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STUDY ON THE "TIN-ENE" REACTION OF α -BROMOACETOPHENONE AND METALLIC TIN WITH ALDEHYDES

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Abstract: β -hydroxy ketones were obtained in good yields by the "tin-ene" reactions of α -bromoacetophenone and metallic tin with aldehydes.

The ene reaction usually involves a concerted reaction of an olefin containing an allylic hydrogen (ene) with an electron-deficient multiple bond (enophile) to form a 1:1 adduct via a six-membered ring transition state¹ (Scheme 1). The ene reaction may also involve the transfer of atoms other than hydrogen. Recently, "metallo-ene" (mainly "magnesium-ene"²⁻⁴) reaction has received interest as a promising tool for synthesis of some natural products, but a cardinal restriction in the use of many organometallic reagents is the strict exclusion of moisture. The solvent and the reagents must be anhydrous and the reaction often

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Scheme 1 The ene reaction.

has to be conducted under an inert atmosphere, and the substrates with functional groups such as hydrogen, halogen, nitro must be appropriately protected during the reaction.

Recently, the active metallic tin has been successfully used in allylation of many aldehydes.⁵⁻⁸ These reactions may offer the following advantages: (1) The reactions can be conducted in aqueous medium. (2) The tedious task of protection-deprotection of certain functional groups can be avoided. So it occurred to us that it might be possible to use metallic tin in other organic reactions.

We report here the reactions of α -bromoacetophenone and metallic tin with aldehydes. These reactions, which afforded β -hydroxy ketones as the products, can hardly carry out in anhydrous THF but proceeded smoothly when a mixture of THF and saturated aqueous solution of ammonium chloride (2:1) was used as solvent.





 α -Bromoacetophenone and tin could react with aliphatic aldehydes and aromatic aldehydes to give β -hydroxy ketones in good yields without difficulty. Only 1,2- addition products were obtained when α , β -unsaturated aldehydes (such as cinnamaldehyde and crotoaldehyde) were used. The reaction carried out smoothly with the substrates containing reactive groups such as halogen, alkoxy or nitro group.

The results, summarized in Table 1, suggest that the reaction proceeded as follow (Scheme 2): α -bromoacetophenone (1) initially reacted with tin to form organotin compound (2), and then (2) tautomerized to its enolate form (3).⁹ So the reaction is actually the "tin-ene" reaction of enolate (3) with aldehyde. In this reaction, the enolate (3) serves as the ene unit and the aldehyde as the enophile.

General procedure

A suspension of 5 mmol of aldehyde, 10 mmol of α -bromoacetophenone, 10 mmol of active tin, THF (20 mL), and saturated aqueous solution of ammonium

LADICI	Т	able	: 1
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Entry	Aldehyde	T/t (°C/h)	Product	Yield (%)
a	СНО	50 / 20	OH O	64
b	Me	60 /20	Me OH O	57
C	CI CHO	60 / 20	CI C	77
d	CHO	50 / 36	O OH O	46
e	CHO	60 / 20	OH O	60
f	NO ₂ CHO	60 / 24	NO ₂ OH O	71
g	СНО	60 / 24	OH O	70
h	~~~Сно	60 / 24	OH O	68
i	~~~	60 / 24		73
j	✓ CHO	60 / 24	OH O	74

chloride (10 mL) is stirred at 50 °C for 20 h. After evaporating of THF, 10 mL of brine is added. The mixture is extracted with ether (20 mL \times 3), the combined extracts are dried over anhydrous sodium sulfate. The ether is removed and the residue is purified by column chromatography to give 4.

For entry **f** the reaction is carried out in two steps that 4- nitrobenzaldehyde is introduced after metallic tin has disappeared.

4a¹⁰: v_{max} : 3500 (s, O-H), 1675 (s, C=O) cm⁻¹; δ_{H} (CCL₄, TMS): 3.07-3.50 (m, 3H, COCH₂, OH), 5.00-5.27 (t, 1H, OCH), 7.00-8.00 (m, 10H, ArH) ppm.

4b¹¹: v_{max} : 3400 (s, O-H), 1675 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 2.23 (s, 3H, CH₃), 3.07-3.50 (m, 3H, COCH₂, OH), 5.00-5.20 (t, 1H, OCH), 6.90-8.00 (m, 9H, ArH) ppm.

4c¹¹: v_{max} : 3500 (s, O-H), 1665 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 3.10-3.30 (d, 2H, COCH₂), 3.50-3.80 (br, 1H, OH), 5.00-5.23 (t, 1H, OCH), 7.00-8.00 (m, 9H, ArH) ppm.

4d: v_{max} : 3500 (s, O-H); 1670 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 2.87-3.20 (m, 3H, COCH₂, OH), 4.93-5.27 (t, 1H, OCH), 5.80 (s, 2H, OCH₂O), 6.40-8.00 (m, 8H, ArH) ppm. Anal. Calcd. for C₁₆H₁₄O₄: C, 71.10; H, 5.22. Found: C, 71.13; H, 5.14.

4e¹⁰: ν_{max}: 3450 (s, O-H), 1675 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 2.67-3.33 (m, 3H, COCH₂, OH), 4.50-4.90 (m, 1H, OCH), 5.83-6.73 (m, 2H, CH=CH), 7.00-8.00 (m, 10H, ArH) ppm.

4f¹²: v_{max} : 3500 (s, O-H), 1680 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 3.00-3.80 (m, 3H, COCH₂, OH), 5.00-5.40 (t, 1H, OCH), 7.23-8.33 (m, 9H, ArH) ppm.

4g¹³: v_{max} : 3450 (s, O-H), 1670 (s, C=O) cm⁻¹; δ_H (CCl₄, TMS): 0.80-1.40 (m, 7H, CH₃, CH₂×2), 2.37-2.57 (d, 2H, COCH₂), 3.00-3.20 (br, 1H, OH), 3.87-4.10 (m, 1H, OCH), 7.30-7.80 (m, 5H, ArH) ppm.

4h¹⁴: v_{max} : 3400 (s, O-H), 1700 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 0.80-1.47 (m, 9H, CH₃, CH₂×3), 2.90-3.03 (br, 1H, OH), 2.37-2.57 (d, 2H, COCH₂), 3.83-4.10 (m, 1H, OCH), 7.30-7.80 (m, 5H, ArH) ppm.

4i¹⁵: v_{max} : 3450 (s, O-H), 1700 (s, C=O) cm⁻¹; δ_{H} (CCl₄, TMS): 0.77-1.47 (m, 13H, CH₃, CH₂×5), 2.33-2.57 (d, 2H, COCH₂), 3.80-4.10 (m, 1H, OCH), 7.33-7.83 (m, 5H, ArH) ppm.

4j¹⁶: v_{max} : 3450 (s, O-H), 1700 (s, C=O), 1640 (w, C=C) cm⁻¹; δ_{H} (CCl₄, TMS): 1.63 (d, 3H, CH₃), 2.60-2.80 (br, 1H, OH), 3.00 (d, 2H, COCH₂), 5.27-5.50 (m, 2H, CH=CH), 7.33-7.80 (m, 5H, ArH) ppm.

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