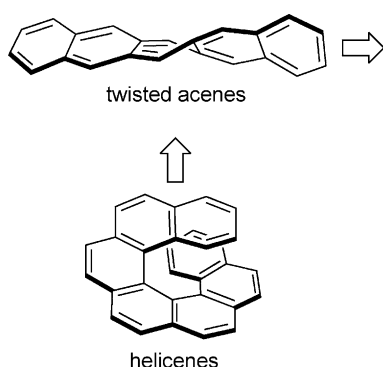


The Hairpin Furans: Easily Prepared Hybrids of Helicenes and Twisted Acenes

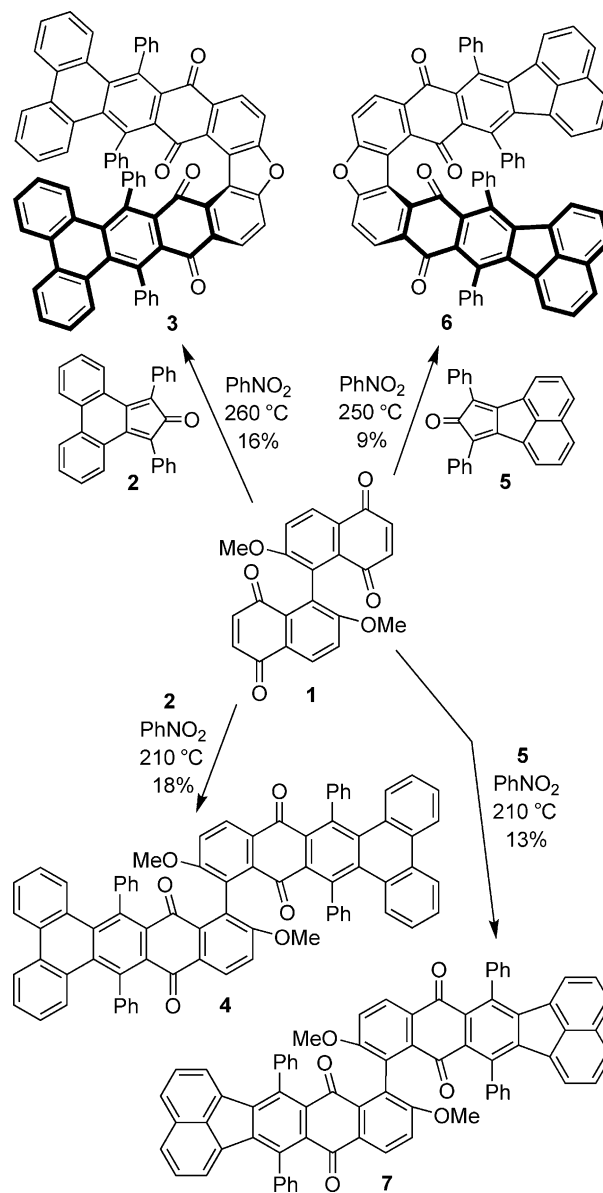
Xin Geng, James P. Donahue, Joel T. Mague, and Robert A. Pascal, Jr.*

Abstract: The thermal reaction of a cyclopentadienone with 6,6'-dimethoxy-5,5'-binaphthoquinone gives, in a single step, a molecular ribbon consisting of two twisted aromatic systems fused to a heteropentahelicene. Such molecules constitute a new class of chiral polycyclic aromatic compounds, the "hairpin furans".

During the last 30 years, we have synthesized and characterized numerous longitudinally twisted polycyclic aromatic compounds, or "twisted acenes".^[1] In these twisted hydrocarbon ribbons, the propagation axis of the molecular helix is parallel to the mean planes of the constituent rings, and thus they stand in contrast to the conventional helicenes,^[2] in which the axis of the helix is perpendicular to the rings. A combination of these two structural classes would yield molecules with highly unusual topologies, but the synthesis of such compounds has long eluded us.



The situation abruptly changed with the heating of 6,6'-dimethoxy-5,5'-binaphthoquinone^[3] (**1**) with two equivalents of phencyclone^[4] (**2**) in nitrobenzene at 260°C; this reaction unexpectedly produced the curious polycyclic furan **3** in 16% yield (Scheme 1). In attempting this reaction, we had merely hoped to improve the yield of the giant biaryl **4**, which had been formed as expected, but in a low 18% yield, by heating **1** and **2** at 210°C. Increasing the temperature by 50°C did not improve the yield, but it dramatically altered the reaction course: at 210°C only traces of **3** could be found in the



Scheme 1. Synthesis of the hairpin furans and related biaryls.

reaction mixture, but at 260°C compound **3** was the only double adduct of bisquinone **1** to be observed.

The identity of compound **3** was clearly evident from its spectroscopic data; mass spectrometry showed a formal loss of dimethyl ether from compound **4**, and no methoxy groups were evident in the proton and carbon NMR spectra of **3**. The presence of 32 aromatic resonances and two carbonyls in the

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carbon NMR spectrum indicated that compound **3** possessed at least time-averaged C_2 symmetry, but the overall conformation of **3**, which must exhibit significant steric crowding, was unknown. Ultimately, single crystals of compound **3** were obtained from CH_2Cl_2 -toluene, and X-ray analysis^[5] yielded the molecular structure illustrated in Figure 1. The molecule

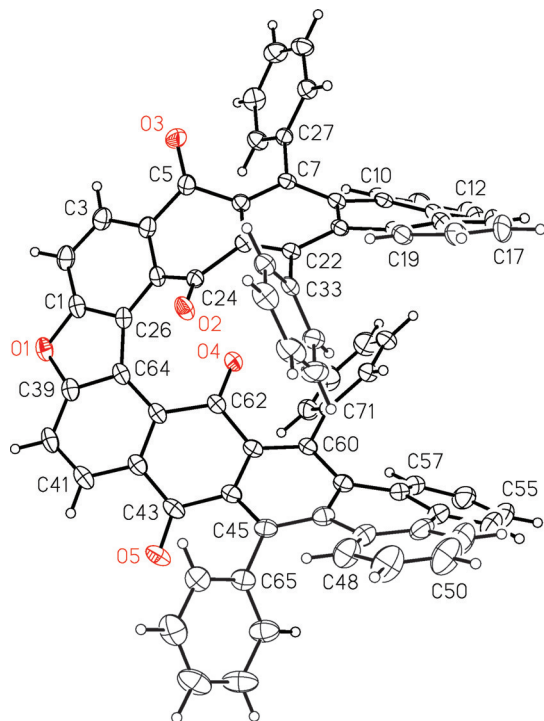


Figure 1. Molecular structure of hairpin furan **3**; thermal ellipsoids are drawn at the 50% probability level.

lies on a general position in the space group $P\bar{1}$ and it adopts an approximately C_2 -symmetric conformation; not surprisingly, the B3LYP/6-31G(d)-calculated lowest energy conformation of **3** possesses exact C_2 symmetry (see the Supporting Information).

The polycyclic core of compound **3** is a continuously twisted, conjugated ribbon consisting of two twisted tetracene quinones fused to a central furan, but the leftmost five rings (as oriented in Figure 1) also constitute a heteropentahelicene. All three components (acene, helicene, and acene) in the structure display left-handed twists; thus we would assign its configuration as (*M,M,M*)-**3**. (Naturally, the enantiomeric (*P,P,P*)-**3** is also present in the centrosymmetric crystal structure.) Several other diastereomeric conformations are possible, with the one of next lowest energy being a C_1 -symmetric (*P,M,M*)-**3**, a mere 3.3 kcal mol⁻¹ higher in energy than the crystal conformation at the B3LYP/6-31G(d) level of theory. The end-to-end twists^[1] of the tetracenequinones are approximately 64° and 59°, slightly less than the HDFT-calculated twist of 69° for both. The twist of the helicene is less clearly defined, but its degree of distortion may be appreciated from the C24-C26-C64-C62 torsion angle of 39° (HDFT: 37°). The two terminal phenanthrene groups are roughly parallel, and they enclose a chiral cleft approximately

4 Å wide between the van der Waals surfaces. This cleft is filled in the crystal by a phenanthrene moiety of an adjacent molecule. We give compounds such as **3** the trivial name of “hairpin furans”, because of the sharp reversal in the direction of propagation of the polycycle at the furan ring.

The syntheses of **3** and **4** may be extended to other cyclopentadienones. For example, when acecyclone^[4] (**5**) was heated with bisquinone **1** at 210°C, the biaryl **7** was the principal double adduct (Figure 2), but when the reaction was

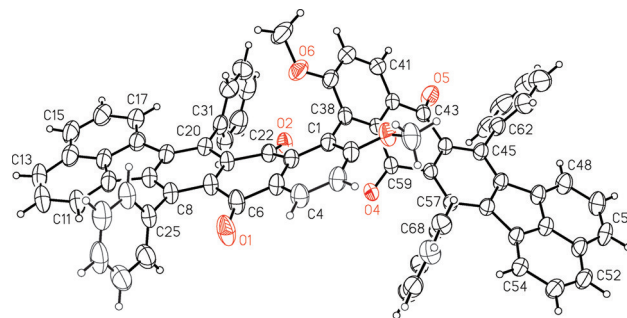


Figure 2. Molecular structure of biaryl **7**; thermal ellipsoids are drawn at the 50% probability level.

carried out at 250°C, the hairpin furan **6** was formed instead. We have also prepared hairpin furans (data not shown) from aceanthrenecyclone,^[4] a di-*tert*-butylphenyclone, and 5,7-diphenyl-6*H*-benzo[*h*]cyclopenta[*f*]quinoline-6-one (an aza-phenyclone),^[6] but tetraphenylcyclopentadienone gives neither biaryl nor furan.^[7] It is likely that most cyclopentadienones that can survive the reaction conditions are suitable precursors of the corresponding hairpin furans. In practice, the limiting factor in these syntheses is the preparation of the bisquinone **1**. For unknown reasons, the multistep synthesis^[3] of this molecule is erratic in our hands, and we have found it preferable to prepare compound **1** by a simple chromic acid oxidation of 2,2'-dimethoxy-1,1'-binaphthalene. The yield of **1** in this process is poor (4%), but its isolation is simple, and the starting material is readily available^[9] (see the Supporting Information).

The hairpin furans **3** and **6** are formed in an unusual reaction, but one that we do not understand. The synthesis of the giant biaryls **4** and **7** is clearly the result of a double Diels–Alder addition of the cyclopentadienones to **1** followed by decarbonylation and dehydrogenation of the adducts. There are numerous similar examples in the chemistry of cyclopentadienones,^[10] and we ourselves have employed this method several times in the past.^[11] But how can the giant biaryls be converted to the hairpin furans? There are several reports of the conversion *o,o'*-dihydroxybiaryls to dibenzofurans by Bronsted acid-catalyzed dehydration^[12] or pyrolytic dehydration over zeolites, silica, or alumina.^[13–15] However, we know of no example where a dialkoxybiaryl is converted to a dibenzofuran, with or without acid catalysis. Our own mechanistic experiments only add to the puzzle. Re-heating compound **7** at 250°C does not convert it to compound **6**, nor is demethylation observed. Even heating compound **7** at 260°C for nine days gave no furan formation; only starting

material was recovered. Interestingly, heating compound **1** alone at 250 °C does not give the corresponding small dibenzofuran-bisquinone; thus the cyclopentadienones may have a role in the reaction beyond that of dienophile. At the suggestion of the referees, further mechanistic experiments were performed with the following results. Heating compound **7** with 2 mol % tosic acid in nitrobenzene at 260 °C gave no reaction; thus trace acid does not seem to promote furan formation. Heating **1** and **2** in diphenyl ether at 260 °C gave a mixture of biaryl **4** and furan **3**, and heating **1** and **2** in 2-methylnaphthalene at 260 °C gave biaryl **4** with only a trace of furan **3**; thus there seems to be a solvent effect, but nitrobenzene remains the best solvent for furan formation.

However, by far the most interesting experiment (again, suggested by a referee) was the heating of **1** (20 μ mol), **2** (80 μ mol), and **7** (20 μ mol) in nitrobenzene at 260 °C to yield furans **3** (0.4 μ mol, 2 %) and **6** (1.9 μ mol, 10 %), and biaryls **4** (1.2 μ mol, 6 %) and recovered **7** (6.8 μ mol, 34 %) (see the Supporting Information). Thus the synthesis of furan **3** from **1** and **2** promotes the conversion of biaryl **7** to furan **6**. This experiment was repeated with three simultaneous controls as follows: (1) **1** + **2** + **7** gave, as before, furans **3** and **6** and biaryl **4**; (2) **1** + **7** gave no reaction; (3) **2** + **7** gave no reaction; and (4) **7** alone gave no reaction. From this we conclude that some intermediate or by-product of the synthesis of the dimethoxybiaryl is a reagent or catalyst necessary for the conversion of the biaryl to the furan. Unfortunately, there are dozens of possible intermediates^[16] to consider for this role, none of which is an obvious choice.

Both the twisted acenes and the helicenes, when resolved into pure enantiomers, are notable for their extreme chiroptical properties, with members of both classes possessing among the highest reported specific rotations.^[17] However, numerous attempts to resolve compounds **3** and **6** on chiral columns have proven unsuccessful.^[18] For this reason, the possible racemization pathways for compound **3** were investigated computationally at the B3LYP/6-31G(d) level.^[19] As is the case for other twisted acenes,^[20,21] the lowest energy racemization pathway is a multistep process: first is twist inversion of one of the tetracenequinones ($\Delta G^\ddagger = 9.5$ kcal mol⁻¹), followed by the two internal carbonyl groups slipping past each other (21.1 kcal mol⁻¹), the two internal phenyl groups slipping past each other (24.1 kcal mol⁻¹), and twist inversion of the other tetracenequinone (9.5 kcal mol⁻¹). (A detailed illustration of the path, intermediates, and transition states is found in the Supporting Information.) The highest, phenyl slip transition state was also located at the B97D/6-31G(d) and M062X/6-31G(d) levels and found to impart very similar barriers of 23.7 kcal mol⁻¹ and 25.3 kcal mol⁻¹, respectively. The former barrier corresponds to a half-life of about 15 h at 20 °C, and the latter more than a week. Thus we have little doubt that compound **3** is resolvable, but it is likely not configurationally stable in the long term.

A great variety of cyclopentadienones exists,^[10] and each one represents a potential hairpin that may be prepared in one step from bisquinone **1**, making hairpin furans an easily accessible new class of large, chiral aromatic polycycles. Because the pi system of hairpin acene **3** is subjected to an overall twist of 180°, conversations about **3** often lead to the

suggestion that it be incorporated into a Moebius polycycle. However, the necessary connection is not so simple to make,^[22] and whether this twisted substructure can be incorporated into larger molecules of unusual topology remains to be seen.

Acknowledgements

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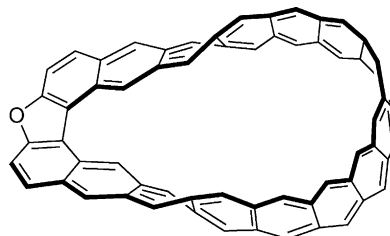
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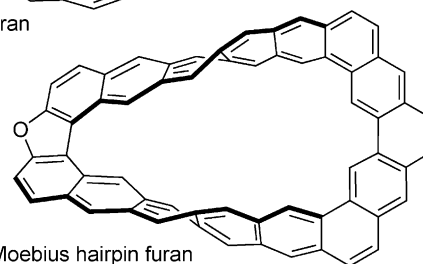
- [1] For a review of twisted acenes: R. A. Pascal Jr., *Chem. Rev.* **2006**, *106*, 4809–4819.
- [2] For a review of helicenes: K. P. Meurer, F. Vogtle, *Top. Curr. Chem.* **1985**, *127*, 1–76.
- [3] E. E. Podlesny, M. C. Kozłowski, *Org. Lett.* **2012**, *14*, 1408–1411.
- [4] W. Dilthey, I. ter Horst, W. Schommer, *J. Prakt. Chem.* **1935**, *143*, 189–210.
- [5] X-ray crystal structure determination for **3**: Formula C₇₆H₄₀O₅·2C₇H₈, *M* = 1217.34, crystal size 0.115 × 0.110 × 0.083 mm, triclinic, *P*1̄, *a* = 13.7401(10) Å, *b* = 15.1398(10) Å, *c* = 15.9430(11) Å, α = 83.3780(9)°, β = 82.6460(10)°, γ = 70.8910(9)°, *V* = 3098.4(4) Å³, *Z* = 2, ρ_{calcd} = 1.307 Mg m⁻³, μ = 0.080 mm⁻¹, Mo *K* α radiation (λ = 0.71073 Å), $2\theta_{\text{max}}$ = 55.2°, *T* = 150(2) K. 54053 reflections were measured, the structure was solved by direct methods, and it was refined by full-matrix least-squares on *F*². *R*(*F*) = 0.058, *wR*(*F*²) = 0.137, and *S* = 1.02 for 9687 reflections with *I* > 2 σ (*I*), and *R*(*F*) = 0.093, *wR*(*F*²) = 0.159, and *S* = 1.02 for 14281 unique reflections, 856 parameters, and 0 restraints. The residual electron density ranged from −0.36 to 0.69 eÅ⁻³. X-ray crystal structure determination for **7**: Formula C₇₄H₄₂O₆·4C₆H₆, *M* = 1339.50, crystal size 0.191 × 0.156 × 0.070 mm, monoclinic, *P*2₁/*n*, *a* = 17.3959(13) Å, *b* = 20.6614(15) Å, *c* = 20.8647(16) Å, β = 110.4220(10)°, *V* = 7027.9(9) Å³, *Z* = 4, ρ_{calcd} = 1.266 Mg m⁻³, μ = 0.078 mm⁻¹, Mo *K* α radiation (λ = 0.71073 Å), $2\theta_{\text{max}}$ = 56.7°, *T* = 150(2) K. 72097 reflections were measured, the structure was solved by direct methods, and it was refined by full-matrix least-squares on *F*². *R*(*F*) = 0.087, *wR*(*F*²) = 0.179, and *S* = 1.02 for 7443 reflections with *I* > 2 σ (*I*), and *R*(*F*) = 0.201, *wR*(*F*²) = 0.242, and *S* = 1.03 for 17452 unique reflections, 928 parameters, and 144 restraints. The residual electron density ranged from −0.44 to 0.65 eÅ⁻³. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-1413109 (**7**) and CCDC-1413110 (**3**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
- [6] R. S. Walters, C. M. Kraml, N. Byrne, D. M. Ho, Q. Qin, F. J. Coughlin, S. Bernhard, R. A. Pascal Jr., *J. Am. Chem. Soc.* **2008**, *130*, 16435–16441.
- [7] Although tetraphenylcyclopentadienone readily adds to olefins, including quinones, at moderate temperatures, with additional heating the resulting adducts often undergo retro-Diels–Alder reactions rather than the decarbonylation necessary to form the

present biaryls. For an example of such a retro-Diels–Alder reaction in preference to decarbonylation, see Ref [8].

- [8] A. P. West Jr., D. Van Engen, R. A. Pascal Jr., *J. Org. Chem.* **1992**, *57*, 784–786.
- [9] S. Brenet, B. Baptiste, C. Philouze, F. Berthiol, J. Einhorn, *Eur. J. Org. Chem.* **2013**, 1041–1045.
- [10] For a review of the chemistry of cyclopentadienones: M. A. Ogliaruso, M. G. Romanelli, E. I. Becker, *Chem. Rev.* **1965**, *65*, 261–367.
- [11] a) R. A. Pascal Jr., D. Van Engen, *Tetrahedron Lett.* **1987**, *28*, 293–294; b) J. Lu, J. Zhang, X. Shen, D. M. Ho, R. A. Pascal Jr., *J. Am. Chem. Soc.* **2002**, *124*, 8035–8041; c) Q. Qin, D. M. Ho, J. T. Mague, R. A. Pascal Jr., *Tetrahedron* **2010**, *66*, 7933–7938.
- [12] J. Areephong, N. Ruangsapichart, T. Thongpanchang, *Tetrahedron Lett.* **2004**, *45*, 3067–3070.
- [13] A. Arienti, F. Bigi, R. Maggi, P. Moggi, M. Rastelli, G. Sartori, A. Trere, *J. Chem. Soc. Perkin Trans. 1* **1997**, 1391–1393.
- [14] X. Xie, T. Y. Zhang, Z. Zhang, *J. Org. Chem.* **2006**, *71*, 6522–6529.
- [15] I. A. Shuklov, N. V. Dubrovina, H. Jiao, A. Spannenberg, A. Börner, *Eur. J. Org. Chem.* **2010**, 1669–1680.
- [16] The formation of a giant biaryl from **1** and a cyclopentadienone requires two cycloadditions, two decarbonylations, and two dehydrogenations (the last of these likely a multistep process), and the two halves of the molecule may react independently.
- [17] For a survey of molecules with very high specific rotations: R. A. Pascal, Jr., A. P. West, Jr., *Tetrahedron* **2013**, *69*, 6108–6115.
- [18] Resolutions were attempted on Chiral Technology IC, IA, AS-H, OD-H, OJ-H, AD-H, OZ-H, and Whelk-01 columns; where supercritical fluid chromatography was used, the mobile phases were 40 % MeOH or EtOH or *i*PrOH in CO₂, and where HPLC was used, the mobile phases were 100 % EtOH, 1:1 heptane/EtOH, and 8:2 heptane/*i*PrOH. We thank Christina Kraml and Neal Byrne of Lotus Separations LLC for the attempted resolutions.
- [19] All HDFT calculations were performed by using GAUSSIAN09, Revision A.02 (M. J. Frisch, et al., Gaussian, Inc., Wallingford CT, **2009**); the built-in defaults for integral accuracy, wavefunction, and gradient convergence were employed. All potential minima and transition state structures were characterized by analytical frequency calculations.
- [20] J. Lu, D. M. Ho, N. J. Vogelaar, C. M. Kraml, S. Bernhard, N. Byrne, L. R. Kim, R. A. Pascal, Jr., *J. Am. Chem. Soc.* **2006**, *128*, 17043–17050.
- [21] R. A. Pascal, Jr., Q. Qin, *Tetrahedron* **2008**, *64*, 8630–8637.
- [22] Connection of the ends of a hairpin furan may lead either to Moebius strip or an ordinary two-sided loop, as illustrated below.



Moebius hairpin furan



not a Moebius hairpin furan

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