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A VERSATILE ROUTE TO MIXED VINYLKETENE ACETALS : USE OF 1-t-BUTYLDIMETHYLSILOXY-1-ETHOXY BUTADIENE IN CYCLOHEXENONE SYNTHESIS

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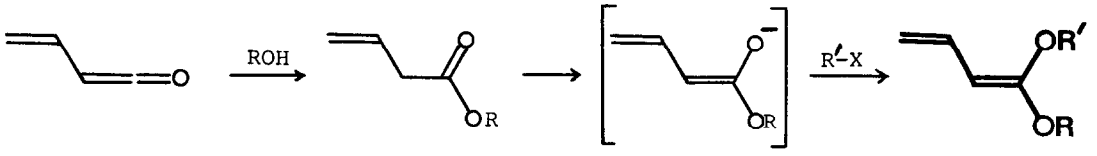
Abstract: The successful entry to the diverse mixed vinylketene acetals **3** extends the participation of these intermediates in cyclohexenone synthesis.

The capacity of vinylketene equivalents[2] and recently[3] even (trimethylsilyl)vinylketene to react as diene components in Diels-Alder reactions has considerably facilitated the synthesis of cyclohexenone derivatives. We became interested in the application of parent vinylketene equivalents **3** (Scheme 1) for this purpose but found that the only known examples **3a** ($R=R'=CH_3$)[4] and **3b** ($R=CH_2CH_3$, $R'=Si(CH_3)_3$)[5] have not been greatly exploited in Diels-Alder reactions. The vinylketene acetal **3a** reacts with both reactive dienophiles[6] and ketones[7] whilst the more easily prepared mixed acetal **3b** has not been used for Diels-Alder cycloaddition, although recently[8a] a 2-substituted derivative of **3b** was used which resulted in the generation of an aromatic ring. The most apparent limitations of these dienes are: (i)



1 2 3

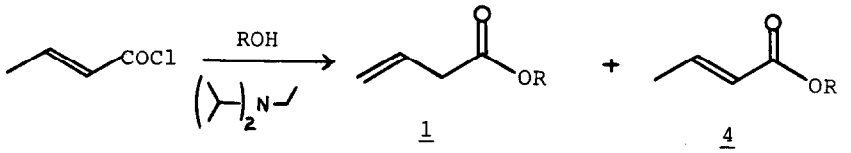
Scheme 1

the sensitivity of the Diels-Alder adduct acetal groups to 1,2-elimination,[2a,8a] occurring at room temperature when the adjacent carbon bears a relatively acidic hydrogen, (ii) the facile 1,5-sigmatropic shift[8b] of the trimethylsilyl group.

In a study to extend the utility of these intermediates in cyclohexenone synthesis and possibly to intramolecular Diels-Alder chemistry we developed a new route (Scheme 1) for the preparation of parent vinylketene acetals **3** that permits the variation of R and R'. We now describe that route where $R'=SiMe_2Bu\text{-}t$ group (Scheme 1) and report a preliminary result of the present study.

The introduction of the group R (Scheme 1) was achieved by acylating its corresponding alcohol with vinylketene. The reported[9] conditions, i.e. crotonoyl chloride/triethylamine/THF resulted in low yields (~ 30%) for volatile[10] cases owing to the difficulty of separation from tetrahydrofuran. When the solvent was changed to dichloromethane little acylation was observed. A simultaneous change of base to diisopropylethylamine (DIPEA), however, gave excellent results and a range of alcohols were acylated using the following procedure: to an

ice-cooled solution of crotonoyl chloride (9.6 mmol) in dichloromethane (5 ml) was added the alcohol (9.6 mmol), followed by DIPEA (11.5 mmol) over 5 min. The mixture was kept in the cold for 30 min and 2,4-dimethylaminopyridine (2.4 mmol, required only in cases where equimolar equivalents of reagent and substrate is used) was added. The work-up was effected immediately[11] by pouring into dilute hydrochloric acid and extraction with ether. Distillation gave the pure products with yields and isomer distribution as shown in the Table (N.B. product **1f** was not volatile).



1 4

Table.

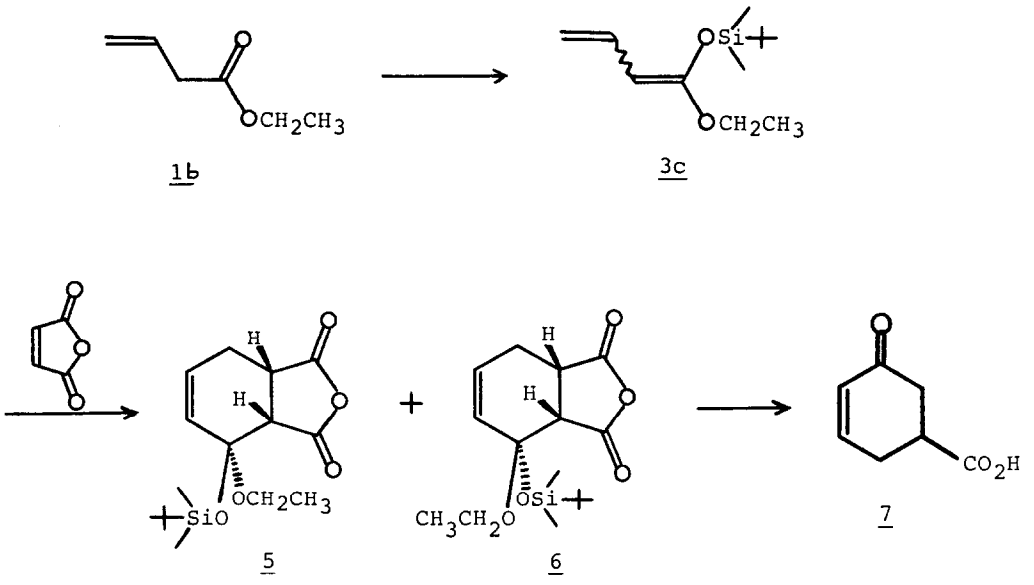
	R	Isolated Yield of butenoate esters	Ratio 1 : 4
a	CH_3-	52%	63 : 37
b	CH_3CH_2-	55%	90 : 10
c	CH_2-	63%	93 : 7
d	$(CH_3)_2CH$-	55%	92 : 8
*e	$(CH_3)_3C$-	60%	96 : 4
*f	CH_2CH_2-	90%	95 : 5

* 2 molar equivalents of reagent was used and addition of 2,4-DMAP was not necessary.

In generating the parent dienolate **2** from ethyl-2-butenoate the problems of self-condensation[12] and nucleophilic addition[13] of the base were overcome by the addition of HMPA. Although 3-butenoate esters **1** have not been used previously to generate the parent dienolate **2** it was expected that such problems would not be encountered provided that proton transfer between the dienolate and unreacted ester was slow. As expected, proton abstraction from ethyl-3-butenoate **1b** with LDA or LiCA proceeded smoothly at -78°C without the addition of HMPA and the vinylketene acetal **3c** (Scheme 2) was prepared simply in the following way; to a solution of ethyl-3-butenoate (0.2g, 1.75 mmol) in tetrahydrofuran at -78°C was added over 10 min a solution of lithium cyclohexylisopropylamide (2.0 mmol). The mixture was kept at -78°C for 30 min, t-butyldimethylsilylchloride (0.35g, 2.3 mmol) was added, the mixture warmed to r.t., HMPA[14] was added and the reaction mixture was worked up after 3hr. The crude product was essentially pure but was distilled in a short path distillation apparatus (base washed glassware), to give the clear colourless vinylketene acetal **3c**[15] b.p. 82-86°C, 1.5mm (0.3g, 75% isolated yield) as a 2:1 mixture of E/Z isomers. The diene was stable in solution at -15°C for long periods. Similar alkylation of esters **1** establishes the versatility of this route to vinylketene acetals **3**.

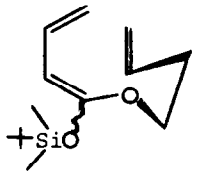
In a test of the utility of these species the mixture of dienes **3c** was heated with

maleic anhydride (equimolar quantities) in carbon tetrachloride at 70°C for 30 min (Scheme 2). To our surprise a 2:1 mixture of adducts[15] **5**, m.p. 69-70°C and **6**, m.p. 116-117°C was obtained with ~10% of impurity according to ^{1}H n.m.r. spectral analysis; none of the 1,2-elimination product could be detected. The respective isomers were assigned on the



Scheme 2

basis of the large upfield shift[16] of the ^{1}H n.m.r. signals of the α-group hydrogen atoms induced by the anhydride carbonyl. A significant amount of decomposition (~50%) occurred during the chromatographic separation of the isomers on deactivated silica gel, so in practice the purification consisted of rapid filtration through a short column of deactivated alumina with ether:petroleum ether, 1:1, yielding the mixture of adducts **5** and **6** in 60-70% yield. This adduct mixture was readily hydrolysed (10% aq HCl/THF, 1:4, r.t. 6 hr) to give as the only product the 5-substituted cyclohexenone **7**, m.p. 83-84°C (Lit.[17] m.p. 85°C) in 80% yield. The mild and unambiguous nature of this route to **7** provides an appealing alternative to the existing procedures[17,18] and shows that vinylketene acetals bearing siloxy substituents can be used in cyclohexenone synthesis.



8

The potential for extending this methodology to intramolecular Diels-Alder reactions was demonstrated by the preparation of **8**, clear liquid, b.p. 65-85°C/0.001 mm, from 1f. Further work is underway to prepare analogues of **8** with more suitable dienophilic moieties.

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15. The structures of all new compounds were consistent with their ^1H n.m.r. spectra, infrared spectra, high resolution mass spectra, and microanalyses.
16. The chemical shift of the methylene protons of the ethoxy group of 5 occurred at δ 1.05, (in 6 at δ 1.25) and the signal for the methyl groups attached to silicon of 6 occur at δ 0.05 and 0.12 (in 5 as one signal at δ 0.20).
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