68. The Circular Dichroism of 5,6-Dimethylidene-2-bicyclo[2.2.n]alkyl Esters. Chiral Exciton Coupling between Benzoate and Exocyclic *s-cis*-Butadiene Chromophores

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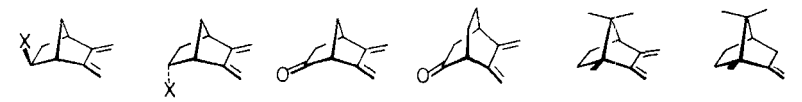
Summary

The optically pure aryl-substituted 5,6-dimethylidene-2-bicyclo[2.2.1]heptyl benzoates **12**–**21** were prepared; their UV absorption and CD spectra are reported. The (−)-(1*S*,2*S*)-esters **17**–**21** with carbonyl groups in *endo*-position exhibit typical exciton-split *Cotton* effects whereas the corresponding (−)-(1*S*,2*R*)-esters **12**–**16** with carbonyl groups in *exo*-position do not present such effects. The chiral exciton coupling between the exocyclic diene and a remote *p*-substituted benzoate chromophore can be used for unambiguous assignment of the absolute configuration of 5,6-dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl derivatives. The method is applied to establish the absolute configuration of 5,6-dimethylidene-2-*exo* and -2-*endo*-bicyclo[2.2.2]octyl *p*-bromobenzoates (−)-**24** and (−)-**25**.

Introduction. – The relationship between the molecular structure of chiral *cisoid*-1,3-dienes and their circular dichroism (CD) spectra has been a subject of long-standing interest [1] [2]. The sign of the *Cotton* effect (CE) associated with the long-wavelength electronic transition (V←N transition) is given by the skewness, *i.e.* helicity of the diene [3] [4] and by contributions of axial groups in allylic position [5] [6]. The contributions of the latter to the CE can outweigh those from the skewed diene [6b]. Recently, the diene helicity and allylic chirality rules have been blended into sector rules for *cisoid*-dienes [4] [7] (see also the planar diene rule [8]). However, chiroptical



X=OH: (+)-**1** (+)-**3** **5** **6** **7** **8**
X=OAc: (+)-**2** (+)-**4**

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effects in a conjugated *cisoid*-diene caused by remote substituents have been little studied [4a] [9] [10] [11]. We reported [9] [11] positive CE's for the exocyclic *s-cis*-butadienes **1–6** in agreement with the 'allylic axial chirality rule' if one considers the C-atoms C(5),C(6) *(Fig. 1)* of the π-system (instead of the methylidene function (C6),C(6') as proposed by *Burgstahler et al.* [5c] for **7** and **8**) and the substituted (therefore most polarizable) C(1),C(2), bond. Our results were in agreement with the proposal of *Gawronski et al.* [5d] which considers the direction of the transition moment and the direction of the substituted allylic bond C(1),C(2) to determine the chirality of the diene chromophore perturbed by remote substituents.

Recently reported crystallographic X-ray data of (−)-camphorquinone and derivatives [11] suggested that the bicyclo[2.2.1]heptane skeleton can adapt to out-of-plane deformations of a π-system grafted onto it. Considering the positive CE's observed for **1–6**, all these dienes might in fact possess some *P*-helicity (right-handed skew). The larger $\Delta\varepsilon$-values measured for the *endo*-alcohol **3** and *endo*-acetate **4** compared with those observed for the *exo*-derivatives **1** and **2**, respectively [8], were consistent with a larger degree of *P*-helicity in **3** and **4** than in **1** and **2**. The latter could be attributed to an *endo*-X...C(6) = CH_2 repulsive effect as shown in *Fig. 2*. *Gauche*-interactions between the methyl group and the exocyclic diene might also induce a left-handed distortion ((*M*)-helicity) in **7** and thus explain the negative CE observed in the CD spectra for this diene. This hypothesis implies that the diene-helicity contribution to the CE of **7** overcomes the expected opposite-sign contribution from the allylic axial methyl-substituted C(1),C(6) bond *(cf. Fig. 3)*. It is assumed again that the diene transition moment determines the chirality of the system [5d].

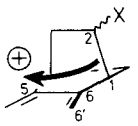


Figure 1

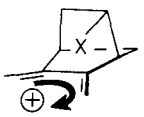


Figure 2

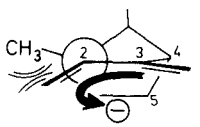
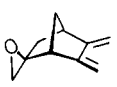


Figure 3

Unfortunately, the out-of-plane distortion of *s-cis*-butadiene moieties grafted onto 'rigid' bicyclo[2.2.1]heptane systems cannot be predicted unequivocally. Indeed, contrary to our expectations, we found that the *exo*- and *endo*-epoxydienes, **9** and **10**, respectively, displayed opposite CE's in their CD spectra [9]. Furthermore, the dimethyl acetal **11** showed a negative CE. This was a surprise as a positive CE was expected based on the above-mentionned 'homo-allylic axial chirality rule' and concurrent (*P*)-diene helicity *(cf. Fig. 2)*. These results demonstrated that the sign of the CE associated with the diene chromophore of 5,6-dimethylidene-2-bicyclo[2.2.1]heptyl derivatives could not be used to establish their absolute configuration.



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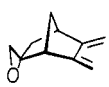

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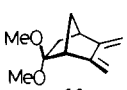

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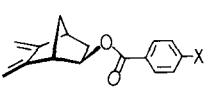
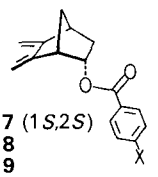
The circular dichroic exciton chirality method [13] has been successfully used to determine the absolute configuration of various organic compounds [14]. The concept of chiral exciton coupling has been extended to nondegenerate systems composed of two different chromophores [14b], namely to the systems benzoate/enone [15], benzoate/olefin (of allylic alcohols) [16], the benzoate/conjugated *s-trans*-diene [14b] [17], and benzoate/phenanthrene [18].

We report the CD spectra of aryl-substituted (1*S*)-5,6-dimethylidene-2-*exo*- and 2-*endo*-bicyclo[2.2.1]heptyl benzoates **12**–**21**. We shall show that the *endo*-esters **17**–**21** exhibit typical exciton-split CE's whereas the *exo*-derivatives **12**–**16** do not display such effects. We also shall establish that the concept of chiral exciton coupling can be extended to exocyclic *s-cis*-butadiene systems remotely substituted and that it can be used for unambiguous assignment of the absolute configuration of 5,6-dimethylidene-2-bicyclo[2.2.n]alkyl derivatives.

Results and Discussion. – The optically pure (−)-(1*S*,2*R*)-5,6-dimethylidene-2-*exo*-bicyclo[2.2.1]heptanol ((−)-**1**) and (−)-(1*S*,2*S*)-5,6-dimethylidene-2-*endo*-bicyclo[2.2.1]-heptanol ((−)-**3**) were prepared as described earlier [9]. Their absolute configuration was established unambiguously by chemical correlation [9] and an X-ray crystal structure analysis of (+)-tricarbonyl[*C*,5,6,*C*-η(*exo*)-(1*S*,2*R*)-5,6-dimethylidene-2-*exo*-bicyclo[2.2.1]heptyl *p*-bromobenzoate]iron [19]. The bicyclic alcohols were transformed into their esters **12**–**21** by treatment with the corresponding *p*-substituted-benzoyl chloride in pyridine (see *Exper. Part*). The UV absorption and CD spectra of compounds **12**–**21** were recorded at room temperature in a polar (EtOH 96%) and apolar solvent (isooctane). They are reported in *Fig. 4–8* and *Table 1*.





X = H:	**12** (1*S*,2*R*)	**17** (1*S*,2*S*)
X = CH_3:	**13**	**18**
X = Cl:	**14**	**19**
X = Br:	**15**	**20**
X = OCH_3:	**16**	**21**

The *exo*-esters **12**–**16** exhibited CD spectra with negative CE's that correspond merely to the superposition of the diene and uncoupled-benzoate CE's (see *Table 1*). The negative sign of these CE's is consistent with the allylic axial chirality rule [5] [6] which considers the σ−C(1),C(2) bond the most polarizable allylic bond and the transition moment of the diene chromophore parallel with the C(5),C(6) bond. It is also consistent with that observed in the CD spectra of the corresponding alcohols (−)-(1*S*)-**1** and (−)-(1*S*)-**3** [9]. The absence of exciton-split CE's for the *exo*-esters **12**–**16** must be ascribed to the large distance between the benzoate and diene moieties.

In contrast, the CD spectra *(Fig. 4–8)* of the *endo*-esters **17**–**21** exhibit typical negative first (λ 248 for **17** in EtOH and 261 nm for **21** in EtOH) and positive second (λ 229 for **17** and 240 nm for **21**) split CE's arising from exciton coupling between the diene

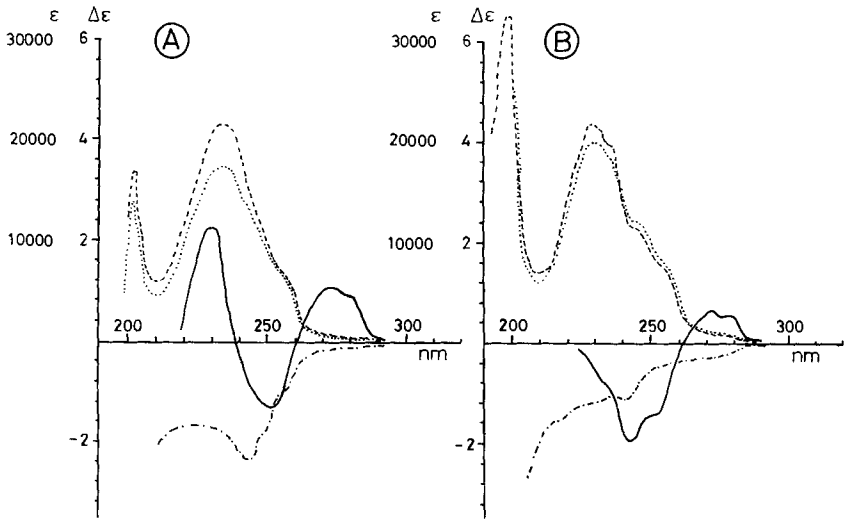


Fig. 4. *UV Absorption Spectra of the* exo-*Benzoate* **12** (– – –) *and* endo-*Isomer* **17** (· · · · ·); *CD Spectra of* (–)-**12** (– · – · –) *and* (–)-**17** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

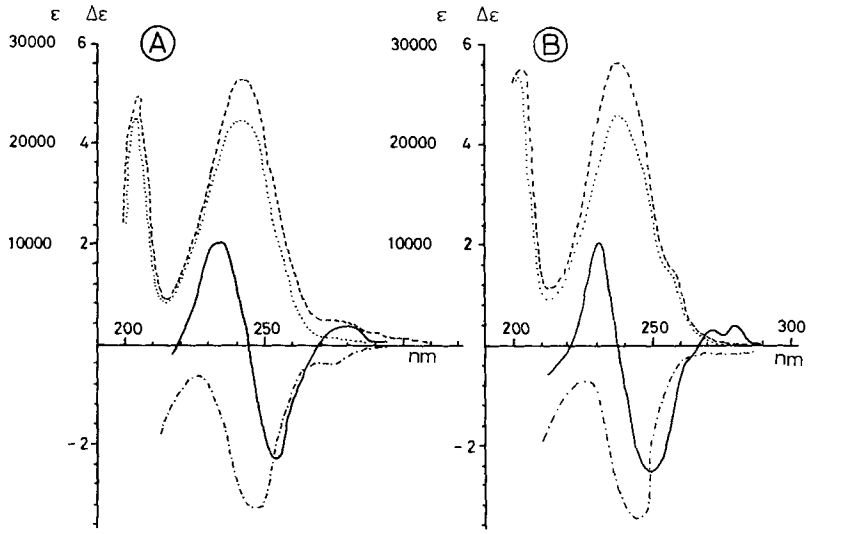


Fig. 5. *UV Absorption Spectra of the* exo-p-*Methylbenzoate* **13** (– – –) *and* endo-*Isomer* **18** (· · · · ·); *CD Spectra of* (–)-**13** (– · – · –) *and* (–)-**18** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

V←N transition and *p*-substituted benzoate ^1L_a transitions (*Table 1* and *Fig. 4–8*). The data confirmed the (–)-chirality of **17–21** ((1*S*,2*S*)) as illustrated in *Fig. 9*. The exciton-coupled CE's of **17** and **18** are perturbed by ^1L_b-transition contributions of the benzoate ($\lambda > 260$ nm) and *p*-methylbenzoate ($\lambda > 268$ nm), respectively [14b]. Such contributions are less important in the CD spectra of esters **19–21** and thus make these

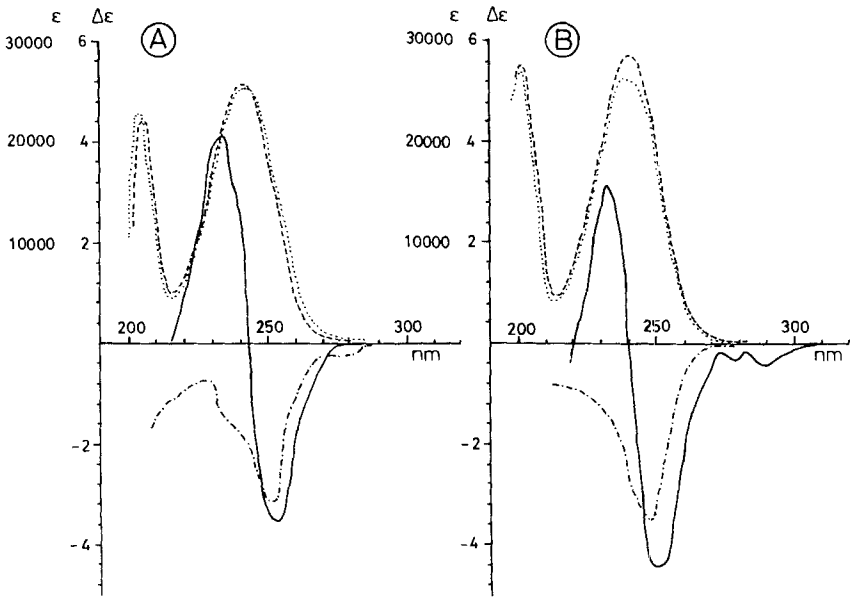


Fig. 6. *UV Absorption Spectra of the* exo-p-*Chlorobenzoate* **14** (– – –) *and* endo-*Isomer* **19** (· · · · ·); *CD Spectra of* (–)-**14** (–·–·–) *and* (–)-**19** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

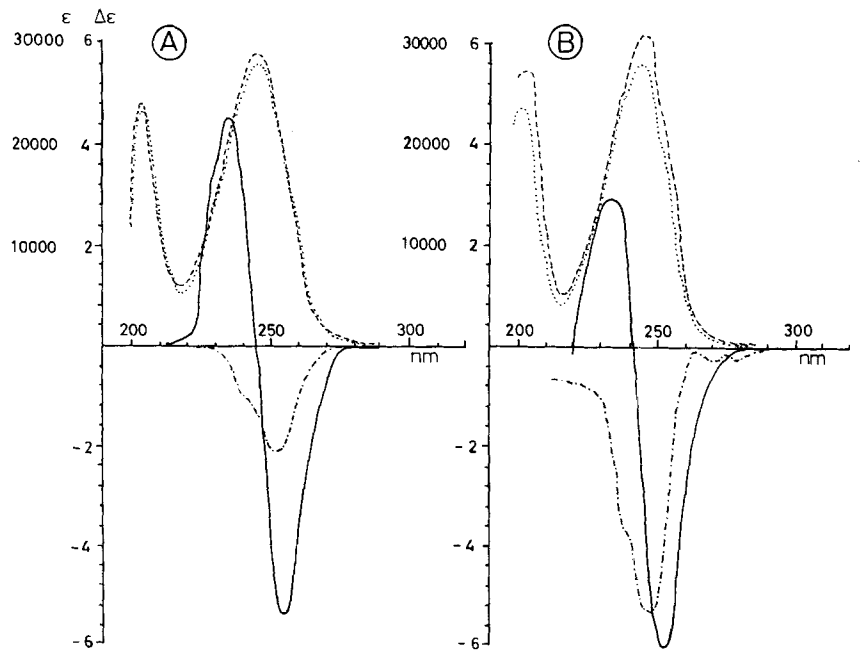


Fig. 7. *UV Absorption Spectra of the* exo-p-*Bromobenzoate* **15** (– – –) *and* endo-*Isomer* **20** (· · · · ·); *CD Spectra of* (–)-**15** (–·–·–) *and* (–)-**20** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

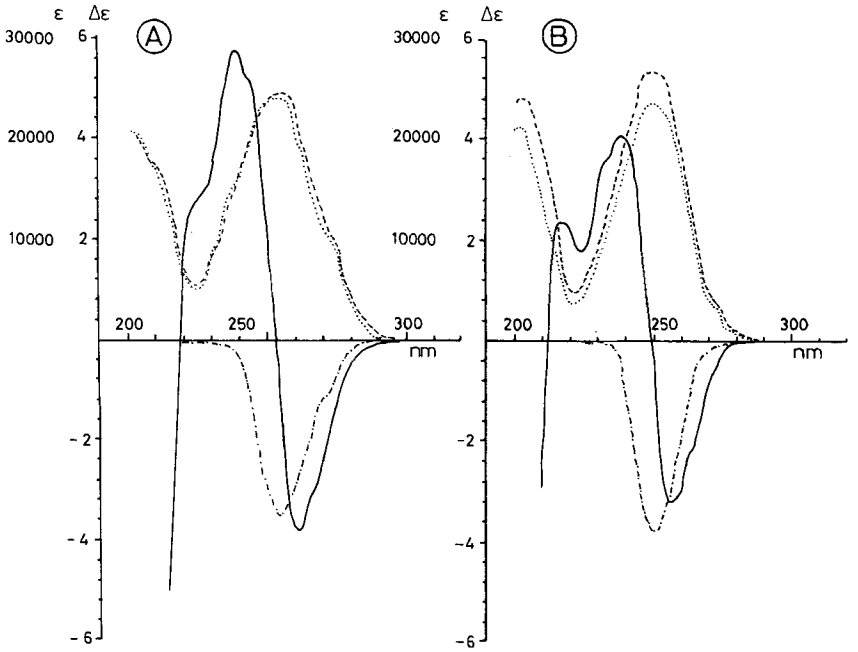


Fig. 8. *UV Absorption Spectra of the* exo-p-*Methoxybenzoate* **16** (----) *and* endo-*Isomer* **21** (·····); *CD Spectra of* (−)-**16** (-·-·-) *and* (−)-**21** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

Table 1. *UV Absorption and CD Spectra of the (−)-(1S)-Benzoates* **12**–**21**, **24**, *and* **25**

Compound		UV ($\lambda_{max}(\varepsilon)$)		CD ($\lambda(\Delta\varepsilon)$)			
X		in isooctane	in EtOH 96%	in isooctane	c^a)	in EtOH 96%	c^a)
H	**12**	198 (32800); 230 (21700); 242 (sh, 11500); 252 (sh, 7700)	202 (16800); 236 (21000); 254 (sh, 7200)	204 (−2.8); 216 (−1.3); 242 (−1.2)	6.175	210 (−2.10); 244 (−2.4); 256 (sh, −1.0)	8.77
	17	230 (19800); 248 (sh, 10900); 256 (sh, 7100)	202 (13900); 233 (17300); 242 (13100)	242 (−2.0); 252 (sh, −1.43); 262 (0); 272 (0.65); 280 (0.54)	3.33	228 (1.50); 238 (0); 252 (−0.91); 260 (0); 272 (0.71); 278 (sh, 0.6)	3.47
CH_3	**13**	202 (27400); 238 (28200)	204 (25000); 240 (26300)	208 (−1.97); 245 (−3.52)	4.47	210 (−1.9); 247 (−3.8)	6.45
	18	202 (26700); 238 (22900); 254 (sh, 7800)	204 (22600); 241 (22200)	221 (0); 230 (2.07); 237 (0); 249 (−2.5); 267 (0); 272 (0.33); 280 (0.4)	2.95	219 (0); 234 (2.1); 243 (0); 254 (−2.3); 269 (0); 281 (0.4)	2.93

Table 1. (continued)

Compound		UV ($\lambda_{max}(\varepsilon)$)		CD ($\lambda(\Delta\varepsilon)$)			
		in isooctane	in EtOH 96%	in isooctane	c[a])	in EtOH 96%	c[a])
Cl	**14**	202 (21900); 240 (28800)	206 (21900); 242 (25800)	248 (−2.6)	5.97	250 (−3.3)	6.63
	19	202 (26800); 240 (26200)	204 (22900); 242 (25300)	221 (0); 232 (3.2); 240 (0); 251 (−4.6); 279 (−0.4); 285 (−0.5)	4.32	214 (0); 234 (4.1); 243 (0); 253 (−3.6); 276 (0)	3.91
Br	**15**	202 (27500); 245 (31100)	204 (24300); 245 (29100)	238 (−3.6); 248 (−5.4)	4.20	252 (−2.0)	6.40
	20	200 (23600); 244 (28200)	204 (23300); 246 (28000)	220 (0); 234 (2.95); 242 (0); 252 (−6.0)	4.65	212 (0); 234 (4.6); 244 (0); 254 (−5.4); 275 (0)	4.37
OCH_3	**16**	202 (24100); 248 (27000)	204 (20400); 255 (24700); 247 (sh, 10000)	250 (−3.94)	6.53	254 (−3.6)	6.28
	21	202 (21000); 249 (23600); 270 (sh, 3300)	202 (21000); 254 (24200); 275 (sh, 8000)	212 (0); 216 (2.4); 238 (4.2); 249 (0); 257 (−3.4); 280 (0)	3.32	218 (0); 225 (sh, 2.7); 238 (5.8); 244 (sh, 5.2); 253 (0); 261 (−3.4); 296 (0)	3.95
	24	204 (28000); 250 (23800)	202 (23800); 246 (23400)	244 (−1.1); 256 (0); 263 (0.4)	2.75	224 (−0.9); 242 (sh, −0.7); 270 (−0.2)	2.10
	25	204 (29000); 252 (25400)	202 (28000); 248 (25000)	232 (3.1); 245 (0); 254 (−1.9); 271 (0); 276 (0.2)	2.90	238 (3.0); 249 (0); 258 (−1.3); 272 (0); 280 (0.3)	2.70

[a]) Concentration c in $10^{-2} \cdot g/dm^3$.

derivatives more useful for absolute-configuration assignment based on the CD exciton chirality method. Ester **20** displayed the largest amplitude ($A = |\Delta\varepsilon_1 - \Delta\varepsilon_2|$) of exciton-split CD CE. This was expected [14] since the ^1L_a-transition energy of the *p*-bromobenzoate (UV: λ_{max} *ca.* 245 nm, $\varepsilon \approx 20000$ [14b]) matches that of the exocyclic *s-cis*-butadiene V←N transition (UV: λ_{max} *ca.* 245 nm, $\varepsilon \approx 10000$ [20]) in this derivative.

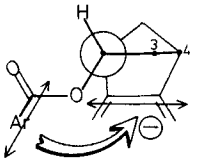
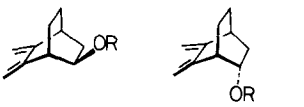


Figure 9



R = H: **22** (1*S*,2*R*) **23** (1*S*,2*S*)
R = *p*-BrC_6H_4CO: (–)-**24** (–)-**25**

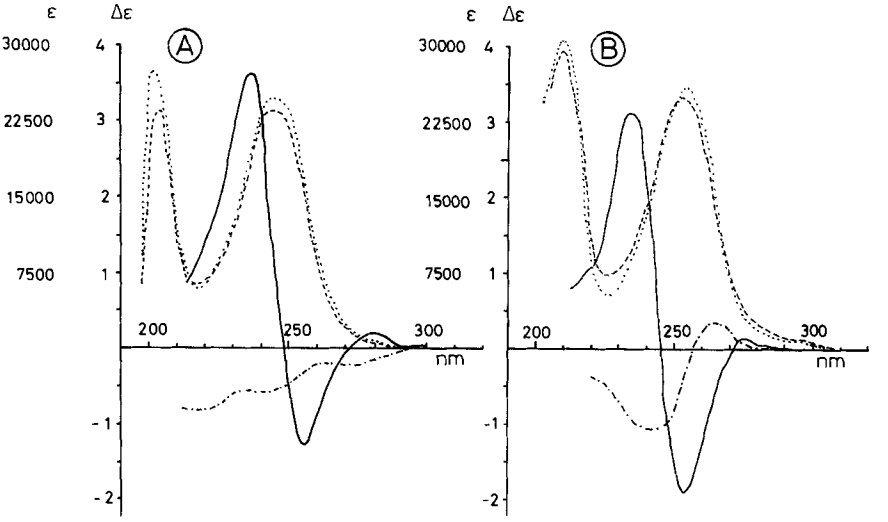


Fig. 10. *UV Absorption Spectra of the* exo-p-*Bromobenzoate* **24** (– – –) *and* endo-*Isomer* **25** (· · · · ·); *CD Spectra of* (–)-**24** (– · – · –) *and* (–)-**25** (——). Ⓐ : in EtOH/H_2O 96:4; Ⓑ : in isooctane.

The absolute configuration of (+)-5,6-dimethylidene-2-bicyclo[2.2.2]octanone (**6**) was deduced from its CD spectrum and by analogy with that of its lower homologue **5** [11]. Reduction of the enantiomer (–)-**6** with $NaBH_4$ in THF yielded a mixture of alcohols **22** and **23** which were separated by HPLC in low yield[2]). The UV and CD spectra of their *exo*- and *endo*-*p*-bromobenzoates (–)-**24** and (–)-**25**, respectively, are reported in *Table 1* and *Fig. 10*.

As in the case of the corresponding bicyclo[2.2.1]heptyl derivatives, the *exo*-ester (–)-**24** did not show any exciton-split CE near 250 nm in its CD spectrum taken in EtOH. In isooctane, the spectrum is less clear *(cf. Fig. 10)*. In contrast, the CD spectra of the *endo*-derivative (–)-**25** displayed typical exciton-split CE's whose amplitudes are somewhat smaller than those observed for **20** *(Fig. 7)* and **21** *(Fig. 8)*. This is consistent with the larger distance between the *p*-substituted benzoate and diene chromophore in (–)-**25** than in **20** and **21**. The signs of the CE's of (–)-**25** confirmed a (–)-chirality

[2]) Stereoselective syntheses of these systems using tricarbonyl(5,6-dimethylidenebicyclo[2.2.2]oct-2-ene)iron precursors will be described elsewhere. The determination of their absolute configuration by X-ray crystallography is under investigation.

and, consequently, the (1*S*,2*S*)-configuration as in the case represented in *Fig. 9*. This result is consistent with the absolute configuration deduced from the CD spectrum of the corresponding dienone **6** [11][2]).

Conclusion. – The method of chiral exciton coupling can be used for unequivocal assignment of the absolute configuration of 5,6-dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl and 5,6-dimethylidene-2-*endo*-bicyclo[2.2.2]octyl derivatives. The CD spectra of the corresponding *p*-substituted benzoates also permit unambiguous distinction between the *exo*- and *endo*-5,6-dimethylidene-2-bicyclo[2.2.n]alkyl derivatives. These assignments for the bicyclo[2.2.2]octyl systems are not always deducible from NMR measurements.

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Experimental Part

General Remarks. See [9] [20a]. CD (λ[nm]): *Roussel-Jouan* dichrograph *III (Jobin-Yvon)*. $[\alpha]^{25}$: *Perkin Elmer 241* polarimeter with mod. *U3* circulatory thermostat. High-resolution MS on *ZAB-2F (VG Analytical)*. Elementary analysis were performed by the microanalytical laboratory of *Ilse Beetz* in Kronach (Germany). Prep. HPLC purifications: *Dupont 830003-904*, UV detector (254 nm), silical gel (*Zorbax Sil*, 7 μm; 21.2 mm × 25 cm); elution solvent: AcOEt/hexane 4:96. The ^{13}C-NMR data are reported in *Table 2*.

General Esterification Procedure. The dienols (−)-**1** and (−)-**3**[9] (0.8 mmol) were dissolved in anh. pyridine (0.5 ml). Pure *p*-substituted-benzoyl chloride (0.735 mmol) was added portionwise to these solutions stirred at 0° under N_2. After the addition, the mixture was allowed to warm to r.t. and stirred for 20 min (**14**, **19**), 30 min (**12**, **17**), 45 min (**13**, **18**), 60 min (**15**, **20**), or 90 min (**16**, **21**). The mixture was poured onto ice/H_2O (20 g) under vigorous stirring and then extracted with pentane (10 ml, 4 times). The combined org. phases were washed successively with sat. aq. $CuSO_4$ (20 ml, 4×) and H_2O (20 ml, 3×). After drying ($MgSO_4$), the solution was evaporated *i.v.* and purified by HPLC.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.1]heptylbenzoate* (**12**). Yield 74%, colourless oil, b.p. 100°/0.1 Torr. $[\alpha]_D^{25} = -60.2°$, $[\alpha]_{578}^{25} = -63.1°$, $[\alpha]_{546}^{25} = -72.7°$, $[\alpha]_{436}^{25} = -135.2°$ $[\alpha]_{365}^{25} = -243.2°$ (c = 12 mg/ml, $CHCl_3$). IR (film): 3090, 2990, 2890, 1796, 1720. ^{1}H-NMR ($CDCl_3$): 8.07 (*m*, 2H); 7.51 (*m*, 3H); 5.36 (*s*, 1H); 5,17 (*s*, 1H); 5.11 (*s*, 1H); 5.05 (*m*, 1H); 4.88 (*s*, 1H); 3.12 (br. *s*, 1H); 2.93 (br. *s*, 1H); 2.05–1.49 (*m*, 4H). MS (70 eV): 242 (0.1), 241 (1.5), 240 (8.2, M^+), 198 (3), 118 (5), 105 (100), 91 (8). Anal. calc. for $C_{16}H_{16}O_2$ (240.203): C 79.97, H 6.71; found: C 80.10, H 6.62.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.1]heptyl* p-*Methylbenzoate* (**13**). Yield 80%, oil, b.p. 120°/0.1 Torr. $[\alpha]_D^{25} = -61.8°$, $[\alpha]_{578}^{25} = -64.9°$, $[\alpha]_{546}^{25} = -75.0°$, $[\alpha]_{436}^{25} = -140.8°$, $[\alpha]_{365}^{25} = -256.6°$ (c = 12.7 mg/ml, $CHCl_3$). IR (film): 3145, 3068, 3045, 2940, 1735, 1628. ^{1}H-NMR ($CDCl_3$): 7.93 (*d*, J = 8, 2H); 7.23 (*d*, J = 8, 2H); 5.32 (*s*, 1H); 5.15 (*s*, 1H); 5.03 (*m*, 1H); 4.88 (*s*, 1H); 3.1 (br. *s*, 1H); 2.9 (br. *s*, 1H); 2.43 (*s*, 3H); 2.25–1.25 (*m*, 4H); 5.0 (*m*, 1H); 3.07 (br. *s*, 1H); 2.89 (br. *s*, 1H); 2.41 (*s*, 3H); 2.18–1.46 (*m*, 4H). MS (70 eV): 254 (12, M^+), 120 (9), 119 (100), 91 (19). Anal. calc. for $C_{17}H_{18}O_2$ (254.33): C 80.28, H 7.13; found: C 80.21, H 7.19.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.1]heptyl* p-*Chlorobenzoate* (**14**). Yield 70%, oil, b.p. 150°/0.1 Torr. $[\alpha]_D^{25} = -61.8°$, $[\alpha]_{578}^{25} = -64.7°$, $[\alpha]_{546}^{25} = -75.3°$, $[\alpha]_{436}^{25} = -140.5°$, $[\alpha]_{365}^{25} = -255.7°$ (c = 13 mg/ml, $CHCl_3$). IR (film): 3150, 3050, 2950, 1755, 1630, 1620. ^{1}H-NMR ($CDCl_3$): 7.95 (*d*, J = 8, 2H); 7.38 (*d*, J = 8, 2H); 5.3 (*s*, 1H); 5.13 (*s*, 1H); 5.05 (*s*, 1H); 4.95 (*m*, 1H); 4.85 (*s*, 1H); 3.08 (br. *s*., 1H); 2.9 (br. *s*, 1H); 2.23–1.25 (*m*, 4H). MS (70 eV): 276 (3), 275 (16), 274 (8.7, M^+), 141 (39), 140 (10), 139 (100). Anal. calc. for $C_{16}H_{15}ClO_2$ (274.75): C 69.95, H 5.50; found: C 69.78, H 5.56.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.1]heptyl* p-*Bromobenzoate* (**15**). Yield 75%, oil, b.p. 150°/0.1 Torr. $[\alpha]_D^{25} = -57.1°$, $[\alpha]_{578}^{25} = -59.7°$, $[\alpha]_{546}^{25} = -69.1°$, $[\alpha]_{436}^{25} = -129.7°$, $[\alpha]_{365}^{25} = -237.3°$ (c = 15 mg/ml, $CHCl_3$). IR (film): 3090, 2990, 2890, 1725, 1595, 1490. ^{1}H-NMR ($CDCl_3$): 7.93 (*d*, J = 8, 2H); 7.6 (*d*, J = 8, 2H); 5.35 (*s*, 1H); 5.18 (*s*, 1H); 5.1 (*s*, 1H); 5.03 (*m*, 1H); 4.88 (*s*, 1H); 3.1 (br. *s*, 1H); 2.93 (br. *s*, 1H); 2.13–1.25

Table 2. *^{13}C-NMR Data of* **12–21**, **24**, *and* **25** *in $CDCl_3$.* δ_C in ppm (δ (TMS) = 0.0 ppm), apparent multiplicities, $^1J_{C,H}$ in Hz[a]).

	C(1)	C(2)	C(3)	C(4)	C(5)	H_2C=C(5)	C(6)	H_2C=C(6)	C(7)	COO	C(arom.)				Others
12	51.1	76.6	38.9	44.7	150.8	100.4	146.4	104.3	36.2	166.0	130.8	129.4	128.2	132.7	
	d, 148	*d*, 158	*t*, 135	*d*, 148	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 163	*d*, 163	*d*, 162	
17	49.5	74.4	36.8	45.0	151.3	100.1	145.8	104.5	37.9	166.6	130.1	129.5	128.2	137.2	
	d, 146	*d*, 156	*t*, 136	*d*, 148	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 164	*d*, 164	*d*, 160	
13	51.0	76.4	38.8	44.7	150.8	100.4	146.5	104.3	36.2	166.1	127.8	129.5	129.0	143.4	21.5
	d, 148	*d*, 158	*t*, 134	*d*, 148	*s*	*t*, 159	*s*	*t*, 159	*t*, 134	*s*	*s*	*d*, 161	*d*, 161	*s*	*q*, 128
18	49.5	74.3	36.8	45.0	151.4	100.0	145.9	104.4	38.0	166.6	127.9	129.6	129.0	143.4	21.6
	d, 146	*d*, 152	*t*, 136	*d*, 148	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 162	*d*, 162	*s*	*q*, 126
14	51.1	76.9	38.9	44.7	150.6	100.5	146.4	104.4	36.2	165.1	129.1	130.8	128.6	139.3	
	d, 148	*d*, 160	*t*, 136	*d*, 148	*s*	*t*, 160	*s*	*t*, 160	*t*, 138	*s*	*s*	*d*, 165	*d*, 167	*s*	
19	49.5	74.7	36.8	45.0	151.2	100.3	145.9	104.4	38.0	166.0	129.1	131.0	128.6	139.2	
	d, 148	*d*, 157	*t*, 137	*d*, 152	*s*	*t*, 158	*s*	*t*, 158	*t*, 137	*s*	*s*	*d*, 166	*d*, 166	*s*	
15	51.1	77.0	38.9	44.7	150.6	100.5	146.4	104.4	36.2	165.3	129.6	131.0	131.6	127.9	
	d, 148	*d*, 162	*t*, 135	*d*, 148	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 166	*d*, 168	*s*	
20	49.6	74.8	36.8	45.0	151.3	100.3	145.9	104.4	38.0	165.8	129.6	131.1	131.7	127.9	
	d, 148	*d*, 155	*t*, 134	*d*, 146	*s*	*t*, 158	*s*	*t*, 158	*t*, 137	*s*	*s*	*d*, 165	*d*, 167	*s*	
16	51.1	76.2	38.9	44.7	150.8	100.3	146.6	104.3	36.2	165.8	123.0	131.4	113.5	163.3	55.3
	d, 148	*d*, 162	*t*, 134	*d*, 148	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 163	*d*, 162	*s*	*q*, 144
21	49.6	74.1	36.9	45.1	151.5	100.0	146.0	104.4	38.0	166.3	123.3	131.6	113.6	163.4	55.4
	d, 148	*d*, 157	*t*, 134	*d*, 147	*s*	*t*, 158	*s*	*t*, 158	*t*, 136	*s*	*s*	*d*, 164	*d*, 164	*s*	*q*, 144
24	41.0	72.7	35.1	36.6	147.6	104.2	145.3	107.2	25.8	165.3	129.5	131.7	131.0	127.9	29.6[b])
	d, 140	*d*, 156	*t*, 131	*d*, 138	*s*	*t*, 158	*s*	*t*, 158	*t*, 135	*s*	*s*	*d*, 166	*d*, 166	*s*	*t*, 135
25	40.8	72.6	35.5	36.1	148.1	103.7	144.0	107.1	22.9	165.3	129.6	131.6	131.0	127.7	24.9[b])
	d, 140	*d*, 156	*t*, 130	*d*, 140	*s*	*t*, 157	*s*	*t*, 158	*t*, 135	*s*	*s*	*d*, 166	*d*, 166	*s*	*t*, 135

[a]) Signal attributions based on comparison with other derivatives [20].

[b]) Signals of $H_2C(8)$ in the bicyclo[2.2.2]octyl derivatives.

(*m*, 4H). MS (70 eV): 321 (0.7), 320 (4), 319 (0.8), 318 (4, M^+), 186 (96), 183 (100). Anal. calc. for $C_{16}H_{15}BrO_2$ (319.2): C 60.21, H 4.74; found: C 60.03, H 4.76.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.1]-heptyl* p-*Methoxybenzoate* (**16**). Yield 75%, white crystals, m.p. 71–73° (pentane). $[\alpha]_D^{25} = -61.3°$, $[\alpha]_{578}^{25} = -64.1°$, $[\alpha]_{546}^{25} = -74.2°$, $[\alpha]_{436}^{25} = -141.3°$, $[\alpha]_{365}^{25} = -264.8°$ (c = 12 mg/ml, $CHCl_3$). IR (KBr): 3090, 2985, 2890, 2850, 1715, 1610, 1515. ^{1}H-NMR ($CDCl_3$): 7.98 (*d*, J = 8, 2H); 6.91 (*d*, J = 8, 2H); 5.33 (*s*, 1H); 5.13 (*s*, 1H); 5.08 (*s*, 1H); 5.00 (*m*, 1H); 4.85 (*s*, 1H); 3.85 (*s*, 3H); 3.08 (br. *s*, 1H); 2.93 (br. *s*, 1H); 2.25–1.4 (*m*, 4H). MS (70 eV): 270 (4, M^+), 136 (9), 135 (100). Anal. calc. for $C_{17}H_{18}O_3$ (270.33): C 75.53, H 6.71; found: C 75.44, H 6.83.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl Benzoate* (**17**). Yield 60%, colourless crystals, m.p. 46–47° (pentane). $[\alpha]_D^{25} = -75.8°$, $[\alpha]_{578}^{25} = -78.9°$, $[\alpha]_{546}^{25} = -90.7°$, $[\alpha]_{436}^{25} = -164°$, $[\alpha]_{365}^{25} = -281°$ (c = 10.5 mg/ml, $CHCl_3$). IR (KBr): 3080, 2975, 2880, 1790, 1715, 1600. ^{1}H-NMR ($CDCl_3$): 8.02 (*m*, 2H); 7.5 (*m*, 3H); 5.35, 5.19, 4.89, 4.88 (4 *s*, 4H); 5.29 (*m*, 1H); 3.26 (*m*, 1H); 2.86 (*m*, 1H); 2.33 (*m*, 1H); 1.59–1.30 (*m*, 3H). MS (70 eV): 240 (5, M^+), 198 (4), 118 (4), 105 (100), 77 (49). Anal. calc. for $C_{16}H_{16}O_2$ (240.303): C 79.97, H 6.71; found: C 79.98, H 6.28.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl* p-*Methylbenzoate* (**18**). Yield 75%, colourless crystals, m.p. 36°–37° (pentane). $[\alpha]_D^{25} = -81.6°$, $[\alpha]_{578}^{25} = -85.5°$, $[\alpha]_{546}^{25} = -98.4°$, $[\alpha]_{436}^{25} = -179°$, $[\alpha]_{365}^{25} = -311°$ (c = 17 mg/ml, $CHCl_3$). IR (film): 3085, 3040, 2980, 2880, 1715, 1615. ^{1}H-NMR ($CDCl_3$): 7.9 (*d*, J = 8, 2H); 7.23 (*d*, J = 8, 2H); 5.35 (*m*, 1H); 5.32 (*s*, 1H); 5.2 (*s*, 1H); 4.9 (*s*, 2H); 3.27 (br. *s*, 1H); 2.89 (br. *s*, 1H); 2.4 (*s*, 3H); 2.33 (*m*, 1H); 1.65–1.25 (*m*, 3H). MS (70 eV): 254 (6, M^+), 212 (2), 119 (100), 91 (40). Anal. calc. for $C_{17}H_{18}O_2$ (254.33): C 80.28, H 7.13; found: C 80.18, H 7.19.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl* p-*Chlorobenzoate* (**19**). Yield 60%, oil, b.p. 150°/0.1 Torr. $[\alpha]_D^{25} = -92.4°$, $[\alpha]_{578}^{25} = -97°$, $[\alpha]_{546}^{25} = -112°$, $[\alpha]_{436}^{25} = -206°$, $[\alpha]_{365}^{25} = -364°$ (c = 10 mg/ml, $CHCl_3$). IR (film): 3095, 2980, 2890, 1800, 1725, 1600. ^{1}H-NMR ($CDCl_3$): 7.93 (*d*, J = 8, 2H); 7.38 (*d*, J = 8, 2H); 5.35 (*s*, 1H); 5.34 (*m*, 1H); 5.2 (*s*, 1H); 4.88 (*s*, 2H); 3.25 (br. *s*, 1H); 2.88 (br. *s*, 1H); 2.33 (*m*, 1H); 1.65–1.2 (*m*, 3H). MS (70 eV): 276 (0.7), 275 (0.4), 274 (2, M^+), 141 (35), 140 (8), 139 (100). Anal. calc. for $C_{16}H_{15}ClO_2$ (274.75): C 69.95, H 5.50; found: C 70.06, H 5.55.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl* p-*Bromobenzoate* (**20**). Yield 70%, oil, b.p. 150°/0.1 Torr. $[\alpha]_D^{25} = -85°$, $[\alpha]_{578}^{25} = -89°$, $[\alpha]_{456}^{25} = -103°$, $[\alpha]_{436}^{25} = -190°$, $[\alpha]_{365}^{25} = -340°$ (c = 10 mg/ml, $CHCl_3$). IR ($CHCl_3$): 3090, 3045, 2990, 2890, 2860, 1715, 1595. ^{1}H-NMR ($CDCl_3$): 7.85 (*d*, J = 8, 2H); 7.53 (*d*, J = 8, 2H); 5.35 (*s*, 1H); 5.34 (*m*, 1H); 5.00 (*s*, 1H); 4.88 (*s*, 2H); 3.25 (br. *s*, 1H); 2.88 (br. *s*, 1H); 2.33 (*m*, 1H); 1.65–1.2 (*m*, 3H). Anal. calc. for $C_{16}H_{15}BrO_2$ (319.2): C 60.21, H 4.74; found: C 60.25, H 4.78.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.1]heptyl* p-*Methoxybenzoate* (**21**). Yield 60%, oil, b.p. 120°/0.1 Torr. $[\alpha]_D^{25} = -77.5°$, $[\alpha]_{578}^{25} = -81°$, $[\alpha]_{546}^{25} = -94°$, $[\alpha]_{436}^{25} = -172°$, $[\alpha]_{365}^{25} = -307°$ (c = 10 mg/ml, $CHCl_3$). IR ($CHCl_3$): 3080, 2980, 2890, 2850, 1695, 1605, 1360. ^{1}H-NMR ($CDCl_3$): 7.95 (*d*, J = 8, 2H); 6.88 (*d*, J = 8, 2H); 5.33 (*s*, 1H); 5.31 (*m*, 1H); 5.08 (*s*, 1H); 4.88 (*s*, 2H); 3.83 (*s*, 3H); 3.23 (br. *s*, 1H); 2.85 (br. *s*, 1H); 2.3 (*m*, 1H); 1.6–1.2 (*m*, 3H). MS (70 eV): 270 (5, M^+), 136 (14), 135 (100), 107 (9), 92 (10), 91 (6). Anal. calc. for $C_{17}H_{18}O_3$ (270.33): C 75.53, H 6.71; found: C 75.42, H 6.77.

*(−)-(1S,2R)-5,6-Dimethylidene-2-*exo*-bicyclo[2.2.2]octyl* p-*Bromobenzoate* (**24**)[2]). Colourless oil. $[\alpha]_D^{25} = -22°$, $[\alpha]_{578}^{25} = -23.1°$, $[\alpha]_{546}^{25} = -26.5°$, $[\alpha]_{436}^{25} = -46.7°$ (c = 20 mg/ml, $CHCl_3$). IR ($CHCl_3$): 3080, 3060, 3020, 1715, 1595, 1270, 1120, 1100, 1010, 910. ^{1}H-NMR ($CDCl_3$): 7.95 (*d*, J = 8, 2H); 7.6 (*d*, J = 8, 2H); 5.43 (*s*, 1H); 5.3 (*s*, 1H); 5.15 (*m*, 1H); 4.95 (*s*, 1H); 4.8 (*s*, 1H); 2.75 (*m*, 1H); 2.45 (*m*, 1H); 2.25–0.65 (*m*, 6H). MS (70 eV): 334 (12), 332 (12, M^+), 291 (8), 290 (3), 185 (94), 183 (100). MS (HR)[3]): compound polymerized.

*(−)-(1S,2S)-5,6-Dimethylidene-2-*endo*-bicyclo[2.2.2]octyl* p-*Bromobenzoate* (**25**)[2]). Colourless oil. $[\alpha]_D^{25} = -13°$, $[\alpha]_{578}^{25} = -13.5°$, $[\alpha]_{546}^{25} = -15.7°$, $[\alpha]_{436}^{25} = -30.7°$ (c = 20 mg/ml, $CHCl_3$). IR ($CHCl_3$): 3040, 3020, 2960, 2880, 1710, 1590, 1490, 1400, 1270, 1120, 1105, 1010, 900. ^{1}H-NMR ($CDCl_3$): 7.9 (*d*, J = 8, 2H); 7.58 (*d*, J = 8, 2H); 5.45 (*s*, 1H); 5.33 (*s*, 1H); 5.23 (*m*, 1H); 4.83 (*s*, 2H); 2.68 (*m*, 1H); 2.48 (*m*, 1H); 2.23 (*m*, 1H); 1.9–0.7 (*m*, 5H). MS (70 eV): 334 (16), 332 (14, M^+), 291 (4), 289 (4), 185 (94), 183 (100). MS (HR)[3]): 332.0384 ($C_{17}H_{17}BrO_2$, calc. 332.0411).

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REFERENCES

[1] *E. Charney*, 'The Molecular Basis of Optical Activity', Wiley, New York, 1979, pp. 217–226; *A. W. Burgstahler, R. C. Barkhurst & J. K. Gawronski*, in 'Modern Methods of Steroid Analysis', E. Heftmann, ed., Academic Press, New York, 1973, *Chap. 16; G. Snatzke & F. Snatzke*, in 'Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism', F. Ciardelli & P. Salvadori, eds., Heydon & Son, New York, 1973, *Chap. 3* and *5*; *G. Snatzke*, in 'Optical Activity and Chiral Discrimination', S. F. Mason, ed., D. Reidel, Dordrecht, 1979, pp. 48–55; *U. Weiss, H. Ziffer & E. Charney, Tetrahedron 21*, 3105 (1965).

[2] *E. Charney, H. Ziffer & U. Weiss*, Tetrahedron *21*, 3121 (1965).

[3] *R. Deen & H. J. C. Jacobs*, Proc. K. Ned. Akad. Wet. *64*, 313 (1961); *A. W. Burgstahler, H. Ziffer & U. Weiss*, J. Am. Chem. Soc. *83*, 4660 (1961); *A. Moscowitz, E. Charney, U. Weiss & H. Ziffer*, ibid. *83*, 4661 (1961); *E. Charney*, Tetrahedron *21*, 3127 (1965).

[4] a) *D. A. Lightner, T. D. Bouman, J. K. Gawronski, K. Gawronska, J. L. Chappuis, B. V. Crist & A. E. Hansen*, J. Am. Chem. Soc. *103*, 5314 (1981); b) *A. W. Burgstahler, G. Wahl, N. Dang, M. E. Sanders & A. Nemirovsky*, ibid. *104*, 6873 (1982).

[5] a) *A. W. Burgstahler & R. C. Barkhurst*, J. Am. Chem. Soc. *92*, 7601 (1970); b) *A. W. Burgstahler, L. O. Weigel & J. K. Gawronski*, ibid. *98*, 3015 (1976); c) *A. W. Burgstahler, D. L. Boger & N. C. Naik*, Tetrahedron *32*, 309 (1976); d) *J. Gawronski & K. Gawronska*, J. Chem. Soc., Chem. Commun. *1980*, 346.

[6] a) *J. S. Rosenfield & E. Charney*, J. Am. Chem. Soc. *99*, 3209 (1977); *E. Charney, C. H. Lee & J. S. Rosenfield*, ibid. *101*, 6802 (1979); b) *A. Rauk & H. A. Peoples*, J. Comput. Chem. *1*, 240 (1980); c) *T. D. Bouman & A. E. Hansen*, Chem. Phys. Lett. *45*, 326 (1977); see also: *A. I. Scott & A. D. Wrixon*, Tetrahedron *26*, 3695 (1970); *iidem*, ibid. *27*, 4787 (1971); *J. Hudec & D. N. Kirk*, ibid. *32*, 2475 (1976).

[7] *O. E. Weigang*, J. Am. Chem. Soc. *101*, 1965 (1979); *R. M. Moriarty, H. E. Paaren, U. Weiss & W. B. Whalley*, ibid. *101*, 6804 (1979).

[8] *M. Duraisamy & H. M. Walborsky*, J. Am. Chem. Soc. *105*, 3264 (1983).

[9] *J. M. Sonney & P. Vogel*, Helv. Chim. Acta *63*, 1034 (1980).

[10] *Z. Zhichen, P. A. Carrupt & P. Vogel*, Tetrahedron Lett. *24*, 3607 (1983).

[11] *P. A. Carrupt & P. Vogel*, Tetrahedron Lett. *22*, 4721 (1981).

[12] *D. L. Cullen, M. M. Mangion, B. V. Crist & D. A. Lightner*, Tetrahedron *39*, 733 (1983).

[13] *W. Kuhn*, Trans. Faraday Soc. *26*, 293 (1930); *J. G. Kirkwood*, J. Chem. Phys. *5*, 479 (1937); *R. A. Grinter & S. F. Mason*, Trans. Faraday Soc. *60*, 274 (1964); *J. A. Schellman*, Acc. Chem. Res. *1*, 144 (1968); *A. D. Buckingham & P. J. Stiles*, ibid. *7*, 258 (1974).

[14] a) *N. Harada & K. Nakanishi*, Acc. Chem. Res. *5*, 257 (1972); b) *iidem*, in 'Circular Dichroic Spectroscopy-Exciton Coupling in Organic Stereochemistry', University Science Books, Oxford Univ. Press, 1983.

[15] *V. Delaroff & R. Viennet*, Bull. Soc. Chim. Fr. *1972*, 277; *M. Koreeda, N. Harada & K. Nakanishi*, J. Am. Chem. Soc. *96*, 266 (1974); *M. Koreeda, G. Weiss & K. Nakanishi*, ibid. *95*, 239 (1973).

[16] *N. Harada, J. Iwabuchi, Y. Yokota, H. Uda & K. Nakanishi*, J. Am. Chem. Soc. *103*, 5590 (1981); *Y. Naya, K. Yoshihara, T. Iwashita, H. Komura, K. Nakanishi & Y. Hata*, ibid. *103*, 7009 (1981); *N. C. Gonnella, K. Nakanishi, V. S. Martin & K. B. Sharpless*, ibid. *104*, 3775 (1982); *W. H. Rastetter, J. Adams & J. Bordner*, Tetrahedron Lett. *23*, 1319 (1982).

[17] *M. A. Adams, K. Nakanishi, W. C. Still, E. V. Arnold, J. Clardy & C. J. Persoons*, J. Am. Chem. Soc. *101*, 2495 (1979).

[18] *D. R. Boyd, G. S. Gadaginamath, N. D. Sharma, A. F. Drake, S. F. Mason & D. M. Jerina*, J. Chem. Soc., Perkin Trans. 1 *1981*, 2233.

[19] *C. Barras, R. Roulet, E. Vieira, P. Vogel & G. Chapuis*, Helv. Chim. Acta *64*, 2328 (1981).

[20] a) *J. M. Sonney, P. Vogel & U. Burger*, Helv. Chim. Acta *63*, 1016 (1980); b) *A. Chollet, C. Mahaim, C. Foetisch, M. Hardy & P. Vogel*, ibid. *60*, 59 (1977); *D. Quarroz, J. M. Sonney, A. Chollet, A. Florey & P. Vogel*, Org. Magn. Reson. *9*, 611 (1977).