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# 2-TRIMETHYLSILYLOXY-1,3-BUTADIENE, A NEW REACTIVE DIENE. PREPARATION AND REACTIONS

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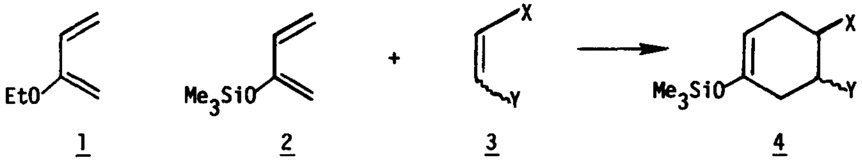
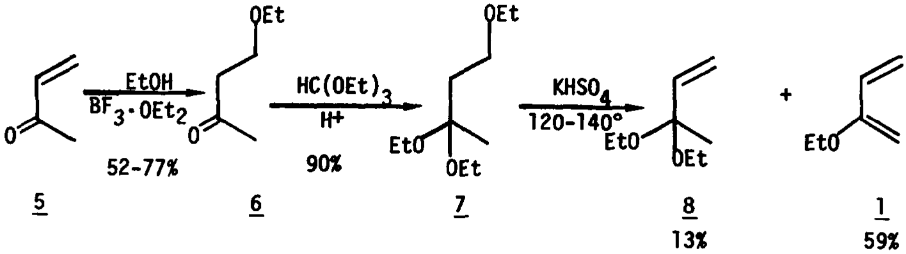
## Introduction

The Diels-Alder reaction is one of the most widely employed and most successful preparative reactions in the hands of synthetic chemists today. The thorough understanding of the stereochemical (Alder endo transition state rules[1]) and regiochemical (concerted but non-synchronous formation of bonds[2]) selectivity of the Diels-Alder reaction which exists today allows one to construct a large variety of specifically substituted cyclohexene derivatives. However the applicability of this reaction to the construction of highly useful cyclohexanone derivatives is rather limited. Because the usual reagent developed for this process, 2-ethoxy-1,3-butadiene, 1, is cumbersome to prepare[3] and possesses very low synthetic flexibility, there existed a need for a new reagent of this type which would circumvent these problems. We report now a solution to this problem with the development of the compound 2-trimethylsilyloxy-1,3-butadiene 2 as a reactive diene component in Diels-Alder reactions.[4] In particular we wish to indicate four important points about this 2-oxygenated-1,3-butadiene: a) the ease of preparation of the diene; b) its reactivity in Diels-Alder reactions; c) the susceptibility of its adducts 4 to various hydrolytic conditions; and d) the synthetic versatility of the adducts 4 especially with regard to the silyl enol ether functionality.

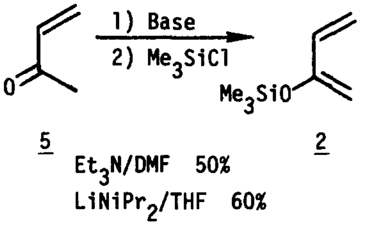


## Preparation of Diene

2-Ethoxy-1,3-butadiene, 1, is usually prepared from methyl vinyl ketone 5 in three steps by acid- or base-catalyzed addition of ethanol, formation of the diethyl ketal, and finally acid-catalyzed elimination of two moles of ethanol[5] to afford the desired ethoxybutadiene 1 and 3,3-diethoxy-1-butene 8 in approximately a 4:1 ratio.[3] This mixture must then be separated by an efficient distillation technique, usually fractional distillation using a spinning-band.[6] In

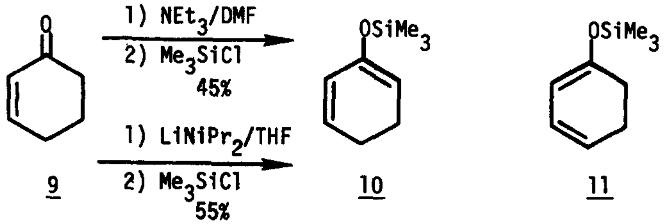


contrast to this rather tedious process, the silyl ether 2 is readily available from methyl vinyl ketone 5 in one easy step. Conia has reported that a solution of 5, triethylamine, and trimethylsilyl chloride in DMF gives the enol ether 2 in 50% yield.[7,8] We have found this preparation very useful especially for large quantities, e.g., up to ~ 1/2 molar. However, on a smaller scale, higher yields (60-65%) can be obtained using lithium diisopropylamide as the base in THF solution. This latter method also allows for the production of the 2-substituted-1,3-dienes from enones with both α' and γ protons.[9] We have found that cyclohexenone 9 under either "kinetic" or "thermodynamic" conditions can be converted into the 2-isomer 10 with none of the 1-isomer 11 being formed.



5 2

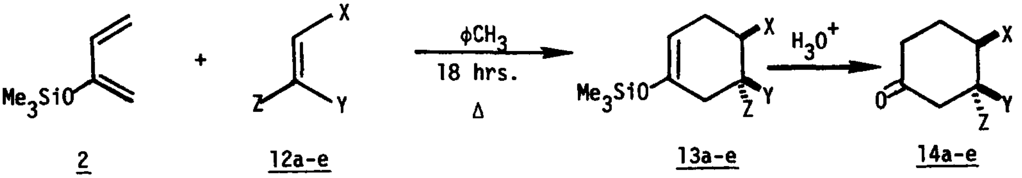
$Et_3N/DMF$ 50%
$LiNiPr_2/THF$ 60%



9 10 11

## Diels-Alder Reaction

2-Ethoxy-1,3-butadiene 1 has been utilized in Diels-Alder reactions quite often. In general it affords moderate yields (35-70%) with dienophiles containing one electron-withdrawing group and somewhat higher yields (50-80%) with dienophiles having two electron-withdrawing groups.[10] These results depend very much on conditions, so that at high temperature and high pressure somewhat better results can be obtained. 2-Trimethylsilyloxy-1,3-butadiene 2 possesses approximately the same reactivity in Diels-Alder reactions with several dienophiles 12a-e to afford the adducts 13a-e as indicated in the Table.[11] The yields of purified products are essentially identical to those obtained with 2-ethoxy-1,3-butadiene 1 and the same dienophiles under similar conditions. However, one difference in reactivity between 1 and 2 was noted. In cases where positional isomers are possible, i.e., 13a and 13b, only the isomer shown (the so-called para isomer) was obtained (>95%). This is in contrast to the usual results with 2-alkoxy-1,3-butadienes which normally yield a mixture in which the major para isomer is accompanied by small amounts of the meta isomer arising from the opposite orientation in the Diels-Alder addition.[10, 12]



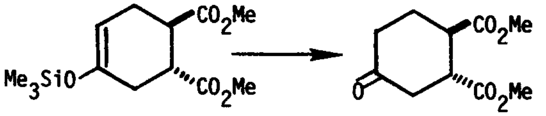
2 12a-e 13a-e 14a-e

| Compound | X | Y | Z | Yield of 13 (%)$^a$ |
|---|---|---|---|---|
| a | $COCH_3$ | H | H | 60 |
| b | $CO_2Me$ | H | H | 35 |
| c | $CO_2Me$ | H | $CO_2Me$ | 71 |
| d | $CO_2Et$ | H | $CO_2Et$ | 77 |
| e | $CO_2Et$ | $CO_2Et$ | H | 39 |

$^a$ Yields are for isolated purified compounds and have not been optimized.

## Hydrolysis of Adducts

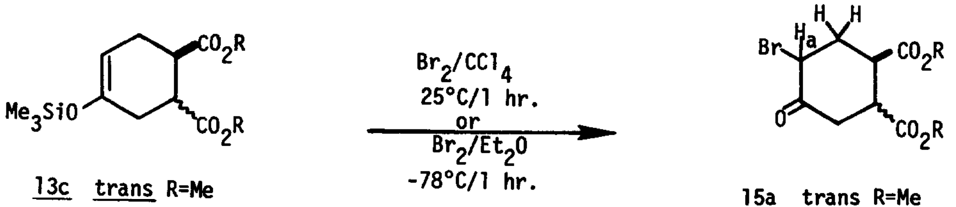
The alkyl enol ethers resulting from the Diels-Alder reaction of 1 with dienophiles are hydrolyzed to ketones only in the presence of strong acid.[13] This is due to the fact that in this case hydrolysis must proceed by a mechanism involving protonation of the double bond followed by attack of water and eventual loss of ethanol. However, in the case of the silyl enol ethers 13 although acidic hydrolysis is still possible, one can now effect hydrolysis under essentially neutral conditions by nucleophilic cleavage of the oxygen-silicon bond. Thus Diels-Alder adducts 13 can be hydrolyzed in essentially quantitative yield to the ketones 14 under extremely mild conditions. For example the dimethyl fumarate adduct 13c could be converted to the ketone 14c by merely stirring in methanol or under totally non-aqueous conditions in >95% yield.



| Conditions | Yield |
|---|---|
| MeOH/25°C/24 hrs. | 95% |
| $MeOH/CF_3CO_2H$/25°C/2 hrs. | |
| $KF\cdot 2H_2O$/THF/25°C/5 hrs. | |

## Versatility of Adducts

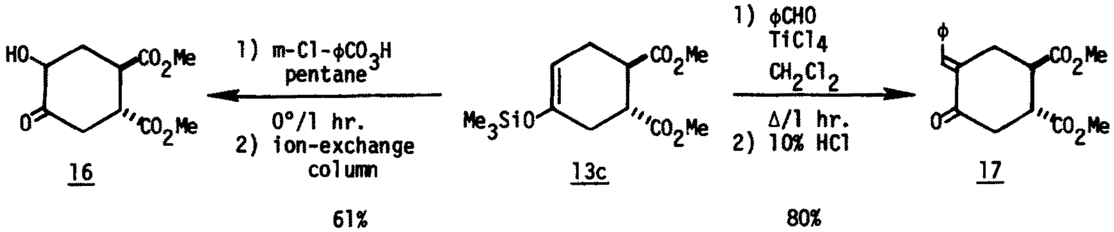
Attempted functionalization of the ketones 14 derived from the Diels-Alder adducts 13 led to mixtures of regioisomers since the two possible enols (and enolates) derived from the ketone are formed at nearly equal rates and in nearly equivalent proportions. However the Diels-Alder adducts 13 contain only one of the two possible silyl enol ether derivatives of the ketones 14. Therefore, it was of interest to investigate whether this enol ether grouping could be utilized to introduce functionality into the molecule specifically at the enol carbon. All attempts at alkylating the specific enolate ion (presumably formed via addition of MeLi, $LiNH_2$, $Me_2CuLi$, $R_4NF$, etc. to 13) proved fruitless, due to complications arising from the presence of the ester functions in the molecule. However, the enol silyl ethers 13 successfully underwent direct bromination, hydroxylation, and Lewis acid-catalyzed aldol condensation. For example, compounds 13c-e were clearly monobrominated (upon treatment with $Br_2$ in $CCl_4$ at 25°C or in $Et_2O$ at -78°C for 1 hour) to afford the bromides 15a-c in good yield. That the bromination had taken place at the expected carbon



| | | |
|---|---|---|
| 13c | trans | R=Me |
| 13d | trans | R=Et |
| 13e | cis | R=Et |

| | | | |
|---|---|---|---|
| 15a | trans | R=Me | 70% |
| 15b | trans | R=Et | 46% |
| 15c | cis | R=Et | 56% |

could be inferred from the 100 MHz NMR spectrum of these compounds which showed a clear doublet of doublets for Ha, the proton $\alpha$ to Br (e.g. in the crystalline 15b, mp. 110-112°C, Ha appears at $\delta$ 4.63, dd J=5, 11). Treatment of 13c with peracid followed by ion exchange chromatography (DOWEX Ag-1-X8, basic) afforded the $\alpha$-hydroxy ketone 16 in 61% yield.[14] Carbon-carbon bond-forming processes could also be effected. For example, refluxing a $CH_2Cl_2$ solution of 13c, benzaldehyde, and $TiCl_4$ for 1 hour, followed by 10% HCl workup afforded the dehydrated aldol product 17 in excellent yield accompanied by small amounts of the bis-aldol product.[15]



## Acknowledgement

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