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A NOVEL METHOD FOR THE ONE-STEP SYNTHESIS OF N-ALKYL IMIDES BY THE USE OF 1,1'-DIMETHYLSTANNOCENE

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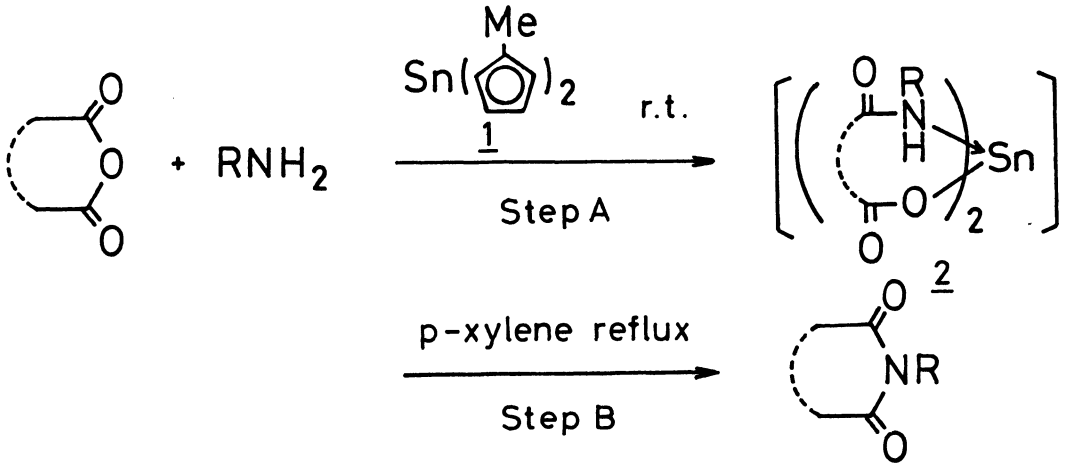
Various N-alkyl imides are easily prepared in good yields under nearly neutral conditions from equimolar amounts of cyclic acid anhydrides and primary amines by the use of 1,1'-dimethylstannocene.

In the course of our synthetic investigation utilizing 1,1'-dimethylstannocene, it was demonstrated that 1,1'-dimethylstannocene functions effectively both as an acid captor[1] and as a dehydrating reagent.[2] These facts prompted us to investigate a one-step synthesis of N-alkyl imides from acid anhydrides and primary amines, which involves two successive reactions; i) amide formation and ii) dehydration. The reaction was expected to proceed by taking advantage of the above mentioned two characteristic properties of 1,1'-dimethylstannocene under nearly neutral conditions.

In the first place, equimolar amounts of 2-phenylethylamine and succinic anhydride were treated with 1,1'-dimethylstannocene and refluxed in p-xylene to afford the corresponding N-alkyl imide directly in 89% yield. To clarify the role of 1,1'-dimethylstannocene, the above reaction was carried out in the absence of 1,1'-dimethylstannocene, and it was found that the desired imide was obtained only in a trace amount. Based on these observations, it is assumed that 1,1'-dimethylstannocene (1) would initially act as an acid captor to form tin(II) salts of amide carboxylic acids (2) (Step A) and then act as a dehydrating reagent (Step B) as shown in the following equation.

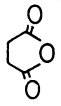
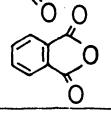


A typical reaction procedure is described for the synthesis of N-(2-phenylethyl)succinimide; to a p-xylene (2 ml) solution of 1,1'-dimethylstannocene

(274 mg, 0.991 mmol) was added 2-phenylethylamine (80 mg, 0.661 mmol) in p-xylene (1.5 ml) at room temperature under an argon atmosphere. After the mixture had been stirred for 1 h, succinic anhydride (66 mg, 0.661 mmol) was added in solid form. The resulting mixture was further stirred for 2 h and then refluxed for 2 h. After cooling, the reaction was quenched with pH 7 phosphate buffer. The aqueous phase was extracted with ethyl acetate three times and the combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the resulted oil was purified by silica-gel thin layer chromatography to afford N-(2-phenylethyl)succinimide (120 mg, 89%).

In a similar manner, various N-alkyl imides were prepared in good yields as summarized in the following Table. It should be noted that the present method is successfully applied to the preparation of imides having bulky alkyl group on nitrogen atom (Entry 2, 3).[3]

Table. Synthesis of N-Alkyl Imides[a]

Entry	Acid Anhydride	Amine	Yield(%)[b]
1		$Ph(CH_2)_2NH_2$	89
2		$PhCH(CH_3)NH_2$	80
3		$PhCH_2C(CH_3)_2NH_2$	75
4		$PhNH_2$	68
5		$Ph(CH_2)_2NH_2$	62
6		$Ph(CH_2)_2NH_2$	82

a) Molar ratio of acid anhydride : amine : 1 = 1 : 1 : 1.5
b) Isolated yield. All samples gave satisfactory ^1H NMR and IR spectra.

Syntheses of N-alkyl imides from cyclic acid anhydrides and primary amines are generally performed at an elevated reaction temperature (about 200°C)[4], with triethylamine in N,N-dimethylformamide (at 110°C) or refluxing toluene[5], or by a two-step procedure.[6] While, the present reaction proceeds smoothly under nearly neutral conditions to provide the corresponding cyclic imides in good yields by a one-step synthesis.

Further synthetic approaches based on the utilization of 1,1'-dimethylstannocene are now in progress.

References

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2) T. Mukaiyama, J. Ichikawa, and M. Asami, Chem. Lett., 1983, 683.
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