Chromatographic Resolution, Circular Dichroism Spectra, and Absolute Configurations of Dimers of 5*H*-Indolo[1,7-*ab*][1]benzazepine and Coumarin with C_2 Symmetry

Anders Hallberg,[1a] Roland Isaksson,[1b] Arnold R. Martin,[1c] and Jan Sandström*,[1b]

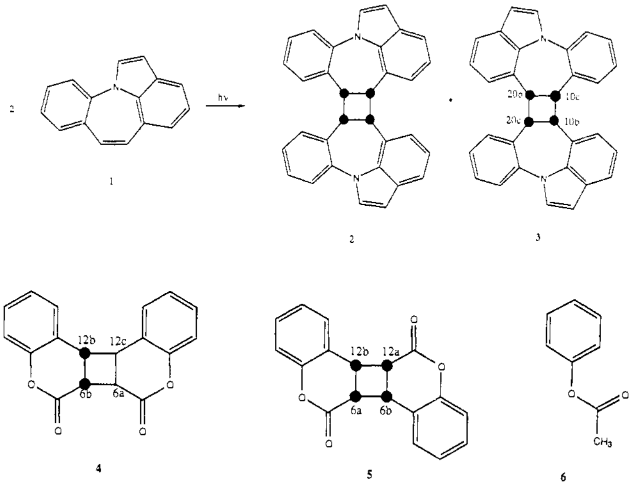
Contribution from the Divisions of Organic Chemistry 1 and 3, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden, and the Department of Pharmaceutical Sciences, University of Arizona, Tucson, Arizona 87521. *Received September 12, 1988*

Abstract: Three photodimers with cyclobutane rings and C_2 symmetry, one (syn, head-to-tail) derived from an indolobenzazepine and two (syn, head-to-tail and anti, head-to-head) from coumarin, have been completely resolved by liquid chromatography on two chiral stationary phases, the indolobenzazepine dimer on microcrystalline triacetylcellulose and the two coumarin dimers on poly(ethyl *S*-2-(acryloylamino)-3-phenylpropionate). The CD spectra have been analyzed and compared with spectra calculated by a semiempirical matrix technique, using transition moments and transition charge densities as input. The generally good agreements between calculated and experimental CD spectra have permitted assignment of the absolute configurations of the three dimers.

5*H*-Indolo[1,7-*ab*][1]benzazepine[2] (**1**) has been shown to undergo photodimerization to give two syn-cyclobutane derivatives, one (**2**, head-to-head) with C_s and one (**3**, head-to-tail) with C_2 symmetry.[3] The photodimerization of coumarin has been the subject of interest for a long time. The triplet dimerization with benzophenone sensitization gives mainly the anti, head-to-head dimer **4** (C_2),[4] and Lewis et al.[5] have shown that singlet dimerization in the presence of boron trifluoride etherate gives a high yield of the pure syn, head-to-tail dimer **5** (C_2).

The dimers with C_2 symmetry, **3**–**5**, are chiral, and analysis of the CD spectra of the enantiomers should in principle permit determination of their absolute configurations. Saigo et al.[6a,c,d] have recently resolved the *anti*-coumarin dimer **4** by separation of the diastereomeric ring-opened *N*-1-phenylethylamides followed by hydrolysis and lactonization. They analyzed the CD spectrum of (+)-**4** by using the coupled oscillator model for the interaction between the $^1L_a \leftarrow {}^1A$ transitions in the (phenyloxy)carbonyl chromophores and concluded that the configuration is 1*R*,2*R*,3*R*,4*R*[6b] with respect to the four carbon atoms in the cyclobutane ring. In a second publication,[6c] the authors describe an X-ray crystallographic study of (−)-**4**, in which by use of the anomalous scattering the absolute configuration was established as 1*R*,2*R*,3*R*,4*R*. However, analysis of the fractional atomic coordinates given in ref 6c shows the absolute configuration to be 1*S*,2*S*,3*S*,4*S*, and a mirror reflection seems to have taken place by mistake in the calculation of the stereostructure.[6d] Thus the initially proposed absolute configuration seems to be the correct one.

Scheme I



We have become aware of the power of chromatographic resolution of enantiomers on a (semi)preparative scale, using e.g. swollen microcrystalline triacetylcellulose (TAC)[7] or synthetic chiral polyacrylamide[8] as the stationary phase. Compound **3** was successfully resolved on a TAC column, but the necessity to use methanol or ethanol as the mobile phase on this column led to partial opening of the lactone rings of the coumarin dimers **4** and **5**. These compounds were resolved on a column with crossbound poly(ethyl *S*-2-(acryloylamino)-3-phenylpropionate)[8] as stationary phase with toluene–dioxane as eluent. In this communication, we will describe the resolutions and the analysis of the CD spectra of **3**–**5** with the purpose of determining the absolute configurations of the enantiomers.

Experimental Section

Materials. The indolobenzazepine dimer **3** was prepared according to Bates et al.[3] This compound must be protected from light. The coumarin anti, head-to-head dimer **4** was prepared according to Hoffman et al.,[4d] and the coumarin syn, head-to-tail dimer **5** according to Lewis et al.[5] The identities of the products were secured by comparison of their

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(1) (a) Division of Organic Chemistry 1, University of Lund. (b) Division of Organic Chemistry 3, University of Lund. (c) University of Arizona.

(2) Hallberg, A.; Martin, A. R. *J. Heterocycl. Chem.* **1981**, *18*, 1255–1256.

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(4) (a) Schenck, G. O.; von Wilucki, I.; Krauch, C. H. *Chem. Ber.* **1962**, *95*, 1409–1412. (b) Hammond, G. S.; Stout, C. A., Lamola, A. A. *J. Am. Chem. Soc.* **1964**, *86*, 3103–3106. (c) Krauch, C. H.; Farid, S.; Schenck, G. O. *Chem. Ber.* **1966**, *99*, 625–633. (d) Hoffman, R.; Wells, P., Morrison, H. *J. Org. Chem.* **1971**, *36*, 102–108.

(5) Lewis, F. D.; Howard, D. K.; Oxman, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 3344–3345.

(6) (a) Saigo, K.; Sekimoto, K.; Yonezawa, N.; Hasegawa, M. *Tetrahedron Lett.* **1983**, *24*, 5381–5384. (b) 6a*R*,6b*R*,12b*R*,12c*R* according to IUPAC rules. (c) Saigo, K.; Yonezawa, N.; Sekimoto, K.; Hasegawa, M.; Ueno, K.; Nakanishi, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1000–1005. (d) This assumption has been kindly verified by Professor K. Saigo. See also: *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2704.

(7) (a) Hesse, G.; Hagel, R. *Justus Liebigs Ann. Chem.* **1976**, 996–1008. (b) Hesse, G.; Hagel, R. *Chromatographia* **1976**, *9*, 62–68. (c) Häkli, H.; Mintas, M.; Mannschreck, A. *Chem. Ber.* **1979**, *112*, 2028–2038. (d) Mannschreck, A.; Eiglsperger, A.; Stühler, G. *Chem. Ber.* **1982**, *115*, 1568–1575. (e) Schlögl, K.; Widhalm, M.; Vogel, E.; Schwamborn, M. *Monatshefte* **1983**, *114*, 605–614. (f) Isaksson, R.; Liljefors, T.; Reinholdson, P. *J. Chem. Soc., Chem. Commun.* **1984**, 137–138.

(8) (a) Blaschke, G.; Schwanghart, A.-D. *Chem. Ber.* **1976**, *109*, 1967–1975. (b) Blaschke, G.; Kraft, H. P.; Markgraf, H. *Chem. Ber.* **1983**, *116*, 3611–3617.

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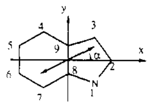
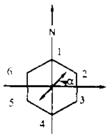
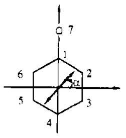
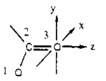
Table I. Input Data for Calculation of CD Spectra

chromophore	transition and direction (α/deg)	energy/ 10^3 cm^{-1}	Δ[a]	transition moment μ/D[b] or M/β[c]	atom	atomic transition charges[d]			
						^1L_b	^1L_a	^1B_b	^1B_a
	^1L_b (−39.0)	31.25	5.0	0.84					
	^1L_a (−64.0)	34.50	22.5	1.60	N(1)	−0.0186	−0.1272	+0.0472	−0.3078
					C(2)	+0.1278	−0.0596	+0.1234	+0.2390
	^1B_b (+5.8)	46.50	10.0	1.36	C(3)	−0.1036	+0.0982	−0.1150	−0.1010
					C(4)	−0.1710	+0.1042	+0.0768	+0.1364
	^1B_a (−39.1)	50.0	10.0	3.81	C(5)	+0.1487	−0.1108	−0.0652	+0.0892
					C(6)	−0.1542	+0.1564	+0.0205	+0.0500
					C(7)	+0.1506	−0.1958	−0.0883	+0.0560
					C(8)	−0.1484	−0.2020	−0.0255	−0.1708
					C(9)	+0.1686	−0.0672	0.0262	+0.0090
	^1L_b (0)	36.90	16.5	2.10	C(1)	0.0000	−0.1114		
					C(2)	−0.0906	−0.0500		
	^1L_a (90)	46.10	10.0	4.13	C(3)	−0.0906	+0.0650		
					C(4)	0.0000	+0.0814		
					C(5)	+0.0906	+0.0650		
					C(6)	+0.0906	−0.500		
	^1L_b (15.0)	35.70	6.5	0.62	C(1)	+0.0080	0.0000		
		36.80	6.5	0.86		+0.0110			
	^1L_a (75.0)	(**4**): 46.50	10.0	3.37	C(2)	+0.0298	+0.1794		
		(**5**): 49.80	10.0	3.37		+0.0418			
					C(3)	+0.0218	−0.0994		
						+0.0302			
					C(4)	−0.0080	−0.0660		
						−0.0110			
					C(5)	−0.0298	−0.1802		
					C(6)	−0.0218	+0.0986		
						−0.0302			
					O(7)	0.0000	+0.0586		
						0.0000			
	nπ^*	45.50	10.0	0.805[c]	C(2)	0.0443;[e]			
						$x, y = \pm 0.479$ Å[f]			
					O(3)	0.2120;[e]			
						$x, y = \pm 0.328$ Å[f]			

[a] Bandwidth (nm) at $\Delta\epsilon_{max}/e$. [b] Electric transition moment. [c] Magnetic transition moment in units of β, Bohr magnetons = 9.274×10^{-21} erg/gauss = 9.274×10^{-24} J T^{-1} (AM^2). [d] In units of the electronic charge. [e] Transition quadrupolar charges. [f] Local coordinates, z-axis along C(2)–O(3) bond.

^{1}H NMR spectra with published spectra.

Chromatographic Resolution. The chromatographic equipment has been described in detail by Isaksson and Roschester.[9] The dimer **3**, 20 mg in 15 mL of ethanol (the eluent), was injected on a 30 × 2.5 cm TAC column. Base-line separation was not achieved, but fractions taken in the first part of the eluate, with positive rotation (E_1), and in the last part of the eluate with negative rotation (E_2) gave CD spectra which were nearly perfect mirror images also with respect to the $\Delta\epsilon$ values, and we therefore consider these fractions to be enantiomerically pure.

Chromatography of the coumarin dimers **4** and **5** on the TAC column with ethanol–water (96/4; v/v) as the eluent gave rise to several optically active bands in the chromatogram, indicating reactions between the substrate and the mobile phase. The TAC column was therefore replaced by two 1 × 35 cm glass columns in series, each packed with 5 g of swollen crossbound poly(ethyl *S*-2-(acryloylamino)-3-phenylpropionate).[8] The columns were connected to a switching valve to allow recycling. The best enantioselectivity was obtained with a binary eluent system consisting of toluene–dioxane (9/1; v/v). Injection of 20 mg of **4** in 15 mL of solvent gave a similar degree of separation as found for **3** on TAC, and fractions collected in the same way gave CD spectra in complete agreement with those reported by Saigo et al.,[6] and these are also considered to be enantiomerically pure. The dimer **5**, 28 mg in 20 mL of solvent, gave a complete base-line separation after three cycles on the columns. Both with **4** and **5** the (−)-enantiomer was eluted first.

The CD measurements were performed on a JASCO Model J 41-A spectrometer, and the solutions were prepared by weighing of crystalline material obtained after evaporation of the chromatography fractions.

Calculations. The CNDO/2 calculations were performed by the standard program,[10] and the CNDO/S calculations by the program described by Guimon et al.[11] The theoretical CD spectra were obtained by the semiempirical Schellman matrix technique,[12] using as input for **3** only the $\pi \rightarrow \pi^*$ transition dipoles and transition charge densities in the distributed monopole approximation. For **4** and **5** the magnetic transition moment and transition quadrupole charges for the $n \rightarrow \pi^*$ transitions, calculated as described by Roschester et al.,[13] were also included (Table I). The static charges, localized in the centers of the atoms, were obtained from the CNDO/2 calculations. The calculations were performed by a computer program, allowing for contributions from the coupled-oscillator,[14] the magnetic–electric-coupling,[15] and the Condon-Altar-Eyring one-electron[16] mechanisms. The geometries used in the calculations are those obtained in X-ray crystallographic studies of **3**,[3] **4**,[6c] and the 7-methoxy analogue of **5**.[17]

The initial transition moments and monopolar transition charges were taken from CNDO/S calculations and scaled to reproduce the experimental UV spectrum. When other polarization directions were tried (vide infra), the corresponding monopoles were obtained by the Lagrangian multiplier technique described by Rizzo and Schellman.[12b] The localization of the transition dipoles has been described before.[18a]

Results and Discussion

The syn, head-to-tail dimer, **3**, of 5-*H*-indolo[1,7-*ab*][1]benzazepine (**1**) contains two *N*-phenylindole chromophores, and in the coupled-oscillator model[14] its CD absorption can be considered to arise through interaction between the $\pi \rightarrow \pi^*$ transitions in the two chromophores. For a complete treatment of the couplings,

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(9) Isaksson, R.; Roschester, J. *J. Org. Chem.* **1985**, *50*, 2519–2521.

(10) Pople, J. A.; Beveridge, D. L. *Approximate Molecular Orbital Theory*; McGraw-Hill; New York, 1970; p 163.

(11) Guimon, C.; Gonbeau, D.; Pfister-Guillouzo, G. *Tetrahedron* **1973**, *29*, 3395–3405.

(12) (a) Bayley, P. M.; Nielsen, E. B.; Schellman, J. A. *J. Phys. Chem.* **1969**, *73*, 228–243. (b) Rizzo, V.; Schellman, J. A. *Biopolymers* **1984**, *23*, 435–470.

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(14) (a) Kirkwood, J. G. *J. Chem. Phys.* **1937**, *5*, 479–491. (b) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy—Exciton Coupling in Organic Chemistry*; Oxford University Press; 1983.

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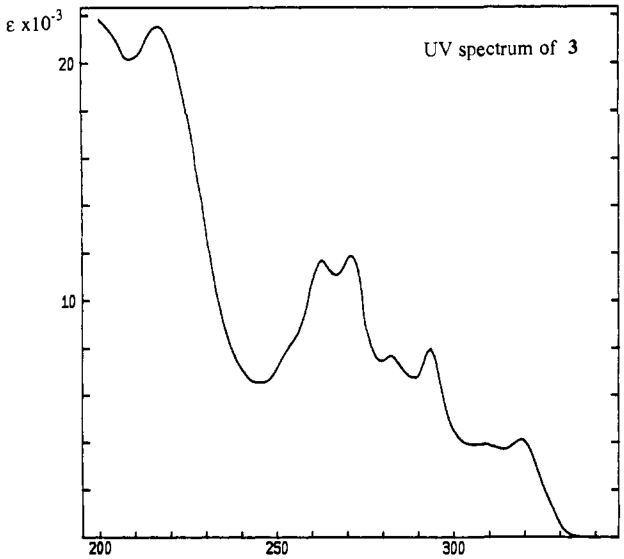
(16) Condon, E. U.; Altar, W.; Eyring, H. *J. Chem. Phys.* **1937**, *5*, 753–775.

(17) Ramasubbu, N.; Guru Row, T. N.; Venkatesan, K.; Ramamurthy, V.; Rao, C. N. R. *J.Chem. Soc., Chem. Commun.* **1982**, 178–179.

(18) (a) Nilsson, I.; Berg, U.; Sandström, J. *Acta Chem. Scand.* **1986**, *B40*, 625–651. (b) Nilsson, I.; Berg, U.; Sandström, J. *Acta Chem. Scand.* **1987**, *B41*, 261–266.



UV spectrum of 3

Figure 1. UV spectrum of 3 in ethanol.

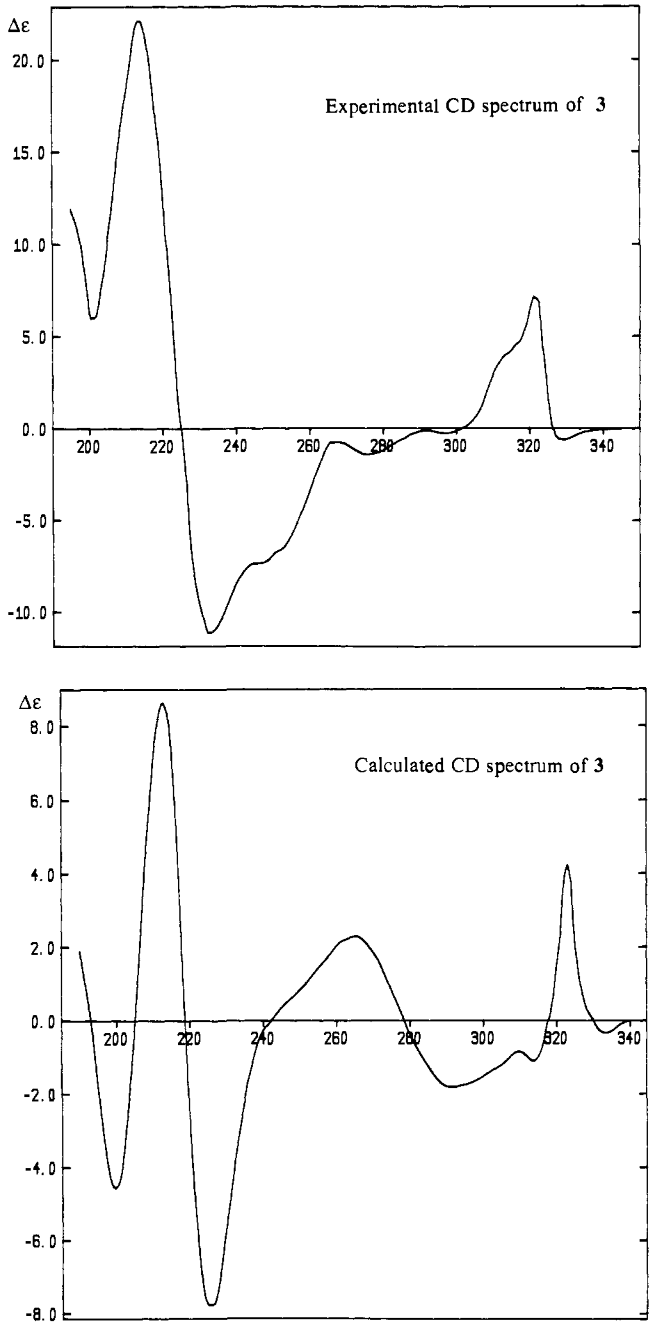
we should need to know the energies of all $\pi \rightarrow \pi^*$ transitions as well as the strengths and directions of the corresponding electric transition dipole moments.

The crystal structure of 3 has been determined by single-crystal X-ray diffraction,[3] and the angle between the indole and phenyl rings was found to be 26.9° in one and 33.4° in the other chromophore. Thus, the *N*-phenylindole chromophore is inherently chiral. Therefore, a rigorous treatment should require a full quantum-mechanical treatment of high quality for the molecule 3, which is not feasible. However, the indole and phenyl π systems are conjugated via the nitrogen atom, which acts as donor atom to both components of the chromophore. This type of cross conjugation leads to only limited interaction between the two parts. This is illustrated by a comparison between the UV spectra of the 1-phenylindole chromophore in 3 (Figure 1, divide ϵ by 2), which is rather similar to that of simple indole derivatives,[19a-e] and 2-phenylindole (λ_{max} 241 and 309 nm with ϵ 22 100 and 29 500),[19f] the latter showing evidence of much stronger conjugation. A similar difference is observed between the spectra of 1-phenylpyrrole (253 nm, 13 500)[19g] and 2-phenylpyrrole (288 nm, 16 600).[19h] Therefore, it seems permissible as a first approximation to treat the twisted 1-phenylindole chromophore as two isolated chromophores, one of indole and one of aniline type, both with a nitrogen atom of reduced donor capacity. This view is supported by a CNDO/S calculation of the transition charge densities, which gives the result that the four lowest $\pi \rightarrow \pi^*$ transitions are considerably localized either in the indole or in the benzene ring. In the UV spectrum of 3, a weak band system with vibrational components at 319 and 307 nm can be ascribed to the indole ^1L_b ($^1L_b \leftarrow {}^1A$,[20] 287 and 281 nm in indole) and two somewhat stronger bands at 293 and 281 nm to the indole ^1L_a transition (270 nm in indole). These transitions have recently been identified in the CD spectra of chiral indoles.[18] A stronger band system with vibrational fine structure around 268 nm is ascribed to ^1L_b type transitions in the benzene rings. The corresponding band for aniline falls at 280 nm (ϵ 1430),[21] and the hypsochromic shift is ascribed to the cross conjugation. The strong band at 217 nm is probably composed of the benzene ^1L_a (230 nm in aniline)[21] and indole ^1B_b (220 nm in indole) transitions, both hypsochromically shifted by the cross conjugation. Besides, an indole ^1B_a transition is assumed at ca. 200 nm[19e] (Table I).

Table II. CD Spectra of Compounds **3–5**

compd	solvent	λ_{max}/nm ($\Delta\epsilon$)
(+)-**3**	ethanol	329 (−0.62), 321 (+7.11), 3.15 (+4.35 S[a]), 297 (−0.25), 277 (−1.44), 245 (−7.28 S[a]), 233 (−11.1), 213.5 (+21.5), 202 (+5.6[b])
(+)-**4**	acetonitrile	285 (−0.11), 280 (+0.59), 272 (+0.38), 228.5 (+18.0), 215.5 (−16.2), 192 (−31.2)
(+)-**5**	acetonitrile	279.5 (+0.56), 274 (+0.53), 233 (+1.86), 207 (+7.6), 196 (−5.5)

[a] Shoulder. [b] Positive minimum.



Experimental CD spectrum of 3

Calculated CD spectrum of 3

Figure 2. (a) CD spectrum of (+)-3 in ethanol and (b) calculated CD spectrum of 3 with geometry from ref 3 and the 10b*R*,10c*S*,20b*R*,20c*S* configuration. The input data are in Table I.

The CD spectrum of (+)-3 (Figure 2a, Table II) in the near UV region is composed of a positive band of medium strength at 319 nm with a shoulder on the short-wavelength side, assigned to the indole ^1L_b transition, and of a stronger negative couplet at 224 nm (peaks at 213.5 and 233 nm). The negative component

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(19) (a) Strickland, E. H.; Horwitz, J.; Billups, C. *Biochemistry* **1969**, *8*, 3205–3213. (b) Strickland, E. H.; Horwitz, J.; Billups, C. *Biochemistry* **1970**, *9*, 4914–4921. (c) Strickland, E. H.; Billups, C.; Kay, E. *Biochemistry* **1972**, *11*, 3657–3662. (d) Strickland, E. H.; Billups, C. *Biopolymers* **1973**, *12*, 1989–1995. (e) Auer, H. E. *J. Am. Chem. Soc.* **1973**, *95*, 3003–3011. (f) Blades, C.; Wilds, A. L. *J. Org. Chem.* **1956**, *21*, 1013–1021. (g) Davoll, J. *J. Chem. Soc.* **1953**, 3802–3811. (h) Elpern, B.; Nachod, F. C. *J. Am. Chem. Soc.* **1950**, *72*, 3379–3382.

(20) Platt, J. R. *J. Chem. Phys.* **1949**, *17*, 484–495.

(21) Doub, L.; Vandenbelt, J. M. *J. Am. Chem. Soc.* **1947**, *69*, 2714–2723.

of the couplet has a shoulder at ca 240 nm, not observed in the UV spectrum. A weak negative band at 330 nm is probably a residue of the ^1L_a band, which in general is broader than the ^1L_b band and often extends to longer wavelengths. The strong UV bands at 260–270 nm (Figure 1) have no strong counterpart in the CD spectrum.

We have attempted to reproduce the experimental CD spectrum of **3** in order to determine its absolute configuration. The most promising feature in the spectrum of the E_1 enantiomer (Figure 2a) is the medium-strong positive band at 321 nm, which should arise through coupling of the indole ^1L_b transition in one chromophore with transitions in the other chromophores. Of these couplings, the one with the other indole ^1L_b transition should have a high weight because of the degeneracy. For the calculations, we need to know the directions of the various transition moments. The directions of the indole ^1L_b and ^1L_a transition have been determined by studies of polarized single-crystal spectra of 3-indolylacetic acid and glycyltryptophane by Yamamoto and Tanaka[22] and by a study of the rotationally resolved UV spectrum of gaseous indole by Philips and Levy.[23] The results show reasonable agreement, with $\alpha = +49°$, $+58°$,[22] and $+45°$,[23] respectively, for the ^1L_b and $-42°$, $-35°$, and $-45°$ for the ^1L_a transition (for definition of α, see Table I). P.P.P. type (π electron SCF) calculations on indole by Yamamoto and Tanaka[22] gave $\alpha = +54°$ and $-41°$ for ^1L_b and ^1L_a, and CNDO/S calculations[18a] gave $+44°$ and $-42°$, whereas a CNDO/S calculation on *N*-phenylindole gave $-39°$ and $-64°$. The directions of the benzene ^1L_b and ^1L_a transition moments are as a first approximation assumed to be governed by the spectroscopic moment of the N atom,[24] in spite of the cross conjugation; the moments are oriented with ^1L_b perpendicular and ^1L_a parallel to the phenyl–nitrogen bond. Similarly oriented transitions are found in the CNDO/S calculation on *N*-phenylindole. The directions of the ^1B_b and ^1B_a transition moments in indole have not been determined experimentally. P.P.P. calculations by Yamamoto and Tanaka[22] gave $\alpha = +18°$ and $-61°$, respectively, whereas a CNDO/S calculation[18a] gave $+6°$ and $-39°$. No transitions unambiguously assignable to ^1B_b and ^1B_a are found in the CNDO/S calculation on *N*-phenylindole. Therefore, the directions for these transitions were taken from the CNDO/S data for indole.[18a]

Calculations of rotational strengths based on interaction between the ^1L_b transitions alone in the 10b*R*,10c*S*,20b*R*,20c*S*[25] configuration (Scheme I) gave positive couplets with a positive band at ca. 322 nm and a negative band at ca. 314 nm for several values of α in the range $-40°$ to $+80°$. It is clear that the rotational strengths have no nodes in this range. Thus, application of the coupled-oscillator model to the indole ^1L_b transition indicates that the $E_1(+)$ enantiomer has the configuration given in the scheme. However, it is a priori possible that strong interactions of the ^1L_b transitions with other transitions could lead to sign reversal of the 322-nm band. To check this, we have successively included other transitions, beginning with indole ^1L_a.

Throughout these calculations, we have used two combinations of α values for the indole ^1L_b and ^1L_a transitions: $\pm 45°$, and $-39°$ and $-64°$. Both combinations gave positive 322-nm bands, but the agreement with the experimental curve was best with the latter combination, which even reproduced the weak negative band at $\lambda > 330$ nm.

Introduction of the benzene ^1L_b transition caused only a slight increase in the intensity of the 322-nm band, but strengthened the negative indole ^1L_a band at ca. 290 nm beside giving rise to a positive band at 264 nm. Changing the direction of the benzene ^1L_b transition by 60° to give the cyclobutyl substituent the same spectroscopic moment as the indole N atom changed the band at 264 nm to strongly negative and worsened the agreement with the experimental curve.

As expected, inclusion of the benzene ^1L_a and indole ^1B_b and ^1B_a transitions did not affect the long-wavelength part of the CD spectrum, but it is worth noticing that the CNDO/S α values for the indole transitions[18a] the couplet at 220 nm was fairly well reproduced. According to the calculations, the benzene ^1L_a and indole ^1B_b transitions contribute about equally to the couplet. Increasing α for the indole ^1B_b transition in steps of 5° from $+5°$ to $+35°$ led to the closest fit with the experimental CD curve for $\alpha = 25°$, whereas decreasing α to $-25°$ led to a worse fit, in both directions without changing the sign of the couplet. No attempts have been made to include the benzene ^1B_b and ^1B_a transitions.

Summing up, the agreement between the experimental (Figure 2a) and calculated (Figure 2b) CD spectra gives credence to the assignment of the E_1 enantiomer of **3** to the 10b*R*,10c*S*,20b*R*,20c*S* configuration. The sign of the 322-nm band has the greatest weight as proof, with the sign and intensity of the 220-nm couplet as a supporting factor.

In several chiral indoles, a CD band has been observed in the range 230–240 nm without a counterpart in the UV spectrum. It has tentatively been assigned to a transition to a ^1C state,[18a,20] and the negative shoulder observed at 240 nm in the CD spectrum of (+)-**3** may have the same origin.

The UV spectrum of the anti, head-to-head coumarin dimer **4** has a strong maximum at 215 nm (ϵ 25 000) and a weaker, structured band with maxima at 280 (ϵ 2000) and 271 nm (ϵ 2500).[6b] The strong band is ascribed to ^1L_a and the weaker to ^1L_b transitions in the benzene chromophore. The syn, head-to-tail dimer **5** has a similar ^1L_b band but then only end absorption down to 200 nm (ϵ 28 000). The basic chromophore of both dimers is also found in phenyl acetate (**6**). The UV spectrum of **6** shows a structured ^1L_b band with maxima at 265 (ϵ 210) and 258 nm (ϵ 250), but then only end absorption down to 200 nm (ϵ 8600).

The ^1L_a band of benzene falls at 204 nm (ϵ 7400) and that of anisole at 215 nm (ϵ 6400).[21] Probably, cross conjugation in phenyl acetate causes a blue-shift of this transition, which cannot fall at much longer wavelength than 200 nm, even if it is overlapped by a stronger band at shorter wavelength. The different positions of the ^1L_a band in the two dimers may be associated with geometric differences. The acyloxy group is ca. 15° out of the plane of the benzene ring in **4** but only ca. 6° in **5**, and cross conjugation should be somewhat more efficient in the latter. However, the spectral differences observed among **4**–**6** may also be explained by different degrees of conjugation through σ bonds in the dimers. Such effects are also seen in the bathochromic shifts and intensity increases in the ^1L_b bands.

The CD spectrum of the anti, head-to-head dimer (+)-**4** (Figure 3a) consists of a residue of a weak negative band at 284 nm, weak positive bands at 280 and 272 nm, and a strong positive couplet at 220 nm followed by a strong negative band at 195 nm.

The CD spectrum of the coumarin syn, head-to-tail dimer (+)-**5** (Figure 4a) is similar to that of (+)-**4**, displaying a weak positive ^1L_b band system at 270 to 280 nm, although less well resolved than for **4**, and a strong pair of bands appearing as a positive couplet centered at 201 nm with peaks at 196 and 206 nm.

The CD spectra of the two coumarin dimers in the near UV should arise primarily through coupling of the ^1L_b and ^1L_a transitions in one chromophore with those in the other. Primarily, one should expect individual couplets for the two kinds of transitions, but only one ^1L_b band is seen. This has also been observed by Canceill et al.[26] in some acetoxylated triveratrylene derivatives. The couplet centered at 221 nm in the spectrum of (+)-**4** and the one found at 201 nm in the spectrum of (+)-**5** appear as normal ^1L_a couplets, with positions in agreement with the positions of the corresponding UV bands.

The positive band at 233 nm ($\Delta\epsilon$ 1.86) in the spectrum of (+)-**5** is ascribed to $n \rightarrow \pi^*$ transitions in the acyloxy groups. This transition gives rise to CD bands in the range 205–230 nm in spectra of saturated γ- and δ-lactones,[27] and the long-wavelength

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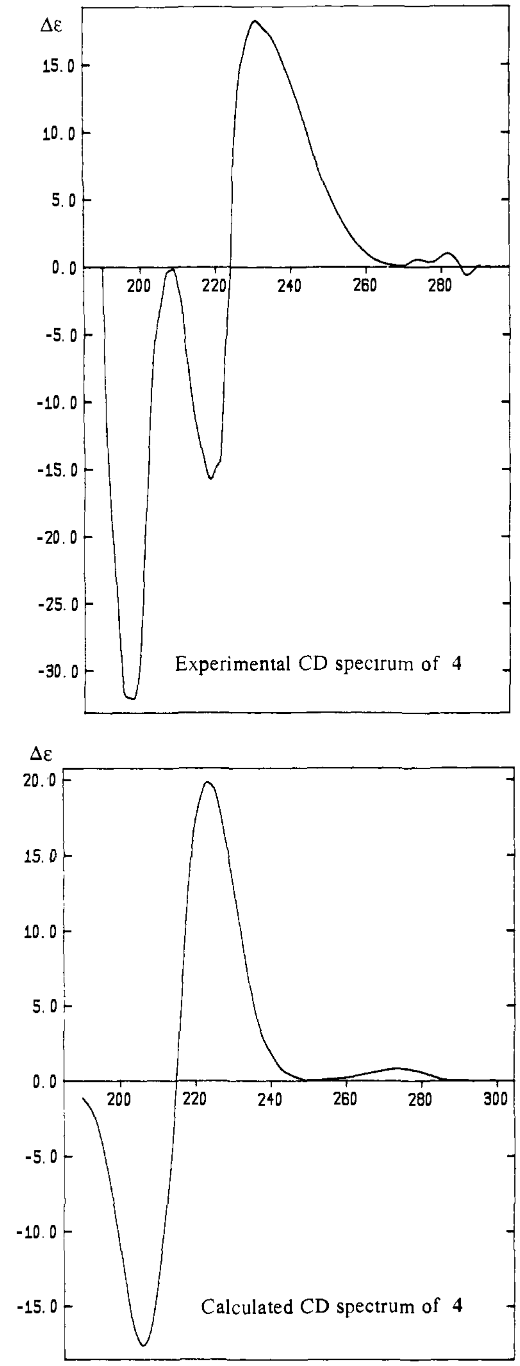

Figure 3. (a) CD spectrum of (+)-**4** in acetonitrile and (b) calculated CD spectrum of **4** with geometry from ref 6c and the 6a*R*,6b*R*,12b*R*,12c*R* configuration. The input data are in Table I.

position for (+)-**5** is as expected considering the cross conjugation and the nonhydroxylic solvent. No similar band is shown by (+)-**4**, which is explained by overlap by the strong band at 228.5 nm, but the broadness of this band is in harmony with an underlying positive band.

In the semiempirical calculations of the CD spectra of **4** and **5** we locate the ^1L_b and ^1L_a transition moments in the center of the benzene rings. The direction of the ^1L_b transition can be estimated from the spectroscopic moments of the acyloxy and cyclobutyl groups. We approximate them as acetoxy and methyl groups and use the spectroscopic moments +10 and +8 (cm·mol/L)$^{-1/2}$ determined by Sagiv[28] for these groups, which gives $\alpha = 41°$ for the ^1L_b transition (see Table I). We also used α = 0°, i.e. neglected the effect of the cyclobutyl group. No spectroscopic moments are known for the ^1L_a transition, and as a first approximation we used $\alpha = 90°$ and $\alpha = 60°$ for this transition. In the first case the direction is along the phenyl–oxygen bond, as proposed by Saigo et al.,[6] and in the second case the acyloxy and cyclobutyl substituents are given equal weights.

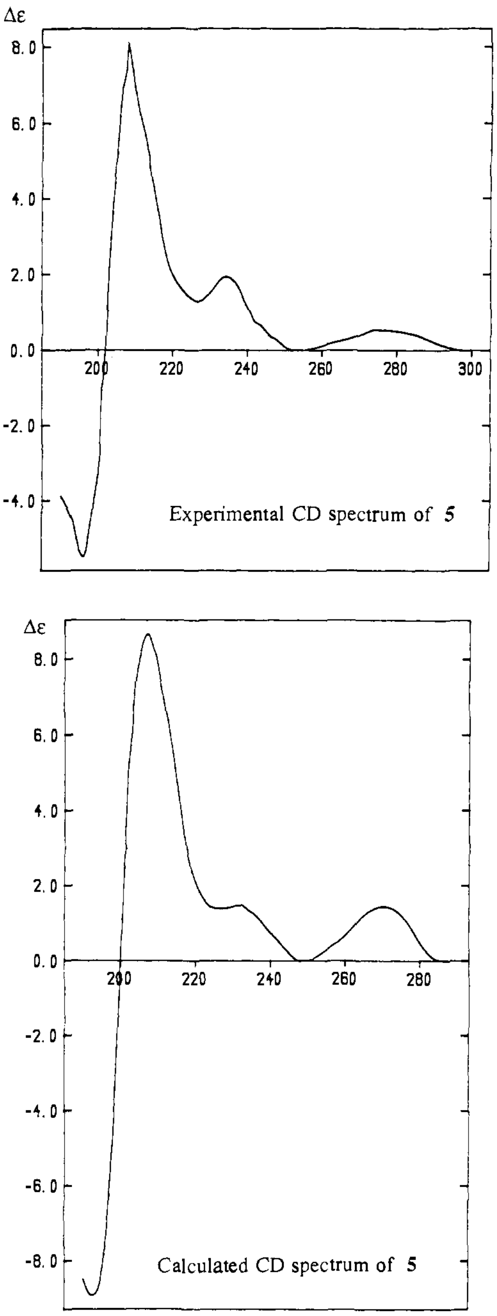

Figure 4. (a) CD spectrum of (+)-**5** in acetonitrile and (b) calculated CD spectrum of **5** with geometry from ref 17 and the 6a*R*,6b*S*,12a*R*,12b*S* configuration. The input data are in Table I.

In the approach we use, the n → π* rotational strength may arise through coupling of the π → π* electric transition moments with the n → π* electric quadrupolar transition moment (the μ–m mechanism)[15] or by the one-electron mechanism of Condon et al.[16] We found the latter to be unimportant, contributing less than Δε 0.1, while the μ–m mechanism gave rise to rotational strengths of the right order of magnitude.

Using the X-ray crystal geometry for **4**[6b] and the 6a*R*,6b*R*,12b*R*,12c*R* configuration, we obtained the correct sign and order of magnitude for the ^1L_a couplet and correct expected (+) sign for the n → π* transitions with all combinations of $\alpha(1L_b)$ = 0 or 41° and $\alpha(^1L_a)$ = 60° or 90°. However, the correct sign (but an exaggerated intensity) of the ^1L_b band was only obtained

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with $\alpha(^1L_b) = 41°$. Changing $\alpha(^1L_b)$ in steps of 5° from 0 to 40° led to the best fit with $\alpha = 15°$ for $\alpha(^1L_a) = 60°$ as well as 90°. The theoretical curve (Figure 3b) is calculated with $\alpha(^1L_b) = 15°$ and $\alpha(^1L_a) = 75°$. The overall good agreement with the experimental curve allows us to assign (+)-**4** to the 6a*R*,6b*R*,12b*R*,12c*R* configuration, also found in the X-ray crystallographic study by Saigo et al.[6c,d]

In the corresponding calculation on **5** (6a*R*,6b*S*,12a*R*,12b*S*) we found a nodal line for the ^1L_a transition between $\alpha = 60°$ and $\alpha = 90°$. The $n \rightarrow \pi^*$ transition gave a positive band with nearly correct intensity for all the combinations of $\alpha(^1L_b)$ and $\alpha(^1L_a)$ discussed above. With $\alpha(^1L_a) = 60°$, the ^1L_a couplet has the right sign with respect to the $n \rightarrow \pi^*$ band but is too intense, but with $(^1L_a) = 90°$ the sign is reversed. The ^1L_b band has the same sign as the $n \rightarrow \pi^*$ band expect with $\alpha(^1L_b) = 0°$, $\alpha(^1L_a) = 60°$. With use of $\alpha(^1L_b) = 15°$ and $\alpha(^1L_a) = 75°$, a rather good agreement was obtained for all transitions in the near UV region (Figure 4b). The influence of the benzene ^1B transitions does not seem to be important for $\lambda > 200$ nm.

Summing up, we propose the 6a*R*,6b*S*,12a*R*,12b*S* configuration for (+)-**5**, and the general agreement between experimental and calculated CD spectra for (+)-**4** and (+)-**5** indicates that the chosen directions for the transition moments are reasonable. Finally, it might be pointed out that the calculations predict only one ^1L_b band, the short wavelength component of the ^1L_b couplet always being weak and cancelled by the neighboring bands of opposite sign.

As has been clearly shown by Collet[29] and also follows from our experience with the ^1L_a transition in **5**, the question of transition moment directions must be treated with great circumspection when using the coupled-oscillator method. Safer conclusions can be drawn when several transitions can be reproduced, like in the present case.

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Reactions of Carbonyl Compounds with Grignard Reagents in the Presence of Cerium Chloride

Tsuneo Imamoto,* Nobuyuki Takiyama, Kimikazu Nakamura, Toshihiko Hatajima, and Yasuo Kamiya

Contribution from the Department of Chemistry, Faculty of Science, Chiba University, Yayoi-cho, Chiba 260, Japan. *Received November 4, 1988*

Abstract: The addition of Grignard reagents to ketones is significantly enhanced by cerium chloride with remarkable suppression of side reactions, particularly enolization. Some esters, which are prone to side reactions, also react readily with Grignard reagents in the presence of cerium chloride to give normal reaction products in reasonable to high yields.

The Grignard reaction of carbonyl compounds to yield alcohols is undoubtedly one of the most fundamental and versatile reactions in all of organic chemistry and has wide-spread synthetic applications.[1] Nevertheless, it is also well recognized that the Grignard reaction is often accompanied by so-called abnormal reactions such as enolization, reduction, condensation, conjugate addition, and pinacol coupling. In some cases such abnormal reactions prevail over the "normal reaction" resulting in poor yields of desired products.

It is synthetically important to enhance the yields of normal reaction products and reduce the yields of abnormal products. Several research groups have devised procedures to suppress abnormal reactions by changing solvent[2] or using additives such as $MgBr_2$,[3] $(n\text{-}C_4H_9)_4N^+Br^-$,[4] $LiClO_4$,[4] $(i\text{-}C_3H_7O)_3TiCl$,[5,6] or $(n\text{-}C_4H_9O)_3ZrCl$.[5] While these reported methods are effective in some cases, they are not always efficient and lack general applicability. For some years, we have been interested in this important problem and have worked to develop a new method which is highly effective in circumventing the abnormal reactions and also one which has broad synthetic applicability.

We previously observed that organocerium(III) reagents, generated by the reaction of organolithiums with cerium(III) halides, undergo efficient carbonyl addition, even though the substrates are susceptible to enolization or conjugate addition with

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