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Unexpected conversion of a polycyclic thiophene to a macrocyclic anhydride

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Abstract—Oxygenation of 2,5,9,12-tetra(*tert*-butyl)diacenaphtho[1,2-*b*:1′,2′-*d*]-thiophene (**1**, $C_{40}H_{44}S$) by peracids gave the cyclic sulfonic ester **4** (2,7,10,13-tetra(*tert*-butyl)diacenaphtho[1,2-*c*:1′,2′-*e*]oxathiin 5,5-dioxide, $C_{40}H_{44}O_3S$) which, when heated in nitrobenzene, is converted into a complex, macrocyclic anhydride **3** ($C_{80}H_{88}O_3$), which is derived from two molecules of **4**. Further investigation found a likely intermediate in this reaction, 4,4′,7,7′-tetra(*tert*-butyl)-1,1′-biacenaphthylenylidene-2,2′-dione (**5**, $C_{40}H_{44}O_2$), apparently formed from **4** by additional oxidation. Anhydride **3** plausibly arises by Diels–Alder reaction of **4** and **5** followed by several ring fragmentations. The structures of **3**, **4**, and **5** were unambiguously established by X-ray crystallography.

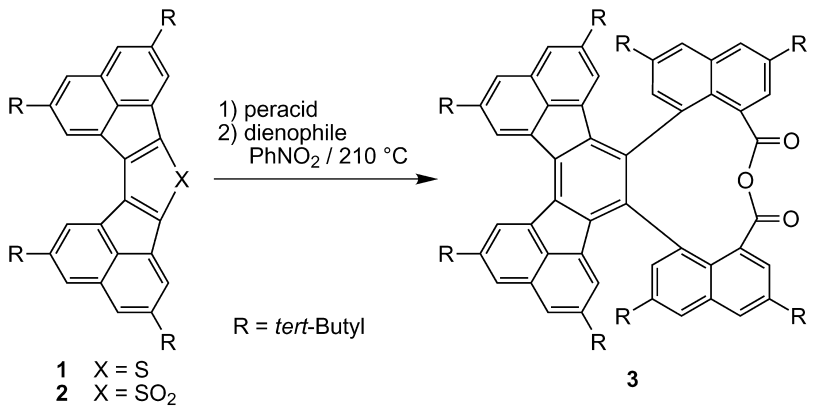
1. Introduction

We recently reported the use of 2,5,9,12-tetra(*tert*-butyl)-diacenaphtho[1,2-*b*:1′,2′-*d*]-thiophene (**1**) in the Diels–Alder synthesis of a large polycyclic aromatic quinone.[1] The reaction of compound **1** is sluggish, however, and the sulfur atom can be difficult to remove from some Diels–Alder adducts. In order to increase the versatility of this building block, we attempted to prepare the thiophene dioxide **2** by oxidation of **1** with peracids. When the resulting red, crystalline product was heated with various dienophiles in refluxing nitrobenzene, a most unusual molecule, the anhydride **3**, was isolated from each reaction mixture. The characterization of **3** and studies related to its formation are the subject of this paper (Scheme 1).

2. Results and discussion

2.1. Crystal and molecular structure of compound 3

The structure of **3** was not immediately evident from its



Scheme 1.

Keywords: Thiophene; Oxidation; Anhydride.
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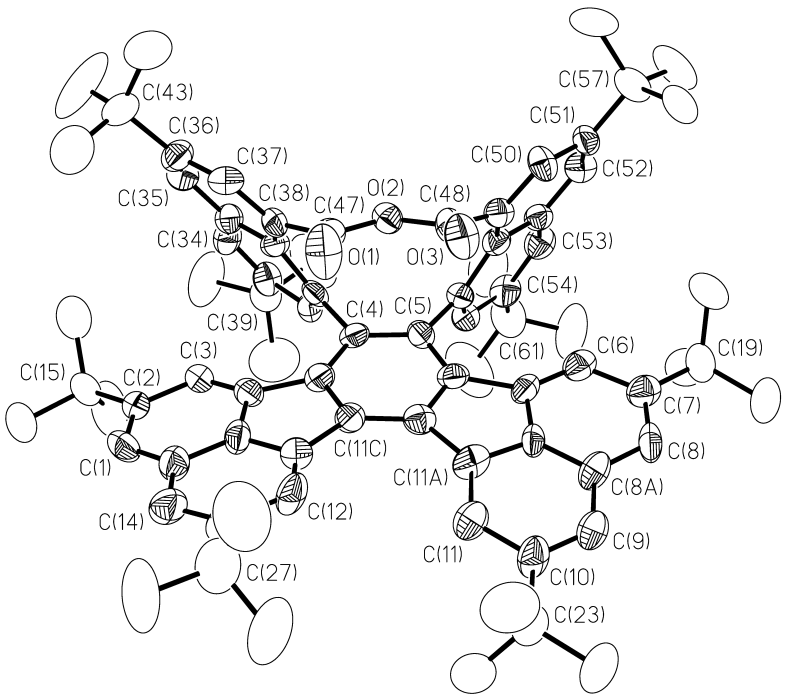


Figure 1. Molecular structure of anhydride **3**. Thermal ellipsoids have been drawn at the 50% probability level, and hydrogen atoms have been omitted for clarity.

spectral data, but its composition was unambiguously established by X-ray crystallography. Its molecular structure is shown in Figures 1 and 2. Compound **3** is clearly derived from two molecules of **1** in what must have been a rather complex series of reactions. In one half of the molecule [C(1)–C(30)], the carbon skeleton of **1** is intact; in the other [C(31)–C(64)], the acenaphthene groups have been cleaved and oxidized to yield a cyclic anhydride with an 11-membered ring. The conformation of this macrocycle is such that the anhydride group is folded over the gently curving acenaphtho[1,2-*j*]fluoranthene substructure. The two remaining naphthalene rings are roughly perpendicular to the rest of the polycycle, and they form a V-shaped cleft with a maximum width of about 8 Å. As a result of this folded structure, the C(3) and C(6) aromatic hydrogens are forced into the faces of naphthalene rings; their ^{1}H NMR resonance is found at δ 4.92.

Large, cleft-containing aromatic compounds such as **3** frequently form crystal structures with networks of solvent-containing channels,[2] and **3** is no exception. Compound **3** crystallized in the chiral space group $P4_3$ as its hexane solvate ($C_{80}H_{88}O_3{\cdot}C_6H_{14}$) (see Table 1), and it adopts a chiral conformation (with C_1 symmetry) so that every crystal contains only a single enantiomer (see Figure 2). Unfortunately, this spontaneous resolution of **3** is of little value, because the interconversion of its enantiomers must be very fast in solution as judged by its symmetric NMR spectra. However, the hexane molecules do lie in chiral channels along the *c* axis of the crystal, and if **3** becomes readily available, it might be interesting to see if small chiral alcohols or alkyl halides would yield similar structures with **3** and thus be resolved themselves.

2.2. Products from oxidation of compound 1

The formation of compound **3** must be a complex process, and **3** cannot arise from **2** without further oxidation. For this reason the products of the peracid treatment of **1** were more carefully investigated. Oxidation of **1** with either MCPBA or H_2O_2/TFA (data not shown for the latter) was found to yield not the sulfone **2** but rather the cyclic sulfonate **4** (Scheme 2). The presence of an extra oxygen atom in **4** was apparent from its mass spectrum and the inequivalence of

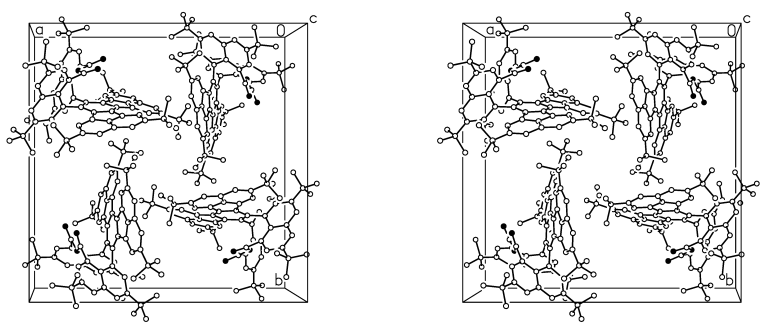


Figure 2. Stereo view of the unit cell of anhydride **3**. Non-hydrogen atoms have been drawn as spheres of arbitrary size, and hydrogen atoms have been omitted for clarity.

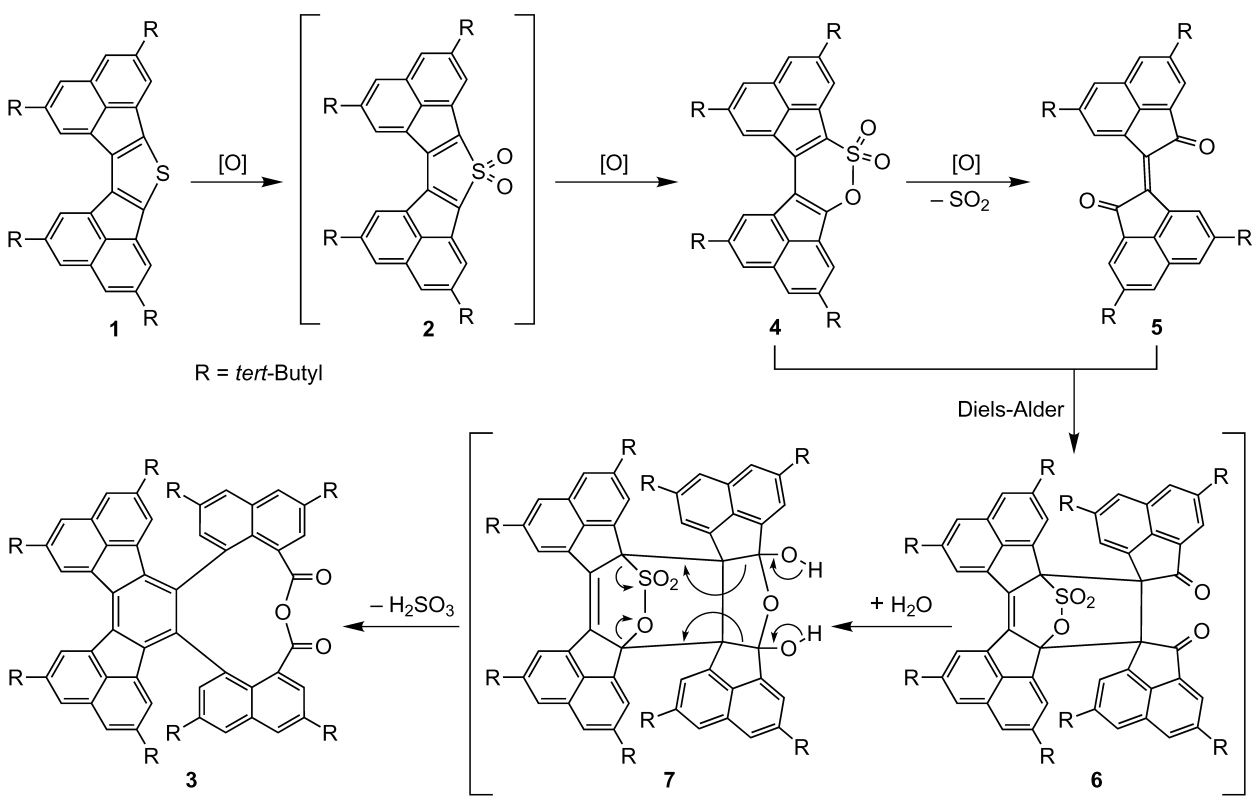
Table 1. Crystallographic data for compounds **3**, **4**, and **5**

	3	**4**	**5**
Chemical formula	$C_{80}H_{88}O_3{\cdot}C_6H_{14}$	$C_{40}H_{44}O_3S{\cdot}CHCl_3$	$C_{40}H_{44}O_2{\cdot}0.5CHCl_3$
Formula weight	1183.68	724.18	616.44
Crystal size (mm)	0.15×0.04×0.03	0.12×0.11×0.07	0.22×0.11×0.10
Space group	$P4_3$ (No. 78)	$P2_1/c$ (No. 14)	$R\bar{3}$ (No. 148)
a (Å)	21.7763 (6)	22.5021 (4)	37.1736 (6)
b (Å)	21.7763 (6)	18.1507 (4)	37.1736 (6)
c (Å)	15.1769 (3)	20.8192 (5)	6.2713 (6)
α (°)	90	90	90
β (°)	90	117.411 (1)	90
γ (°)	90	90	120
V (Å^3)	7197.0 (3)	7548.5 (3)	7505.1 (7)
Z	4	8	9
ρ_{calcd} (g/cm^3)	1.092	1.274	1.228
μ (mm^{-1})	0.064	0.335	0.189
T (K)	200 (2)	200 (2)	200 (2)
θ_{max} (°)	22.50	22.51	27.50
Reflections			
Total	53201	38049	33746
Unique	9178	9863	3811
Observed [$I>2\sigma(I)$]	5526	6973	2312
$R(F)$ (obs. data)[a]	0.0878	0.0679	0.0693
$wR(F^2)$ (obs. data)[a]	0.1713	0.1473	0.1846
S (obs. data)[a]	1.188	1.098	1.171
$R(F)$ (all data)[a]	0.1520	0.1054	0.1110
$wR(F^2)$ (all data)[a]	0.1970	0.1664	0.2141
S (all data)[a]	1.033	1.024	1.025

[a] $R(F)=\sum||F_o|-|F_c||/\sum|F_o|$; $wR(F^2)=[\sum w(F_o^2-F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$; S=goodness-of-fit on $F^2=[\sum w(F_o^2-F_c^2)^2/(n-p)]^{1/2}$, where n is the number of reflections and p is the number of parameters refined.

the signals for the two acenaphthene groups in its ^{1}H and ^{13}C NMR spectra. X-ray diffraction confirmed its structure (Fig. 3). Compound **4** may arise by a Baeyer–Villiger-like insertion of oxygen into the sulfone **2**. Thus far, compound **2** itself has not been observed.

When thiophene **1** was oxidized with MCPBA, a second oxidation product (in addition to **4**) was isolated in substantial amounts. This material possessed an NMR spectrum consistent with C_{2h} or C_{2v} molecular symmetry, as expected for **2**. However, X-ray diffraction established the



Scheme 2.

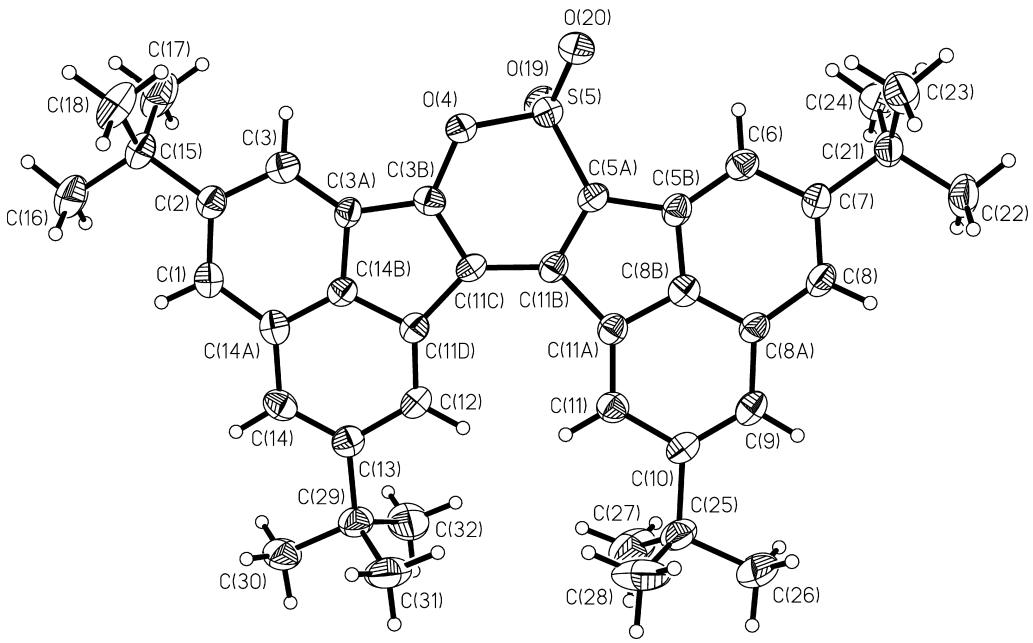


Figure 3. Molecular structure of sulfonic ester **4**. Thermal ellipsoids have been drawn at the 50% probability level.

structure as the diketone **5** (Fig. 4). This material is presumably formed by further oxidation of **4**.

Interestingly, a diketone identical to **5** but lacking the *tert*-butyl groups has been prepared previously.[3] Despite the heavy substitution of its central olefin, this molecule has been reported to undergo Diels–Alder reactions with cyclopentadiene, butadiene, and isoprene.[3] This observation provides a reasonable explanation for the formation of anhydride **3**. Diels–Alder reaction of **4** and **5** would yield the polycyclic adduct **6** (Scheme 2). Hydration of the adduct **6** would give the lactol **7**, which can plausibly fragment to give the macrocyclic anhydride **3**. Other, similar fragmentation reactions may be envisioned, and the participation of water is not an absolute requirement, inasmuch as the sulfonate may provide the extra oxygen for the anhydride formation.

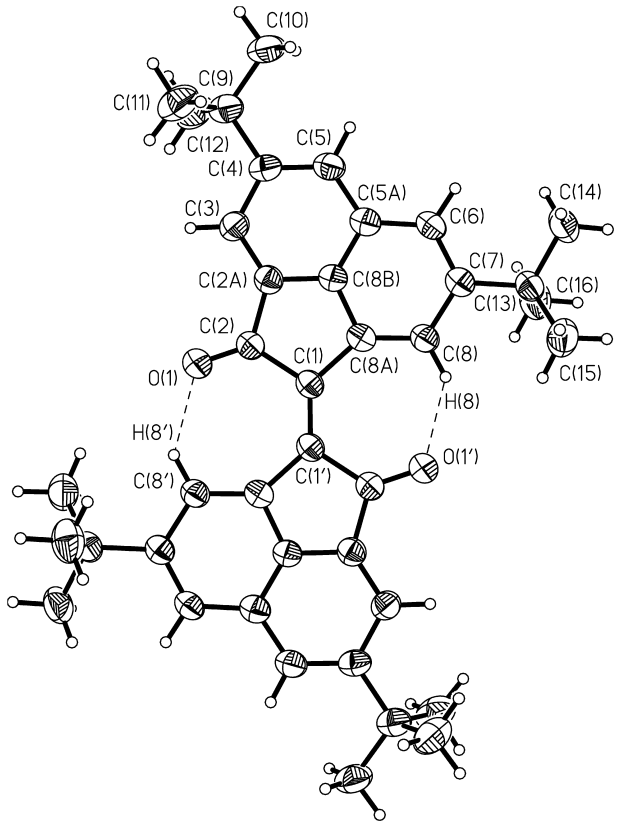


Figure 4. Molecular structure of diketone **5**. Thermal ellipsoids have been drawn at the 50% probability level.

The early reactions of dienophiles with sulfonic ester **4** (at the time thought to be **2**) had given the anhydride **3**, but the mechanism postulated in Scheme 2 requires an additional oxidation step to obtain diketone **5** from **4**. Several questions arose with regard to the formation of **5** and **3**. First, the yields of anhydride **3** in the early reactions were very low, thus it was possible that all of this material arose from the reaction of sulfonic ester **4** with the small amounts of **5** that are found as an impurity in most samples of **4**. Second, did sulfonic ester **4** undergo oxidation to diketone **5** in nitrobenzene solution? Both of these questions could be answered by heating **4** in nitrobenzene in the absence of any other reagents. In the event, carefully purified **4** (>97% pure by NMR) was heated in nitrobenzene at 200 °C for 20 h, and both anhydride **3** and diketone **5** were obtained as products (in 22 and 10% yields, respectively). This result unequivocally establishes that both **3** and **5** may be formed from **4**, and it is consistent with the mechanism outlined in Scheme 2, but it does not establish that **5** is an intermediate in the formation of **3**.

In order to garner support for the intermediate role for diketone **5**, equimolar amounts of **4** and **5** (0.0895 mmol each) were heated in nitrobenzene under the same conditions as the previous experiment (200 °C for 20 h) giving 0.0165 mmol of **3** (18% yield relative to **4**). In the previous experiment, 0.160 mmol of **4** had given 0.0177 mmol of **3**. If 2 mol of **4** were consumed to generate

3, then this represents a yield of 22%, and thus the yields of the two experiments were comparable (18 and 22%). If diketone **5** were not an intermediate in the formation of **3**, then the yield of **3** in the latter experiment should have been only half as great. These data clearly indicate that **5** is involved in the generation of **3**, if one assumes that the Diels–Alder reaction is much faster than the decomposition of **4** into **5**.

3. Conclusion

It is not obvious that the structure of anhydride **3** would have been determined by ordinary spectroscopic means from the very small amounts of material isolated from the reactions where it was originally observed. This is not to say that it could not have been done, but the effort required would have been far too great to invest on an unknown 'decomposition product'. However, compound **3** is highly crystalline, its surprising structure was determined in relatively short order by X-ray diffraction, and once the result was known, our curiosity with regard to its mechanism of formation was irreversibly aroused. The unique shape of compound **3**, and the presence of the anhydride for further elaboration, suggests that this or similar structures might find use someday as scaffolds in host–guest chemistry. For now, however, we present this highly unusual reaction for the amusement of the reader.

4. Experimental

4.1. Data for compounds

4.1.1. 2,7,10,13-Tetra(*tert*-butyl)diacenaphtho[1,2-*c*:1′,2′-*e*]oxathiin 5,5-dioxide (4) and 4,4′,7,7′-tetra(*tert*-butyl)-1,1′-biacenaphthylenylidene-2,2′-dione (5). Following the method of Furukawa et al.[4] for the oxidation of thiophenes, compound **1** (603 mg, 1.08 mmol), MCPBA (77%, 649 mg, 2.89 mmol), and CH_2Cl_2 (10 mL) were stirred at room temperature for 24 h. The dark red solution was concentrated to dryness on to silica gel powder, and this material was loaded on to a silica gel column. The initial material to elute (solvent, 97:3 hexanes–ethyl acetate) was yellow, unreacted **1** (248 mg, 0.45 mmol, 41%). The solvent was then changed to 95:5 hexanes–ethyl acetate, which eluted first the orange diketone **5** (128 mg, 0.22 mmol, 20%) and then the red sulfonic ester **4** (137 mg, 0.22 mmol, 20%). For **4**: mp 270–273 °C (dec). ^{1}H NMR ($CDCl_3$) δ 1.51 (s, 9H), 1.52 (s, 9H), 1.59 (s, 9H), 1.60 (s, 9H), 7.91 (d, J=1 Hz, 1H), 7.92 (d, J=1 Hz, 1H), 7.99 (d, J=1 Hz, 1H), 8.10 (d, J=1 Hz, 1H), 8.11 (d, J=1 Hz, 1H), 8.18 (d, J=1 Hz, 1H), 8.51 (d, J=1 Hz, 1H), 8.74 (d, J=1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 31.8, 31.9, 32.0, 32.1, 32.2, 32.5, 35.96, 36.0, 116.8, 122.0, 122.2, 122.5, 123.1, 123.3, 124.0, 124.3, 124.8, 126.4, 127.3, 127.6, 128.3, 128.8, 129.5, 131.6, 132.2, 133.0, 140.6, 151.7, 152.0, 152.4, 152.9, 156.0 (32 of 32 expected resonances); EI MS, *m*/*z* 604 (M^+, 72), 588 (M−O, 48), 572 (M−2O, 85), 556 (M−3O, 100). Single crystals of **4** were obtained from chloroform. For **5**: mp 305–315 °C (dec). ^{1}H NMR ($CDCl_3$) δ 1.50 (s, 18H), 1.61 (s, 18H), 7.96 (s, 2H), 8.11 (s, 2H), 8.19 (s, 2H), 9.66 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 31.9, 35.9, 36.4, 119.5, 123.0, 126.7, 127.2, 130.3, 132.2, 132.8, 138.9, 139.5, 151.4, 152.4, 196.1 (15 of 16 expected resonances); EI MS, *m*/*z* 556 (M^+, 100). Single crystals of **5** were obtained from chloroform.

4.1.2. 4,5-Bis[3,6-di(*tert*-butyl)-8-carboxynaphthyl]-2,7,10,13-tetra(*tert*-butyl)-acenaphtho[1,2-*j*]fluoranthene cyclic anhydride (3). Reaction A—the initial observation. Sulfonic ester **4** (50 mg, 0.083 mmol) and 1,4-diphenyl-1,3-butadiyne (8.1 mg, 0.04 mmol) were heated in refluxing nitrobenzene (8 mL) for 30 h. The volume of nitrobenzene was reduced to 2 mL by distillation at atmospheric pressure, and methanol (10 mL) was then added to yield a brown precipitate. This material was subjected to preparative TLC (9:1 hexanes–$CHCl_3$, then 3:1 hexanes–$CHCl_3$), and isolation of the band with R_f=0.04 yielded a few milligrams of anhydride **3**; mp 358–360 °C (dec). ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 18H), 1.27 (s, 18H), 1.48 (s, 18H), 1.62 (s, 18H), 4.92 (d, J=1 Hz, 2H), 7.50 (d, J=1 Hz, 2H), 7.53 (d, J=2 Hz, 2H), 7.76 (d, J=1 Hz, 2H), 7.94 (d, J=2 Hz, 2H), 8.00 (d, J=2 Hz, 2H), 8.09 (d, J=2 Hz, 2H), 8.92 (d, J=1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 31.2, 31.4, 31.9, 32.2, 34.9, 35.2, 36.0, 121.4, 121.5, 122.5, 123.1, 125.4, 127.8, 128.6, 129.0, 129.2, 129.6, 130.9, 131.6, 135.2, 135.7, 136.0, 136.20, 136.23, 136.3, 140.6, 147.7, 149.7, 150.5, 150.7, 164.5 (31 of 32 expected peaks, but the δ 35.20 resonance is of double intensity); FAB MS, *m*/*z* 1098 (M+H [$^{13}C_1$], 100). Single crystals of **3** were obtained from hexanes–ethyl acetate.

4.1.3. Compound 3. Reaction B—formation from compound 4 and nitrobenzene. Carefully purified sulfonic ester **4** (99.8 mg, 0.160 mmol, >97% pure by ^{1}H NMR) was dissolved in nitrobenzene (1.5 mL) and placed in a screw-capped vial. The vial was placed in a sand bath held at 190–200 °C for 20 h. After cooling, the reaction mixture was loaded on to a short silica gel column. Hexanes were used to elute the nitrobenzene, and $CHCl_3$ was used to elute the larger organic products. After removal of the solvent, the latter material was fractionated by preparative TLC (9:1 cyclohexane–$CHCl_3$, then 3:1 cyclohexane–$CHCl_3$). The products isolated were anhydride **3** (19.4 mg, 0.0177 mmol, 22%), diketone **5** (9.5 mg, 0.0160 mmol, 10%), and recovered **4** (5.5 mg, 0.0091 mmol, 6%).

4.1.4. Compound 3. Reaction C—formation from equal amounts of 4 and 5. Sulfonic ester **4** (54.0 mg, 0.0895 mmol), diketone **5** (52.6 mg, 0.0895 mmol), and nitrobenzene (1.5 mL) were placed in a screw-capped vial. The vial was placed in a sand bath held at 190–200 °C for 20 h. After cooling, the reaction mixture was fractionated by silica gel column chromatography and preparative TLC as described above. The products isolated were anhydride **3** (18.1 mg, 0.0165 mmol, 18% yield if the reaction is **4**+**5**→**3**, 37% yield if the reaction is **4**+**4**→**3**), diketone **5** (25.9 mg, 0.0440 mmol, 49%), and recovered **4** (6.3 mg, 0.0104 mmol, 12%).

4.2. General X-ray crystallographic procedures

X-ray data were collected by using graphite monochromated Mo Kα radiation (0.71073 Å) on a Nonius KappaCCD diffractometer. The diffraction data were processed by using the program DENZO.[5] All structures were solved by direct methods using Siemens SHELXTL,[6]

and all were refined by full-matrix least-squares on F^2 using SHELXTL. All non-hydrogen atoms were refined anisotropically, and hydrogens were included with a riding model. The structures of **3**·C_6H_{14} and **5**·$CHCl_3$ contained highly disordered solvent molecules, and they were further processed by using the SQUEEZE/BYPASS method[7] implemented in PLATON.[8] Specific crystal, reflection, and refinement data are contained in Table 1. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 207773-207775. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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