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Novel Lewis Acid Promoted Spiroannulation *versus* [2+2] - Cycloaddition of Dihydrofuran and Dihydropyran to Quinones

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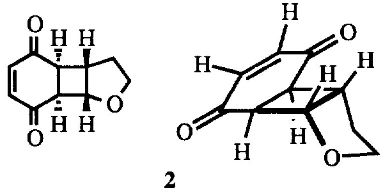
Abstract: *Dihydrofuran was found to undergo dimethylaluminium chloride promoted [2+2] - cycloaddition with benzo- and naphthoquinone. The first example of a novel spiroannulation was observed with methoxybenzoquinone. With dihydropyran, spiroannulation only, occurred in all cases investigated.*

We have reported the annulation of enaminoesters and enaminoketones with quinones and applied these findings to the synthesis of mitosenes[1] and benzocarbazoles.[2] Addition of other electron rich alkenes, such as enol ethers,[3] styrenes[4] and ketene acetals[5] to quinones is also well established. Mildly nucleophilic allylsilanes[6] and allylstannanes[7] also undergo Lewis acid promoted addition to quinones. These reactions have provided the basis of the synthesis of a wide range of natural products such as neolignans,[8] pterocarpans,[9] naturally occuring benzofurans[10] and vitamin K.[7]

We have initiated a study of the Lewis acid promoted reaction of enol ethers with *p* - quinones employing dihydrofuran (DHF) and dihydropyran (DHP) and now report the results of our preliminary investigations. The first reaction studied was that between DHF and benzoquinone **1** in dichloromethane at - 78°. The [2+2] adduct **2** was the only product.[11] The *cis* - *anti* - *cis* stereochemistry was assigned to it on the basis of 1D - and 2D - nmr and by analogy.[12]



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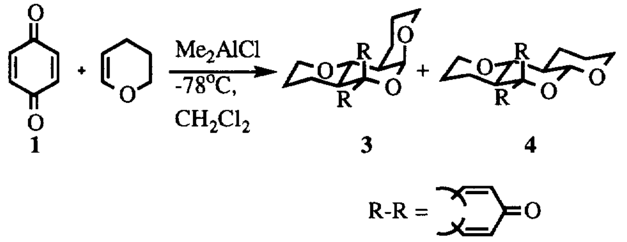
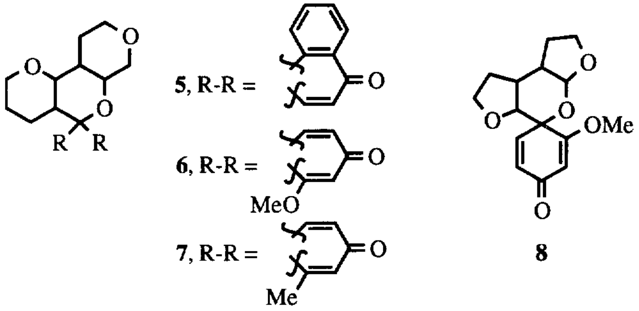
Extension of this reaction with benzoquinone to DHP provided a unique and unexpected result. Two diastereomeric products **3** and **4** only, were formed. The stereochemistries were assigned by careful analysis of the ^{1}H, ^{1}H COSY nmr spectra. The regiochemistry was assigned by comparison with ^{13}C nmr data of analogous systems.[15] None of the [2+2] - cycloadduct or the potential benzofurofuran, derivable therefrom,[14] was detected. This is the first example of this spiroannulation reaction. In addition, the ultimate products represent the first examples of a new tricyclic ring system.[16]

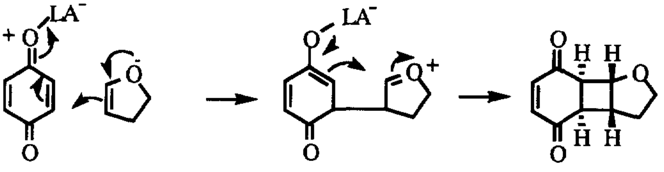


Scheme 1

The spiroannulated products - as separable diastereomeric mixtures - **5**, **6**, **7** and **8**, were isolated in yields of 66, 33, 54 and 33% respectively, when the corresponding quinone was treated with either DHP or DHF (3 equivalents) in the presence of dimethylaluminium chloride (1.5 equivalents). There were no cycloaddition products detected in these reactions. Notably, stoichiometric amounts of the Lewis acid were required for complete reaction. The use of $TiCl_4$ as the promoter gave an intractable mixture, presumably due to acid catalysed side reactions. This problem was not encountered with dimethylaluminium chloride due to it's dual nature as a Lewis acid and Brönsted base.[17]



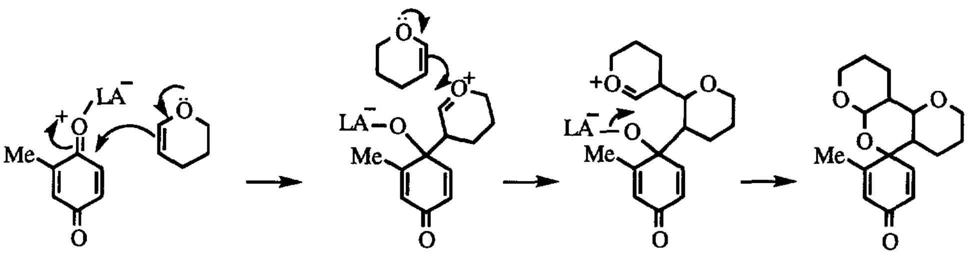
The mechanisms employed by other investigators in this area have been extended to explain the formation of these products.[9, 18] Thus it is proposed that [2+2] - cycloaddition occurs by initial Lewis acid coordination to the quinone, then Michael addition of DHF, followed by rapid ring closure of the intermediate dipolar ion **9**, Scheme 2.



9

Scheme 2

It is proposed that the first step in the spiroannulation reaction is 1,2 - attack by the DHP or DHF on the activated quinone. Although the dipolar ion, **10**, thus formed may now undergo cyclisation to the spiropyranoöxetane, it chooses to react in a cascade process with excess enol ether to give the ' homologated ' intermediate, **11**. This cyclises readily with formation of a new pyran ring, to afford **7**, Scheme 3.



10 11 7

Scheme 3

There are a number of tantalising questions which remain to be answered. It will be necessary to determine the scope and limitations of spiroannulation, as well as the factors affecting stereochemistry and regiochemistry. However, the central issue of the factors which influence the relative rates of the 1,2 - and 1,4 - addition reactions and hence the formation of spiroannulation or [2+2] - cycloaddition products remains unclear. Additionally, it is of note that the proposed intermediates **9** and **10** differ so markedly in their mode of action. One, **9**, Scheme 2, chooses to cyclise whereas the other, **10**, Scheme 3, chooses to react with excess enol ether. Examples of Lewis acid promoted reaction sequences initiated by conjugate addition and leading to a variety of products such as Sakurai products,[19] [2+2] - cycloadducts[9, 18] and benzofurans[9] are well established. On the otherhand Lewis acid promoted 1,2 - addition reactions of mild nucleophiles to quinones are rare.[20]

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11. All new compounds gave satisfactory spectroscopic and analytical data.
12. The basis of this structural assignment was the 270 MHz ^{1}H and ^{1}H, ^{1}H COSY spectra. In particular the two vinyl protons are observed as an AB quartet δ6.80 and 6.84 ppm. The similarity of these chemical shifts is consistent only with the stereochemistry shown since otherwise in the alternative *cis-syn-cis* configuration one proton would lie proximate to the furan oxygen with consequent deshielding.[13] The *anti* arrangement between the fused rings is indicated by the anticipated coupling, $J = 2.4$ Hz. Finally, we obtained the same *cis-anti-cis* [2+2] - cycloadduct between indene and methoxybenzoquinone as had Engler and co - workers,[14] when dimethylaluminium chloride was employed as the Lewis acid promoter.
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