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LETTERS

Chirality transmission in flexible 5,5′-dinitrodiphenic esters connected with chiral secondary alcohols

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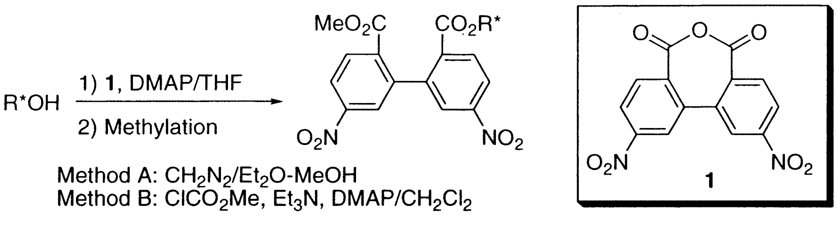
Abstract—Induced circular dichroism (CD) was observed with dinitrodiphenic esters of chiral secondary alcohols. The CD spectra of the esters prepared from a pair of antipodal alcohols were symmetrical to each other relative to the *x*-axis, indicating the enantiomeric nature of the esters. The sign of the Cotton effect at around 270 nm was found to reflect the absolute configuration of the original alcohol. In the case of aliphatic mono-alcohols, negative Cotton effect was observed for the esters of (*R*)-alcohols and a positive effect for the esters of (*S*)-alcohols. On the contrary, unsaturation or an oxygen atom at the vicinal position reversed the sign of the Cotton effect. © 2001 Elsevier Science Ltd. All rights reserved.

CD spectroscopic analysis has been regarded as a reliable tool as the X-ray diffraction method for stereochemical elucidation, and the exciton-coupled CD has been extensively applied to various organic compounds to determine their absolute configurations in a nonempirical manner.[1] However, application of this method has been limited to chiral compounds with two or more functional groups.[2] Recently, Harada and co-workers[3] reported a new CD spectroscopic method to determine the absolute configuration of mono-functional chiral alcohols. They employed an achiral carboxylic acid with two chromophores, di(1-naphthyl)acetic acid, as a CD auxiliary to derivatize chiral alcohols, and showed that the chirality of the substrates induced exciton-coupled CD arising from an interaction of the two chromophores on the auxiliary, which, coupled with conformational analysis of the derivatives, can be used for determining the absolute configuration of the substrates. It occurred to us that if the two chromophores on the auxiliaries were directly bound, a more effective exciton couplet could be expected. Here we describe that induced CD was observed for the dinitrodiphenic esters of chiral secondary alcohols. The sign of the Cotton effect at around 270 nm was found to reflect the absolute configuration of the alcohol moieties.

5,5′-Dinitrodiphenic anhydride **1**[4] was selected as a CD chromophoric reagent based on its relatively large transition moment and low transition energy[5] (Scheme 1). Condensation of **1** with *l*- and *d*-menthol followed by methylation gave methyl esters **2b** and **3b** in good yields, respectively.

Although the esters **2b** and **3b** could exist as a mixture of diastereomers arising from the chiral center of the alcohol part and the axial chirality of the biphenyl system, they showed completely identical ^{1}H NMR spectra. This indicates that **2b** and **3b** are enantiomeric



Scheme 1. Derivatization of chiral alcohols.

Keywords: absolute configuration; alcohols; asymmetric induction; axial chirality; circular dichroism; Cotton effect.

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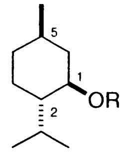
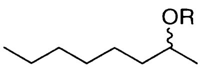
to each other in a solution. In spite of the achiral nature of the dinitrodiphenyl chromophore, the CD spectra of **2b** and **3b** in cyclohexane showed symmetrical CD curves relative to the *x*-axis, indicating that the chirality of the substrates was effectively transmitted to and induced axial chirality on the dinitrodiphenyl chromophore (Fig. 1).[6] Other types of chiral alcohols **4a**–**18a** were similarly converted to the corresponding

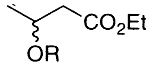
Table 1. UV and CD data of dinitrodiphenyl derivatives



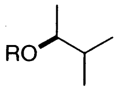
2 (1*R*, 2*S*, 5*R*)
3 (1*S*, 2*R*, 5*S*)



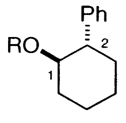
4 (*R*)
5 (*S*)



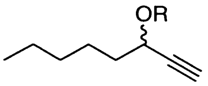
6 (*R*)
7 (*S*)



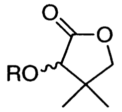
8 (*S*)



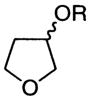
9 (1*R*, 2*S*)
10 (1*S*, 2*R*)



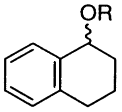
11 (*R*)
12 (*S*)



13 (*R*)
14 (*S*)

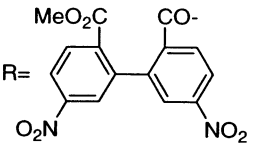


15 (*R*)
16 (*S*)



17 (*R*)
18 (*S*)

a: R=H; b: R=



Group	Product	Yield (%)[a,b]	UV λ_{max} (ε) nm[c]	CD λ_{ext} (Δε) nm[c,d]	Sign of Cotton effect[e]	Absolute config.
A	**2b**	74 83 (A)	206.5 (26000)[f] 261.5 (21700)	272.9 (−5.6)[f]	−	*R*
	3b	77 97 (A)	204.5 (27200)[f] 260.5 (22500)	271.8 (+6.0)[f]	+	*S*
	4b	70 88 (A)	208.0 (24200)[f] 260.5 (21200)	271.7 (−2.9)[f]	−	*R*
	5b	68 87 (A)	206.0 (25200)[f] 261.0 (21200)	271.9 (+3.1)[f]	+	*S*
	6b	71 79 (B)	203.0 (27700) 262.5 (19100)	271.5 (−2.5)	−	*R*
	7b	62 76 (B)	204.0 (29000) 262.5 (20700)	273.1 (+2.4)	+	*S*
	8b	58 93 (A)	202.5 (20200) 262.5 (13100)	271.2 (+2.2)	+	*S*
	9b	69 96 (A)	205.5 (27000) 263.0 (16200)	270.5 (−2.9)	−	*R*
	l0b	64 96 (A)	205.5 (27300) 263.0 (16700)	273.9 (+3.0)	+	*S*
B	**11b**	79 24 (A)	203.0 (22600)[f] 260.0 (16900)	272.6 (+1.8)[f]	+	*R*
	12b	74 19 (A)	203.0 (23200)[f] 260.0 (17000)	272.6 (−1.7)[f]	−	*S*
	13b	78 66 (A)	203.5 (30800) 262.0 (20400)	271.4 (+4.1)	+	*R*
	14b	87 70 (B)	203.0 (27900) 262.5 (18000)	270.5 (−3.7)	−	*S*
	15b	80 62 (B)	202.5 (15800) 262.5 (9900)	273.5 (+0.4)	+	*R*
	16b	84 71 (B)	203.0 (25600) 262.5 (16400)	272.1 (−0.7)	−	*S*
	17b	79 85 (A)	210.0 (28000)[f] 261.0 (20300)	271.2 (+6.2)[f]	+	*R*
	18b	75 85 (A)	208.5 (26600)[f] 260.5 (18300)	270.7 (−5.4)[f]	−	*S*

[a] In the first step, an alcohol was reacted with the anhydride **1** (1.0 equiv.) in the presence of 4-dimethylaminopyridine (DMAP) (3.0 equiv.) in THF at room temperature. In the second step, either of the following reaction conditions were employed: (A) CH_2N_2 in MeOH–Et_2O; (B) $ClCO_2Me$, Et_3N, DMAP/CH_2Cl_2, 0°C–rt.

[b] Isolated yield.

[c] Measured in MeOH.

[d] Only the data at around 270 nm are shown.

[e] At around 270 nm.

[f] Measured in cyclohexane.

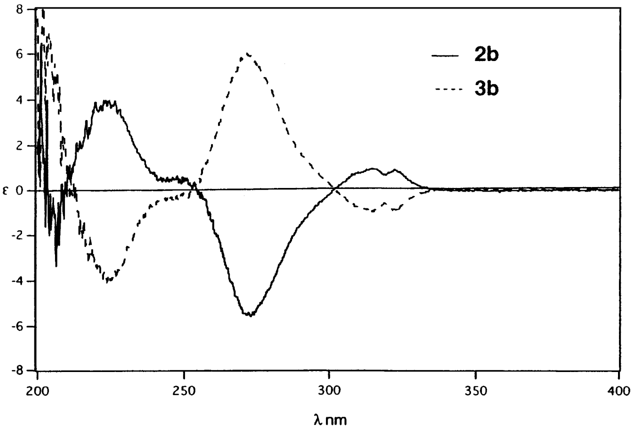


Figure 1. CD spectra of dinitrodiphenyl derivatives **2b** and **3b** in cyclohexane.

derivatives **4b**–**18b**. Their ^{1}H NMR and CD spectra clearly indicated that the derivatives prepared from a pair of antipodes are enantiomeric to each other. Considering the relationship between the observed Cotton effect at around 270 nm and the absolute configuration of the substrate, the derivatives could be classified into two groups (Table 1). In group A, comprised of compounds having no unsaturation nor an oxygen atom on the vicinal carbons, negative Cotton effect was observed for the esters of (R)-alcohol and a positive effect for the esters of (S)-alcohols. In contrast, unsaturation or an oxygen atom at the vicinal position in group B reversed the sign of the Cotton effect.

In summary, we have found that *the chirality of secondary alcohols induced axial chirality in their dinitrodiphenic esters*. The CD spectra of the esters prepared from antipodal pairs of alcohols employed were symmetrical relative to the x-axis. The sign of the Cotton effect at around 270 nm was shown to have good correlation to the absolute configuration of the substrate alcohols. Further studies on the factors controlling the chiral transmission mentioned above are currently under way.

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2. Although there are several reports on determination of the absolute configuration of mono-functional compounds by introduction of a single CD auxiliary, the substrates in these reports already have chromophores, which enable application of the CD exciton method. For example, see: Adam, W.; Luckacs, Z.; Viebach, K.; Humpf, H.-U.; Saha-Moller, C. R.; Shreier, P. *J. Org. Chem.* **2000**, *65*, 186–190.
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4. Pufahl, F. *Chem. Ber.* **1929**, *62*, 2817–2824.
5. UV data of the related chromophores in MeOH: dimethyl 5,5′-dinitrodiphenyl-2,2′-dicarboxylate $\lambda_{\max}$ (ε) 211 (21600), 264 (19200) nm; methyl p-nitrobenzoate $\lambda_{\max}$ (ε) 204 (9000), 256 (12600) nm.
6. The CD spectra of **2b** and **3b** did not show a split CD curve and the A values were quite smaller than expected. They also showed the same tendency in other solvents (MeOH, MeCN). The reason for this may be as follows; (i) there is only a small difference in the population of stable conformers with positive and negative Cotton effects; (ii) two p-nitrophenyl rings were connected at a central part of the longitudinal ^1L_a transition moment of the chromophore; (iii) the angle between the two chromophores was not suitable for their effective interaction. To our knowledge, few investigations have reported on an induced axial chirality for a system in which an achiral chromophoric component is connected covalently with a chiral component: see Ref. 3 and Zahn, S.; Canary, J. W. *Org. Lett.* **1999**, *1*, 861–864. For an induced chirality based on intermolecular association (hydrogen bonding), see: Brittain, H. G. *Tech. Instrum. Anal. Chem.* **1994**, *14*, 307–341; Mizutani, T.; Takagi, H.; Hara, O.; Horiguchi, T.; Ogoshi, H. *Tetrahedron Lett.* **1997**, *38*, 1991–1994.