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Novel appearance of chirality in a 2,5-di(*p*-tolyl)thiophene π-system by the aid of a remote chiral carboxyl group

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Abstract

A tweezers-type dicarboxylic acid (**1**), which has two chiral (*R*)-1,1′-binaphthyl systems bridged by a 2,5-(*p*-tolyl)thiophene spacer, exhibited the Cotton effect at 337 nm (Δε−16.5) in its CD spectrum in chloroform. This is attributable to the twisted spacer and the mechanism for the appearance of this effect is discussed. © 1999 Elsevier Science Ltd. All rights reserved.

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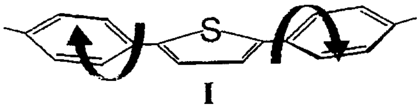
To date, much attention has been paid to chiral compounds without centers of chirality. Common π-systems such as biphenyl and terphenyl are optically inactive because their chiral conformations are convertible. However, these π-systems can exist in a stable, optically active form in which case they are so highly strained or bulky that a symmetrical conformation cannot be adopted and, in result, one chiral conformer is not converted easily to its mirror image. This is exemplified by optical isomers by restricted rotation (atropisomerism),[1] helicenes,[2] chiral olefins,[3] helical polymers bearing chiral arms.[4] Here we report a novel concept for the appearance of chirality which was observed in a 2,5-di(*p*-tolyl)thiophene π-system (**I**) which does not have any obstacle in the bond rotation between the neighboring aromatic rings, but a chiral carboxyl group at a remote position to make the aromatic ring chiral by OH–π interaction.[5]



I

In the course of our investigation on asymmetric molecular recognition, we synthesized a tweezers-type dicarboxylic acid (**1**), which has two chiral (*R*)-1,1′-binaphthyl systems bridged by a 2,5-(*p*-

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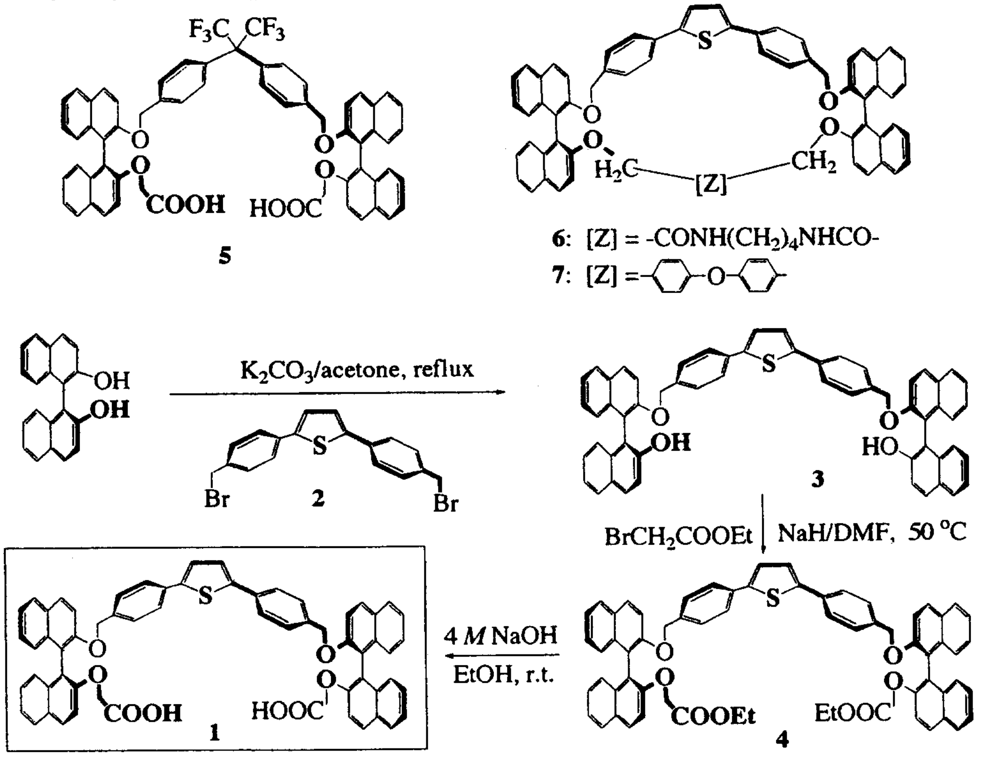
tolyl)thiophene spacer: the reaction of 2,5-bis[*p*-(bromomethyl)phenyl]thiophene (**2**) with 2 mol equiv. of 1,1′-binaphthol (K_2CO_3 in refluxing acetone) gave a 1:2 substitution product (**3**), which was allowed to react with ethyl bromoacetate (NaH in DMF, 50°C) to afford a diester derivative (**4**) (Scheme 1). The final alkaline hydrolysis (4 M aqueous NaOH in EtOH, room temperature) afforded **1**[6] in 80% yield.



Scheme 1.

To our surprise, the dicarboxylic acid (**1**) exhibited three Cotton effects in its CD spectrum in chloroform (1.00×10^{-5} M)[7] as shown in Fig. 1 [λ_{ext} 337 nm ($\Delta\varepsilon$ −16.5), λ_{ext} 316 nm ($\Delta\varepsilon$ +9.5), and λ_{ext} 291 nm ($\Delta\varepsilon$ +18.7)]. The first (−)-Cotton effect of **1** around 340 nm was considered to come from the 2,5-(*p*-tolyl)thiophene spacer, based on the following points: (*R*)-1,1′-binaphthol exhibited a very weak Cotton effect in this region, if any, though the UV spectrum of **1** is regarded as a simple combination of those of **2** and the 2,5-di(*p*-tolyl)thiophene, as shown in Fig. 1. The compound (**5**) which has a 2,2-hexafluoro-propylidene group instead of the 2,5-thienylene of **1** exhibited no Cotton effect around 340 nm.

One happens to think of the possibility that the conformation of **1** is locked by the intramolecular interaction between the carboxyl groups at both ends to make the 2,5-di(*p*-tolyl)thiophene spacer chiral. However, this possibility was ruled out by a CPK model study suggesting that these carboxyl groups are too far apart to interact one another. We also synthesized a cyclized derivative (**6**) of **1** and its analog (**7**). These compounds exhibited a significant Cotton effect around 340 nm, but the sign was positive [λ_{ext} 338 nm ($\Delta\varepsilon$ +72.3) and λ_{ext} 337 nm ($\Delta\varepsilon$ +39.5), respectively, as shown in Fig. 2].

Noteworthily, the carboxyl group was shown to be vital for the appearance of chirality in the 2,5-di(*p*-tolyl)thiophene spacer of **1**. The corresponding ethyl ester (**4**) and the diol derivative (**3**) exhibited no (−)-Cotton effect around 340 nm [the first Cotton effect: λ_{ext} 279 nm ($\Delta\varepsilon$ +16.1) and 310 nm ($\Delta\varepsilon$ +16.1), respectively]. The first Cotton effect of **1** at λ_{ext} 337 nm in $CHCl_3$ disappeared when THF was employed

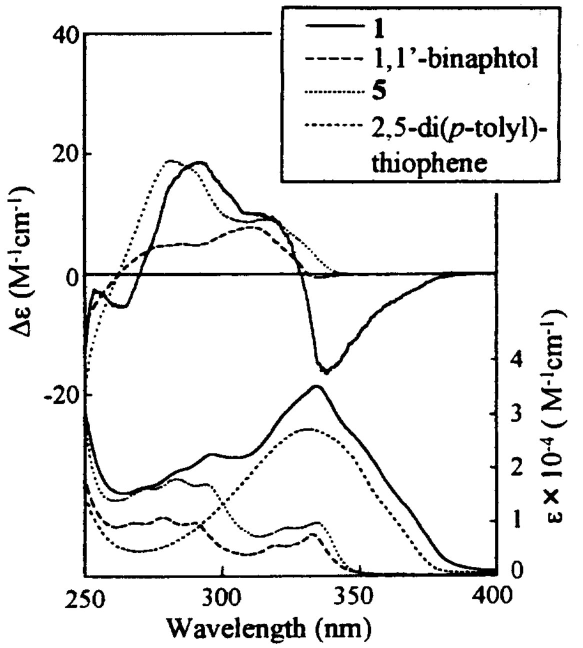


Figure 1. CD (top) and UV (bottom) spectra of **1** and its related compounds ($CHCl_3$; 1.00×10^{-5} M)

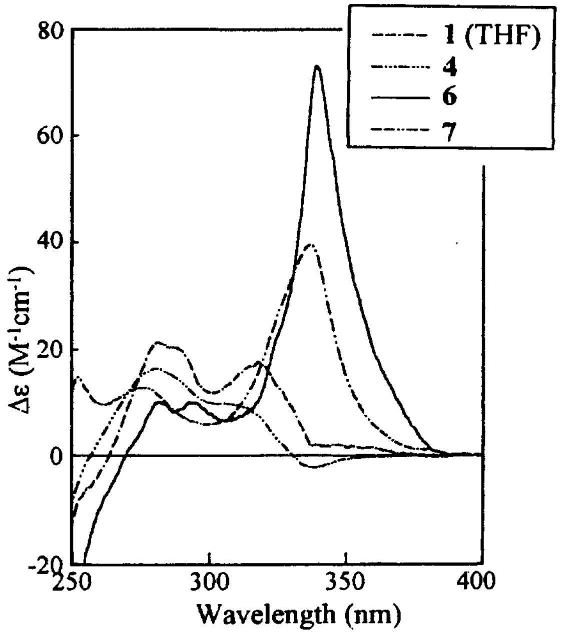
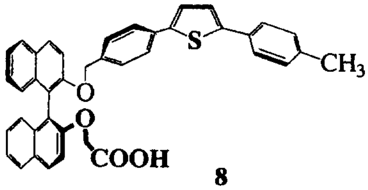


Figure 2. CD spectra of **1** (THF; 1.00×10^{-5} M), **4**, **6**, and **7** ($CHCl_3$; 1.00×10^{-5} M)

as a solvent which interacts with the carboxyl group. Even in chloroform, the CD spectrum of **1** became broad at a higher concentration of 1.20×10^{-3} M. This is probably because intermolecular interaction took place. These facts emphasize that the carboxyl group takes an important role in the restriction of the conformation of the intramolecular 2,5-di(*p*-tolyl)thiophene moiety of **1**. This phenomenon is reasonably explained in terms of an intramolecular OH–π interaction[5] between the carboxylic proton and the central π-system: when the carboxylic proton interacts with the benzene ring in an asymmetric manner, the benzene ring can be regarded to be chiral and, in result, affects the conformation of the neighboring thiophene. At the present time, we cannot rule out another possibility that the carboxyl group interacts directly with the central thiophene ring.

In either case, it was expected that a 2,5-di(*p*-tolyl)thiophene derivative (**8**) having one (*R*)-1,1′-binaphthyl moiety would exhibit a similar phenomenon. Hence, we synthesized this compound (**8**) and, in its CD spectrum $CHCl_3$, observed the first (–)-Cotton effect at λ_{ext} 338 nm with $\Delta\varepsilon$ of –9.9 which is about half so much as that of **1**.



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In conclusion, we found a novel π-system which becomes chiral by OH–π interaction with a chiral carboxyl group at a remote position. Now we are making efforts to extend the present compounds (**1** and **8**) to various simpler systems in order to elucidate a precise mechanism for this intriguing phenomenon.

Acknowledgements

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6. Pale yellow crystals; mp 109–110°C (from cyclohexane-ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$): δ 8.05–7.80 (m, 8H), 7.52 (d, 2H, J=8.9 Hz), 7.41–7.12 (m, 16H), 6.97 (d, 2H, J=8.4 Hz), 6.80 (d, 2H, J=7.8 Hz), 5.06 (s, 4H), 4.70 (d, 2H, J=16.5 Hz), 4.55 (d, 2H, J=16.5 Hz); IR (KBr) 3422, 1732, 1620, 1590, 1262, 1104, 806 cm^{-1}. Anal. calcd for $C_{62}H_{44}O_8S\cdot CH_3COOC_2H_5\cdot 0.5C_6H_{12}$: C, 76.78; H, 5.42. Found: C, 76.82; H, 5.52.
7. M=mol dm^{-3}