Reductive Coupling Cyclization of 1,1-Dicyanoalkenes Promoted by Sm^0/cat. $HgCl_2$ System

ZHANG, Ji-Ming[a](张纪明) **ZHANG, Yong-Min**[*,a,b](张永敏)

[a] *Department of Chemistry, Zhejiang University, Hangzhou, Zhejiang 310028, China*

[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

The intermolecular reductive coupling cyclization reactions of 1,1-dicyanoalkenes promoted by Sm^0/cat. $HgCl_2$ were studied. A possible reaction mechanism was proposed.

Keywords samarium, mercuric dichloride, 1,1-dicyanoalkenes, reductive coupling cyclization

Carbon-carbon bond formation is the essence of organic synthesis. The reductive dimerization of carbonyl derivatives by active metal is one of the most valuable methods for establishing carbon-carbon bonds. In a general fashion, the carbonyl derivatives are aldehydes, ketones, carboxylic esters and acid chlorides,[1] and the active metals are alkali or alkaline earth metals. Recently, reductive dimerization cyclization of arylmethylidenemalononitrile induced by samarium(II) diiodide was reported.[2] Although samarium(II) diiodide has been developed as a mild, neutral and ether-soluble one-electron transfer reductant and therefore has been used in many reductive reactions or couplings of various functional groups,[3] there are some drawbacks when it is used as a reductant, such as its sensitivity to air and moisture, difficult storage, and it has been used invariably in stoichiometric amounts. On the other hand, metallic samarium is stable in the air and its strong reducing power ($Sm^{3+}/Sm = -2.41$ V) is similar to that of magnesium ($Mg^{2+}/Mg = -2.37$ V), and superior to that of zinc ($Zn^{2+}/Zn = -0.71$ V). These properties prompted us to use the more convenient and cheaper samarium directly as a reductant instead of samarium(II) iodide. In order to improve the activity of metallic samarium, some additives are needed, such as $HgCl_2$,[4] NH_4Cl (aq.),[5] TMSCl,[6] *etc*. In these additives, $HgCl_2$ is an efficient one, for it can be reduced by samarium metal to form liquid mercury, and then Sm(Hg) amalgam is obtained *in situ*. Our group has applied this reducing system to the reduction of RSCN,[7] ArSeSeAr,[8] pinacolic coupling of aromatic aldehydes and ketones,[9] and so on. Here, the results on the reductive coupling cyclization of 1,1-dicyanoalkenes promoted by Sm/cat. $HgCl_2$ system in tetrahydrofuran were reported.

When 1,1-dicyanoalkenes (**1**) were treated with Sm/cat. $HgCl_2$ system in THF, the intermolecular reductive coupling cyclization products **2** and **3** were formed (Scheme 1). The results were summarized in Table 1.

Considering the toxicity of metallic mercury produced by metallic samarium and mercuric dichloride, a catalytic amount of $HgCl_2$ was used to decrease the toxicity of the reducing system and the satisfactory results were got. From the results of experiments (Table 1, Entry 1), the idealic ratio ($HgCl_2$: Sm) is 15 mol%. When metallic samarium and the catalytic amount of $HgCl_2$ were mixed in THF, the catalytic $HgCl_2$ was reduced by metallic samarium, and then Sm^{2+} and Sm(Hg) amalgam were formed. Through the single-electron transfer process, Sm^{2+} was oxidized to Sm^{3+}. Sm(Hg) amalgam reacts with Sm^{3+} to give the Sm^{2+} to finish the catalytic cycle (Scheme 2).

* E-mail: yminzhang@mail.hz.zj.cn

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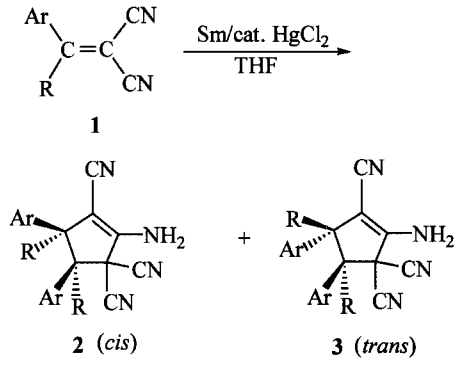
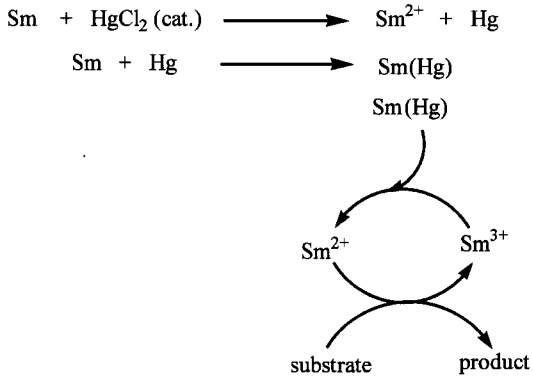
Scheme 1

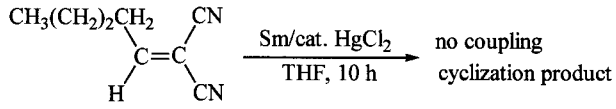


Scheme 2



All the reactions were completed within 6 h and afforded the corresponding substituted cyclopentenes in good yields. In these reactions, the cleavage takes place at carbon-nitrogen triple bond and the carbon-carbon double bond. The chloro, bromo and alkoxyl groups of the substrates could not be reduced under the current reaction conditions and have no influence on the rate of cyclodimerization. As shown in Table 1, it is found that substrates **1** derived from aromatic aldehydes give products **2** and **3** in good to excellent yields at room temperature, and the major product is *trans*-form product **3**. The range of **3/2** ratio is 75/25 to 85/15. Substrates **1** derived from aromatic ketones give products **2** and **3** in good yields at 50 ℃. The ratio of **3/2** is 60/40. Unfortunately, when substrate **1** derived from aliphatic aldehyde (such as pentanal) was used (Scheme 3), no reductive coupling cyclization product was isolated. It is probably owing to the different stability of the radical anion intermediate. A benzyl radical anion intermediate from 1,1-dicyanoalkenes derived from aromatic aldehydes or ketones is stabilizad by the neighbouring aromatic ring, so that it is easy to form and has enough time to react with another benzyl radical anion to form a dianion and eventually to give **2** and **3**.

Scheme 3



The configurations of **2** and **3** were determined by ^{1}H NMR spectra. The coupling constants of the two protons on the ring in substituted cyclopentene **2** and **3** were in the range of 7—8 Hz and 9—10 Hz, respectively. Thus, it was assigned that the two protons whose the coupling constant between 7—8 Hz are oriented *cis* to each other, and the two protons whose coupling constant between 8—9 Hz are oriented *trans* to each other. Although the detailed mechanism has not been clarified yet, the cyclopentene formation may be explained by a postulated mechanism presented in Scheme 4.

Table 1 Cyclodimerization of 1,1-dicyanoalkenes (**1**) promoted by Sm/cat. $HgCl_2$ system

Entry	Compound	Ar	R	Yield (%)[a]	3/2[b]
1	**a**	C_6H_5	H	65,[c] 72,[d] 72[e]	80/20
2	**b**	4-$CH_3OC_6H_4$	H	60	75/25
3	**c**	4-$CH_3C_6H_4$	H	70	78/22
4	**d**	4-BrC_6H_4	H	81	85/15
5	**e**	3-BrC_6H_4	H	78	80/20
6	**f**	4-ClC_6H_4	H	79	84/16
7	**g**	C_6H_5	CH_3	53	60/40
8	**h**	4-BrC_6H_4	CH_3	57	60/40

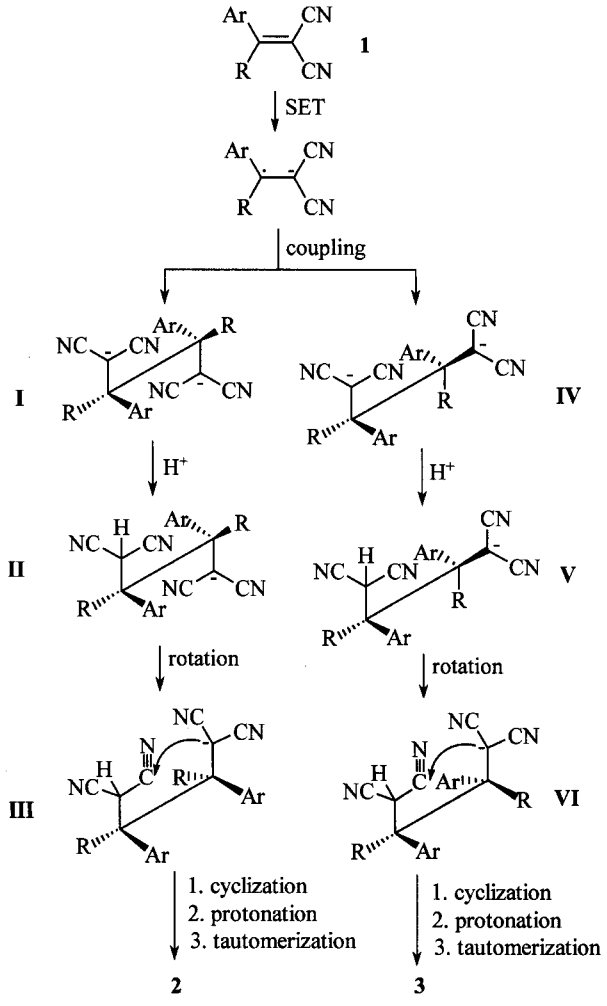
[a] Isolated yield. [b] Ratio determined from the intensities of methenyl protons of products (Entries 1—6) or methyl protons of products (Entries 7,8) in the ^{1}H NMR spectra. [c] The molar ratio of Sm to $HgCl_2$ is 10:1. [d] The molar ratio of Sm to $HgCl_2$ is 10:1.5. [e] The molar ratio of Sm to $HgCl_2$ is 10:3.

A radical anion of the electron deficient olefin **1** may be formed by single-electron transfer process under the reaction conditions, and it reacts with another radical anion of **1** to form a dianion **I** or **IV**. Eventually, dianion gives the functionalized cyclopentene through the protonation and cyclization, protonation and tautomerization. Anion **III** and **VI** are key intermediates in the course of the formation of **2** and **3**, respectively. Considering the stability

of anion **III**, **VI** and products, it is obvious that the formation of **3** is favable.

In conclusion, the combination of Sm and cat. $HgCl_2$ is an efficient system in the reductive coupling cyclization of 1,1-dicyanoalkenes. The notable advantages of this reaction are using catalytic amount of $HgCl_2$, lower toxicity, mild reaction conditions and simple operation.

Scheme 4



Experimental

General

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. Infrared spectra were recorded on Bruker vector 22 spectrometers in KBr with absorptions in cm^{-1}. ^1H NMR spectra were determined in Bruker AC-80 spectro meters in $CDCl_3$. J values are in Hz. Chemical shifts are downfield from internal tetramethylsilane. Mass spectra were recorded on an HP 5989B MS spectrometer. Microanalysis was carried out on a EA1101 instrument.

General procedure for the cyclodimerization reactions

A solution of 1,1-dicyanoalkene (**1**, 1 mmol) in anhydrous THF (3 mL) was added to the mixture of Sm (0.75 mmol) and $HgCl_2$(0.11 mmol) in THF(10 mL) at room temperature under dry nitrogen atmosphere. The reaction was completed in 6 h. Then the reaction mixture was quenched with dilute HCl (1 mol/L, 1 mL) and extracted with ether (3 × 40 mL). The combined extracts were washed with saturated solution of NaCl (15 mL), and dried over anhydrous Na_2SO_4. After evaporating the solvent under the reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (V:V, 1:3) as the eluent.

2a and **3a** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 3.74 (d, J = 9.5 Hz, 0.8H, **3a**-CH), 4.51 (d, J = 9.5 Hz, 0.8H, **3a**-CH), 3.21 (d, J = 7.2 Hz, 0.20H, **2a**-CH), 4.32 (d, J = 7.2 Hz, 0.20H, **2a**-CH), 5.30 and 5.44 (brs, 2H, NH_2), 7.24—7.40 (m, 10H, ArH × 2); IR (KBr) ν: 3378, 3215, 3051, 2943, 2216, 1680, 1671, 1630, 1503, 1455, 697 cm^{-1}.

2b and **3b** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 3.64 (s, 3H, CH_3), 3.71—3.90 (m, 3.75H, CH_3O- and **3b**-CH), 4.40 (d, J = 9.4 Hz, 0.75H, **3b**-CH), 4.06 (d, J = 7.2 Hz, 0.25H, **2b**-CH), 3.12 (d, J = 7.2 Hz, 0.25H, **2b**-CH), 5.30 and 5.42 (brs, 2H, NH_2), 7.01—7.21 (m, 8H, ArH × 2); IR (KBr) ν: 3380, 3230, 3051, 2948, 2210, 1684, 1662, 1645, 1620, 1520, 1466, 1382, 810 cm^{-1}.

2c and **3c** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 2.14 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 3.84 (d, J = 9.4 Hz, 0.78H, **3c**-CH), 4.60 (d, J = 9.4 Hz, 0.78H, **3c**-CH), 3.21 (d, J = 7.2 Hz, 0.22H, **2c**-CH), 4.31 (d, J = 7.2 Hz, 0.22H, **2c**-CH), 5.30 and 5.40 (brs, 2H, NH_2), 7.08—7.25 (m, 8H, ArH × 2); IR (KBr) ν: 3380, 3221, 3044, 2948, 2211, 1680, 1663, 1645, 1620, 1510, 1465, 1380, 821 cm^{-1}.

2d and **3d** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz)

δ: 3.72 (d, J = 9.5 Hz, 0.85H, **3d**-CH), 4.50 (d, J = 9.5 Hz, 0.85H, **3d**-CH), 3.33 (d, J = 7.2 Hz, 0.15H, **2d**-CH), 4.22 (d, J = 7.2 Hz, 0.15H, **2d**-CH), 5.29 and 5.41 (brs, 2H, NH_2), 7.22—7.39 (m, 8H, ArH × 2); IR (KBr) ν: 3380, 3213, 3052, 2942, 2210, 1680, 1668, 1657, 1630, and 1504, 1462, 827 cm^{-1}.

2e and **3e** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 3.57 (d, J = 9.4 Hz, 0.80H, **3e**-CH), 4.49 (d, J = 9.4 Hz, 0.80H, **3e**-CH), 3.11 (d, J = 7.2 Hz, 0.20H, **2e**-CH), 4.14 (d, J = 7.2 Hz, 0.20H, **2e**-CH), 5.50 and 5.60 (brs, 2H, NH_2), 7.22—7.43 (m, 8H, ArH × 2); IR (KBr) ν: 3375, 3210, 3077, 2962, 2220, 1680, 1662, 1630, 1500, 1464, 789, 700 cm^{-1}; MS (70 eV) m/z (%): 470 (M^+ + 4, 44), 468 (M^+ + 2, 100), 466 (M^+, 46), 390 (22), 389 (48), 388 (33), 308 (28), 156 (17), 155 (41), 128 (18), 127 (23), 101(17), 77 (24), 76 (33), 75 (33), 63 (20), 51 (32). Anal. calcd for $C_{20}H_{12}Br_2N_4$: C 51.31, H 2.58, N 11.97; found C 51.54, H 2.81, N 12.10.

2f and **3f** (lit.[10]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 3.75 (d, J = 9.2 Hz, 0.84H, **3f**-CH), 4.52 (d, J = 9.2 Hz, 0.84H, **3f**-CH), 3.43 (d, J = 7.0 Hz, 0.16H, **2f**-CH), 4.26 (d, J = 7.0 Hz, 0.16H, **2f**-CH), 5.30 and 5.41 (brs, 2H, NH_2), 7.20—7.41 (m, 8H, ArH × 2); IR (KBr) ν: 3381, 3204, 3072, 2945, 2220, 1680, 1661, 1630, 1500, 1460, 826 cm^{-1}.

2g and **3g** (lit.[6(a)]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 1.21 (s, 0.40 × 3H, **2g**-CH_3), 1.45 (s, 0.60 × 3H, **3g**-CH_3), 1.88 (s, 0.40 × 3H, **2g**-CH_3), 2.01 (s, 0.60 × 3H, **3g**-CH_3), 5.38 (br, 2H, NH_2), 7.04—7.20 (m, 10H, ArH × 2); IR (KBr) ν: 3380, 3224, 3052, 2950, 2224, 1685, 1661, 1600, 1500, 1460, 1379, 690 cm^{-1}.

2h and **3h** (lit.[6(a)]) ^1H NMR ($CDCl_3$, 80 MHz) δ: 1.20 (s, 0.40 × 3H, **2g**-CH_3), 1.45 (s, 0.60 × 3H, **3g**-CH_3), 1.88 (s, 0.40 × 3 H, **2h**-CH_3), 2.01 (s, 0.60 × 3H, **3h**-CH_3), 5.36 (br, 2H, NH_2), 7.02—7.17 (m, 8H, ArH × 2); IR (KBr) ν: 3370, 3234, 3058, 2950, 2220, 1690, 1661, 1600, 1520, 1460, 1380, 824 cm^{-1}; MS (70 eV) m/z (%): 498 (M^+ + 4, 41), 496 (M^+ + 2, 100), 494 (M^+, 48), 248 (23), 247 (19), 170 (32), 169 (77), 168 (32), 140 (21), 115 (27), 102 (25), 77 (34), 76 (23), 75 (24), 51 (31). Anal. calcd for $C_{22}H_{16}Br_2N_4$: C 53.25, H 3.25, N 11.29; found C 53.51, H 3.55, N 11.09.

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