, dioxane)),[1] and freshly-distilled methanesulfonyl chloride (2.2 m*l*) in pyridine (30 m*l*) was heated under reflux for one hour in a nitrogen atmosphere. A volatile material was then removed by distillation under reduced pressure. The residue was dissolved in ethyl acetate, after which the solution was washed with

water and dried over anhydrous sodium sulfate. After the evaporation of the ethylacetate under reduced pressure, the residue was crystallized from benzene-*n*-hexane to give prisms (2.14 g). mp 183—184°C, $[\alpha]_D$ +66.2° (*c* 0.998, chloroform). IR $\nu_{max}^{CHCl_3}$ 1368 cm^{-1}.

Found: C, 61.49; H, 6.56; S, 13.22%. Calcd for $C_{25}H_{32}O_6S_2$: C, 60.95; H, 6.55; S, 13.02%.

(R)-(+)-3,3,5,3',3',5'-Hexamethyl-bis-1,1'-spiroindane (R)-(+)-VI. A solution of the above obtained (+)-dimesyate (2.0 g) in dry tetrahydrofuran (10 m*l*) was added to liquid ammonia (150 m*l*). A small piece of sodium metal was then added under reflux with vigorous stirring. The end point of the reaction was shown by a persistent blue color of the reaction mixture. After stirring for 15 more min, ammonium chloride (0.5 g) was added and the ammonia was evaporated. Water (50 m*l*) was then added to the residue. The aqueous layer was extracted with ether and the combined organic layer was washed with water and dried on anhydrous sodium sulfate. The solvent was distilled under reduced pressure, and the residue was crystallized from methanolic water. Recrystallization from methanol gave prisms (811 mg, 65.6%). mp 76—78°C, $[\alpha]_D$ +1.8° (*c* 2.285, chloroform). NMR τ: 8.68 (6H, singlet), 8.63 (6H, singlet), 7.73 (4H, singlet), 7.67 (6H, singlet), 3.31 (2H, doublet, J=7.8 Hz), 2.9—3.2 (4H, multiplet).

Found: C, 90.56; H, 9.21%. Calcd for $C_{23}H_{28}$: C, 90.73; H, 9.27%.

(R)-(−)-3,3,3',3'-Bis-1,1'-spiroindane-5,5'-dicarboxylic Acid (R)-(−)-VII. Chromium trioxide (1.2 g) was added, in one portion, to a solution of (+)-VI (300 mg) in acetic acid (15 m*l*), water (9 m*l*), and concentrated sulfuric acid (1.5 m*l*). The mixture was heated under reflux for 7.5 hr and then poured into ice water (50 m*l*). After this mixture had been allowed to stand overnight, crystals were collected, washed with water, and then extracted with aqueous sodium hydroxide. The alkaline solution was acidified with dilute hydrochloric acid, and the resultant gel set aside overnight. The precipitated solid was dried and recrystallized from acetone-water (142 mg, 31.5%). mp>300°C, $[\alpha]_D$ −53.2° (*c* 0.468 dioxane). IR ν_{max}^{Nujol} 1690 cm^{-1}.

Found: C, 75.78; H, 6.64%. Calcd for $C_{23}H_{24}O_4$: C, 75.80; H, 6.68%.

(R)-(−)-3,3,3',3'-Tetramethyl-bis-1,1'-spiroindane (R)-(−)-V. A mixtur of (R)-(−)-VII (105 mg) and copper chromite (119 mg) in quinoline (3 m*l*, freshly distilled from copper chromite) was heated under reflux for 90 min. To the cooled reaction mixture, ether (20 m*l*) was added, after which an undissolved solid was removed by filtration. The solution was washed with 50% hydrochloric acid, aqueous sodium bicarbonate, and then water, and dried on anhydrous sodium sulfate. The ether was evaporated, and the residue was crystallized and recrystallized from ethanol to give colorless needles (42 mg, 52.7%). mp 124—125°C, $[\alpha]_D$ −30.4° (*c* 0.471, dioxane). The IR spectrum of this compound was identical with that of an authentic sample.[1]

(R)-(+)-5,5'-Diamino-bis-1,1'-spiroindane (R)-(+)-VIII. Into a solution of (R)-(−)-VII (147 mg) in concentrated sulfuric acid (6.5 m*l*), sodium azide (215 mg) was added in small portions over a 50-min period at 40—45°C with stirring, Foaming occurred and stirring was continued at 50—55°C for 2 hr. The reaction mixture was allowed to stand overnight and then poured into ice water (50 m*l*). After this mixture had been made alkaline with 40% aqueous sodium hydroxide (35 m*l*) under cooling, yellow powders were collected, washed with water, and dried *in vacuo*. The crude powders were dissolved in benzene, and an amorphous solid was removed by filtration. After it had been concentrated to *ca.* 2 m*l* under reduced pressure, the solution was allowed to stand overnight; then the product was collected and dried *in vacuo* to give needles (64 mg). mp 208—210°C, $[\alpha]_D$ +8.3° (*c* 0.350, MeOH). IR ν_{max}^{Nujol} 3440, 3355 cm^{-1}.

Found: C, 82.55; H, 8.49; N, 9.41%. Calcd for $C_{21}H_{26}N_2$: C, 82.31; H, 8.55; N, 9.14%.