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Communications

Facile Synthesis of Vicinal Di- and Tricarbonyl Compounds by SmI_2-Mediated Double Insertion of Isocyanides into Organic Halides

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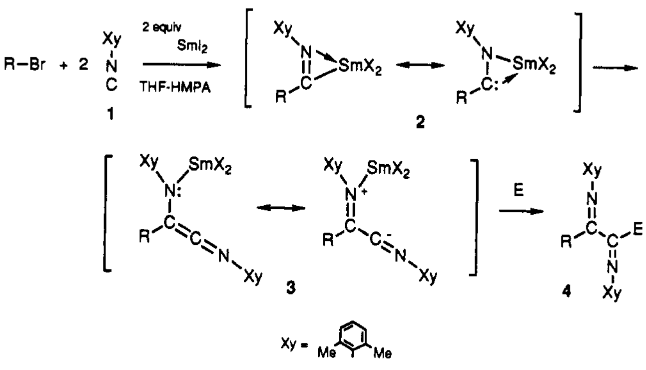
Summary: Selective double insertion of aryl isocyanide into organic halide was mediated by samarium(II) iodide, which provided a facile method for the synthesis of di- and tricarbonyl compounds.

Unlike carbon monoxide, isocyanides have been known to undergo successive polyinsertion into some organometallic compounds to give poly(N-substituted iminomethylene).[1] However, it has not been so far achieved to control the polyinsertion of isocyanides leading to a useful synthetic methods. Recently, we have reported that samarium(II) iodide mediated coupling reaction of benzyl chloromethyl ether with isocyanide generates [2-(benzyloxy)-1-(2,6-xylylimino)ethyl]samarium, which acts as α-hydroxyacetyl anion equivalent.[2] We now report that selective double insertion of aryl isocyanide into organic halides is efficiently mediated by samarium(II) iodide providing a useful synthetic method for vicinal di- and tricarbonyl compounds.

Ethyl bromide was treated with 2,6-xylyl isocyanide (**1**, 2.0 equiv) and samarium iodide (2.5 equiv) in THF-HMPA at −15 °C for 10 h and 1,2-bis(2,6-xylylimino)butane (**4a**),[3] i.e. double insertion product of isocyanide **1**, was obtained in 90% yield after usual aqueous workup. The intermediate organosamarium species **3**, thus formed from **1** and alkyl bromide, underwent an addition to carbonyl compounds giving hydroxy diimine in good yields (Table I, entries 3–5). Furthermore, the intermediate **3** was so nucleophilic as to react with esters to produce the corresponding acylated diimine derivatives (entries 6–8). The structures and reactions of the precedent 1-(N-substituted imino)alkyl and acyl complexes of lanthanide and actinide metal[4] may rationalize the formation of the intermediate **3**, i.e., insertion of isocyanide into alkylsamarium, formed by reduction of alkyl bromide with SmI_2, gave η^2-1-(2,6-xylylimino)alkylsamarium (**2**). Subsequent coupling of **2** with the second equivalent of isocyanide produced samarium ketenimine complex (**3**). Triple insertion of isocyanide did not occur even by use of 3 equiv of **1** under the similar conditions (−15 °C, 33 h).

Scheme I



Successive double insertion of two different isocyanides (**1** and **5**) was achieved by stepwise treatment of ethyl bromide (1.4 equiv) with **1** (1 equiv) in the presence of SmI_2 (2 equiv) for 2 h,[5] and then with **5** (1.4 equiv) for 15

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[1] Drenth, W.; Nolte, R. J. M. *Acc. Chem. Res.* **1979**, *12*, 30. Millich, F. *Macromol. Rev.* **1980**, *15*, 207.

[2] Murakami, M.; Kawano, T.; Ito, Y. *J. Am. Chem. Soc.* **1990**, *112*, 2437.

[3] A total of 28 carbon resonances are observed in the ^{13}C NMR spectrum, suggesting **4a** is a mixture of two isomers with respect to the directions of 2,6-xylyl groups. This also supports the ^{1}H NMR spectrum.

[4] (a) Moloy, K. G.; Fagan, P. J.; Manriquez, J. M.; Marks, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 56. (b) Evans, W. J.; Hanusa, T. P.; Meadows, J. H. *Organometallics* **1987**, *6*, 295. (c) Evans, W. J.; Meadows, J. H.; Hunter, W. E.; Atwood, J. L. *Organometallics* **1983**, *2*, 1252.

[5] The addition of H_2O instead of the second isocyanide (**5**) afforded 1-(2,6-xylylimino)propane.

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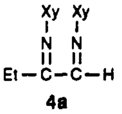
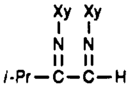
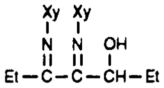
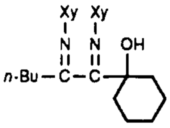
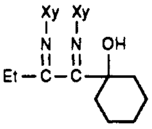
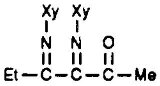
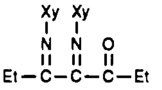
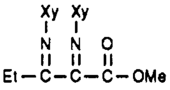
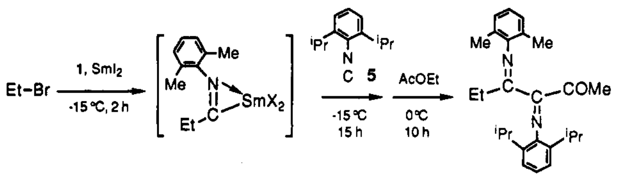
Table I. Reaction of 3 with Electrophiles[a]

entry	RBr	E, conditions	product	yield, %
1	EtBr	H_2O, 0 °C, 15 min	 $\mathrm{Et{-}C({=}NXy){-}C({=}NXy){-}H}$ **4a**	90
2	*i*-PrBr	H_2O, 0 °C, 15 min	 $\mathrm{\textit{i}\text{-}Pr{-}C({=}NXy){-}C({=}NXy){-}H}$ **4b**	60[b]
3	EtBr	EtCHO, 0 °C, 12 h	 $\mathrm{Et{-}C({=}NXy){-}C({=}NXy){-}CH(OH){-}Et}$ **4c**	70
4	*n*-BuBr	cyclohexanone, 0 °C, 12 h	 **4d**	77
5	EtBr	cyclohexanone, 0 °C, 12 h	 **4e**	92
6	EtBr	AcOEt, 0 °C, 5 h	 $\mathrm{Et{-}C({=}NXy){-}C({=}NXy){-}C({=}O){-}Me}$ **4f**	83
7	EtBr	$EtCO_2Me$, 0 °C, 6 h	 $\mathrm{Et{-}C({=}NXy){-}C({=}NXy){-}C({=}O){-}Et}$ **4g**	79
8	EtBr	$MeOCO_2Me$, 0 °C, 20 h	 $\mathrm{Et{-}C({=}NXy){-}C({=}NXy){-}C({=}O){-}OMe}$ **4h**	63

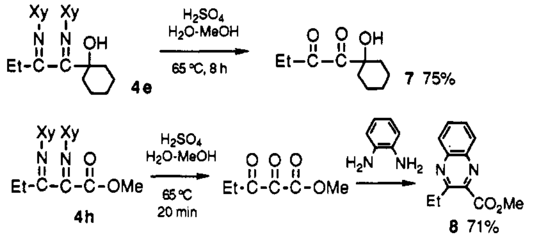
[a] Unless otherwise noted, alkyl bromide (1 equiv) was added to a mixture of 2,6-xylyl isocyanide (2.5 equiv), HMPA (5.8 equiv), and SmI_2 (0.1 M in THF, 2.0–2.5 equiv) at −15 °C. After stirring for 10 h, an electrophile (1.5 equiv) was added, and the reaction mixture was stirred under the conditions specified above. All products have been fully characterized by spectroscopic methods plus elemental analysis or HRMS. [b] Double insertion was carried out at 0 °C for 10 h.

Scheme II



6 81%

Scheme III



h at −15 °C. After the reaction with AcOEt, a cross double insertion product (**6**) was obtained in 81% yield based on **1**. The homo double insertion product, which might arise from double insertion of two molecules of **1**, was not detected. This finding suggested that the double insertion is irreversible and that the first insertion proceeds rather faster than the coupling with the second isocyanide.

The diimines thus obtained were hydrolyzed in acidic media to the corresponding polycarbonyl compounds[6] in good yields (Scheme III). Of particular interest was that this procedure provides a novel and convenient method for the construction of 1,2,3-tricarbonyl functionality, which has recently attracted a growing attention; 1,2,3-tricarbonyl system is a peculiar and pharmacologically interesting structural feature of the powerful immunosuppressant FK-506, whose synthetic study is currently being undertaken by several groups.[7] In addition, the synthetic utility of 1,2,3-tricarbonyl compounds for nitrogen-containing heterocycles has been reported.[8]

Application of the present methodology to the synthesis of 1,2,3-tricarbonyl segment of FK-506 is under progress in our laboratory.

Supplementary Material Available: Experimental details and spectroscopic and microanalytical data for **4** and **6–8** (4 pages). Ordering information is given on any current masthead page.

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[6] The tricarbonyl compound appeared to be in the hydrated form based on ^{13}C NMR of the crude product mixture and was trapped as the quinoxaline derivative (**8**) for isolation: Hoffman, R. V.; Kim, H.-O.; Wilson, A. L. *J. Org. Chem.* **1990**, *55*, 2820.

[7] Villalobos, A.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 2776 and references cited therein.

[8] Wasserman, H. H.; Cook, J. D.; Vu, C. B. *J. Org. Chem.* **1990**, *55*, 1701.

Electroorganic Chemistry. 130.[1] A Novel Trifluoromethylation of Aldehydes and Ketones Promoted by an Electrogenerated Base

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Summary: A base generated by the electroreduction of 2-pyrrolidone deprotonated trifluoromethane to form a trifluoromethyl anion equivalent. In the presence of hexamethyldisilazane, this species reacted with a variety of aldehydes and ketones to afford (trifluoromethyl)carbinols in high yield.

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