Samarium(II) Iodide-Promoted Intermolecular and Intramolecular Ketone-Nitrile Reductive Coupling Reactions

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Received 21 June 1999; revised 9 August 1999

Abstract: Samarium (II) iodide, a strong one-electron transfer reducing reagent, has been successfully utilized for the intermolecular and intramolecular reductive coupling reactions of ketones with nitriles. α-Hydroxy ketones, monocyclic, fused bicyclic α-hydroxy ketones and monocyclic α-amino alcohols composed of a number of substitution patterns have been prepared in good yields at room temperature or reflux under neutral conditions. The procedure can avoid overreduction of the resulting of α-hydroxy ketones or α-amino alcohols. The crystal structures of monocyclic α-amino alcohols are reported.

Key words: samarium diiodide, ketone-nitrile, reductive coupling, cyclizations, α-ketols, α-amino alcohols, aldehydes, ketones, heterocycles

Introduction

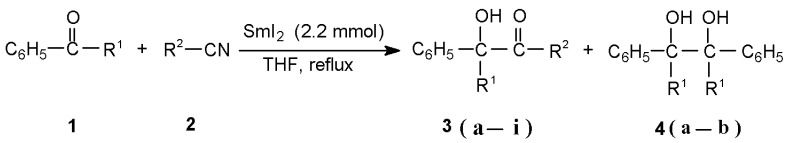
Applications of samarium(II) iodide to organic synthesis have significantly grown in the last decade.[1] Pioneering work performed by Kagan with SmI_2 has served to outline the uses of this reagent in synthetic organic chemistry. Kagan and co-workers' investigations have been followed by reports from other scientists, revealing that SmI_2 is an exceedingly reliable, mild, neutral, selective and versatile single electron transfer agent for promoting reductive reactions difficult to accomplish by other existing methodologies.

Carbonyl coupling reactions passing through a ketyl intermediate constitute an important class of reactions in organic chemistry. For instance, ketone-olefin couplings,[2] and intermolecular and intramolecular pinacol coupling reactions[3] have been conducted using SmI_2 as the reagent. It has been reported that ketyls can also be produced by photochemical[4] and electrochemical processes,[5] low-valent titanium reagent[6] and other reductants.[7]

α-Ketols are versatile synthetic intermediates and partial structures of various biologically active compounds such as cortisone acetates[8] and adriamycin acetate.[9] The methods for synthesis of α-ketols from alkenes[10] and mono-oxygenated compounds such as enol ethers[11] and enolates[12] have been studied extensively. α-Ketols can also be produced by ketyl-nitrile reductive coupling using one-electron reducing agents such as Cp_2TiPh,[13] Zn/TMSCl[14] and SmI_2 [15] in addition to the electroreductive method.[16] Although the reaction of other functional groups promoted by SmI_2 have been studied, little attention has been given to the reaction of nitriles with this agent.[17] It is well known that the carbonyl group can easily be reduced by SmI_2. However, the cyano group is more stable to samarium diiodide than the carbonyl group and could not be coupled by this reagent.[18] In our previous work, we have reported a novel cyclodimerization of arylidenemalononitriles and arylidenecyanoacetates, and intermolecular and intramolecular reductive coupling of nitriles with nitro compounds promoted by SmI_2.[19] Recently Molander reported the intramolecular ketyl-nitrile coupling promoted by SmI_2 under irradiation with a 250 W floodlamp. [15] Herein, we wish to report our results on intermolecular and intramolecular ketone-nitrile reductive couplings promoted by SmI_2 in tetrahydrofuran at room temperature or under reflux conditions.

Intermolecular Ketone-Nitrile Cross Reductive Coupling Reactions

Reaction of 1 equivalent of ketones (or aldehydes) **1** and about 1.2 equivalents of nitriles **2** with 2.2 equivalents of SmI_2 gave α-hydroxy ketones **3** (or pinacols **4**) (Scheme 1). Table 1 summarizes the results on the intermolecular ketone-nitrile reductive couplings. When benzophenone and aromatic nitriles were heated at reflux with SmI_2 un-



1 **2** **3 (a— i)** **4 (a — b)**

Scheme 1

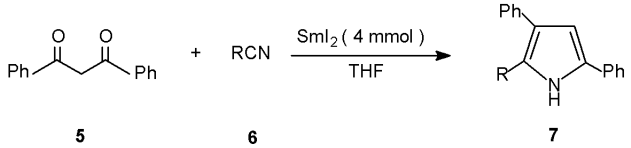
Table 1 The Intermolecular Cross Reductive Coupling of Ketones with Nitriles

Entry	R^1	R^2	Reaction Time (h)	Yield (%)[a,b]	
				3	**4**
1	Ph	Ph	4	78[c]	–
2	Ph	4-ClC_6H_4	5	75[c]	–
3	Ph	3-MeC_6H_4	5	87[c]	–
4	Ph	4-MeC_6H_4	4	76[c]	–
5	Ph	4-$MeOC_6H_4$	6	75[c]	–
6	4-MeC_6H_4	Ph	2.5	83[c]	–
7	4-MeC_6H_4	4-MeC_6H_4	4	70[c]	–
8	4-$MeOC_6H_4$	4-ClC_6H_4	5	77[c]	–
9	Ph	Ph	24	45[d]	–
10	H	4-ClC_6H_4	8	–	81[c]
11	H	4-ClC_6H_4	8	–	86[d]
12	Me	Ph	10	30[c]	44[c]

[a] Yields of isolated products **3a–i** and **4a**,**b**
[b] 1 mmol of **1** and about 1.2 mmol of **2** were used
[c] Reaction was carried out under reflux
[d] Reaction was carried out at room temperature

der nitrogen, α-hydroxy ketones **3** were obtained in good yields (Entries 1–8). If the reaction was carried out at room temperature, it was slow and gave lower yields (Entry 9). Addition of HMPA[20] or LiCl[21] to the reaction mixture gave no evident change. On the other hand, treatment of aromatic aldehydes and nitriles with SmI_2 at room temperature, even under reflux conditions did not give α-hydroxy ketones **3**, only pinacol coupling products **4a,b** were obtained in good yields (Entries 10 and 11). Reaction of acetophenone and benzonitrile with SmI_2, gave α-hydroxy ketones **3i**, along with pinacol **4b** (Entry 12). For comparison, when the same reaction was carried out using $TiCl_4$/Zn as the reductant at reflux temperature, the cross coupling product ketone was obtained along with an olefin[22] while α-hydroxy ketone was not found.

The intramolecular pinacol coupling reaction of diketones can be promoted smoothly by SmI_2.[1,3] Attempts to induce the cross coupling between nitriles and diketones were unsuccessful. Ketones are far more reactive than nitriles and intramolecular reaction could occur much easier than intermolecular one. An exception is the case of dibenzoylmethane (**5**). When dibenzoylmethane (**5**) and nitriles **6** were treated with SmI_2 at reflux conditions, pyrroles **7** were formed in moderate yield (Table 2). The great steric strain for the intramolecular cyclization of dibenzoylmethane is probably the reason why the coupling reaction is driven to take an intermolecular way.



5 6 7

Scheme 2

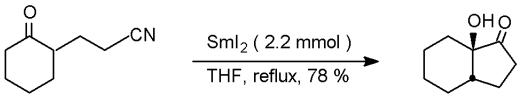
Table 2 Intermolecular Reductive Coupling of Dibenzoylmethane with Nitriles

Entry	R	Reaction Time (h)	Yield (%)[a]
1	Ph	48	61
2	4-MeC_6H_4	40	45

[a] Yield isolated products **7a** and **b**.

Intramolecular Ketone-Nitrile Reductive Coupling Reactions

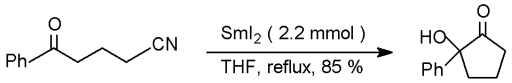
The intramolecular reductive coupling of the keto nitrile **8** was found to be similar to the intermolecular one. When a solution of 1 equivalent of **8** in anhydrous THF was allowed to react with 2.2 equivalents SmI_2 in anhydrous THF under the same reaction conditions, the reductive cyclization took place to provide a 78% yield of the α-hydroxy ketone **9**.



8 9

Scheme 3

The *cis* stereochemistry of **9** was determined by comparison of its ^{13}C NMR spectrum with the reported data. Hence it is reasonable to suggest that the strain of transition structure does not lead to the formation of *trans*-fused bicyclo[4,3,0]system.[15c, 16] The keto nitrile **10** was cyclized to give the α-hydroxy ketone **11** in 85% under the same reaction conditions.

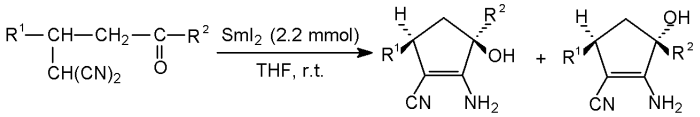


10 11

Scheme 4

Substrates **12**, which possess a carbonyl group and a dicyano group, can undergo intramolecular ketyl-nitrile reductive coupling reaction smoothly even if at room temperature under nitrogen. The reductive cyclization products 1,4-diaryl-2-amino-3-cyanocyclopent-2-ene-1-ols **13** were obtained along with their diastereomers **14** (Scheme 5).

Table 3 summarizes the results on the intramolecular cyclization of γ-keto nitriles. All substrates were cyclized in good yields. The reaction is highly chemoselective; only



12 13 14

Scheme 5

two isomers were obtained. The pinacol coupling products of ketones were not detected. The yield of product **14** is much higher than that of **13**. The chloro and alkoxyl groups of the substrates could not be reduced under the reaction conditions. The structures and relative configuration of the products have been established using spectroscopic data and by X-ray analysis. The X-ray diffraction studies on single crystals of **13c** and **14c** indicate that the products **13** (1,4-*cis*) and **14** (1,4-*trans*) are diastereoisomers (Figure 1 and Figure 2).

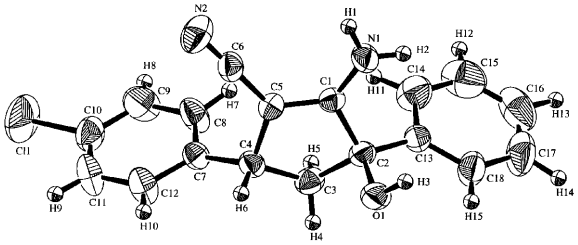


Figure 2 ORTEP diagram of **14c**

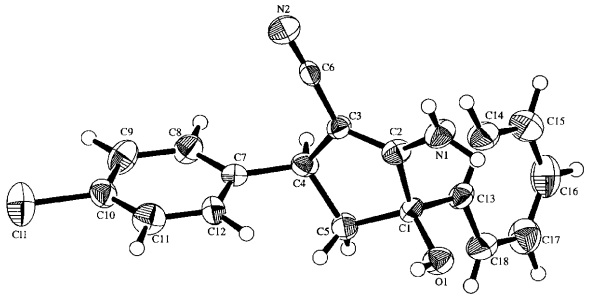


Figure 1 ORTEP diagram of **13c**

Though the detailed mechanism of the above reductive coupling reaction has not been clarified yet, the formation of monocyclic α-amino alcohols and α-hydroxy ketones may be explained by the possible mechanism presented in Scheme 6.

In the intramolecular ketone-nitrile coupling reaction (Scheme 5), after the formation of ketyl anion (**A**), ring closure occurs via radical addition to the nitrile group. Then the carbon-nitrogen double bond is transformed to form a carbon-carbon double bond due to stabilization by the cyano group. In the intermolecular reaction (Scheme 1) and other intramolecular reaction (Schemes 3 and 4), however, the carbon-nitrogen double bond could not be transferred to form a carbon-carbon double bond and in the absence of a cyano group, α-hydroxy ketones are formed. On the other hand, the ketyl radical **(A')** from aromatic aldehydes has less steric hindrance than that of benzophenone and the pinacol coupling reaction could proceed prior to the ketone-nitrile reaction.

In summary, the behavior of SmI_2 applied to the ketone-nitrile reductive coupling reactions has been studied. Although the cross coupling reaction of aldehyde with nitrile did not occur, the reactions afford a variety of α-hydroxy ketones or α-amino alcohols in good yield. Further studies to develop other new reactions using SmI_2 are now in progress.

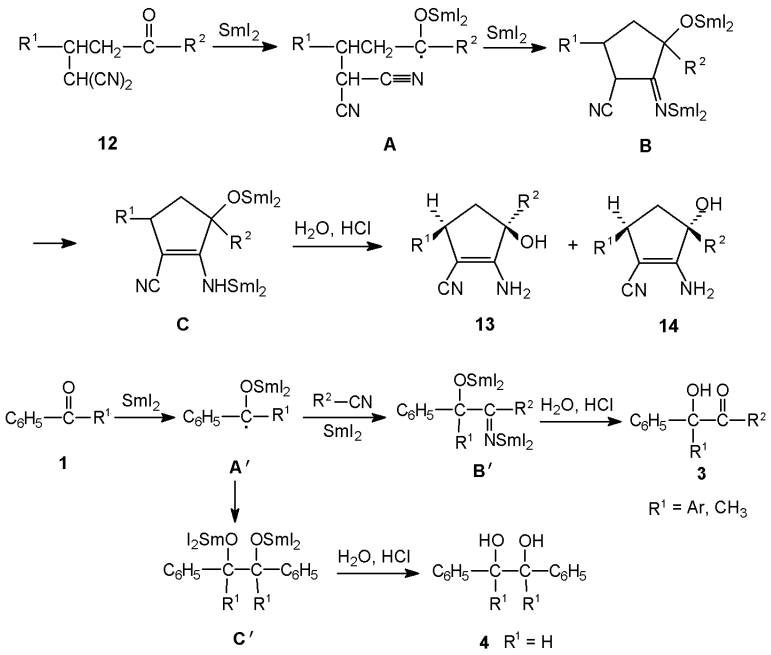
Table 3 The Intramolecular Reductive Coupling of γ-Keto Nitriles

Entry	R^1	R^2	Reaction Time (h)	Yield (%)[a,b]	
				13	**14**
1	Ph	Ph	2	23	49
2	4-ClC_6H_4	4-MeC_6H_4	1	30	54
3	4-ClC_6H_4	Ph	2	25	55
4	3,4-$OCH_2OC_6H_3$	Ph	2.5	21	48
5	2-ClC_6H_4	Ph	1.5	23	53
6	Ph	4-MeC_6H_4	2	27	47
7	4-MeC_6H_4	Ph	2	–	68

[a] Reactions were carried out at room temperature. Yields of isolated products **13a–f** and **14a–g**.
[b] 2.2 mmol SmI_2 and 1 mmol of **1** were used.

THF was distilled from sodium/benzophenone immediately prior to use. All reactions were performed under N_2 using syringes and Schlenk-type techniques.

Melting points are uncorrected. IR spectra were recorded on Perkin Elmer 683 or FTIR-8101 spectrometers in KBr or CCl_4 solution. NMR spectra were recorded on a Bruker AC-300 (^1H, 300 MHz, ^{13}C, 75 MHz) or a JEOL PMX-60 spectrometer. *J* values are in Hertz. Chemical shifts are expressed in ppm downfield from internal TMS. Mass spectra were recorded on a HP 5989A or a Finnigan MAT GCMS spectrometer. Microanalysis were carried out on a Carlo-Erba 1106 instrument.



Scheme 6

SmI_2-Promoted Preparation α-Hydroxy Ketones; General Procedure

To Sm (331 mg, 2.2 mmol) in anhyd THF (22 mL) was added I_2 (558 mg, 2.2 mmol). The resultant orange slurry was stirred vigorously for 2 h at r.t. The resulting SmI_2 solution had a deep blue-green colour. A solution of ketone (or aldehyde) **1** (1 mmol) and nitrile **2** (1.2 mmol) in anhyd THF (3 mL) was added at r.t. under dry N_2. The mixture was then stirred at reflux. After the reaction was complete, the mixture was quenched with dil HCl (5% HCl, 2 mL). The solution was extracted with Et_2O (3 × 40 mL) and the combined extracts were washed with aq satd solution of $Na_2S_2O_3$ (15 mL), brine (15 mL), and dried (Na_2SO_4). After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using EtOAc/cyclohexane (1:10) as eluent.

2-Hydroxy-1,2,2,-triphenylethanone (3a)

Compound **3a** was obtained from benzophenone (182 mg, 1 mmol) and benzonitrile (134 mg, 1.3 mmol) as a white solid in 78% yield; mp 85−86°C (Lit.[23] mp 84°C).

IR (KBr) ν = 3510, 1680 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.96 (1 H, br s, OH, exchangeable), 7.13−7.72 (15 H, m, ArH).

2-Hydroxy-1-(4-chlorophenyl)-2,2,-diphenylethanone (3b)

Compound **3b** was obtained from benzophenone (182 mg, 1 mmol) and 4-chlorobenzonitrile (165 mg, 1.2 mmol) as a white solid in 75% yield; mp 86−88°C (Lit.[24] mp 87−88°C).

IR (KBr) ν = 3490, 1690 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.55 (1 H, s, OH), 6.80−7.80 (14 H, m, ArH).

2-Hydroxy-2,2-diphenyl-1-(*m*-tolyl)ethanone (3c)

Compound **3c** was obtained from benzophenone (182 mg, 1 mmol) and *o*-tolunitrile (141 mg, 1.2 mmol) as an oil in 76% yield; bp 180−187°C/0.2 Torr (Lit.[24] mp 175 − 180°C/0.1 Torr).

IR (neat): ν = 3470, 1680 cm^{-1}.

^1H NMR (CCl_4): δ = 2.07 (3 H, s, CH_3), 4.80 (1 H, s, OH), 6.75−7.60 (14 H, m, ArH).

2-Hydroxy-2,2,-diphenyl-1-(*p*-tolyl)ethanone (3d)

Compound **3d** was obtained from benzophenone (182 mg, 1 mmol) and *p*-tolunitrile (141 mg, 1.2 mmol) as a white solid in 76% yield; mp 56−57°C (Lit.[24] mp 57−59°C).

IR (KBr): ν = 3480, 1680 cm^{-1}.

^1H NMR (CCl_4): δ = 2.16 (3 H, s, CH_3), 5.10 (1 H, s, OH), 6.86−7.75 (14 H, m, ArH).

2-Hydroxy-1-(4-methoxyphenyl)-2,2-diphenylethanone (3e)

Compound **3e** was obtained from benzophenone (182 mg, 1 mmol) and 4-methoxybenzonitrile (160 mg, 1.2 mmol) as a white solid in 75% yield; mp 131−133°C (Lit.[24] mp 132−133.5°C).

IR (KBr): ν = 3410, 1675 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.78 (3 H, s, OCH_3), 5.08 (1 H, s, OH), 6.70−7.90 (14 H, m, ArH).

2-Hydroxy-1,2-diphenyl-2-(*p*-tolyl)ethanone (3f)

Compound **3f** was obtained from 4-methylbenzophenone (196.3 mg, 1 mmol) and benzonitrile (144 mg, 1.4 mmol) as a pale yellow oil in 83% yield (Lit.[25] bp 216−219°C/2.7 Torr).

IR (neat): ν = 3460, 1680 cm^{-1}.

^1H NMR (CCl_4): δ = 2.27 (3 H, s, CH_3), 4.70 (1 H, br s, OH), 6.90−7.70 (14 H, m, ArH).

2-Hydroxy-2-phenyl-1,2-di(*p*-tolyl)ethanone (3g)

Compound **3g** was obtained from 4-methylbenzophenone (196.3 mg, 1 mmol) and *p*-tolunitrile (129 mg, 1.1 mmol) as a colorless oil in 70% yield.[26]

IR (neat): ν = 3480, 1680 cm^{-1}.

^1H NMR (CCl_4): δ = 2.20 (3 H, s, CH_3), 2.27 (3 H, s, CH_3), 4.75 (1 H, br s, OH), 6.90−7.80 (13 H, m, ArH).

1-(4-Chlorophenyl)-2-hydroxy-2-(4-methoxyphenyl)-2-phenylethanone (3h)
Compound **3h** was obtained from 4-methoxybenzophenone (21.3 mg, 1 mmol) and 4-chlorobenzonitrile (151 mg, 1.1 mmol) as a white solid in 77% yield; mp 92−94°C (Lit.[26] mp 93−94°C).

IR (KBr): ν = 3480, 1690 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.60 (3 H, s, OCH_3), 4.23 (1 H, br s, OH), 6.50 − 7.80 (13 H, m, ArH).

2-Hydroxy-2-methyl-1,2-diphenylethanone (3i)
Compound **3i** was obtained from acetophenone (120.2 mg, 1 mmol) and benzonitrile (124 mg, 1.2 mmol) as a solid in 30% yield; mp 66−68°C (Lit.[25] mp 68−69°C).

IR (KBr): ν = 3470, 1690 cm^{-1}.

^1H NMR (CCl_4): δ = 1.43 (3 H, s, CH_3), 3.40 (1 H, br s, OH), 6.90−7.50 (9 H, m, ArH).

SmI_2-Promoted Preparation of Pyrroles 7
To SmI_2 (1.62 g, 4 mmol) in anhyd THF (40 mL) was added a solution of dibenzoylmethane (**5**; 224 mg, 1 mmol) and nitrile **6** (1.5 mmol) in anhyd THF (3 mL) at r.t. under N_2. The mixture was then stirred at reflux about 2 d. After this period, TLC analysis of the mixture showed the reaction to be complete. The reaction was quenched with aq 10% K_2CO_3 solution (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 30 mL) and the combined extracts were washed with brine (15 mL), and dried (Na_2SO_4). After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using Et_2O/petroleum (1:6) as eluent.

2, 3, 5-Triphenylpyrrole (7a)
Compound **7a** was obtained from dibenzoylmethane and benzonitrile in 61% yield; mp 139−140°C (Lit.[27] mp 142°C).

IR (KBr): ν = 3460, 1610, 1510, 1495, 1455, 1265, 1180, 1070, 955, 760, 690 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.50 (1 H, s, CH), 7.05−7.75 (15 H, m, ArH), 8.20 (1 H, s, NH).

3, 5-Diphenyl-2-(*p*-tolyl)pyrrol (7b)
Compound **7b** was obtained from dibenzoylmethane and 4-methylbenzonitrile in 45% yield; mp 104−105°C.

IR (KBr): ν = 3420, 1600, 1480, 1450, 1260, 1070, 810, 790, 760, 700 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.30 (3 H, s, CH_3), 6.65 (1 H, s, CH), 7.05−7.70 (14 H, m, ArH), 8.30 (1 H, s, NH).

MS (EI, 70 eV): *m*/*z* (%) = 309 (M^+, 100), 191 (11), 146 (7), 105 (8).

Anal. Calcd for $C_{23}H_{19}N$: C, 89.28; H, 6.10; N, 4.53. Found: C, 88.95; H, 6.10; N, 4.62.

***cis*-6-Hydroxybicyclo[4.3.0]nonan-7-one (9)**
Compound **9** was prepared from the keto nitrile **8** according to the general procedure for **3**. Purification by preparative TLC on silica gel using EtOAc/cyclohexane (1:4) as eluent afforded **9** as a colorless oil in 78% yield.

IR (neat): ν = 3460, 1750 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.13−1.30 (1 H, m), 1.40−1.83 (9 H, m), 2.05−2.47 (3 H, m,), 3.60 (1 H, br s, OH).

^{13}C NMR ($CDCl_3$): δ = 20.60, 20.72, 20.95, 24.35, 29.37, 33.28, 40.80, 77.75, 219.80.

MS (EI, 70 eV): *m*/*z* (%) = 154 (M^+, 13), 98 (100), 70 (32), 55 (32).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 9.40.

2-Hydroxy-2-phenylcyclopentan-1-one (11)
Compound **11** was prepared from the keto nitrile **10** according to the general procedure for **3**. Purification by preparative TLC on silica gel using EtOAc/cyclohexane (1:4) as eluent afforded **11** as a pale yellow oil in 85% yield.[28]

IR (neat): ν = 3450, 2980, 1750 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.73−1.89 (1 H, m), 1.96−2.10 (1 H, m), 2.15−2.26 (1 H, m,), 2.38−2.50 (3 H, m), 3.19 (1 H, br s, OH), 7.24−7.35 (5 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 176 (M^+, 7), 148 (100), 120 (98), 105 (97), 91 (18), 77 (39), 51 (15).

SmI_2-Promoted Preparation of α-Amino Alcohols
To SmI_2 (331 mg, 2.2 mmol) in anhyd THF (22 mL) was added a solution of keto nitrile **12** (1 mmol) in anhyd THF (3 mL) at r.t. under N_2. The mixture was then stirred at r.t. for about 2 h. After this period, the TLC analysis of the mixture showed the reaction to be complete. The reaction was quenched with 5 % dil HCl (2 mL). The mixture was extracted with Et_2O (3 × 30 mL) and the combined extracts were washed with aq satd $Na_2S_2O_3$ solution (10 mL), brine (15 mL), and dried (Na_2SO_4). After evaporating the solvent under reduced pressure, the crude product purified by preparative TLC on silica gel using EtOAc/cyclohexane (1:2) as eluent.

***cis*-2-Amino-3-cyano-1,4-diphenylcyclopent-2-en-1-ol (13a)**
Compound **13a** was obtained from **12a** as a white solid in 23% yield; mp 168−170°C.

IR (KBr): ν = 3440, 3320, 2200, 1670, 1610, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.98−2.23 (2 H, dd, *J* = 13.2, 7.5 Hz, C^5-H, OH), 2.68−2.93 (1 H, dd, *J* = 13.2, 7.1 Hz, C^5-H), 3.83−4.01 (1 H, dd, *J* = 7.5, 7.1 Hz, C^4-H), 4.65 (2 H, br s, NH_2), 7.23−7.42 (10 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 34), 258 ($M^+ - H_2O$, 100), 257 (61), 181 (25), 171 (9), 155 (20), 154 (23), 105 (69), 77 (75).

Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.83; N, 10.14. Found: C, 78.50; H, 5.60; N, 9.97.

***trans*-2-Amino-3-cyano-1,4-diphenylcyclopent-2-en-1-ol (14a)**
Compound **14a** was obtained from **12a** as a white solid in 49% yield; mp 164−165°C.

IR (KBr): ν = 3480, 3360, 2200, 1660, 1610, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.05−2.32 (2 H, dd, *J* = 14.2, 7.5, C^5-H, OH), 2.58−2.85 (1 H, dd, *J* = 14.2, 7.3, C^5-H), 4.21−4.40 (3 H, dd, *J* = 7.5, 7.3, C^4-H, NH_2), 7.26−7.50 (10 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 59), 258 ($M^+ - H_2O$, 100), 181 (24), 171 (10), 155 (22), 154 (23), 105 (66), 77 (67).

Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.83; N, 10.14. Found: C, 78.47; H, 5.57; N, 9.88.

***cis*-2-Amino-4-(4-chlorophenyl)-3-cyano-1-(*p*-tolyl)cyclopent-2-en-1-ol (13b)**
Compound **13b** was obtained from **12b** as a white solid in 30% yield; mp 187 − 189°C.

IR (KBr): ν = 3470, 3420, 3365, 2180, 1675, 1615, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.90 − 2.17 (1 H, dd, *J* = 13.0, 7.5, C^5-H), 2.37 (3 H, s, CH_3), 2.64−2.89 (2 H, dd, *J* = 13.0, 7.1, C^5-H, OH), 3.77−3.95 (1 H, dd, *J* = 7.5, 7.1, C^4-H), 4.58 (2 H, br s, NH_2), 7.14−7.40 (8 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 326 ($[M + 2]^+$, 7), 324 (M^+, 21), 308 (37), 306 ($M^+ - H_2O$, 100), 289 (28), 271 (26), 256 (14), 215 (16), 205 (5), 189 (6), 188 (4), 119 (64), 91 (55).

Anal. Calcd for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.27; N, 8.62. Found: C, 70.50; H, 5.45; N, 8.36.

***trans*-2-Amino-4-(4-chlorophenyl)-3-cyano-1-(*p*-tolyl)cyclopent-2-en-1-ol (14b)**
Compound **14b** was obtained from **12b** as a white solid in 54% yield; mp 170−172°C.

IR (KBr): ν = 3490, 3390, 3250, 2190, 1660, 1605, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.94−2.21 (1 H, dd, *J* = 14.2, 7.4 Hz, C^5-H), 2.34 (3 H, s, CH_3), 2.52−2.79 (2 H, dd, *J* = 14.2, 7.3 Hz, C^5-H, OH), 4.41−4.32 (1 H, dd, *J* = 7.4, 7.3 Hz, C^4-H), 4.51 (2 H, br s, NH_2), 7.11−7.38 (8 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 326 ([M + 2]$^+$, 17), 324 (M^+, 49), 308 (35), 306 ($M^+ - H_2O$, 99), 289 (80), 271 (55), 256 (24), 215 (10), 205 (7), 189 (8), 188 (6), 119 (100), 91 (74).

Anal. Calcd for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.27; N, 8.62. Found: C, 70.04; H, 5.13; N, 8.81.

***cis*-2-Amino-4-(4-chlorophenyl)-3-cyano-1-phenylcyclopent-2-en-1-ol (13c)**
Compound **13c** was obtained from **12c** as a white solid in 25% yield; mp 178−180°C.

IR (KBr): ν = 3490, 3420, 3360, 2180, 1680, 1625, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.93−2.19 (2 H, dd, *J* = 13.0, 7.5 Hz, C^5-H, OH), 2.66−2.91 (1 H, dd, *J* = 13.0, 7.0 Hz, C^5-H), 3.79−3.97 (1 H, dd, *J* = 7.5, 7.0 Hz, C^4-H), 4.70 (2 H, br s, NH_2), 7.25−7.50 (9 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 312 ([M + 2]$^+$, 10), 310 (M^+, 29), 294 (36), 292 ($M^+ - H_2O$, 100), 275 (53), 257 (41), 215 (10), 205 (8), 189 (7), 105 (62), 77 (48).

Anal. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.87; N, 9.01. Found: C, 69.82; H, 4.99; N, 8.87.

***trans*-2-Amino-4-(4-chlorophenyl)-3-cyano-1-phenylcyclopent-2-en-1-ol (14c)**
Compound **14c** was obtained from **12c** as a white solid in 55% yield; mp 191−193°C.

IR (KBr): ν = 3500, 3390, 2200, 1660, 1605, 1500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.00−2.27 (2 H, dd, *J* = 14.1, 7.5 Hz, C^5-H, OH),2.57−2.84 (1 H, dd, *J* = 14.1, 7.3 Hz, C^5-H), 4.18−4.37 (3 H, dd, *J* = 7.5, 7.0 Hz, C^4-H, NH_2), 7.13−7.41 (9 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 312 ([M + 2]$^+$, 14), 324 (M^+, 39), 294 (33), 292 ($M^+ - H_2O$, 95), 275 (100), 257 (48), 215 (6), 205 (7), 189 (7), 105 (85), 77 (58).

Anal. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.87; N, 9.01. Found: C, 69.75; H, 4.65; N, 9.17.

***cis*-2-Amino-3-cyano-4-(3, 4-methylenedioxyphenyl)-1-phenylcyclopent-2-en-1-ol (13d)**
Compound **13d** was obtained from **12d** as pale yellow crystals in 21% yield; mp 164 − 166°C.

IR (KBr): ν = 3470, 3390, 3250, 2200, 1660, 1610, 1510, 1455 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.93−2.16 (2 H, dd, *J* = 13.0, 7.5 Hz, C^5-H, OH), 2.64−2.91 (1 H, dd, *J* = 13.0, 7.0 Hz, C^5-H), 3.75−3.94 (1 H, dd, *J* = 7.5, 7.0 Hz, C^4-H), 4.68 (2 H, br s, NH_2), 5.94 (2 H, s, OCH_2O), 6.72−6.78 (3 H, m, ArH), 7.35−7.61 (5 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 320 (M^+, 100), 302 ($M^+ - H_2O$, 47), 105 (33), 77 (23).

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.04, N, 8.74. Found: C, 71.51; H, 5.16; N, 8.61.

***trans*-2-Amino-3-cyano-4-(3,4-methylenedioxyphenyl)-1-phenylcyclopent-2-en-1-ol (14d)**
Compound **14d** was obtained from **12d** as a pale yellow crystal in 48% yield; mp 162−164°C.

IR (KBr): ν = 3500, 3370, 3260, 2200, 1660, 1610, 1490, 1450 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.00−2.27 (2 H, dd, *J* = 14.2, 7.5 Hz, C^5-H, OH), 2.54−2.81 (1 H, dd, *J* = 14.2, 7.3 Hz, C^5-H), 4.13−4.32 (1 H, dd, *J* = 7.5, 7.3 Hz, C^4-H), 4.41 (2 H, br s, NH_2), 5.94 (2 H, s, OCH_2O), 6.75 (3 H, s, ArH), 7.30−7.50 (5 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 320 (M^+, 100), 302 ($M^+ - H_2O$, 38), 105 (28), 77 (16).

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.04; N, 8.74. Found: C, 71.61; H, 5.35; N, 8.61.

***cis*-2-Amino-3-cyano-4-(2-chlorophenyl)-1-phenylcyclopent-2-en-1-ol (13e)**
Compound **13e** was obtained from **12e** as a white solid in 23% yield; mp 171−172°C.

IR (KBr): ν = 3430, 3370, 3250, 2180, 1675, 1605, 1455 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.87−2.12 (2 H, dd, *J* = 13.5, 6.4 Hz, C^5-H, OH), 2.82−3.02 (1 H, dd, *J* = 13.5, 7.6 Hz, C^5-H), 4.38−4.47 (1 H, dd, *J* = 7.6, 6.4 Hz, C^4-H), 4.66 (2 H, br s, NH_2), 7.19−7.49 (9 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 312 ([M + 2]$^+$, 17), 310 (M^+, 48), 294 (28), 292 ($M^+ - H_2O$, 74), 275 (4), 257 (31), 215 (7), 205 (5), 189 (5), 105 (64), 77 (100).

Anal. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.87; N, 9.01. Found: C, 69.83; H, 4.65; N, 9.18.

***trans*-2-Amino-3-cyano-4-(2-chlorophenyl)-1-phenylcyclopent-2-en-1-ol (14e)**
Compound **14e** was obtained from **12e** as a white solid in 53% yield; mp 183−185°C.

IR (KBr): ν = 3460, 3370, 3250, 2190, 1660, 1610, 1460 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.92−2.19 (1 H, dd, *J* = 14.3, 6.8 Hz, C^5-H), 2.73−3.00 (2 H, dd, *J* = 14.3, 7.7 Hz, C^5-H, OH), 4.57 (2 H, br s, NH_2), 4.67−4.83 (1 H, dd, *J* = 7.7, 6.8 Hz, C^4-H), 7.15−7.36 (9 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 312 ([M + 2]$^+$, 21), 310 (M^+, 47), 294 (34), 292 ($M^+ - H_2O$, 89), 275 (5), 257 (12), 215 (5), 205 (4), 189 (3), 105 (68), 77 (100).

Anal. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.87; N, 9.01. Found: C, 69.79; H, 4.63; N, 9.25.

***cis*-2-Amino-3-cyano-4-phenyl-1-(*p*-tolyl)cyclopent-2-en-1-ol (13f)**
Compound **13f** was obtained from **12f** as a white solid in 27% yield; mp 196−98°C.

IR (KBr): ν = 3420, 3370, 3250, 2190, 1675, 1640, 1610 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.96−2.00 (1 H, dd, *J* = 13.4, 7.3 Hz, C^5-H), 2.38 (3 H, s, CH_3), 2.65−2.88 (2 H, dd, *J* = 13.4, 7.3 Hz, C^5-H, OH), 3.80−3.98 (1 H, dd, *J* = 7.3, 7.3 Hz, C^4-H), 4.65 (2 H, br s, NH_2), 7.23−7.45 (9 H, m, ArH).

MS (EI, 70 eV): *m*/*z* (%) = 290 (M^+, 38), 272 ($M^+ - H_2O$, 100), 257 (22), 198 (21), 181 (14), 171 (6), 155 (10), 154 (7), 119 (42), 91 (34).

Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.60; H, 6.25; N, 9.65. Found: C, 78.78; H, 6.12; N, 9.82.

***trans*-2-Amino-3-cyano-4-phenyl-1-(*p*-tolyl)cyclopent-2-en-1-ol (14f)**
Compound **14f** was obtained from **12f** as a white solid in 47% yield; mp 165−166.

IR (KBr): ν = 3500, 3400, 2200, 1650, 1640, 1600 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.01−2.28 (1 H, dd, *J* 14.2, 7.5 Hz, C^5-H), 2.34 (3 H, s, CH_3), 2.54−2.61 (2 H, dd, *J* = 14.2, 7.3, C^5-H, OH),

4.18−4.36 (1 H, dd, J = 7.5, 7.3 Hz, C^4-H), 4.46 (2 H, br s, NH_2), 7.11−7.41 (9 H, m, ArH).

MS (EI, 70 eV): m/z (%) = 290 (M^+, 73), 272 (M − H_2O, 100), 257 (34), 198 (8), 181 (7), 163 (16), 155 (12), 154 (8), 119 (52), 91 (36).

Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.60; H, 6.25; N, 9.65. Found: C, 78.38; H, 5.98; N, 9.77.

***trans*-2-Amino-3-cyano-1-phenyl-4-(*p*-tolyl)cyclopent-2-en-1-ol (14g)**

Compound **14g** was obtained from **12g** as a white solid in 68% yield; mp 166−68°C.

IR (KBr): ν = 3450, 3370, 3260, 2190, 1670, 1620, 1520 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.13−2.20 (1 H, dd, J = 14.3, 7.4 Hz, C^5-H), 2.32 (3 H, s, CH_3), 2.63−2.70 (1 H, dd, J = 14.3, 7.3 Hz, C^5-H), 2.85 (1 H, br s, OH), 4.23−4.28 (1 H, dd, J = 7.4, 7.3, C^4-H), 4.41 (2 H, br s, NH_2), 7.12−7.49 (9 H, m, ArH).

MS (EI, 70 eV): m/z (%) = 290 (M^+, 41), 272 (M^+ − H_2O, 100), 257 (28), 198 (15), 181 (6), 163 (15), 155 (34), 154 (27), 119 (58), 91 (41).

Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.60; H, 6.25; N, 9.65. Found: C, 78.31; H, 5.96; N, 9.60.

Crystallographic Data for Compounds 13c and 14c[32]

Crystals of **13c** and **14c** suitable for X-ray analysis were obtained by crystallization from EtOH solution.

Data for **13c**: $C_{18}H_{15}ClN_2O$ (310.78), colorless; monoclinic; space group C2/c: a = 24.416 (2), b = 12.215 (4), c = 10.772 (4) Å; β = 97.78 (1)°; V = 3183 (1) $Å^3$; Z = 8; D_c = 1.297 g cm^{-3}; F (000) = 1296. Data were collected with a Rigaku AFC7R diffractometer with ω -scan technique, graphite - monochromated M_o-K_α radiation (λ = 0.71069Å, μ = 0.242 mm^{-1}) at 293K. 3028 reflections were measured, of which 2953 were independent reflections with 2θ in the range of 6 to 50°, 1071 reflections having I > 2σ (I). The structure was solved by direct methods[29] and expanded using Fourier techniques.[30] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-sequares refinement give R = 0.058 and R_w = 0.054 with $w = 1/\sigma^2(F_0)$, S = 1.36. The maximum and the minimum peak on the final difference Fourier map corresponded to 0.26 and −0.26 e/$Å^3$, respectively. All calculations were performed using TEXSAN program package.[31]

Data for **14c**: $C_{18}H_{15}ClN_2O$ (310.78), colorless; orthorhombic; space group Pbcn: a = 13.370 (5), b = 10.481 (5), c = 23.350 (6) Å; V = 3272 (3) $Å^3$; Z = 8; D_c = 1.262 g cm^{-3}; F (000) = 1296. Data were collected with a Rigaku AFC7R diffractometer with ω-scan technique, graphite - monochromated M_o-K_α radiation (λ = 0.71069Å, μ = 0.236 mm^{-1}) at 293K. 3278 reflections were measured with 2θ in the range of 6 to 50°, 1551 reflections having I > 2σ (I). The structure was solved by direct methods[29] and expanded using Fourier techniques.[30] All non-hydrogen atoms were refined anisotropically. hydrogen atoms were refined isotropically. The final cycle of full-matrix least-sequares refinement give R = 0.048 and R_w = 0.051 with $w = 1/\sigma^2(F_0)$, S = 1.54. The maximum and the minimum peak on the final difference Fourier map corresponded to 0.20 and − 0.22 e/$Å^3$, respectively. All calculations were performed using TEXSAN program package.[31]

Acknowledgement

We are grateful to the National Natural Science Foundation of China (Project No. 29672007 and 29872010), the NSF of Zhejiang Province, China and the Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Science for financial support.

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13c: O(1) − C(1) 1.425(6), N(1) − C(2) 1.338(7), N(2) − C(6) 1.156(7), C(1) − C(2) 1.528(8), C(1) − C(5) 1.535(8), C(1) − C(13) 1.533(8), C(2) − C(3) 1.341(7), C(3) − C(4) 1.526(7), C(3) − C(6) 1.417(8), C(4) − C(5) 1.533(7), C(4) − C(7) 1.503(8); O(1) − C(1) − C(2) 111.7(5), O(1) − C(1) − C(5) 112.2(5), O(1) − C(1) − C(13) 105.3(4), C(2) − C(1) − C(5) 101.8(4), C(2) − C(1) − C(13) 113.4(5), C(5) − C(1) − C(13) 112.7(5), N(1) − C(2) − C(1) 118.6(5), N(1) − C(2) − C(3) 131.0(5), C(1) − C(2) − C(3) 110.4(5), C(2) − C(3) − C(4) 112.9(5), C(2) − C(3) − C(6) 125.9(5), C(4) − C(3) − C(6) 121.1(5), C(3) − C(4) − C(5) 100.9(4), C(3) − C(4) − C(7) 113.9(5), C(5) − C (4) − C(7) 114.2(5), C(1) − C(5) − C(4) 107.2(5), N(2) − C(6) − C(3) 177.4(7).
14c: O(1) − C(2) 1.431(4), N(1) − C(1) 1.331(4), N(2) − C(6) 1.150(4), C(1) − C(2) 1.536(4), C(2) − C(3) 1.530(5), C(2) − C(13) 1.511(5), C(1) − C(5) 1.353(4), C(4) − C(5) 1.521(4), C(5) − C(6) 1.406(5), C(3) − C(4) 1.531(5), C(4) − C(7) 1.520(4); O(1) − C(2) − C(1) 106.8(3), O(1) − C(2) − C(3) 106.2(3), O(1) − C(2) − C(13) 112.1(3), C(1) − C(2) − C(3) 101.8(3), C(1) − C(2) − C(13) 114.4(3), C(3) − C(2) − C(13) 114.6(3), N(1) − C(1) − C(2) 120.7(3), N(1) − C(1) − C(5) 129.3(3), C(2) − C(1) − C(5) 109.7(3), C(1) − C(5) − C(4) 112.6(3), C(1) − C(5) − C(6) 124.2(3), C(4) − C(5) − C(6) 123.1(3), C(3) − C(4) − C(5) 101.0(3), C(5) − C(4) − C(7) 112.7(3), C(3) − C(4) − C(7) 116.0(3), C(2) − C(3) − C(4) 106.7(3), N(2) − C(6) − C(5) 179.4(4).

Article Identifier:
1437-210X,E;2000,0,01,0091,0098,ftx,en;F03999SS.pdf