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A new samarium diiodide-mediated coupling reaction between *N*-acyl lactams and ketones or aldehydes

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Abstract

A new SmI_2-mediated coupling reaction between *N*-acyl lactams and ketones or aldehydes is reported. The ring opening of these imides with samarium diiodide gives acyl samarium species, which are trapped by ketones or aldehydes to yield amido α-ketols. With an excess of SmI_2, in the presence of ethanol, the end products are amidoketones. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: coupling reactions; acyl lactams; amidoketones; amidoketols; samarium diiodide.

The samarium(II)-mediated reactions involving a variety of carbonyl compounds (ketones, aldehydes, esters, acid chlorides, acid anhydrides) have been extensively studied.[1] On the other hand, it has been proved that, except in some cases,[2,3] amides have a low reactivity, which permits selective reactions, for example Barbier-type reaction with amidoketones.[4] The carbonyl group of imides should be more reactive, even though, to our knowledge, only two examples are known, namely an intramolecular Barbier-type reaction of some *N*-iodoalkyl cyclic imides[5] and recently a pinacolic coupling between phthalimides and carbonyl compounds.[6]

We report here some results concerning a new samarium diiodide-mediated coupling reaction between some *N*-acyl lactams and ketones or aldehydes. We found that *N*-acyl lactams react with ketones or aldehydes, at room temperature in a few minutes, to give amido α-ketols **1** in good yields. The reactions are performed in THF without any additives such as HMPA or nickel salts[7] (Table 1). Although the cleavage of the endocyclic *N*-carbonyl bond always occurs preferentially, better results are obtained with pivaloyl lactams (R^1 = *tert*-butyl) than with compounds having a less hindered exocyclic *N*-carbonyl bond ($R^1 = n\text{-}C_7H_{15}$ or $n\text{-}C_4H_9$). In the reactions involving an aldehyde (entries 9 and 12), a 1:1 mixture of two isomeric amido α-ketols is obtained. This observation can be rationalized by the assumption that the corresponding samarium α-ketolates are in equilibrium via their enolates (Scheme 1).

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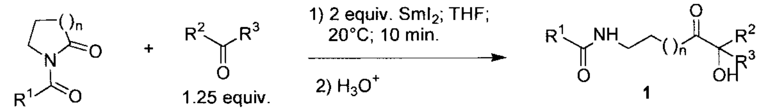
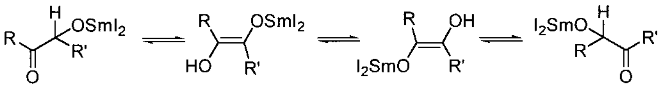
Table 1
Preparation of amido α-ketols



entry[a]	n	R[1]	R[2], R[3]	isolated yield (%)
1	1	*n*-C_7H_{15}	-$(CH_2)_5$-	69
2	1	*n*-C_7H_{15}	CH_3, *n*-C_6H_{13}	62
3	1	*n*-C_4H_9	-$(CH_2)_5$-	65
4	1	*n*-C_4H_9	CH_3, *n*-C_6H_{13}	60
5	1	*tert*-C_4H_9	-$(CH_2)_5$-	75
6	1	*tert*-C_4H_9	CH_3, C_2H_5	72
7	1	*tert*-C_4H_9	CH_3, *n*-C_6H_{13}	67
8	1	*tert*-C_4H_9	-$(CH_2)_3$-	85
9	1	*tert*-C_4H_9	H, *n*-C_4H_9	62[b]
10	2	*tert*-C_4H_9	-$(CH_2)_5$-	30
11	2	*tert*-C_4H_9	-$(CH_2)_3$-	26
12	2	*tert*-C_4H_9	H, *n*-C_4H_9	56[b]
13	3	*tert*-C_4H_9	-$(CH_2)_5$-	60
14	3	*tert*-C_4H_9	-$(CH_2)_3$-	72
15	3	*tert*-C_4H_9	CH_3, C_2H_5	54

a) In a Schlenk tube under argon, to 20 mL of a 0.1 M solution of SmI_2 in THF (2.0 mmol) was quickly added a mixture of a ketone or an aldehyde (1.25 mmol) and an *N*-acyl lactam (1 mmol) in THF (10 mL) at 20°C. Stirring was continued for 10 min, then the reaction mixture was quenched with HCl (0.1 M). After the usual work-up,[9] the crude material was purified by flash chromatography on silica gel.

b) Mixture (1:1) of two isomeric amido α-ketols (see scheme 1).

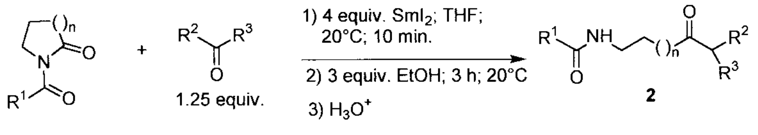


Scheme 1.

Alternatively, an intramolecular MPV/O reaction could account for this result. Due to an over-reduction of the samarium α-ketolates, small amounts (5–10%) of the deoxygenated coupling products **2** (amidoketones) are detected. This reaction can be achieved with 4 equivalents of SmI_2 (instead of 2 equivalents) and 2 equivalents of ethanol within 3 h (Table 2). With *N*-pivaloyl-2-piperidinone, the yields of heterocoupling products decrease (Table 1: entries 10 and 11; Table 2: entries 9 and 10), mainly because of a competing reductive homocoupling reaction of the imide. Interestingly, this reaction takes place readily in the absence of a ketone or an aldehyde, giving diamidodiketones **3** in 55–70% isolated yields (Scheme 2). The reaction requires only one equivalent of SmI_2.

Under similar conditions, but with two equivalents of the reagent, a complex mixture of products is obtained. In the presence of a proton donor (ethanol), the treatment of the imides with SmI_2 (2 equivalents) furnishes the amidoaldehydes **4** in good yields, though accompanied by minor amounts (10–15%) of the amido ethyl esters **5** (Scheme 3). These last products might arise from nucleophilic attack of samarium ethoxide on the lactam carbonyl group.

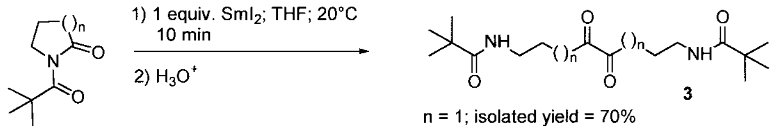
Table 2
Preparation of amidoketones



entry[a]	n	R^1	R^2, R^3	isolated yield (%)
1	1	*n*-C_7H_{15}	-$(CH_2)_5$-	66
2	1	*n*-C_7H_{15}	CH_3, *n*-C_6H_{13}	60
3	1	*n*-C_4H_9	-$(CH_2)_5$-	60
4	1	*n*-C_4H_9	CH_3, *n*-C_6H_{13}	58
5	1	*tert*-C_4H_9	-$(CH_2)_5$-	77
6	1	*tert*-C_4H_9	CH_3, C_2H_5	79
7	1	*tert*-C_4H_9	CH_3, *n*-C_6H_{13}	82
8	1	*tert*-C_4H_9	-$(CH_2)_3$-	83
9	2	*tert*-C_4H_9	-$(CH_2)_5$-	38
10	2	*tert*-C_4H_9	-$(CH_2)_3$-	42
11	2	*tert*-C_4H_9	H, *n*-C_4H_9	45[b]
12	3	*tert*-C_4H_9	-$(CH_2)_5$-	58
13	3	*tert*-C_4H_9	-$(CH_2)_3$-	65
14	3	*tert*-C_4H_9	CH_3, C_2H_5	50

a) In a Schlenk tube under argon, to 40 mL of a 0.1 M solution of SmI_2 in THF (4.0 mmol) was quickly added a mixture of a ketone or an aldehyde (1.25 mmol) and an acyl lactam (1 mmol) in THF (10 mL) at 20°C. After 10 min, ethanol (3 mmol) was added and stirring was continued for 3 hours, then the reaction mixture was quenched with HCl (0.1 M). After the usual work-up,[9] the crude material was purified by flash chromatography on silica gel.

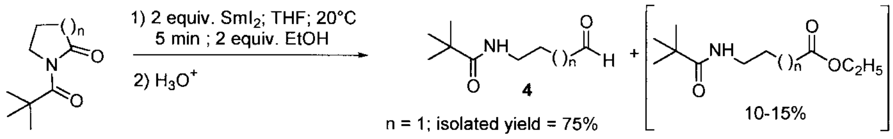
b) Mixture (1:1) of two isomeric amidoketones (see scheme 2).



n = 1; isolated yield = 70%

n = 2; isolated yield = 55%

Scheme 2.



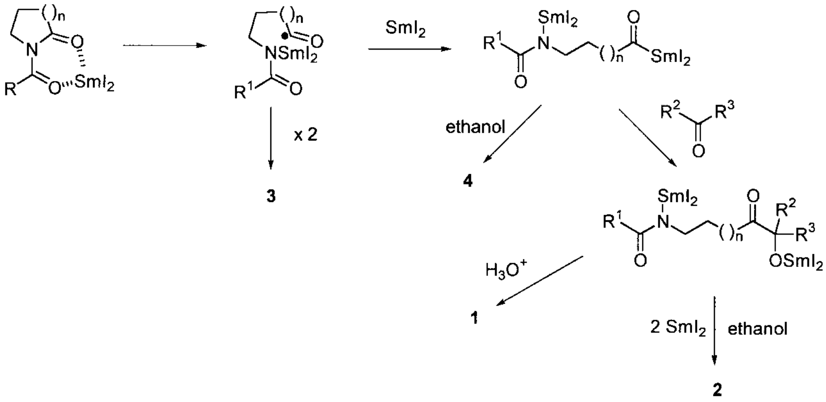
n = 1; isolated yield = 75%

n = 2; isolated yield = 85%

n = 3; isolated yield = 70%

Scheme 3.

All these results are reminiscent of those reported in Sm(II)-mediated reactions of acid chlorides.[8] They support the hypothesis of the formation of an acyl radical that is reduced into a transient acyl samarium species, which is then trapped by an electrophile (ketone, aldehyde or ethanol). Coupling of acyl radicals accounts for the formation of diamidodiketones **3** in the absence of an electrophile (Scheme 4).



Scheme 4.

Finally, it is worth noting that *N*-methylsuccinimide and *N*-methylglutarimide are unreactive under similar experimental conditions. Consequently, it could be assumed that the ring cleavage of *N*-acyl lactams occurs in an SmI_2–acyl lactam complex whose samarium is chelated by the carbonyl groups (Scheme 4).

In conclusion, we have found a new coupling reaction mediated by SmI_2, which allows the synthesis of polyfunctionalized compounds and links the imide and the acid chloride reactivities. We are currently exploring the scope of the coupling reactions of imides or related structures, including oxycarbonyllactams, with a variety of electrophiles.

Acknowledgements

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