

## New Metathesis Methodology Leading to Angularly-Fused Polycyclic Quinones and Related Compounds

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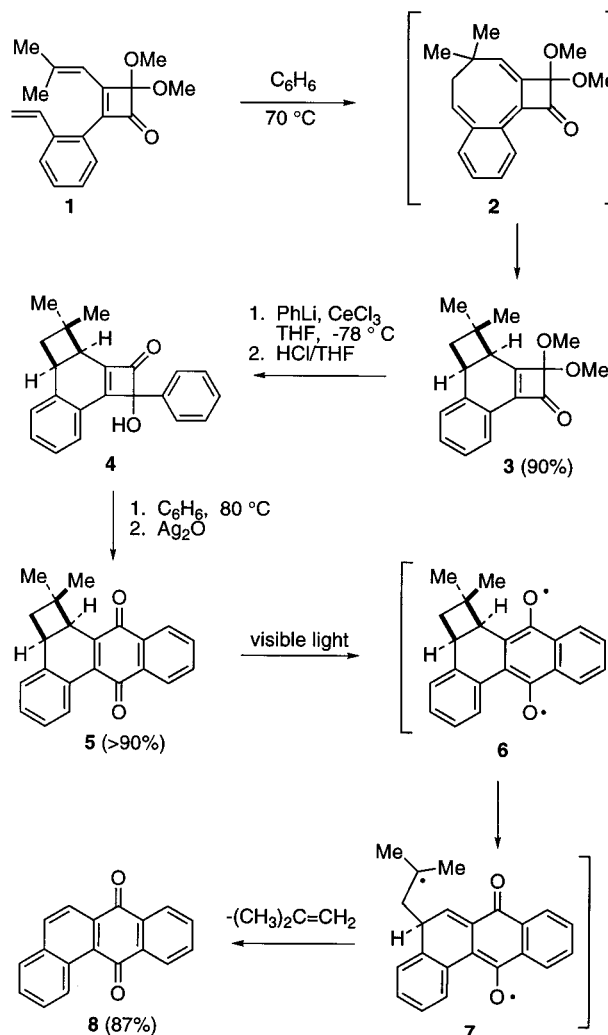
Reported here is a new method for the regiospecific synthesis of phenanthraquinones and related angularly fused polycyclic compounds from squaric acid derived cyclobutenones.<sup>1</sup> The method rests on dual annulation reactions. One involves the well-known electrocyclic ring opening of appropriately substituted cyclobutenones to vinylketenes and their subsequent reactions with proximally placed ketenophiles.<sup>2</sup> The other constitutes a new metathesis sequence leading to aromatic rings which arise from a photofragmentation of cyclobutyl-substituted quinones as the ultimate step.<sup>3</sup>

The salient details are outlined in Scheme 1. Cyclobutenone **1** undergoes ring closure to the tetracyclic cyclobutenone **3** (85%) upon mild thermolysis (benzene, 70 °C), a transformation envisaged to involve an  $8\pi$  electrocyclization to cyclooctatriene intermediate **2**, followed by a  $6\pi$  electrocyclic ring closure to the observed product **3**.<sup>4</sup> Treatment of **3** with phenylcerium(III) chloride<sup>5</sup> followed by acid hydrolysis (concentrated HCl) gave cyclobutenone **4**, which was immediately thermolyzed (benzene, 80 °C).<sup>2</sup> The resulting ring expanded hydroquinone was not isolated but directly oxidized ( $\text{Ag}_2\text{O}$ ) to quinone **5** in >90% overall yield from **3**.

When the red-colored benzene solution of **5** was exposed to fluorescent laboratory light it underwent an efficient photofragmentation reaction to yield yellow benzo[*a*]anthracene-7,12-dione (**8**)<sup>6</sup> (87%), a compound representing the basic framework of the angucycline group of antibiotics.<sup>7–9</sup> The mechanism of this unusual photofragmentation is envisaged to involve the excited-state diradical **6** whose strain energy is relieved upon cleavage of the cyclobutane ring to give **7**. Subsequent expulsion of isobutylene provides **8**.

The following data suggest this method to be a general, regiospecific route to angularly fused polycyclic aromatic compounds (Scheme 2). For example, **3** was converted to **9** (89%),

Scheme 1



**10**<sup>9</sup> (71%), and **11** (75%) by using respectively 1-hexynylcerium(III) chloride, 2-anisoylcerium(III) chloride, and 2-lithiofuran. For comparison, **12** (obtained from **22** in 91% yield) gave the regioisomers **13** (73%), **14**<sup>10</sup> (83%), and **15** (75%).

A particularly interesting example is the conversion of cyclobutenone **16** to 6-(4-pentenyl)benzo[*a*]anthracene-7,12-dione (**19**) (Scheme 3). Here, **16** gave **17** in 89% yield upon mild thermolysis at 80 °C. Ring expansion of **17**, using phenylcerium(III) chloride, gave the quinone **18** in 93% yield. Photofragmentation of **18** then gave **19** in 81% yield (75% from **17**).

Syntheses of the requisite cyclobutenones **1**, **22**, and **16** were accomplished as outlined in Scheme 4.<sup>11</sup> Specifically, treatment of dimethyl squarate<sup>12</sup> (**20**) with 2-lithiostyrene followed by methanolysis (TFAA, MeOH) of the resulting  $\beta$ -hydroxyenol ether gave cyclobutenone **21** in 86% yield. This was converted to **1** (88%) upon treatment with 1-lithio-2-methylpropene. Similarly, **20** gave **22** (64% overall) by changing the addition order of the organometallic reagents, i.e., 1-lithio-2-methylpropene preceded

(10) Manning, W. B.; Muschik, G. M.; Tomaszewski, J. E. *J. Org. Chem.* **1979**, *44*, 699.

(11) For examples of analogous synthetic methodology see: Gayo, L.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 6896. Santora, V. J.; Moore, H. W. *J. Am. Chem. Soc.* **1995**, *117*, 8486.

(12) Liu, H.; Tomooka, C. S.; Moore, H. W. *Synth. Commun.* **1997**, *27*, 2177.

(1) For a listing of naturally occurring phenanthraquinones see: Thomson, R. H. *Naturally Occurring Quinones*; Chapman and Hall: New York, 1987; Vol. III.

(2) For a recent review on the ring expansion of cyclobutenones see: Moore, H. W.; Yerxa, B. R. *Adv. Strain Org. Chem.* **1995**, *4*, 81–162.

(3) For a review of olefin metathesis in organic chemistry see: Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036.

(4) For an elegant application of this electrocyclic cascade in natural products synthesis see: Nicolaou, K. C.; Patisis, N. A.; Zipin, R. E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555.

(5) Imamoto, T.; Sugiora, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233.

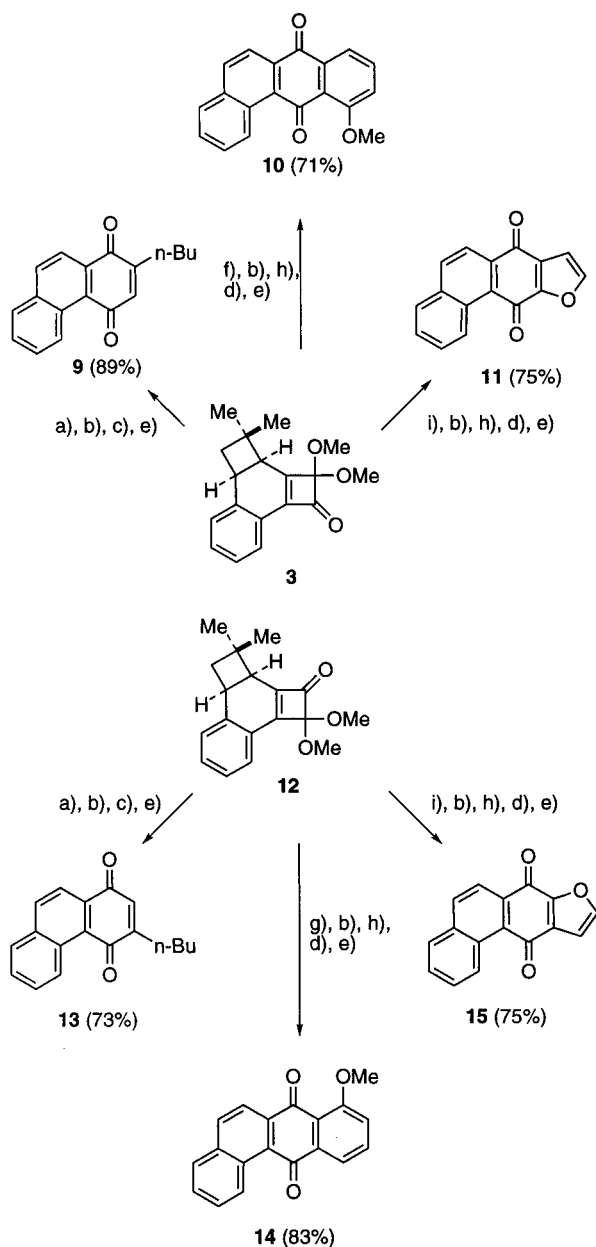
(6) Elbs, K. *Ber.* **1886**, *19*, 2209. Badger, G. M. *J. Chem. Soc.* **1939**, 802.

(7) The photolysis is carried out by exposing a benzene solution of the quinone to two 40 W fluorescent lights for a few hours.

(8) For a recent review on these compounds see: Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, 103. Also see: (a) Krohn, K.; Ballwanz, F.; Baltus, W. *Liebigs Ann. Chem.* **1993**, 911. (b) Larsen, D. S.; O'Shea, M. D. *Tetrahedron Lett.* **1993**, *34*, 1373. (c) Krohn, K.; Khanbabaee, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 99. (d) Larsen, D. S.; O'Shea, M. D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1019. (e) Kim, K.; Sulikowski, G. A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2397. (f) Matsuo, G.; Miki, Y.; Nakata, M.; Matsumura, S.; Toshima, K. *Chem. Commun.* **1996**, 225. (g) Carreno, M. C.; Urbano, A.; Fischer, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1621. (h) Larsen, D. S.; O'Shea, M. D.; Brooker, S. *Chem. Commun.* **1996**, 203.

(9) The structure assignments of all new compounds reported here are based upon characteristic spectral and analytical data (see Supporting Information).

Scheme 2



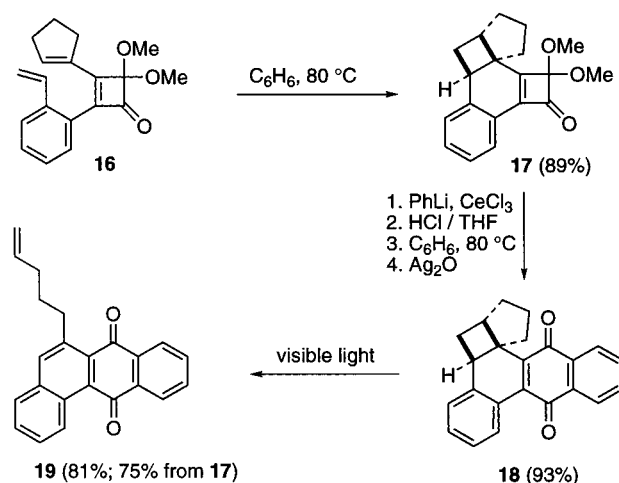
a) 1-lithiohexyne/CeCl<sub>3</sub>, THF, -78 °C; b) HCl, 0 °C; c) diethyl ether, reflux; d) Ag<sub>2</sub>O; e) benzene, visible light; f) 2-lithioanisole/CeCl<sub>3</sub>, THF, -78 °C; g) 2-lithioanisole, THF, -78 °C; h) benzene, reflux; i) 2-lithiofuran, THF, -78 °C;

2-lithiostyrene. Finally, **16** was obtained in 88% yield upon treatment of **21** with 1-lithiocyclopentene.<sup>13</sup>

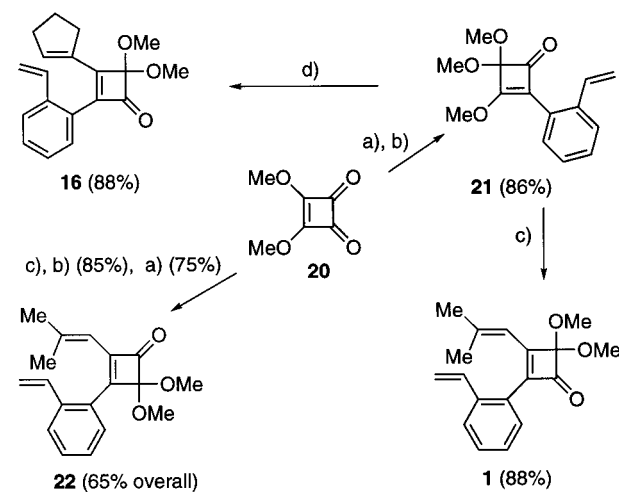
The significant points to arise from this study include the following: (1) a general synthesis of 2-(2-ethenylphenyl)-3-alkenyl-4,4-dimethoxycyclobutenones and their regioisomers is presented along with the observation that the octatetraene unit in these compounds undergoes facile ring closure to the corresponding bicyclo[4.2.0]octadienes; (2) the cyclobutanylquinones derived

(13) Pross, A.; Sternhell, S. *Aust. J. Chem.* **1970**, *23*, 989. Barton, H. R.; Bashiardes, G.; Fourrey, J. L. *Tetrahedron Lett.* **1983**, *24*, 1605.

Scheme 3



Scheme 4



a) 2-lithiostyrene, THF, -78 °C  
b) TFAA, MeOH  
c) 1-lithio-2-methylpropene, THF, -78 °C  
d) 1-lithiocyclopentene, THF, -78 °C

from these cyclobutenones undergo a new photofragmentation reaction leading to aryl ring formation; (3) this methodology provides a useful route to angularly fused polycyclic quinones, including those having the basic framework of the angucycline antibiotics; and (4) although other synthetic routes to angularly fused quinones are available (for example, by Diels–Alder methods<sup>8</sup>), the dual annulation sequence presented here illustrates a potentially powerful, regio-specific method leading to highly substituted examples.

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**Supporting Information Available:** Procedures and characterization data (12 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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