Synthesis, Circular Dichroism and Absolute Stereochemistry of Chiral Spiroaromatic Compounds. 9,9′-Spirobifluorene Derivatives

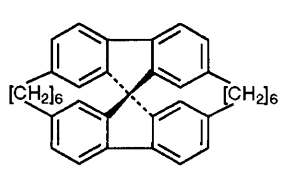
Nobuyuki Harada,* Hiroshi Ono, Toru Nishiwaki and Hisashi Uda

Institute for Chemical Reaction Science, Tohoku University, 2-1-1 Katahira, Aoba, Sendai 980, Japan

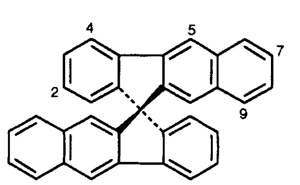
The chiral spiroaromatic compounds (+)-**2** and (+)-**3** with 9,9′-spirobifluorene skeletons have been synthesized and their absolute stereostructures have been unambiguously determined to be *R*, by application of the CD exciton chirality method; the *R* absolute stereochemistry of (−)-[6,6]-vespirene **1** was established by chemical correlation with these compounds.

Among chiral spiroaromatic compounds, the optically active [6,6]-vespirene **1** is a unique member of the chiral 9,9′-spirobifluorene type, because the optical activity of **1** arises from the 9,9′-spirobifluorene chromophore twisted by the side-chain bridge.[1,2] [6,6]-Vespirene was first synthesized and optically resovled by Prelog and coworkers,[1,2] who determined the absolute stereochemistry of (−)-**1** to be *R* by analysis of its CD spectrum on the basis of exciton coupling.[2–4] Their assignment was based on the interpretation that the CD spectrum of (−)-**1** exhibited, in the region of the 270 nm UV transition, negative first and positive second Cotton effects at 297 and 272 nm, respectively, and hence a negative exciton chirality between two fluorene chromophores, *i.e.* *R* absolute configuration, was assigned. However, [6,6]-vespirene (−)-**1** is not an ideal case of exciton coupling, becasue its CD spectrum shows a third Cotton effect (255 nm) of negative sign in the exciton region, and also shows a very intense negative Cotton effect at 320 nm which is stronger than the exciton Cotton effects at 297 and 272 nm. In most cases, exciton Cotton effects are the strongest.[4] These complex phenomena imply that the 9,9′-spirobifluorene chromophore of **1** is strongly twisted and strained. Therefore, it is difficult to be certain whether the CD exciton chirality method[4] is applicable to such a strongly twisted and strained system or not. To establish the absolute stereochemistry of a series of chiral 9,9′-spirobifluorene compounds including [6,6]-vespirene by application of the CD exciton chirality method,[5,6] we designed and synthesized optically active 9,9′-spirobifluorene derivatives **2** and **3** which have two naphthalene and anthracene chromophores, respectively. These spiroaromatic compounds are more suitable for application of the CD exciton chirality method than [6,6]-vespirene **1**, because of their less strained structures and clear definition of exciton chirality between two chromophores.

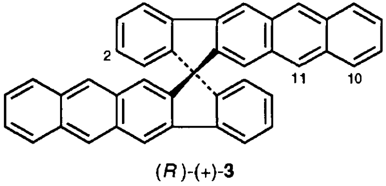
The optical resolution method for the dicarboxylic acid **4** reported by Prelog and Hass[1] was slightly modified; racemic acid (±)-**4** was condensed with (+)-dehydroabietylamine using 2-chloro-1-methylpyridinium toluene-*p*-sulfonate[7] to



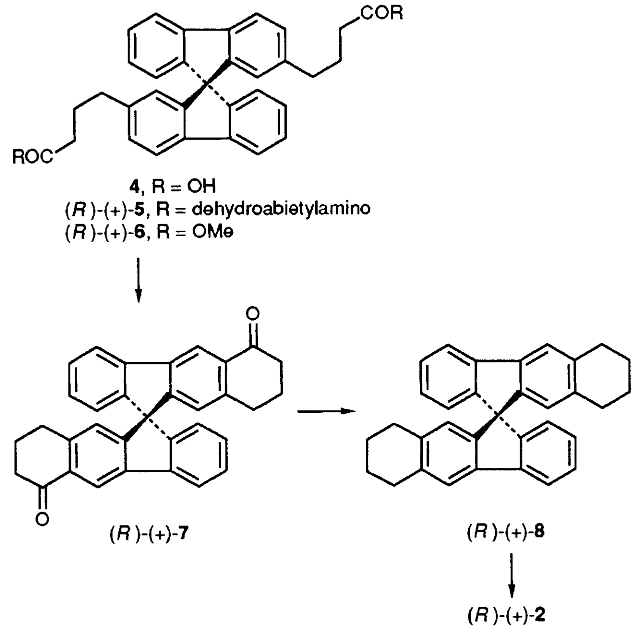
(*R*)-(−)-**1**



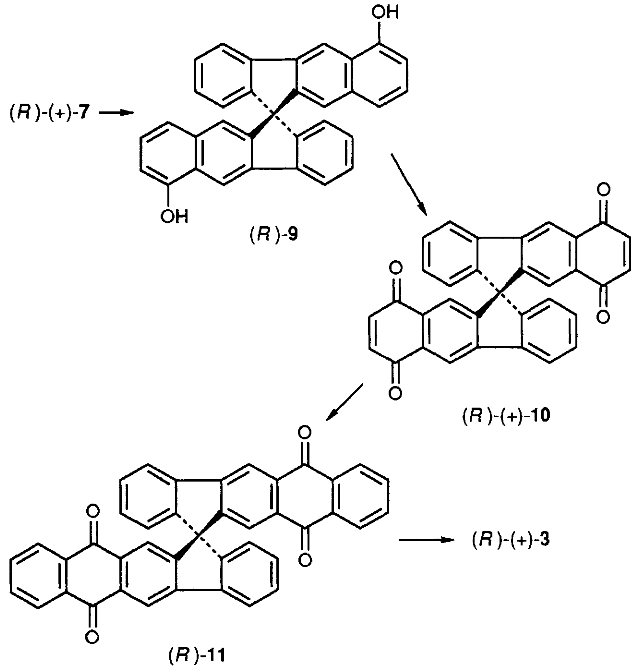
(*R*)-(+)-**2**



(*R*)-(+)-**3**



Scheme 1



Scheme 2

yield bisamide **5** (Scheme 1). The two diastereoisomers of **5** were separated by HPLC on silica gel (hexane–EtOAc, 1 : 1) to afford (*R*)-(+)-**5**, $[\alpha]_D$ + 26.6° (*c* 1.80, $CHCl_3$), as the first-eluted fraction.† Bisamide (*R*)-(+)-**5** was treated with $NaNO_2$ in acetic anhydride–acetic acid, and the unstable nitrosamide obtained was immediately hydrolysed with KOH in ethanol to give dicarboxylic acid (*R*)-**4**: methyl ester (*R*)-(+)-**6**, $[\alpha]_D$ + 28.0° (*c* 1.78, $CHCl_3$).

Dicarboxylic acid (*R*)-**4** was cyclized with polyphosphoric acid to yield diketone (*R*)-(+)-**7**, $[\alpha]_D$ + 3.4° (*c* 1.437, $CHCl_3$), which was then subjected to Huang–Minlon reduction to yield octahydro derivative (*R*)-(+)-**8**, $[\alpha]_D$ +51.0° (*c* 1.256, $CHCl_3$); ref. 1, $[\alpha]_D$ +52° (*c* 0.82, $CHCl_3$). The dehydrogenation of (*R*)-(+)-**8** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded the desired compound with two naphthalene chromophores, (*R*)-(+)-**2**, as prisms: m.p. 273 °C; $[\alpha]_D$ +426° (*c* 0.308, $CHCl_3$).‡

Diketone (*R*)-(+)-**7** was treated with isopropenyl acetate and toluene-*p*-sulfonic acid in acetic anhydride to give the enol acetate, which was dehydrogenated with DDQ in benzene and then hydrolysed with K_2CO_3 in aqueous ethanol (Scheme 2).

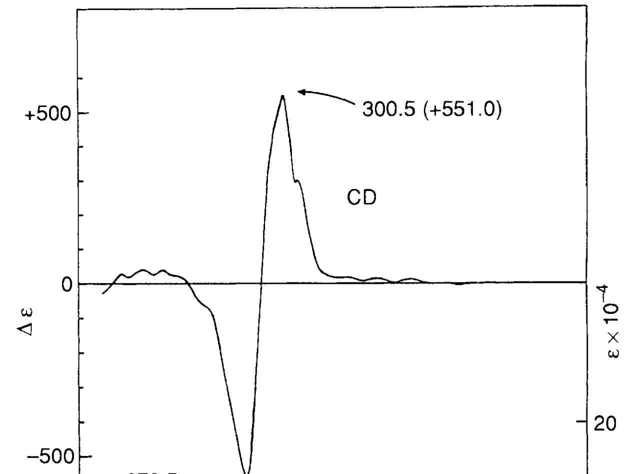


Fig. 1 CD and UV spectra of the bis(anthracene) compound (*R*)-(+)-**3** in ethanol

The phenol (*R*)-**9** obtained was oxidized with oxygen in acetonitrile in the presence of a catalytic amount of salcomine to yield quinone (*R*)-(+)-**10**, $[\alpha]_D$ +57.2° (*c* 0.278, $CHCl_3$). The Diels–Alder reaction of (*R*)-(+)-**10** with 1-acetoxybutadiene at 80 °C followed by heating in acetic acid afforded the

---

† The absolute configuration of the spiro centre was determined as discussed below.

‡ (*R*)-(+)-**2**: IR (KBr) ν_{max}/cm^{-1} 880, 755 and 740; ^1H NMR (500 MHz, $CDCl_3$) δ 6.783 (2 H, d, *J* 7.5 Hz, 1-H), 7.152 (2 H, ddd, *J* 7.5, 7.5, 1.1 Hz, 2-H), 7.210 (2 H, s, 10-H), 7.323 (2 H, ddd, *J* 8.2, 6.8, 1.3 Hz, 8-H), 7.430 (2 H, ddd, *J* 7.5, 7.5, 1.1 Hz, 3-H), 7.436 (2 H, ddd, *J* 8.2, 6.8, 1.3 Hz, 7-H), 7.371 (2 H, d, *J* 8.2 Hz, 9-H), 7.958, (2 H, d, *J* 8.2 Hz, 6-H), 8.038 (2 H, d, *J* 7.5 Hz, 4-H) and 8.303 (2 H, s, 5-H); ^1H NMR NOESY (500 MHz, $CDCl_3$) 1-H/2-H, 2-H/3-H, 3-H/4-H, 4-H/5-H, 5-H/6-H, 6-H/7-H, 7-H/8-H, 8-H/9-H and 9-H/10-H; ^{13}C NMR (125 MHz, $CDCl_3$) δ 65.0, 118.2, 120.7, 123.1, 124.6, 125.6, 125.9, 128.0, 128.2, 128.3, 128.6, 133.6, 133.7, 140.1, 140.9, 148.1 and 150.4; MS *m/z* 416 (M^+, 100%), 208 (16); HRMS calc. for $C_{33}H_{20}$: 416.1565. Found: *m/z* 416.1572.

(*R*)-(+)-**3**: IR (KBr) ν_{max}/cm^{-1} 3051, 3016, 1637, 1601, 1545, 1471, 1462, 1431, 1313, 1286, 1155, 895, 741, 692, 681 and 469; ^1H NMR (600 MHz, $CDCl_3$) δ 6.852 (2 H, d, *J* 7.6 Hz, 1-H), 7.187 (2 H, ddd, *J* 7.6, 7.3, 1.0 Hz, 2-H), 7.360 (2 H, ddd, *J* 8.4, 6.5, 1.0 Hz, 9-H), 7.415 (2 H, s, 12-H), 7.417 (2 H, ddd, *J* 8.5, 6.5, 1.0 Hz, 8-H), 7.460 (2 H, ddd, *J* 7.7, 7.3, 1.0 Hz, 3-H), 7.811 (2 H, d, *J* 8.4 Hz, 10-H), 7.991 (2 H, d, *J* 8.5 Hz, 7-H), 8.083 (2 H, s, 11-H), 8.102 (2 H, d, *J* 7.7 Hz, 4-H), 8.464 (2 H, s, 5-H) and 8.531 (2 H, s, 6-H); MS *m/z* 516 (M^+, 100%); HRMS calc. for $C_{41}H_{24}$: 516.18779. Found: *m/z* 516.18771.

anthraquinone derivative (*R*)-**11**, which was finally reduced with zinc dust in a mixture of aqueous NaOH and benzene to give the desired bis(anthracene) compound (*R*)-(+)-**3** as a yellow solid: $[\alpha]_D$ +1050° (*c* 0.08350, $CHCl_3$).§

The UV spectrum of the bis(anthracene) compound (+)-**3** exhibits an intense ^1B_b band (λ_{max} 288.6 nm, ε 152 000), the electric transition moment of which is polarized along the long axis of the chromophore (Fig. 1). In the ^1B_b transition region, the CD spectrum shows intense positive first and negative second Cotton effects: λ_{ext} 300.5 nm, $\Delta\varepsilon$ +551.0 and λ_{ext} 278.5 nm, $\Delta\varepsilon$ −560.7; *A* = +1111.7. Although the UV spectrum shows the ^1L_a band around 330–400 nm, the CD Cotton effects in the corresponding region were negligibly small in comparison with the strong exciton Cotton effects in the ^1B_b region. The present results clearly indicate that the long-axis electric transition moments of the two chromophores constitute a clockwise screw sense, *i.e.* positive exciton chirality. The absolute stereochemistry of (+)-**3** was hence unambiguously determined to be *R*.

The bis(naphthalene) compound (+)-**2** gave similar data leading to the *R* absolute configuration. The UV spectrum of (+)-**2** shows an intense absorption band (λ_{max} 251.5 nm, ε 86 100) which can be easily assigned to the long-axis polarized ^1B_b transition. In the corresponding region, the CD spectrum exhibits strong and typical exciton-split Cotton effects of positive first and negative second signs: λ_{ext} 272.3 nm, $\Delta\varepsilon$ + 188.3 and λ_{ext} 252.0 nm, $\Delta\varepsilon$ − 207.2; *A* = + 395.5. From the positive sign of the *A*-value, the absolute stereochemistry of (+)-**2** was definitely determined to be *R*.

The determination of the absolute stereochemistry of (*R*)-(+)-**2** and (*R*)-(+)-**3** described above leads to the *R* absolute configuration of the starting materials, the first-eluted amide (+)-**5** and dimethyl ester (+)-**6**. Since compounds (+)-**5** and (*R*)-(+)-**6** were converted to (−)-[6,6]-vespirene by Prelog and Hass,[1]§ the *R* absolute configuration of [6,6]-vespirene (−)-**1**{$[\alpha]_D$ − 360° (*c* 0.587, $CHCl_3$)} was established.

We thank Mr Akira Saito, Nissan Chemical Industry Ltd., for ^1H NMR measurements (500 MHz). This work was supported in part by grants from the Ministry of Education, Science, and Culture, Japan [General (A) No. 59430005 and General (B) No. 01470026, Priority Areas Nos. 01648501, 02230201 and 0321407, and International Joint Research No. 02044014 to N. H.].

Received, 26th July 1991; Com. 1/03865F

References

1 G. Hass and V. Prelog, *Helv. Chim. Acta*, 1969, **52**, 1202.
2 G. Haas, P. B. Hulbert, W. Klyne, V. Prelog and G. Snatzke, *Helv. Chim. Acta*, 1971, **54**, 491.
3 See also: J. Sagiv, A. Yogev and Y. Mazur, *J. Am. Chem. Soc.*, 1977, **99**, 6861.
4 N. Harada and K. Nakanishi, *Circular Dichroic Spectroscopy—* Exciton *Coupling in Organic Stereochemistry*, University Science Books, Mill Valley, California, and Oxford University Press, Oxford, 1983.
5 N. Harada, Y. Tamai and H. Uda, *J. Org. Chem.*, 1984, **49**, 4266 and references cited therein.
6 N. Harada, J. Iwabuchi, Y. Yokota and H. Uda, *Croat. Chem. Acta*, 1989, **62**, 267 and references cited therein.
7 T. Mukaiyama, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 707 and references cited therein.

---

§ The conversion of (*R*)-(+)-**6** to (−)-[6,6]-vespirene **1** was also confirmed by us.