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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 5867–5869

Novel synthesis of a unique helical quinone derivative by coupling reaction of 2-hydroxybenzo[*c*]phenanthrene

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Received 6 June 2005; revised 22 June 2005; accepted 24 June 2005
Available online 14 July 2005

Abstract—Oxidative coupling reaction of both 3-hydroxychrysene and 2-hydroxybenzo[*c*]phenanthrene by using $Cu(NO_3)_2$–$3H_2O$ under atmospheric air is described. The former gave the aimed coupled biaryl derivative. However, the latter gave a further oxidized helical quinone derivative. The unique helical structure was characterized by X-ray and NMR analysis.

Oxidative coupling reaction of phenolic compounds has been utilized for the synthesis of chiral ligands for asymmetric synthesis.[1] To improve asymmetric and chemical yields, novel chiral ligands such as modified BINOL derivatives have been intensively investigated.[2]

Recently, we have reported a novel synthetic method for 9-acetoxydibenzo[*c*,*g*]phenanthrene based on an oxy-Cope rearrangement as a key reaction, which would be accessible for a wide range of functionalized polycyclic aromatic hydrocarbons.[3] Thus, as an extension of these results, we were keen to explore the preparation of polycondensed biaryl derivatives for their application to synthesis of axially chiral ligands. According to this strategy, we conducted oxidative coupling of 3-hydroxychrysene **1**[4] and 2-hydroxybenzo[*c*]phenanthrene **2**[5], respectively. The former gave the aimed coupled biaryl derivative **3**. However, the latter gave a further oxidized quinone derivative **4**. The formation of quinone derivatives has long been pointed out as the undesired by-product of the oxidative coupling reaction of phenols.[6] However, the discriminating structure of **4** is of importance in considering its applications.[7] In this communication, we report the synthesis and characterization of the helical quinone derivative **4** obtained from **2**.

The starting **1** and **2** were synthesized by oxy-Cope rearrangement as a key reaction, according to a previously published procedure and a modified procedure.[3]

Oxidative coupling of **1** was conducted by using 2.5 equiv of $Cu(NO_3)_2$–$3H_2O$ in the presence of 6.0 equiv of (*S*)-1-phenyl-2-(*p*-tolyl)ethylamine ((*S*)-PTEA) under atmospheric air,[8] which gave bis-3-hydroxychrysene derivative **3** in 84% yield (<1%ee). On the other hand, oxidative coupling of **2** under the same conditions gave quinone derivative **4**[9] in 60% yield (Scheme 1). Similarly, when the reaction was conducted with CuCl(OH)–TMEDA[10] in EtOH it gave **4** in 82% yield.

The single crystal of **4** obtained from the ethanol solution was measured by X-ray crystal analysis. It revealed that the fully eclipsed helical structure of **4** consists of a symmetrical bigeminal moiety connected by a *Z*-configured double bond as shown in Figure 1.[11] The bond length of the *Z*-oriented double bond is 1.352 Å, which indicates that the strain is delocalized.

The ^1H NMR spectrum supports the structure determined by X-ray analysis. That is, all of the signals in the ^1H NMR spectrum of **4** in $CDCl_3$ were assigned

Keywords: Helicenes; Oxy-Cope rearrangement; Phenol coupling; Air-oxidation; Chrysene.
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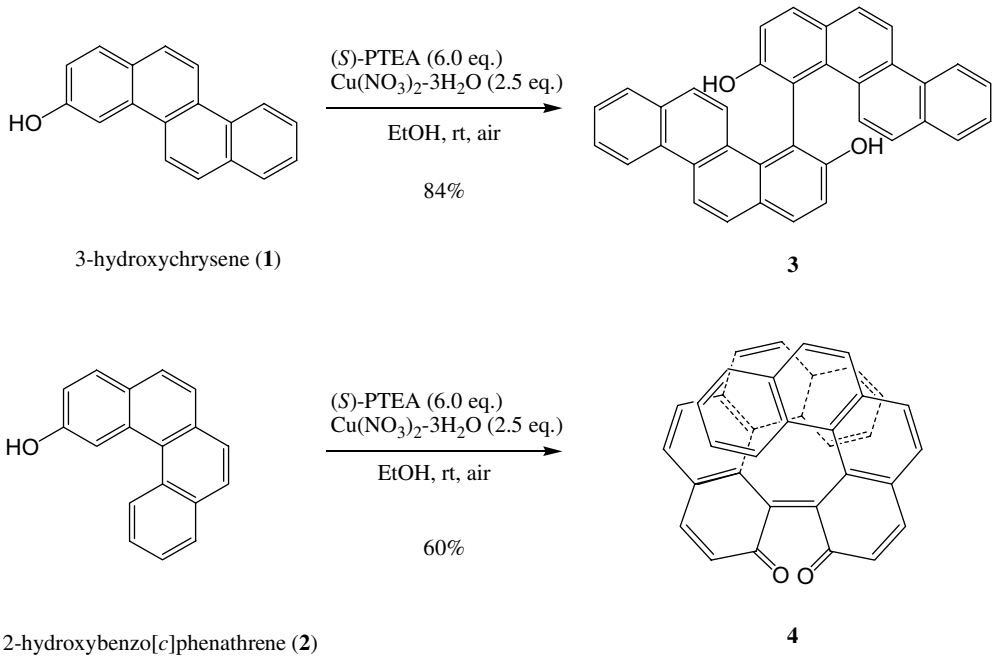
doi:10.1016/j.tetlet.2005.06.142



Scheme 1.

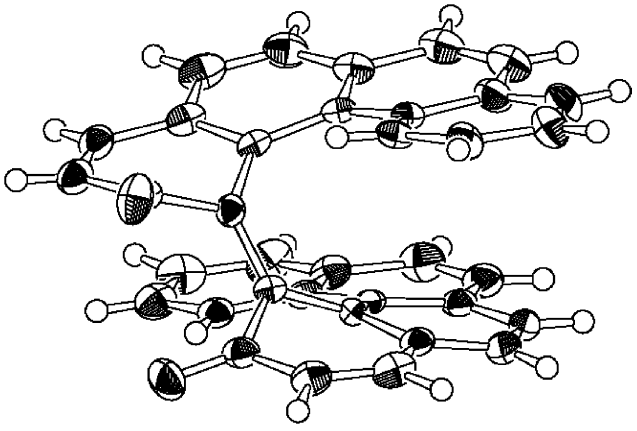


Figure 1. Molecular structure of **4** determined by X-ray diffraction.

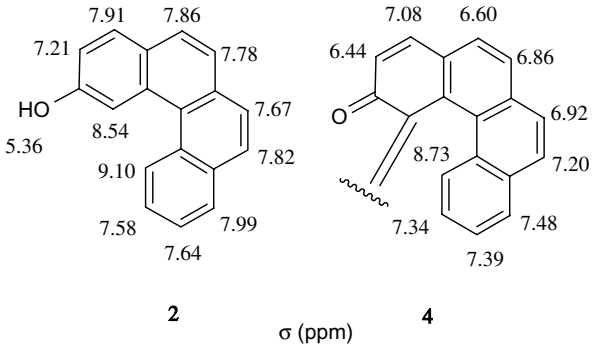
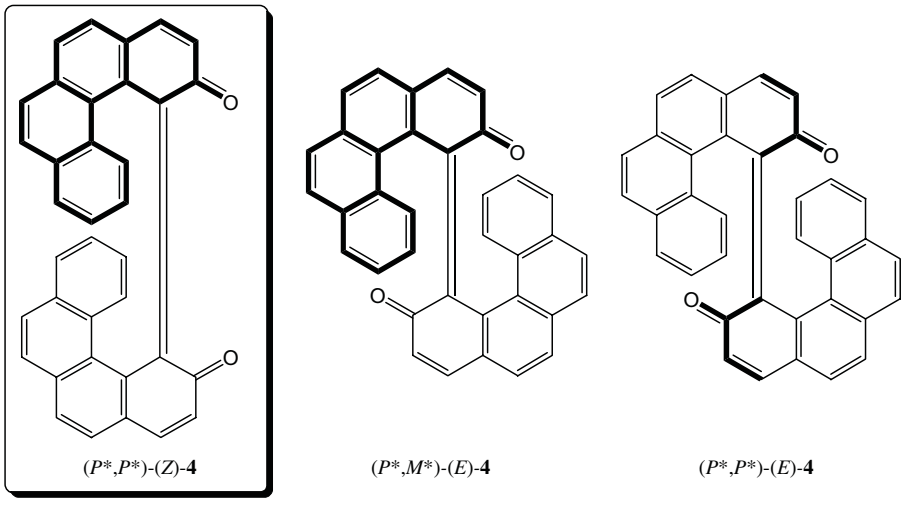


Figure 2. The ^{1}H NMR chemical shift data of **2** and **4** in $CDCl_3$.



Scheme 2.

on the basis of chemical shifts, coupling constants, and ^1H–^1H gCOSY experiments. It is significant that these signals shift upfield (ca. $\Delta\delta = 0.24$–1.26 ppm) compared to **2** (Fig. 2).

It is noteworthy that the formation of the possible *E* isomers, (*P**,*M**)-(*E*)-**4** and (*P**,*P**)-(*E*)-**4** was not detected. The mechanism of this stereoselection is not clear at this stage and further studies in this direction are being carried out (Scheme 2).

In summary, we have synthesized a novel quinone derivative **4** by oxidative coupling of 2-hydroxybenzo[*c*]phenanthrene **2**. From the X-ray crystal analysis, it is evident that **4** shows helical configuration. The 3-hydroxychrysene **1** gave the aimed coupled biaryl product **3** in the usual manner. However, 2-hydroxybenzo[*c*]phenanthrene **2** gave the helical quinone derivative **4**, which consisted of two helical molecules connected by a double bond (Scheme 1). A helical compound has its own value for considering its applications. Therefore, our strategy offers a feasible methodology for the construction of novel helical molecules. Further studies on the asymmetric synthesis of helical quinones are currently in progress.

Acknowledgments

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture of the Japanese Government (12490004).

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9. (*P**,*P**)-(*E*)-1,1′-Bibenzo[*c*]phenanthryliden-2,2′-dione (**4**): red crystals; mp 234–236 °C (dec); crystallographic data for **4**: $C_{36}H_{20}O_2$, triclinic space group, $P\bar{1}$, $a = 10.5348(3)$ Å, $b = 22.9604(6)$ Å, $c = 9.9355(3)$ Å, $\alpha = 90.024(1)°$, $\beta = 90.0052(6)°$, $\gamma = 103.192(1)°$, $V = 2339.81(1)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.375$ g/cm, $T = 193$, $R_1 = 0.049$, $R_w = 0.109$; spectral data for **5**, IR (KBr) 1683, 1654 cm^{-1}; UV (EtOH) $\lambda(\log\varepsilon) = 455$ (2.59), 356 (3.67), 317 (3.96); ^1H NMR (300 MHz, $CDCl_3$) δ 8.73 (1H, dd, $J = 8.1$, 1.5 Hz), 7.48 (1H, dd, $J = 8.1$, 1.5 Hz), 7.39 (1H, td, $J = 8.1$, 1.5 Hz), 7.34 (1H, td, $J = 8.4$, 1.5 Hz), 7.20 (1H, d, $J = 8.7$ Hz), 7.08 (1H, d, $J = 9.6$ Hz), 6.92 (1H, d, $J = 8.7$ Hz), 6.85 (1H, d, $J = 8.1$ Hz), 6.59 (1H, d, $J = 8.1$ Hz), 6.43 (1H, d, $J = 9.6$ Hz); MS (70 eV) *m*/*z* 486 $[M+2]^+$ (100), 485 $[M+1]^+$ (46), 484 $[M]^+$ (81); The enantiomeric ratios of the quinone **4** were determined using HPLC through Daicel CHIRALPAK IA column (0.80 mL/min, *n*-hexane/AcOEt = 6/4, 452 nm). It only showed low enantioselectivity of 2% ee, $[\alpha]_D^{25}$ −31 (*c* 0.84, $CHCl_3$).
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11. (a) Similar type of helical quinone derivative was reported by coupling of dibenzo[*c*,*g*]phenanthren-1-ol using Ag_2O as an oxidizing agent. However, the configuration of the quinone was assumed as *E*, based on the presence of the dipole–dipole interaction. See Dreher, S. D.; Katz, T. J.; Lam, K.-C.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 815–822; In the case of 5-hydroxybenzo[*c*]phenanthrene, both *Z* and *E* stereoisomers were obtained. See (b) Nakano, D.; Hirano, R.; Yamaguchi, M.; Kabuto, C. *Tetrahedron Lett.* **2003**, *44*, 3683–3686; (c) Guo, H.-X.; Liu, Y.-C.; Li, C.-L. *Res. Chem. Intermed.* **1992**, *17*, 137–143.