by GLC): IR (neat) 1690 (s), 1080 (m), 1025 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 4.00 (t, J = 7 Hz, 1 H), 4.5–4.8 (m, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.07, 22.51, 24.01, 25.08, 29.92, 31.36, 32.33, 34.24, 36.30, 40.64, 87.68, 95.03, 155.03. Its stereoisomeric purity is ca. 97% by ^{13}C NMR analysis, and its purity by GLC is ca. 97%.

The above results point to a significant difference between this new approach to cyclic enol ethers and the base-induced β elimination of halo ethers.[2] Namely, in contrast with the latter reaction, in which one of the two diastereomers is either inert or of low reactivity to an external base, hence requiring its chromatographic separation prior to the final elimination step, the former can proceed readily with either diastereomer, presumably because β elimination of **17** does not require attack by an external base.

We then turned our attention to the synthesis of enol lactones **2**. Treatment of **7a** with Jones reagent gave **9a** (82%). Its treatment with MCPBA directly gave a cyclization product **10a** (ca. 80%). To our chagrin, direct treatment of **10a** with either KH suspended in THF or $BF_3{\cdot}OEt_2$ in CH_2Cl_2[7b] did not give the desired product **2a** in any significant amount (<2–3% by GLC). A few other bases, such as $KN(SiMe_3)_2$, were also totally unsatisfactory. On the other hand, acetylation of **10a** followed by treatment with n-Bu_4NF[17] in HMPA cleanly produced **2a**[16] (72% based on **10a**, E/Z ratio of 99) presumably via anti elimination:[18] IR (neat) 1800 (s), 1700 (s), cm^{-1}; ^1H NMR ($CDCl_3$), Me_4Si) δ 1.8–2.1 (m, 2 H), 2.5–3.1 (m, 4 H), 5.22 (tt, J = 2, 7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 103.31, 149.51, 174.94. To our knowledge, this represents the first reported synthesis of an (E)-γ-alkylidene γ-lactone. In an analogous manner, **2b** was prepared in 85% yield (Z/E ratio of 99) via **9b** (83%) and **10b** (92%). The spectral data for **2b**[16] are as follows: IR (neat) 1800 (s), 1700 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_3Si) δ 1.9–2.3 (m, 2 H), 2.3–3.1 (m, 4 H), 4.60 (t, J = 7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_3Si) δ 104.91, 147.70, 175.78.

The following conversion of **9a** into **2a** is representative. To **9a** (1.21 g, 5 mmol) in 10 mL of CH_2Cl_2 was added MCPBA (1.04 g, 6 mmol) in 30 mL of CH_2Cl_2 for 2 h at 0 to 25 °C. Quenching (aqueous sodium sulfite), extraction (Et_2O), washing (aqueous sodium sulfite), drying ($MgSO_4$), and distillation gave 1.01 g (78% yield) of **10a**, 130–135 °C (0.2 mm). Acetylation of **10a** (0.77 g, 3 mmol) was carried out with AcCl (0.35 g, 4.5 mmol) and pyridine (0.36 g, 4.5 mmol) in THF (−78 to +25 °C, 8 h). Quenching (aqueous NH_4Cl), extraction (Et_2O), drying ($MgSO_4$), and concentration under reduced pressure yielded the acetate which was ≥98% pure by GLC and ^{13}C NMR. Without further purification 0.60 g (2 mmol) of the acetate dissolved in HMPA was added to n-Bu_4NF (3 mmol) in THF at 0 °C, and the mixture was stirred for 0.5 h at 25 °C. Quenching-extraction (water-pentane), drying ($MgSO_4$), and concentration provided 0.28 g (72%) of **2a**, which was stereoisomerically 99% pure but was contaminated with a minor unidentified compound (ca. 5%). The product can be further purified by low temperature distillation without being accompanied by stereoisomerization.

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Supplementary Material Available: ^1H and ^{13}C NMR, IR, and mass spectral data as well as purity figures based on ^{13}C NMR and GLC (5 pages). Ordering information is given on any current masthead page.

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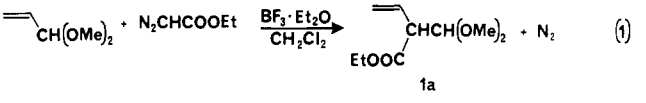
Homologation of Acetals of α,β-Unsaturated Carbonyl Compounds with Diazo Esters. Synthesis of Acetals of β,γ-Unsaturated Carbonyl Compounds

Summary: β,γ-Unsaturated acetals are conveniently prepared in good yields by boron trifluoride etherate catalyzed homologation of acetals of α,β-unsaturated aldehydes with ethyl diazoacetate.

Sir: There are few preparative methodologies that utilize a specific bond migration as an integral feature of the synthetic transformation.[1] In those most useful for organic synthesis, migration takes place unidirectionally to a developing electrophilic center to produce a relatively stable carbocation.[2] Aldehyde and ketone homologation reactions by diazo compounds,[3-7] like the related pinacol rearrangement,[8] take advantage of carbocation stabilization by an adjacent oxygen. However, mixtures of products are generally obtained when two different groups can undergo migration to the developing electrophilic center, epoxide formation competes with bond migration in homologation reactions when diazomethane is employed,[3] and α,β-unsaturated aldehydes and ketones are not amenable to homologation with diazo compounds.[6] We now report a new design for aldehyde and ketone homologation reactions through which acetals or ketals of α,β-unsaturated carbonyl compounds are transformed into acetals or ketals of β,γ-unsaturated carbonyl compounds.

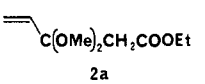
Treatment of acrolein dimethyl acetal with ethyl diazoacetate in the presence of a catalytic amount of boron trifluoride etherate results in the product (**1a**) from formal insertion of the carboethoxy carbenoid group between the vinyl and acetal carbons (eq 1). Formal acetal carbon–



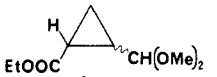
(1)

1a

hydrogen insertion (**2a**) and cyclopropane formation (**3a**)



2a



3a

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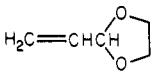
Table I. Product Yields from $BF_3 \cdot Et_2O$-Catalyzed Reactions of Acetals and Ketals with Ethyl Diazoacetate[a]

run	acetal (ketal)	temp, °C	yield of 1-4, %	rel yield, % C-C insertion, 1	rel yield, % C-H insertion, 2	rel yield, % cyclopropane 3 (t/c ratio)	1/2 ratio	1/3 ratio
a	H_2C=CHCH(OMe)$_2$	0	72[b]	68	14	18 (1.03)	5.0	3.6
		−15	70	75	10	15 (1.05)	7.4	5.1
b	PhCH(OMe)$_2$	25	85[c]	97	3	<1 (4b)	32	
		25[d]	79	92	4	4 (4b)	23	
c	(E)-PhCH=CHCH(OMe)$_2$	0	70[e]	100	<1	<1	>100	>100
		−15	61	100	<1	<1	>100	>100
d	PhC≡CCH(OMe)$_2$	25	22[f]	100	<1		>100	
e	PhC(OMe)$_2$CH$_3$	25	88[g]	63	12[h]	25 (4e)	4.8	
		0	88	62	15[h]	23 (4e)	4.1	
f	H_2C=CHCH(OEt)$_2$	0	36[i]	32	54	14 (1.04)	0.59	2.4
		−15	51	50	26	24 (1.07)	2.0	2.1
g		−25	58[j]	29	12	59 (1.02)	2.5	0.50

[a] Reactions were performed by dropwise addition of 10.0 mmol of ethyl diazoacetate over 4 h to a cooled solution of 25 mmol of acetal or ketal in 25 mL of freshly distilled dichloromethane containing 0.50 mmol of $BF_3 \cdot Et_2O$. After gas evolution was complete, the reaction solution was extracted, and products were isolated by distillation. Structural analyses were performed on the isolated products by NMR and mass spectral determinations. Elemental compositions of compounds 1 were in agreement with calculated values. [b] Bp 54–56 °C (0.5 torr). [c] Bp 87–89 °C (0.4 torr). [d] 0.5 mol % of $BF_3 \cdot Et_2O$ was employed. [e] Bp 106–109 °C (0.025 torr). [f] Bp 110–113 °C (0.3 torr). [g] Bp 94–96 °C (0.4 torr). [h] Product from methyl migration: ethyl 3,3-dimethoxy-2-methyl-3-phenylpropanoate. [i] Bp 70–72 °C (0.5 torr). [j] Bp 72–76 °C (0.5 torr).

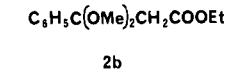
compete with the production of **1a**, but the yields of these products are low relative to that of **1a** and decrease with decreasing temperature. For the reaction performed at −15 °C in dichloromethane, **1a–3a** were obtained in 70% yield, and the product ratios **1a**/**2a** and **1a**/**3a** were 7.4 and 5.1, respectively.

The absence of products from carbon–oxygen insertion (<0.2%) is surprising in view of prior reports that these compounds are the only products obtained from reactions of diazo compounds with acetals and ketals.[9-11] Schönberg and Praefcke have described formation of carbon–heteroatom insertion products as the sole outcome of reactions of acetals and thioacetals with ethyl diazoacetate under conditions remarkably similar to those employed for the formation of **1a**.[12] Their structural interpretation, which is consistent with the intervention of vinyl cations derived from diazocarbonyl compounds[13] but is inconsistent with results from aldehyde and ketone homologation reactions,[6] has not been challenged. this apparent conflict has now been resolved through reinvestigation of the $BF_3 \cdot Et_2O$-promoted reaction of benzaldehyde dimethyl acetal with ethyl diazoacetate. Instead of the previously reported carbon–oxygen insertion product, the formal carbon–carbon insertion product **1b** is actually obtained (eq 2).[14]

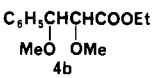
$$C_6H_5CH(OMe)_2 + N_2CHCOOEt \xrightarrow[CH_2Cl_2]{BF_3 \cdot Et_2O} \underset{\displaystyle COOEt}{C_6H_5CHCH(OMe)_2} + N_2 \quad (2)$$

1b

When only 0.5 mol % of $BF_3 \cdot Et_2O$ is employed, rather than the normal 5.0 mol %, the carbon–hydrogen (**2b**) and



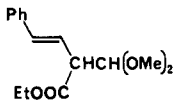
2b



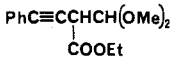
4b

carbon oxygen (**4b**) insertion products are more evident, but even at 25 °C under these conditions the **1b**/**2b** and **1b**/**4b** ratios are greater than 20.

The general applicability of acetal homologation is indicated by the results described in Table I. Dimethyl acetals of α,β-unsaturated aldehydes yield the corresponding carbon–carbon insertion products **1a–d** with a high degree of selectivity. Only **1c** is obtained in the



1c



1d

$BF_3 \cdot Et_2O$-catalyzed reaction of cinnamaldehyde dimethyl acetal with ethyl diazoacetate, and, although the yield of **1d** is low, this is the only volatile product produced from the dimethyl acetal of 3-phenyl-2-propynal. Carbon–oxygen insertion products are not observed,[15] except as minor components in reactions with benzaldehyde dimethyl acetal, and **1** is not subject to double bond isomerization under the reaction conditions employed. With ketals, however, carbon–hydrogen and carbon–oxygen insertion products are significant. Application of this methodology to the dimethyl ketal of 3-buten-2-one produced a complex mixture of products due, in part, to competing elimination of methanol to form 2-methoxy-1,3-butadiene.

The synthetic utility of these homologation transformations was examined by treating equivalent amounts of selected acetals and ethyl diazoacetate in dichloromethane (5 mL/mmol) with 2.5 mol % of $BF_3 \cdot Et_2O$. In this manner, acrolein dimethyl acetal gave a mixture composed of **1a** (78%), **2a** (7%), and **3a** (15%, trans/cis ratio of 1.00) in 51% yield when this reaction was performed at −25 °C.

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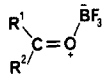
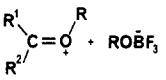
(14) **1b**: ^{1}H NMR ($CDCl_3$) δ 7.65–7.25 (m, Ph), 5.01 (d, J = 8.9 Hz, C*H*(OMe)$_2$), 4.18 (q, J = 7.1 Hz, CH_2O), 3.92 (d, J = 8.9 Hz, PhC*H*COOEt), 3.49 (s, OCH_3), 3.20 (s, OCH_3), 1.25 (t, J = 7.1 Hz, CH_3CH_2O). The mass spectrum of **1b** exhibits a characteristic M − 1 peak at m/e 237, and the base peak at m/e 75 can be attributed to the $(MeO)_2CH$ fragment.
(15) Authentic samples of carbon–oxygen insertion products were employed for GC, NMR, and GC/mass spectral comparisons.

However, nearly quantitative yields of 1 were obtained when the dimethyl acetal of benzaldehyde (**1b**, 98% yield) and cinnamaldehyde dimethyl acetal (**1c**, 95% yield) were exposed to an equivalent amount of ethyl diazoacetate in the presence of 2.5 mol % of $BF_3{\cdot}Et_2O$ at 25 °C. In these latter cases addition of $BF_3{\cdot}Et_2O$ to the combined acetal/diazo compound, rather than addition of ethyl diazoacetate to the acetal/$BF_3{\cdot}Et_2O$ combination (Table I), minimizes polymerization of these acetals and represents the optimum condition for synthetic utilization of this transformation.

Homologation of acetals and ketals is analogous to similar reactions performed with aldehydes and ketones but with three important differences. In aldehyde or ketone homologation reactions, Lewis acid activation of the carbonyl carbon (**5**) is responsible for subsequent addition to



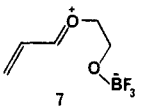
5



6

the nucleophilic diazo compound. However, in acetal or ketal homologation reactions, alkoxide removal by the Lewis acid forms the reactive oxonium salt **6**. Second, the product-forming step in acetal or ketal homologation reactions is the recapture of alkoxide either from $(ROBF_3)^-$ or from another acetal or ketal. In contrast, catalysis of aldehyde or ketone homologation reactions occurs with Lewis acid release from the reaction product and, as a result of the normal greater basicity of the homologation product obtained with ethyl diazoacetate, requires the use of at least 10 times more acid than is effective for acetal or ketal homologation.[6] Lastly, SbF_5-promoted reactions of diazocarbonyl compounds with α,β-unsaturated aldehydes and ketones form cyclopropane derivatives[16] rather than homologation products observed from reactions with acetals of corresponding α,β-unsaturated aldehydes.

The acrolein acetal series (Table I) demonstrates the substantial structural influence of the acetal on the course of Lewis acid catalyzed reactions with diazo compounds. The diethyl acetal is inferior to the dimethyl acetal in both overall yield and selectivity for carbon-carbon bond insertion. With the ethylene acetal of acrolein, however, product yields are higher, but the cyclopropane product is dominant. This reversal of selectivity for nucleophilic attack by the diazo compound suggests intramolecular competition from the BF_3-bound oxygen of **7** that inhibits attack by the diazo compound at the 1-position.



7

Migration of an unsaturated group to a developing electrophilic center, such as is represented by the products from carbon–carbon insertion in Table I, is now demonstrated to be preferred over methoxyl migration. As indicated by results with benzaldehyde and acetophenone dimethyl acetal or ketal, methoxyl migration only occurs when a carbocation of comparable stability to a methoxy-stabilized carbocation can be produced. This selectivity, the convenience in access to reactant acetals and ketals,[17] and the utilization of exceptionally mild conditions for these homologation reactions offer a convenient synthesis of a useful group of polyfunctional organic compounds that are not readily available by alternate methods. Extensions of this approach are currently under investigation.

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