Tetrahedron: Asymmetry Vol. 4, No. 3, pp. 383-392, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Chiroptical Properties of Benzene Chromophore in Substituted 1,1-Diphenylcyclopropanes*

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(*Received in UK* 14 *December* 1992; *accepted* 12 *January* 1993)

Abstract - The CD spectra of 29 derivatives of 1,1-diphenylcyclopropane of known absolute configuration have been measured. The minimum energy "perpendicular" conformation of these molecules follows from the MMX calculations as well as from available X-ray data. A contribution of substituents X and Y in the 2-position of the cyclopropane ring to the rotatory strength of the phenyl chromophores is evaluated and a simple rule relating the size and donor character of the substituent to the sign of the ^1L_b and L_a^1 Cotton effects is proposed.

INTRODUCTION

Optical activity of chiral molecules containing isolated benzene ring has been a subject of numerous investigations[1]. Since the benzene chromophore is highly symmetrical the rotational power is gained through interaction with chirally disposed substituents. A number of sector rules have been developed to correlate the optical activity of the benzene chromophore associated with the forbidden ^1L_b and ^1L_a bands with the substitution pattern[1,2]. Snatzke has studied the effect of the substitution pattern of the benzene ring on the sign and magnitude of the ^1L_b band Cotton effect[3,4].

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* Dedicated to the memory of Professor Günther Snatzke

Particularly difficult to interpret are chiroptical data for monosubstituted benzene derivatives, as these molecules show significant conformational mobility[1]. Within this group of compounds a number of benzene derivatives having a chiral center at β-position have been investigated[5-8], but no general rule relating the chiroptical data to absolute configuration has been proposed.

1,1-Diphenylcyclopropanes are good model compounds to study, as such molecules, unlike ordinary benzene derivatives with alkyl chain substituent, have restricted rotation around the phenyl - cyclopropyl bond. In this report we present the CD data for 1,1-diphenylcyclopropanes of the general formula shown in Fig.1 (X ≠ Y).

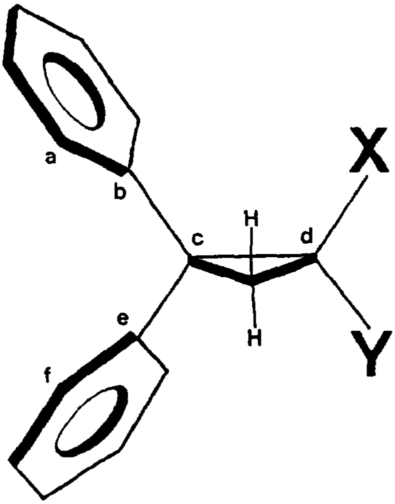


Fig.1

Previously published CD data on phenylcyclopropane derivatives have been reviewed by Runge[9].

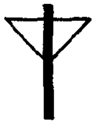
ABSOLUTE CONFIGURATION

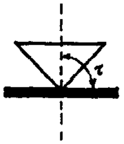
All of the compounds studied here (Table 2) have absolute configurations known due to a series of chemical correlations carried out in one of the authors' laboratory (see references in EXPERIMENTAL).

CONFORMATION

For phenylcyclopropane derivatives two extreme conformations of the phenyl ring with respect to the cyclopropane ring are possible : the bisected conformation (A) and the perpendicular one (B), as viewed along the C-C bond joining the two rings. A comprehensive analysis of the

X-ray structural data of cyclopropane derivatives carried out by Allen[10] revealed systematic geometrical changes that constitute evidence for conjugation of the cyclopropane with the π-acceptor group. In particular, π-donation from the HOMO of the cyclopropyl into the LUMO of the phenyl group occurs in a bisected conformation (A), while no effects due to orbital overlap are observed in the perpendicular conformation (B)[10,11].


A (τ=0)



B (τ=90°)

Numerous X-ray data show that while many phenylcyclopropane derivatives show preference for conformation A (τ = 0–20°)[12], those with steric constraints that render the bisected conformation unfavourable would prefer perpendicular conformation B (τ = 70–90°)[13]. In particular, 1,1-diphenylcyclopropane derivatives invariably show preference for the perpendicular conformation of both phenyl rings as judged from the available X-ray data[14], including those for the three 2,2-diphenylcyclopropanecarboxylic acids 4[14d], 11[14d] and 22[14e].

Our MMX[15] calculations on the derivatives of 1,1-diphenylcyclopropane show consistently the minimum of steric energy for the perpendicular conformation. Table 1 lists the calculated torsion angles α and β, as defined in Fig. 1, for the minimum energy conformers. Large differences between α and β values are found for 1,1-diphenylcyclopropanes having a bulky substituent X and a hydrogen atom as Y. These compouds have significant values of angle γ (Table 1) which is the measure of twist of the two phenyl rings with respect to each other caused by the two substituents X and Y (Fig.1).

The values in Table 1 for compounds 4, 11 and 22 differ slightly from the values α and β determined by the X-ray structural analysis (4 : $\alpha = -121^\circ$, $\beta = 107^\circ$ [14d]; 11 : $\alpha = -122^\circ$, $\beta = 109^\circ$ [14d]; 22 : $\alpha = -103.5^\circ$, $\beta = 108.1^\circ$ [14e]), but the support for a slightly distorted perpendicular conformation remains unchallenged.

CIRCULAR DICHROISM

With the configurational and conformational data at hand we have sound basis for the analysis of the chiroptical data of 1,1-diphenylcyclopropanes 1-29, collected in Table 2.

Table 1. Conformation (MMX) of 1,1-diphenylcyclopropanes

No.	X	Y	Torsion angles α (abcd)	 β (fecd)	 γ (abef)
1	H	Me	−125.5	116.3	- 7.3
2	H	Bu	−127.1	114.3	- 9.9
3	H	CH_2OH	−127.9	112.9	−11.2
4	H	COOH	−128.3	112.6	−11.6
5	H	COOMe	−128.5	108.4	−14.8
6	H	F	−126.6	119.9	- 5.0
7	H	Cl	−126.1	115.2	- 8.5
10	Me	CH_2OH	−117.9	114.3	- 2.7
11	Me	COOH	−118.4	113.8	- 3.2
12	Me	F	−116.8	122.0	4.2
13	Me	Cl	−117.7	115.7	- 1.3
14	Me	Br	−117.4	114.8	- 1.8
17	CH_2OH	OMe	−114.6	122.4	6.0
18	CH_2OH	F	−115.7	122.0	5.0
19	CH_2OH	Br	−115.6	114.9	- 0.4
21	COOH	OMe	−112.1	123.9	8.5
22	COOH	F	−115.2	123.1	5.9
23	COOH	Cl	−114.2	117.5	2.3
24	COOH	Br	−113.9	116.3	1.6

Due to restricted rotation of the phenyl groups these compounds generally display moderate to large Cotton effects within the ^1L_b and ^1L_a absorption bands. The ^1L_b Cotton effect in the 275–250 nm range is composed of vibronic bands of which only the well-defined ones at the longer-wavelength side of the ^1L_b band are reported. These include the bands with the maxima around 270, 263 and 257 nm, which are the most intense ones, with the exception of 19 and 20 (see Table 2). These vibronic bands are in several cases accompanied by the second progression of CD maxima of opposite sign at 274 and 266 nm, usually of lower intensity. In several cases there is only a small "hump" observed at 276 nm (1–3, 6, 10, 23, 25). A common feature of the compounds showing a second progression of vibronic bands is the presence of at least one bulky substituent.

The ^1L_a band Cotton effect appears in the spectral range close to the corresponding UV maximum (219–225 nm), although in some cases it is red-shifted down to 233 nm – depending on the sign and intensity of the

Table 2. CD and UV data (acetonitrile solution) for substituted 1,1-diphenylcyclopropanes 1-29

No.	X	Y	Configuration and sign of rotation	^1L_b		^1L_a	
				$\Delta\varepsilon$ (λ_{max})		$\Delta\varepsilon$ (λ_{max})	ε (λ_{max})
1	H	Me	(R)-(-)	+0.19(276) -1.48(263)	-1.12(270) -1.10(257)	- 9.0(225)	13400(222)
2	H	n-Bu	(R)-(-)	+0.15(276) -2.24(263)	-1.55(270) -1.50(257)	-10.1(221)	13300(222)
3	H	CH_2OH	(R)-(-)	+0.03(276) -1.45(263)	-1.21(270) -1.05(257)	- 9.8(217)	13200(221)
4	H	COOH	(R)-(-)	-1.50(268) -1.45(258)	-1.90(263)	-18.0(218)	13200(221)
5	H	COOMe	(R)-(-)	-1.26(269) -1.12(256)	-1.48(263)	-16.6(218)	13300(221)
6	H	F	(R)-(+)	+0.04(274) -0.51(261)	-0.40(268) -0.33(256)	- 2.6(219)	13000(219)
7	H	Cl	(R)-(-)	-0.90(269) -0.64(256)	-1.04(262)	- 5.2(215)[a]	13600(220)
8	H	NC	(R)-(-)	-0.88(269) -0.72(255)	-1.00(262)	-10.7(215)	13300(219)
9	H	NHCHO	(R)-(-)	-1.13(269) -0.80(256)	-1.18(263)	- 3.1(227)	13700(219)
10	Me	CH_2OH	(R)-(-)	-0.03(274) +0.24(263)	+0.27(270) +0.11(257)	- 2.7(231)	14000(224)
11	Me	COOH	(R)-(+)	+0.70(270) +0.50(257)	+0.80(263)	- 3.9(223)[b]	13800(223)
12	Me	F	(R)-(+)	+0.47(271) +0.38(257)	+0.54(264)	+ 8.0(224)	13300(222)
13	Me	Cl	(R)-(-)	+0.31(272) +0.10(258)	+0.25(265)	+ 8.8(230)	13000(223)
14	Me	Br	(R)-(-)	+0.37(272) +0.15(257)	+0.28(265)	+11.5(232)	11600(225)
15	Me	NC	(R)-(-)	+0.25(271) +0.12(257)	+0.23(264)	+ 2.8(225)	13600(221)
16	Me	NHCHO	(R)-(-)	-0.33(272) -0.22(258)	-0.30(265)	- 5.2(232)	13400(222)
17	CH_2OH	OMe	(R)-(-)	+0.45(272) +0.49(258)	+0.46(265)	+ 7.2(228)	13000(223)
18	CH_2OH	F	(R)-(+)	+0.37(271) +0.32(258)	+0.44(264)	+ 6.8(224)	13000(221)

Table 2 continued

19	CH_2OH	Br	(R)-(-)	+0.24(272) +0.15(266)	-0.05(269) -0.09(262)	+11.8(231)	14000(222)
20	CH_2OMe	Br	(R)-(-)	+0.19(273) +0.13(266)	-0.08(269) -0.10(262)	+12.5(232)	11600(225)
21	COOH	OMe	(R)-(+)	+0.38(272) +0.19(258)	+0.30(265)	+13.0(216)[c]	13800(223)
22	COOH	F	(R)-(+)	+0.26(271) +0.19(257)	+0.26(264)	+10.7(217)[d]	13100(222)
23	COOH	Cl	(R)-(-)	+0.10(274) -0.40(262)	-0.34(269) -0.10(257)	+ 7.5(226)	13300(224)
24	COOH	Br	(R)-(-)	+0.13(274) +0.09(266)	-0.28(269) -0.18(262)	+ 6.4(232)	12200(224)
25	COOMe	Br	(R)-(-)	+0.09(274) +0.30(262)	-0.35(269)	+ 6.3(233)	12500(224)
26	F	Cl	(R)-(-)	-0.13(269) -0.12(257)	-0.17(262)	- 2.0(220)[e]	12800(220)
27	F	Br	(R)-(-)	-0.13(271) -0.16(256)	-0.19(263)	- 2.0(218)[f]	12600(221)
28	F	J	(R)-(-)	-0.14(271)	-0.06(265)	+ 2.0(224)[g]	12000(220)
29	F	NHCOOtBu	(S)-(-)	-0.36(269) -0.32(256)	-0.41(262)	-10.4(215)	12600(219)

Additional bands :

[a] +1.0 at 231 nm; [b] +1.8 at 233 nm; [c] +0.8 at 243 nm;
[d] +0.4 at 243 nm, -0.9 at 232 nm; [e] +0.7 at 231 nm;
[f] +2.6 at 231 nm; [g] +0.9 at 247 nm, -0.8 at 233 nm

strong CD band at still shorter wavelength. An additional CD maximum may precede the ^1L_a Cotton effect (see footnotes to Table 2) which may either be due to the $n-\pi^*$ Cotton effect of the carboxylic group (11, 21, 22) or due to a halogen substituent.

All derivatives with X = H and absolute configuration (R) (1-9, Fig. 1) display negative ^1L_b and ^1L_a Cotton effects, hence allowing the unambiguous correlation of the absolute configuration with the sign of these Cotton effects. It is of interest to note here that the absolute configuration does not correlate unambiguously with the sign of $[\alpha]_D$, as compound 6, unlike others in the series 1-9, has positive rotation.

Since two phenyl chromophores are present in the compounds studied here it is pertinent to evaluate the contribution of each phenyl group to the rotational strength associated with the ^1L_b and ^1L_a bands.

The superposition of the two projections along the $C_{aryl}-C_{cyclopropane}$ bond with the phenyl ring perpendicular to the plane of projection shows the two contributions, trans and cis, from substituent Y (Fig. 2).

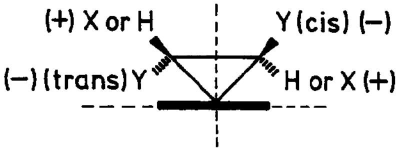
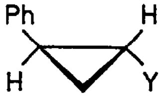
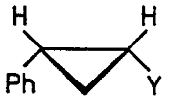


Fig. 2

According to Schellman[16] a regional quadrant rule can be devised for both ^1L_b and ^1L_a band Cotton effects, as defined by the nodal plane of the benzene p orbitals and the plane orthogonal to the preceding one and passing through the $C_{aryl}-C_{cyclopropane}$ bond. The trans-Y substituent gives a negative contribution as corroborated by the fact that the ^1L_b and ^1L_a Cotton effects of (−)-(1R,2R)-trans-1-methyl-2-phenylcyclopropane (C, Y = Me) and (−)-(1R,2R)-trans-2-phenylcyclopropanecarboxylic acid (C, Y = COOH) are also negative[17] but of lower amplitudes. As the cis stereoisomers of the two compounds mentioned above (D) also have negative rotations[18] it is reasonable to assume that in 1 and 4 both phenyl groups cis and trans to the substituent Y give negative rotatory contributions to the ^1L_b and ^1L_a Cotton effects, relative to hydrogen atoms.



C



D

Concerning the relative magnitude of the contribution of different Y substituents it can readily be deduced that carbon substituents give the strongest contributions (1–5), followed by isonitrile (8), formamido (9) and chlorine (7) substituents, with fluorine (6) substituent providing the smallest contribution (Table 3).

For disubstituted derivatives 10–29 the observed ^1L_b and ^1L_a Cotton effects should result from the difference of contributions of substituents X and Y, according to Fig. 2. However, the order of contributions of different substituents does not seem to follow strictly the order established for monosubstituted derivatives (Table 3).

Table 3. Decreasing contributions of substituents X, Y to the rotatory strength of ^1L_b and ^1L_a bands of 1,1-diphenylcyclopropanes

	Monosubstituted (X or Y = H)	Disubstituted (X, Y ≠ H)
^1L_b	n-Bu, COOR, CH_2OH, Me, NHCHO, NC, Cl, F, H	NHCOR, Me, CH_2OH, I, Br, Cl, NC, COOR, F, OMe
^1L_a	COOR, n-Bu, CH_2OH, Me, NC, Cl, NHCHO, F, H	NHCOR COOR, CH_2OH, Me, NC, Br, Cl, F, OMe

The Cotton effects of derivatives having X = Me (**10**–**16**) indicate a dominating contribution of the Y = NHCHO substituent (**16**), as both ^1L_a and ^1L_b Cotton effects are negative. Two other Y substituents, CH_2OH (10) and COOH (**11**) give stronger contributions, compared to X = Me, to the ^1L_a Cotton effect - but not to the ^1L_b Cotton effect. For other derivatives having hetero substituents (**12**–**15**, **17**–**20**) the dominant contribution of the methyl or hydroxymethyl group is evident. Derivatives of 2,2-diphenyl-1-cyclopropanecarboxylic acid (X = COOH, **21**–**25**) follow the above order for disubstituted 1,1-diphenylcyclopropanes, giving positive ^1L_a and ^1L_b Cotton effects (however additional strong negative vibronic bands are associated with the ^1L_b Cotton effect of halogenoacids 23 and **24**). Finally, the halogenated 1,1-diphenylcyclopropanes **26**–**29** give Cotton effects reflecting the relative magnitudes of the contribution of heteroatom substituents (the relative contribution of F and I to the ^1L_a Cotton effect in **29** is difficult to assess due to the multiplicity of the CD bands in the region 220-250 nm).

Comparison of the substituent contributions to the Cotton effects of mono- (**1**–**9**) and disubstituted (**10**–**25**) 1,1-diphenylcyclopropanes suggests that two factors are operative : steric effects and substituent electronic properties. In cases where X = H steric effects of the Y substituent appear to dominate. Thus alkyl, CH_2OH and COOR groups contribute stronger than other Y substituents. This may correlate to some extent with the degree to which the two phenyl rings are twisted with respect to each other (angle γ in Table 1). When X ≠ H steric effects appear to contribute to a smaller extent, as the derivatives **13** and **14** with similar van der Waals radii of X and Y substituents still produce strong Cotton effects, particularly the one associated with the ^1L_a band. In this case a combination of donor properties and the size of the substituents seems to determine their magnitudes of contribution, as shown in Table 3. Thus, for 1,1-diphenylcyclopropane derivatives of the general formula given in Fig. 1 positive ^1L_a and ^1L_b Cotton effects are expected when Y gives a stronger contribution compared to X and negative Cotton effect when the stronger contribution is from the X substituent; the sequence of contributions being determined according to Table 3.

Finally it should be noted that while Cotton effects of disubstituted 1,1-diphenylcyclopropane derivatives can satisfactorily be correlated with the absolute configuration of these compounds, the negative sign of $[\alpha]_D$ value for derivatives **13-15**, **17**, **19** and **20** is rather confusing in view of the positive ${}^1L_b$ and ${}^1L_a$ Cotton effects measured for these compounds.

EXPERIMENTAL

The CD spectra were recorded with either a JASCO Model J-500 spectropolarimeter or with a Jobin-Yvon III dichrograph. The UV spectra were recorded with a Cary 219 spectrophotometer.

Enantiomers of some compounds reported here were actually measured and the CD data were correlated to 100 % e.e. Sources of compounds : 1[19], 2[20], ent-3[21], ent-4[21,22], ent-5 (prepared by CH_2N_2 estrification of ent-4), 6[23], 7[24], ent-8[22], ent-9[22], 10[25], ent-11[21,26], 12[27], ent-13[27,28], 14[28], 15[29], ent-16[29], 17[24], 18[24], ent-19[30], ent-20[31], ent-21[24], 22[24], 23[28], 24[19], 25 (prepared by CH_2N_2 estrification of 24), ent-26[23], ent-27[23], ent-28[23], and ent-29[32].

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