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Acid-catalysed Rearrangement of the Diels–Alder Adducts of Activated Quinones

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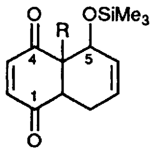
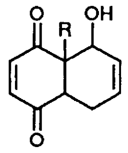
The Diels–Alder adducts (**1**)–(**5**) in the presence of the hydrochloric acid undergo a 4a,5 carbon–carbon bond fission to give rearranged compounds of type (**9**), (**10**), or the dihydrobenzofurans (**11**)–(**14**). Compound (**16**), obtained by hydrolysis of the adduct (**15**), rearranges to (**17**) in the presence of ethanol and silica gel.

In the course of studies on the synthesis of rabelomycine analogues[1,2] we were interested in the conversion of the Diels–Alder adduct (**1**) into the corresponding alcohol (**6**) under mild conditions. We have, however, found that (**1**) under acidic conditions undergoes a facile rearrangement to produce the dihydrobenzofuran (**11**) in 99% yield. This transformation, which presumably involves a selective cleavage of the 4a,5 carbon–carbon bond,[3] has received relatively little attention[4–6] in spite of its synthetic potential. Only recently Kraus[7] has reported the use of a similar base-catalysed rearrangement in the synthesis of two naturally occurring pyranquinones.

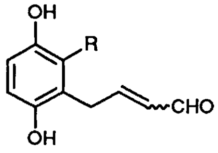
In order to explore the scope of the above rearrangement we have examined the behaviour of various Diels–Alder adducts structurally related to (**1**) and the results are described herein.



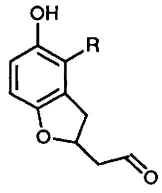
(**1**) R = Ac
(**2**) R = CHO
(**3**) R = CO2Me
(**4**) R = CN
(**5**) R = NO2



(**6**) R = Ac
(**7**) R = CO2Me
(**8**) R = NO2



(**9**) R = CHO (*E*)
(**10**) R = CN (*E* + *Z*)



(**11**) R = Ac
(**12**) R = CHO
(**13**) R = CO2Me
(**14**) R = NO2

A range of such angularly substituted adducts (**2**)–(**5**), obtained from the corresponding substituted benzoquinone and (*E*)-1-trimethylsilyloxybuta-1,3-diene,[8] were treated with hydrochloric acid in water–THF (1:9), at room temperature.

First, the adducts (**2**)–(**5**) were allowed to react under the same conditions as those under which the rearrangement of the adduct (**1**) into (**11**) was observed. A typical experimental procedure is as follows: to a stirred solution of the adduct (**1**) (740 mg, 2.35 mmol) in water–tetrahydrofuran (1:9; 15 ml) was added 6 drops of 1.3M hydrochloric acid. After 2.5 h at room temperature, the mixture was diluted with water (30 ml) and extracted with chloroform (30 ml). The organic layer was washed with water (2 × 30 ml), dried ($MgSO_4$), and evaporated to furnish (**11**) as a yellow solid (550 mg, 99%), m.p. 82–84 °C (from hexane);† δ_H(100 MHz; $CDCl_3$) 2.56 (3 H, s, COMe), 2.70–3.30 (3 H, m, 1′-H and 3-H), 3.75 (1 H, dd, *J* 18, 10 Hz, 3-H′), 5.00–5.50 (1 H, m, 2-H), 6.80 (1 H, d, *J* 9 Hz, 6-H), 6.96 (1 H, d, *J* 9 Hz, 7-H), 9.90 (1 H, br s, CHO), and 12.20 (1 H, s, OH). Under these conditions, adducts (**3**) and (**5**) were hydrolysed to the corresponding alcohols (**7**) (91%) and (**8**) (97%), respectively. In contrast, acidic treatment of the adducts (**2**) and (**4**) gave the aryl substituted crotonaldehydes (**9**) (96%) and (**10**) (70%), respectively.

When the adducts (**2**), (**3**), and (**5**) were treated in a similar way but using 8.0M hydrochloric acid the dihydrobenzofurans (**12**), (**13**), and (**14**) were obtained in 73, 70, and 88% yields, respectively.

It should be noted that the alcohol (**8**) also underwent the rearrangement to the dihydrobenzofuran (**14**) when its purification was attempted by column chromatography on silica gel, using chloroform as eluant.

All these results indicate that the rearrangment of the adducts (**1**)–(**3**) and (**5**) to the dihydrobenzofurans (**11**)–(**14**) involves a sequence which is probably initiated by the hydrolysis of the TMSO group followed by fission of the 4a,5 carbon–carbon bond in the corresponding alcohols and cyclisation.

The above results prompted us to examine the behaviour of adduct (**15**), obtained from naphthodiquinone and (*E*)-1-trimethylsilyloxybuta-1,3-diene.[8] Acid-treatment of (**15**) for 1 h, under the above mentioned conditions, afforded the corresponding alcohol (**16**) in 68% yield. Additional attempts to effect the rearrangement of alcohol (**16**), under a variety of reaction conditions, led only to the unchanged starting material, no rearrangement products being detected.

Taking into account formation of the furan (**14**) by rearrangement of the alcohol (**8**) on silica gel, we studied the behaviour of the alcohol (**16**) under similar conditions. Interestingly, when compound (**16**) was filtered through silica gel using chloroform stabilised with 1% ethanol, the furan derivative (**17**) was isolated in moderate yield. Moreover, compound (**17**) was prepared in 70% yield by stirring (**16**) with silica gel in chloroform–ethanol (3:1).

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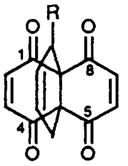
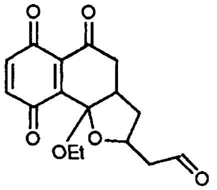
† Satisfactory spectroscopic and analytical data were obtained for all new compounds.



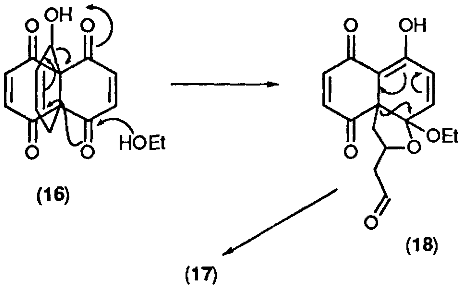
(15) R = $OSiMe_3$
(16) R = OH



(17)

In the absence of ethanol, the furan derivative (**17**) was not formed from (**16**). This fact was also established in an additional experiment in which the alcohol (**16**) was adsorbed on silica gel and eluted with pure chloroform (HPLC grade, stabilized with *p*-cymene). Under these conditions no reaction products were detected by TLC, only the unchanged alcohol (**16**) being recovered.

The transformation of the alcohol (**16**) into the furan derivative (**17**) can be rationalized in terms of the intermediate (**18**), generated by a concerted rearrangement in which formation of the furan ring and the cleavage of the carbon–carbon bond are induced by ethanol attack on the carbonyl group at the 5-position. The intermediate (**18**) presumably undergoes an alkyl sigmatropic [1,5] shift to give the product (**17**). These transformations are shown in the Scheme.



Scheme.

There are examples reported in the literature of reactions of anthracenediquinone and naphthalenediquinone with 1,1-bis(*O*,*O*-substituted) dienes.[9] These reactions have been interpreted as Michael-type additions on the basis of the reaction of similar *O*-silylated ketene acetals and because no Diels–Alder adducts were observed as intermediates. The present results demonstrate, however, the formation of such Diels–Alder type adducts with 1-trimethylsilyloxybuta-1,3-diene followed by an acid-catalysed carbon–carbon bond fission to give rearranged products. Therefore, this two-steps process may not be excluded as an alternative interpretation to the proposed direct Michael addition for the above mentioned examples.

The rearranged products reported here may be valuable intermediates in organic synthesis, especially compounds of type (**17**) as appropriate BC synthons for the elaboration of anthracyclinones.

Acknowledgements

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