Optically Active Phthalocyanines and Their Circular Dichroism

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Following their first syntheses early this century, phthalocyanines (Pcs) have been intensively studied as a result of their chemical robustness and versatility. In addition to a large amount of fundamental academic research, interest has also been recently expanding in applied fields such as xerography, photovoltaics, electrochromism, optical discs, laser dyes, liquid crystals, molecular metals, electrocatalysis, chemical sensors, and photodynamic cancer therapy.[1] In spite of this growing importance in many areas, however, there has been no report to date of an optically active Pc. Optical activity is omnipresent in living organisms and has become established in organic, organometallic, and theoretical chemistry. In this communication, we report the first syntheses of two types of Pc possessing optically active binaphthyl units and, in particular, two important results on their circular dichroism (CD), one concerned with a monomer and the other with a stacked dimer in solution.

In synthesizing optically active compounds from optically pure starting materials, it is important to avoid racemization at each reaction step. In the present study, optically active (−)-(*S*)- and (+)-(*R*)-2,2′-dihydroxy-1,1′-binaphthyl (1*S* and 1*R*, respectively) (Scheme I) were chosen as the starting material, since their optical stability has been well studied in the past[2] and they produce a strong chiral field[3] which is convenient in analyzing CD data. The design of the synthetic route shown in Scheme I was based on the known[4] optical stability of these and other binaphthyl derivatives. The optical purity of the compounds at each reaction step was examined[5] either by comparative experiments or by confirming that the recovered unreacted materials had very little or no rotational loss. Thus, optically active CuPcs 3*S* and 3*R*[5a] were prepared by reaction[4a] of 1*S* or 1*R* with 1,2-dibromo-4,5-bis(bromomethyl)benzene[6] and subsequent treatment of the resultant dibromo derivatives 2*S* and 2*R*[4b] with CuCN in DMF.[7] After purification using basic alumina, the products were recrystallized from toluene (*ca.* 4–5%).[5a,8] In a separate preparation, the optically active dialcohols 4*S* and 4*R*[2a,4c] were converted[5b] by reaction with 4-nitrophthalonitrile in the presence of potassium

Scheme I
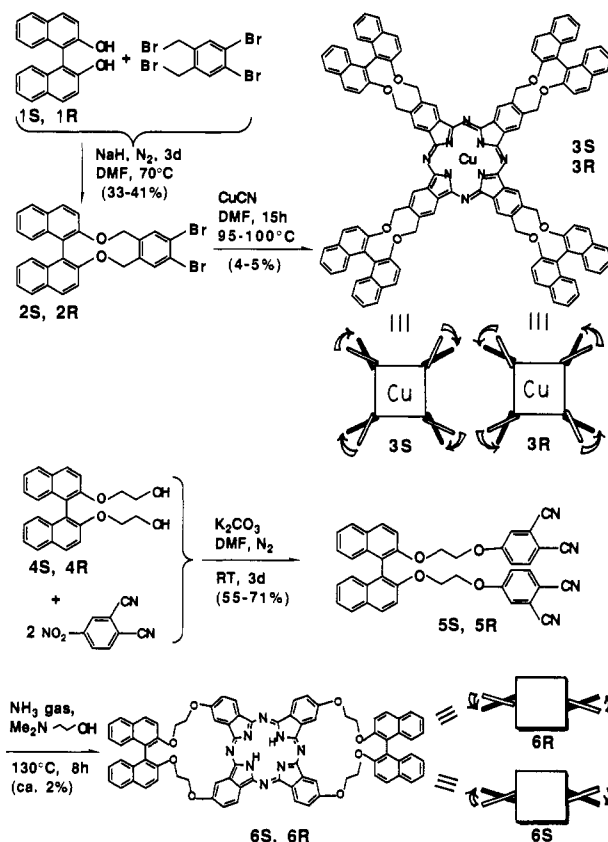
carbonate[9] to 5*S* and 5*R* in *ca.* 55–71% yields, which were then condensed by treatment[5c] with ammonia in refluxing (*N,N*-dimethylamino)ethanol[10] to give another type of optically active Pc, 6*S* and 6*R*,[8] in *ca.* 2% yield (purified by column chromatography).[11] These showed the desired parent ion peaks at 1255

(1) (a) *Phthalocyanines-Properties and Applications*; Leznoff, C. C., Lever, A. B. P., Eds.; VCH: New York, 1989. (b) Moser, F. H.; Thomas, A. H. *The Phthalocyanines*; CRC Press: Boca Raton, FL, 1983; Vols. I and II. (c) Lever, A. B. P. *CHEMTECH,* **1987,** 506–510. (d) Simon, J.; Sirlin, C. *Pure Appl. Chem.* **1989,** *61,* 1625–1629. (e) Orti, E.; Bredas, J.-L. *J. Am. Chem. Soc.* **1992,** *114,* 8669–8675 and references therein.

(2) (a) Kyba, E. P.; Gockel, G. W.; Jong, F.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogar, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977,** *42,* 4173–4184. (b) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moleau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogar, G. D. Y. *J. Org. Chem.* **1978,** *43,* 1930. (c) Pincock, R. E.; Johnson, W. M.; Wilson, K. R.; Farmer, J. H. *J. Am. Chem. Soc.* **1973,** *95,* 6477–6478. (d) Kyba, E. B.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Cram, D. J. *J. Am. Chem. Soc.* **1973,** *95,* 2692–2693.

(3) (a) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy-Exciton Coupling in Organic Stereochemistry*; University Science Books: New York, 1983. (b) Akimoto, H.; Shioiri, T.; Iitaka, Y.; Yamada, S. *Tet. Lett.* **1968,** 97–102. (c) Akimoto, H.; Iitaka, Y. *Acta Crystallogr., Sect. B* **1969,** *25,* 1491–1500.

(4) The following information is already known concerning compounds related to this study. (a) When 1*S* or 1*R* were reacted for 3 days to obtain 2*S* or 2*R*, no racemization was observed under the same conditions as shown in Scheme I.[2a] (b) An optically active 1,1′-binaphthyl whose 2,2′-positions were linked by a crown ether unit, which has a structure fairly similar to that of 2, did not racemize when heated in ethylene glycol at 200 °C for 6 h, but 8.6% optical loss was observed when it was kept at 205 °C for 202 h.[2a] (c) Compounds 4*S* and 4*R* were optically stable when heated to reflux under N₂ in the presence of *t*-BuOK in THF for 14 h.[2a]

(5) (a) After 3*S* was obtained, the unreacted 2*S* which was recovered from the reaction mixture showed a small rotational loss of 1.2%; however, this may reflect a small amount of compound decomposition. Hence, it is thought that 3*S* and 3*R* were optically pure when they were recrystallized until a constant value of the optical rotation was obtained. 3*S* and 3*R* were accordingly recrystallized three times from toluene at temperatures lower than 95 °C. (b) In the present study, 4*S* and 4-nitrophthalonitrile were reacted at room temperature for 3 days ([K₂CO₃]/M = *ca.* 0.5). When this experiment was performed at 60 °C for 3 days, the [α]₅₈₉ of the resultant 5*S* was smaller by 2.3% than that of 5*S* obtained by reaction at room temperature. Since this value could not be improved even after three recrystallizations (solvent, ethanol), 4*S* may racemize only slightly under these conditions. (c) Separately, when 5*S* was heated to reflux (*ca.* 130 °C) in (*N,N*-dimethylamino)ethanol for 20 h, no rotational loss was observed. In addition, after 6*R* was obtained, the [α]₅₈₉ of the recovered unreacted 5*R* was 69.2°, compared to 69.9° for the original 5*R*.

(6) Piechoki, C.; Simon, J. *Nouv. J. Chim.* **1985,** *9,* 159–166.

(7) Metz, J.; Schneider, O.; Hanack, M. *Inorg. Chem.* **1984,** *23,* 1065–1071.

(8) Purification and analytical data on new compounds. 2: Pale yellow solid (silica–benzene, *R* = 0.69), recrystallized from benzene–acetone–methanol. Anal. Calcd for C₂₈H₁₈O₂Br₂: C, 61.56; H, 3.32; Br, 29.26. Found: C, 61.19; H, 3.51; Br, 29.70 for 2*S* and C, 61.22; H, 3.43, Br, 28.68 for 2*R*. 3: Anal. Calcd for C₁₂₀H₇₂N₈O₈Cu: C, 79.30; H, 3.99; N, 6.17. Found: C, 78.25; H, 4.20; N, 5.90 for 3*S* and C, 78.41; H, 4.26; N, 5.67 for 3*R*. 5: White solid (silica–benzene:CH₂Cl₂ = 3:1 v/v, *R_f* = 0.09), recrystallized from ethanol. Anal. Calcd for C₄₀H₂₆N₄O₄: C, 76.66; H, 4.18; N, 8.94. Found: C, 76.83; H, 4.40; N, 8.68 for 5*S* and C; 76.81; H, 4.42; N, 8.75 for 5*R*. 6: Anal. Calcd for C₈₀H₅₄N₈O₈: C, 76.54; H, 4.34; N, 8.93. Found: C, 75.92; H, 4.52; N, 8.77 for 6*S* and C, 76.09; H, 4.60; N, 8.71 for 6*R*. [α]₅₈₉ = −50.1, 49.9, −69.5, and 69.9 for 2*S*, 2*R*, 5*S*, and 5*R*, respectively (*c* 1.00 g/dL, CH₂Cl₂). mp = 87–88 °C for 5, but 2*S* and 2*R* decompose at above 240 °C. ¹H NMR (60 MHz, CDCl₃): 2, δ 7.0–8.1 (m,14H), 5.18 (s,4H); 5, δ 7.6–8.0 (m,4H), 6.8–7.4 (m,10H), 6.4–6.8 (m,4H), 4.1–4.4 (m,4H), 3.85–4.10 (m,4H) For 6, ¹H NMR (500 MHz, CDCl₃): δ 6.4–8.3 (m, 36H), 3.7 (m, 8H), 4.4 (m, 8H), −5.5 (br s, 2H).

(9) Keller, T. M.; Price, T. R.; Griffith, J. R. *Synthesis* **1980,** 613–613.

(10) Brach, P. J.; Grammatica, S. J.; Ossanna, O. A.; Weinberger, L. *J. Heterocycl. Chem.* **1970,** *7,* 1403–1405.

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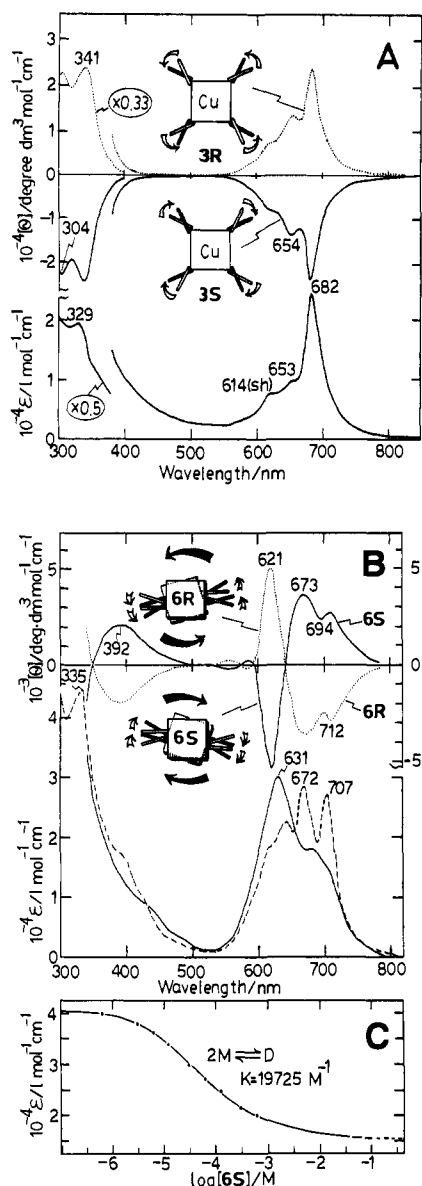
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Figure 1. (A) Absorption (bottom) and circular dichroism (top) spectra of 3S (—) and 3R (···) in toluene. (B) Absorption spectra (bottom) of 6S in CHCl₃ (---) or in acetone–DMF (1:2 v/v) (—) and circular dichroism spectra (top) of 6S (—) and 6R (···) in acetone–DMF (1:2 v/v). The spectra shown as solid lines were recorded at [6S or 6R]/M ≅ 1.2 × 10⁻³ using a 0.5-mm cuvette. (C) Absorption coefficients (dots) of 6S at 703 nm at various concentrations in acetone–DMF (1:2 v/v) and their digital simulations were obtained assuming a monomer–dimer equilibrium. Cells of path lengths of 0.5, 1, 2, 5, 10, 20, 50, and 100 mm were used.

(M⁺) in mass spectra using the FAB technique, with NMR data supporting the structure,[8] and have good solubility in DMF, DMSO, and chloroform containing *acetone* (more than *ca.* 5% v/v). In the above procedures, optical purity appears to have been preserved.[2,4,5]

Figure 1A shows the electronic absorption and CD spectra of *monomeric 3S* and *3R* in toluene. In the case of *3S*, the sign of the CD is negative over the entire spectrum, while, conversely, *3R* shows a positive CD sign, with peaks and shoulders corresponding to the absorption spectrum of the Pc. Since *1S* and *1R* are known to be right- and left-handed conformers, respectively (see illustration in Scheme I),[3] the results indicate that *negative CD is induced in the field of the right-handed conformer*, while *positive CD is generated in the field of the left-handed conformer*. This result is applicable to many systems. For example, if an

optically inactive chromophore shows positively induced CD in the wavelength region of its electronic absorption, then the asymmetric field surrounding the molecule may be determined to be left-handed.[12]

Figure 1B shows the electronic absorption and CD spectra of *6S* and *6R*. Of several solvents studied, chloroform gave a spectrum showing the highest proportion of monomeric species;[13a] however, the weakening of strong peaks at 707 and 672 nm indicated that some amount of Pc was present in aggregated forms.[13,14] Therefore, to simplify the interpretation, a solvent which gave a spectrum showing mainly aggregated Pc species, *i.e.*, acetone–DMF (1:2 v/v), was chosen for the CD experiments. The shape of the Q-band absorption in Figure 1B (solid line) indicates that *6S* and *6R* exist either as dimers or as oligomers in a cofacial conformation.[13b,c] To clarify the nature of the aggregate, Beer's law experiments were carried out at Pc concentrations of 6.1 × 10⁻⁷–6.1 × 10⁻⁴ M. At low concentrations, four peaks were present at 703, 670, 640, and 609 nm, while at higher concentrations the two longer-wavelength peaks disappeared and a new peak developed at 631–633 nm, with an isosbestic point at 651–652 nm, indicating that the spectrum in Figure 1B (solid line) may be that of a dimer. To obtain the dimerization constant K, the absorption coefficients ϵ at 703 nm were plotted as a function of [6S] (Figure 1C), and the data were computer-fitted[15] assuming a monomer(M)–dimer(D) equilibrium; *i.e.*, 2M ⇌ D. Using this, together with the values of ϵs of the pure monomer and dimer (40 200 and 15 500 M⁻¹ cm⁻¹, respectively), K was estimated to be 19 725 M⁻¹. Since the spectra shown as solid lines in Figure 1B were recorded at log[6S or 6R] ≅ -3, it is concluded from Figure 1C that these spectra are approximately those of dimers. Corresponding to the absorption spectrum (Figure 1B, solid line), the sign of the CD spectrum in the Q-band region changes from positive to negative for *6S* and from negative to positive for *6R* on going from longer to shorter wavelengths. These changes in CD sign indicate that *6S* and *6R* have opposite chirality of Pc stacking, plausibly right-handed for *6S* and left-handed for *6R* (see illustration in Figure 1B).[3a,16] *Chirality control of the Pc stacking* has been achieved in this way for the first time by introducing optically active conformers as substituent groups. Since several interesting characteristics of Pcs, such as one-dimensional high conductivity and columnar discotic liquid crystals,[1d] appear when the Pc molecules form cofacial stacks, chirality control of the Pc stacking may be useful in developing new areas in these fields.

(11) Since *5S* and *5R* contain two phthalonitrile units, large amounts of oligomeric Pcs were formed, but the yield of 6S and 6R was low. From columns of basic alumina (Act. III–CH₂Cl₂), a portion of R_f = 0.67 was collected and further purified by Bio-Beads-SX2 (Bio-Rad) columns.

(12) Hemoproteins generally show either positive or negative CD curves throughout both the Soret and the Q-band regions, and hence their shape is quite often similar to that of the absorption spectrum. However, the correspondence between the asymmetric environment surrounding the heme and the sign of the induced CD has not yet been determined. According to theoretical calculations (Hsu, M. C.; Woody, R. W. *J. Am. Chem. Soc.* **1971**, *93*, 3515–3525), the induced CD sign is determined solely by a coupled oscillator interaction between the heme transitions and allowed π–π* transitions in nearby aromatic side chains. Therefore, our observation that a Pc having aromatic substituent groups with a right-handed conformer induces negative CD at both the Soret bonds and the Q-bands suggests that the asymmetry of a heme environment which shows a negative CD sign is right-handed. Conversely, a heme environment which produces a positive CD sign would appear to be left-handed.

(13) (a) Stillman, M. J.; Nyokong, T. In *Phthalocyanines-Properties and -Applications*; Leznoff, C. C.; Lever, A. B. P. Eds.; VCH: New York, 1989; Chapter 3. (b) Gouterman, M.; Holten, D.; Lieberman, E. *Chem. Phys.* **1977**, *25*, 139–153. (c) It is difficult to judge from the absorption spectra whether the Pc planes of aggregated 6S are completely parallel or not since it has been found previously that 1,8-naphthalene-linked dinuclear Pcs, in which two Pc planes stretch apart from each other, display spectra similar to those of 1,8-anthracene-linked Pcs, where the two Pc planes are thought to be parallel (Kobayashi, N.; Lam, H.; Nevin, W. A.; Janda, P.; Leznoff, C. C.; Lever, A. B. P. *Inorg. Chem.* **1990**, *29*, 3415–3425. Kobayashi, N.; Yanagisawa, Y.; Osa, T.; Lam, H.; Leznoff, C. C. *Anal. Sci.* **1990**, *6*, 813–817).

(14) Kobayashi, N.; Lever, A. B. P. *J. Am. Chem. Soc.* **1987**, *109*, 7433–7441.

(15) White, W. I. In *The Porphyrins*; Dolphin, D. Ed.; Academic Press: New York, 1978; Vol. 5, pp 303–339.

(16) Charney, E. *The Molecular Basis of Optical Activity*; John Wiley & Sons: New York, Chichester, Brisbane, 1980. Kobayashi, N.; Saito, R.; Hino, H.; Ueno, A.; Osa, T. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1031–1035.