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CIRCULAR DICHROISM OF OPTICALLY ACTIVE 1,2-DISUBSTITUTED 1,2-DIPHENYLETHANES—PART I: THE COTTON EFFECTS WITHIN THE α-BAND[1]

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Zusammenfassung—Die zwei Phenylchromophore eines optisch aktiven 1,2-disubstituierten 1,2-Diphenylethans geben unabhängig voneinander Cotton-Effekte innerhalb des Wellenlängenbereichs der α-Bande. Durch Bildung der Summen-und Differenz-CD-Kurve für ein threo/erythro Paar erhält man CD-Spektren, die für jedes "Halbmolekül" charakteristisch sind, und die im allgemeinen zwei 0–0—Linien um 37230 cm^{-1} aufweisen. Aus deren Vorzeichen kann die absolute Konfiguration an jedem der Chiralitätszentren eindeutig bestimmt werden.

Abstract—The two phenyl chromophores of optically active 1,2-disubstituted 1,2-diphenylethanes give independent Cotton effects within the wavelength range of the α-band. By drawing the sum and difference CD curves for a threo/erythro pair CD spectra characteristic for each "half-molecule" are obtained, in which generally two 0–0-lines appear near 37230 cm^{-1}. From their signs the absolute configuration at each centre of chirality can be determined unequivocally.

1,2-Disubstituted 1,2-diphenylethanes contain two phenyl chromophores, which do not interact (or at least do not interact strongly) with each other within the energy range corresponding to the absorption within the α-band (250–280 nm). In a following paper we will give details about all Cotton effects found for such compounds, and also on the determination of their absolute configuration from their circular dichroism bands at shorter wavelengths.

In general within the range of the α-band in the UV-spectrum one finds only weak absorption, but very pronounced fine structure. At least two series can be identified also in solution spectra, namely the one which has its origin in the 0–0-transition (spac-

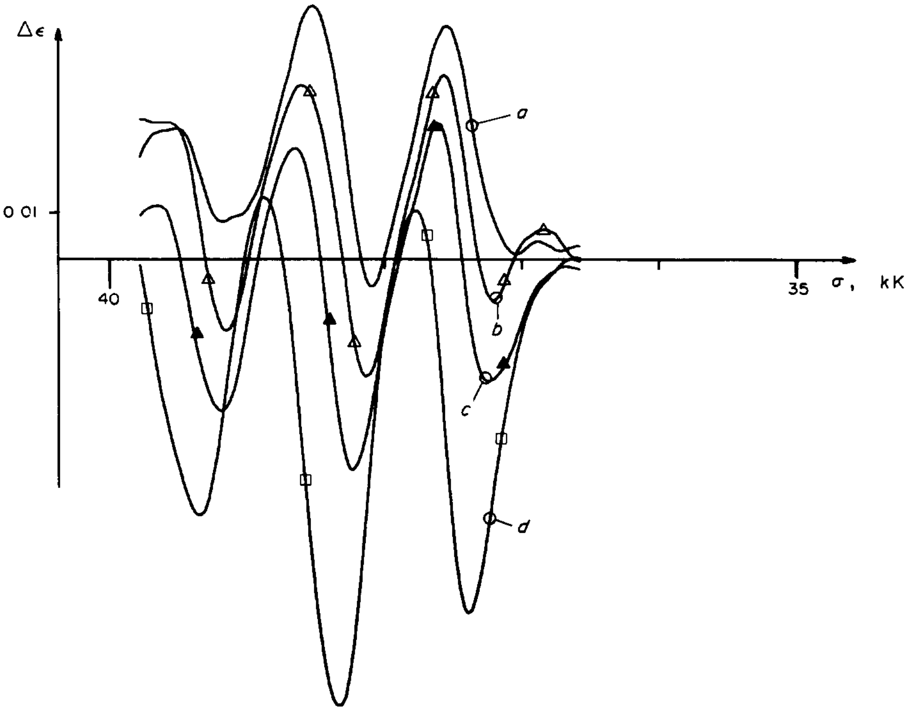
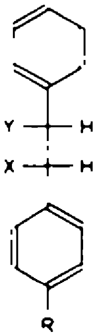


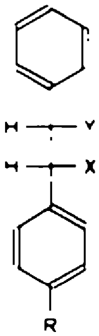
Fig. 1. Solvent dependence of the CD spectrum of **26** (a) ethanol; (b) ethanol–acetonitrile 3:1; (c) ethanol–acetonitrile 1:1; (d) acetonitrile. Abscissa linear in wavenumbers (1 unit = 10^3 cm^{-1}).

ing approx. 920 cm^{-1}), whereas the second is shifted to the blue by approx. 520 cm^{-1} (1 quantum of the non-totally-symmetric vibration ν_6).[7] In the CD spectra both series can also be identified and have even sometimes opposite signs.[7] We noticed empirically that such bisignate CD-curves appear only very rarely with erythro compounds, but are quite frequently found for their threo-isomers. In such cases the shape of these fine structure bands changes also quite drastically with a change of the solvent. One extreme such case is shown in Fig. 1.

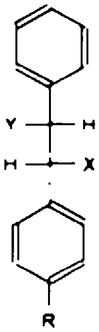
For each optically active 1,2-diphenylethane deriv-

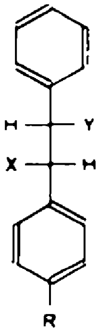


	X	Y	R	Lit.
1	HO	HOCH$_2$	Cl	6b
2	HO	MenOOC	Cl	6b,9
3	HO	MenOOC	OCH$_3$	6b,9
4	AcO	AcOCH$_2$	Cl	6b
5	MenOOC	HO	Cl	6b,9



	X	Y	R	Lit.
6	CH$_3$	NH$_2$	H	10
7	CH$_2$Br	NH$_2$	H	10
8	CH$_2$OH	OH	H	6a
9	CH$_2$OH	OH	Cl	6b
10	CH$_2$OH	NH$_2$	H	10,11
11	CH$_2$OH	NH$_3^+$	H	6b
12	CH$_2$OAc	OAc	H	6b
13	CH$_2$OAc	OAc	Cl	6b
14	CH$_2$OAc	NHAc	H	-
15	OH	COOMen	H	6b,9
16	OH	COOMen	Cl	6b,9
17	NH$_2$	CH$_2$NH$_2$	H	12
18	NH$_2$	COOMen	H	10,11
19	NH$_3^+$	CH$_2$NH$_3^+$	H	12
20	NH$_3^+$	COOMen	H	10,11
21	NHCOCH$_2$Cl	OH	H	13
22	NHCONH$_2$	COOMen	H	14
23	COOMen	OH	H	6a
24	COOMen	OH	Cl	6b,9
25	COOMen	NH$_2$	H	10,11
26	COOMen	NH$_3^+$	H	10,11
27	COOMen	NHCONH$_2$	H	14





	X	Y	R	Lit.
28	CH_2OH	HO	H	6b
29	CH_2OH	HO	Cl	6b
30	CH_2OAc	AcO	H	6b
31	CH_2OAc	AcO	Cl	6b
32	[illegible]	$HOCH_2$	Cl	6b
33	OH	$HOCH_2CONH$	H	[illegible]
34	OH	MeOOC	Cl	6b,9
35	OAc	[illegible]	Cl	6b
36	COOMent	HO	–	6b,9
37	COOMent	HO	Cl	6b,9
38	COOMe	[illegible]	–	10,11
39	COOMe	[illegible]	–	10,11
40	COOMe	[illegible]	H	14

	X	Y	R	Lit.
41	H_3C	NH_2	H	10
42	$BrCH_2$	NH_2	H	10
43	$HOCH_2$	NH_2	H	10,11
44	$HOCH_2$	NH_3^+	H	10,11
45	$AcOCH_2$	NHAc	H	-
46	H_2NCH_2	NH_2	H	12
47	$H_3N^+CH_2$	NH_3^+	H	12
48	HO	COOMent	Cl	6b,9
49	HO	COOMent	OCH_3	6b,9
50	MentOOC	OH	H	6b,9
51	MentOOC	OH	Cl	6b,9
52	MentOOC	NH_2	H	10,11
53	MentOOC	NH_3^+	H	10,11
54	MentOOC	$NHCONH_2$	H	14

ative we thus expect at least four distinct series, and it seems a hopeless task to determine the absolute configuration for one such compound from its Cotton effects within the α-band region because of their overlap. If on the other hand the corresponding threo/erythro pair with the same constitution is available, we can make use of the fact that the two chromophores absorb quite independently. Under this assumption the sum of the two CD-spectra should give a curve characteristic for one "half-molecule", and the difference another one for its second "half-molecule". Using 54 differently substituted compounds of this type (cf Scheme 1) we checked empirically this assumption and found that in nearly all cases one can indeed determine unequivocally the absolute configuration of each "half-molecule". This procedure did not work for a few positively charged ammonium salts, for most of the investigated carboxylic esters of (−)-menthol it is not difficult to determine the absolute configuration, although we are dealing here with diastereomers including one additional chiral alcohol moiety. Which of the two compounds of such a pair is the threo and which the erythro isomer is, of course, easily deduced from ^{1}H-NMR spectra,[4] if it is not known from chemical correlations.

In order to avoid difficulties which might arise from the presence of several CD series we concentrate on the 0–0-transitions, whose positions can be surprisingly well predicted from Petruska's formula,[2] for which one needs two parameters (l and v), which are tabulated for many substitutents. These parameters have been obtained from the UV spectra. For substituents lacking rotational symmetry, they refer of course to weighted average values over all possible conformations. For a detailed discussion of the CD bands such average values are however not sufficient, since even such lines which are lying very close to each other can easily be resolved in the CD spectrum, if they have different signs. As these bathochromic shifts (similar to the transition moments, which can be predicted from Platt's "spectroscopic moments"[2,3]) are caused by p–π-conjugation ("hyperconjugation"), the contribution of any bond not coplanar with the plane of the benzene ring can be described by a $\cos^2$-function

$$A\sigma = -A_l \cos^2 \omega_l$$

if A_l is a parameter characteristic for the C–Z-bond of the moiety C_6H_5–C–Z, and ω_l is the torsional angle between the bond C–Z and the line perpendicular to the plane of the ring.

Figure 2 shows the six conformations which are believed to correspond to energy minima during a full rotation around the pivot-bond of one phenyl (Bn refers to the second (substituted) benzyl moiety). Of these II and IV can be safely excluded (at least if Z is not H or F), and also III is not too probable. Of the remaining three conformations VI will give only a very small contribution to the Cotton-effect, because Z and Bn adopt enantiotopic positions, so their contributions to the Cotton-effects will cancel to a great extent. We are thus left with mainly conformations I and V, which must for mere reason of symmetry give contributions to the CD of opposite signs, and this irrespective of the special type of sector rule or helicity rule which might be applicable. At least in the case that Z is a hetero atom with greater electronegativity than that of carbon its parameter A_l will be smaller than A_{Bn}, i.e. the 0–0-band of conformer V will be slightly more shifted towards the red than that of conformer I. This situation is depicted in

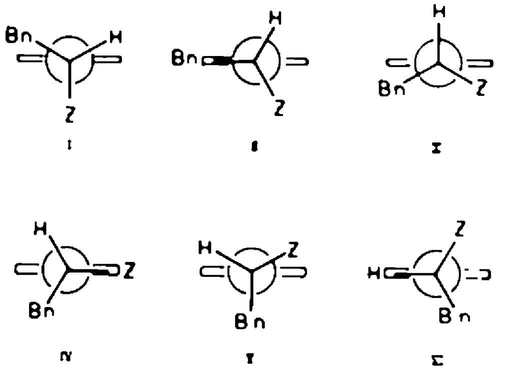
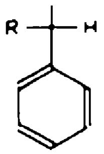


Fig. 2. The six preferred conformations of a phenyl moiety of a 1,2-disubstituted 1,2-diphenylethane around one of the Ph–C bonds (Z is a substituent, Bn the second (substituted) benzyl grouping).



R = H_3C
I: 41–6 (E)

R = $BrCH_2$
II: 42–7 (E)

R = $HOCH_2$
III: 41–10 (F)
53–11 (F,W)
F-III: 2+32 (A)
8+28 (A, A+H$^+$, C, D)

R = $AcOCH_2$
IV: --
F-IV: 4+25 (A,D,F)
12+30 (A,D,F)
14–42 (A)

R = Et_2NCH_2
V: 13+46 (E)

R = $H_2N^+CH_2$
VI: 29+47 (E)

R = HO
VII: 8–26 (A, A+H$^+$, C, D)
9–22 (A)
21–23 (A,C)
24+51 (A,D)
F-VII: 5+27 (A,H)
5–[illegible] (A)

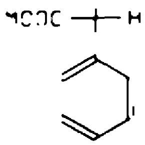
R = AcO
VIII: 12–30 (A,D,F)
13–41 (A)

R = H_2N
IX: 6+41 (E)
7+52 (E)
10+52 (E)
46–[illegible] (F)

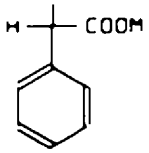
R = H_3N^+
X: 17+43 (E,W)
17–10 (E)

R = AcNH
XI: 15+42 (A)

R = $ClCH_2CONH$
XII: —
F-XII: 21+42 (A,C)



XIII: 17+31 (A)
17–36 (A,D)
16+48 (D)
16–34 (D)
18+54 (A,E,D)
18–36 (A,E,D)
25+33 (A,F)
25–39 (A,F)
22+54 (A,D)
22–40 (A,D)
4[illegible]



XIV: 2+24 (A,D)
23+36 (A)
23–26 (A)
25+28 (A,E,D)
25–52 (A,E,D)
26+39 (A,E)
26–23 (E)
27+42 (A,D)
27–54 (A,D)
33–30 (C)

Abbreviations: A [illegible] acetonitrile, [illegible] ethanol.
[illegible] dioxane, [illegible] diethylether isopentane ethanol [illegible] 2.
[illegible] water, [illegible] A [illegible]

Fig 3 together with the signs of the sector rule for the B_{2u}-band as earlier[1] derived empirically (B_{2u} refers, of course, as usual to the full symmetry of the benzene chromophore) For the absolute configuration of the "half-molecule" given in Fig 3 one should then obtain for the two 0 0-lines the bisignate CD shown The relative magnitudes of the two CD lines depend of course on the nature of Z, the preferred conformation of the second benzyl moiety, the second substitutent on the other C of the ethane moiety, and (mainly) on the position of the conformational equilibrium I ⇄ V As the different groups Z contribute only to the CD of conformer V but not to that of I the first mentioned band (the one at longer wavelengths) will show stronger variation than the other band in the CD spectra of different compounds.

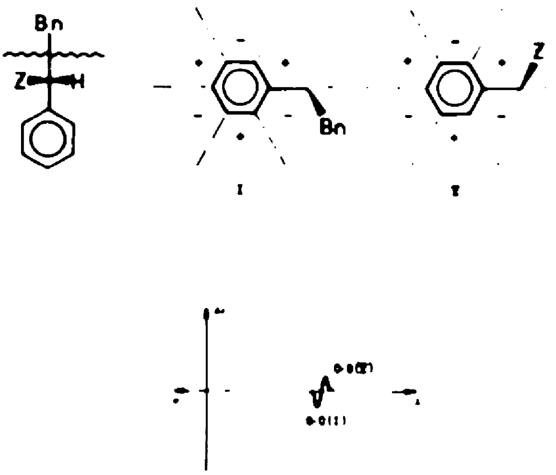


Fig 3. Top Projections onto a plane perpendicular to the benzene ring of conformations I and V (*cf* Fig 2) of the absolute configuration shown left Bottom Bisignate CD curve within the range of the two 0–0-lines for a mixture of these two conformers (for details see text)

As in a few rare cases one of the two lines does not well show up in these sum or difference spectra one should note that the border-line between these two 0 0-lines is found to be 37,230 cm^{-1}. The first CD line always occurs at wavenumbers smaller than this, whereas the second line is found at this wavenumber or at a slightly larger one The first might be too small to be detectable, the second is always present, but it might appear only as a minimum (of opposite sign) in between two other sharp lines rather than as the usual maximum

Scheme 2 gives an overview over all "half-molecules", how their CD-spectra were obtained, and the solvent used For convenience only one possible enantiomer is presented, although in some cases the CD spectra have been constructed for both enantiomers, or even only for the mirror image to that given in Scheme 2 As usual the enantiomer of Q is called E–Q. Only for the diasteromeric (–)-menthol

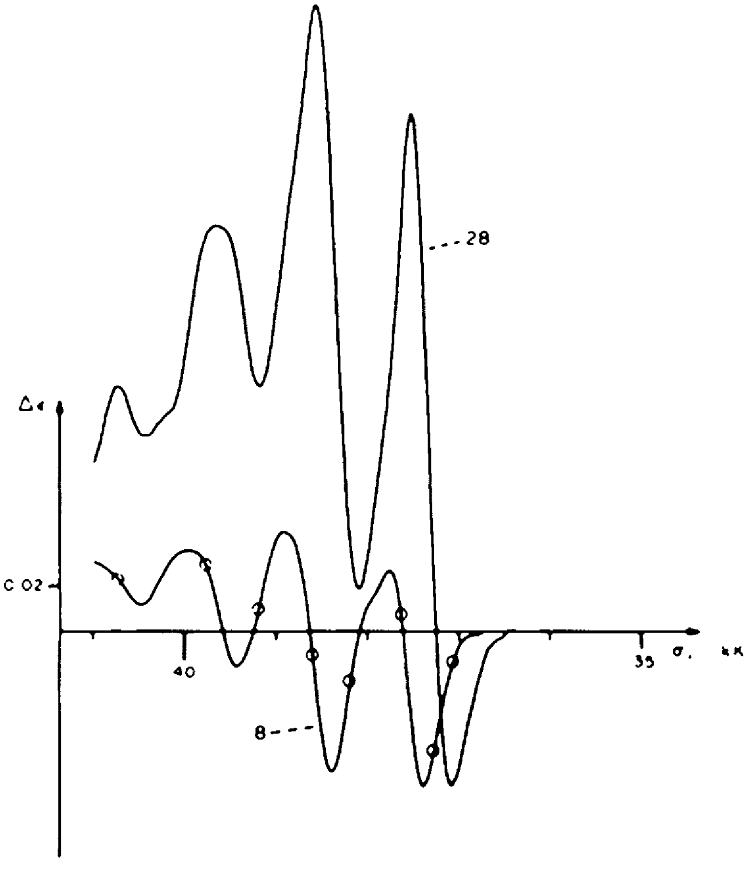


Fig 4 CD curves of **8** and **28** (in acetonitrile), abscissa as in Fig 1

Table 1. Positions and (twice the) Δε-values for the first two 0–0-lines of "half-molecules" I through XIV as obtained by addition or subtraction of original CD-curves

"half-molecule"	parent molecules	solvent$^{a)}$	first 0–0 - line	second 0–0 - line
I	41-6	F	-	37425 (−0.430)
II	42-7	F	36873 (+0.037)	37369 (−0.322)
III	43-10	F	37064 (+0.129)	37509 (−0.141)
	44-11	F	37286 (+0.519)$^{b)}$	
		N	37369 (+0.190)$^{b)}$	
E-III	1+32	A	37037 (−0.179)	37453 (+0.205)
	8+28	A	37120 (−0.089)	37566 (+0.188)
		A+H^{+}	37175 (−0.124)	37594 (+0.248)
		C	36879 (−0.029)	37453 (+0.312)
		D	-	37594 (+0.342)
IV	-			
E-IV	4+25	A	36470 (−0.169)$^{c)}$ 37202 (−0.330)	-
		O	36364 (−0.141)$^{c)}$ 37120 (−0.234)	37509 (+0.147)
		P	36364 (−0.142)$^{c)}$ 37120 (−0.272)	37509 (+0.104)
	16+30	A	37147 (−0.221)	37538 (+0.107)
		O	37064 (−0.108)	37453 (+0.219)
		P	37120 (−0.137)	37481 (+0.204)
	14-45	A	37120 (−0.399)	-
V	17+46	F	36955 (−0.080)	37453 (−0.255)
VI	19+47	F	37313 (+0.329)$^{b)}$	
VII	8-28	A	37037 (+0.054)	37481 (−0.280)
		A+H^{+}	37092 (+0.066)	37509 (−0.323)
		C	-	37509 (−0.441)
		D	-	37369 (−0.386)
	9-29	A	36023 (+0.029)$^{c)}$ 36390 (−0.058)$^{c)}$	37284 (−0.493)
	27-33	A	-	37425 (−0.237)
		C	-	37341 (−0.193)
	23+52	A	36075 (−0.077)$^{c)}$ 36711 (−0.090)$^{c)}$	37313 (−0.307)
		H	36049 (−0.259)$^{c)}$	37230 (−0.501)
E-VII	5+27	A	36779 (−0.049)$^{c)}$ 36879 (−0.024)$^{c)}$	37425 (+0.162)
		H	36232 (+0.105)$^{c)}$	37313 (+0.267)
	3-21	A	36701 (+0.031)$^{c)}$ 36730 (+0.048)$^{c)}$	37315 (+0.216)
VIII	12-30	A	37120 (+0.197)	37481 (−0.076)
		O	37037 (+0.102)	37425 (−0.241)
		F	37094 (+0.136)	37453 (−0.167)
	13-31	A	35945 (+0.036)$^{c)}$ 36443 (−0.030)$^{c)}$	37313 (−0.441)
IX	6+41	E	-	37425 (−0.413)
	7+42	E	36928 (+0.085)	37453 (−0.122)
	10+43	F	37092 (+0.171)	37481 (−0.113)
	46-12	F	36955 (+0.075)	37453 (−0.277)
X	11+44	F	-	37258 (+0.381) 37620 (−0.085)
	11+44	W	-	37341 (+0.316) 37700 (−0.035)
	47-19	E	-	37286 (+0.323)

Table 1 (*Contd*)

"half-molecule"	isomer molecules	solvent[a]	first 0-0 - line	second 0-0 -line
XI	**14**+**45**	A	36955 (+0.133)	37369 (−0.613)
XII	-			
F-XII	**21**+**33**	A	-	37509 (+0.798)
		C	-	37397 (+0.500)
XIII	**15**+**40**	A	-	37341 (−0.189)
	15-**36**	A	36928 (−0.031)	37369 (−0.234)
		O	-	37258 (−0.742)
	16+48	O	-	37258 (−0.642)
	18+**52**	A	36819 (+0.046)	37481 (−0.248)
		E	-	37397 (−0.370)
		O	-	37369 (−0.672)
	18-38	A	36900 (+0.081)	37453 (−0.215)
		F	-	37397 (−0.434)
		O	-	37425 (−0.670)
	20+**53**	A	37175 (+0.098)	37793 (−0.164)
		E	37092 (+0.066)	37707 (−0.169)
	20-**39**	A	37120 (+0.116)	37707 (−0.121)
		F	37092 (+0.093)	37679 (−0.157)
	22+**24**	A	-	37453 (−0.359)
		D	-	37313 (−0.384)
	22-**40**	A	37037 (+0.059)	37425 (−0.335)
		D	36955 (+0.076)	37369 (−0.256)
	49-**3**	O	35714 (−0.520)[d]	37258 (−1.000)
XIV	**2**+**34**	A	36982 (−0.065)	37538 (+0.164)
		O	-	37258 (+0.674)
	23+**36**	A	36955 (−0.052)	37369 (+0.177)
	23-**50**	A	-	37341 (+0.132)
	25+**38**	A	36955 (−0.114)	37481 (+0.162)
		F	-	37397 (+0.364)
		O	-	37425 (+0.573)
	25-**52**	A	37010 (−0.078)	37481 (+0.199)
		E	-	37397 (+0.300)
		C	-	37397 (+0.567)
	26+**29**	A	37092 (−0.106)	37622 (+0.132)
		E	37120 (−0.095)	37651 (+0.143)
	26-**51**	E	37120 (−0.069)	37707 (+0.152)
	27+**40**	A	37064 (−0.105)	37425 (+0.246)
		D	37037 (−0.200)	37425 (+0.085)
	27-**54**	A	37064 (−0.054)	37453 (+0.295)
		D	36982 (−0.092)	37369 (+0.190)
	34-**16**	O	36127 (−0.014)[c]	37092 (+0.191)[e] 37481 (−0.070)[e]

a) For abbreviations cf. Formula scheme 2.
b) only one line in wrong position (ammonium salts involved).
c) additional line from not fully compensated CD of p-chloro-phenyl moiety.
d) additional line from not fully compensated CD of p-methoxy-phenyl moiety.
e) formally wrong signs.

esters of the "half-molecules" containing the acid grouping both formulae are presented.

As an illustration the procedure is outlined for the CD spectra of "half-molecules" III and VII, which can e.g. be obtained from the CD-curves of the diastereomeric pair **8** and **28**. Their relative (as well as absolute) stereochemistry is known from chemical methods[8] but could also have been obtained from the ^{1}H-NMR spectra: the splitting of the signals for the two hydrogen atoms of the ethane moiety is 9.2 Hz for **28** (threo-isomer) and 6.1 Hz for **8** (erythro-isomer).[7] The CD spectra in the range between 300 and 244 nm of **8** and **28** (recorded with a computer-resolution of 0.2 nm) are shown in Fig. 4, their difference and sum curves in Fig. 5. The first corresponds to twice the CD-curve of "half-molecule" VII.

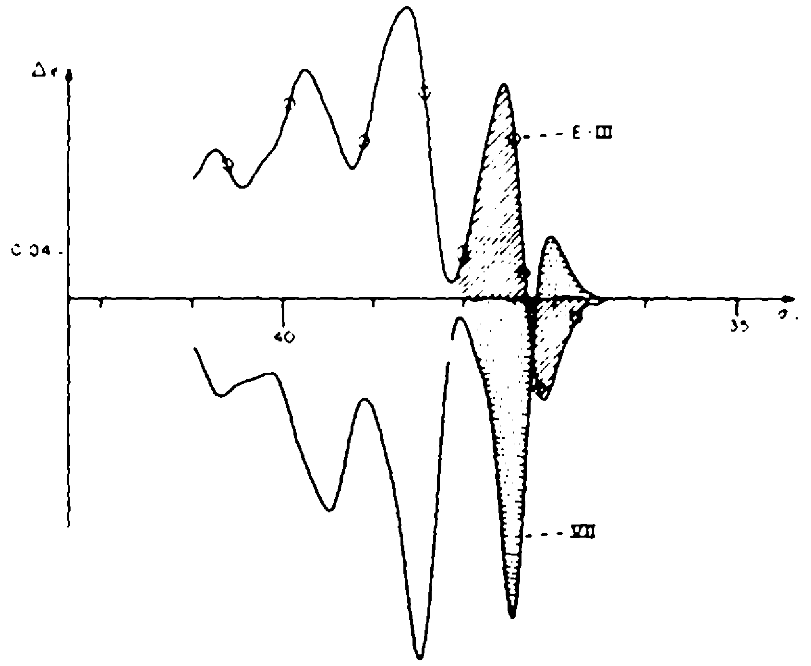


Fig 5 CD curves for the two "half-molecules" VII and E-III, obtained as the difference and sum curves, resp. of 8 and 28 Abscissa as in Fig 1. Δε-values are double those for the "half-molecules"

the two 0–0-lines are marked by hatching, and only these two are used for the determination of absolute configuration The sum spectrum corresponds to twice the CD of the "half-molecule" E-III, and again only the first two CD-lines (hatched) are used. In both spectra the two 0–0-lines are easily discernible and their signs are in agreement with those given in Fig 3

Table 1 summarizes the results and demonstrates convincingly that by this combination of the two curves of a corresponding threo/erythro pair the absolute configuration for both centres of chirality can be determined unequivocally, provided that the amines are measured in their neutral forms Only in one other case apparently wrong signs are obtained (XIV = 34 – 16), this might be due to the fact that we are here dealing with diastereomeric and not with enantiomeric halves, or (more probably) due to incomplete compensation of the CD lines of the *p*-chlorophenyl moiety In all other examples of diastereomers including the chiral menthol moiety into the "half-molecule" no such deviations from the rule are found

The data show furthermore, that the (substituted) benzyl group (at least when we discuss the introduced bathochromic shifts) is in each case a more powerful perturber for the benzene chromophore than the group Z, even if the latter is not a heteroatom

EXPERIMENTAL

CD data were obtained with a Dichrograph Mark III (ISA Jobin-Yvon) connected on-line to a PDP-8e Noise was eliminated by curve-smoothing according to the Golay-Savitzky algorithm[8] (best parabola of degree 3 fitted to 25 consecutive points) The detailed data of all Cotton effects are given in a following paper

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[1] This paper forms Part LXXIX of the series Circular Dichroism of the Bochum author, Part LXXVIII G Snatzke, A Konowal, A Sabljic, N Blažević and V Šunjić, *Croatica Chem Acta*, 55, 435 (1982)

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