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Nucleophilic Acylation of Esters by Acid Chlorides Mediated by Samarium Diiodide: Formation and Use of Samarium Enediolates.

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Abstract : Acid chlorides react with esters in the presence of samarium diiodide and catalytic amounts of NiI_2 to afford samarium enediolates which can further react with electrophiles such as water or aldehydes to give respectively α-ketols or α-dihydroxyketones. © 1997 Published by Elsevier Science Ltd.

We recently discovered the beneficial effect of catalytic amounts of some transition metal salts such as NiI_2 on many reactions mediated by diiodosamarium.[1] Strong accelerations were noticed, for instance, in Barbier reactions with ketones and in acid chloride couplings. It was also found that intermolecular Barbier type reactions were possible with esters.

We wish to describe here a new coupling reaction between acid chlorides and esters mediated by SmI_2 in the presence of catalytic amounts of NiI_2.

As a reaction model, we investigated the reaction between benzoyl chloride and ethyl acetate in the presence of 4 eq. of SmI_2 and 1 mol % (with respect to SmI_2) of NiI_2 in tetrahydrofuran (THF) at 0°C. There was a fast oxidation of Sm(II) to Sm(III) as evidenced by the color change of the reaction medium. Acidic workup allowed the isolation of α-ketol **1** with trace amounts of the isomeric ketol **2** (Scheme 1).[2] Without NiI_2, the yield of α-ketol **1** is less than 30% ; by-products such as ketol resulting from the self-coupling of the acid chloride, or esters, arising from the ring opening of THF are produced.[3] Optimisation of the experimental conditions[4] allowed the preparation of **1** in 82% isolated yield (with respect to the acid chloride). The transient formation of the enediolate **3** was established by deuterolysis (D_2O) giving **1'** with 83% deuteration. The enediolate was also quenched by acetic anhydride, leading to acetylated enediol **4** (*Z* isomer, isolated yield 83%) and with propanal, affording dihydroxyketone **5** (mixture of diastereomers) in 76% isolated yield.[5] These results are depicted in Scheme 1.

Coupling between the acid chloride and the ester probably proceeds through a transient acyl samarium species,[7,8] the resulting α-diketone being quickly reduced into an enediolate by samarium diiodide,[10] (Scheme 2).

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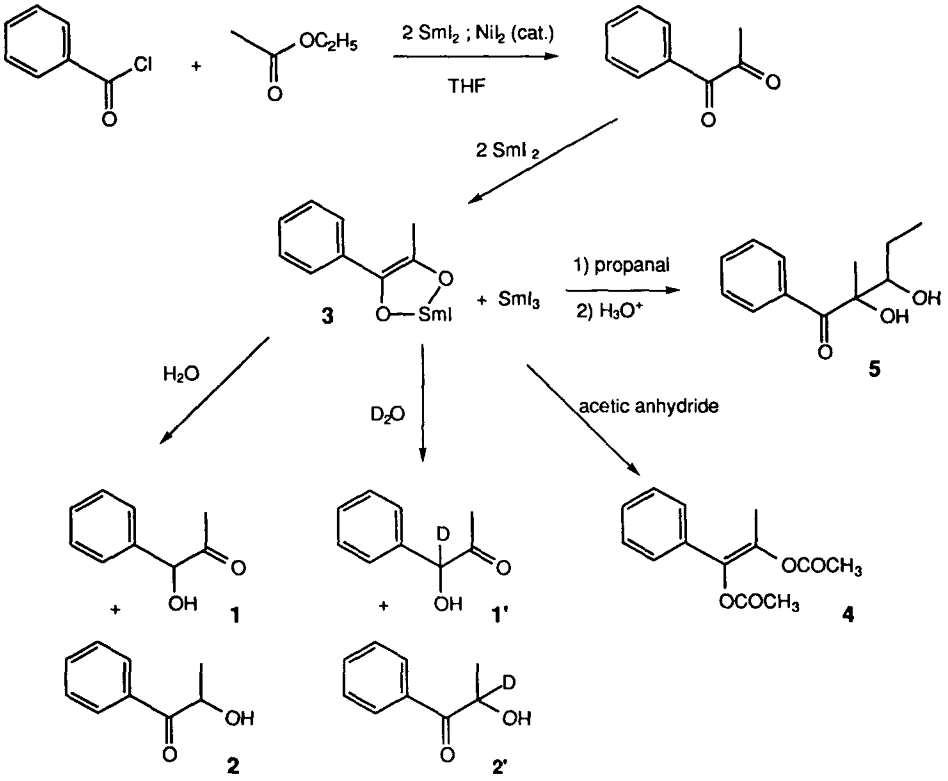
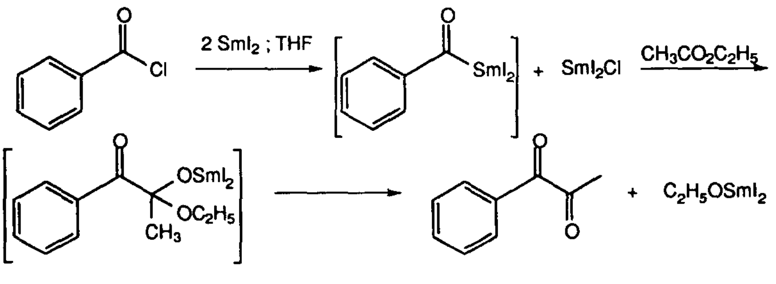
Scheme 1: Coupling Reactions of Benzoyl Chloride and Ethyl Acetate.



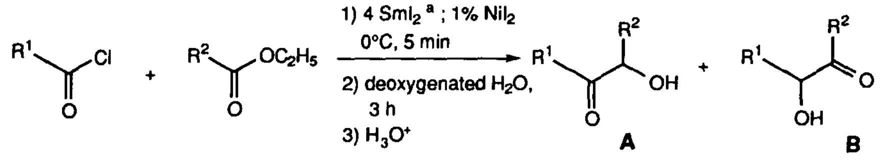
Scheme 2: Reaction of Acyl Samarium Species with Ethyl Acetate.



In a further investigation the above results were generalized to other classes of acid chlorides and esters. The results are gathered in Table 1

Use of an excess of ester allows formation of α-ketols, after hydrolysis, in good isolated yields. At the present time the distribution between the two isomeric ketols which results from the reaction of water with samarium enediolate is unpredictable. It is worthy of note that benzoyl chloride and nonanoyl chloride give almost exclusively α-ketols with the carbonyl group on the ester side (**B** isomer), thus reaction with ester and reaction with aldehyde (exclusive formation of the other α-ketols[3]) are complementary to each other.

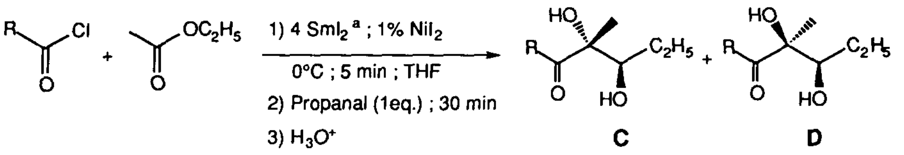
Table 1: Coupling Reactions of Acid Chlorides and Esters.



R^1	R^2	Ester/Acid Chloride (eq.)	Isolated yield % (A + B)	A/B[b]
Phenyl	CH_3	10	82	2/98
2-chlorophenyl	CH_3	10	83	70/30
n-C_8H_{17}	CH_3	10	62[c]	0/100
Phenyl	*n*-C_7H_{15}	3	68	20/80
Adamantyl	CH_3	10	70	80/20
Cyclohexyl	*n*-C_7H_{15}	3	74	60/40
1-methylcyclohexyl	CH_3	10	77	48/52
Cyclohexyl	CH_3	10	85	33/67
Cyclohexyl	C_2H_5	1	0[d]	-
Cyclohexyl	C_2H_5	10	68	53/47
Cyclohexyl	*i*-C_3H_7	10	43	52/48

a) Reaction performed in THF with a slurry of SmI_2, $[SmI_2]=1$ M; mole ratio of SmI_2/acid chloride=4. b) Determined by glc. c) Solution of SmI_2 in THF, $[SmI_2]=0.1$ M d) Exclusive formation of the α-ketol resulting from self coupling of the acid chloride.

Table 2: Quenching of Samarium Enediolates with Propanal.



R	Isolated yield % (C+D)	C/D[b]
Adamantyl	56	58/42
Cyclohexyl	65	61/39
Phenyl	76	52/48

a) Reaction performed in THF with the slurry of SmI_2, $[SmI_2]=1$ M

b) Determined by glc; relative stereochemistries of C and D were assigned by analogy with ref. 6

We have checked that samarium enediolates are able to react with propanal, as indicated above for benzoyl chloride and ethyl acetate. Carbon-carbon bond formation occurs on the less hindered side of the enediolate but unfortunately, diastereoselectivity is low with this aldehyde (Table 2).

We are currently investigating the scope of the coupling reaction of acid chloride with esters and the reactivity of disymmetric samarium enediolates towards various electrophiles such as protonating agents (including chiral protonating agents) and carbonyl compounds.

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4. To a slurry of SmI_2 (4×10^{-3} mol) in THF (4 mL) is added a solution of NiI_2 (4×10^{-5} mol) in THF (4 mL) and ethyl acetate (40×10^{-3} mol). The mixture is cooled to 0°C and acid chloride (10^{-3} mol) in THF (5 mL) is dropwise added within 5 min. The initially deep blue solution turns brown, the electrophile (H_2O, D_2O, propanal or acetic anhydride) is then added. Finally the mixture is quenched with HCl (0.1 M) to obtain a clear solution and extracted with ether. The combined extracts are washed with sodium thiosulfate and brine. The organic layer is dried over $MgSO_4$ the crude material is purified by flash chromatography on silica gel.
5. Coupling between samarium enediolates and aldehydes has been previously reported, see ref. 6.
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