

## Reductive cyclodimerization of arylmethylenemalononitriles promoted by samarium and catalytic amount of iodine: facile synthesis of cyclopentene derivatives\*

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**Abstract:** Samarium and a catalytic amount of iodine were used to obtain functionalized cyclopentenes by reductive dimerization followed by intramolecular cyclization of 1,1-dicyanoalkenes under mild conditions.

**Key words:** Metallic samarium, Catalyzed by iodine, 1,1-dicyanoalkenes, Reductive cyclodimerization, Cyclopentene derivatives

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### INTRODUCTION

Carbon-carbon bond formation is the essence of organic synthesis and the reductive dimerization of carbonyl derivatives by means of active metals is one of the most valuable methods for establishing carbon-carbon bonds. The reported reductive cyclodimerization of  $\alpha,\beta$ -unsaturated nitriles provides novel access to functionalized five-membered ring products (Fan and Zhang, 2001; Zhong and Zhang, 2000; Zhou and Zhang, 1997; 1998). The products of enamine comprise important synthetic intermediates in organic synthesis (Cook, 1969). Enamine is not only an intermediate for the indirectly selective alkylation or acylation of an aldehyde or ketone

(Stork *et al.*, 1963), but can also be converted into carbonyl compound, or into a carboxylic acid or its derivatives (Helmers and Kaiser, 1971; Seitz and Monnighoff, 1971).

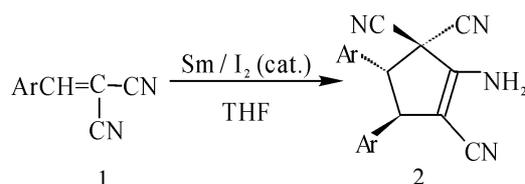
The chemistry by the use of metallic samarium is of current interest in organic synthesis. Although samarium diiodide is a good synthetic tool and ether-soluble one-electron transfer agent (Molander, 1992; Molander and Harris, 1996), its sensitivity to air makes it difficult to handle. It was noted that cheap and stable metallic samarium can be used directly as a reductant instead of  $\text{SmI}_2$  in organic synthesis (Huang and Zhang, 1997; Huang *et al.*, 1997; Ogawa *et al.*, 1994). Yanada reported that the diastereoselective allylation and alkylation of optically active imines with Sm and a catalytic amount of iodine (Yanada *et al.*, 1999). We wish to report our preliminary results on novel intermolecular reductive cyclodimerization and intramolecular

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reductive cyclizations of arylmethylidenemalononitriles by samarium and a catalytic amount of iodine.

## METHOD

When arylmethylidenemalononitriles **1** were treated with Sm and a catalytic amount of iodine in anhydrous tetrahydrofuran, intermolecular reductive cyclodimerization products 2-amino-1,3,3-tricyano-4,5-diarylcyclopentenes **2** were formed. Through careful separation of the reaction mixture, only one isomer, the 4,5-*trans* isomer was obtained, indicating that this cyclodimerization process is highly stereoselective. The assignments of the structure of **2** are based on their physical data and spectral characteristics, and are all in agreement with data in literature (Fig.1).



**Fig.1 Reduction of 1,1-dicyanoalkenes**

## RESULTS AND DISCUSSION

Table 1 summarizes the results on the reaction of a number of substrates. The chloro, bromo and alkoxy groups of the substrates were tolerated under the reaction conditions. In addition, we found catalytic amounts of iodine to be necessary because

**Table 1 Reduction of 1,1-dicyanoalkenes with Sm and a catalytic amount of iodine**

Entry	Ar	T (°C)	t (h)	Yield (%) <sup>a</sup>
2a	4-ClC <sub>6</sub> H <sub>4</sub>	60	8	78
2b	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	60	8	75
2c	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	60	8	74
2d	4-BrC <sub>6</sub> H <sub>4</sub>	60	8	71
2e	3-BrC <sub>6</sub> H <sub>4</sub>	60	8	70
2f	C <sub>6</sub> H <sub>5</sub>	60	8	68
2g	3,4-(OCH <sub>2</sub> O)C <sub>6</sub> H <sub>3</sub>	60	8	69

<sup>a</sup> Isolated yields

the reduction did not proceed in the presence of samarium only.

Although the detailed mechanism of the above reaction has not been clarified yet, according to the previous work of our group, it is proposed that the reaction may proceed via a single-electron transfer (SET) process (Fig.2), with Sm<sup>2+</sup>, which is generated in situ from the reaction of metal samarium with iodine, supplying electrons to substrate **1** to generate radical anion A. Radical anion A then extracts a proton from solvent (THF) to form radical B. Promoted by Sm<sup>2+</sup>, radical B dimerizes with substrate **1** to give anion C, which undergoes ring closure reaction to yield aminocyclopentene derivatives **2**.

Based on the mechanism depicted in Fig.2, the observed stereoselectivity of the reaction can be explained by the existence of two different conformations for the anionic intermediate (C). Conformation I, being non-eclipsed, may be favored since two aryl groups are in *anti*-positions and the steric interactions are minimized. Thus, when the five-membered ring is formed, the *trans* conformation product should be obtained. On the other hand, the eclipsed conformation (conformation II), from which the *cis*-product could be obtained, is much less favored since the steric interactions are maximized (the two aryl groups being in *syn*-positions). In fact, no *cis*-product was obtained in our experiments.

## CONCLUSIONS AND EXPERIMENTAL DETAILS

In conclusion, we have provided a new route to cyclopentamine derivatives, the advantages of which include high yields, simple and mild reaction conditions, and high chemo- and stereoselectivity. Further studies to develop other new uses of Sm and a catalytic amount of iodine are now in progress in our laboratory.

**General procedure** Powdered samarium (0.17 g, 1.1 mmol) and iodine (0.05 g, 0.2 mmol) were mixed in a three necked round bottom flask under nitrogen. A solution of arylmethylidenemalononitrile (**1** mmol) in THF (10 ml) was added to the suspension in one portion by syringe. After stirring for 8 h at 60 °C,

**Fig.2 The depicted mechanism of reduction of 1,1-dicyanoalkenes**

the mixture was quenched with dilute HCl (0.1 mol/L, 5 ml) and extracted with ether (3×20 ml). The combined extracts were washed with saturated brine (15 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:4) as eluent. All the cyclopentene products have physical data (m. p.) and spectral characteristics (IR, MS and <sup>1</sup>H NMR) in agreement with data in literature.

2a,  $\nu_{\max}$  3372, 3210 (NH<sub>2</sub>), 2218 (CN), 1678 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  3.75 (1H, d, J 9.5 Hz, ArCH), 4.50 (1H, d, J 9.5 Hz, ArCH), 5.31 (2H, br s, NH<sub>2</sub>), 6.90–7.45 (8H, m, ArH).

2b,  $\nu_{\max}$  3378, 3220 (NH<sub>2</sub>), 2210 (CN), 1670 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  3.75 (1H, d, J 9.5 Hz, ArCH), 4.50 (1H, d, J 9.4 Hz, ArCH), 5.35 (2H, br s, NH<sub>2</sub>), 6.87–7.50 (8H, m, ArH).

2c,  $\nu_{\max}$  3380, 3240 (NH<sub>2</sub>), 2215 (CN), 1670 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  2.25 (3H, s, CH<sub>3</sub>), 2.30 (3H, s, CH<sub>3</sub>), 3.75 (1H, d, J 9.6 Hz, ArCH), 4.51 (1H, d, J 9.6 Hz, ArCH), 5.45 (2H, br s, NH<sub>2</sub>), 7.02–7.42 (8H,

m, ArH).

2d,  $\nu_{\max}$  3375, 3260 (NH<sub>2</sub>), 2220 (CN), 1665 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  2.25 (3H, s, CH<sub>3</sub>), 2.32 (3H, s, CH<sub>3</sub>), 3.78 (1H, d, J 9.6 Hz, ArCH), 4.53 (1H, d, J 9.6 Hz, ArCH), 5.42 (2H, br s, NH<sub>2</sub>), 7.02–7.45 (8H, m, ArH).

2e,  $\nu_{\max}$  3385, 3212 (NH<sub>2</sub>), 2215 (CN), 1675 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  3.60 (1H, d, J 9.4 Hz, ArCH), 4.49 (1H, d, J 9.4 Hz, ArCH), 5.33 (2H, br s, NH<sub>2</sub>), 6.79–7.55 (8H, m, ArH).

2f,  $\nu_{\max}$  3385, 3220 (NH<sub>2</sub>), 2210 (CN), 1678 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  3.95 (1H, d, J 9.2 Hz, ArCH), 4.65 (1H, d, J 9.2 Hz, ArCH), 5.45 (2H, br s, NH<sub>2</sub>), 7.20–7.80 (10H, m, ArH).

2g,  $\nu_{\max}$  3390, 3245 (NH<sub>2</sub>), 2218 (CN), 1670 (C=C-NH<sub>2</sub>) cm<sup>-1</sup>,  $\delta$  4.20 (1H, d, J 9.2 Hz, ArCH), 4.63 (1H, d, J 9.2 Hz, ArCH), 5.34 (2H, br s, NH<sub>2</sub>), 9.95 (4H, s, 2OCH<sub>3</sub>O), 6.34–7.05 (6H, m, ArH).

## References

Cook, A.G., 1969. Enamines: Their Synthesis, Structure and Reaction. Marcel Dekker, New York.

- Fan, X.S., Zhang, Y.M., 2001. Reductive cyclodimerization of  $\alpha,\beta$ -unsaturated ketones promoted by  $\text{AlCl}_3/\text{Sm}$  system: a facile synthesis of 2-aryl-1,3,3-triaryl cyclopentanol derivatives. *Chin. J. Chem.*, **19**(6):616-619(in Chinese).
- Helmers, R., Kaiser, W., 1971. Ueber eine alkylierende retro-thorpe-reaktion. *Tetrahedron Lett.*, **12**: 3853-3855.
- Huang, Y., Zhang, Y.M., 1997. Preparation of disulfides by reduction of sodium alkyl thiosulfates with metallic samarium and catalytic amount of iodine. *Synth. Commun.*, **27**(6):1043-1047.
- Huang, Y., Zhang, Y.M., Wang, Y.L., 1997. Facile reduction of azides to the corresponding amines with metallic samarium and catalytic amount of iodine. *Tetrahedron Lett.*, **38**(6):1065-1066.
- Molander, G.A., 1992. Application of lanthanide reagents in organic synthesis. *Chem. Rev.*, **92**(1):29-68.
- Molander, G.A., Harris, C.R., 1996. Sequencing reactions with samarium(II) iodide. *Chem. Rev.*, **96**(1):307-338.
- Ogawa, A., Nanke, T., Takami, N., Takam, Y., 1994. Enhanced reducing ability by the combination of  $\text{SmI}_2$  and Sm metal in the reduction of alkyl halides. *Chem. Lett.*, (2):379-380.
- Seitz, G., Monnighoff, H., 1971. Die thorpe-ziegler-cyclisierung zur synthese von substituierten cyclopenta thiophene. *Tetrahedron Lett.*, **12**:4889-4890.
- Stork, G., Brizzolaro, A., Landesman, H., Szmuszkovicz, J., Terrel, R., 1963. The enamine alkylation and acylation of carbonyl compounds. *J. Am. Chem. Soc.*, **85**:207-222.
- Yanada, R., Negoro, N., Okaniwa, M., Ibuka, T., 1999. Diastereoselective allylation and alkylation of optically active imines with metallic samarium and a catalytic amount of iodide. *Tetrahedron*, **55**(49):13947-13956.
- Zhong, W.H., Zhang, Y.M., 2000. Samarium diiodide mediated simultaneous reduction of nitro group and azide group in o-nitrophenylazide: a new access to 2,3-dihydro-1H-1,5-benzodiazepines. *J. Chem. Res.*, (8):532-534.
- Zhou, L.H., Zhang, Y.M., 1997. A novel cyclodimerization of Arylidenecyanoacetate promoted by samarium diiodide. *Tetrahedron Lett.*, **38**(46):8063-8066.
- Zhou, L.H., Zhang, Y.M., 1998. A novel reductive cyclization of arylmethylidenemalononitrile promoted by samarium diiodide. *J. Chem. Soc., Perkin Trans.I*, (15): 2399-2402.

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