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A Convenient Preparation of α-(p-Hydroxy- or p-Aminophenyl) Carbonyl Compounds. Addition-Reduction Reaction of Tin(II) Enolate with p-Benzoquinone and Its Mono-N-tosylimino Derivative

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Tin(II) enolates react with p-benzoquinone and its mono-N-tosylimino derivative to give 1,2-adducts in good yield. These can be reduced in situ to α-(p-hydroxy- or p-aminophenyl) carbonyl derivatives by addition of dichloromethylsilane and dimethylaminopyridine.

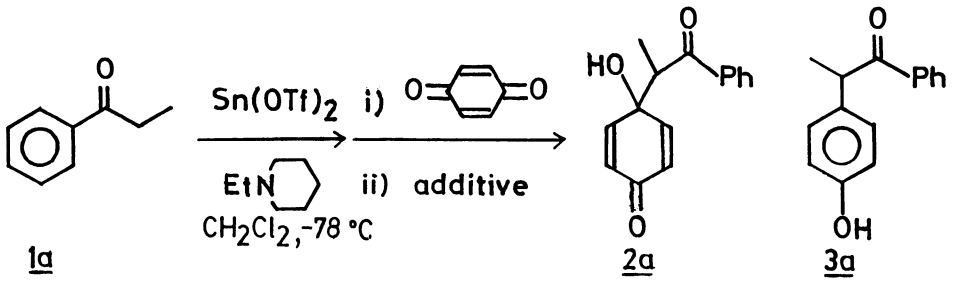
The addition of organometallic reagents to quinones is often complicated by the occurrence of undesired side-reactions such as electron transfer to the quinone leading to self-coupling of the nucleophile,[1] and by the difficulty of achieving selective 1,2 or 1,4 additions and selective mono- or diaddition of the nucleophile to the quinone. Recently the use of alkyllithium reagents in ether[2] or the use of allyl stannanes[3] has allowed selective 1,2 or 1,4 alkylation of quinones. However, although the addition of enolates derived from active methylene compounds to quinones has been studied,[4] there are few reports of similar reactions using the enolates of ketones or carboxylic acid derivatives.[5]

Recently we have been studying the reactions of tin(II) enolates and have developed various characteristic aldol reactions using these species, such as the asymmetric reaction using chiral diamine ligands.[6] However, the reducing property of tin(II) has not so far been used for in situ transformation of the aldol products. We have now examined the reaction of the tin(II) enolates of ketones and 3-acyloxazolidine-2-ones with 1,4-benzoquinone and would like to report here the successful use of this characteristic.

When the tin(II) enolate derived from propiophenone 1a was allowed to react with 0.45 equivalents of 1,4-benzoquinone at -78 °C for 30 min, the 1,2-adduct 2a, was formed in 68% yield.[7] On the other hand, when the reaction was carried out in the presence of chlorotrimethylsilane, which we expected to behave as a mild Lewis acid[8] compatible with the presence of an enolate, the phenol 3a, a reduction product of 2a, was produced in 63% yield.

The intermediacy of 2a in the reaction leading to 3a was confirmed by reduction of the isolated adduct 2a to 3a in 81% yield by treatment with tin(II) triflate and chlorotrimethylsilane, a reaction which did not proceed in the absence of the chloride.

To examine the effect of the silicon substituents on the yield, various other chlorosilanes were screened. These results are listed in Table 1.



1a 2a 3a

Table 1. Examination of the Additives

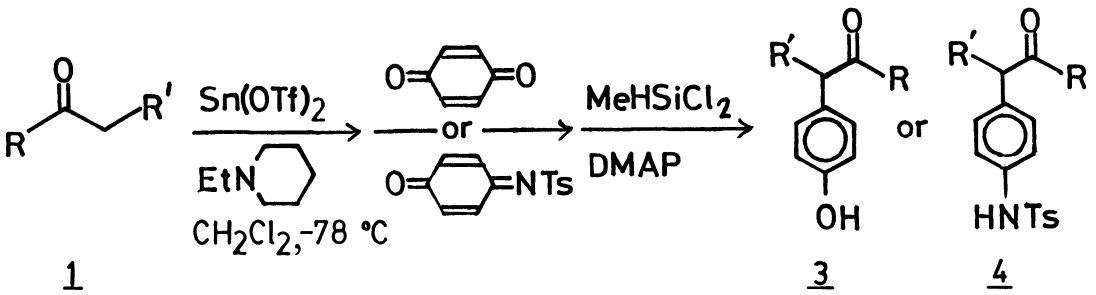
Entry	Additive	Reaction time/h	Yield/% 2a	Yield/% 3a
1	——	0.5	68	—
2	TMSCl 2 equiv.	overnight	—	63
3	$MeHSiCl_2$ 2 equiv.	overnight	—	58
4	$MeHSiCl_2$ 2 equiv. + DMAP 1 equiv.	2	—	83
5	Me_2SiCl_2 2 equiv. + DMAP 1 equiv.	2	—	74
6	TMSCl 2 equiv. + DMAP 1 equiv.	overnight	40	33

The combination of dichloromethylsilane and 4-dimethylaminopyridine(DMAP)[9] gave the best yields and also led to a marked shortening of the reaction time from overnight to thirty minutes. The following four points should be noted. Firstly, to get the best yields, it is necessary to use 1 equivalent of DMAP, as although a catalytic amount increases the rate of the reduction, the yield remains about the same; Secondly, other amines such as pyridine or N-methylimidazole are not effective catalysts; Thirdly, only silanes bearing two chlorine atoms are effective as promoter in combination with DMAP (compare entires 4 and 5 with 6) and lastly, the order of addition of chloride and amine is important, as adding the amine first leads to suppression of reduction, 2a being isolated as the major product.

Under the optimised reaction conditions, the following yields were obtained for various substrates (Table 2).

In every case except entry 8, a yield of around 70% was obtained. Furthermore the reaction can also be applied to imino quinone derivative to produce 4-aminophenyl derivatives (entry 10-12), and by using 3-acyloxazolidine-2-ones as the carbonyl component, potentially useful 2-arylpropanoic acid derivatives[10] can be produced.

A typical procedure is as follows; Propiophenone (1a, 0.44 mmol) in dichloromethane (1 ml) was added dropwise at -78 °C to a stirred mixture of tin(II) trifluoromethanesulphonate (0.55 mmol) and N-ethylpiperidine (0.61 mmol) in dichloromethane (1 ml). The resulting mixture was stirred at -78 °C for 40 min. 1,4-Benzoquinone (0.19 mmol) in dichloromethane (2 ml) was added dropwise at -78 °C to the resulting yellow-green suspension, and stirring was continued for a further 30 min, after which dichloromethylsilane (0.97 mmol in 2 ml CH_2Cl_2) and dimethylaminopyridine (0.44 mmol in 2 ml CH_2Cl_2) were added dropwise in quick succession. Stirring was continued at -78 °C until thin layer chromatography (50% ethyl



1 3 4

Table 2. Reaction of Various Carbonyl Compounds[a)]

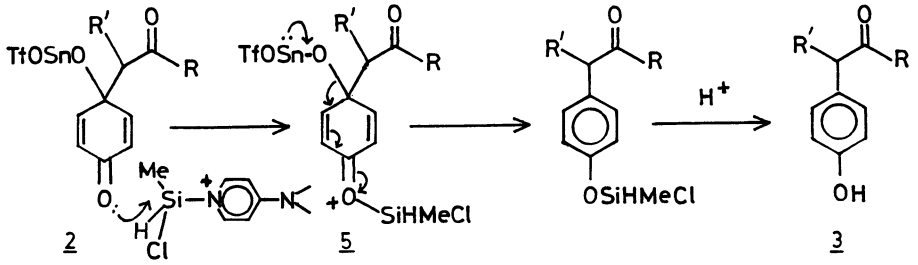
Entry	Carbonyl			Substrate	Yield/%	Product[b,c)]
	R	R^1				
1	Ph	Me	(1a)	1,4-benzoquinone	83	3a
2	Ph	Et	(1b)	1,4-benzoquinone	72	3b
3	Ph	CH_2Ph	(1c)	1,4-benzoquinone	66	3c
4	Ph	H	(1d)	1,4-benzoquinone	65	3d
5	iPr	H	(1e)	1,4-benzoquinone	65	3e
6	Et	Me	(1f)	1,4-benzoquinone	68	3f
7	iPr	Me	(1g)	1,4-benzoquinone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

a) For entries 1-4, 8, and 10, molar ratio is; $Sn(OTf)_2$:Carbonyl:Quinone:$MeHSiCl_2$:DMAP = 1.2:1.0:0.45:2.0:1.0. For entries 5-7, 9, 11, and 12, molar ratio is; $Sn(OTf)_2$:Carbonyl:Quinone:$MeHSiCl_2$:DMAP = 1.2:1.0:0.6:2.0:1.0. Aliphatic enolates gave benzofuran side-products when 0.45 equivalents of quinone were used.[11)]
b) All the products gave satisfactory NMR, IR, and mass spectra.
c) The structures of the products obtained in entries, 1, 6, 7, 8, and 9 were confirmed by independent synthesis, and the other structures were confirmed by comparison of NMR and IR spectra.

acetate/hexane) showed consumption at all the intermediate (~30 min). The reaction was then quenched with 10% aqueous citric acid solution (10 ml) and the resulting two-phase mixture was extracted with dichloromethane (3x10 ml). The combined extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give an oily residue which was purified by preparative thin layer chromatography on silica gel using 30% ethyl acetate/hexane as eluent. This gave

the phenol 3a (0.16 mmol 83%) as a colorless oil, which slowly solidified on standing.

Although a number of possible mechanisms can be postulated for the present reaction, the following is the most reasonable to explain the efficiency of the DMAP/dichloromethylsilane combination. After initial formation of the aldol intermediate 2, the quinol carbonyl reacts with the activated silane to give a complex 5 which in turn undergoes a ready internal reduction /oxidation reaction to give 3, after cleavage of the O-Si bond.[12)]



Thus it has now become possible to utilize the reducing ability of tin(II) to reduce certain aldol products in situ, in particular the adducts with 1,4-benzoquinone and its mono-N-tosylimino derivative, when a silyl chloride is used as a promoter. We are currently investigating the asymmetric version of this reaction, and its application to the preparation of medicinally important compounds. Also under examination is the use of the adducts 2 for the preparation of various polyfunctionalized aromatic species.

References

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5) M. C. Lasne, J. L. Ripoll, and A. Thuillier, Chem. Ind., 20, 830 (1980).
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7) In contrast to these results the lithium enolate of 1 did not add efficiently to 1,4-benzoquinone under any conditions examined.
8) H. Oshino, E. Nakamura, and I. Kuwajima, J. Org. Chem., 50, 2802 (1985); and references therein.
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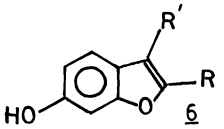
11) Based on spectral and chemical evidence, the structures of these products are believed to be 6.



12) It is possible that the Lewis acidity of the silane is enhanced by complexation with tin(II) (N. Iwasawa and T. Mukaiyama, Chem. Lett., submitted for publication).

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