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Generation and Intramolecular Cyclization of (2-Ethenylphenyl)bisketenes. Synthesis of Benzofuranones

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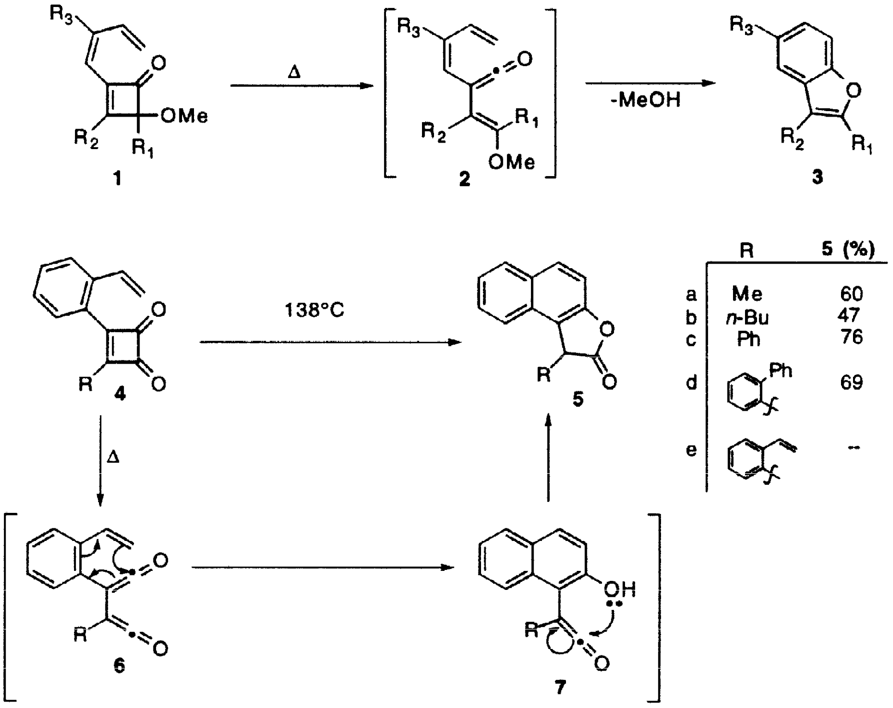
Abstract : Several new differentially substituted cyclobutenediones **4a-e** have been prepared. Their thermal rearrangement to substituted naphthofuranones **5a-d** is reported. This rearrangement involves an unprecedented intramolecular cyclization of a reactive bisketene **6**, and forms the naphthofuranone system in good yield. © 1998 Elsevier Science Ltd. All rights reserved.

The thermal rearrangement of 2-dienylcyclobutenones **1** to highly substituted annulated furans **3** was previously described (Scheme-1).[1] This transformation centered on the well precedented electrocyclic ring opening of the cyclobutenones to dienylketene intermediates **2** followed by their 6π electrocyclization and subsequent addition/elimination of the resulting phenol to the enol ether linkage.[2] We now report a complementary ring expansion of representative members of a 3-dienylcyclobutenedione series, *i.e.*, 3-(2-ethenylphenyl)cyclobutenediones **4** to naphtho[2,1-b]furan-2(3H)-ones **5**.



Scheme 1

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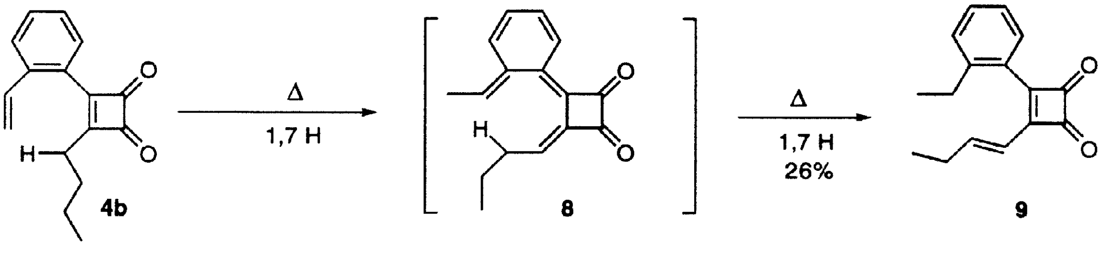
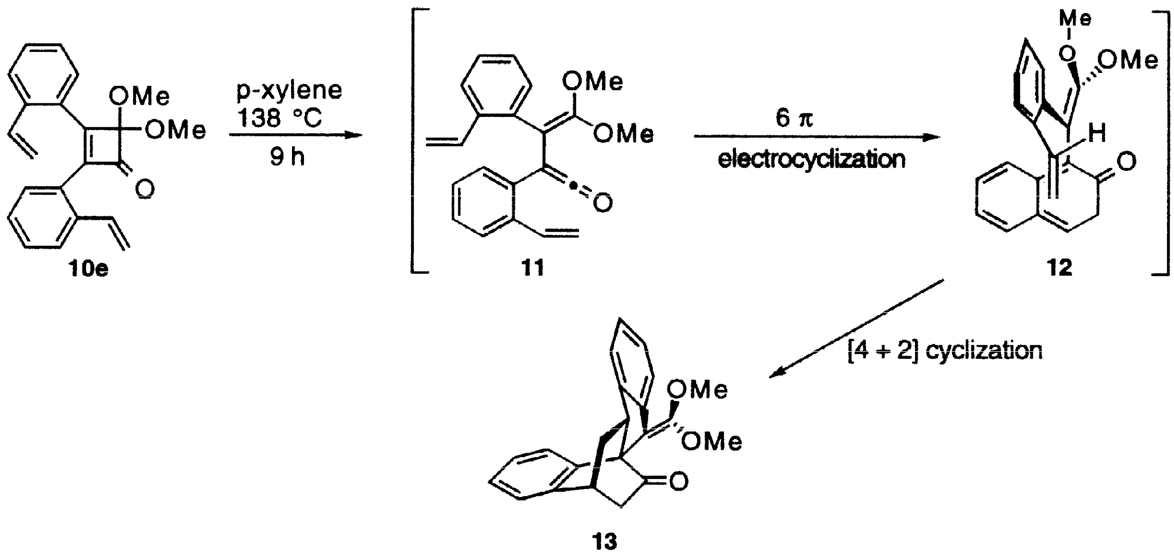
Thermolysis of **4a-d** (*p*-xylenes, 138°C) gave naphthofuranones **5a-d** in yields ranging from 47-76%. The rearrangement is envisaged to arise *via* a mechanism involving initial electrocyclic ring opening of the cyclobutenediones to the corresponding bisketenes **6** which then undergo a 6π electrocyclization followed by aromatization to the naphthols **7**. Finally, addition of the naphtholic hydroxyl group to the remaining ketene gives the observed products **5a-d**. Interestingly, thermolysis of **4b** gave 2-(2-ethylphenyl)-3-(1-butenyl)cyclobutene-1,2-dione (**9**) (26%) in addition to the benzofuranone **5d** (47%) (Scheme-2). This unusual transformation is envisaged to arise from an initial 1,7-hydrogen shift to give the quinodimethane intermediate **8** followed by rearomatization *via* an analogous 1,7-shift to produce the observed product **9**.[3]



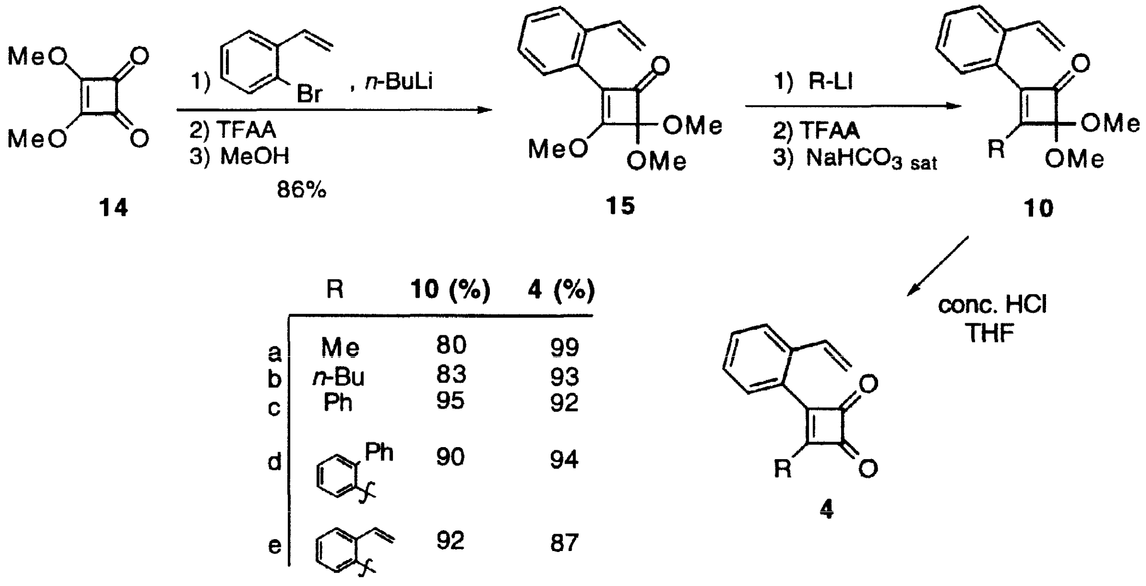
Scheme 2

Thermolysis of **4e** was studied as a possible new route to binaphthols, but, unfortunately, no isolable product was obtained. In comparison, the ketal precursor to **4e**, i.e., 2,3-di-(2-ethenylphenyl)-4,4-dimethoxycyclobutenone (**10e**) undergoes a most unusual thermal rearrangement (*p*-xylene, 138°C). Specifically, the polycyclic compound **13** was isolated in 72% yield (Scheme-3). As in the previous examples, the vinylketene intermediate **11** is envisaged to undergo electrocyclization to give the naphthol tautomer **12**. However, rather than tautomeric aromatization this quinodimethane is trapped by an intramolecular Diels-Alder cyclization to give **13**. The structure and stereochemistry of this product was established by X-ray crystallographic analysis.[4]



Scheme 3

Synthesis of the requisite 3-(2-ethenylphenyl)cyclobutenediones was accomplished by employing the key synthetic intermediate, 2-(2-ethenylphenyl)-3,4,4-trimethoxycyclobutenone (**15**), which was prepared by a modification of a previously described general method for the regiospecific synthesis of cyclobutenones starting with dimethyl squarate (**14**) (Scheme-4).[5] Specifically, treatment of **14** with 2-lithio-1-ethenylbenzene followed by trifluoroacetic anhydride (TFAA) and then methanol gave cyclobutenone **15** in 86% yield.[6] 1,2 Addition of methyl- and *n*-butyllithium to **15** followed by hydrolysis (TFAA, H_2O) gave **10a** (80%) and **10b** (83%), respectively. Interestingly, treatment of **15** with the softer aryllithium reagents gave only 1,4 addition-elimination products. In this manner, the methoxy group at position-3 was directly replaced upon treatment with the respective aryllithium reagents to give **10c** (95%), **10d** (90%), and **10e** (92%). Hydrolysis of ketals **10a-e** gave 3-(2-ethenylphenylcyclobutene-1,2-diones **4a-e** in excellent yields (87-99%).[7]



	R	10 (%)	4 (%)
a	Me	80	99
b	*n*-Bu	83	93
c	Ph	95	92
d	Ph	90	94
e		92	87

Scheme 4

In conclusion the results presented here add to a growing but still limited data base concerning the chemistry of 1,2-bisketenes. The majority of the work concerning this class of reactive intermediates has focused primarily on their generation, stability, reactivity with nucleophiles and intermolecular cyclizations.[8] The work outlined herein represents a new aspect of their chemistry and has direct analogies in the synthetically important ring expansion reactions of cyclobutenones.[2] Finally, it is noted that benzofuranones are found in a number of natural products and synthetic bio-active compounds.[9] The fact that the starting cyclobutenediones are readily prepared from squaric acid and various organometallic reagents speaks to a potentially general route to this class of compounds.

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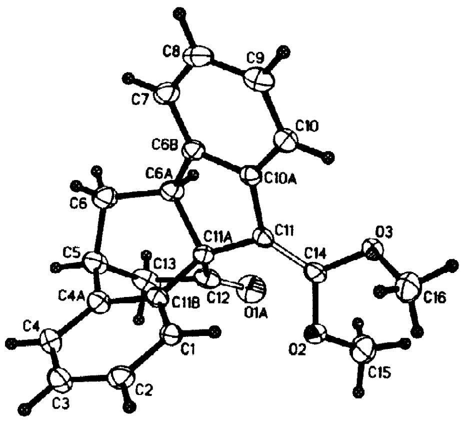

Figure 1. ORTEP Drawing of Compound **13**

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