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Novel Alkylaluminium Chloride Promoted [2+2] Cycloaddition Reactions of Styrenes with 1,4-Naphthoquinones and Bromoquinones: A Facile Route to Orthoquinodimethane Precursors

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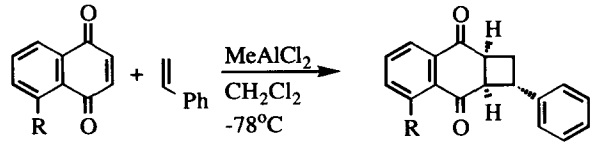
Abstract: The first examples of a Lewis acid catalysed [2+2]cycloaddition between styrenes and naphthoquinones have been observed. The reactions of both methoxyl and acetoxylnaphthoquinones were both regio- and stereospecific. When *m*-methoxystyrene was employed a novel tetracycle was also formed, and by an unexpected mechanistic pathway. Extension to bromoquinones resulted ultimately in the formation of arylnaphthocyclobutenes, common precursors of the orthoquinodimethanes.

We have recently reported the dimethylaluminium chloride promoted stereospecific [2+2] cycloaddition of dihydrofuran with 1,4-benzo- and naphthoquinones.[1] Indeed Lewis acid promoted [2+2] cycloadditions of unactivated alkenes to enones has been an area of hectic activity, accordng to the recent literature.[2a-e] In particular, Engler and co-workers have shown that Ti(IV) promotes [2+2] cycloadditions between propenyl benzenes and 1,4-benzoquinones.[3a,b]

Scheme 1



1 R=H
3 R=OMe
4 R=$OCOCH_3$

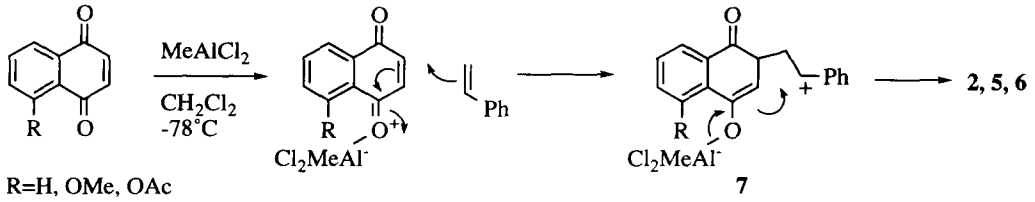
2 R=H
5 R=OMe
6 R=$OCOCH_3$

In the course of an investigation into a possible Lewis acid catalysed [4+2] cycloaddition of styrene with 1,4-naphthoquinone **1**, we unexpectedly isolated the cyclobutane **2** when $MeAlCl_2$ was employed as the promoter. This is the first recorded example of a Lewis acid promoted [2+2] cycloaddition of styrene to the naphthoquinone **1**.[4,5] Furthermore, the unsymmetrical quinones **3** and **4**, afforded regio- and stereospecifically

the cyclobutanes **5** and **6**, Scheme **1**, also in good yield. None of the naphthofurans potentially derivable from the cyclobutane products were detected.[3,6] We therefore initiated a study of this novel reaction.

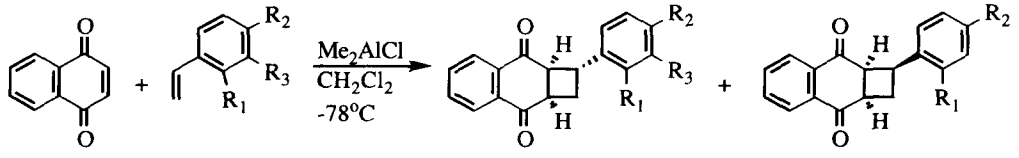
The mechanisms employed by other investigators in this general area have been extended to explain the formation of these products.[2a,f] Thus, it is proposed that [2+2] cycloaddition occurs by initial Lewis acid coordination to the quinone,subsequent Michael addition of styrene, followed by rapid ring closure of the intermediate dipolar ion **7**, Scheme 2, affording stereospecifically,[7] the cyclobutane with *exo* stereochemistry. The cyclobutanes **5** and **6** are formed regiospecifically, probably as a result of bidentate coordination of the Lewis acid at the C-4 carbonyl oxygen and the C-5 oxygen substituent.

Scheme 2



Extension of this reaction with quinone **1** to the activated styrenes, *o*- and *p*-methoxystyrene, **8** and **9**, afforded in both cases an approximately 3:2 mixture of diastereomers **10**,**11** and **12**,**13**, respectively, upon quenching the reaction after 30 minutes. Interestingly, treatment of the separated cyclobutane epimers **10** and **11**, with two equivalents of Me_2AlCl at -78°C, resulted in complete conversion of the *endo* adduct **11** to the *exo* adduct **10**, within one hour. Under the same conditions the *exo* adduct **10** remained unchanged.

Scheme 3



1

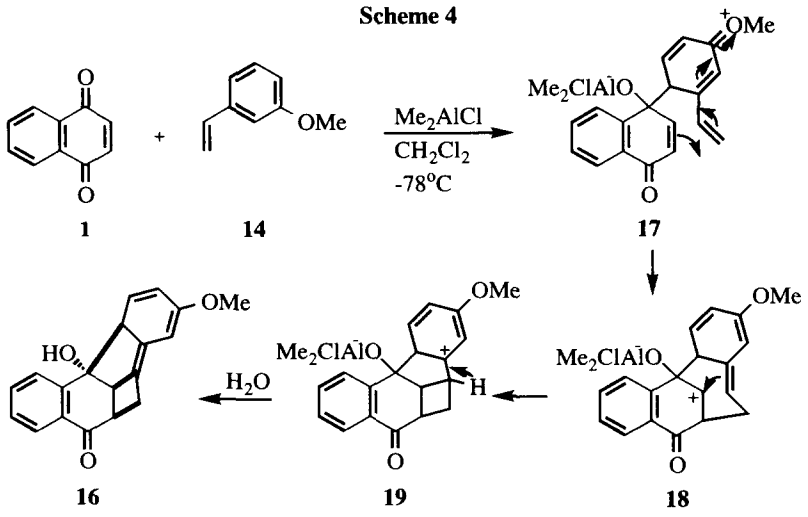
8 R_1=OMe, R_2=R_3=H
9 R_1=R_3=H, R_2=OMe
14 R_1=R_2=H, R_3=OMe

10 R_1=OMe, R_2=R_3=H
12 R_1=R_3=H, R_2=OMe
15 R_1=R_2=H, R_3=OMe

11 R_1=OMe, R_2=H
13 R_1=H, R_2=OMe

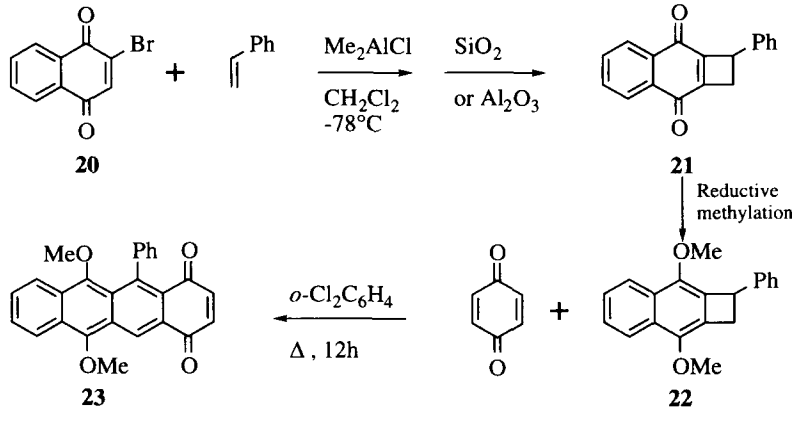
The use of *m*-methoxystyrene **14** in the reaction with quinone **1** afforded the *exo* [2+2] adduct **15** and the transannulated tetracycle **16**.[8] None of an *endo* adduct, the epimer of **15**, was detected. We initially assumed that **16** had been formed *via* the *endo* [2+2] adduct by a Lewis acid catalysed transannular nucleophilic attack by the pendant aryl group on the neighbouring carbonyl group. Fortunately, we were enabled to test this mechanistic proposal. When 2-methylbenzoquinone was treated under the usual conditions with *m*-methoxystyrene, both the *endo* and *exo* [2+2] cycloadducts, together with the tetracycle corresponding to **16**, were formed. When the pure *endo* [2+2] adduct was treated with Me_2AlCl conversion to the *exo* [2+2] adduct only was observed. None of the tetracycle was detected. To explain the formation of **16**, we now propose initial 1,2 addition to the carbonyl[9] with formation of the intermediate **17.** Subsequent sequential intramolecular [2+2] cycladdition ultimately results in the formation of the tetracycle **16**, Scheme 4.

Scheme 4



Interestingly, extension of the reaction to bromoquinones, such as **20**, resulted in the formation of the cyclobutene **21**, following facile dehydrobromination of the labile bromoadduct with either silica or alumina. Subsequent reductive methylation[10] afforded the naphthocyclobutene **22**, in good overall yield. This methodology represents a facile approach to these valuable *o*-quinodimethane precursors which are otherwise difficultly accessed.[11] The cyclobutene **22** was thermally ring opened and trapped with benzoquinone and after exposure to air, yielded the [4+2] cycloadduct **23**.

Scheme 5



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4. The chemistry is related to that described by Engler,[3a,b] however attempts to employ $TiCl_4$ as promoter in the reactions with 1,4-naphthoquinones gave no isolable product. Our chemistry was equally applicable to 1,4-benzoquinones. For examples of photochemical [2+2] cycloadditions of 1,4-naphthoquinone with styrene see: (a) Krauch, C.H.; Farid, S. *Tetrahedron Lett.* **1966**, 4783. (b) Maruyama, K.; Otsuki, T.; Takuwa, A.; Kako, S. *Bull. Inst. Chem. Res., Kyoto Univ.* **1972**, 50, 344.
5. All new compounds gave satisfactory spectroscopic and analytical data.
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7. We believe that the (5+2)[4π+2π] cycloaddition mechanism proposed by Engler[3a,b] does not occur in these reactions since such a mechanism would result in loss of aromaticity of the aryl ring in quinone **1**. No products derived from such intermediates were detected.
8. m.p.200-200°C; υ_{max} (KBr), 3426 (br), 1648 (s), 1474 (w) and 1110 (w) cm^{-1}; δ_H (270 MHz) 8.02 (1H, dd,*J*. 8.40, 1.35 Hz, Ar*H*), 7.84 (1H, dd,*J* 8.40, 1.35 Hz, Ar*H*), 7.63 (1H, ddd, *J* 8.40, 8.40, 1.35 Hz, Ar*H*), 7.46 (1H, ddd, *J* 8.40, 8.40, 1.35 Hz, Ar*H*), 7.25 (1H, d,*J* 7.31 Hz), 7.00 (1H, d, *J* 1.96 Hz), 6.77 (1H, dd, *J* 7.31, 1.96 Hz), 3.83 (3H, s, OCH_3), 3.55 (1H, s), 3.24 (1H, d, *J* 4.82 Hz), 2.70 (1H, ddd, *J* 8.68, 1.93, Hz), 2.41 (1H, brs, D_2O exchangeable), 2.00 (1H, ddd, *J* 13.50, 4.82, 1.93 Hz) and 1.68 (1Hdd, *J* 13.50, 8.68 Hz); δ_C (67.80 MHz) 200.50(C), 159.51(C), 148.23(C), 143.64(C), 134.20(CH), 132.60(C), 130.17(C), 127.96(CH), 126.48(CH), 126.43(CH), 124.60(CH), 111.81(CH), 109.82(CH), 91.60(C),60.32(CH), 55.50(CH_3), 52.62(CH), 49.91(CH) and 32.90(CH_2); LREIMS 292 (M^+, 57%), 172(100) and 158(44).
9. For a related intramolecular 1,2-nucleophilic addition of a dienone see: Majetich, G.; Khetani, V. *Tetrahedron Lett.* **1990**, 31, 2243-2246.
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