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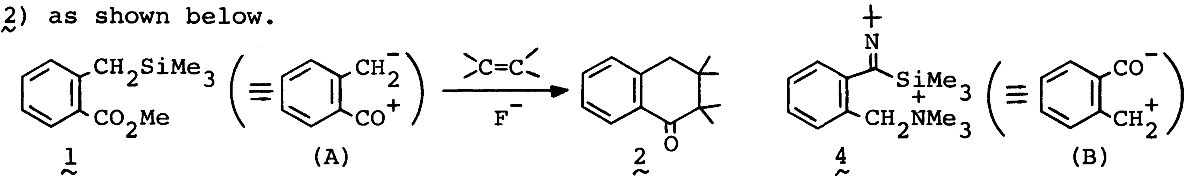
A NEW FLUORIDE ANION-PROMOTED 1,4-CYCLOADDITION LEADING TO SYNTHESIS OF α-TETRALONES

Masahiro AONO, Yoshiyasu TERAO, and Kazuo ACHIWA*
Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422

Fluoride anion-promoted 1,4-cycloaddition of methyl o-trimethylsilylmethylbenzoate to conjugated olefins was found to give α-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.$^{1)}$ 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.$^{2)}$

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

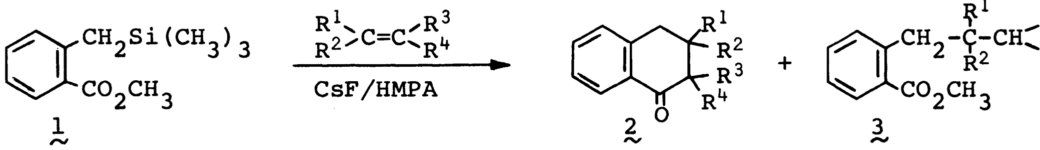


Although Ito et al. reported recently the fluoride anion-promoted 1,4-cycloaddition of 4 as the synthon B leading to α-tetralones,$^{3)}$ present method included the use of the more simple compound (1) as the synthon A, which has the formally reverse-charged structure of the synthon B.

As shown in Table 1, treatment of methyl o-trimethylsilylmethylbenzoate (1)$^{4)}$ with conjugated olefins in the presence of CsF in hexamethylphosphoramide (HMPA) afforded α-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 $MgSO_4$, 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 cm^{-1}; MS m/z 262 (M^+); ^1H NMR($CDCl_3$) δ 3.55(s), 3.72(s), 3.86(s)(6H, OCH_3), 3.13-3.96(3.5H, m, CH_2CHCH & CH_2CHC=), 7.10-7.53, 7.89-7.97(4H, m, C_6H_4), 12.60(0.5H, s, OH); ^{13}C NMR($CDCl_3$) δ

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



Olefin				Reaction conditions		Product (Yield/%)	
R^1	R^2	R^3	R^4	Temp/°C	Time/h	2	3
CO_2CH_3	H	CO_2CH_3	H	60	3	2a 43	3a 15
CO_2CH_3	H	H	CO_2CH_3	60	3	2a 41	3a 28
H	H	H	CO_2CH_3	rt	3.5	2b[a] 17	3b 21
H	H	CH_3	CO_2CH_3	40	3	2c 32	3c 0
$-CH_2-CH_2-CO-$				60	3	2d 14	3d 33
C_6H_5	H	CO_2CH_3	CO_2CH_3	60	3	2e 0	3e 70
$-CH_2-CH_2-CH_2-CO-$				rt	4	2f 0	3f 26

a) $R^3 = CH_2CH_2CO_2CH_3$.

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

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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^{-1}; ^1H NMR($CDCl_3$) δ 0.05(9H, s, $Si(CH_3)_3$), 2.18(2H, s, CH_2Si), 3.82(3H, s, OCH_3), 6.80-7.75, 7.68-7.88(4H, m, C_6H_4).

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