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The Tin(II) Enolate Addition Reactions to α,β-Unsaturated Ketones and Quinones

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Abstract: The reaction of tin(II) enolates with various α,β-unsaturated carbonyl compounds is examined. When TMSCl is added as an activator of the α,β-unsaturated ketones, the Michael addition reaction proceeds smoothly to give the corresponding 1,4-adduct in good yield. When 1,4-benzoquinone and its mono-imino derivative are employed as acceptors in conjunction with dichloromethylsilane-DMAP activator, a novel addition-reduction reaction takes place to afford the α-arylcarbonyl compounds.

The Michael addition reaction is a basic carbon-carbon bond forming reaction widely employed in organic synthesis. This reaction has great potential as a versatile method for the stereoselective synthesis of acyclic systems including the construction of adjacent tertiary carbon centers.[1)]

During the last decade, the use of various metal enolates has brought about a high degree of stereoselection in aldol reactions.[2)] As the Michael reaction may be considered to be a vinylogous aldol addition reaction, the application of metal enolate nucleophiles to the Michael reaction emerges as a promising method for the realization of stereocontrol in this reaction.

The Michael addition reaction of active methylene compounds such as malonic esters to α,β-unsaturated carbonyl compounds under basic conditions is a well established method in organic synthesis. On the other hand, the use of ordinary ketones or esters as the donor in this reaction is still severely limited due to the occurrence of various side reactions. In addition, the reactivity of these substrates in the Michael reaction is generally low and therefore vigorous reaction conditions are usually required. Under such conditions, the process can be plagued by side reactions such as further transformation of the product, self-condensation of the acceptor, competitive 1,2-addition and the retrograde Michael reaction.[3)]

Recently, the reaction of lithium enolates with various Michael acceptors has been reported by several groups. Yamaguchi has studied extensively the stereoselective Michael reaction of lithium ester enolates with α,β-unsaturated esters.[4)] Heathcock has reported on the reaction of various lithium enolates and α,β-unsaturated ketones where the aforementioned side reactions are

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Dedicated to Professor Hans Wynberg on the occasion of his 65th birthday.

suppressed by employing sterically hindered acceptors.[5] However, the Michael reaction of metal enolates, especially with α,β-unsaturated ketones, still remains as a formidable problem.[6]

Over the past few years, we have been studying the chemistry of tin(II) enolates, and have succeeded in realizing a highly diastereoselective and enantioselective cross aldol reaction.[7] As the tin(II) enolate is generated under mild conditions (addition of carbonyl compound to tin(II) triflate in the presence of N-ethylpiperidine as base at -78°C), it was expected that various side reactions which take place in the Michael reaction of other metal enolates generated under more basic conditions would be suppressed.

First the reaction between 2-cyclohexen-1-one and the tin(II) enolate generated from 3-propanoyl-1,3-oxazolidin-2-one was examined. No reaction was observed when 2-cyclohexen-1-one was added to the tin(II) enolate at -78°C. The same reaction, when carried out at an elevated temperature resulted in the formation of a complex mixture from which both 1,2-addition and 1,4-addition products were isolated in low yields. Therefore, the addition of Lewis acid activators was examined with the expectation that the coordination of the Lewis acid to the carbonyl oxygen of the enone would enable the reaction to proceed at lower temperatures. The addition of $SnCl_4$ failed to promote the reaction, while use of $BF_3 \cdot OEt_2$ lead to the formation of the desired product in 28% yield. This result prompted us to examine other activators which exhibit a strong affinity towards the oxygen atom. Subsequently, it was found that in the presence of chlorotrimethylsilane (TMSCl), the reaction was promoted dramatically to give the Michael addition product in 84% yield (Table 1).

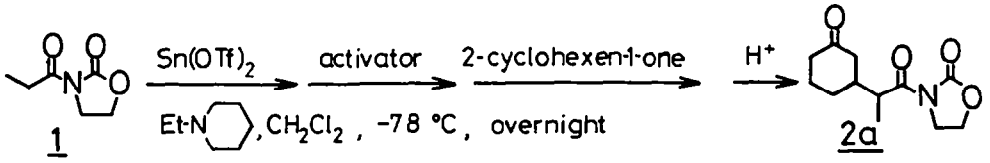
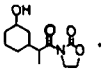


Table 1. Examination of activators[a]

Activator		Yield/%	Diastereomer ratio[b]
1)	none	0	———
2)	$SnCl_4$	0	———
3)	Me_3SnCl	0	———
4)	$BF_3 \cdot OEt_2$	28	69:31
5)	Ph_2BCl	17	53:47
6)	TMSCl	84	62:38
7)	TMSOTf	82	62:38
8)	Me_2SiCl_2	76	58:42
9)	Me_2HSiCl	66	———[c]
10)	$MeSiCl_3$	0	———
11)	$Me_2{}^tBuSiCl$	0	———

a) Molar ratio of $Sn(OTf)_2$: N-ethylpiperidine: 3-propanoyl-1,3-oxazolidin-2-one: activator: 2-cyclohexen-1-one=1.0:1.2:0.8:1.2-1.5:0.6.

b) Diastereomer ratio was determined by ^{1}H-NMR.

c) In this case, further reduction of 2a occurred to give  .

The reaction proceeded smoothly at -78°C, and no side products such as the 1,2-adduct were obtained. Other silyl compounds, such as chlorodimethylsilane, dichlorodimethylsilane, and trimethylsilyl triflate (TMSOTf) also effectively activated the reaction. Trichloromethylsilane and chlorodimethyl-t-butylsilane, however, failed to give any of the desired product. The former gave a complex mixture, while no reaction took place using the latter. The reaction of tin(II) enolates with various enones is shown in Table 2.

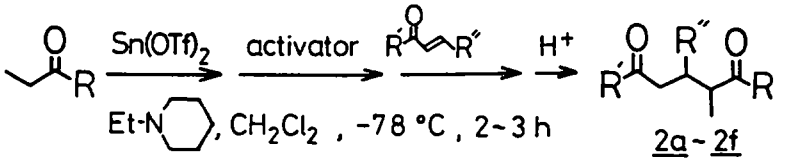
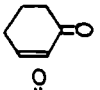


Table 2. The Michael reaction of tin(II) enolates

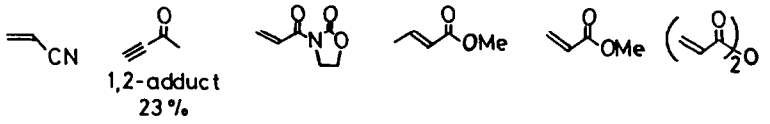
Entry	R	Acceptor	Product	Yield/%	Diastereomer[b] ratio	Activator[a]
1)			2b	77	92:8	A
2)	"	"	2b	78	29:71	B
3)	"		2c	56	95:5	A
4)	"	"	2c	56	71:29	B
5)	"		2d	85	75:25	A
6)	"		2a	84	62:38	B
7)	Et		2e	72	_____[c]	B
8)	Ph	"	2f	54	_____[c]	B

a) Activator A; chlorodimethylsilane, B; TMSCl.

b) Diastereomer ratio was determined by ^{1}H-NMR and ^{13}C-NMR.

c) Diastereomer ratio not determined.

No reaction was observed when the following compounds were used as acceptors.



In all cases the reaction is effectively promoted by the silyl compound and the desired Michael addition product is obtained in moderate to good yields. It is noted that the diastereomer ratio of the products obtained was dependent on the activator employed and in some cases, either diastereomer could be obtained predominantly by choosing either TMSCl or chlorodimethylsilane as activator. It is also noted that various enolates derived from ordinary ketones could be successfully employed in the present reaction, although the yields were slightly lower. The reaction with Michael acceptors other than α,β-unsaturated ketones, as shown in Table 2, was also tried. However, under the present reaction conditions none of the desired product was obtained.

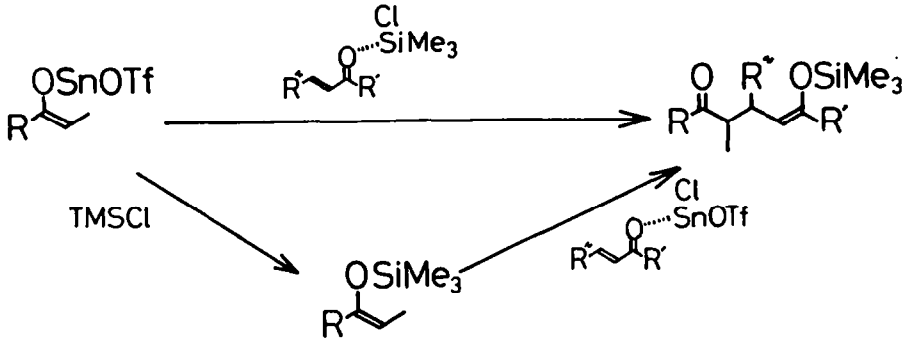
Regarding the mechanism of this reaction, two alternative reasonable pathways can be postulated.

In one possible pathway, the nucleophilic species is the tin(II) enolate, with activation of the acceptor by TMSCl. A similar activation by TMSCl has been reported in the conjugate addition of organocopper reagents to α,β-unsaturated carbonyl compounds.[8] In the present reaction this activation of the enone by TMSCl in the presence of tin(II) enolates would be feasible, due to the fact that tin(II) enolates, in contrast to lithium enolates, are not promptly silylated by TMSCl at -78°C. Furthermore, we have reported in a previous communication that the combination of catalytic amounts of tin(II) chloride and TMSCl leads to the formation of an extremely active complex which exhibits a highly Lewis acidic character.[9] Such an interaction between the tin(II) atom of the enolate and TMSCl could induce an extremely strong activation of the enone.

The other possibility is that the nucleophile is the silyl enol ether formed by metal exchange of the tin(II) enolate with TMSCl. The formation of the silyl enol ether, under the reaction conditions employed, can be observed on the tlc, although the rate of this silyl enol ether formation appears to be rather slow. Activation of the enone by the newly generated tin(II) triflate chloride or excess TMSCl could then promote the Michael reaction.

Although, at present, the latter pathway cannot be completely ruled out, the following experimental results suggest that the nucleophilic species is in fact the tin(II) enolate and not the silyl enol ether. The reaction between the silyl enol ether of propiophenone and phenyl propenyl ketone did not proceed in the presence of tin(II) triflate-chiral diamine. On the other hand, the addition of chiral diamine to the tin(II) enolate of propiophenone, followed by the addition of phenyl propenyl ketone and trimethylsilyl triflate gave an optically active Michael addition product. These results indicate that, in the presence

of a diamine, tin(II) triflate is not strong enough a Lewis acid to promote the Michael reaction between silyl enol ethers and α,β-unsaturated ketones, and the



reaction proceeds predominantly via the tin(II) enolate. Although the presence of diamine renders an exact comparison impossible, these facts imply that the tin(II) enolate is the active nucleophilic species in the present reaction. Further studies directed towards clarification of the mechanism as well as further applications of this reaction are currently in progress in our laboratory.

We have also examined quinone as the acceptor molecule as part of our study of the reaction of tin(II) enolates with α,β-unsaturated carbonyl compounds.

It is well documented in the literature that the addition of organometallic reagents to a quinone is often complicated because of undesired side reactions.[10,11,12] For example, when Grignard reagents are employed, electron transfer from the anionic species to the quinone often predominates and the self-coupling product of the nucleophile is obtained as a major product.[16] Also, in some cases, it is rather difficult to achieve selective 1,2- or 1,4-additions and mono- or di-additions of the nucleophile.

Recently, several successful results have been obtained using alkyllithium[13] reagents in ether, trialkylborane,[14] π-allyl Ni complex,[20] or allylstannanes[23] which give respectively either selective 1,2- or 1,4-alkylation products. However, addition of metal enolates derived from ketones or carboxylic acid derivatives has rarely been reported[13] probably due to the accompanying side reactions. As tin(II) enolates are highly nucleophilic and relatively low in basicity, it was expected that they might be successfully employed in addition reactions to quinones. Therefore we have examined these reactions, and particularly those of the silane/enolate system.

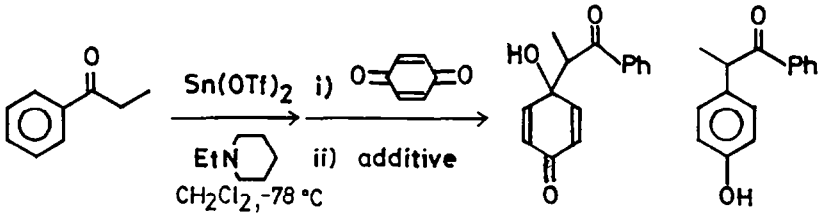
First, we examined the reaction of the tin(II) enolate derived from propiophenone with 1,4-benzoquinone. When the enolate was made to react with 0.45 equivalents of 1,4-benzoquinone at -78°C without any additives, a clean 1,2-addition reaction occurred and the adduct 4a was obtained in 68% yield with no trace of any Michael addition product.

[redacted]

addition of 1,4-benzoquinone, it was found that the 1,2-addition product 4a was gradually converted to a new compound, which was isolated in 63% yield after the

usual work-up. The structure of the new compound was assumed, based on NMR and IR spectra, to be the phenol 5a, the reduction product of 4a, and this was verified by independent synthesis. That the adduct 4a was indeed an intermediate in the formation of the phenol 5a was confirmed by treating isolated 4a with tin(II) triflate and TMSCl, which gave the phenol 5a in 81% yield, a reaction which did not proceed in the absence of TMSCl. Thus, a novel 1,2-addition-reduction reaction of a tin(II) enolate to quinone can be achieved just by adding TMSCl as an activator.

At this stage, it was ascertained that, in this reaction, the 1,2-addition of tin(II) enolate was a quick reaction (within 10 min), whereas the reduction step required rather a long period of time (usually overnight). Therefore, to increase the yield of phenol 5a and to accelerate the rate of reduction, the effect of altering the silicon reagent was examined. (Table 3)



3a 4a 5a

Table 3. Examination of silanes[a)]

Entry	Additive	Reaction time	Yield/% 4a	5a
1)	-	0.5 h	68	-
2)	-	overnight	62	7
3)	Me_3SiCl	overnight	-	63
4)	Me_3SiCl[b)]	overnight	c)	23
5)	Me_2HSiCl	overnight	-	55
6)	Me_2SiCl_2	overnight	-	56
7)	$MeHSiCl_2$	overnight	c)	58
8)	Me_3SiOTf	overnight	-	26
9)	$Me_2{}^tBuSiCl$	overnight	31	-
10)	$Ph_2MeSiCl$	overnight	28	48

a) Molar ratio of $Sn(OTf)_2$: N-ethylpiperidine: propiophenone: additive: quinone = 1.0:1.1:0.8:1.6:0.36.
b) 0.08eq of TMSCl is employed.
c) Product isolated in low yield.

Although increase of the yield of 5a had not been achieved at this point, the following three points ought to be emphasized here. Firstly, a very slow reduc-tion reaction takes place in the absence of any silanes, and an additive is essential to achieve a clean reduction (entries 2 and 3). Secondly, a

catalytic amount of promoter is not sufficient (compare entry 3 and 4) to give complete reduction and 2 equivalents of silane are routinely used. Thirdly, although several simple silanes give yield around 60% (entries 5-7), use of bulkier promoters leads to less efficient reaction (entries 9 and 10).

As the yield was still unsatisfactory, we turned to the use of potential activators of the silane. Consideration of a possible mechanism for the reaction (see below) led us to investigate reagents which might promote the attack of nucleophiles on the silane, i.e. nucleophilic catalysts. As amines such as 4-dimethylaminopyridine(DMAP) are a class of compounds often used for this purpose, we examined their effect on this reaction (Table 4).

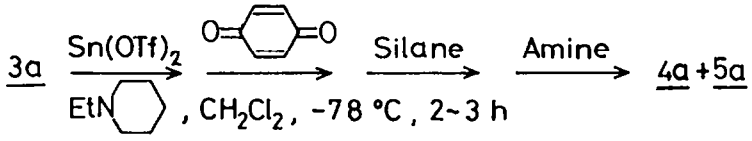


Table 4. Examination of silane-amine combinations[a)b)]

Entry	Additive	Reaction time	Yield/% 4a	5a
1)	Me_3SiCl 2eq + DMAP leq[c)]	overnight	40	33
2)	Me_2HSiCl 2eq + DMAP leq[c)]	overnight	17	36
3)	Me_2SiCl_2 2eq + DMAP leq[c)]	2 h	-	74
4)	$MeHSiCl_2$ 2eq + DMAP leq[c)]	2 h	-	78
5)	$MeHSiCl_2$ 2eq + DMAP 0.leq	2 h	-	63
6)	$MeHSiCl_2$ 2eq + pyridine leq[c)]	overnight	20	50
7)	$MeHSiCl_2$ 2eq + pyridine leq[c)]	overnight	42	-
8)	$MeHSiCl_2$ 2eq + pyridine leq[c)] + DMAP 0.leq[c)]	overnight	-	63

a) Molar ratio of $Sn(OTf)_2$: N-ethylpiperidine: propiophenone: silane: 1,4-benzoquinone = 1.0:1.1:0.8:1.6:0.36.

b) The order of addition was; quinone, silane, amine.

c) Eq to propiophenone.

As expected, when DMAP was used in conjunction with a dichlorosilane[8)], the reduction step was dramatically accelerated taking only about 2 h, and the yield of the product 5a was increased to 78% (entries 3 and 4). In contrast, the combination of DMAP and a monochlorosilane was ineffective (entries 1 and 2). Acceleration of the reduction step was achieved even when only a catalytic amount of activator was used, although a full equivalent was necessary for the best yield. It was also found that the order of addition influences the product distribution (Table 5).

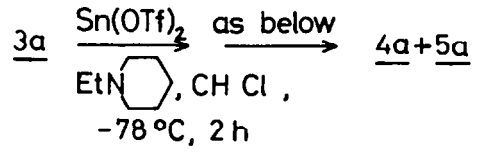


Table 5. Effect of order of addition[a)b)]

Entry	Order of addition	Yield/% 4a	5a
1)	quinone + $MeHSiCl_2$, DMAP	-	55
2)	DMAP, quinone, $MeHSiCl_2$	32	-
3)	quinone, DMAP, $MeHSiCl_2$	84	-
4)	quinone, $MeHSiCl_2$, DMAP	-	76
5)	quinone, $MeHSiCl_2$, 10 min, DMAP	-	78
6)	quinone, $MeHSiCl_2$, 30 min, DMAP	-	83

a) Molar ratio of $Sn(OTf)_2$: N-ethylpiperidine: propiophenone: silane: quinone = 1.0:1.1:0.8:1.6:0.36.

b) Unless otherwise noted, the components were added successively.

In Table 4, DMAP was added just after the addition of quinone and chlorosilane, however, when DMAP was added before silane, complete suppression of the reduction occurred (entries 2 and 3). On the other hand, a further increase in the yield of the phenol 5a was achieved when the aldol reaction was allowed to go to completion before the addition of the DMAP (entries 4-6), and a maximum yield of 83% was obtained.

Four mechanisms that can be postulated for this reaction are;

A) Elimination of HOSnOTf from the 1,2-adduct 4, followed by reduction with tin(II).

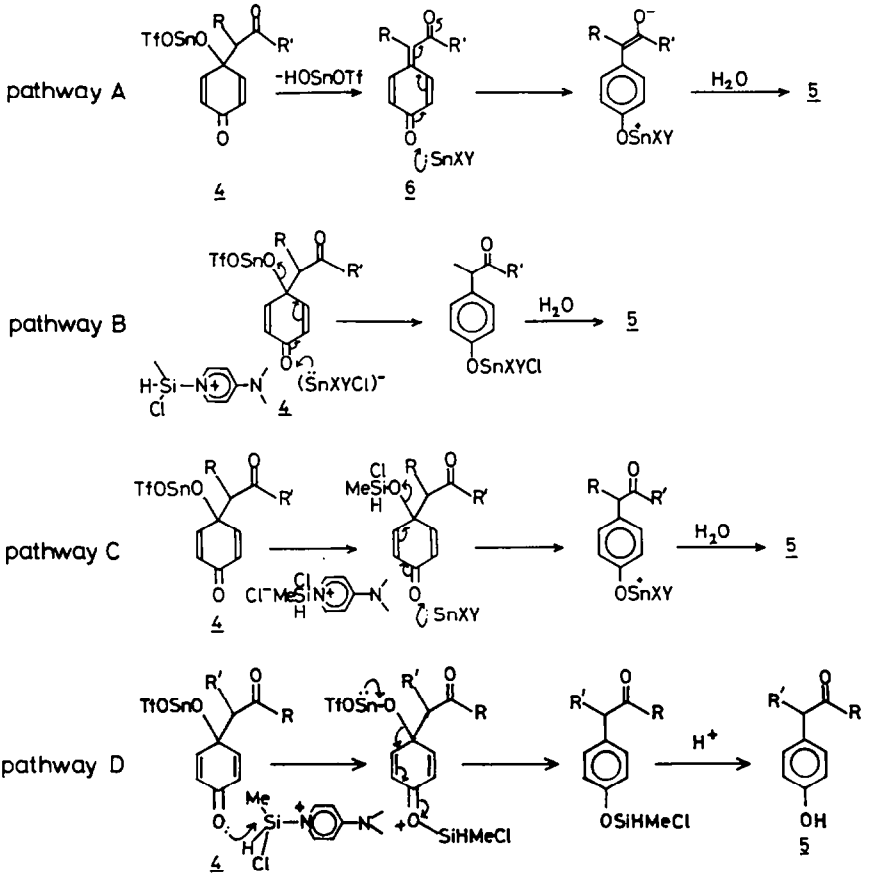
B) Reduction of the 1,2-adduct 4 with an external tin(II) species. In this case, the role of the chlorosilane is to form the $[SnX_2Cl]^-$ complex, which is assumed to have a higher reducing ability than SnX_2.

C) Silylation of the 1,2-adduct 4 followed by reduction with an external tin(II) species. In this case, it is assumed that silylation is necessary for rapid reduction.

D) Internal reduction-oxidation of the 1,2-adduct facilitated by activation of the diene carbonyl with silicon.

In both C and D, it is quite probable that the silylating ability (in C) or the Lewis acidity (in D) of silicon is enhanced by complexation with tin(II).[9] At this stage, both pathway A and B seem unlikely based on the following experi-

mental results. Firstly, when the reaction was carried out in the presence of the chiral diamine, and the intermediate 4a was reduced in situ, the product 5a was obtained in optically active form. This rules out the intermediacy of a planar species such as 6, at least as the major reaction pathway. Secondly, addition of metal chlorides, KCl/18-C-6 or n-Bu_4NCl, which would also be expected to lead to the formation of $[SnX_2Cl]^-$ species, does not have an effect on the reduction rate or yield. These results make both pathways A and B unlikely.



As for pathways C and D, we have not yet been able to determine which is the correct reaction mechanism. However, both mechanisms can explain why the order of addition of silane and DMAP effects this reaction. Thus, when DMAP is added before the silane, DMAP coordinates to tin and the catalytic activity of DMAP is lost. However, when DMAP is added after the silane, DMAP coordinates preferentially to silane. Also the fact that use of TMSCl-DMAP renders the reduction step slower can be explained as TMSCl is a weaker silylating agent than $MeHSiCl_2$ and thus DMAP may coordinate preferentially to tin even in the presence of TMSCl. At present we are in the process of clarifying the exact mechanism.

Having discovered the optimal reaction conditions, we next applied this reaction to various substrates and the results are summarized in Table 6.

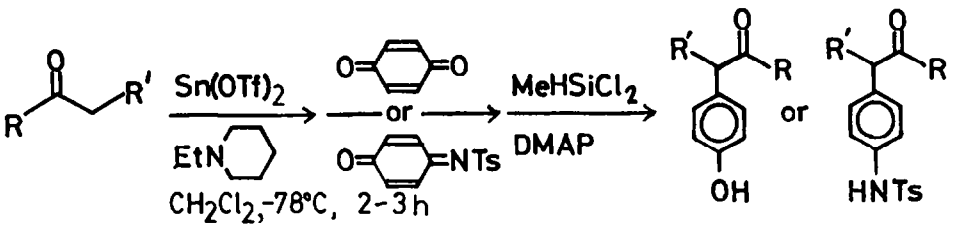


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Table 6. The reaction of tin(II) enolates with quinones[a)b)]

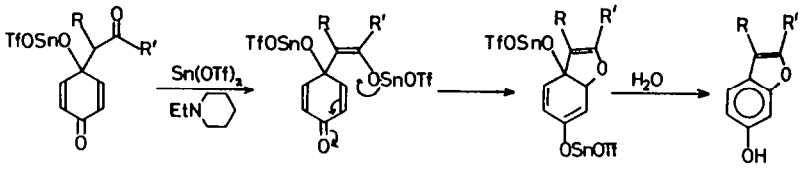
Entry	R	R'	Substrate		Product	Yield/%
1)	Ph	Me	1,4-benzoquinone		5a	83
2)	Ph	Et	1,4-benzoquinone		5b	72
3)	Ph	CH_2Ph	1,4-benzoquinone		5c	66
4)	Ph	H	1.4-benzoquinone		5d	65
5)	iPr	H	1,4-benzoquinone		5e	65
6)	Et	Me	1,4-benzoquinone		5f	68
7)	iPr	Me	1,4-benzoquinone		5g	70
8)		H	1,4-benzoquinone		5h	48
9)		Me	1,4-benzoquinone		5i	71
10)	Ph	Me	1,4-benzoquinone	mono-N-tosylimine	7a	77
11)	Et	Me	1,4-benzoquinone	mono-N-tosylimine	7f	78
12)		Me	1.4-benzoquinone	mono-N-tosylimine	7i	67

a) For entries 1,2,3,4,8,9 and 10 procedure a (see experimental) was followed, for entries 5,6,7,11 and 12 procedure b was used.

b) The structures of products 5a, 5f, 5h and 5i were proved by independent synthesis, and the others confirmed by comparison of IR, NMR and mass spectra.

In nearly every case, a yield of around 70% was obtained. One problem is the formation of benzofuran side products when a dialkyl ketone enolate is used. We believe these arise *via* the pathway shown in the following scheme, that is, enolization of the intermediate 4, cyclization, and dehydration to give the furan 8. Although from the NMR of this compound it was not possible to assign the aromatic substitution pattern conclusively, the weight of spectroscopic and

chemical evidence makes it virtually certain that 8 is the isomer shown. Optimization of the reaction of dialkyl ketone enolates by adjusting the ketone/quinone molar ratio to 1:0.6 led to suppression of this side reaction.



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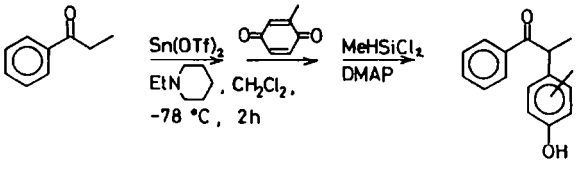
This reaction can also be applied to an iminoquinone derivative to produce 4-aminophenyl derivatives (entries 10-12), and by using 3-acyl-1,3-oxazolidin-2-ones as the carbonyl component, potentially useful 2-arylpropanoic acid derivatives can be produced.[25] The reaction was also applied to 2-methyl-1,4-benzoquinone and a single isomer 9 was obtained in 59% yield, although the regiochemistry has not yet been determined. This shows the reaction has considerable promise for the regioselective synthesis of trisubstituted phenols.



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In conclusion, this reaction provides a useful, conceptually new route to the one-pot synthesis of 2-arylcarbonyl compounds, including potentially useful 2-aryl propanoic acid derivatives. Furthermore, it also combines the high reactivity of tin(II) enolate with the reducing properties of tin(II), permitting for the first time *in situ* reduction of the aldol intermediate.

Thus, we have successfully used tin(II) enolates both for the Michael addition to α,β-unsaturated ketones and for the conversion of quinone to the corresponding α-arylcarbonyl compounds *via* an addition-reduction process. Both of these two reactions are made possible only when tin(II) enolates are employed together with silyl chloride, and we believe this kind of reaction promoted by the combined use of two essentially neutral reagents will find a wide variety of applications in synthetic reactions.

We are currently investigating the asymmetric version of these reactions, both for the synthesis of some medicinally important compounds[25] and for the clarification of the exact reaction mechanisms.

Experimental

All m.p.s are uncorrected. IR spectra were recorded as films for oils and as KBr discs for solids on a Hitachi 260-30 infrared spectrophotometer. ^{1}H-NMR spectra were obtained on a Hitachi R-24B spectrometer and low and high resolution mass spectra were recorded on a JEOL JMS-D300 mass spectrometer. Column

chromatography was performed on Wakogel C-200 silicagel and preparative thin layer chromatography on Wakogel B5F. All reactions were carried out under an argon atmosphere in dried glassware.

Typical procedure for the reaction of tin(II) enolates with α,β-unsaturated ketones in the presence of TMSCl: The addition of 3-propanoyl-1,3-oxazolidin-2-one to phenyl propenyl ketone.

$Sn(OTf)_2$ (343mg, 0.82mmol) in a two-necked flask was cooled to -78°C and N-ethylpiperidine (116mg, 1.03mmol) in dichloromethane (2ml) was added to it dropwise. After 10 min a solution of 3-propanoyl-1,3-oxazolidin-2-one (97mg, 0.67 mmol) in dichloromethane (1.5ml) was added dropwise with stirring to the resulting yellow-green suspension, and stirring was continued at -78°C for a further 1 h. Phenyl propenyl ketone (77mg, 0.53mmol) and TMSCl (107mg, 0.99mmol) were added successively to the mixture and after stirring for 2 h the reaction was quenched at -78°C with 10% citric acid (10ml). Dichloromethane (10ml) was added and the organic and aqueous phases were separated. The aqueous phase was extracted with dichloromethane (10ml x 3) and the combined organic layers were dried ($MgSO_4$) filtered and evaporated under reduced pressure. To completely hydrolyze the trimethylsilyl ether product, the residue was dissolved in methanol and citric acid was added to this solution. After stirring for 1 h the reaction was quenched with pH7 phosphate buffer. The organic layer was extracted with dichloromethane (10ml x 3) and the combined extracts were dried ($MgSO_4$). After evaporation of the solvent, the crude product was purified by preparative thin layer chromatography to afford the Michael adduct 2d (120mg, 79%).

Spectral data of the Michael adducts are presented below.

2a: A white, crystalline solid. IR(KBr) 2950, 1760, 1700, 1380, 1220, 760, 700cm^{-1}; NMR($CDCl_3$)δ 1.1(3H,d,J=6Hz), 1.3-2.6(9H,br), 3.5-4.7(5H,m). Precise mass calc for $C_{12}H_{17}O_4N$ m/z 239.1158. Found 239.1188.

2b: A white, crystalline solid. IR(KBr) 3000, 1770, 1700, 1380, 1220, 760, 700cm^{-1}; NMR($CDCl_3$)δ 0.9(3H,d,J=5Hz), 1.9(3H,s), 2.4-3.1(2H,m), 3.3-3.6(1H,m), 3.9-4.5(5H,m), 7.1(5H,s). Calc for $C_{16}H_{19}O_4N$: C, 66.42; H, 6.62; N, 4.84%. Found: C, 66.13; H, 6.68; N, 4.65%.

2c: A white, crystalline solid. IR(KBr) 2970, 1780, 1680, 1380, 1200, 760, 700cm^{-1}; NMR($CDCl_3$)δ 0.8-1.2(6H,m), 2.1(3H,s), 2.2-2.8(3H,m), 3.5-4.6(5H,m).

2d: A white, crystalline solid. IR(KBr) 2970, 1760, 1680, 1380, 1240, 760, 690cm^{-1}; NMR($CDCl_3$)δ 0.9-1.3(6H,m), 2.4-3.3(3H,m), 3.6-4.5(5H,m), 7.2-7.6(3H,m), 7.8-8.1(2H,m). Precise mass calc for $C_{16}H_{19}O_4N$ m/z 289.1315. Found 289.1307.

2e: A colorless oil. IR(neat) 2980, 1710, 1690, 1600, 1450, 760, 690cm^{-1}; NMR($CDCl_3$)δ 0.8-1.2(9H,m), 2.3-3.2(6H,m), 7.2-7.6(3H,m), 7.8-8.0(2H,m). Precise mass calc for $C_{15}H_{20}O_2$ m/z 232.1464. Found 232.1482.

2f: A colorless oil. IR(neat) 2970, 1680, 1600, 1450, 1220, 760, 690cm^{-1}; NMR($CDCl_3$)δ 1.0(3H,d,J=6Hz), 1.2(3H,d,J=6Hz), 2.5-3.2 (3H,m), 3.4-3.7(1H,m), 7.2-7.6(3H,m), 7.7-8.0(2H,m). Precise mass calc for $C_{19}H_{20}O_2$ m/z 280.1464. Found 280.1462.

Procedure for the 1,2-addition of tin(II) enolates to quinones: The addition of propiophenone to 1,4-benzoquinone.

$Sn(OTf)_2$ (313mg, 0.75mmol) in a two-necked flask was cooled to -78°C and N-ethylpiperidine (95mg, 0.84mmol) in dichloromethane (1.5ml) was added to it dropwise. After 10 min a solution of propiophenone (81mg, 0.61mmol) in dichloromethane (1.5ml) was added dropwise with stirring to the resulting yellow-green suspension, and stirring was continued at -78°C for a further 30 min. Then, 1,4-benzoquinone (29mg, 0.27mmol) in dichloromethane (1.5ml) was added dropwise at -78°C to the mixture and after stirring for 30 min the reaction was quenched at -78°C with 10% citric acid (10ml). Dichloromethane (10ml) was added and the organic and aqueous phases were separated. The aqueous phase was extracted with dichloromethane (10ml x 3) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure. This left a colorless solid residue which was purified by flash column chromatography on silica gel to give the 1,2-adduct 4 (45mg, 68%) as a white crystalline solid, m.p.110-112°C(recrystallised from toluene).

IR(KBr) 3400, 1680, 1620, 1600, 1250cm^{-1}; NMR($CDCl_3$)δ 1.3(3H,d,J=7Hz), 3.7(1H,q,J=7Hz), 3.8(1H,br), 6.0-6.3(2H,m), 6.7-7.3(2H,m), 7.4-7.6(3H,m), 7.9-8.1(2H,m). Calc for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83%. Found: C, 74.65; H, 5.77%.

Procedure for the 1,2-addition-reduction reaction of tin(II) enolates and quinones: The addition of propiophenone to 1,4-benzoquinone with the addition of

TMSCl.

$Sn(OTf)_2$ (1346mg, 3.20mmol) was placed in a two-necked round-bottomed flask and N-ethylpiperidine (399mg, 3.50mmol) in dichloromethane (11ml) was added to it dropwise at -78°C. Stirring was continued for a further 10 min, and then propiophenone (367mg, 2.70mmol) in dichloromethane (2ml) was added dropwise. Stirring was continued for a further 30 min at -78°C, and then 1,4-benzoquinone (133mg, 1.20mmol) in dichloromethane (2ml) was added dropwise to the suspension, followed after 10 min by a solution of TMSCl (588mg, 5.40mmol) in dichloromethane (2ml). After stirring for 30 min at -78°C the reaction was quenched by addition of 10% citric acid (50ml) and dichloromethane (50ml). The layers were separated and the aqueous layer was extracted with dichloromethane (50ml x 2). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give an oily, yellow residue. This was purified by flash column chromatography to give the phenol 5a (175mg, 0.77mmol) (63%) as fluffy, white crystals, m.p. 89-90°C (recrystallised from chloroform/hexane).

IR(KBr) 3400, 1660, 1605, 1590, 1570, 1505, 1220, 730cm^{-1}; NMR($CDCl_3$) 1.5(3H,d,J=7Hz), 4.6(1H,q,J=7Hz), 6.7(2H,d,J=7Hz), 7.1(2H,d,J=7Hz), 7.4(3H,m), 7.8-8.0(2H,m). Calc for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24%. Found: C, 79.46; H, 6.28%.

Reduction of dienone (2) to phenol (3a).

$Sn(OTf)_2$ (230mg, 0.55mmol) was placed in a two-necked flask and acetonitrile (3.5ml) was added to it. The resulting suspension was cooled to -40°C, and the dienone 4 (67mg, 0.28mmol) in acetonitrile (1.5ml) was added dropwise with stirring. After 10 min TMSCl (342mg, 3.20mmol) in acetonitrile (1.5ml) was added dropwise to the mixture and thereafter stirring was continued at -40°C for a further 3 h. The reaction was then quenched by addition of 10% citric acid (15ml) and ether (15ml). The two phases were separated, and the aqueous phase was extracted with ether (18ml x 3). The combined organic layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a colorless paste which was purified by preparative thin layer chromatography on silica gel to give the phenol 5a (52mg, 0.23mmol)(84%), identical to that obtained by the aldol reaction of the tin(II) enolate of propiophenone with 1,4-benzoquinone in the presence of TMSCl.

Typical procedure for the reaction of a tin(II) enolate with a quinone followed by in situ reduction with DMAP/dichloromethylsilane.

Procedure (a). The carbonyl compound (0.40mmol) in dichloromethane (1ml) was added dropwise at -78°C to a stirred mixture of $Sn(OTf)_2$ (0.50mmol) and N-ethylpiperidine (0.55mmol) in dichloromethane (1ml). The resulting mixture was stirred at -78°C for 40 min. The quinone (0.18mmol) in dichloromethane (2ml) was added dropwise at -78°C to the resulting yellow-green suspension, and stirring was continued for a further 30 min, after which dichloromethylsilane (0.97mmol) in dichloromethane (2ml) and dimethylaminopyridine (0.44mmol) in dichloromethane (2ml) were added dropwise, with an interval of about 30 min. Stirring was continued at -78°C until analytical thin layer chromatography showed consumption of all the intermediate (30 min to 2 h). The reaction was then quenched with 10% aqueous citric acid solution (10ml) and the resulting two phase mixture was extracted with dichloromethane (3 x 10ml). The combined extracts were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give an oily or semi-solid residue which was purified by preparative thin layer chromatography on silica gel.

Procedure (b). Identical to procedure (a) excepting that 0.24mmol of quinone was used.

Spectral data of the phenol and amine products are presented below.

5b: A white, crystalline solid, m.p. 90-91°C (recrystallised from chloroform/hexane at -78°C) IR(neat) 3400, 1660, 1610, 1595, 1580, 1510, 1220cm^{-1}; NMR($CDCl_3$) δ 0.9(3H,t,J=6Hz), 1.5-2.4(2H,m), 4,4(1H,t,J=7Hz), 6.0(1H,br), 6.7(2H,d,J=8Hz), 7.1(2H,d,J=8Hz), 7.3-7.5(3H,m), 7.9-8.0(2H,m). Calc for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71%. Found: C, 79.71; H, 6.69%.

5c: A white, crystalline solid, m.p. 154-155°C (recrystallised from toluene). IR(KBr) 3350, 1660, 1610, 1595, 1580, 1510, 1275, 1220cm^{-1}; NMR ($CDCl_3$) δ 3.0(1H,dd,J=14,7Hz), 3.5(1H,dd,J=14,7Hz), 4.7(1H,t,J=7Hz), 5.2(1H,brs), 6.7(2H,d,J=7Hz), 6.9-7.4(10H,m), 7.7-7.9(2H,m). Precise mass calc for $C_{21}H_{18}O_2$ m/z 302.1305. Found 302.1279.

5d: A white, crystalline solid, m.p. 136-138°C (recrystallised from toluene). IR(KBr) 3250, 1680, 1610, 1590, 1570, 1505, 1440, 1210cm^{-1}; NMR($CDCl_3$) δ 4.2(2H,s), 5.2-5.8(1H,br), 6.7(2H,d,J=8Hz), 7.1(2H,d,J=8Hz), 7.2-7.5(3H,m), 7.8-

8.0(2H,m). Precise mass calc for $C_{14}H_{12}O_2$ m/z 212.0837. Found 212.0852.
5e: A colorless oil. IR(neat) 3250, 1710, 1615, 1600, 1510, 1170cm^{-1}; NMR($CDCl_3$) δ 1.1(3H,d,J=7Hz), 2.7(1H,nanoplet,J=7Hz), 3.6(2H,s), 6.5-6.8(1H,br), 6.7(2H,d,J=8Hz), 7.0(2H,d,J=8Hz). Precise mass calc for $C_{11}H_{14}O_2$ m/z 178.0993. Found 178.0998.
5f: A colorless oil. IR(neat) 3250, 1710, 1615, 1600, 1515, 1160cm^{-1}; NMR($CDCl_3$) δ 1.0(3H,t,J=7Hz), 1.4(3H,d,J=7Hz), 2.4(1H,q,J=7Hz), 3.7(1H,q, J=7Hz), 5.5-5.8(1H,br), 6.7(2H,d,J=8Hz), 7.1(2H,d,J=8Hz). Precise mass calc for $C_{11}H_{14}O_2$ m/z 178.0993. Found 178.1005.
5g: A colorless oil. IR(neat) 3350, 1700, 1610, 1585, 1505, 1220cm^{-1}; NMR($CDCl_3$) δ 1.0(3H,d,J=7Hz), 1.1(3H,d,J=7Hz), 1.4(3H,d,J=7Hz), 2.7(1H, nanoplet, J=7Hz), 3.9(1H,q,J=7Hz), 5.9-6.4(1H,br), 6.7(2H,d,J=8Hz), 7.0(2H,d, J=8Hz).
5h: A white, crystalline solid, m.p. 147-149°C (recrystallised from toluene). IR(KBr) 3370, 1770, 1695, 1615, 1600, 1520, 1400cm^{-1}; NMR(DMSO-d_6)δ 3.9(2H,s), 3.6-4.5(5H,m), 6.6(2H,d,J=8Hz), 7.0(2H,d,J=8Hz). Calc for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33%. Found: C, 59.48; H, 4.99; N, 6.34%.
5i: A white, crystalline solid, m.p. 164-166°C (recrystallised from toluene). IR(KBr) 3350, 1760, 1700, 1620, 1600, 1520, 1400cm^{-1}; NMR($CDCl_3$)δ 1.5(3H,d,J=7Hz), 3.8-4.5(4H,m), 5.0(1H,q,J=7Hz), 6.0(1H,br), 6.7(2H,d,J=8Hz), 7.2(2H,d,J=8Hz). Calc for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.96%. Found: C, 61.20; H, 5.43; N, 5.66%.
7a: A white, powdery solid, m.p. 144-145°C (recrystallised from butan-1-ol). IR(KBr) 3250, 1680, 1610, 1595, 1510, 1160cm^{-1}; NMR($CDCl_3$)δ 1.5(3H,d,J=7Hz), 2.4(3H,s), 4.6(1H,q,J=7Hz), 6.7-8.0(14H,m). Calc for $C_{22}H_{21}NO_3S$: C, 69.63; H, 5.58; N, 3.69%. Found: C, 69.62; H, 5.51; N, 3.47%.
7f: A colorless gum. IR(KBr) 3250, 1710, 1615, 1600, 1515, 1160cm^{-1}; NMR($CDCl_3$) δ 1.0(3H,t,J=7Hz), 1.4(3H,d,J=7Hz), 2.4(1H,q,J=7Hz), 2.4(3H,s), 4.1(1H,q,J=7Hz), 7.0-7.8(9H,m). Precise mass calc for $C_{18}H_{21}NO_3S$ m/z 331.1243. Found 331.1284.
7i: A colorless gum. IR(KBr) 3250, 1780, 1700, 1615, 1605, 1520cm^{-1}; NMR($CDCl_3$) δ ;1.4(3H,d,J=7Hz), 2.4(3H,s), 3.8-4.5(4H,m), 5.0(1H,q,J=7Hz), 7.0-7.8(9H,m). Precise mass calc for $C_{19}H_{20}N_2O_5S$ m/z 388.1092. Found 388.1127.

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