

Silicon Assisted Halogenation I: A Convenient Synthesis of β -chloroketones via Reaction of α,β -unsaturated ketones with Tetrachlorosilane-Phenol

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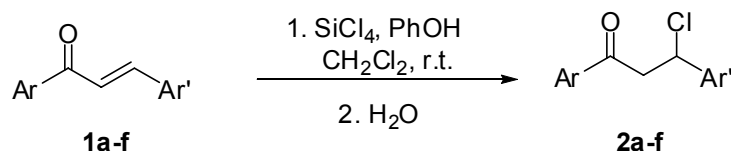
ABSTRACT- A combination of tetrachlorosilane (TCS) and phenol in dichloromethane was found to be an efficient reagent for hydrochlorination of α,β -unsaturated ketones to afford the corresponding β -chloroketones in good yield at ambient temperature.

INTRODUCTION

β -Haloketones are useful intermediates in organic synthesis as they undergo a number of substitution reactions at halogen, as well as protonation and addition reactions at the carbonyl group.¹ However, whereas the methods of synthesis of α -haloketones are numerous, it is apparently more difficult to obtain β -halo derivatives which suffer spontaneous dehydrohalogenation if the conditions are too drastic. Olefin acylation² and addition of hydrogen halides to α,β -unsaturated ketones³ are mainly the most applicable procedures for the synthesis of β -haloketones. The latter reaction often leads to salts by protonation of the carbonyl oxygen, which then renders the carbon-carbon double bond unreactive toward hydrogen halide addition. The reaction of an enone with a tetraalkylammonium halide in anhydrous trifluoroacetic acid is a convenient synthesis for β -iodo ketones but remains less efficient for β -chloroketones.⁴ The Mukaiyama reaction can lead to β -chloroketones as unexpected side products.⁵ Halosilanes have been used in the preparation of β -haloketones. For example, iodotrimethylsilane (TMSI) adds to α,β -unsaturated carbonyl compounds to give β -iodo carbonyl derivatives⁶ or their acetals,⁷ in the presence of diols. Some β -haloketones have been obtained by direct coupling of a ketone with itself⁸ or with benzaldehyde⁹ in the presence of a halosilane. β -Haloketones were also prepared through the halogenation of β -siloxyketones with a halosilane under $\text{BiCl}_3\text{-ZnI}_2$ catalysis.¹⁰ On the other hand, combinations of some silicon derivatives and phenol have been explored for the cleavage of tert-butyl protecting groups in solid phase peptide synthesis.¹¹ In conjunction with our interest in exploring the utility of *in situ* reagents based on tetrachlorosilane (TCS)¹² in organic synthesis, the present communication describes a facile and mild procedure for the hydrochlorination of α,β -unsaturated ketones to give the corresponding β -chloroketones in good yields utilizing the inexpensive and readily available tetrachlorosilane-phenol system.^{12c}

RESULTS AND DISCUSSION

The reaction of α,β -unsaturated ketones with SiCl_4 -PhOH works well giving good yields of respective β -chloroketones after aqueous work up (Scheme 1, Table 1). The structure of isolated β -chloroketones was assigned based on their spectral analyses as well as by matching their melting points with reported analogues.



1a, 2a; Ar = Ar' = Ph
1b, 2b; Ar = Ph, Ar' = 4-ClC₆H₄-
1c, 2c; Ar = Ph, Ar' = 3-ClC₆H₄-
1d, 2d; Ar = 4-MeOC₆H₄-, Ar' = Ph
1e, 2e; Ar = 4-MeC₆H₄-, Ar' = 4-ClC₆H₄-
1f, 2f; Ar = 4-MeOC₆H₄-, Ar' = 4-ClC₆H₄-

Scheme 1

Table 1. Reaction of α,β -unsaturated ketones with TCS-PhOH reagent

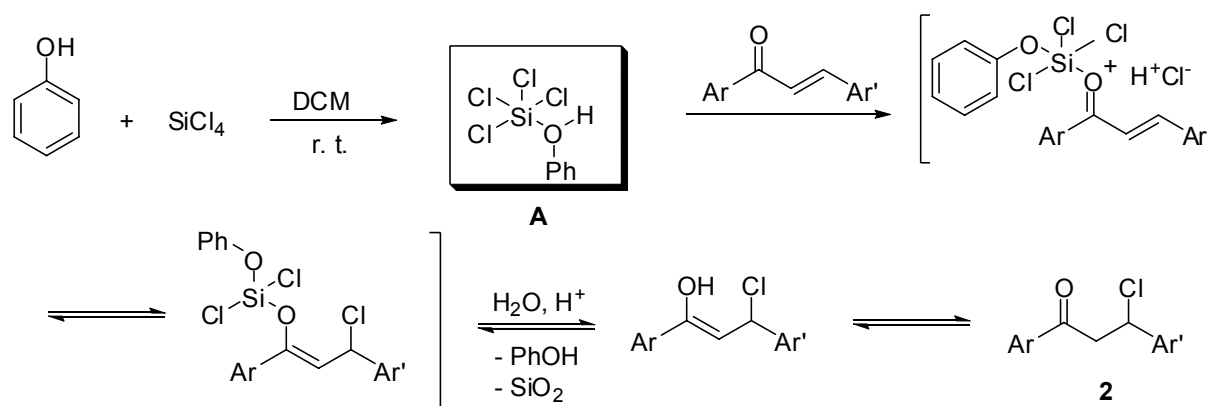
Entry	Substrate	Time (h)	Product	Yield (%) ^a
1	Benzalacetophenone	11	2a	82
2	4-Chlorobenzalacetophenone	16	2b	74
3	3-Chlorobenzalacetophenone	15	2c	65
4	Benzal-4-methoxyacetophenone	14	2d	67
5	4-Chlorobenzal-4-methylacetophenone	16	2e	71
6	3-Chlorobenzal-4-methoxyacetophenone	17	2f	61
7	2,6-Dibenzal cyclohexanone	24	-	-
8	2-(4'-Methylbenzal)-1-tetralone	21	-	-

^a Isolated yield

It is noteworthy to mention that no reaction was observed in the absence of either the PhOH or SiCl_4 . The generality of the process was examined through applying the reaction to various examples of α,β -unsaturated ketones, however, unfortunately, the reaction failed with arylidenes of alicyclic ketones. For example, dibenzalacetone and 2,6-dibenzal cyclohexanone were recovered without reaction (entries 7,8, Table 1). The structure of β -chloroketones **2** was supported by analytical and spectral data. First, in the IR spectra of **2**, the absorption at 1680-1690 cm^{-1} attributed for carbonyl stretching of saturated system showed a clear shift than that corresponding to starting α,β -unsaturated ketones. The ¹H-NMR spectra of **2e** for example showed two doublet of doublets at δ 3.88 and δ 3.59 as well as a triplets at δ 5.57

These were assigned to the C-2 and C-3 protons respectively. The EI-MS showed a characteristic peak at m/z 256 attributed to $M^+ - HCl$ which is expected due to a dehydrohalogenation during the ionization process.

The mechanism of synthesis of β -chloroketones **2** has not been exactly determined. However, a plausible pathway for the present reaction may proceed as depicted in Scheme 2 through 1,4- addition of stoichiometric reagent generated in situ from the reaction of TCS and phenol in 1:1 molar ratio (proposed phenoxychlorosilane **A**) to α,β -unsaturated ketones. Formation of **A** may find a support from the reported reaction of chlorotrimethylsilane (TMSCl) with phenol in which a complex similar to **A** was proposed.^{11b} In addition, 1,4-addition of halosilanes to enones is well-documented.^{6,7}



Scheme 2

CONCLUSION

In conclusion, we have presented herein a new convenient route to the synthesis of β -chloroketones via the reaction of α,β -unsaturated ketones with the cheap and readily available tetrachlorosilane and phenol in dichloromethane at ambient temperature. However, the superior method to prepare β -chloroketones is probably by reaction of the enones with gaseous HCl, the present procedure does offer a milder method which may have some applications exploring the versatile role of tetrachlorosilane in organic synthesis.

EXPERIMENTAL

General procedure for the synthesis of β -chloroketones:

To a mixture of α,β -unsaturated ketone (5 mmol) and phenol (10 mmol) in CH_2Cl_2 (20ml), $SiCl_4$ (10 mmol) was added and the reaction mixture was stirred at room temperature. On completion (the reaction was monitored by TLC), the mixture was quenched with cold water, extracted with $CHCl_3$, dried over anhydrous $MgSO_4$ and the solvent was vaporized under vacuum and the residue was

chromatographed using the eluent system pet.ether-ethyl acetate (20:1) to give pure **2c-f** or treated with ethanol (5ml) to give pure **2a,b**. Data for **4f** as representative example are showed below:

3-Chloro-3-(4-chlorophenyl)-1-p-tolylpropan-1-one 2e. Yield 71%; Purification by column chromatography using pet. ether-ethyl acetate (20:1) as eluent system; 87 °C; IR (KBr plate, cm^{-1}) ν 3094, 3027, 2920, 1679 (COCH_2), 1599 ($\text{C}=\text{C}$), 1515, 1451, 1413, 1357, 1329, 1237, 1063, 856, 753, 726, 699; $^1\text{H-NMR}$ (CDCl_3) δ 7.84 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.42 (d, $J = 7.4$ Hz, Ar-H), 7.34-7.22 (m, 4H, Ar-H), 5.57 (t, 1H, $J = 6.2$ Hz), 3.88 (dd, $J = 5.4, 16.5$ Hz, 1H), 3.59 (dd, $J = 5.4, 16.5$ Hz, 1H), 2.41 (s, 3H); EI-M.S.(m/z, %): 256 ($\text{M}^+ - \text{HCl}$, 81), 241 (33), 221 (35), 178 (31), 165 (32), 119 (84), 91 (100); Anal. Calcd. For $\text{C}_{16}\text{H}_{12}\text{Cl}_2\text{O}$ (293.19): C, 65.55; H, 4.81. Found: C, 65.32; H, 4.68

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