reported by S. Omura, A. Nakagawa, A. Neszmélyi, S. D. Gero, A.-M. Sepulchre, F. Piriou, and G. Lukacs, *J. Am. Chem. Soc.*, **97,** 4001 (1975). Melting points were uncorrected. Significant NMR spectral data are listed herein. **2**: ^{13}c nmr 202.6 (C-9), 105.3 (C-1′), 103.6 (C-18), 84.8 (C-5), 73.4 (C-5′), 68.5 (C-4′). **4**: ^{13}C NMR 103.6 (C-18), 84.0 (C-4), 72.6 (C-5), 64.8 and 64.3 (ethylene carbons of the acetal). **6**: ^{13}C NMR 103.4 (C-18), 100.6 (C-1′), 85.5 (C-5). **8**: ^{1}H NMR 6.38 (d, $J = 6$ Hz, H-1), 4.82 (d, H-2). **9**: ^{1}H NMR 5.25 (d, $J \sim 1$ Hz, H-1″), 3.97 (d, H-2″); ^{13}C NMR 105.3 (C-1′), 103.8 (C-18), 100.2 (C-1″), 73.0 (C-4′), 72.5 (C-5′), 53.4 (C-2″). **10**: ^{1}H NMR 5.21 (d, $J \sim 1$ Hz, H-1), 3.97 (d, H-2). **11**: ^{13}C NMR 200.9 (C-18), 104.0 (C-1′), 100.3 (C-1″), 53.4 (C-2″).

(8) S. Ōmura, A. Nakagawa, K. Suzuki, T. Hata, A. Jakubowski, and M. Tishler, *J. Antibiot.*, **27,** 147 (1974).

(9) The drastic condition required for the acetylation of 4 suggests that the C-5 hydroxyl group has little reactivity for the glycosylation because of some hindrance.

(10) Prepared by treatment of tri-*O*-acetylmycaminose[2a] with hydrogen bromide in methylene chloride (23 °C, 1 h), ^{1}H NMR 6.77 (d, $J = 3.5$ Hz, H-1).

(11) Improvements of the yield will be sought in further experimentation. It should be noted, however, that the glycosylation was achieved without protection of the C-2′ and C-3″ hydroxyl and C-3′ dimethylamino groups.

(12) Prepared from isopropyl alcohol and **8** in the same manner as described above (91%), $[\alpha]^{21}{}_{D}$ −65° (c 1.0, $CHCl_3$).[5]

(13) Synthetic carbomycin B has mp 193–195 °C (prisms from acetone–hexane). Anal. Calcd for $C_{42}H_{67}NO_{15}$: C, 61.07; H, 8.18; N, 1.70. Found: C, 61.10; H, 8.09; N. 1.64.

Kuniaki Tatsuta,* Akihiro Tanaka
Koichi Fujimoto, Mitsuhiro Kinoshita
Department of Applied Chemistry, Keio University
832 Hiyoshi, Yokohama, Japan 223

Sumio Umezawa
Institute of Bioorganic Chemistry
1614 Ida, Nakahara, Kawasaki, Japan 211

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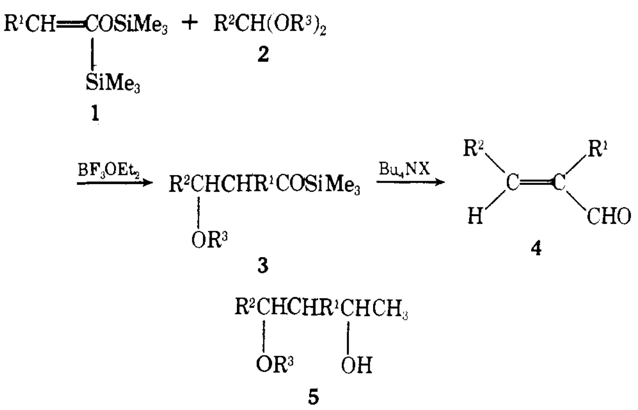
An Effective Preparative Method of α,β-Unsaturated Aldehydes via β-Alkoxyacylsilanes

Sir:

Formal "directed aldol coupling" between two types of aldehydes to afford α,β-unsaturated aldehyde, RCH=CR′CHO, is one of the most versatile synthetic organic reactions and a number of masked carbonyl equivalents have hitherto been devised.[1] Brook's pioneering works on acylsilane types of compounds have shown that silylcarbonyl groups can also be used as formyl synthon.[2] Unfortunately, their characteristic features have not been fully utilized yet for synthetic purpose because of limited applicability with moderate success. We have recently developed a method for effective conversion of 1,1-bis(trimethylsilyl)alkan-1-ol[3] into the trimethylsilyl enol ether of the corresponding trimethylacylsilane **1**.[4] This paper describes the reaction of this silyl enol ether **1**, which provides a facile preparative method of α,β-unsaturated aldehyde effected through the following two stages: (1) preparation of β-alkoxyacylsilane **3** by BF_3·OEt_2-catalyzed[5] reaction of acetal **2** with the silyl enol ether **1** and (2) its conversion into α,β-unsaturated aldehyde **4** under the influence of catalytic amounts of quaternary ammonium hydroxide or substituted phenoxides. Both of these reactions proceed under very mild conditions in high yield. This makes this method of considerable synthetic interest. The following procedures are illustrative. The trimethylsilyl enol ether of propionyltrimethylsilane (1.010 g, 5 mmol) and benzaldehyde diethyl acetal (0.900 g, 5 mmol) in methylene chloride (10 mL) were added to a methylene chloride (5 mL) solution of BF_3·OEt_2 (0.710 g, 5 mmol) at −78 °C under an argon atmosphere. After stirring for 1 h at −78 °C and 2 h at −30 °C, the reaction mixture was quenched with aqueous $NaHCO_3$ and was extracted with ether. Removal of the solvent and distillation afforded the corresponding adduct **3**[6] ($R^1 = CH_3$; $R^2 = C_6H_5$; $R^3 = C_2H_5$) (1.214 g, 92%, bp 105∼106 °C (2 mm). The alkoxyacylsilane (1.056 g, 4 mmol) thus obtained was treated with a 25% methanolic solution of tetrabutylammonium hydroxide (0.832 g, 0.8 mmol) in acetonitrile (15 mL) at room temperature for 15 min. The reaction mixture was then neutralized with dilute HCl, washed with aqueous $NaHCO_3$, and extracted with ether. Removal of the solvent followed by bulb-to-bulb distillation gave 2-methyl-3-phenylpropenal (0.549 g, 94%). Various acetals react similarly to afford the corresponding unsaturated aldehyde **4** in good yield by the above-mentioned two successive procedures, while ketals usually fail to react with the silyl enol ether **1** under the reaction conditions described above.[7] The aldehydes obtained are usually the *E* isomers exclusively.[8]



Stronger Lewis acids, e.g., $TiCl_4$, $AlCl_3$, or $SnCl_4$, cannot

Table I. Preparation of β-Alkoxyacylsilane **3** and Its Conversion into α,β-Unsaturated Aldehyde **4**

Reactant			**3**[a],		**4**,
R^1	R^2	R^3	% yield	X	% yield
CH_3	C_3H_7	CH_3	87	OH[b]	91[f]
	C_6H_5	C_2H_5	92	OH[c]	94
	$C_6H_5CH{=}CH$	C_2H_5	86	OH[c]	89
C_2H_5	C_3H_7	CH_3	81	OH[b]	85
$C_6H_5CH_2$	CH_3	C_2H_5	90	OH[c]	71
				F[d]	45[g]
				o-$CH_3OC_6H_4$-O[e]	81
	C_3H_7	CH_3	75	OH[b]	92
	C_6H_5	C_2H_5	88	OH[c]	93[h]
				F[d]	98[i]
	$C_6H_5CH{=}CH$	C_2H_5	87	OH[c]	90[j]
				F[d]	92[k]

[a] All of the reactions were carried out under the same condition described in the text. [b] The reaction was performed for 50 min in the presence of 25% methanolic solution of Bu_4NOH (0.2 equiv). [c] The reaction was performed for 15∼20 min in the presence of 25% methanolic solution of Bu_4NOH (0.2 equiv). [d] The reaction was performed for 12 h in the presence of Bu_4NF (0.08 equiv) and methanol (4 equiv). [e] The reaction was performed for 46 h in the presence of *o*-methoxyphenoxide (0.4 equiv) and methanol (4 equiv). [f] The *E* isomer was formed exclusively, otherwise noted. [g] Methyl transfer product **5** was also formed in 5% yield. [h] *E*:*Z*, 89:4. [i] *E*:*Z*, 90:8. [j] *E*:*Z*, 85:5. [k] *E*:*Z*, 84:8.

be employed for stage 1; they appear to induce the facile decomposition of β-alkoxyacylsilane **3** initially formed.[9]

For effecting the transformation of stage 2, tetrabutylammonium hydroxide is a preferable reagent of the wide applicability of the facile and relatively clean formation of the product **4**. For efficient conversion, however, it is crucial to use it in an amount as small as possible, because this strong base sometimes catalyzes the polymerization reaction of the aldehyde formed, which results in appreciable decrease of the yield especially when the product is labile to base. For certain β-alkoxyacylsilanes, tetrabutylammonium fluoride (TBAF)[10] is also employable. For example, the acylsilane **3** derived from the diethyl acetal of benzaldehyde or of cinnamaldehyde can be converted into the corresponding product **4** in higher yield under the catalytic effect of TBAF (~0.08 equiv), although the reaction proceeds much more slowly (12 h at room temperature). However, clean conversion can not generally be achieved with TBAF, because the side product **5**, resulting from methyl transfer from silicon to carbon,[2] is often formed in substantial amount. Lithium or sodium alkoxide are also found to be much less effective for the **3** → **4** transformation.

It should be noted that a weaker nucleophile, such as tetrabutylammonium *o*-methoxyphenoxide,[11,12] also catalyzes a conversion of **3** into **4**. This appears to be better reagent, especially for the preparation of base-labile unsaturated aldehydes such as 2-substituted crotonaldehydes, although it is a very slow process.

In contrast to the successful transformation of β-alkoxyacylsilanes into the corresponding unsaturated aldehydes, similar treatment of simple saturated acylsilane leads to the formation of the aldol condensation product of the aldehyde formed,[13] along with the methyl transfer product, even if quaternary ammonium *o*-methoxyphenoxide is employed. Further, the reaction with unsaturated acylsilane is found to give a complex mixture containing a small amount of the corresponding aldehyde[14] during similar procedure with hydroxide or *o*-methoxyphenoxide.

Further elucidation of the reaction mechanism is now under investigation.

References and Notes

(1) (a) G. Wittig and H. Reiff, *Angew. Chem., Int. Ed. Engl.*, **7**, 7 (1968); (b) E. J. Corey, D. Enders, and M. G. Bock, *Tetrahedron Lett.*, 7 (1976), and references cited therein.

(2) A. G. Brook, *Adv. Organomet. Chem.*, **7**, 95 (1968).

(3) I. Kuwajima, T. Sato, N. Minami, and T. Abe, *Tetrahedron Lett.*, 1591 (1976).

(4) I. Kuwajima, M. Arai, and T. Sato, *J. Am. Chem. Soc.*, **99**, 4181 (1977).

(5) For Lewis acid catalyzed reactions of vinyl ethers with acetals to afford α,β-unsaturated aldehydes, see R. I. Hoaglin and D. H. Hirsh, *J. Am. Chem. Soc.*, **71**, 3468 (1949); O. Isler, H. Lindlar, M. Montavon, R. Reugg, and P. Zeller, *Helv. Chim. Acta*, **39**, 249 (1956); O. Isler, *Adv. Org. Chem.*, **4**, 128 (1963). For similar reactions of silyl enol ethers of ketones with acetals, see T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 15 (1974); K. Narasaka, K. Soai, Y. Aikawa, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **49**, 779 (1976); A. Ishida and T. Mukaiyama, *ibid.*, **50**, 1161 (1977); E. Nakamura and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 961 (1977).

(6) This alkoxyacylsilane exhibited the following spectral data: NMR (CCl_4, methylene chloride as internal standard) δ 0.22 (s, 9 H), 0.52 (d, J = 7 Hz, 3 H), 1.03 (t, J = 7 Hz, 3 H), 3.0–3.6 (m, 3 H), 4.22 (d, J = 10 Hz, 1 H), 7.27 (s, 5 H); IR (neat) 3020, 2963, 1640, 1600, 1490, 1250, 1093, 842, 760 cm^{-1}.

(7) Under forcing reaction condition, the following reaction is observed: $R^1R^2C(OC_2H_5)_2 + R^3CH{=}C(SiMe_3)OSiMe_3 \rightarrow R^1R^2C{=}CHR^3$.

(8) For a facile isomerization of *Z* isomer of this type of aldehyde into its *E* isomer, see, for example, G. Büchi and H. Wüest, *J. Am. Chem. Soc.*, **96**, 7573 (1973).

(9) Depending on the Lewis acid employed, the following two types of decomposition products are obtained: **3** → $R^2CH{=}CHR^1$ or $R^2CH(OH)CHR^1SiMe_3$. These interesting decompositions reactions will be described in a separate note.

(10) On the specific action of fluoride ion to silicon atom, see I. Kuwajima, *J. Syn. Org. Chem. Jpn.*, **34**, 964 (1976).

(11) Tetrabutylammonium phenoxides are prepared as follows. A slight excess amount of the corresponding substituted phenol is treated with an aqueous solution of tetrabutylammonium hydroxide. Excess phenol is extracted out with ether and most of the water is removed with a rotary evaporator. The remaining solid is used as its solution in methanol.

(12) Various phenoxides were examined for the transformation of **3** (R^1 = $C_6H_5CH_2$; R^2 = CH_3; R^3 = C_2H_5) into the corresponding aldehyde and the following results were obtained: unsubstituted phenoxide (60% **4**, 3 h for complete disappearance of **3**), *o*-methyl- (67%, 6 h), *m*-methyl- (72%, 42 h), *p*-methyl- (72%, 3 days), and *o-tert*-butylphenoxide (62%, 14 h).

(13) Treatment of 3-phenylpropionyltrimethylsilane with 0.2 equiv of Bu_4NOH at room temperature for 10 min afforded 2-benzyl-5-phenyl-2-pentenal (79%) and 4-phenylbutan-2-ol (7%).

(14) Treatment of 3-phenylpropenoyltrimethylsilane with Bu_4NOH (0.2 equiv, 10 min at room temperature) or *o*-methoxyphenoxide (0.4 equiv, 35 min at room temperature) afforded cinnamaldehyde in 23% and 52% yields, respectively, along with other many unidentified products.

Toshio Sato, Masahiko Arai, Isao Kuwajima*
Department of Chemistry, Tokyo Institute of Technology
Ookayama, Meguro-ku, Tokyo 152 Japan

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Cation and Solvent Effects on the Alkylation of Two Alkali β-Ketoenolates

Sir:

In the course of an extended investigation of ion pairing and reactivity of alkali β-diketoenolates, we have observed several phenomena which we think are striking enough to communicate prior to publication of our complete results.

Sodium and potassium dibenzoylmethides (MDBM) are completely carbon alkylated by methyl iodide in Me_2SO, as shown by ^1H NMR and HPLC analysis of the products. Combination of rate data for the process with conductance data[1] shows that the dissociated anions engage in typical S_N2 attack on MeI with a rate constant that is three or four orders of magnitude greater than attack by the alkali enolate ion pair.

When dimethyl sulfate (Me_2SO_4) is used as alkylating agent, clean formation of the oxygen-methylated product (the β-keto vinyl ether) is observed. In dramatic contrast to the kinetics of all other enolate alkylation studies known to us, the reaction *turns out to be only 0.24 order*[2] *in enolate, although still first order in* Me_2SO_4. This suggests that much of the reaction occurs through a highly reactive intermediate generated from Me_2SO_4. This was demonstrated through independent observation of an exothermic reaction[3] between Me_2SO_4 and Me_2SO with a pseudo-first-order rate constant $k_1 = 6.81 \times 10^{-4}\ s^{-1}$ which is roughly comparable to the pseudo-first-order alkylation rates listed in the third column of Table I. The kinetic complications of competing reactions during alkylation (see below) make closer agreement unlikely. The product solution generated after an hour by this process reacted instantly with KDBM and NaDBM to give oxygen-alkylated product. This experiment confirmed the formation of a highly reactive intermediate and showed that it was generated by interaction of Me_2SO_4 with the solvent.

The identity of the intermediate as the dimethylmethoxysulfonium ion[4] Me_2SOMe^+ was substantiated by observation of the ^1H NMR spectrum of a solution of dimethyl sulfate following its solution in Me_2SO-d_6. A single spike at 3.97 ppm was replaced by two peaks of equal heights at 4.02 ppm (assigned to $(CD_3)_2SO^+CH_3$) and 3.44 ppm (assigned to the anion $^-OSO_2OCH_3$). The first-order rate of conversion (at 38 °C) was roughly equivalent to that expected on the basis of the first-order calorimetric rate at 25 °C.

Treatment of the rate data as competing first- and second-order processes[10] led to results typified by the data in Table I, which show (last two columns) that product formation occurs with comparable speed through both pathways under these conditions. More extensive analysis of the results, again using conductance data,[11] confirms the supposition that for the S_N2 process the dissociated enolate anions are the only effective nucleophiles, with essentially no competition from ion pairs.