

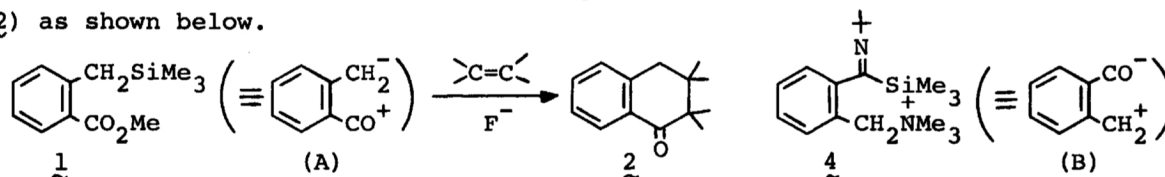
A NEW FLUORIDE ANION-PROMOTED 1,4-CYCLOADDITION LEADING TO  
SYNTHESIS OF  $\alpha$ -TETRALONES

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Fluoride anion-promoted 1,4-cycloaddition of methyl o-trimethylsilylmethylbenzoate to conjugated olefins was found to give  $\alpha$ -tetralones and uncyclized Michael adducts in moderate yields.

Fluoride anion-promoted generation of the carbanions from organosilicons in the neutral medium under mild conditions is one of the most useful methods in organic synthesis.<sup>1)</sup> Recently, we also reported that trifluoroacetic acid- or fluoride anion-promoted desilylation of trimethylsilylmethylamine derivatives underwent new 1,3-cycloadditions to conjugated olefins and acetylenes leading to the pyrrolidines and 2,5-dihydropyrroles.<sup>2)</sup>

We wish to describe here a new fluoride anion-promoted 1,4-cycloaddition of methyl o-trimethylsilylmethylbenzoate (**1**) leading to the synthesis of  $\alpha$ -tetralones (**2**) as shown below.



Although Ito et al. reported recently the fluoride anion-promoted 1,4-cycloaddition of **4** as the synthon B leading to  $\alpha$ -tetralones,<sup>3)</sup> present method included the use of the more simple compound (**1**) as the synthon A, which has the formally reverse-charged structure of the synthon B.

As shown in Table 1, treatment of methyl o-trimethylsilylmethylbenzoate (**1**)<sup>4)</sup> with conjugated olefins in the presence of CsF in hexamethylphosphoramide (HMPA) afforded  $\alpha$ -tetralones (**2**) and Michael adduct (**3**) in moderate yields. Ratios of the products, **2** and **3**, depend on the structures of used olefins. A typical experiment is described below.

A solution of **1** (222 mg, 1 mmol) and dimethyl maleate (173 mg, 1.2 mmol) in HMPA (1 ml) was added to a stirred mixture of CsF (151 mg, 1 mmol), dried on an open flame under reduced pressure, in HMPA (1 ml). After stirring for 3 h at 60 °C, the mixture was diluted with benzene, washed with water and saturated aqueous sodium chloride, dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure. The resulted residue was subjected to preparative TLC (silica gel, THF/hexane = 1/9). **2a**: 113 mg (43%), mp 61-62 °C; IR(KBr) 3340, 1740, 1728, 1690  $\text{cm}^{-1}$ ; MS  $m/z$  262 ( $\text{M}^+$ );  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$  3.55(s), 3.72(s), 3.86(s) (6H,  $\text{OCH}_3$ ), 3.13-3.96(3.5H, m,  $\text{CH}_2\text{CHCH}$  &  $\text{CH}_2\text{CHC=}$ ), 7.10-7.53, 7.89-7.97(4H, m,  $\text{C}_6\text{H}_4$ ), 12.60(0.5H, s, OH);  $^{13}\text{C}$  NMR( $\text{CDCl}_3$ )  $\delta$

Table 1. Reaction of Methyl o-(Trimethylsilylmethyl)benzoate (**1**) with Conjugated Olefins

				Reaction conditions		Product (Yield/%)	
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Temp/°C	Time/h	<b>2</b>	<b>3</b>
CO <sub>2</sub> CH <sub>3</sub>	H	CO <sub>2</sub> CH <sub>3</sub>	H	60	3	<b>2a</b> 43	<b>3a</b> 15
CO <sub>2</sub> CH <sub>3</sub>	H	H	CO <sub>2</sub> CH <sub>3</sub>	60	3	<b>2a</b> 41	<b>3a</b> 28
H	H	H	CO <sub>2</sub> CH <sub>3</sub>	rt	3.5	<b>2b</b> <sup>a)</sup> 17	<b>3b</b> 21
H	H	CH <sub>3</sub>	CO <sub>2</sub> CH <sub>3</sub>	40	3	<b>2c</b> 32	<b>3c</b> 0
	-CH <sub>2</sub> -CH <sub>2</sub> -CO-			60	3	<b>2d</b> 14	<b>3d</b> 33
C <sub>6</sub> H <sub>5</sub>	H	CO <sub>2</sub> CH <sub>3</sub>	CO <sub>2</sub> CH <sub>3</sub>	60	3	<b>2e</b> 0	<b>3e</b> 70
	-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CO-			rt	4	<b>2f</b> 0	<b>3f</b> 26

a) R<sup>3</sup> = CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>.

30.88(t), 31.04(t), 37.60(d), 43.07(d), 51.79(q), 52.06(q), 52.44(q), 56.34(d), 95.68(s), 124.83(d), 127.05(d), 127.21(d), 127.48(d), 127.70(s), 127.81(d), 128.79(d), 129.22(s), 131.11(s, d), 134.48(d), 136.75(s), 140.81(s), 166.22(s), 169.63(s), 172.56(s), 173.70(s), 191.37(s). These data indicate that **2a** is a mixture of keto-enol tautomers. The structure of **3a** was also determined by its spectral and elementary analyses.

It should be noted that several attempts at direct cycloaddition of methyl o-tolylbenzoate to dimethyl maleate under such basic conditions as LDA or BuLi in HMPA/THF failed to give α-tetralones (**2a**) or Michael adduct (**3a**) and the present reaction provides a useful procedure for synthesis of α-tetralones under mild and neutral conditions. Its further application for synthesis of anthracycline antibiotics is under investigation.

#### References

- 1) E. Colvin, "Silicon in Organic Synthesis," Butterworth, London (1981); W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, New York (1983).
- 2) K. Achiwa and M. Sekiya, Chem. Lett., 1981, 1213; Tetrahedron Lett., 23, 2589 (1982); Y. Terao, N. Imai, K. Achiwa, and M. Sekiya, Chem. Pharm. Bull., 30, 3167 (1982); K. Achiwa, T. Motoyama, and M. Sekiya, ibid., 31, 3939 (1983); K. Achiwa, N. Imai, T. Inaoka, and M. Sekiya, ibid., 32, 2878 (1984); K. Achiwa, N. Imai, T. Motoyama, and M. Sekiya, Chem. Lett., 1984, 2041; Y. Terao, N. Imai, H. Kotaki, and K. Achiwa, Chem. Pharm. Bull., in press.
- 3) Y. Ito, E. Nakajo, and T. Saegusa, Tetrahedron Lett., 25, 3139 (1984).
- 4) This compound was prepared from methyl o-tolylbenzoate and trimethylsilyl chloride in the presence of LDA in ether. **1**: bp 120-122 °C (20 Torr); IR(neat) 1726 cm<sup>-1</sup>; <sup>1</sup>H NMR(CDCl<sub>3</sub>) δ 0.05(9H, s, Si(CH<sub>3</sub>)<sub>3</sub>), 2.18(2H, s, CH<sub>2</sub>Si), 3.82(3H, s, OCH<sub>3</sub>), 6.80-7.75, 7.68-7.88(4H, m, C<sub>6</sub>H<sub>4</sub>).

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