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Contrasting Reactivity in Lewis Acid-Promoted Reactions of Thio- and Silyl-Allenes with 1,4-Benzoquinones

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Abstract: In Ti(IV)-promoted reactions with 2-methoxy-1,4-benzoquinones 3, thioallenes 1 give 2+2 and/or 3+2 products via attack on a C=C moiety of the quinone, whereas silylallene 2 gives products derived from attack on a carbonyl group of the quinone.

Lewis acid-promoted reactions of various alkenyl systems with 1,4-benzoquinones are remarkably versatile providing selective access to several different types of products. Diels-Alder products are formed in reactions with dienes,^{1a} and bicyclo[4.2.0]octenediones, bicyclo[3.2.1]octenediones, and/or 2,3-dihydrobenzofuranols have been found in reactions with styrenyl systems.^{1b-f} Some electron-rich alkenes yield products derived from 1,4-addition and allylsilanes and -stannanes give products of 1,2- or formal 1,4-addition, depending upon substituents present on the reactants.² As an unexplored area, we became interested in potential Lewis acid-promoted reactions of quinones with allenyl systems. Thioallenes have been shown to give products of formal 2+2 cycloaddition with various Michael acceptors³ and silylallenes react with α , β -unsaturated ketones in the presence of Lewis acids to give 3-silyl-2-cyclopentenyl ketones in a useful 3+2 annulation procedure.^{4,5} Seeking to develop similar processes utilizing quinones as the α , β -unsaturated carbonyl component in these reactions, we have examined Lewis acid-promoted reactions of thioallene 1 and silylallene 2 with various 2-alkoxy-1,4-benzoquinones. Our preliminary results reported herein indicate that the two allenes give very different kinds of products; thioallene 1 products derived form them, via attack on a C=C moiety of the quinone, whereas silylallene 2 gives 6 and 7, or products derived from them, via attack on a carbonyl group of the quinone.



Treatment of quinones 3a/b with Ti(IV), as mixtures of TiCl₄:Ti(OiPr)₄, in CH₂Cl₂ at -78 °C followed by addition of allene $1a^6$ gave, after quenching with solid NaHCO₃/iPrOH and then H₂O, extraction (CH₂Cl₂) and chromatography (silica gel, acetone/hexanes), cyclobutanes $4a/b^{7a}$ (Scheme I and Table 1). Reaction of allene 1b with quinone 3a gave cyclobutane $4c^{7a}$ and benzofuran 5c.^{7b} Upon warming the reactions to -20 °C or room temperature, the major products were benzofurans 5^{7b} as inseparable mixtures of double bond isomers in which the *E*-isomer predominated (>2:1). Reaction of quinone 3c with allene 1a required warming to room temperature and gave only the benzofuran product 5d,^{7a} exclusively as the opposite Z-isomer, presumably for steric reasons. Selective decoupling of the allylic methyl groups in 4a identified the H-6 and H-8 NMR signals and, by default, the H-1 signal as well. The position of the C-3 methoxy group in 4a was then determined by an HMBC experiment and the stereochemistry assigned by ¹H-¹H NOE experiments.⁸ The substitution pattern and stereochemistry in 4b/c were assigned by spectral comparison with 4a and confirmed by single crystal X-ray analysis of 4c. In benzofurans 5a-c, the appearance of H-4 and H-7 as noncoupled singlets supports the assignment of the C-6 methoxy group. The stereochemistry in benzofurans 5 was again established from ¹H-¹H NOE experiments.⁸



Table 1. Ti(IV)-Promoted Reactions of Thioallenes 1a/b with Quinones 3.

Entry	Allene	Quinone	Lewis acid ^a	Temp (°C)	Product(s) (% yield) ^b
1	la	3a	2.8:1 TiCl4:Ti(OiPr)4	-78	4a (29)
2	1a	3b	3:1 TiCl4:Ti(OiPr)4	-78	4b (53)
3	1b	3a	2:1 TiCl4:Ti(OiPr)4	-85	4c (35) + 5c (21)
4	1a	3a	3:1 TiCl4:Ti(OiPr)4	-78 -> -20	5a (69)
5	1a	3b	2.8:1 TiCl4:Ti(OiPr)4	-78 -> -20	5b (64)
6	1b	3a	2.8:1 TiCl4:Ti(OiPr)4	-78 -> -20	4c(15) + 5c(39)
7	1a	<u>3c</u>	1:1 TiCl4:Ti(OiPr)4	<u>-78 -> rt</u>	5d (37)

^aOne equiv Ti(IV) with respect to quinone. ^bNot optimized.

Mechanistically, these reactions probably proceed via regioselective nucleophilic attack of the thioallene on the Lewis acid-activated quinone to give carbocations 8/9 (LA=Ti⁺³); at low temperature, 8 closes to cyclobutanes 4a-c, whereas at higher temperature, benzofuran 5 is found through C-O bond formation and loss of H⁺.⁹ In related experiments, treatment of 4a/b with p-TsOH/CH₂Cl₂ at room temperature effects their rearrangement to 5a/b (~62/85%), again as a mixture of isomers, presumably through carbocation 8 (LA=H). Intermediate carbocation 9 gives only benzofuran 5d via C-O bond formation and loss

of H+, most likely due to steric hindrance to C-C bond formation.

On the other hand, TiCl₄-promoted reactions of allenylsilane 2^{4f} with quinones 3a/c gave the spirocyclic ethers 10/11 and 13/14, respectively, as major products, accompanied by homopropargylic alcohols 12 and 15 (Scheme II);⁷ similar products are found in Lewis acid-promoted reactions of silylallenes with aldehydes.^{4e} Although ketal 11 was formed as a single diastereomer, the relative configuation at C-1 and C-9 has not been assigned. The positions of the substituents in spirocyclic ethers 10/13, ketal 11 and homopropargylic alcohol 12 were assigned from HMBC NMR experiments.¹⁰ The structure of alcohol 15 was assigned by spectral comparison to alcohol 12 and ether 13, and that of desilylated dihydrofuran 14 was assigned by spectral comparison to 13; in the latter comparison, the major differences were the absence of a TMS group in 14 along with the appearance of a signal at 4.63 ppm which was coupled to the C-7 CH₂ in the ¹H NMR (all other spectral data was as expected).



The formation of spirocyclic ethers 10 and 13 probably involves 1,2-alkylation of the Ti(IV)-quinone complex 16 by the allenylsilane to give the β -silylcarbocation 17 which can be represented as 17a, b or c. A [1,2]-silyl group migration with C-O bond formation, i. e. from 17a/b, or C-O bond formation in 17c, then gives 10/13. Alternatively, desilylation of 17a-c, perhaps by chloride ion present in the reaction mixture, followed by aqueous workup accounts for the formation of homopropargylic alcohols 12/15. Compound 14 may be formed from 13 by desilylation under the reaction conditions or by reaction with HCl generated during quenching the reaction. Similarly, ketal 11 may be formed from 10 by prototopic desilylation and acid-catalyzed addition of iPrOH on workup.



We continue to explore the generality, limitations and synthetic utility of these reactions.

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6. Allenes 1a/b were prepared by reaction of 3-methoxythiophenol and thiophenol, respectively, with 3-chloro-3,3-dimethylpropyne in the presence of K2CO3 and KI in refluxing acetone.

7. a) These compounds exhibited expected spectral data (300 HMz¹H NMR, 75 MHz¹³C NMR, IR and mass) and exact mass and/or elemental analyses. b) Identified by NMR and by desulfurization (nickel boride, EtOH/H₂O, gentle reflux) of the mixture to a 1:1 mixture of **18** and 6-methoxy-2,2,3-trimethyl-2,3dihydrobenzofuran-5-ol (87%) followed by further reduction of this mixture (H₂, Pd/C, EtOH, rt) to afford only the latter compound (91%).



8. Selected data from an HMBC experiment on 4a (Fig. 1) and ${}^{1}H{}^{-1}H$ NOE experiments on 4a (Fig. 2), 5c (Fig. 3) and 5d (Fig. 4, see below).

9. A preference for cyclobutane formation at low temperature in Ti(IV)-promoted reactions of styrenes with quinones, which are thought to proceed via intermediates similar to 8/9, has been noted; see references 1b/f.

10. Selected data from HMBC experiments on 10-13 (Fig. 5).



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