

ALDOL REACTION OF ALUMINIUM ENOLATE RESULTING FROM 1,4-ADDITION OF
 Me_2AlSPh TO α,β -UNSATURATED CARBONYL COMPOUND.
 A 1-ACYLETHENYL ANION EQUIVALENT

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Abstract: Me_2AlSPh or Me_2AlSeMe adds to α,β -unsaturated carbonyl compounds in 1,4-fashion. The resulting aluminium enolates react with aldehydes effectively to afford the adducts of the title anion after formal PhSH (or MeSeH)-elimination.

A recent publication¹ on the joining reaction of thiolate anion, an activated olefin and a carbonyl component prompts us to report independent results along the similar line involving (1) 1,4-addition of R_2AlX to α,β -unsaturated carbonyl compound to give the aluminium enolate, (2) aldol reaction² of the resulting aluminium enolate, and (3) elimination of HX providing α -substituted α,β -unsaturated carbonyl compound. The overall transformation provides an access to a 1-acylethenylanion V adding to the aldehyde component³ to form IV. Among many candidates for X, phenylthio and methylseleno group have been found effective (Table 1).

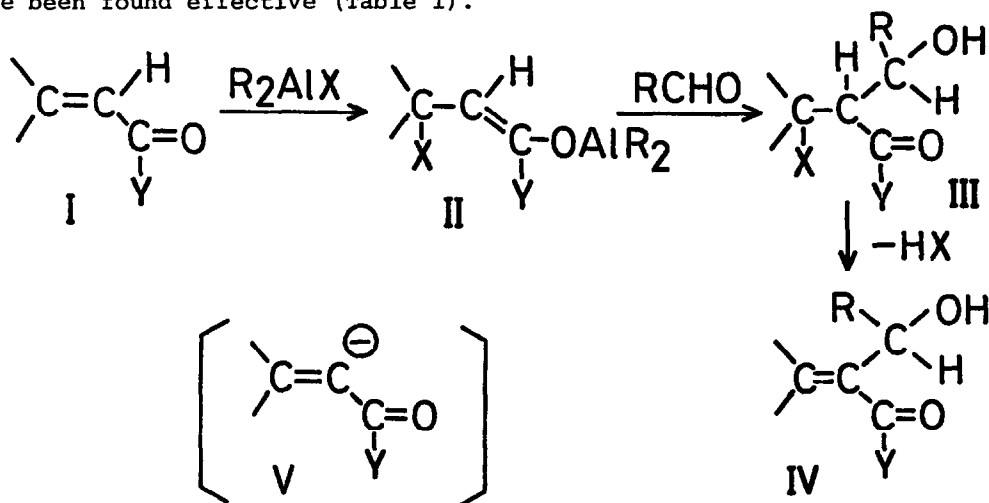





Table 1. Reaction between α,β -unsaturated carbonyl compound and aldehyde by means of Me_2AlSPh or Me_2AlSeMe ^a

Run	α,β -Unsaturated Carbonyl Compound	X	Aldehyde RCHO	Method	III Yield ^b (%)	IV Yield from III ^b (%)
1	2-cyclohexenone	SPh	CH_3CHO	A	94	92
2	2-cyclohexenone	SeMe ^c	CH_3CHO	A	77	77
3	2-cyclohexenone	SPh	$\text{CH}_3(\text{CH}_2)_7\text{CHO}$	A	90	71
4	2-cyclohexenone	SPh	methacrolein	A	97	84
5		SPh	CH_3CHO	A	75	—
6		SPh	CH_3CHO	A	—	50 ^e
7	$\text{CH}_2=\text{CHCOCH}_3$	SPh	CH_3CHO	A	60	57
8	$\text{CH}_2=\text{CHCOCH}_3$	SeMe ^c	CH_3CHO	A	55	50
9	2-cyclopentenone	SPh	HCHO	A	56	30 ^f
10	2-cyclopentenone	SPh	$\text{CH}_3(\text{CH}_2)_7\text{CHO}$	A	76	60
11	$\text{CH}_2=\text{CHCOOC}_2\text{H}_5$	SPh	CH_3CHO	B ^d	73	87
12		SPh	PhCHO	B ^d	77	74

a. Reactions were performed on 2.0 mmol scale. b. Satisfactory spectroscopic and elemental analyses of all the products. Diastereomer ratios have not been determined. c. Me_2AlSeMe was prepared in situ according to ref. 4. d. An ate complex $\text{Me}_3\text{Al}^- \text{SPhLi}^+$ was used instead of Me_2AlSPh . e. Phenylthio group has been eliminated in the reaction mixture without further treatment with CuCl_2 and NaOAc . f. See ref. 7.

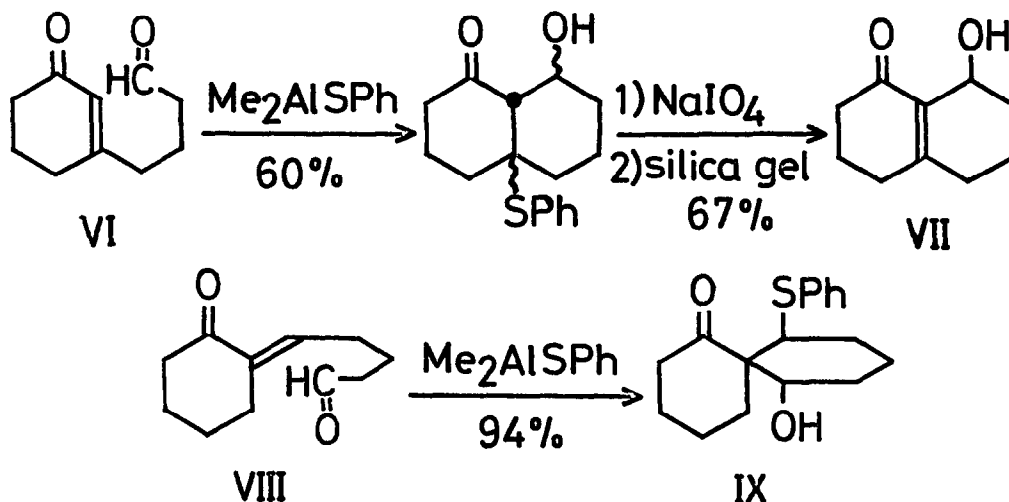
To a solution of PhSH (0.26 g, 2.4 mmol) in dichloromethane (2 ml) was added Me_3Al (1.0 M solution in hexane, 2.4 ml, 2.4 mmol) at 0 °C under argon atmosphere and the reaction mixture was kept there for an additional 20 min. A solution of 2-cyclohexenone (0.19 g, 2.0 mmol) in dichloromethane (2 ml) was added at -78 °C. After the completion of 1,4-addition of thiolate (15 min),⁵ the reaction mixture was diluted with tetrahydrofuran (10 ml)⁶ and a solution of nonanal (0.34 g, 2.4 mmol) in THF (2 ml) was added dropwise. Stirring was continued at -78 °C for 15 min and the reaction mixture was diluted with ethyl acetate (20 ml) and poured into ice-cooled 1N hydrochloric acid. The organic phase was washed with brine, dried, and freed of the solvent. Purification

by column chromatography on silica gel afforded the desired β -hydroxy carbonyl compound III (0.64 g, 90% yield) as a colourless oil (method A).

Unfortunately Me_2AlSPh was not effective in the reaction of α,β -unsaturated esters because of sluggish addition of thiolate and thiol ester formation.⁸ The use of a new ate complex⁹ $\text{Me}_3\text{Al}^-\text{SPhLi}^+$ has been found to be much more advantageous possibly due to the increased reactivity of thiolate ion itself and the resulting enolate anion corresponding to II.

Spontaneous elimination of phenylthio group in the reaction mixture was observed in run 6. Frequently the conversion of III to IV was achieved by the oxidation (NaIO_4 for SPh and H_2O_2 for SeMe) and successive elimination¹⁰ as given in the Table 1. Moreover, the overall transformation could be performed in one pot, for instance, the addition of cupric chloride (5 mmol) and sodium acetate (5 mmol) before work up in the run 1 afforded the desired compound IV directly in 52% isolated yield.

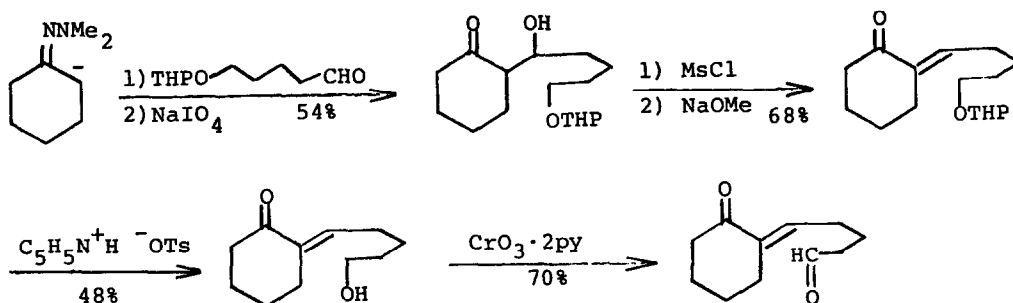
Treatment of the α,β -unsaturated carbonyl compounds VI¹¹ and VIII¹² with Me_2AlSPh provided an efficient method for the cyclization affording VII¹³ and IX,¹⁴ respectively.^{15,16}



References and notes

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5. Disappearance of the starting enone was monitored by analytical tlc.
6. THF was found to be the best solvent for the aldol reaction of aluminium enolate. See also ref. 2.
7. This product is a key compound for the synthesis of cyclopentenoid antibiotics (See ref. 3). The research described here was started to exploit an another versatile route to this compound.
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9. A hexane solution of Me_3Al (1.0 mol) was added to a solution of LiSPh derived from PhSH (1.0 mol) and $n\text{-BuLi}$ (1.0 mol) in THF at 0°C . The reagent was used without isolation.
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12. The compound VIII was prepared as follows:



13. The product VII exhibited: IR(neat) 3480, 1655, 1630(sh) cm^{-1} ; NMR(CCl_4) δ 1.60-2.40 (m, 12H), 2.97 (m, 1H), 4.42 (bs, 1H); exact mass spectrum m/e 166.0980 (calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$ 166.0992).
14. A mixture of diastereomers. IR(neat) 3440, 1702 cm^{-1} ; NMR(CCl_4) δ 2.28-2.47 (m, 2H), 3.81 (m, 2H), 7.13-7.48 (m, 5H).
15. The reagent Me_2AlSPh (3.0 mmol) was prepared described above and diluted with THF (9.0 ml). A solution of VI or VIII (1.0 mmol) in THF (1.0 ml) was added over 40 min at 0°C and the resulting mixture was stirred for an additional 30 min.
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