Note

Synthesis of the Cyclopentenylamine Derivatives Promoted by SmI_2

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The intermolecular reductive coupling of 1,1-diaryl-2,2-dicyanoethylenes with cinnamic esters promoted by samarium(II) iodide was studied. Functionalized cyclopentenylamine derivatives were prepared in good yields under neutral and mild conditions.

Keywords samarium diiodide, 1,1-diaryl-2,2-dicyanoethylene, cinnamic ester, cyclopentenylamine

Since Kagan had shown a simple method for the preparation of samarium diiodide from samarium metal and 1,2-diiodoethane,[1] SmI_2 was widely used in synthetic organic chemistry.[2] Hong and Kang reported the decyanation of α-alkoxylcarbonyl substituted nitrile derivatives by samarium diiodide.[3] Yacovan and co-workers reported that 1,1-diaryl-2,2-dicyanoethylenes were quantitatively reduced to diarylmethyl malononitrile without contamination by any dimeric products by this reagent,[4] because 1,1-diaryl-2,2-dicyanoethylenes can form radical anions like diaryl ketones due to the similarity between the $C=C(CN)_2$ and the C=O groups.[4,5] Our group reported the cyclodimerization of arylmethylidenemalonotrile[6a] and the reductive coupling reactions of ketones and nitriles[6b] promoted by SmI_2. Recently, we reported the preparation of polysubstituted 3*H*-pyrroles from 1,1-diaryl-2,2-dicyanoethylenes or 1,1-diaryl-2-cyano-2-ethoxycarbonylethylenes and aromatic nitriles mediated by samarium diiodide.[7]

The enamine is one of the important synthetic intermediate in organic synthesis.[8] It is not only an intermediate for the directly selective alkylation or acylation of an aldehyde or ketone,[9] but it also can be converted into carbonyl compound, or into a carboxylic acid or its derivaties.[10] It is well known that the Thorpe-Ziegler method is an effective synthetic route to enamino-nitriles.[11] The base-catalyzed condensation of two molecules of nitriles or a dinitrile yields imines which tautomerize to enamines, but usually a strong base such as sodium ethoxide or sodium methyl anilide is used in the reaction. It is desirable to develop milder methods for enamine preparation. Herein, we wish to report our results on the preparation of polysubstituted cyclopentenylamines from 1,1-diaryl-2,2-dicyanoethylenes and cinnamic esters promoted by samarium diiodide in tetrahedrofuran (Scheme 1).

Scheme 1

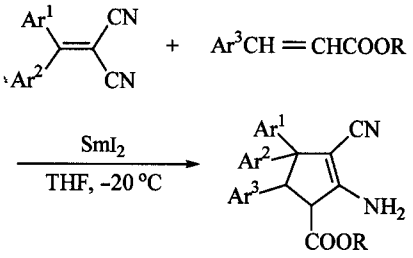

Table 1 summarized our results. In the reaction, substrates **1** could react with cinnamic esters **2** to produce polysubstituted cyclopentenylamines (**3**) in moderate to good yields and the structures of the products were confirmed by ^1H NMR, IR, MS and elemental analyses. The reaction was completed at -20 ℃ to room temperature for 1—1.5 h. When the substrates were 1,1-dicyanoalkene and cinnamic ester, only the reductive dimerization cyclization product of 1,1-dicyanoalkene was obtained. The yields of the reaction were almost the same either in the presence or absence of hexamethyl phosphoramide(HMPA).

Though the detailed mechanism of the reaction has not been clarified yet,[4-7,10] it can be assumed that the formation of polysubstituted cyclopentenylamines may be described by the possible mechanism presented in Scheme 2.

In the initial step, the transfer of an electron from SmI_2 to substrate **1** results in the formation of radical aninon **A**, which is then protonated by THF[12] to form radical **B**. The radical **B** attacks another substrate cinnamic ester **2** to form the carbon-carbon bond and affords an electron to generate **C**. The latter results in the formation of carbon-carbon bond intramolecularly and produce intermediate **D**. Then the form **D** would be isomerized to product **3**.

In conclusion, polysubstituted cyclopentenylamine derivatives are readily obtained via intermolecular reductive

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Received March 14, 2002; revised July 9, 2002; accepted September 8, 2002.

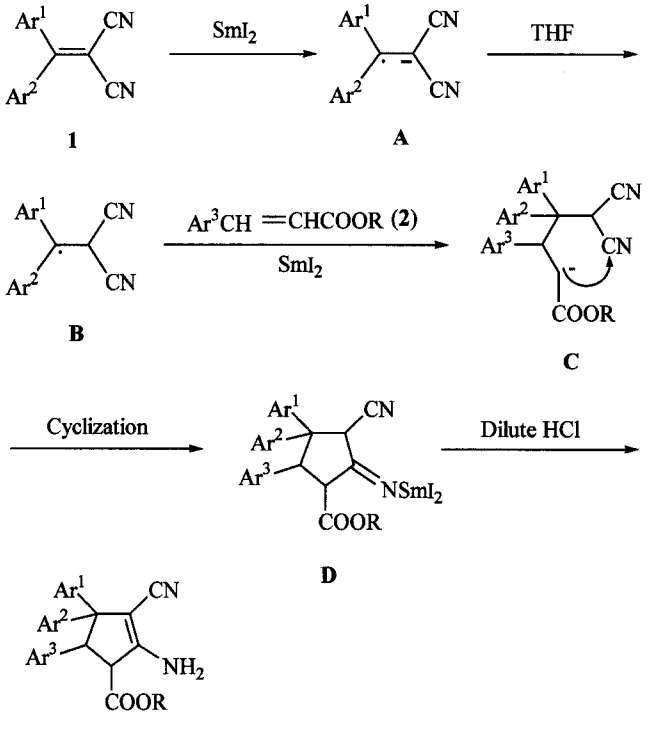
Project supported by the National Natural Science Foundation of China (No. 20072033) and the Natural Science Foundation of Zhejiang Province, China.

Table 1 Synthesis of polysubstituted cyclopentenylamines promoted by SmI_2

Entry	Ar^1	Ar^2	Ar^3	R	T (h)	Yield (%)[a]
1	C_6H_5	C_6H_5	C_6H_5	CH_2CH_3	1.5	82, 81[b] (**3a**)
2	C_6H_5	C_6H_5	C_6H_5	CH_3	1.5	73 (**3b**)
3	C_6H_5	C_6H_5	C_6H_5	$(CH_3)_2CH$	1.5	79 (**3c**)
4	C_6H_5	C_6H_5	C_6H_5	$CH_2CH=CH_2$	1.5	90 (**3d**)
5	C_6H_5	C_6H_5	4-ClC_6H_4	CH_3	1.5	65 (**3e**)
6	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	C_6H_5	CH_2CH_3	1	78 (**3f**)
7	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	C_6H_5	$CH_2CH=CH_2$	1	81 (**3g**)
8	C_6H_5	H	C_6H_5	CH_2CH_3	1	0[c]

[a] Isolated yields; 1,1-diaryl-2,2-dicyanoethylenes (1 mmol), cinnamic esters (1.2 mmol) and SmI_2 (2.2 mmol) were used. [b] In the presence of HMPA. [c] Only the reductive dimerization cyclization product of 1,1-dicyanoalkene was obtained.

Scheme 2



cyclization of 1,1-diaryl-2,2-dicyanoethylenes with cinnamic esters promoted by samarium(II) iodide. The advantages of our method are convenient manipulation, easily accessible starting materials and good yields.

Experimental

General

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atomsphere. Melting points are uncorrected. ^1H NMR spectra were recorded on a Bruker 400 MHz instrument as $CDCl_3$ or DMSO-d_6 solutions using TMS as internal standard. IR spectra were recorded using KBr disks with a Vector-22 infrared spectrometer. Elemental analyses were performed on an EA-1110 instrument. Metallic samarium and all solvents were purchased from commercial sources, without further purification before use.

General procedure for the synthesis of compounds **3**

A solution of 1,1-diaryl-2,2-dicyanoethylene (1 mmol) and cinnamic ester (1.2 mmol) in dry THF (2 mL) was added to the solution of SmI_2 (2.2 mmol) in THF (15 mL) at −20 ℃ under a nitrogen atmosphere. After being stirred for a given time (Table 1, the reaction was monitored by TLC), the reaction was quenched with dilute HCl (0.1 mol/L, 5 mL) and extracted with ethyl acetate (3 × 30 mL). The organic phase was washed with water (20 mL), brine (15 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude product, which was purified by preparative TLC using ethyl acetate and cyclohexane (1:4, $V:V$) as eluant.

1-Amino-2-cyano-5-ethyloxycarbonyl-3, 3, 4-triphenylcyclopentene (**3a**) White solid, yield 82%, m.p. 192—194 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.56—7.04 (m, 11H), 6.68—6.63 (m, 4H), 5.16 (brs, 2H), 4.98—4.95 (d, J = 10.72 Hz, 1H), 4.15—4.11 (q, J = 7.13 Hz, 2H), 3.90—3.87 (d, J = 10.76 Hz, 1H), 1.15—1.12 (t, J = 7.12 Hz, 3H); IR (KBr) ν: 3448, 3345, 3060, 3029, 2193, 1729, 1681, 1634, 1103, 1026 cm^{-1}; MS (70 eV) m/z (%): 408 (M^+, 51.80), 407 (100), 361 (53.25), 77 (35.42). Anal. calcd for $C_{27}H_{22}N_2O_2$: C 79.38, H 5.92, N 6.86; found C 79.26, H 5.77, N 6.98.

1-Amino-2-cyano-5-methoxycarbonyl-3, 3, 4-triphenylcyclopentene (**3b**) White solid, yield 73%, m.p. 150—151 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.54—7.03 (m, 11H), 6.68—6.62 (m, 4H), 5.14 (brs, 2H), 4.94—4.91 (d, J = 10.93 Hz, 1H), 3.85—3.82 (d, J = 10.89 Hz, 1H), 3.68 (s, 3H); IR (KBr) ν: 3452, 3353, 3032, 2953, 2193, 1734, 1669, 1633, 1116, 1033 cm^{-1}; MS (70 eV) m/z (%): 394 (M^+, 50.25), 393(100). Anal. calcd for $C_{26}H_{22}N_2O_2$: C 79.16, H 5.62, N 7.10; found C 79.33, H 5.61, N 7.34.

1-Amino-2-cyano-5-iso-propyloxycarbonyl-3, 3, 4-triphenylcyclopentene (**3c**) White solid, yield 79%, m.p. 180—182 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.55—6.98 (m, 11H), 6.68—6.62 (m, 4H), 5.16 (brs, 2H),

5.00—4.91 (m, 2H), 3.86—3.84 (d, J = 10.84 Hz, 1H), 1.13—1.10 (m, 6H); IR (KBr) ν: 3448, 3360, 2981, 2191, 1733, 1641, 1606, 1103 cm^{-1}; MS (70 eV) m/z (%): 422 (M^+, 82.82), 379 (63.75), 335 (85.45), 77 (38.38), 43 (100). Anal. calcd for $C_{28}H_{26}N_2O_2$: C 79.59, H 6.20, N 6.63; found C 79.71, H 6.42, N 6.03.

1-Amino-2-cyano-5-allyloxycarbonyl-3, 3, 4-triphenylcyclopentene (**3d**) White solid, yield 90%, m.p. 163—165 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.56—6.97 (m, 11H), 6.68—6.64 (m, 4H), 5.73—5.81 (m, 1H), 5.18—5.08 (m, 4H), 5.01—4.98 (d, J = 10.79 Hz, 1H), 4.59—4.54 (m, 2H), 3.95—3.92 (d, J = 10.79 Hz, 1H); IR (KBr) ν: 3452, 3395, 3029, 2195, 1733, 1645, 1609, 1160, 1020 cm^{-1}; MS (70 eV) m/z (%): 420 (M^+, 30.95), 419 (32.05), 379 (1.53), 335 (19.84), 77 (28.29), 41 (100). Anal. calcd for $C_{28}H_{24}N_2O_2$: C 79.97, H 5.75, N 6.66; found C 79.72, H 5.76, N 6.68.

1-Amino-2-cyano-5-methoxycarbonyl-3,3-diphenyl-4-(4-chlorophenyl) cyclopentene (**3e**) White solid, yield 65%, m.p. 199—200 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.52—7.50 (d, J = 8.52 Hz, 2H,), 7.35—6.88 (m, 12H), 5.18 (brs, 2H), 4.95—4.92 (d, J = 10.80 Hz, 1H), 3.85—3.83 (d, J = 10.80 Hz, 1H), 3.67 (s, 3H); IR (KBr) ν: 3452, 3345, 2950, 2193, 1722, 1684, 1643, 1110, 1013 cm^{-1}; MS (70 eV) m/z (%): 428 (M^+, 65.40), 430 (M^+ + 2, 23.58), 427 (100), 395 (37.93), 77 (38.00). Anal. calcd for $C_{26}H_{21}ClN_2O_2$: C 72.80, H 4.94, N 6.53; found C 72.75, H 4.88, N 6.41.

1-Amino-2-cyano-5-ethyloxycarbonyl-3,3-di(4-methylphenyl)-5-phenylcyclopentene (**3f**) White solid, yield 78%, m.p. 172—174 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.42—7.40 (d, J = 8.27 Hz, 2H), 7.25—6.78 (m, 7H), 6.66—6.64 (d, J = 7.06 Hz, 2H), 6.55—6.53 (d, J = 8.21 Hz, 2H), 5.12 (brs, 2H), 4.92—4.89 (d, J = 10.96 Hz, 1H), 4.15—4.10 (q, J = 7.20 Hz, 2H), 3.88—3.85 (d, J = 10.88 Hz, 1H), 2.35 (s, 3H), 2.28 (s, 3H), 1.13 (t, J = 7.19 Hz, 3H); IR (KBr) ν: 3461, 3348, 3087, 2979, 2191, 1726, 1678, 1636, 1559, 1102, 1021 cm^{-1}; MS (70 eV) m/z (%): 436 (M^+, 28.30), 435 (51.79), 421 (49.28), 77 (100). Anal. calcd for $C_{29}H_{28}N_2O_2$: C 79.78, H 6.46, N 6.42; found C 79.53, H 6.33, N 6.39.

1-Amino-2-cyano-5-allyloxycarbonyl-3,3-di(4-methylphenyl)-5-phenylcyclopentene (**3g**) White solid, yield 81%, m.p. 153—154 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.42—7.39 (d, J = 8.31 Hz, 2H), 7.25—6.85 (m, 7H), 6.67—6.65 (d, J = 7.25 Hz, 2H), 6.55—6.53 (d, J = 8.23 Hz, 2H), 5.76—5.72 (m, 1H), 5.17—5.08 (m, 4H), 4.94—4.91 (d, J = 10.91 Hz, 1H), 4.59—4.54 (m, 2H), 3.93—3.90 (d, J = 10.89 Hz, 1H), 2.31 (s, 3H), 2.26 (s, 3H); IR (KBr) ν: 3455, 3350, 3030, 2193, 1728, 1632, 1158, 1033 cm^{-1}; MS (70 eV) m/z (%): 448 (M^+, 4.27), 433 (17.66), 41 (100). Anal. calcd for $C_{30}H_{28}N_2O_2$: C 80.33, H 6.29, N 6.24; found C 80.27, H 6.08, N 6.37.

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(E0203145 ZHAO, X. J.; DONG, L. J.)