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Samarium diiodide-mediated intermolecular coupling of organic halides with cyclic imides

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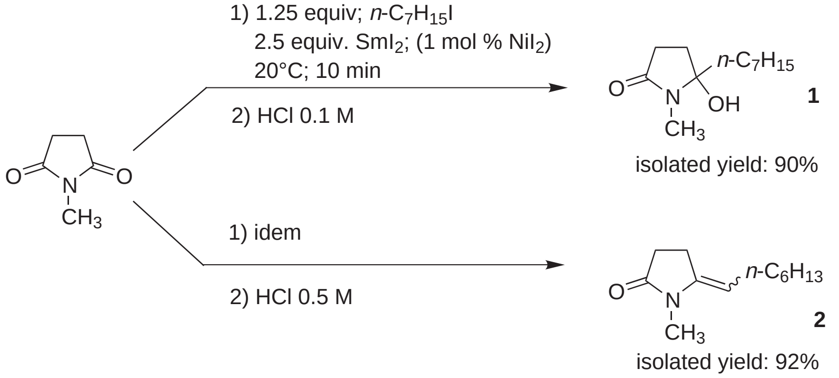
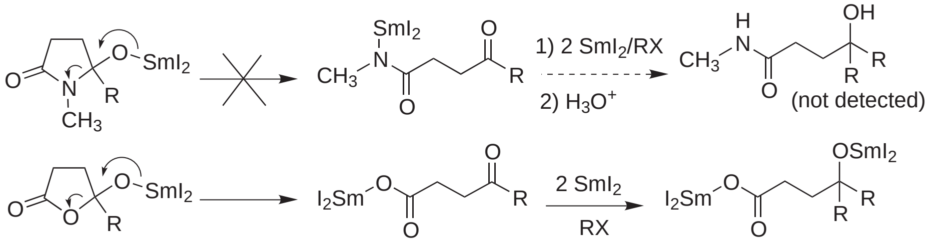
Abstract—SmI_2-mediated couplings between a variety of organic halides and cyclic imides have been performed giving either hydroxylactams from *N*-methylsuccinimide and *N*-methylphthalimide or δ-ketoamides from *N*-methylglutarimide. In the latter case, ring opening occurs during hydrolysis. Couplings of imides with alkyl halides require a catalytic amount of NiI_2. © 2001 Elsevier Science Ltd. All rights reserved.

Intramolecular as well as intermolecular couplings of organic halides with carbonyl compounds, mediated by samarium(II) derivatives, have been widely investigated.[1] However, few studies have been devoted to coupling with imides. To the best of our knowledge, only intramolecular Barbier-type reactions with *N*-(iodoalkyl)succinimides and *N*-(iodoalkyl)phthalimides have been reported.[2,3] These reactions are slow (2–3 h



Scheme 1.



Scheme 2.

Keywords: samarium diiodide; imides; nickel diiodide; organic halides; coupling reactions.

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at 0°C), they require a catalyst (Fe(DBM)$_3$) and afford, in most cases, the dehydration products (enamides) in moderate to good yields.

We wish to report some results concerning *intermolecular* Barbier-type and Reformatsky-type reactions mediated by samarium diiodide with *N*-methylsuccinimide, *N*-methylphthalimide and *N*-methylglutarimide. We found that samarium diiodide in the presence of a catalytic amount of nickel diiodide (1 mol% with respect to SmI$_2$) mediates a fast coupling reaction between *N*-methylsuccinimide and 1-iodoheptane to give an hydroxylactam **1**. Whether dehydration takes place or not depends on the hydrolysis conditions. Thus, quenching with 0.5 M HCl instead of 0.1 M HCl leads to the formation of an alkylene pyrrolidinone **2** (Scheme 1).

No reaction occurs without NiI$_2$, exemplifying again the beneficial effect of this additive.[4] Besides, by using an excess of the reagents (SmI$_2$: 5 equiv.; 1-iodoheptane: 2.5 equiv.) and with a longer reaction time (3 h), the same products are obtained, showing that only one carbonyl group is reactive. In addition, contrary to the result obtained in a Barbier-type reaction with succinic anhydride,[5] the ring opening is never observed. This difference might be ascribed to a weaker affinity of samarium for nitrogen than for oxygen (Scheme 2).

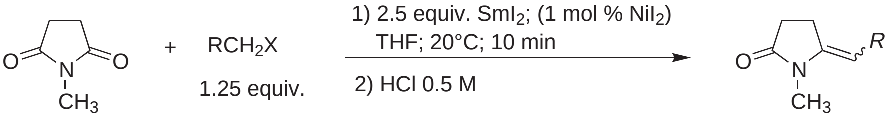
The results concerning *N*-methylsuccinimide are gathered in Table 1.

Hydrolysis has been achieved with 0.5 M HCl. In every case only dehydration products have been isolated. Reformatsky-type reactions have been performed with an α-halogenoester (entry 5) and α-halogenoamides (entries 6 and 7), giving polyfunctionalized compounds in good yields. For these reactions and the one involving benzyl bromide (entry 4), nickel diiodide is not necessary. Reactivity of the SmI$_2$ (NiI$_2$ catalytic)/RX system differs from those of organomagnesium and organolithium. With these reagents, proton abstraction and subsequent dimerization are always observed.[7] Interestingly, less basic organocerium reagents (RMgX/CeCl$_3$) give selective nucleophilic substitution, but afford amidoketones in moderate yields.[8]

In another set of experiments, Barbier-type reactions have been carried out with *N*-methylphthalimide in the presence of the SmI$_2$ (NiI$_2$ catalytic) system, giving hydroxylactams in good yields with short reaction times (Scheme 3).

In contrast with *N*-methylsuccinimide, dehydration does not occur even if hydrolysis is achieved with HCl 1 M.

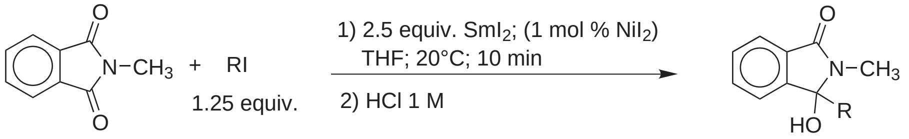
Table 1. Coupling reactions with *N*-methylsuccinimide



Entry[a]	R	X	Isolated yield (%)
1	n-C_3H_7	I	95
2	n-C_6H_{13}	I	92
3	n-$C_{11}H_{23}$	I	89
4[b]	C_6H_5	Br	81
5[b]	CH_3OCO	Br	85
6[b]	C_6H_5NHCO	Cl	55
7[b]	$(C_6H_5)_2NCO$	Cl	70

[a] In a Schlenk tube under argon, to 25 mL of a 0.1 M solution of SmI$_2$ in THF (2.5 mmol) were successively added a solution of NiI$_2$ (2.5×10^{-3} mmol) in THF (2.5 mL), and a mixture of an organic halide (1.25 mmol) and *N*-methylsuccinimide (1 mmol) in THF (10 mL) at 20°C. After 10 min stirring, the reaction mixture was quenched with HCl (0.5 M). After the usual work-up,[6] the crude material was purified by flash chromatography on silica gel.

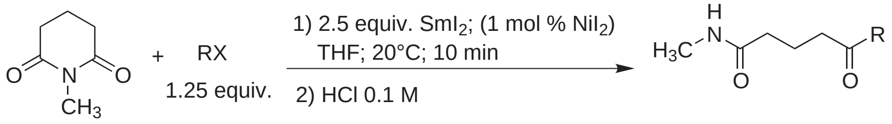
[b] Without NiI$_2$.



R = C_2H_5 ; isolated yield = 79%
R = n-C_4H_9 ; isolated yield = 82%
R = n-C_7H_{15} ; isolated yield = 68%

Scheme 3.

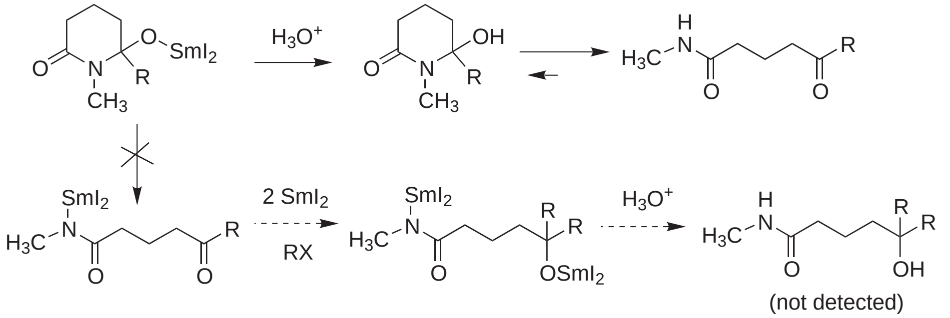
Table 2. Coupling reactions with *N*-methylglutarimide



Entry[a]	R	X	Isolated yield (%)
1	n-C_4H_9	I	85
2	n-C_7H_{15}	I	83
3	n-$C_{12}H_{25}$	I	72
4[b]	$C_6H_5CH_2$	Br	75

[a] The experimental procedure is similar to the one described in footnote a in Table 1, except quenching with 0.1 M HCl.

[b] Without NiI_2.



Scheme 4.

Coupling reactions with *N*-methylglutarimide have been also investigated (Table 2).

In contrast with *N*-methylsuccinimide, *N*-methylglutarimide undergoes a ring opening giving, in every case, exclusively δ-ketoamides in good yields. As with *N*-methylsuccinimide, the reactions of halogenoalkanes (entries 1–3) require a catalytic amount of NiI_2, but Reformatsky-type reactions have failed, even in the presence of NiI_2. The use of an excess of the reagents (5 equiv. SmI_2; 2.5 equiv. organic halide) gives the same results (products and yields). This can be explained assuming the ring opening occurs during the hydrolysis (whatever conditions used: 0.1 M HCl or $NaHCO_3$/Rochelle's salt[9]). Thus, δ-ketoamides would be formed through a tautomeric equilibrium between an hydroxylactam and a δ-ketoamide, which is shifted towards the latter species in a six-membered ring, as previously reported (Scheme 4).[10]

In conclusion, *N*-methylsuccinimide *N*-methylphthalimide and *N*-methylglutarimide are reactive in samarium diiodide-mediated coupling reactions with organic halides; with alkyl halides a catalytic amount of nickel diiodide is required. In contrast with acid anhydrides, ring opening never occurs before hydrolysis. With *N*-methylglutarimide it readily takes place during hydrolysis furnishing δ-ketoamides. It turns out then that the use of a samarium(II) mediated coupling reaction of RX with imides can be an interesting alternative to previously reported reactions of organomagnesium, organolithium or organocerium.

We are currently studying coupling of organic halides with some other imides, in particular acyl lactams.

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References

1. Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, 745.
2. Ha, D.-C.; Yun, C.-S.; Yu, E. *Tetrahedron Lett.* **1996**, *37*, 2577.
3. Ha, D.-C.; Yun, C.-S.; Lee, Y. *J. Org. Chem.* **2000**, *65*, 621.
4. Kagan, H. B.; Namy, J.-L. *Topics in Organometallic Chemistry*; Springer: Berlin, 1999; Vol. 2, p. 155.
5. Machrouhi, F.; Pârlea, E.; Namy, J.-L. *Eur. J. Org. Chem.* **1998**, 2431.
6. Girard, P.; Namy, J.-L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.
7. Katritzky, A. R.; Yao, J.; Qi, M.; Chou, Y.; Sikora, D. J.; Davis, S. *Heterocycles* **1998**, *48*, 2677.
8. Bailey, P. D.; Morgan, K. M.; Smith, D. I.; Vernon, J. M. *Tetrahedron Lett.* **1994**, *35*, 7115.
9. Schwaebe, R.; Little, R. *Synth. Commun.* **1997**, *27*, 837.
10. Chiron, R.; Graff, Y. *Bull. Soc. Chim. Fr.* **1971**, 2145.