

REGIOSPECIFICALLY CONTROLLED FORMATION
 OF TETRASUBSTITUTED TRIBUTYLTIN KETONE
 ENOLATES CATALYZED BY A PALLADIUM COMPLEX

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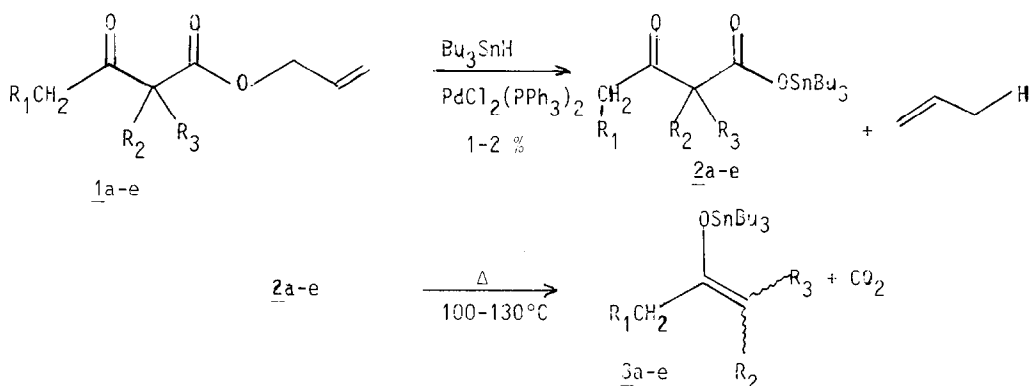
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Summary : The palladium-catalyzed hydrostannolysis of α -disubstituted allyl β -keto esters yields the corresponding tributyltin β -keto carboxylates which lose carbon dioxide at very moderate temperature, thus leading to the regioselective formation of tributyltin tetrasubstituted enolates.

Owing to their ability to react with various electrophilic carbon species, ketone enolates are very important intermediates in organic chemistry for the formation of carbon-carbon bonds². However, their synthetic potentiality is often plagued by the problem of obtaining the desired enolate regioisomer in a high state of purity.

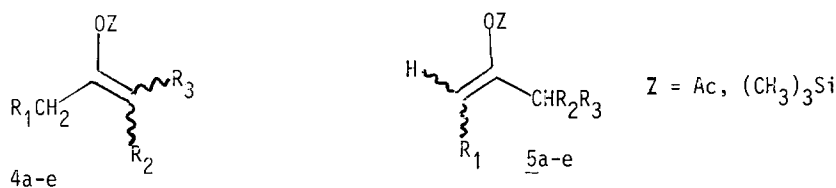
House and coworkers have shown that this problem is particularly acute for the preparation of tetrasubstituted enolates by proton abstraction from the parent ketone³. Although several new recent techniques⁴⁻⁶ have been developed to achieve selective deprotonation of ketones, their generality has not as yet been thoroughly established. Alternative routes to tetrasubstituted enolates involve the action of organometallics on or the partial reduction of α,β -unsaturated ketone or α -bromo ketone systems^{2c-e,7,8}. Tetrasubstituted silyl enol ethers have been prepared under rather drastic conditions by silatropic rearrangement of the corresponding silyl β -keto esters⁹.

We report here a two-step, "one pot" method, for the regiocontrolled formation of tetrasubstituted tributyltin enolates starting from easily available allyl β -keto esters 1 (see the scheme and the table).



The palladium-catalyzed hydrostannolysis of the carboxylic allyl group¹⁰ of 1 occurs instantaneously leading to 2 with evolution of propene¹¹. The thermal decarboxylation of the intermediate tributyltin β -keto carboxylates 2 into tributyltin enolates 3 then occurs by heating at very moderate temperature (100-130°C). This is in sharp contrast to the corresponding silatropic rearrangement of trimethylsilyl β -keto esters which requires much higher temperatures (240-470°C)⁹. The cyclic compounds 2a-c were found to decarboxylate faster than the acyclic ones 2c-e.

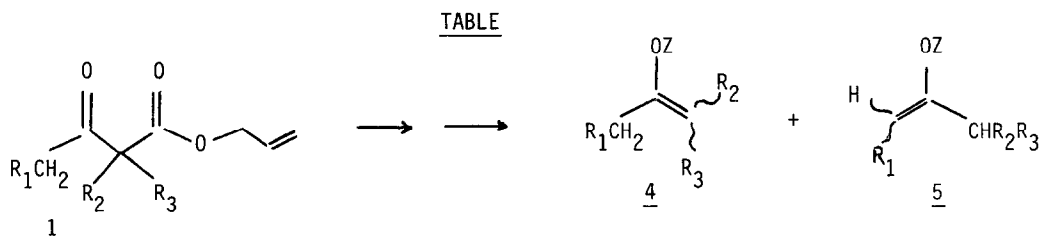
For analytical purposes, at the end of the reaction¹², the tin enolates 3 were converted to the corresponding silyl enol ethers or enol acetates by trapping at room temperature with trimethylsilyl or acetyl chloride. The structures, the yields and the regioisomeric composition of the resulting products 4 and 5 were determined by IR and NMR spectroscopy and by GC/MS analysis (see the table).



For the sake of comparison, the composition of the 4 + 5 mixtures obtained by treatment of the parent ketone under thermodynamic control (Et₃N/Me₃SiCl in DMF or H₂C=C(Me)OAc/TsOH) are also included in the table. These conditions are known to generally, but not always, favour the formation of the enol derivative with the more substituted double bond.

The total yields of the above enol derivatives are all reasonably good. The main by-product is generally the parent ketone which probably arises from hydrolysis of the tin enolates by adventitious water¹³. Some polymeric material is undoubtedly also formed on decarboxylation of 2d,e. *In all the cases studied, the tin enolates are formed with a near-to-total regioselectivity both in the cyclic and the acyclic series.* The transformation of 2e to 4e is a particularly good illustration of the regiospecific character of the present method and the regiostability of the tributyltin enolates obtained. Indeed, in the parent benzyl isopropyl ketone, the benzylic hydrogens are both the thermodynamically and kinetically more acidic ones. As a result, only the acetate 5e is formed under either thermodynamic or kinetic (triphenylmethyl lithium, Ac₂O^{3b}) conditions.

Owing to their specific reactivity in various condensation reaction, tributyltin enolates have received increasing attention in the recent years¹⁴. Furthermore, tin enolates may be converted to other enolates or enol derivatives by straightforward reactions. Finally, allyl β -keto esters are available by a number of classical condensation reactions^{2a,15}, which allows a great flexibility in the choice of the substituents in the molecules. For all these reasons, the present method of regiospecific formation of tetrasubstituted tributyltin enolates should be very useful in synthetic chemistry.



R_1	R_2	R_3	Decarboxylation conditions ^(a)	Yield ^(b) <u>4</u> + <u>5</u>	Regioisomeric ^(b) composition <u>4/5</u>	Regioisomeric composition <u>4/5</u> at equilibrium ^(b)	
a	$-(CH_2)_2-$	CH_3	110°C, 15 min	85-90 %	98/2	57/43 ^(c)	
b	$-(CH_2)_3-$	CH_3	110°C, 15 min	85-95 %	99/1	78/22 ^(c)	
c	H	CH_3	110°C, 90 min	85-90 %	96/4	18/82 ^(c,d)	
d	H	CH_3	CH_2-Ph	130°C, 20 min	60-70 %	98/2 ^(e)	22/78 ^(f)
e	Ph	CH_3	CH_3	130°C, 30 min	65-75 %	> 95/5	0/100 ^(g)

(a) Decarboxylation at 130°C were performed after removal of toluene on a vacuum line.

(b) Z = $(CH_3)_3Si$ for entries a-c ; Z = Ac for entries d,c. Identification of products: see footnote h. (c) From ref 3c. (d) For $R_1=R_2=R_3=CH_3$. (e) 4d-E/4d-Z = 35/65. (f) Obtained in this laboratory from the parent ketone by the isopropenyl acetate/TsOH method^{3a} ; 4d-E/4d-Z = 40/60.

(g) Obtained in this laboratory from the parent ketone by the Ph_3CLi/Ac_2O method^{3b} ; 5e-E/5e-Z = 30/70. The isopropenylacetate/TsOH method gives also exclusively the enol acetate 5e but in very low yield. (h) Compounds 4 a-c and 5 a-c were identified by comparison with authentic samples prepared according to literature procedures^{3c}. Main spectroscopic characteristics for compounds 4d, 5d and 4e, 5e :

4d IR (CCl_4) : 1750 cm^{-1} (OAc), ~ 1695 cm^{-1} (C=C) ; 1H RMN ($CDCl_3$) : δ 2.01 (s, $OCOCH_3$), 3.29 and 3.38 (broad s, benzylic hydrogens E and Z isomers) ; GC/MS 70 eV m/e (rel. intensity) : the E and Z isomers have different retention time ; Z isomer : 204 (3%, M^+), 162 (25%, $M - CH_2=C=O$), 147 (22%), 144 (3%), 91 (25%, C_7H_7), 43 (100%, CH_3CO) ; E isomer : 204 (2%), 162 (21%), 147 (19%), 144 (2%), 91 (25%), 43 (100%)

5d IR (CCl_4) : 1760 cm^{-1} (OAc), 1660 cm^{-1} (C=C) ; 1H NMR ($CDCl_3$) : δ 2.01 (s, $OCOCH_3$), 4.65 (m, $H_2C=$) ; GC/MS : 162 (10%, $M - CH_2=C=O$), 147 (5%), 144 (42%, $M - CH_2=C=O, -H_2O$), 91 (80%), 43 (100%)
4e IR (CCl_4) : 1745 cm^{-1} (OAc), 1680 cm^{-1} (C=C) ; 1H RMN ($CDCl_3$) : δ 2.02 (s, $OCOCH_3$), 3.60 (broad s, benzylic hydrogens) ; GC/MS : 204 (4.5%, M^+), 162 (100%, $M - CH_2=C=O$), 147 (11%), 144 (13%), 118 (0.5%), 92 (52%), 91 (56%), 70 (14%), 43 (55%).

5e IR (CCl_4) : 1758 cm^{-1} (OAc), 1670 cm^{-1} (C=C) ; 1H NMR ($CDCl_3$) : δ 2.02 (s, $OCOCH_3$), 5.55 and 6.03 (two s, vinylic hydrogens for Z and E isomers respectively) ; GC/MS : the E and Z isomers are not separated by GC : 204 (9%, M^+), 162 (100%), 147 (28%), 144 (2.5%), 118 (7%), 92 (9%), 91 (4%), 70 (<0.5%), 43 (70%).

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References and Notes

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- 12- All our experiments were performed on millimoles scales under an argon atmosphere and with dry reagents. The first step simply involves a dropwise addition of tributyltin hydride (1.2 equivalents) to a toluene solution (1 M) of **1** in the presence of **1** to $2 \cdot 10^{-2}$ equivalents of dichloro bis(triphenylphosphine) palladium(II). In the decarboxylation step, metallic palladium immediately forms upon heating. It was checked in separate experiments where the precipitate was removed by filtration that the metal has no effect on the decarboxylation rate. The whole process of the formation of **2** and its decarboxylation to **3** may be followed by infra-red spectroscopy. Both the tin carboxylate and the tin enolate functionalities give a strong absorption in the 1640-1660 cm^{-1} range ; the tin enolate absorption however is immediately replaced by the carbonyl absorption of the parent ketone upon addition of minute amounts of methanol to the infra-red (CCl_4) solution.
- 13- No deuterium incorporation could be detected in the ketone by-product when the reaction was carried out with Bu_3SnD , which excludes any possible role of the tin hydride in the formation of the ketone.
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