

QUATERNARY AMMONIUM ENOLATES AS SYNTHETIC INTERMEDIATES.  
GENERATION OF ESTER ENOLATES BY THE AID OF  $\alpha$ -TRIMETHYLSILYLESTERS  
AND QUATERNARY AMMONIUM FLUORIDE, AND THEIR REACTIONS WITH CARBONYL COMPOUNDS

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Regiospecific alkylation of ketone enolates generated from trimethylsilyl-enol ethers and quaternary ammonium fluoride was reported previously.<sup>1</sup> A study about the reaction of ethyl trimethylsilylacetate and tetra-*n*-butylammonium fluoride (ETSA-TBAF) has recently led us to develop an effective procedure for the silylation of compounds with acidic hydrogens.<sup>2</sup> This letter describes an unprecedented selectivity of the reagent, ETSA-TBAF, and some evidence for the involvement of quaternary ammonium ester enolate in this reaction

In aldol<sup>3</sup> and Reformatsky-type<sup>4</sup> reactions, Lewis acid-metal counteractions have proved effective in the activation of the carbonyl group and the stabilization of the transition state. In this respect, the reactivity of quaternary ammonium ester enolate has been of considerable interest. An expedient similar to one employed for the alkylation of ketones<sup>1</sup> was applied to the reaction of trimethylsilylacetates. When a trimethylsilylacetate<sup>5</sup> and a carbonyl compound were treated in an aprotic solvent, e.g., tetrahydrofuran (THF), dimethoxyethane, and acetonitrile, with a catalytic amount (0.03 equiv - 0.003 equiv) of anhydrous tetra-*n*-butylammonium fluoride (TBAF)<sup>6</sup>, a  $\beta$ -trimethylsilyloxyester or a silyl enol ether<sup>2</sup> derived from the carbonyl compound was, in most cases, obtained in good yields. Reactions of ethyl trimethylsilylacetate (ETSA) with various carbonyl compounds are representative of this catalyzed reaction (Table I).<sup>7</sup> Except for the case with aliphatic aldehydes, only small amounts of isolable by-products were detected in the crude reaction mixture, and the product was generally isolated by distillation after non-aqueous work-up. The adduct,  $\beta$ -silyloxyester, was quantitatively hydrolyzed with AcOH-H<sub>2</sub>O or methanol to give the corresponding  $\beta$ -hydroxyester, when desired. On the other hand, aliphatic aldehydes underwent self-condensation to an appreciable extent, and afforded a small amount of the expected adduct.

The course of this catalyzed reaction is most reasonably explained by the involvement of quaternary ammonium enolate 1, and the subsequent silylation by trimethylfluorosilane (TMS-F). The following facts may substantiate this

Table I. Reactions of ETSA with Carbonyl Compounds Catalyzed by TBAF.<sup>a</sup>

RR'C=O	$\beta$ -Siloxyster, <sup>b</sup> %	Bp, <sup>c</sup> °C	Recovered RR'C=O, <sup>b</sup> %
Cinnamaldehyde	81	120 <sup>d</sup> (0.10 mm)	0
Citral	79	110 <sup>d</sup> (1 mm)	(5)
<u>trans</u> -2-Hexenal	82	75 <sup>d</sup> (0.17 mm)	
Crotonaldehyde	(69) <sup>e</sup>	(68) (0.5 mm) <sup>f</sup>	
Benzaldehyde	76	90 <sup>d</sup> (0.11 mm) <sup>g</sup>	0
$\beta$ -Phenylpropionaldehyde	(24)	(120) <sup>d</sup> (0.07 mm)	(21)
Benzylacetone	0		88
$\beta$ -Ionone	0		(91)
Benzophenone	88	130 <sup>d</sup> (0.09 mm)	0

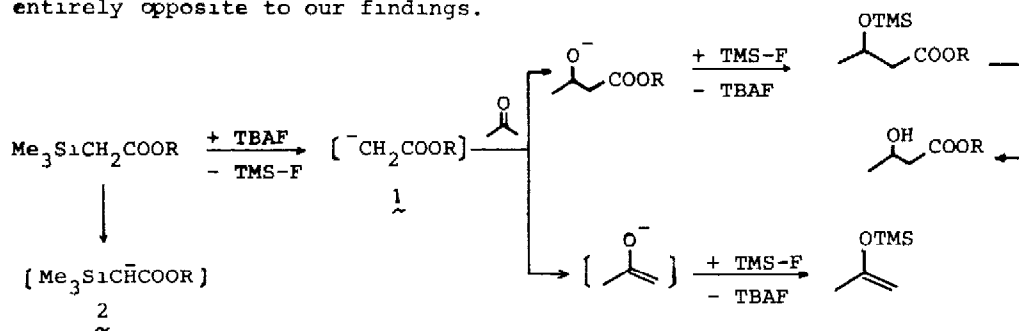
<sup>a</sup>Reactions were carried out in ca. 3 mmol scale in 1M THF solution at -20°C, with a reactant ratio: ETSA · RR'C=O : TBAF = 1.3 : 1.0 · 0.03. Reaction periods were 2-4 hours where adducts were obtained and 1 hour where not. <sup>b</sup>Isolated yields of silylated products: isolated yields after hydrolysis in parentheses.

<sup>c</sup>Boiling points of  $\beta$ -hydroxyesters in parentheses.

<sup>d</sup>Bath temperature. <sup>e</sup>About 15 mmol scale reaction <sup>f</sup>W Jawarsky and S. Reformatzky, Chem. Ber., 35, 3633 (1902). <sup>g</sup>Ref 6b

mechanism, and rule out a possible alternative, the formation of an anion 2:<sup>6b</sup>

(a) Ethyl  $\alpha$ -trimethylsilylisobutyrate<sup>8</sup> which has no  $\alpha$ -protons also underwent this fluoride catalyzed addition reaction with aldehydes, and the reaction rate appeared to be similar to that of silylacetates.<sup>9</sup> (b) The reaction of the anion 2 and carbonyl compounds is known to afford readily the mixture of E and Z isomers of  $\alpha,\beta$ -unsaturated esters, instead of  $\beta$ -trimethylsiloxyesters,<sup>10</sup> which is entirely opposite to our findings.



The selectivity disclosed here (Table I) presents a striking contrast to that of the previously known Reformatsky reactions<sup>4</sup> in which most of aldehydes and ketones are equally good electrophiles. In this catalyzed reaction of trimethylsilylacetates, carbonyl compounds without acidic  $\alpha$ -protons uniformly gave adducts in high yields, while those with  $\alpha$ -protons gave a little or none of them. An examination of the isomer composition of silyl enol ethers revealed that the deprotonation occurred mostly in a kinetically controlled manner.<sup>2</sup> Consequently, the dominant factor that controlled the reaction paths is considered to be the availability of the kinetically acidic  $\alpha$ -protons of the carbonyl compounds. A comparison of this catalyzed reaction and the conventional Reformatsky reaction suggests that addition of ester enolates to ketones is not an unfavorable process, yet acidic counteranions greatly facilitate the nucleophilic addition reaction relative to the proton abstraction from ketones.

It was reported, for the reaction of carbon nucleophiles with ketones,<sup>11</sup> that proton abstraction prevails over addition when the counteranion passes from smaller ones to larger ones.<sup>12</sup> When compared with the corresponding lithium or zinc enolate, the present reaction is the first clear indication that an enolate anion also exhibits a marked cation-dependent change of reactivities.<sup>13</sup> In addition, KF-dicyclohexyl-18-crown-6 also catalyzed the reaction of trimethylsilylacetates, which coincides with what is generally accepted; quaternary ammonium and crown solvated potassium cation behave similarly.

In conclusion, the enolate species reported here exhibit very unique reactivities toward carbonyl compounds. Since these reactivities differ even from those of anions similarly generated from a silyl enol ether and a silyl acetylene,<sup>14</sup> further studies concerning the structure variation of enolate anions are under way.

#### Ethyl 3-Phenyl-3-trimethylsilyloxypropanoate:

To a suspension of anhydrous TBAF (42 mg, 0.16 mmol) in 2 ml of THF kept under argon at  $-78^\circ$  was added a mixture of ETSA (4.07 g, 25.4 mmol) and benzaldehyde (2.65 g, 25.0 mmol) in 10 ml of THF during 5 min. After stirring for 5 min at  $-78^\circ$ , a cooling bath was removed and the yellow reaction mixture was stirred for additional 3 hr. Diluted with 70 ml of hexane, the reaction mixture was filtered, and concentrated in vacuo. The residual yellow oil was submitted to short-path distillation to afford a little forerun and 5.07 g (76%) of the pure  $\beta$ -trimethylsilyloxyester, bp  $99^\circ$ , 1 mm.

## References and Notes

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5. (a) Unlike the corresponding trimethylsilylketene acetals,  $\alpha$ -trimethylsilyl-esters are quite stable. (b) Trimethylsilylacetates such as ethyl, methyl, and isobutyl esters were prepared in ca. 70% yields from bromoacetates: R. J. Fessenden and J. S. Fessenden, J. Org. Chem., 32, 3535 (1967).
6. (a) TBAF was prepared by neutralizing 10% aqueous tetra-*n*-butylammonium hydroxide with dilute aqueous HF. The bulk of water was removed, and the paste was dried at 90°, 0.5 mm for 15 hr. The resulting hygroscopic mass, TBAF, was pulverized and stored over P<sub>2</sub>O<sub>5</sub> cf. P. W. Kent and R. C. Young, Tetrahedron, 27, 4057 (1971). (b) A similar reaction was reported with catalysts, KOH and KAl(OCH<sub>3</sub>)<sub>4</sub>, under rather drastic conditions, and only aromatic aldehydes reacted with moderate success. L. Birkofer, A. Ritter, and H. Wieden, Chem. Ber., 95, 971 (1962); L. Birkofer and A. Ritter, Angew. Chem., 77, 414 (1965).
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