

THE 2,2'-SPIROBICHROMAN - 1,1'-SPIROBIINDAN-4,4'-DIOL REARRANGEMENT. II

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Abstract — The reaction of 2,2'-spirobichroman derivatives with either hydrobromic acid in the acetic acid solution or aluminum chloride in the chlorobenzene solution yielded 1,1'-spirobiindan-4,4'-diol analogues. The reaction is peculiar as compared with the reaction of alkyl aryl ethers with the same reagents in the same media.

Introduction. For all the prevalence of the thermal and the acid-catalyzed Claisen rearrangement¹ in the synthetic accomplishments, the conversion of alkyl aryl ethers into their respective alkylphenols remains to raise mechanistic studies in arguments.² Due evidences were adduced either in favor of or against the alternative mechanisms of intermolecular³ or intramolecular⁴ rearrangement.

In most of the reactions substantiating the effective rearrangement to yield *o*- and *p*-alkylphenols, the alkyl aryl ethers were treated with Lewis acid in the absence of any solvents.⁵ In the presence of chlorobenzene as solvent, the reactions of alkyl aryl ethers with aluminum chloride invariably yielded alkylchlorobenzene derivatives⁶ instead of alkylated phenols indicating the fact that the alkyl carbenium ions, formed by the attack of the Lewis acid on the ethers, react with the solvent rather than the aromatic nuclei of the phenol moieties of the ethers.

It is also well known that the reaction of alkyl aryl ethers with hydrobromic acid in the acetic acid solutions yields alkyl bromides and phenols.

A peculiar illustration is the rearrangement of 2,2'-spirobichroman derivatives (I) into 1,1'-spirobiindan-4,4'-diol analogues (II) which was effected either by heating the formers with hydrobromic acid in the acetic acid solution⁷ or by the reaction of the formers with anhydrous aluminum chloride in the chlorobenzene solution,⁸ as preliminarily reported.

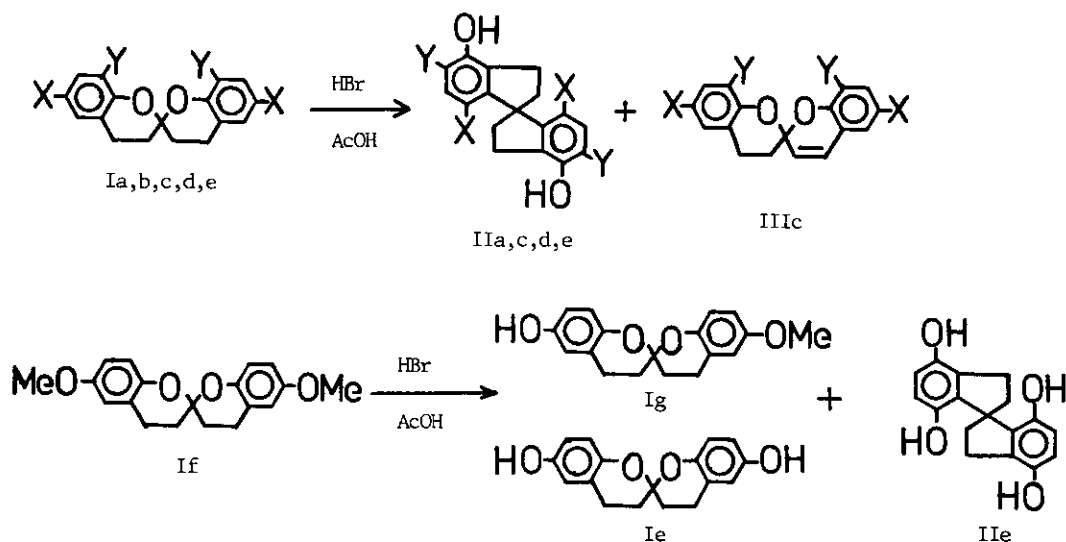
The rearrangement reactions. The rearrangement of I having electron-donating substituents into II was effected with moderate yields by the reaction with hydrobromic acid-acetic acid at 95°C, while 6,6'-dichloro-2,2'-spirobichroman (Ib) having substituents specified by their electron-attracting

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dipoles, on reaction with hydrobromic acid - acetic acid at 95°C for 60 h, was recovered unscathed implicating the electrophilic nature of the rearrangement reaction. The results are summarized in Figure I and Table I.

Figure I. The reaction of 2,2'-spirobichroman derivatives with hydrobromic acid - acetic acid



a: X = Y = H ; b: X = Cl, Y = H ; c: X = Me, Y = H ; d: X = Y = Me ; e: X = OH, Y = H ;
f: X = OMe, Y = H ; g: X = OH, OMe, Y = H

Table I. Summary of the reaction of 2,2'-spirobichroman derivatives in the acetic acid solution.

Reactant	Reagent	Temp. °C	Time h	Products (%)
Ia	HBr ^a	95	60	IIa (1.8), Ia (88.5)
Ib	HBr	95	60	no appreciable products
Ib	HBr-HI ^b	reflux	16	
Ic	HBr	95	60	IIc (10.8), IIIc (6.0), Ic (58.1)
Ic	HBr-HI	reflux	16	IIc (15.3), IIIc (3.0)
Id	HBr	95	52	IIId (62.2)
Ie	HBr	95	3	IIe (80.0)
If	HBr	80	4	If (28.8), Ig (25.6), Ie (11.3), IIe (3.5)
If	HBr	80	40	Ie (9.9), IIe (40.8)
If	HBr	95	14	Ie (2.8), IIe (64.7)

a. 12 ml CH₃COOH and 2 ml HBr per 100 mg reactant. b. 4 ml CH₃COOH, 2-3 ml HBr and 0.2-0.3 ml HI per 100 mg reactant.

On the inspection of Table I, it is pointed out that the reaction of 2,2'-spirobichroman-6,6'-diol dimethyl ether (If) with hydrobromic acid - acetic acid at 80°C resulted in stepwise elimina-

tion of two methyl groups from the methoxyl groups to yield successively the monomethyl ether (Ig) and the diol (Ie) rather than the migration of methyl groups onto the aromatic nuclei. It is, therefore, inferred that the fissions of two methyl groups preceded the rearrangement reaction which proceeded very slowly at 80°C and in substantial rate at 95°C.

Jacquesy et al.^{2b} reported that the rearrangement of *p*-alkyl phenetole derivatives in superacid (HF-SbF₅) medium yielded exclusively 4-alkyl-3-ethylphenol derivatives and proved the intermolecular mechanism by cross-alkylation experiments. They also proved that the reaction went forward via direct attack of the carbenium ion toward carbon meta to the oxygen function rather than the o,p-substitution followed by migration to the meta position. And in the related experiments made by the same authors, bromination of *p*-alkylphenol and *p*-alkylanisol derivatives in the same medium yielded m-bromophenol derivatives.^{9, #3}

In contrast to this conclusion, the reaction which we are dealing with proceeds intramolecularly because the migrating groups are tied up to the phenyl rings in which they are bound to anchor. On the basis of such foregoing results, it is reasonable to consider that the increase of plus charge at C-2 (C-2'), i.e. the use of stronger Lewis acid as well as the increase of the electron density of the aromatic rings particularly at C-5 and C-5', i.e. electron releasing substituents at C-6 and C-6', facilitate the rearrangement reaction. The effects of electron releasing substituents were already confirmed. Therefore, another choice to be examined may be the use of strong Lewis acid such as anhydrous aluminum chloride.

The rearrangement of I was effected by aluminum chloride in chlorobenzene solution as summarized in Figure II and Table II.

2,2'-Spirobichroman (Ia) and Ib which could not effectively be rearranged by the hydrobromic acid - acetic acid method, yielded 1,1'-spirobiindan-4,4'-diol (IIa) and 7,7'-dichloro-1,1'-spirobiindan-4,4'-diol (IIb) in 35.5 and 38.5 % yield, respectively. IIa crystallized from benzene-heptane (1:1) as a (2:1) clathrate compound with benzene having mp 105°C, which was debenzenized at 110°C under vacuum (25 mm Hg) to yield crystals having mp 129-30°C. 1-[2-(2-Hydroxyphenyl)ethyl]-4-indanol (IV) was also isolated as a clathrate compound with heptane having mp 108°C which on deheptanization at 110°C under vacuum yielded crystals having mp 138°C.

Although higher temperature assured the energy to pass over the transition state, competing de-

#3. Jacquesy et al. seem to suggest implicitly the meta-directing influence of protonated oxygen functions although it also seems likely that phenol oxygen atom as well as that of its methyl ether, even when protonated at its oxygen function, still retains in its P_z orbital of sp² hybridized oxygen atom a pair of unshared electrons available to the mesomeric displacement toward the benzene nucleus to effect a weak o,p-directing influence. Orbital overlap between oxygen and benzene ring of the alkyl (except tert-butyl) aryl ethers was observed.¹⁰

Figure II. The reaction of 2,2'-spirobichroman derivatives with aluminum chloride

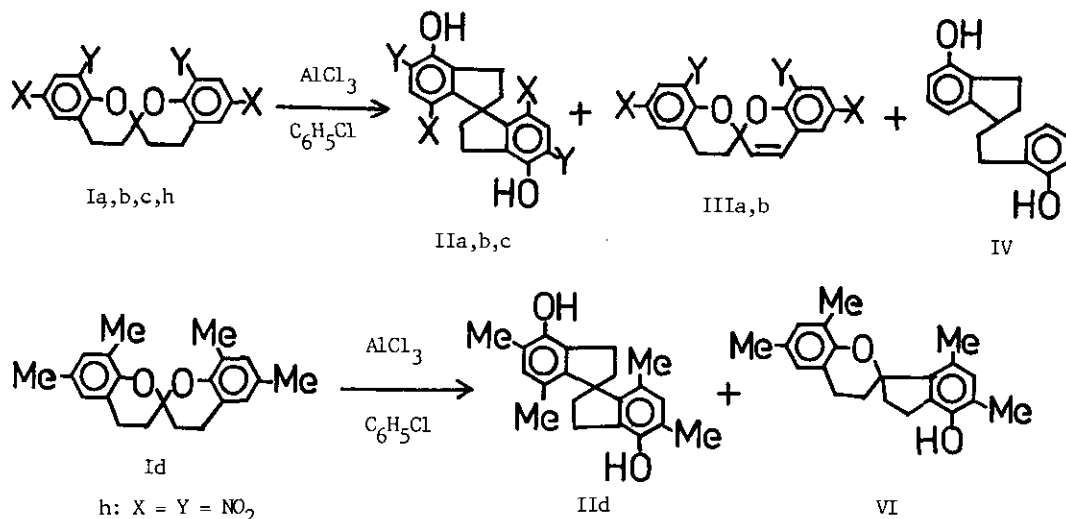


Table II. Summary of the reaction of 2,2'-spirobichroman derivatives in chlorobenzene solution.

Reactant	AlCl ₃ /I	Temp. °C ^a	Time h	Products (%)
Ia	2.5	100	4	IIIa (25.5), IV (3.4)
Ia	2.3	140	1	IIa (35.5), IIIa (23.8), IV (5.7)
Ib	2.5	100	3	IIb (38.5), IIIb (12.2)
Ib	2.6	135	1	IIb (22.1), IIIb (38.1)
Ic	2.5	100	2.6	IId (65.8)
Id	3	20 ^b	1.5	IId (67.8), VI (10.1)
Ih ^c	2.5	135	2	no appreciable products

a: Bath temperature. b: On the addition of aluminum chloride the temperature of the reaction mixture rose to 50°C. c: 6,6',8,8'-Tetranitro-2,2'-spirobichroman.¹³

hydrogenation reactions¹¹ leading to 3,4-dihydro-2,2'-spirobi[2H-chromene] (IIIa) and 6,6'-dichloro-3,4-dihydro-2,2'-spiro[2H-chromene] (IIIb) restricted the yields of IIa and IIb in a lower limit. However, much improvement of the yield was realized of the rearrangement of Ic and Id exemplifying the reaction accelerating effect of the Lewis acid.

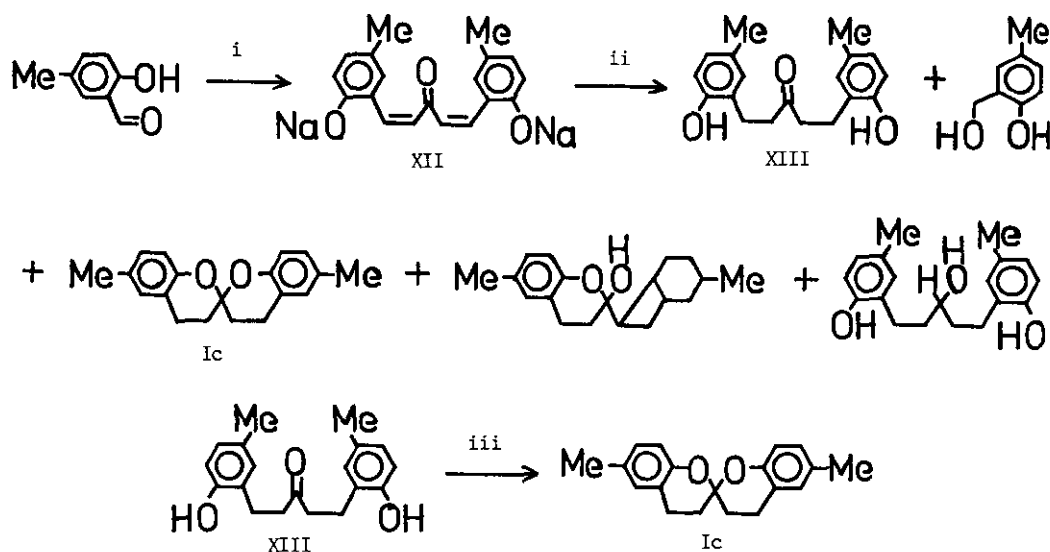
Comparing the aptitudes toward rearrangement due to both reagents, the order of reactivity of the substituted 2,2'-spirobichroman derivatives to form 1,1'-spirobiindan-4,4'-diol analogues was,

6,6'-dihydroxy > 6,6'-dimethoxy > 6,6',8,8'-tetramethyl > 6,6'-dimethyl > 6,6'-dichloro > unsubstituted > 6,6',8,8'-tetranitro

It should be added that aluminum chloride-catalyzed rearrangement substantiated the syntheses of IIa and IIb which otherwise were difficult to synthesize.¹²

Synthesis of 2,2'-spirobichroman derivatives. As represented by the synthesis of 6,6'-dimethyl derivative (Ic) in Figure III, 2,2'-spirobichroman derivatives were prepared by a modification of the method which Mora and Szeki reported on their study of disalicylideneacetone derivatives.¹³ The

Figure III. Synthesis of 6,6'-dimethyl-2,2'-spirobichroman

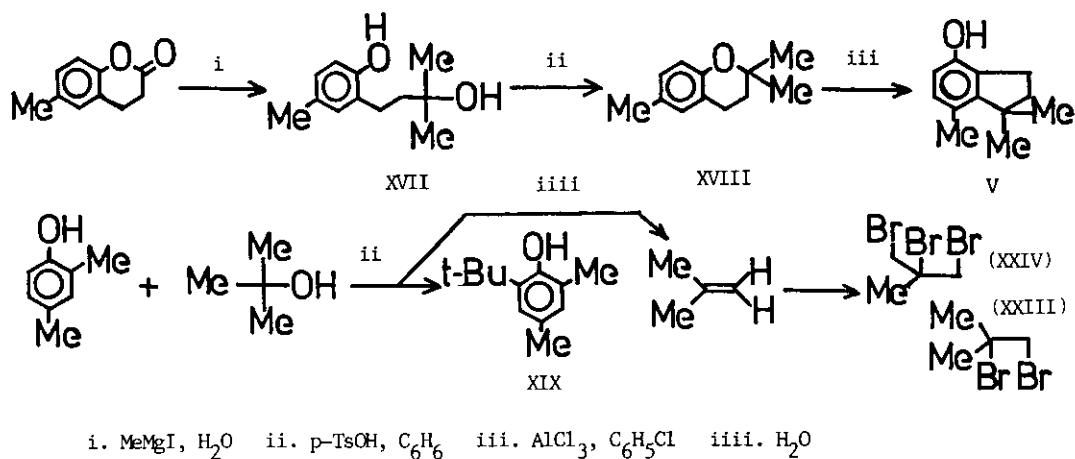


i. MeCOMe, aq. NaOH, EtOH ii. H₂, Pd-C iii. H₂SO₄-EtOH

cyclization of XIII into Ic was effected at 0°C in the alcoholic sulfuric acid in 2 h. The extreme ease with which the cyclization of 1,5-bis(2-hydroxyphenyl)-3-pentanone derivatives into 2,2'-spirobichroman derivatives occurs, may be ascribed to the "tied up group" reactivity¹⁴ because the reaction of p-cresol and 2,4-xyleneol with 3-pentanone in the same media at 0°C and 60°C for 6 h resulted in complete recovery of the starting materials. It should also be suggested that the rearrangement of I into II, which means meta-substitution, may also be due to the "tied up group" state. We may add another instance of the varied reactivity due to "tied up group". As illustrated in Figure IV, by azeotropically distilling water off from the benzene solution of 3-(2-hydroxy-5-methylphenyl)-1,1-dimethylpropan-1-ol (XVII) using p-toluenesulfonic acid as catalyst, 78 % yield of 3,4-dihydro-2,2,6-trimethyl-2H-1-benzopyran (XVIII)¹⁵ was obtained. Rearrangement of XVIII was effected by the reaction with aluminum chloride in chlorobenzene solution to give 85.6 % yield of 2,3-dihydro-1,1,7-trimethyl-1H-inden-4-ol (V), a product of meta-substitution.

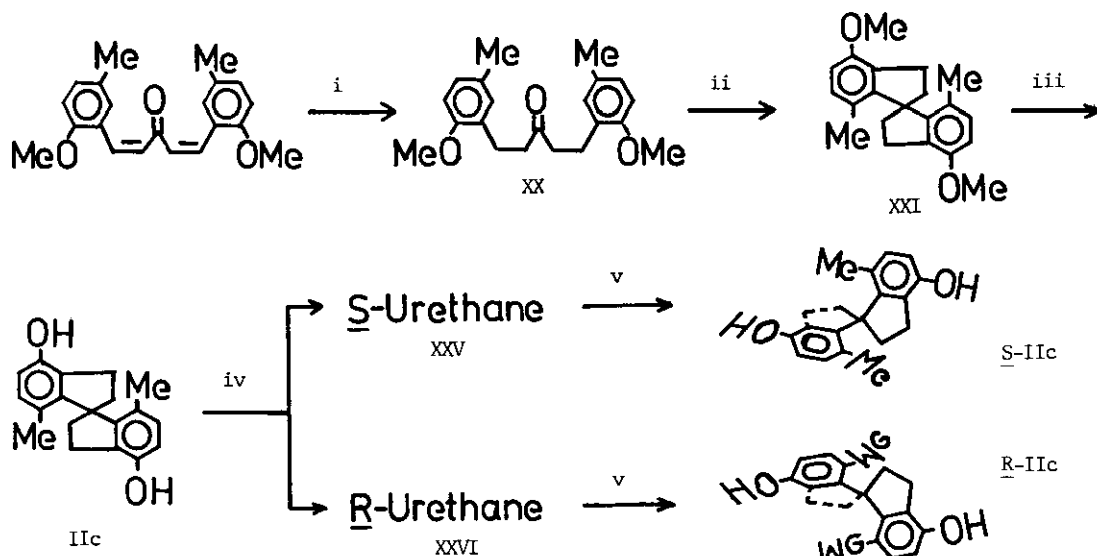
In a comparative experiment, the reaction of 2,4-xyleneol and tert-butanol (both of 2,3-seco-species out of XVII) yielded 2,4-dimethyl-6-tert-butylphenol (XIX) instead of 2,4-dimethylphenyl tert-butyl ether. In the experiment, refluxing without distilling water off resulted in low yield of XIX, the main product being isobutene which was trapped as dibromo- and tribromo-isobutane. The water as a hard base plays an important role in the dehydration reaction.

Figure IV. Reaction of tert-alcohols with phenols.



Structure of 1,1'-spirobiindan-4,4'-diol derivatives. The structure of II was verified on their nmr spectra as well as by the synthesis¹⁶ of racemic 7,7'-dimethyl-1,1'-spirobiindan-4,4'-diol (IIc) and its resolution into optical isomers as illustrated in Figure V. The cyclization of 1,5-

Figure V. Synthesis and optical resolution of 7,7'-dimethyl-1,1'-spirobiindan-4,4'-diol



bis(2-methoxy-5-methylphenyl)pentan-3-one (XX) into dimethyl ether of IIc (XXI) could not be effected by the method by which Nakagawa et al.^{16a} succeeded in cyclizing 1,5-bis(3-methoxyphenyl)-3-pentanone into 1,1'-spirobiindan-5,5'-diol dimethyl ether, but was achieved in 51.6 % yield by the addition of stannic chloride to the phosphorous oxychloride - benzene solution of XX followed by 30 h refluxing.

Optical resolution of IIc. The diastereoisomeric urethanes were prepared by refluxing the toluene solution of racemic IIc with (+)-1-phenylethyl isocyanate and a drop of pyridine for 46 h. On evaporation of the solvent followed by treatment of the residue with benzene, precipitated the urethane of S(+)-IIc having mp 152°C, $[\alpha]_D^{15} -26^\circ$ (EtOH, c = 0.17) while urethane of R(-)-isomer having mp 104°C, $[\alpha]_D^{15} -118^\circ$ (EtOH, c = 0.45) was obtained from the benzene solution on chromatography through silica gel column. R(-)-IIc having mp 194°C, $[\alpha]_D^{15} -67^\circ$ (EtOH, c = 0.55) and S(+)-IIc having mp 194°C, $[\alpha]_D^{15} +62^\circ$ (EtOH, c = 0.56), obtained by hydrolyses of the respective urethanes, were estimated to be of ee 100 and 96 %^{#4}, respectively, on the high performance liquid chromatography through Chiralpak OT(+) column¹⁷ as illustrated in Figure VI and a calculation based on their $[\alpha]_D$ values.

Figure VI. High performance liquid chromatography of R- and S-IIc

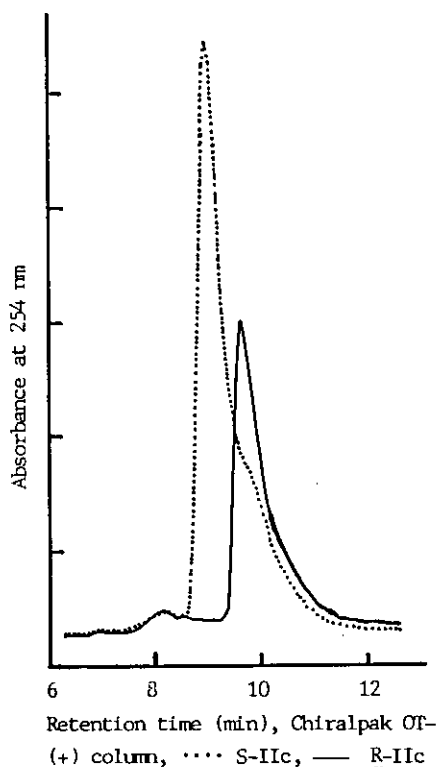
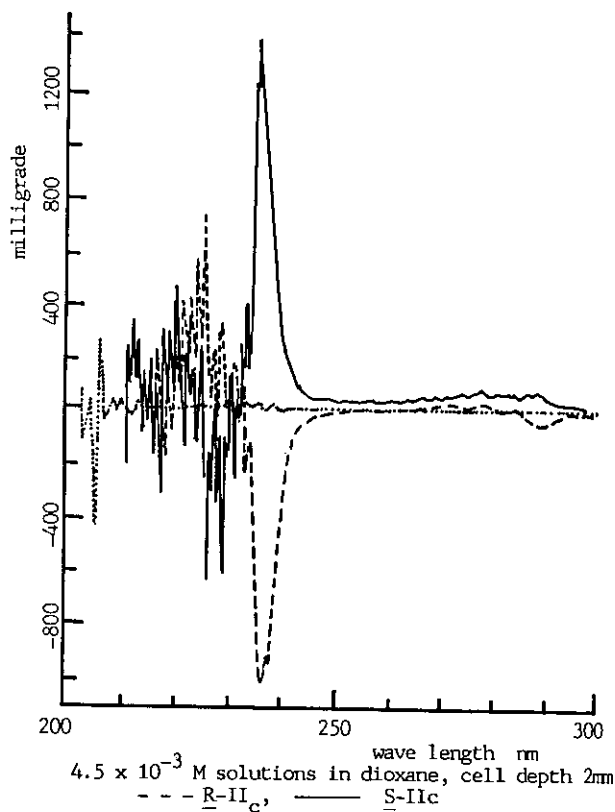


Figure VII. cd Spectra of R- and S-IIc



#4. We also got ee 97 % on the $[\alpha]_D$ values -280° (dioxane, c = 0.13) and $+263^\circ$ (dioxane, c = 0.13).

Assignment of S- and R-structures was made on their cd spectra shown in Figure VII as well as on their high performance liquid chromatographic analyses on a column mentioned above through which, it is known, S-isomers are eluted in less retention times than those of the R-isomers.¹⁸

EXPERIMENTAL

Melting points are uncorrected. ¹H nmr spectra were recorded in CDCl₃ solution containing tetramethylsilane as a standard at room temperature with a JEOL INM-MH-100 and FT nmr GX-270 instruments, ms and ir spectra were taken on JEOL JMS-D-300 and Hitachi EPI-G-2 instruments, cd and high performance liquid chromatography were determined on JASCO J-20 automatic ord recorder and Trirotar II instrument, respectively. Analysis of sodium was made on the flame photometric method. Columns for silica gel chromatography were packed with Wakogel C-200.

2,2'-Spirobichroman (Ia).¹³ A convenient method to prepare Ia is as follows : a solution of 30 g of disalicylideneacetone disodium salt heptahydrate (VII) in 200 ml of water was stirred with 2 g of 5 % palladium-charcoal under hydrogen atmosphere at 55°C for 12 h to absorb 3 l of hydrogen. The solution was filtered and the palladium-charcoal was extracted twice with 50 ml of hot water and the combined filtrate was poured into a mixture of 20 ml of conc. hydrochloric acid and 100 ml of ice-water, which was extracted twice with 250 ml of benzene-ether (1 : 1). The combined organic layer was shaken with 5 % aq. sodium carbonate solution followed by brine, dehydrated with anhydrous sodium sulfate and evaporated. The residue was dissolved in small amount of ethanol and the solution was poured into stirred ice-cold ethanol (90 ml) containing 12 ml of conc. sulfuric acid. In 30 min pink-colored gruel ensued. Stirring was continued for another 2 h in the ice bath and the gruel was filtered, recrystallized from ethanol to yield 9.1-9.5 g pure Ia having mp 107-108°C. The crystals obtained from the mother liquor of crystallization, combined with the crystals obtained from the ethanol-sulfuric acid filtrate by treatment with water, was chromatographed through silica gel column to yield 0.8-1.2 g Ia having mp 108°C as the benzene elute. Total yield 57.1-61.7 %.

Bis(2-methoxybenzylidene)acetone (VIII). To a refluxing solution of 21 g of VII in 250 ml of ethanol containing 2.0 g of sodium hydroxide was gradually added 25 g of methyl iodide and the refluxing was continued for 5 h. The resultant solution was evaporated and the residue was treated with 50 ml of 10 % aq. sodium hydroxide solution and extracted twice with ether-benzene (1 : 1). The combined organic layer was washed with water, dehydrated with sodium sulfate, evaporated and the residue was crystallized from ethanol to give 11.72 g (81.7 %) yellow crystals: mp 124°C, ir 1675 cm⁻¹ (C=O).

1,5-Bis(2-methoxyphenyl)-3-pentanone (IX). A solution of 10g of VIII in 180 ml of acetone was hydrogenated over 0.5 g of palladium-charcoal at room temperature for 24 h to absorb 1.3 l of hydrogen. The solution was filtered and the charcoal was extracted twice with hot acetone. The combined filtrate was evaporated and the residue on chromatography through silica gel column yielded white crystals as the benzene elute which on crystallization from methanol weighed 6.52 g (64.4 %): mp 92°C.

Anal. Found: C, 76.51; H, 7.50 %. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43 %; $\text{ir } 1718 \text{ cm}^{-1}$ (C=O); $\text{nmr } \delta=2.72$ (4H, t $J=7$ Hz, CH_2), 2.79 (4H, t $J=7$ Hz, CH_2), 3.80 (6H, s, OCH_3), 6.80 (2H, d $J=8$ Hz, Ar), 6.88 (2H, d $J=8$ Hz, Ar), 7.10 (4H, dd $J=2$ and 8 Hz, Ar).

Attempted cyclization of IX. By refluxing a solution of 10.4 g of IX, 44 ml of POCl_3 and 8.7 g of SnCl_4 in 114 ml of heptane or benzene for 42 h, no substantial amounts of 2,2'-spirobichroman derivatives could be obtained.

6,6'-Dichloro-2,2'-spirobichroman (Ib).^{19,7b} To a mechanically stirred mixture of 9.1 g (1/20 mole) of 6-chloro-3,4-dihydrocoumarin²⁰ and 40 ml of heptane heated at $100\text{--}110^\circ\text{C}$, was added a mixture of 12.5 g (1/20 mole) of boron tribromide and 10 ml of heptane. From the clear yellow solution which ensued on the addition, in 30 min precipitate began to separate. The precipitate became a hard mass which prevented stirring, in which event the mass must be crushed by a glass rod to assure effective stirring to continue for 5 h. The reaction mixture, on cooling, was poured into 200 ml of ice-water and the precipitate was filtered. The aqueous organic filtrate was extracted twice with 200 ml of ether-benzene (1:1) and the combined extract was washed with brine, dehydrated with sodium sulfate and evaporated. The precipitate, together with the residue of the extract, was dissolved in benzene and chromatographed through silica gel to yield Ib as the first benzene elute. Recrystallization from heptane or ethanol yielded 1.2 g (15.2 %) of white needles having $\text{mp } 207^\circ\text{C}$.²¹ Anal. Found: C, 63.87; H, 4.54; Cl, 21.72 %; M^+ , 306. Calcd. for $C_{17}H_{14}O_2Cl_2$: C, 63.57; H, 4.39; Cl, 22.08 %; M^+ , 306.

Bis(2-hydroxy-5-chlorobenzylidene)acetone disodium salt heptahydrate (X). To a solution of 29.18 g of 5-chlorosalicylaldehyde and 5.20 g of acetone in 85 ml of ethanol was added 13.94 g of sodium hydroxide in 20 ml of water, when yellow precipitate separated. The reaction mixture was shaken for 1 h and left to stand overnight. The dark red mass was filtered and recrystallized from 70 % ethanol to yield 23.56 g (50.1 %) red crystals with green metallic luster. Anal. Found: C, 39.98; H, 5.01; Na, 10.23 %. Calcd. for $C_{17}H_{10}O_3Cl_2Na_2 \cdot 7H_2O$: C, 40.40; H, 4.78; Na, 9.10 %.

Ib via hydrogenation of X. A mixture of 4.99 g of X, 0.7 g of 5 % palladium-charcoal and 120 ml of acetic acid was stirred in the hydrogen atmosphere at 30°C for 7 h. The solution was filtered and the charcoal was extracted twice with 30 ml of acetic acid and the combined filtrate was poured into 500 ml of ice-water, when yellow precipitate separated. The precipitate was filtered and recrystallized from ethanol. Yield 0.30 g (9.4 %): $\text{mp } 205\text{--}206^\circ\text{C}$.

Hydrogenation of X in the aqueous solution yielded a mixture of Ia and Ib in which the former predominated. Separation of Ib from Ia was effected by chromatography through silica gel column of sufficient length using benzene-heptane (1:1) as solvent. Ib came out first.

Chlorination of Ia was effected in the acetic acid solution to yield tetrachloro derivative.

Bis(2-methoxy-5-chlorobenzylidene)acetone (XI). By the procedure described on the synthesis of IX, reaction of 24.4 g of X, 25.1 g of methyl iodide and 1.0 g of sodium hydroxide in the 250 ml of eth-

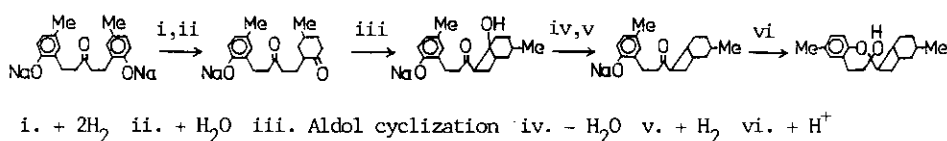
anolic solution yielded 8.6 g (49.2 %) of XI having mp 156–158°C. Anal. Found: C, 62.63; H, 4.39 %. Calcd. for $C_{19}H_{16}O_3Cl_2$: C, 62.82; H, 4.44 %.

Bis(2-hydroxy-5-methylbenzylidene)acetone disodium salt heptahydrate (XII). To a solution of 100 g of 5-methylsalicylaldehyde and 20.5 g of acetone in 340 ml of ethanol was added a solution of 55 g of sodium hydroxide in 85 ml of water, when yellow crystals of sodium salt of the aldehyde precipitated. The mixture was shaken for 30 min and left to stand overnight, when the whole mass solidified. The precipitate was filtered and recrystallized from 70 % ethanol to yield 136.1 g (73.8 %) of red crystals with green metallic luster. Anal. Found: C, 49.82; H, 6.31; Na, 10.17 %. Calcd. for $C_{19}H_{16}O_3Na_2 \cdot 7H_2O$: C, 49.13; H, 6.51; Na, 9.90 %.

1,5-Bis(2-hydroxy-5-methylphenyl)-3-pentanone (XIII). A solution of 35.5 g of XII in 650 ml of water was treated with 3 g of palladium-charcoal and hydrogenated at 55°C for 18 h. The resultant clear solution was filtered and the charcoal was extracted twice with hot water and filtered. The combined filtrate was acidified with 30 ml of acetic acid, extracted three times with 300 ml of ether-benzene (1 : 1). The combined extract was washed with 5 % aq. sodium carbonate solution followed by water, dehydrated with anhydrous sodium sulfate and evaporated under reduced pressure to yield 22.3 g of an oil, which was dissolved in benzene and chromatographed through a column packed with 500 ml of silica gel. Every 50 ml elute fraction was tested on thin-layer chromatography and fractions which revealed spots of the same Rf values were combined and evaporated.

Fraction 1. Benzene elute 0.16 g, which was crystallized from heptane to give a mixture containing Ic: mp 121–126°C. Fraction 2. Benzene elute 0.48 g (2.2 %), which was recrystallized twice from heptane to yield white crystals having mp 165°C. 6-Methyl-2-(3-methyl[4.2.0]bicyclooct-7-yl)-2-chroman-ol^{#5}; ir 1150 (tert-OH), 1225 cm^{-1} (phenyl ether); nmr δ =0.89 (3H, d J=7 Hz, CH_3), 1.00 (2H, broad, cyclobutane CH_2), 1.08 (3H, broad, 3 cyclobutane CH), 1.45 (1H, overlapped, CH), 1.55 (4H, d J=5 Hz, $2CH_2$), 1.69 (2H, t J=3 Hz, CH_2), 1.92 (2H, dd J=6 and 2 Hz, CH_2), 2.12 (1H, s, OH), 2.24 (3H, s, CH_3), 2.69 (2H, dd J=6 and 2 Hz, CH_2), 6.69 (1H, d J=8 Hz, Ar), 6.89 (1H, s, Ar), 6.92 (1H, d J=8 Hz, Ar). Anal. Found: C, 79.53; H, 9.15 %; M^+ 286 [fragment ions: 286 ($M-18$)⁺, 211 ($M-18-57(C_4H_9)$)⁺, 171 ($M-18-97(C_7H_{13})$)⁺, 165 ($M-121(C_8H_9O)$)⁺, 158 ($M-18-110(C_8H_{14})$)⁺, 147 ($C_{10}H_{11}O$)⁺, 121 (C_8H_9O)⁺, 108 (C_7H_8O)⁺, 91 (C_7H_7)⁺]. Calcd. for $C_{19}H_{26}O_2$: C, 79.67; H, 9.15 %; M^+ 286. Fraction 3, Benzene elute

#5. A possible mechanism of the formation of this by-product may be the reduction of one of the phenol rings of XIII into cyclohexanone system²² followed by the successive reactions of aldol cyclization, dehydration and hydrogenation as formulated below.



0.42 g (1.9 % yield), which on recrystallization from heptane yielded Ic having mp 131-132°C.

Fraction 4. Ether-benzene (1 : 10) elute 10.54 g (46.3 % yield) which on evaporation was isolated as oil and crystallized gradually on standing. Recrystallization from benzene-heptane (1 : 5) yielded white crystal: mp 87°C. 1,5-Bis(2-hydroxy-5-methylphenyl)-3-pentanone (XIII); ir 1690 cm^{-1} (C=O); nmr δ =2.10 (2H, s, OH), 2.22 (6H, s, 2CH_3), 2.76 (8H, s, 4CH_2), 6.70 (2H, d J=8 Hz, Ar), 6.82 (2H, s, Ar), 6.90 (2H, d J=8 Hz, Ar). Anal. Found: C, 76.70; H, 7.42 %. Calcd. for $\text{C}_{19}\text{H}_{22}\text{O}_3$: C, 76.48; H, 7.43 %. Fraction 5. Ether-benzene (1 : 10) elute 0.69 g, which was recrystallized from benzene-heptane (1 : 3) to yield crystals having mp 103°C. 2-Hydroxy-5-methylbenzyl alcohol. Anal. Found: C, 69.68; H, 7.21 %. Fraction 6. Ether-benzene (2 : 5) elute 0.75 g (3.3 % yield), which was recrystallized from benzene-heptane (1 : 1) to yield white crystals having mp 116-118°C. 1,5-Bis(2-hydroxy-5-methylphenyl)-3-pentanol; nmr δ =1.74 (4H, t J=6 Hz broad, 2CH_2), 2.20 (6H, s, 2CH_3), 2.67 (2H, t J=6 Hz, CH_2), 2.73 (2H, t J=6 Hz, CH_2), 3.56 (1H, broad, CH), 4.50 (1H, s broad, OH), 6.72 (2H, d J=8 Hz, Ar), 6.84 (2H, d J=8 Hz, Ar), 6.84 (2H, s, Ar), 7.74 (2H, s broad, OH). Anal. Found: C; 75.86; H, 8.02 %. Calcd. for $\text{C}_{19}\text{H}_{24}\text{O}_3$: C, 75.97; H, 8.05 %.

6,6'-Dimethyl-2,2'-spirobichroman Ic from XIII. According to the procedure described in the preparation of Ia, 10 g of XIII on treatment with 60 ml of ethanol containing 8 ml of conc. sulfuric acid yielded 5.93 g (63.1 %) of Ic having mp 131-132°C; nmr δ =1.90 (2H, td J=12, 12 and 6 Hz, CH_2), 2.25 (8H, s, 2CH_3 , CH_2 overlapped), 2.68 (2H, ddd J=12, 6 and 2 Hz, CH_2), 3.22 (2H, ddd J=14, 12 and 6 Hz, CH_2), 6.68 (2H, d J=8 Hz, Ar), 6.92 (2H, d J=8 Hz, Ar), 6.95 (2H, s, Ar). Anal. Found: C, 81.45; H, 7.18 %; M^+ 280. Calcd. for $\text{C}_{19}\text{H}_{20}\text{O}_2$: C, 81.39; H, 7.19 %; M^+ 280.

Bis(2-hydroxy-3,5-dimethylbenzylidene)acetone disodium salt heptahydrate (XIV). Prepared by the procedure described for the synthesis of XII. When 100 ml of ethanolic solution of 30 g of 3,5-dimethylsalicylaldehyde²³ and 6 g of acetone was shaken with 8 g of sodium hydroxide in 15 ml of water for 1 h, the reaction proceeded slowly. After two days' standing, the color of the precipitate, which was bright-orange when filtered, on exposure to the air rapidly turned into dark-red. On the basis of this observation and analysis the formula containing one mole of oxygen was assigned. Recrystallization from 90 % ethanol yielded 32 g (61.1 % yield) of red crystals, ir 1590 cm^{-1} (conjugated C=O). Anal. Found: C, 48.03; H, 6.24; Na, 10.11 %. Calcd. for $\text{C}_{21}\text{H}_{20}\text{O}_3\text{Na}_2 \cdot 7\text{H}_2\text{O} \cdot \text{O}_2$: C, 48.09; H, 6.53; Na, 8.77 %.

1,5-Bis(2-hydroxy-3,5-dimethylphenyl)-3-pentanone (XV). Reduction of 16 g of XIV was effected with 1.7 g of 5 % palladium-charcoal in 200 ml of water under hydrogen atmosphere at 50°C to the absorption of 600 ml of hydrogen. The product was chromatographed through a column packed with 300 ml of silica gel. As a benzene elute a small amount of Id was detected but not isolated pure. XV was isolated as ether-benzene (1 : 10) elute and recrystallized from benzene-heptane (1 : 3) to yield 1.63 g (16.6 % yield) white crystals having mp 140°C; ir 1703 cm^{-1} (C=O); nmr δ =2.20 (12H, s, 4CH_3), 2.82

(8H, s, 4CH₂), 6.52 (2H, s, OH), 6.79 (1H, s, Ar), 6.90 (3H, s, Ar). Anal. Found: C, 77.52; H, 8.08 %. Calcd. for C₂₁H₂₆O₃: C, 77.27; H, 8.03 %.

Compound XV was also obtained by the reaction of 6,8-dimethyl-3,4-dihydrocoumarin with boron tribromide in the heptane solution at 100-110°C with 15.6 % yield. Crystals of XV obtained by this method are golden-yellow colored.^{7b,19}

Catalytic reduction of XIV in the acetic acid solution. Reduction of 10 g of XIV with 1.5 g of palladium-charcoal in 300 ml of acetic acid under hydrogen, on the absorption of 750 ml of hydrogen, yielded 0.32 g (3.4 % yield) Id as a benzene elute and 1.57 g (15.6 % yield) of 1,5-bis(2-hydroxy-3,5-dimethylphenyl)-3-pentanol (XVI) as ether-benzene (1 : 5) elute. The latter on crystallization from benzene-heptane (1 : 3) melted at 153°C.²⁴ Anal. Found: C, 76.66; H, 8.63 %. Calcd. for C₂₁H₂₈O₃: C, 76.79; H, 8.53 %. Structure of XVI was confirmed by its conversion into triacetate. By refluxing 0.74 g of XVI with 0.45 g of fused sodium acetate and 50 ml of acetic anhydride for 2.5 h, 0.68 g (66.7 % yield) of triacetate was obtained. The crystals on crystallization from heptane melted at 71°C; ir 1735 and 1725 cm⁻¹ (ester C=O); nmr δ=1.77 (2H, t J=6 Hz, CH₂), 1.83 (2H, t J=6 Hz, CH₂), 2.00 (3H, s, COCH₃), 2.03 (6H, s, 2CH₃), 2.23 (6H, s, 2CH₃), 2.40 (4H, t J=6 Hz, CH₂), 4.86 (1H, m, OCH), 6.80 (4H, s, Ar). Anal. Found: C, 71.18; H, 7.65 %. Calcd. for C₂₇H₃₄O₆: C, 71.40; H, 7.54 %.

6,6',8,8'-Tetramethyl-2,2'-spirobichroman (Id) from XV. By the procedure described in the preparation of Ia, treatment of 1 g of XV with 30 ml of ethanol containing 4 ml of conc. sulfuric acid yielded 0.78 g (82.1 % yield) of Id having mp 166°C; nmr δ=1.91 (5H, s, CH₃, CH₂ overlapped), 2.04 (3H, s, CH₃), 2.20 (8H, s, 2CH₃, CH₂ overlapped), 2.64 (2H, ddd J=2, 7 and 16 Hz, CH₂), 6.67 (4H, s, Ar). Anal. Found: C, 81.53; H, 7.84 %. Calcd. for C₂₁H₂₄O₂: C, 81.78; H, 7.84 %.

Bis(2-hydroxy-5-methoxybenzylidene)acetone disodium salt hexahydrate (XXII). According to the procedure described for the synthesis of XII, 75 ml of ethanolic solution of 22.2 g of 5-methoxysalicylaldehyde²⁵ and 4.3 g of acetone by treatment with 11.7 g of sodium hydroxide in 20 ml of water yielded, on recrystallization from ethanol-water (4 : 1), 21.5 g (61.6 % yield) red crystals of XXII; ir 1580 cm⁻¹ (C=O). Anal. Found: C, 68.10; H, 5.76; Na, 9.71 %. Calcd. for C₁₉H₁₆O₅Na₂·6H₂O: C, 47.70; H, 5.90; Na, 9.61 %.

1,1'-Spirobichroman-6,6'-diol dimethyl ether (If). By the procedure described in the synthesis of Ia, catalytic reduction of 200 ml of aqueous solution of 20 g of XXII with 2 g of 5 % palladium-charcoal at 50-55°C in the hydrogen atmosphere yielded 9 g of a resinous product which was dissolved in 30 ml of ethanol and treated with 45 ml of ethanol containing 6 ml of conc. sulfuric acid at 0°C for 1 h. Chromatography of the product through a column packed with silica gel yielded 6.63 g (50.8 % yield) of white crystals of If having mp 142°C as a benzene elute; nmr δ=1.96 (2H, td J=12.9, 12.9 and 6 Hz, CH₂), 2.19 (2H, ddd J=12.9, 6 and 2 Hz, CH₂), 2.70 (2H, ddd J=16, 6 and 2 Hz, CH₂), 3.25 (2H, ddd J=16, 12.9 and 6 Hz, CH₂), 3.74 (6H, s, OCH₃), 6.64 (6H, d J=1.5 Hz, Ar). Anal. Found: C, 72.97; H,

6.45 %. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45 %.

Rearrangement of 2,2'-spirobichroman (Ia) into 1,1'-spirobiindan-4,4'-diol (IIa). To a stirred refluxing (bath temperature 140°C) solution of 2.52 g of Ia in 40 ml of chlorobenzene was added 3.0 g of powdered anhydrous aluminum chloride in a lot. Vigorous reaction occurred and in 10 min precipitates separated. Stirring was continued for 1 h and the reaction mixture was cooled, treated with 50 ml of ice-water and extracted twice with ether-benzene (1 : 1). The combined organic layer was washed with brine, dehydrated with sodium sulfate, evaporated and the residue was chromatographed through a column packed with 150 ml of silica gel. The first benzene elute containing 3,4-dihydro-2,2'-spiro[2H-chromene] (IIIa) was evaporated and the residue was rechromatographed through silica gel column using benzene-heptane (1 : 1) as solvent to isolate 0.71 g of crude IIIa which on recrystallization from heptane yielded 0.60 g of white crystals having mp 90°C ; nmr δ =1.95 (1H, dd J =6 and 14 Hz, CH_2), 2.24 (1H, ddd J =2, 6 and 14 Hz, CH_2), 2.30 (1H, ddd J =2, 6 and 14 Hz, CH_2), 3.18 (1H, dd J =6 and 14 Hz, CH_2), 5.67 (1H, d J =9 Hz, =CH), 6.60 (1H, d J =9 Hz, =CH), 6.80 (8H, m, Ar). Anal. Found: C, 81.39; H, 5.78 %. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64 %.

From the second benzene elute fractions, on evaporation and crystallization of the residue from benzene-heptane (1 : 1), 1.03 g (35.5 % yield) of the clathrate compound of 1,1'-spirobiindan-4,4'-diol (IIa) with benzene having mp 105°C was obtained; nmr δ =2.26 (4H, t J =7 Hz, CH_2), 2.96 (4H, t J =7 Hz, CH_2), 4.78 (2H, s, OH), 6.58 (2H, d J =8 Hz, Ar), 6.70 (2H, d J =8 Hz, Ar), 7.12 (2H, t J =8 Hz, Ar), 7.40 (3H, s, benzene, this absorption peak was not observed in the spectrum of debenzenized sample). Anal. Found: C, 82.27; H, 6.59 %. Calcd. for $C_{17}H_{16}O_3 \cdot 1/2C_6H_6$: C, 82.44; H, 6.57 %. Debenzenization was effected by heating at 110°C under 25 mm Hg for 3 h to yield white crystals having mp $129\text{--}130^\circ\text{C}$. Anal. Found: C, 80.82; H, 6.36 %. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.36 %.

From the rapidly coming fractions of the ether-benzene (1 : 10) elute, on evaporation and crystallization of the residue from benzene-heptane (1 : 3), was obtained white needles of 1-[2-(2-hydroxyphenyl)ethyl]-4-indanol (IV) having mp 108°C . The compound, however, was proved on the nmr spectrum to contain heptane which was removed by heating at 110°C under 25 mm Hg for 3 h. The yield of deheptanized IV having mp 138°C was 0.13 g (5.7 % yield). nmr δ =1.80 (1H, t J =4 Hz, CH_2), 1.94 (1H, t J =8 Hz, CH_2), 2.34 (2H, m, CH_2), 2.76 (2H, t J =8 Hz, CH_2), 2.84 (2H, t J =8 Hz, CH_2), 3.20 (1H, m, CH), 4.70 (1H, s, OH), 4.78 (1H, s, OH), 6.90 (7H, m, Ar). Anal. Found: C, 79.72; H, 7.03 %; M^+ 254. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13 %; M^+ 254.

By the reaction of 2.50 g of Ia with 3.0 g of anhydrous aluminum chloride in 50 ml of chlorobenzene solution at 100°C for 4 h, 0.63 g (25.5 % yield) of IIIa and 0.09 g (3.4 % yield) of IV were obtained.

Rearrangement of 6,6'-dichloro-2,2'-spirobichroman (Ib) into 7,7'-dichloro-1,1'-spirobiindan-4,4'-diol (IIb). By the reaction of 538 mg of Ib with 619 mg of anhydrous aluminum chloride in 40 ml of

chlorobenzene solution at 135°C for 1 h and 1.143 g of Ib with 1.21 g of anhydrous aluminum chloride in 20 ml of chlorobenzene solution at 100°C for 3 h, 129 mg (22.1 % yield) of IIb, 221 mg (38.1 % yield) of IIIb and 440 mg (38.5 % yield) of Iib, 138 mg (12.2 % yield) of IIIb, respectively, were obtained. IIIb was obtained as the benzene elute on the silica gel column chromatography of the reaction product and was purified by rechromatography through a column packed with silica gel using benzene-heptane (1 : 1) as solvent followed by recrystallization from heptane. Iib was obtained as the ether-benzene (1 : 10) elute and was recrystallized from benzene-heptane (1 : 3). IIb: white crystals having mp 193°C; nmr δ =2.29 (4H, t J=7 Hz, CH₂), 2.93 (2H, t J=7 Hz, CH₂), 2.99 (2H, t J=7 Hz, CH₂), 6.75 (2H, d J=8 Hz, Ar), 7.00 (2H, d J=8 Hz, Ar), 8.34 (2H, s, OH). Anal. Found: C, 63.80; H, 4.40; Cl, 21.46 %. Calcd. for C₁₇H₁₄O₂Cl₂: C, 63.57; H, 4.39; Cl, 22.08 %. IIIb: white crystals having mp 177°C; nmr δ =2.02 (1H, dd J=6 and 14 Hz, CH₂), 2.32 (1H, dd J=6 and 2 Hz, CH₂), 2.79 (1H, dd J=2 and 6 Hz, CH₂), 3.25 (1H, dd J=6 and 14 Hz, CH₂), 5.77 (1H, d J=8 Hz, =CH), 6.56 (2H, d J=8 Hz, Ar), 6.72 (1H, d J=8 Hz, =CH), 7.04 (2H, s, Ar), 7.08 (2H, d J=8 Hz, Ar). Anal. Found: C, 63.97; H, 3.92 %. Calcd. for C₁₇H₁₂O₂Cl₂: C, 63.97; H, 3.79 %.

Rearrangement of 6,6'-dimethyl-2,2'-spirobichroman (Ic) into 7,7'-dimethyl-1,1'-spirobiindan-4,4'-diol (IIc). When 2.10 g of Ic was treated with 2.38 g of anhydrous aluminum chloride in 30 ml of chlorobenzene solution at 100°C for 2.6 h, on pouring the reaction mixture into ice water precipitated white amorphous product which was filtered and crystallized from benzene-heptane (1 : 1) to yield 1.22 g of IIc having mp 219°C, granular crystals of slightly pinkish tint. The aqueous filtrate was extracted twice with ether-benzene (1 : 1), from which via routine procedure 0.16 g of IIc was obtained. The total yield amounted to 65.8 %. nmr δ =2.18 (2H, t J=8 Hz, CH₂), 2.28 (8H, s, 2 CH₃, CH₂ overlapped), 2.76 (2H, t J=8 Hz, CH₂), 2.84 (2H, t J=8 Hz, CH₂), 4.36 (2H, s, OH), 6.08 (2H, d J=8 Hz, Ar), 6.93 (2H, d J=8 Hz, Ar). Anal. Found: C, 80.47; H, 7.19 %. Calcd. for C₁₉H₂₀O₂: C, 81.39; H, 7.19 %.

Rearrangement of 6,6',8,8'-tetramethyl-2,2'-spirobichroman (Id) into 5,5',7,7'-tetramethyl-1,1'-spirobiindan-4,4'-diol (IIId). To a stirred solution of 0.366 g of Id in 30 ml of chlorobenzene at room temperature (20°C), was added 0.48 g of anhydrous aluminum chloride in a lot, when vigorous exothermic reaction occurred and the temperature of the reaction mixture temporarily rose to 50°C. After stirring at room temperature for 1.5 h, the mixture was poured into ice water. Via a routine procedure, the reaction product which was practically a mixture of two compounds, was chromatographed through a column packed with silica gel. From the benzene elute, 5',6,7',8-tetramethylspiro[chroman-2,1'-indan]-4'-ol (VI) was isolated and recrystallized from benzene-heptane (1 : 5) to give 0.037 g (10.1 % yield) of faintly yellow-colored crystals having mp 106°C²⁶; nmr δ =1.92 (2H, m, CH₂), 2.14 (3H, s, CH₃), 2.25 (6H, s, 2CH₃), 2.29 (5H, s, CH₃, CH₂ overlapped), 2.76 (2H, t J=8 Hz, CH₂), 2.84 (2H, t J=8 Hz, CH₂), 4.44 (1H, s, OH), 6.85 (1H, s, Ar), 6.89 (2H, s, Ar). Anal. Found:

C, 80.92; H, 8.23 %. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84 %.

From the last benzene elute and ether-benzene (1 : 10) elute, IIId was isolated and recrystallized from benzene-heptane (1 : 5) as 0.247 g (67.5 % yield) of white crystals having mp 185°C; nmr δ =1.70 (6H, s, $2CH_3$), 2.20 (10H, s, $2CH_3$, $2CH_2$ overlapped), 2.96 (2H, t J=3 Hz, CH_2), 3.00 (2H, dd J=4 and 12 Hz, CH_2), 4.50 (2H, s, OH), 6.90 (2H, s, Ar). Anal. Found: C, 81.20; H, 7.82 %. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84 %.

Reaction of 2,2'-spirobichroman (Ia) with hydrobromic acid - acetic acid. A solution of 1.01 g of Ia in a mixture of 120 ml of acetic acid and 20 ml of hydrobromic acid was heated at 95°C for 60 h. The mixture was treated with 30 ml of water and evaporated at 60-70°C under reduced pressure to yield 1.17 g of a residue which solidified on standing. The residue was treated with water, filtered, dried, dissolved in benzene and chromatographed through a column packed with silica gel. As a benzene elute 894 mg (88.5 %) of Ia was recovered and 18 mg (1.8 % yield) of IIa was obtained as an ether-benzene (1 : 10) elute.

Reaction of 6,6'-dichloro-2,2'-spirobichroman (Ib) with hydrobromic acid - acetic acid. The reaction of 0.6 g of Ib with a mixture of 12 ml of hydrobromic acid and 72 ml of acetic acid at 95°C for 60 h as well as a reaction of 0.5 g of Ib with 15 ml of hydrobromic acid and 1.5 ml of hydroiodic acid in 20 ml of acetic acid at 140°C for 16 h, resulted in complete recovery of the starting material.

Reaction of 6,6'-dimethyl-2,2'-spirobichroman (Ic) with hydrobromic acid - acetic acid. A mixture of 520 mg of Ic, 10 ml of hydrobromic acid and 60 ml of acetic acid was heated at 95°C for 60 h. The reaction mixture was poured into 300 ml of water. The precipitate, which was filtered, weighed 465 mg. The filtrate was evaporated to yield 76 mg of a residue. The combined product was dissolved in benzene and chromatographed through a column packed with silica gel. On rechromatography of the benzene elute, 302 mg (58.1 %) of Ic was recovered as a benzene-heptane (1 : 1) elute and following Ic 31 mg (6.0 % yield) of 6,6'-dimethyl-3,4-dihydro-2,2'-spiro[2H-chromene] (IIIC) was eluted and was recrystallized from hexane, mp 87°C; nmr δ =2.06 (1H, td J=6, 14 and 14 Hz, CH_2), 2.36 (3H, s, CH_3), 2.38 (3H, s, CH_3), 2.66 (1H, ddd J=3, 6 and 14 Hz, CH_2 , partly overlies CH_3 signal), 2.90 (1H, ddd J=3, 6 and 16 Hz, CH_2), 3.42 (1H, ddd J=6, 14 and 16 Hz, CH_2), 6.01 (1H, d J=10 Hz, =CH), 6.86 (2H, d J=8 Hz, Ar), 7.06 (1H, d J=10 Hz, =CH), 7.21 (2H, s, Ar), 7.22 (2H, d J=8 Hz, Ar). Anal. Found: C, 81.92; H, 6.60 %. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52 %. As the ether-benzene (1 : 10) elute, 56 mg (10.8 % yield) of IIc was obtained as crystals having mp 217°C.

Reaction of Ic with hydrobromic acid - hydroiodic acid - acetic acid. A mixture of 0.7 g of Ic, 21 ml of hydrobromic acid, 2 ml of hydroiodic acid and 42 ml of acetic acid, was refluxed at 140°C for 16 h. The reaction mixture, on cooling, was poured into 300 ml water. The precipitate was filtered, dried, and extracted exhaustively with benzene-heptane (1 : 5) to yield 260 mg of the extract.

The aqueous filtrate was evaporated up to yield 47 mg of a residue which was combined with 260 mg of the extract and chromatographed to afford 107 mg (15.3 % yield) of IIc and 21 mg (3 % yield) of IIId.

Reaction of 6,6',8,8'-tetramethyl-2,2'-spirobichroman (Id) with hydrobromic acid - acetic acid. A mixture of 640 mg of Id, 96 ml of acetic acid and 12 ml of hydrobromic acid, was heated at 95°C for 52 h. By a procedure described in the reaction of Ic, 398 mg (62.2 % yield) of IIId having mp 183°C was obtained.

Reaction of 2,2'-spirobichroman-6,6'-diol dimethyl ether (If) with hydrobromic acid - acetic acid. A mixture of 965 mg of If, 12 ml of hydrobromic acid and 70 ml of acetic acid was heated at 80°C for 4 h. The reaction mixture was treated with 20 ml of water, evaporated to dryness at 60-70°C under reduced pressure. The residue was dissolved in benzene and chromatographed through a column packed with silica gel. Fraction I. From benzene elute, 278 mg (28.8 %) of If was recovered. Fraction II. From ether-benzene (1 : 10) elute was isolated 2,2'-spirobichroman-6,6'-diol monomethyl ether (Ig), which on recrystallization from benzene-heptane (1 : 5), melted at 152°C, 236 mg (25.6 % yield); nmr δ =1.93 (2H, td J=6, 13 and 13 Hz, CH₂), 2.18 (2H, dd J=6 and 13 Hz, CH₂), 2.68 (1H, td J=6.5, 6.5 and 20 Hz, CH₂), 2.69 (1H, td J=6.5, 6.5 and 20 Hz, CH₂), 3.22 (2H, ddd J=6.5, 13 and 20 Hz, CH₂), 3.74 (3H, s, CH₃), 4.50 (1H, s, OH), 6.52 (1H, dd J=8.5 and 2.4 Hz, Ar), 6.56 (2H, d J=8.5 Hz, Ar), 6.59 (1H, dd J=8.5 and 2.4 Hz, Ar), 6.64 (2H, s, Ar). Anal. Found: C, 72.25; H, 6.10 %. Calcd. for C₁₈H₁₈O₄: C, 72.46; H, 6.08 %. Fraction III. From ether-benzene (1 : 5) elute was obtained 100 mg (11.3 % yield) of 2,2'-spirobichroman-6,6'-diol (Ie)²⁷ which on recrystallization from benzene melted at 224°C; nmr δ =1.90 (2H, td J=6, 13 and 13 Hz, CH₂), 2.14 (2H, ddd J=2.4, 6 and 13 Hz, CH₂), 2.63 (2H, ddd J=2.4, 6 and 16 Hz, CH₂), 3.13 (2H, ddd J=6, 13 and 16 Hz, CH₂), 6.48 (2H, d J=8.4 Hz, Ar), 6.53 (2H, dd J=2 and 8.4 Hz, Ar), 6.59 (2H, d J=2 Hz, Ar), 7.80 (2H, s, OH). Anal. Found: C, 71.82; H, 5.59 %. Calcd. for C₁₇H₁₆O₄: C, 71.82; H, 5.67 %. Fraction IV. From ether-benzene (2 : 3) elute was isolated 31 mg (3.5 % yield) of 1,1'-spirobiindan-4,4',7,7'-tetrol (IIe), which on recrystallization from benzene yielded colorless crystals having mp 234°C; nmr [(CD₃)₂SO] δ =2.08 (2H, t J=5 Hz, CH₂), 2.20 (2H, t J=8 Hz, CH₂), 2.80 (2H, t J=8 Hz, CH₂), 2.92 (2H, t J=5 Hz, CH₂), 6.36 (2H, d J=8 Hz, Ar), 6.44 (2H, d J=8 Hz, Ar), 7.94 (2H, s, OH), 8.40 (2H, s, OH broad); uv $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ): 201.5 (5.32), 277 (sh 4.60), 291 (4.32), 368 (2.72). Anal. Found: C, 71.60; H, 5.63 %. Calcd. for C₁₇H₁₆O₄: C, 71.82; H, 5.67 %. By crystallization of IIe from ether-benzene (1 : 5) in the ambient atmosphere, deep blue crystals of its dihydrate having mp 232°C were isolated; uv $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ): 216 (sh 4.42), 259 (3.81), 266 (3.82), 292 (4.07), 361 (2.49), 530 (reflectance). Anal. Found: C, 62.65; H, 6.13 %. Calcd. for C₁₇H₁₆O₄·2H₂O: C, 63.74; H, 6.29 %. Dehydration of IIe dihydrate was effected by heating at 110°C under reduced pressure for 1 h.

By a reaction of 799 mg of If with 10 ml of hydrobromic acid and 55 ml of acetic acid at 80°C for

40 h, 72 mg (9.9 % yield) of Ie and 297 mg (40.8 % yield) of IIe were obtained, while by the reaction of 1 g of If with 12 ml of hydrobromic acid and 60 ml of acetic acid at 95°C for 14 h, 26 mg (2.8 % yield) of Ie, 144 mg (15.8 % yield) of IIe and 504 mg (48.9 % yield) of IIe dihydrate were obtained. In these operations, portions of the products which were insoluble in benzene were dissolved in either ether-benzene (1 : 5) or (2 : 3) and chromatographed.

3-(2-Hydroxy-5-methylphenyl)-1,1-dimethylpropan-1-ol (XVII). A solution of 16.18 g (0.1 M) of 6-methyl-3,4-dihydrocoumarin in 100 ml of THF was added to 250 ml of THF solution containing 0.25 M methylmagnesium bromide in 1 h, followed by refluxing for 2 h under argon atmosphere. The reaction mixture was cooled, treated with 75 ml of 15 % hydrochloric acid, extracted three times with 150 ml of benzene and the combined organic layer was treated with brine, dehydrated over sodium sulfate and evaporated. The residual reddish solid was dissolved in benzene and chromatographed through a column packed with silica gel. Most of the by-product (10.4 g) was eluted with ether-benzene (1 : 5). XVII was eluted with ethanol-benzene (1 : 3) and was recrystallized from benzene, 6.44 g (33.2 % yield), mp 100-102°C; nmr δ =1.29 (6H, s, 2CH₃), 1.78 (2H, t J=7.3 Hz, CH₂), 2.22 (1H, s, OH broad), 2.24 (3H, s, CH₃), 2.68 (2H, t J=7.3 Hz, CH₂), 6.73 (1H, d J=8 Hz, Ar), 6.80 (1H, s, OH broad), 6.88 (1H, d J=8 Hz, Ar). Anal. Found: C, 73.98; H, 9.21 %. Calcd. for C₁₂H₁₈O₂: C, 74.19; H, 9.34 %.

3,4-Dihydro-2,2,6-trimethyl-2H-1-benzopyran (XVIII).¹⁵ A solution of 5.99 g of XVII and 0.65 g of p-toluenesulfonic acid in 150 ml of benzene was refluxed for 22 h while azeotropically distilling water off from the reaction mixture. The benzene solution, on cooling, was washed with water, dried over sodium sulfate, evaporated and distilled. XVIII was obtained as colorless oil (4.64 g; 78 % yield), bp 85-89°C/4 mm Hg. Satisfactory analytical and nmr results were obtained.

Reaction of XVIII with aluminum chloride. To a solution of 1 g of XVIII in 30 ml of chlorobenzene being stirred at 55°C, was added 1.02 g of anhydrous aluminum chloride in a lot. The color of the solution changed into blue-green which in 10 min faded and turned to red. Stirring was continued for 1 h at the temperature. By the ordinary procedure, 1.02 g of an oil, which solidified on standing, was obtained and chromatographed through a column packed with silica gel. 2,3-Dihydro-1,1,7-trimethyl-1H-inden-4-ol (V) was obtained as benzene elute and was recrystallized from aqueous methanol, 0.856 g (85.6 % yield), mp 76°C; nmr δ =1.34 (6H, s, 2CH₃), 1.93 (2H, t J=7.3 Hz, CH₂), 2.31 (3H, s, CH₃), 2.76 (2H, t J=7.3 Hz, CH₂), 4.43 (1H, s, OH), 6.55 (1H, d J=8 Hz, Ar), 6.81 (1H, d J=8 Hz, Ar). Anal. Found: C, 81.71; H, 9.09 %. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.07 %. As a by-product eluted by benzene-heptane (1 : 3), was obtained 31 mg (1.9 % yield) of 4-(2-hydroxy-5-methylphenyl)-2-(4-chlorophenyl)-2-methylbutane as a resinous oil; nmr δ =1.36 (6H, s, 2CH₃), 1.87 (1H, dd J=2 and 4.8 Hz, CH₂), 1.90 (1H, t J=2 Hz, CH₂), 2.22 (5H, s, CH₃, CH₂ overlapped), 4.40 (1H, s, OH), 6.60 (1H, d J=8 Hz, Ar), 6.82 (1H, s, Ar), 6.84 (1H, d J=8 Hz, Ar), 7.28 (2H, d J=8 Hz, Ar), 7.31 (2H, d J=8 Hz, Ar). Anal. Found: C, 75.47; H, 7.86 %. Calcd. for C₁₈H₂₁OCl: C, 74.85; H, 7.33 %.

Reaction of 2,4-xyleneol with tert-butanol. A solution of 14.78 g of 2,4-xyleneol, 9.65 g of tert-butanol and 1.64 g of p-toluenesulfonic acid in 150 ml of benzene was refluxed for 3 h while azeotropically distilling off water from the reaction mixture. The top of the reflux condenser was connected to a series of two wash bottles each containing a solution of 10 g of bromine in 30 ml of chloroform. The reaction mixture was cooled, washed with water, dried over sodium sulfate, evaporated and chromatographed through a column packed with silica gel. As benzene elutes, 5.57 g (25.8 % yield) of 2,4-dimethyl-6-tert-butylphenol (XXII) having bp 104-105°C/1 mm Hg was obtained together with 83 mg of 4-methyl-2-tert-butylphenol having bp 95-100°C (bath)/2 mm Hg as the sole by-product derived from 2,4-xyleneol. From the wash bottles, the solvent and bromine were purged off and the residue (1.84 g) was distilled to yield 0.72 g of 1,2-dibromo-2-methylpropane (XXIII) having bp 50-55°C/25 mm Hg and 0.49 g of 1,2,3-tribromo-2-methylpropane (XXIV) having bp 105-110°C/25 mm Hg. When a solution of the same amounts of the reagents described above was refluxed without distilling water off, 1.02 g (4.7 % yield) of XXII, 4.53 g (16.1 % yield) of XXIII and 3.24 g (8.4 % yield) of XXIV were obtained. Water formed in the reaction accelerates the dehydration reaction.

Bis(2-methoxy-5-methylbenzylidene)acetone (dimethyl ether of XII). Prepared by refluxing a solution of 100 g of XII, 2.94 g of sodium hydroxide and 135 g of methyl iodide in 1.2 l of ethanol for 6 h. On recrystallization from methanol, XII dimethyl ether melted at 119°C, yield 61.54 g (88.7 %); ir 1570 (C=O), 1260 cm^{-1} (OCH_3); nmr δ =2.30 (6H, s, CH_3), 3.88 (6H, s, OCH_3), 6.84 (2H, d J=8 Hz, Ar), 7.16 (2H, d J=16 Hz, =CH), 7.18 (2H, dd J=2 and 8 Hz, Ar), 7.44 (2H, d J=2 Hz, Ar), 8.60 (2H, d J=16 Hz, Ar). Anal. Found: C, 78.16; H, 6.93 %. Calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_3$: C, 78.23; H, 6.88 %.

1,5-Bis(2-methoxy-5-methylphenyl)-3-pentanone (XX). Hydrogenation of 12 g of dimethyl ether of XII, was effected in the acetone solution (150 ml) containing 1 g of 5 % palladium-charcoal at 30°C in 6 h. On chromatography of the product through a column packed with silica gel, 8.7 g (71.2 % yield) of XX was obtained as ether-benzene (1 : 10) elute, and was recrystallized from methanol, mp 62°C; ir 1710 cm^{-1} (C=O); nmr δ =2.26 (6H, s, 2CH_3), 2.74 (4H, t J=6 Hz, CH_2), 2.87 (4H, t J=6 Hz, CH_2), 3.80 (6H, s, OCH_3), 7.04 (2H, d J=8 Hz, Ar), 7.00 (2H, s, Ar, overlapped), 7.80 (2H, d J=8 Hz, Ar). Anal. Found: C, 77.22; H, 8.05 %. Calcd. for $\text{C}_{21}\text{H}_{26}\text{O}_3$: C, 77.27; H, 8.03 %. As a by-product, 1,5-bis(2-methoxy-5-methylphenyl)-3-pentanol having mp 101°C was obtained, yield 0.31 g (2.5 %); nmr δ =1.78 (4H, dt J=6, 8 and 8 Hz, CH_2), 2.28 (6H, s, 2CH_3), 2.75 (4H, t J=8 Hz, CH_2), 3.46 (1H, quin J=6 Hz, CH), 3.83 (6H, s, OCH_3), 6.70 (2H, d J=8 Hz, Ar), 6.95 (2H, Ar, overlapped), 7.00 (2H, d J=8 Hz, Ar). Anal. Found: C, 76.64; H, 8.68 %. Calcd. for $\text{C}_{21}\text{H}_{28}\text{O}_3$: C, 76.79; H, 8.58 %.

7,7'-Dimethyl-1,1'-spirobiindan-4,4'-diol dimethyl ether (XXI). A solution of 2.7 g of XX in 30 ml of benzene was treated with 12 ml of phosphorus oxychloride followed by 4.6 g of stannic chloride and refluxed for 10 h. On the addition of another 1 g of stannic chloride, refluxing was continued for further 20 h. After the ordinary workup, the purple reaction product was chromatographed through

a column packed with 150 g of alumina to yield 2.03 g of benzene elute which was rechromatographed through a column packed with silica gel. Pure XXI was obtained as a hexane elute and recrystallized from hexane to yield 1.32 g (51.6 % yield) of white crystals having mp 143°C; nmr δ =1.76 (6H, s, 2 CH₃), 2.13 (2H, t J=9 Hz, CH₂), 2.19 (2H, dd J=4 and 9 Hz, CH₂), 2.92 (2H, t J=9 Hz, CH₂), 2.98 (2H, dd J=4 and 9 Hz, CH₂), 3.83 (6H, s, 2OCH₃), 6.62 (2H, d J=8 Hz, Ar), 6.88 (2H, d J=8 Hz, Ar). Anal. Found: C, 81.65; H, 7.84 %. Calcd. for C₂₁H₂₄O₂: C, 81.78; H, 7.84 %.

Conversion of XXI into IIc. A mixture of 2.03 g of XXI, 25 ml of hydrobromic acid, 2 ml of hydroiodic acid and 35 ml of acetic acid was refluxed for 30 h. After cooling, the whole mixture was poured into 200 ml of water to yield 1.75 g of precipitate which together with the evaporation residue of the filtrate was chromatographed. The yield of pure IIc was 1.15 g (62.2 %). Diacetate of IIc was prepared by heating 163 mg of IIc, 3 ml of pyridine and 1 ml of acetic anhydride at 100°C for 4.5 h. The yield of white crystals of the diacetate having mp 168°C, was 121 mg (57.1 %); ir 1760 cm⁻¹ (C=O). Anal. Found: C, 75.30; H, 6.70 %; M⁺, 364. Calcd. for C₂₃H₂₄O₄: C, 75.80; H, 6.64 %; M⁺, 364.

Optical resolution of 7,7'-dimethyl-1,1'-spirobiindan-4,4'-ylene di-(+)-(N-1-phenylethyl)carbamate.

A solution of 2 g of IIc, 1 drop of pyridine and 5 ml of (+)-1-phenylethyl isocyanate in 50 ml of toluene was refluxed for 46 h. After evaporation of the solvent, remained resinous mass which on trituration with 50 ml of benzene solidified. The precipitate was filtered and recrystallized from benzene-heptane (1 : 5) to yield 1.26 g white crystals of S-IIc di-(+)-(N-1-phenylethyl)carbamate (XXV) having mp 152°C; $[\alpha]_D^{15}$ -26° (EtOH, c = 0.55); ir 1720 cm⁻¹ (C=O); nmr δ =1.60 (6H, d J=8 Hz, 2CH₃), 1.80 (6H, s, 2CH₃), 2.19 (2H, t J=10 Hz, CH₂), 2.22 (2H, t J=4 Hz, CH₂), 2.76 (2H, dd J=4 and 10 Hz, CH₂), 2.98 (2H, dd J=4 and 10 Hz, CH₂), 5.00 (2H, q J=8 Hz, CH), 5.32 (2H, s, NH), 6.96 (4H, s, Ar), 7.44 (10H, s, Ar). Anal. Found: C, 77.49; H, 6.71; N, 5.04 %. Calcd. for C₃₇H₃₈O₄N₂: C, 77.32; H, 6.67; N, 4.87 %. The benzene filtrate was chromatographed through a column packed with 400 ml of silica gel. From the ether-benzene (1 : 20) elute, 1.43 g (35 % yield) of R-IIc di-(+)-(N-1-phenylethyl)carbamate (XXVI) was obtained. On recrystallization from benzene-heptane (1 : 5) it melted at 104°C. Its ir and nmr spectra were identical with those of XXV. $[\alpha]_D^{15}$ -118° (EtOH, c = 0.45). Anal. Found: C, 78.17; H, 6.75; N, 4.56 %. Calcd. for C₃₇H₃₈O₄N₂: C, 77.32; H, 6.67; N, 4.87 %. From ether-benzene (1 : 10) elute, 0.13 g of XXV was isolated. The total yield of XXV amounted to 1.39 g (34 %).

Isolation of S-IIc by the hydrolysis of XXV. A solution of 0.5 g of XXV, 1.5 g of potassium hydroxide and a drop of water in 15 ml of ethanol was refluxed for 10 h. After cooling, the solution was decanted from sodium carbonate, acidified with hydrochloric acid and the mixture containing some crystals was evaporated to yield 176 mg of precipitate from which on recrystallization 141 mg (57.8 % yield) of S-IIc having mp 194°C was obtained; $[\alpha]_D^{15}$ +62° (EtOH, c = 0.56), +263° (dioxane, c =

0.13); ϵ 236.5 nm (dioxane, $\Delta\epsilon$ +31.1); high performance liquid chromatography, retention time 9 min (Chiralpak OT(+)) column 4.6 x 250 mm, flow rate 0.5 ml/min, uv detector at 254 nm); uv nm ($\log \epsilon$), 206 (4.9), 228 (sh, 4.5), 277 (3.5), 283.5 (3.5). Anal. Found: C, 80.60; H, 7.22 %. Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19 %.

Isolation of R-IIc by the hydrolysis of XXVI. According to the procedure described above, 0.5 g of XXVI yielded 152 mg (62.3 % yield) of R-IIc having mp 194 °C; $[\alpha]_D^{15}$ -67° (EtOH, c = 0.55), -280° (dioxane, c = 0.13); ϵ 237 nm (dioxane, $\Delta\epsilon$ -26.7); high performance liquid chromatography, retention time 9.7 min. Anal. Found: C, 80.71; H, 7.23 %. Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19 %.

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REFERENCES

1. R. P. Lutz, Chem. Rev., 1984, 84, 205; J. H. Hoare, P. P. Policastro and G. A. Berchtold, J. Am. Chem. Soc., 1983, 105, 6264; R. D. H. Murray and Z. D. Jorge, Tetrahedron, 1984, 40, 5529; M. Anastasia, P. Allevi, P. Ciufredda and A. Fiecchi, J. Chem. Soc. Perkin. Trans. I, 1983, 2365.
2. a: F. Johnson, 'Friedel-Crafts and Related Reactions', eds, by G. A. Olah, Wiley, New York, 1964, vol. IV. p. 25; b: J. P. Gesson, L. D. Giusto and J. C. Jacquesy, Tetrahedron, 1978, 34, 1715.
3. W. F. Short, J. Chem. Soc., 1928, 528; F. J. Sowa, H. O. Hinton and J. A. Nieuwland, J. Am. Chem. Soc., 1933, 55, 3402.
4. H. Hart and R. J. Elia, J. Am. Chem. Soc., 1954, 76, 3031; W. L. Gilbert and E. S. Wallis, J. Org. Chem., 1940, 5, 184.
5. R. A. Smith, J. Am. Chem. Soc., 1933, 55, 849, 3718; ibid., 1934, 56, 717; M. J. S. Dewar and N. A. Puttnam, J. Chem. Soc., 1960, 959.
6. D. S. Tarbell and J. C. Petropoulos, J. Am. Chem. Soc., 1952, 74, 244; H. S. Mason, J. Am. Chem. Soc., 1947, 69, 2241; T. Tanaka and Y. Tsuchihashi, Abstracts of papers of the 50th annual meeting of the Japan Chemical Society, Tokyo, Jpn. 1985, II, 1234; M. Matsuoka, M. Tsuchiya and T. Nishida, Ger. Offen. DE 3,334,951, Chem. Abst., 1984, 101, P. 23333d.
7. a: T. Tanaka, Chem. Lett., 1980, 739; b: Abstracts of papers of the 8th congress of heterocyclic chemistry, Kyoto, Jpn., 1975, 194; T. Tanaka and T. Tomimatsu, Heterocycles, 1975, 3, 1137; T. Tanaka, Abstracts of papers of the 33rd symposium on organic reaction mechanism, Kyoto, Jpn.

- 1982, 136.
8. T. Tanaka, M. Murakami, Y. Kitajima, Y. Ota, M. Yamamura and H. Furukawa, Abstracts of papers of the 34th symposium on organic reaction mechanism, Sapporo, Jpn. 1983, 122.
 9. J. C. Jacquesy, M. P. Jouannetaud and S. Makani, Chem. Comm., 1980, 110.
 10. P. S. Dewar, E. Ernstbrunner, J. R. Gilmore, M. Godfrey and J. M. Mellor, Tetrahedron, 1974, 30, 2455.
 11. R. D. Fisher and T. D. Bogard, J. Am. Chem. Soc., 1972, 94, 7599; R. Markovits-Kornis, Chem. Ber., 1971, 104, 3080.
 12. No substantial amount of 1,1'-spirobiindan-4,4'-diol derivative was obtained from 1,5-bis(2-methoxyphenyl)-3-pentanone by the procedure which effected the cyclization of 1,5-bis(2-methoxy-5-methylphenyl)-3-pentanone (see experimental).
 13. A. T. Mora and T. Szeki, J. Am. Chem. Soc., 1950, 72, 3009.
 14. Following the ingenious work of Stork et al., effective syntheses have been reported on the implicit "tied up group" concept. G. Stork, S. Malhotra, H. Thompson and M. Uchibayashi, J. Am. Chem. Soc., 1965, 87, 448; R. Breslow, Acc. Chem. Res., 1980, 13, 170; R. Breslow and D. Heyer, Tetrahedron Lett., 1983, 24, 5039; M. S. South and L. S. Liebeskind, J. Am. Chem. Soc., 1984, 106, 4181.
 15. L. Bolzoni, G. Casiraghi, G. Casnati and D. Sartori, Angew. Chem., 1978, 90, 727; E. K. Aleksandrova, E. I. Bunina-Krivorukova and K. V. Bal'yan, Zh. Org. Khim., 1980, 16, 459, Chem. Abst., 1980, 93, 45637z.
 16. a: S. Hagishita, K. Kuriyama, M. Hayashi, Y. Nakano, K. Shingu and M. Nakagawa, Bull. Chem. Soc. Jpn., 1971, 44, 196; R. K. Hill and D. A. Cullison, J. Am. Chem. Soc., 1973, 95, 1229; J. H. Brewster and R. T. Prudence, ibid., 1973, 95, 1217.
 17. Y. Okamoto, K. Suzuki, K. Ohta, K. Hatada and H. Yuki, J. Am. Chem. Soc., 1979, 101, 4769; Y. Okamoto, S. Honda, I. Okamoto and H. Yuki, ibid., 1981, 103, 6971; Y. Okamoto, I. Okamoto and H. Yuki, Chem. Lett., 1981, 835.
 18. N. Harada, J. Iwabuchi, Y. Yokota, H. Uda, Y. Okamoto, H. Yuki and Y. Kawata, Abstracts of papers of the 15th symposium on structural organic chemistry, Kyoto, Jpn. 1982, 3B, 35; N. Harada, T. Ai and H. Uda, Chem. Comm., 1982, 232.
 19. T. Tanaka, T. Tomimatsu, R. K. Mochisuki and M. Okamoto, Abstracts of papers of the 32nd symposium on organic reaction mechanism, Tsukuba, Jpn. 1981, 151.
 20. K. Sato, T. Amakasu and S. Abe, J. Org. Chem., 1964, 29, 1971.
 21. nmr Spectrum of Ib was reported in reference 7a.
 22. A. C. Whitaker, J. Am. Chem. Soc., 1947, 69, 2414; R. B. Thompson, Org. Synth., 1947, 27, 21.
 23. 3,5-Dimethylsalicylaldehyde was prepared from 2,4-xyleneol by Duff reaction with 29 % yield. 2,4-

Dinitrophenylhydrazone, mp 291°C.

24. This compound can be purified by sublimation under reduced pressure.
25. 5-Methoxysalicylaldehyde was prepared by the modified Reimer-Tiemann reaction with 40 % yield.
Y. Sasson and M. Yanovich, Tetrahedron Lett., 1979, 39, 3753.
26. It is suggested that this compound is racemic as on the high performance liquid chromatogram (Chiralpak OT(+)) column; flow rate 0.5 ml/min; uv detector at 254 nm) two peaks having retention times 11.5 and 12.2 min, respectively, were observed.
27. This compound could not be prepared by a scheme described in Figure III. Reaction of gentis-aldehyde with acetone yielded ambiguous product which on catalytic hydrogenation changed into black polymeric compound.

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