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Intermolecular and Intramolecular Ketone–Nitrile Reductive Coupling Reactions Promoted by $TiCl_4$–Sm System

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Abstract—The intermolecular and intramolecular reductive coupling reactions of ketones with nitriles have been successfully promoted by low-valent titanium prepared by the $TiCl_4$–Sm system. Substituted ketones, monocyclic α-amino alcohols and monocyclic amines composed of a number of substitution patterns have been prepared in good yields at room or THF reflux temperature under neutral conditions. The procedure can avoid over reduction of the resulting of ketones, α-amino alcohols or amines. The crystal structures of two monocyclic α-amino alcohols are reported.

Introduction

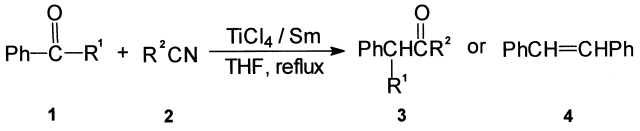
Carbon–carbon bond formation is the essence of organic synthesis and the reductive coupling of carbonyl derivatives is one of the most valuable methods for making carbon–carbon bonds. Low-valent titanium reagent has an exceedingly high ability in promoting reductive coupling of carbonyl compounds and is attracting increasing interest in organic synthesis. A lot of other functional groups can also be coupled by this reagent.[1] Recently, we have reported a reductive cleavage reaction of Se–Se and Te–Te bonds using the $TiCl_4$–Sm system.[2] Here we wish to report a reductive cross-coupling reaction of nitrile derivatives with carbonyl compounds promoted by $TiCl_4$–Sm in anhydrous THF.

It has been shown that the cyano group is relatively more stable to low-valent titanium reagent than the carbonyl group and it could only be reduced under reflux for a long time in low yield.[3] We considered that the intermediate derived from a more active functional group by its treatment with low-valent titanium could perhaps attack a more stable functional group, which otherwise would not react with low-valent titanium. Therefore, we have studied the behavior of the cyano group and the carbonyl group with low-valent titanium prepared by $TiCl_4$–Sm in THF at room or reflux temperature.

Results and Discussion

Intermolecular ketone–nitrile cross-reductive coupling reactions

Treatment of 1 equiv. of ketones (or aldehydes) **1** and 1.2 equiv. of nitriles **2** with low-valent titanium which was prepared from 2 equiv. of $TiCl_4$ and 2 equiv. of Sm powder, gave substituted ketones **3** (or olefins **4**) (Scheme 1). Table 1 summarizes the results on the intermolecular ketone–nitrile



Scheme 1.

Table 1. $TiCl_4$–Sm induced cross-coupling of ketones with nitriles

Entry	R^1	R^2	t (h)	Product (%)[a]
a	Ph	Ph	10	**3a** (81)[b]
b	Ph	4-ClC_6H_4	8	**3b** (82)[b]
c	4-$CH_3C_6H_4$	Ph	10	**3c** (70)[b]
d	Ph	4-$CH_3C_6H_4$	12	**3d** (66)[b]
e	Ph	$C_6H_5CH_2$	12	**3e** (73)[b]
f	4-$CH_3OC_6H_4$	Ph	12	**3f** (70)[b]
g	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	10	**3g** (72)[b]
h	4-ClC_6H_4	Ph	10	**3h** (78)[b]
i	Ph	Ph	18	**3a** (41)[c]
j	H	Ph	10	**4a** (63)[c]
k	H	Ph	10	**4a** (79)[b]

[a] Isolated yield.
[b] Reaction is carried out under reflux.
[c] Reaction is carried out at room temperature.

Keywords: reductive coupling; ketones; α-amino alcohols.
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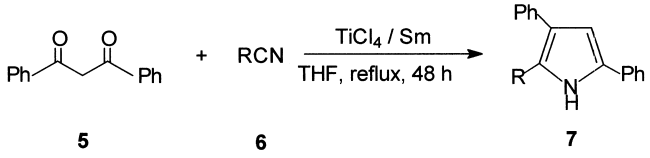
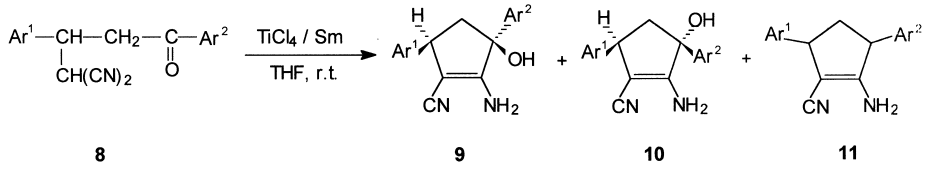


5 6 7

Scheme 2. 7a: R=Ph, yield 51%; **7b**: R=4-$CH_3C_6H_4$, yield 42%.



8 9 10 11

Scheme 3.

reductive couplings. When benzophenone and nitriles were heated under reflux with $TiCl_4$–Sm in a nitrogen atmosphere, ketones **3** were obtained in good yields (entries a–h); if carried out at room temperature, the reaction is slow and gives lower yields (entry 9). On the other hand, treatment of aromatic aldehydes and nitriles with $TiCl_4$–Sm at room or reflux temperature did not give ketones **3**, only olefins **4** were obtained in good yields (entries j–k). For comparison when the same reaction was carried out using SmI_2 as the reductant at reflux temperature, the cross-coupled product (α-hydroxy ketone) was obtained and ketone **3** was not found.[4]

The intramolecular pinacol coupling reaction of diketones can be promoted satisfactorily by low-valent titanium to afford three-membered ring compounds.[1] Attempts to induce the cross-coupling between nitriles and diketones were unsuccessful. Ketones are far more reactive than nitriles and intramolecular coupling could occur much easier than the cross-coupling reaction. An exception is the case of dibenzoylmethane. When dibenzoylmethane **5** and nitriles **6** were treated with $TiCl_4$–Sm at reflux temperature, pyrroles **7** were formed in moderate yield (entries a and b). The great steric strain for the pinacol coupling of dibenzoylmethane is probably the reason why the reaction is driven to take the cross-coupling way (Scheme 2).

Intramolecular ketone–nitrile reductive coupling reactions

On the other hand, the intramolecular ketone–nitrile reductive coupling is dissimilar to the intermolecular one. Substrates **8**, which possess a carbonyl group and two cyano groups, can undergo intramolecular ketyl–nitrile reductive coupling reaction smoothly even at room temperature under a nitrogen atmosphere. The reductive cyclization products 2-amino-3-cyano-1,4-diaryl-2-cyclopenten-1-ols **9** were obtained along with their diastereoisomers **10** in addition to 1-amino-2-cyano-3,5-diaryl-1-cyclopentenes **11** (Scheme 3). The intramolecular ketyl–nitrile reductive coupling reaction products are different from those obtained using one-electron reducing agents such as Cp_2TiPh,[5] Zn/TMSCl,[6] SmI_2[4,7] and electroreductive method,[8] which produce α-hydroxyketones. When the same reaction is carried out at −20°C, only cyclopentenes **9** and **10** were formed and products **11** were not detected. However, if the reaction was carried out at about 65°C, cyclopentenes **11** were obtained in good yield along with a smaller amount of cyclopentenes **10** and products **9** were not found.

Table 2 summarizes the results of the intramolecular cyclization of γ-ketonitriles. All substrates were cyclized in good yields. The reaction is highly chemoselective: only cyclization products were obtained. The pinacol coupling products

Table 2. $TiCl_4$–Sm induced intramolecular ketone–nitrile coupling reaction

Entry	Substr.	Ar^1	Ar^2	*T* (°C)	*t* (h)	Isolated yield (%)		
						9	**10**	**11**
1	**8a**	Ph	Ph	rt	3	**9a** (20)	**10a** (32)	**11a** (17)
2	**8a**	Ph	Ph	−20	4	**9a** (30)	**10a** (43)	–
3	**8a**	Ph	Ph	65	3.5	–	–	**11a** (77)
4	**8b**	4-ClC_6H_4	4-$CH_3C_6H_4$	−20	6	**9b** (34)	**10b** (45)	–
5	**8b**	4-ClC_6H_4	4-$CH_3C_6H_4$	65	3	–	**10b** (5)	**11b** (74)
6	**8c**	4-ClC_6H_4	Ph	−20	4	**9c** (29)	**10c** (51)	–
7	**8c**	4-ClC_6H_4	Ph	65	3	–	–	**11c** (74)
8	**8d**	3,4-$OCH_2OC_6H_3$	Ph	−20	5	**9d** (30)	**10d** (43)	–
9	**8d**	3,4-$OCH_2OC_6H_3$	Ph	65	3	–	**10d** (8)	**11d** (72)
10	**8e**	2-ClC_6H_4	Ph	−20	6	**9e** (26)	**10e** (40)	–
11	**8e**	2-ClC_6H_4	Ph	65	3.5	–	–	**11e** (81)
12	**8f**	4-$CH_3C_6H_4$	Ph	−20	8	–	**10f** (71)	–
13	**8f**	4-$CH_3C_6H_4$	Ph	65	2.5	–	–	**11f** (77)

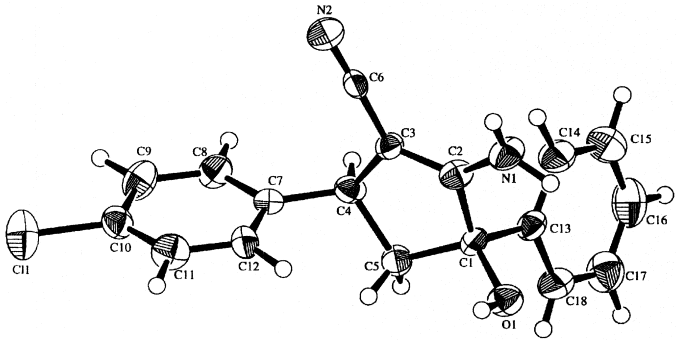


Figure 1. ORTEP diagram of **9c**.

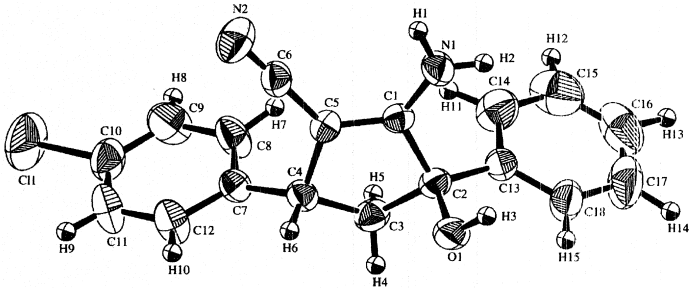
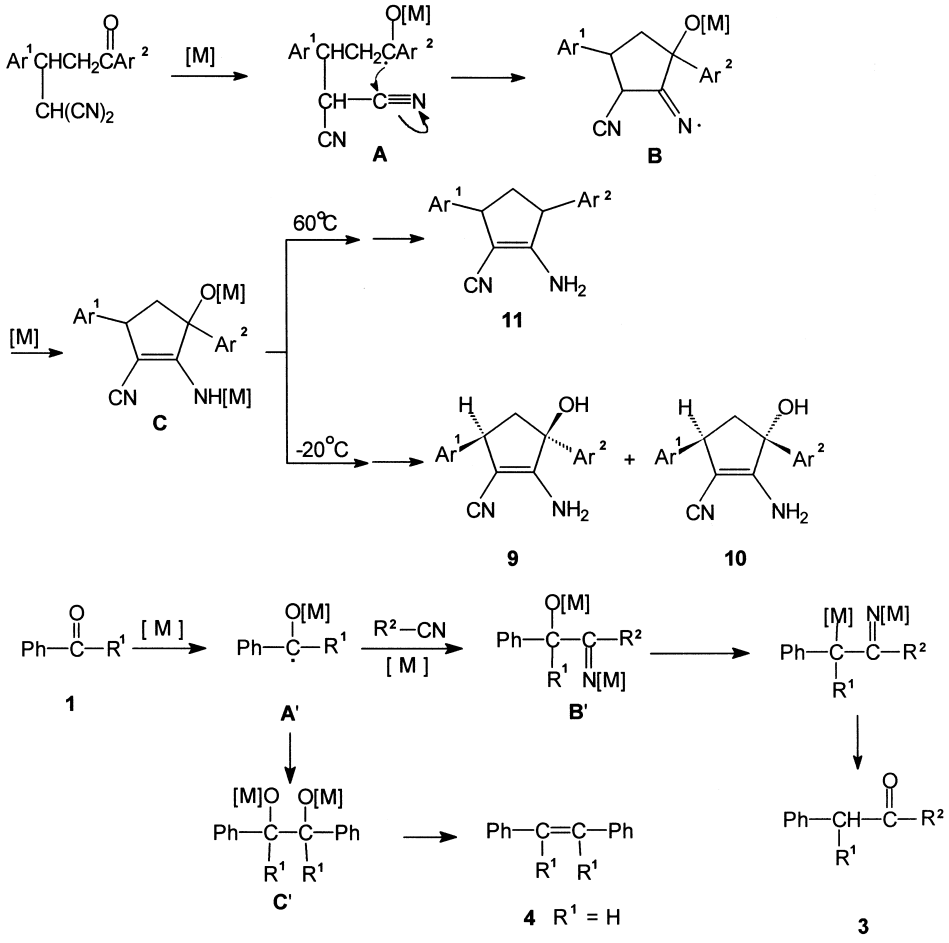


Figure 2. ORTEP diagram of **10c**.



Scheme 4.

of ketones were not detected. 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 as well as X-ray analysis. The X-ray diffraction studies on a single crystal of **9c** and **10c** indicate that the products **9** (1,4-*cis*) and **10** (1,4-*trans*) were diastereoisomers (Figs. 1 and 2).

Though the detailed mechanism of the above reductive coupling reaction has not yet been clarified, the formation of monocyclic α-amino alcohols and amines or ketones may be explained by a possible mechanism presented in Scheme 4.

In the intramolecular ketone–nitrile coupling reaction (Scheme 4), after the formation of ketyl anion (**A**), ring closure occurs via radical addition with the nitrile group; then the carbon–nitrogen double bond is transferred to form a carbon–carbon double bond due to stabilization by the cyano group. If the reaction is carried out at lower temperature (−20°C), the intermediates can be protonated to 2-amino-3-cyano-1,4-diaryl-2-cyclopenten-1-ols **9** and **10**. At higher temperature (65°C), however, the intermediates can be further reduced by the low-valent titanium, thereby forming 1-amino-2-cyano-3,5-diaryl-1-cyclopentenes **11**. In the intermolecular reaction (Scheme 4), however, the carbon–nitrogen double bond (in intermediate **B′**) could not proceed to form a carbon–carbon double bond due to the absence of a cyano group, and ketones **3** are formed.[9] On the other hand, the ketyl radical (**A′**) derived from aromatic aldehydes has less steric hindrance than that of benzophenone and the pinacol coupling reaction could proceed prior to the ketone–nitrile reaction, with further reduction to olefin **4**.

In conclusion, low-valent titanium, prepared by $TiCl_4$–Sm system, induced ketone–nitrile reductive coupling reactions have been studied. Although the cross-coupling reaction of an aldehyde with a nitrile did not occur, the reactions afford a variety of substituted ketones or α-amino alcohols and amines in good yields. Further studies of this low-valent reagent on other chemical transformations are now in progress.

Experimental

General details

Melting points are uncorrected. IR spectra were measured with Perkin–Elmer 683 or FTIR-810 spectrophotometer in KBr or CCl_4. ^1H NMR spectra were obtained on Bruker AC 300, Bruker AC 80 or JEOL PMX-60 spectrometers for samples dissolved in $CDCl_3$ or CCl_4 using TMS as internal standard; *J* values are given in Hz. Elemental analyses were performed on a Carlo Erba 1106 instrument. Mass spectra were obtained on a HP 5989A mass spectrometer using electron impact mode (70 eV). Thin layer chromatography (TLC) was performed on 0.5 mm silica gel (GF254) pre-coated microscope slides and visualised with UV light (254 nm). Preparative TLC was carried out on 1.5 mm silica gel (GF254) pre-coated plate glass (20×20 cm) and visualised with UV light (254 nm).

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. All reactions were performed under a nitrogen atmosphere, using syringes and Schlenk-type techniques. Titanium tetrachloride, metallic samarium, aldehydes, dibenzoylmethane, diaryl ketones, nitriles were purchased from commercial sources and used without purification. γ-Ketonitriles **8**[10] were prepared from the reaction of chalcones with malononitrile using KF–Al_2O_3 as catalyst at room temperature.

General procedure for the preparation of ketones promoted by low-valent titanium

Under an inert atmosphere of nitrogen, $TiCl_4$ (0.22 mL, 2 mmol) was added dropwise using a syringe to stirred suspension of powdered samarium (0.30 g, 2 mmol) in freshly distilled dry THF (20 mL) at room temperature. After the completion of addition, the mixture was refluxed for 2 h. A suspension of the low-valent titanium reagent was formed and cooled to room temperature; then a solution of diarylketone **1** (1 mmol) and nitrile **2** (1 mmol) in THF (3 mL) was added dropwise. The mixture was stirred at reflux temperature for the time indicated in Table 1. Then, dilute HCl (5%, 4 mL) solution was added and the mixture then extracted with ether (3×3 mL). After usual work-up, the crude product was then purified by preparative thin layer chromatography of silica gel with dichloromethane-petroleum ether (30–60°C) (2:3) as the eluent to afford the product.

2,2-Diphenylacetophenone 3a. Mp 134–136°C (lit.[11] 138–138.5°C); ν_{max}(KBr)/cm^{-1} 3100, 3080, 3045, 2940, 1690, 1640, 1600, 1500, 1400, 1360, 1205, 1030, 1010, 995, 760, 755, 735, 690; δ_H ($CDCl_3$) 6.00 (1H, s, CH), 7.13–8.10 (15H, m, ArH).

2,2-Diphenyl-(4′-chloro)acetophenone 3b. Mp 108–110°C (lit.[12] 108–109°C); ν_{max} (KBr)/cm^{-1} 3040, 2980, 1690, 1600, 1580, 1500, 1405, 1210, 1030, 1090, 1005, 995, 835, 810, 745, 695; δ_H (CCl_4) 5.90 (1H, s, CH), 7.15–7.95 (14H, m, ArH).

2-Phenyl-2-(4′-methylphenyl)acetophenone 3c. Mp 97–98°C (lit.[13] 97.5–98.5°C); ν_{max} (KBr)/cm^{-1} 3040, 2930, 1695, 1600, 1500, 1450, 1360, 1205, 1005, 790, 750, 735, 710; δ_H ($CDCl_3$) 2.26 (3H, s, CH_3), 6.00 (1H, s, CH), 7.10–8.20 (14H, m, ArH).

2,2-Diphenyl-4′-methylacetophenone 3d. Mp 99–101 (lit.[13] 100–101°C); ν_{max} (KBr)/cm^{-1} 3040, 2940, 1690, 1615, 1505, 1460, 780, 740, 695; δ_H (CCl_4) 2.33 (3H, s, CH_3), 5.97 (1H, s, CH), 7.05–7.60 (12H, m, ArH), 7.89 (2H, d, *J*=7.2 Hz, ArH).

α,α,α-Triphenylacetone 3e. Mp 82–83 (lit.[14] 84°C); ν_{max} (KBr)/cm^{-1} 3050, 1680, 1610, 1500, 1460, 1060, 735, 690; δ_H (CCl_4) 3.67 (2H, s, CH_2), 5.10 (1H, s, CH), 6.95–7.40 (15H, m, ArH).

2,2-Diphenyl-4′-methoxyacetophenone 3f. Mp 128–129 (lit.[15] 128–130°C); ν_{max} (KBr)/cm^{-1} 3045, 1685, 1605, 1515, 1360, 1275, 1165, 1010, 820, 740, 720, 690; δ_H (CCl_4) 3.65 (3H, s, OCH_3), 5.90 (1H, s, CH), 6.87 (2H, d,

J=9.0 Hz, ArH), 7.20–7.40 (10H, m, ArH), 8.01 (2H, d, J=9.0 Hz, ArH).

2-Phenyl-2-(4′-methoxyphenyl)-4′-methoxyacetophenone 3g. Low mp solid; ν_{max} (KBr)/cm^{-1} 3050, 3015, 2950, 2950, 2860, 1690, 1610, 1510, 1470, 1260, 1215, 1170, 1030, 830, 780, 695, δ_H (CCl_4) 3.58 (6H, s, 2×OCH_3), 5.87 (1H, s, CH), 6.80 (4H, d, J=9.0, ArH), 7.20–7.40 (10H, m, ArH), 8.01 (2H, d, J=9.0, ArH); m/z 332 (M^+, 2%), 197 (31), 165 (5), 153 (9), 135 (100), 107 (4), 92 (5), 77 (10). Anal. for $C_{22}H_{20}O_3$: Calcd (Found) C, 79.50 (79.81), H, 6.06 (6.18)%.

2-Phenyl-2-(4′-chlorophenyl)acetophenone 3h. Mp 105–106°C; ν_{max} (KBr)/cm^{-1} 1690, 1640, 1605, 1590, 1500, 1455, 1220, 1090, 1020, 790, 740, 710, 690; δ_H ($CDCl_3$) 6.15 (1H, s, CH), 7.30–7.70 (12H, m, ArH), 7.98–8.20 (2H, m, ArH); m/z 306 (M^+, 1%), 201 (9), 166 (10), 165 (18), 105 (100), 77 (20); Anal. for $C_{20}H_{15}ClO$: Calcd (Found) C, 78.30 (78.52); H, 4.92 (5.20)%.

General procedure for the low-valent titanium promoted preparation of pyrroles 7

To low-valent titanium (prepared from 2 mmol $TiCl_4$ and 2 mmol powdered samarium) in dry THF (20 mL) was added to a solution of dibenzoylmethane **5** (1 mmol) and nitrile **6** (1.5 mmol) in anhydrous THF (3 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was then stirred under reflux for about 2 days. After the reaction was completed, as monitored by TLC, the reaction was quenched with 10% K_2CO_3 (10 mL). The mixture was extracted with dichloromethane (3×30 mL) and the combined extracts were washed with saturated solution of NaCl (15 mL), and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative thin layer chromatography on silica gel using diethyl ether–petroleum (1:6) as the eluent.

2,3,5-Triphenylpyrrole 7a. 7a (154 mg) was obtained from dibenzoylmethane (230 mg) and benzonitrile (155 mg) in 51% yield. mp 139–140°C (lit.[16] 142°C). ν_{max} (KBr)/cm^{-1} 3460, 1610, 1510, 1495, 1455, 1265, 1180, 1070, 955, 760, 690. δ_H ($CDCl_3$) 6.50 (1H, s, CH), 7.05–7.75 (15H, m, ArH), 8.20 (1H, s NH).

3,5-Diphenyl-2-(*p*-methylphenyl)pyrrole 7b. 7b (132 mg) was obtained from dibenzoylmethane (230 mg) and 4-methylbenzonitrile (176 mg) in 42% yield mp 104–105°C, ν_{max} (KBr)/cm^{-1} 3420, 1600, 1480, 1450, 1260, 1070, 810, 790, 760, 700. δ_H ($CDCl_3$) 2.30 (3H, s, CH_3), 6.65 (1H, s, CH), 7.05–7.70 (14H, m, ArH), 8.30 (1H, s, NH); m/z 309 (M^+, 100%), 191 (11), 146 (7), 105 (8); Anal. for $C_{23}H_{19}N$: Calcd (Found) C, 89.28 (88.95); H, 6.10 (6.10); N, 4.53 (4.62)%.

General procedure for the low-valent titanium promoted preparation of α-amino alcohols 9 and 10

To low-valent titanium (prepared from 2 mmol $TiCl_4$ and 2 mmol powdered samarium) in dry THF (20 mL) was added a solution of ketonitrile **8** (1 mmol) in anhydrous THF (3 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was then stirred at −20°C according to the reaction time in Table 2 and quenched with dilute hydrochloric acid (5% HCl, 2 mL). The mixture was extracted with diethyl ether (3×30 mL) and the combined extracts were washed with saturated aqueous NaCl (15 mL), and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative thin layer chromatography on silica gel using ethyl acetate–cyclohexane (1:2) as the eluent.

***cis*-2-Amino-3-cyano-1,4-diphenyl-2-cyclopentene-1-ol (9a). 9a** (83 mg) was obtained from ketonitrile **8a** (275 mg) as a white solid in 30% yield. Mp 168–170°C, ν_{max} (KBr)/cm^{-1} 3440, 3320, 2200, 1670, 1610, 1500. δ_H ($CDCl_3$) 2.10 (1H, dd, J=13.2, 7.5 Hz, H-5), 2.18 (1H, br s, OH), 2.80 (1H, dd, J=13.2, 7.1 Hz, H-5), 3.92 (1H, dd, J=7.5, 7.1 Hz, H-4), 4.65 (2H, br s, NH_2), 7.23–7.42 (10H, m, ArH); m/z 276 (M^+, 34%), 258 ($M-H_2O$, 100), 257 (25), 171 (9), 155 (20), 154 (23), 105 (69), 77 (75). Anal. for $C_{18}H_{16}N_2O$: Calcd (Found) C, 78.24 (78.50); H, 5.83 (5.60); N, 10.14 (9.97)%.

***trans*-2-Amino-3-cyano-1,4-diphenyl-2-cyclopenten-1-ol (10a). 10a** (119 mg) was obtained from ketonitrile **8a** (275 mg) as a white solid in 43% yield. Mp 164–165°C, ν_{max} (KBr)/cm^{-1} 3480, 3360, 2200, 1660, 1610, 1500. δ_H ($CDCl_3$) 2.18 (1H, dd, J=14.2, 7.5 Hz, H-5), 2.25(1H, br s, OH), 2.72 (1H, dd, J=14.2, 7.3 Hz, H-5), 4.31 (1H, dd, J=7.5 Hz, H-4), 4.41(2H, br s, NH_2) 7.26–7.50 (10H, m, ArH); m/z 276 (M^+, 59%), 258 ($M-H_2O$, 100), 181 (24), 171 (10), 155 (22), 154 (23), 105 (66), 77 (67). Anal. for $C_{18}H_{16}N_2O$: Calcd (Found) C, 78.24 (78.47); H, 5.83 (5.57); N, 10.14 (9.88)%.

***cis*-2-Amino-3-cyano-1-(*p*-methylphenyl)-4-(*p*-chlorophenyl)-2-cyclopenten-1-ol (9b). 9b** (110 mg) was obtained from ketonitrile **8b** (320 mg) as a white solid in 34% yield. Mp 187–189°C. ν_{max} (KBr)/cm^{-1} 3470, 3420, 3365, 2180, 1675, 1615, 1500. δ_H ($CDCl_3$) 2.04 (1H, dd, J=13.0, 7.5 Hz, H-5), 2.37 (3H, s, CH_3), 2.67 (1H, br s, OH), 2.77 (1H, dd, J=13.0, 7.1 Hz, H-5), 3.86 (1H, dd, J=7.5, 7.1 Hz, H-4), 4.58 (2H, br s, NH_2), 7.14–7.40 (8H, m, ArH); 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. for $C_{19}H_{17}ClN_2O$: Calcd (Found) C, 70.26 (70.50); H, 5.27 (5.47); N, 8.62 (8.36)%.

***trans*-2-Amino-3-cyano-1-(*p*-methylphenyl)-4-(*p*-chlorophenyl)-2-cyclopenten-1-ol (10b). 10b** (145 mg) was obtained from ketonitrile **8b** (320 mg) as a white solid in 45% yield. Mp 170–172°C. ν_{max} (KBr)/cm^{-1} 3490, 3390, 3250, 2190, 1660, 1605, 1500. δ_H ($CDCl_3$) 2.08 (1H, dd, J=14.2, 7.4 Hz, H-5), 2.34 (3H, s, CH_3), 2.66 (1H, dd, J=14.2, 7.3 Hz, H-5), 2.75 (1H, br s, OH), 4.21 (1H, dd, J=7.4, 7.3 Hz, H-4), 4.51 (2H, br s, NH_2), 7.11–7.38 (8H, m, ArH); 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. for $C_{19}H_{17}ClN_2O$: Calcd (Found) C, 70.26 (70.04); H, 5.27 (5.13); N, 8.62 (8.81)%.

***cis*-2-Amino-3-cyano-1-phenyl-4-(*p*-chlorophenyl)-2-cyclopenten-1-ol (9c). 9c** (90 mg) was obtained from keto nitrile **8c** (310 mg) as a white solid in 29% yield. Mp 178–180°C. ν_{max} (KBr)/cm^{-1} 3490, 3420, 3360, 2180, 1680, 1625, 1500. δ_H ($CDCl_3$) 2.06 (1H, dd, J=13.0, 7.5 Hz, H-5), 2.15 (1H, br s, OH), 2.78 (1H, dd, J=13.0, 7.0 Hz, H-5), 3.88 (1H, dd, J=7.5, 7.0, H-4), 4.70 (2H, br s, NH_2), 7.25–7.50 (9H, m, ArH); 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. for $C_{18}H_{15}ClN_2O$: Calcd (Found) C, 69.57 (69.82); H, 4.87 (4.99); N, 9.01 (8.87)%.

Crystallographic data for **9c**: $C_{18}H_{15}ClN_2O$ (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 Mo-K_α radiation (λ=0.71069 Å, μ=0.242 mm^{-1}) at 293 K. 3028 reflections were measured, of which 2953 were independent reflections with 2θ in the range of 6 to 50°, 1071 reflections having $I>2\sigma$ (I). The structure was solved by direct methods[17] and expanded using Fourier techniques.[18] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares 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.[19]

***trans*-2-Amino-3-cyano-1-phenyl-4-(*p*-chlorophenyl)-2-cyclopenten-1-ol (10c). 10c** (158 mg) was obtained from ketonitrile **8c** (310 mg) as a white solid in 51% yield. Mp 191–193°C. ν_{max} (KBr)/cm^{-1} 3500, 3390, 2200, 1660, 1605, 1500. δ_H ($CDCl_3$) 2.13 (1H, dd, J=14.1, 7.5 Hz, H-5), 2.21 (1H, br s, OH), 2.71 (1H, dd, J=14.1, 7.3 Hz, H-5), 4.28 (1H, dd, J=7.5, 7.0 Hz, H-4), 4.36 (2H, br s, NH_2), 7.13–7.41 (9H, m, ArH); 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. for $C_{18}H_{15}ClN_2O$: Calcd (Found) C, 69.57 (69.75); H, 4.87 (4.65); N, 9.01 (9.17)%.

Crystallographic data for **10c**: $C_{18}H_{15}ClN_2O$ (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 Mo-K_α radiation (λ=0.71069 Å, μ=0.236 mm^{-1}) at 293 K. 3278 reflections were measured with 2θ in the range of 6 to 50°, 1551 reflections having $I>2\sigma$ (I). The structure was solved by direct methods[17] and expanded using Fourier tecnhiques.[18] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares 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.

***cis*-2-Amino-3-cyano-1-phenyl-4-(3,4-methylenedioxyphenyl)-2-cyclopenten-1-ol (9d). 9d** (97 mg) was obtained from ketonitrile **8d** (320 mg) as a pale yellow crystal in 30% yield. Mp 164–166°C. ν_{max} (KBr)/cm^{-1} 3470, 3390, 3250, 2200, 1660, 1610, 1510, 1455. δ_H ($CDCl_3$) 2.05 (1H, dd, J=13.0, 7.5 Hz, H-5), 2.14(1H, br s, OH), 2.78 (1H, dd, J=13.0, 7.0 Hz, H-5), 3.85 (1H, dd, J=7.5, 7.0 Hz, H-4), 4.68 (2H, br s, NH_2), 5.94 (2H, s, OCH_2O), 6.72–6.78 (3H, m, ArH), 7.35–7.61 (5H, m, ArH); m/z 320 (M^+, 100%), 302 (M−H_2O, 47), 105 (33), 77 (23). Anal. for $C_{19}H_{16}N_2O_3$: Calcd (Found) C, 71.24 (71.51); H, 5.04 (5.16), N, 8.74 (8.61)%.

***trans*-2-Amino-3-cyano-1-phenyl-4-(3,4-methylenedioxyphenyl)-2-cyclopenten-1-ol (10d). 10d** (140 mg) was obtained from ketonitrile **8d** (320 mg) as a pale yellow crystal in 43% yield. Mp 162–164°C, ν_{max} (KBr)/cm^{-1} 3500, 3370, 3260, 2200, 1660, 1610, 1490, 1450. δ_H ($CDCl_3$) 2.06 (1H, br s, OH), 2.13 (1H, dd, J=14.2, 7.5 Hz, H-5), 2.68 (1H, dd, J=14.2, 7.3 Hz, H-5), 4.23 (1H, dd, J=7.5, 7.3 Hz, H-4), 4.41 (2H, br s, NH_2), 5.94 (2H, s, OCH_2O), 6.75 (3H, s, ArH), 7.30–7.50 (5H, m, ArH); m/z 320 (M^+, 100%), 302 (M−H_2O, 38), 105 (28), 77 (16). Anal. for $C_{19}H_{16}N_2O_3$: Calcd (Found) C, 71.24 (71.61); H, 5.04 (5.35); N, 8.74 (8.61)%.

***cis*-2-Amino-3-cyano-1-phenyl-4-(*o*-chlorophenyl)-2-cyclopenten-1-ol (9e). 9e** (81 mg) was obtained from ketonitrile **8e** (310 mg) as a white solid in 26% yield. Mp 171–172°C. ν_{max} (KBr)/cm^{-1} 3430, 3370, 3250, 2180, 1675, 1605, 1455, δ_H ($CDCl_3$) 1.99 (1H, dd, J=13.5, 6.4 Hz, H-5), 2.08 (1H, br s, OH), 2.92 (1H, dd, J=13.5, 7.6 Hz, H-5), 4.43 (1H, dd, J=7.6, 6.4, H-4), 4.66 (2H, br s, NH_2), 7.19–7.49 (9H, m, ArH); 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. for $C_{18}H_{15}ClN_2O$: Calcd (Found) C, 69.57 (69.83); H, 4.87 (4.65); N, 9.01 (9.18)%.

***trans*-2-Amino-3-cyano-1-phenyl-4-(*o*-chlorophenyl)-2-cyclopenten-1-ol (10e). 10e** (124 mg) was obtained from ketonitrile **8e** (310 mg) as a white solid in 40% yield. Mp 183–185°C. ν_{max} (KBr)/cm^{-1} 3460, 3370, 3250, 2190, 1660, 1460. δ_H ($CDCl_3$) 2.05 (1H, dd, J=14.3, 6.8 Hz, H-5), 2.75 (1H, br s, OH), 2.86 (1H, dd, J=14.3, 7.7 Hz, H-5), 4.57 (2H, br s, NH_2), 4.75 (1H, dd, J=7.7, 6.8 Hz, H-4), 7.15–7.36 (9H, m, ArH); 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. for $C_{18}H_{15}ClN_2O$: Calcd (Found) C, 69.57 (69.79); N, 9.01 (9.25)%.

***trans*-2-Amino-3-cyano-1-phenyl-4-(*p*-methylphenyl)-2-cyclopenten-1-ol (10f). 10f** (207 mg) was obtained from ketonitrile **8g** (290 mg) as a white solid in 71% yield. Mp 166–168°C. ν_{max} (KBr)/cm^{-1} 3450, 3370, 3260, 2190, 1670, 1620, 1520. δ_H ($CDCl_3$) 2.17 (1H, dd, J=14.3, 7.4 Hz, H-5), 2.32 (3H, s, CH_3), 2.67 (1H, dd, J=14.3, 7.3 Hz, H-5), 2.85 (1H, br s, OH), 4.26 (1H, dd, J=7.4, 7.3 Hz, H-4), 4.41 (2H, br s, NH_2), 7.12–7.49 (9H, m, ArH); 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. for $C_{19}H_{18}N_2O$: Calcd (Found) C, 78.60 (78.31); H, 6.25 (5.96); N, 9.65 (9.60)%.

General procedure for the low-valent titanium promoted preparation of amines 11

To low-valent titanium (prepared from 2 mmol $TiCl_4$ and 2 mmol samarium powder) in dry THF (20 mL) was added a solution of ketonitrile **8** (1 mmol) in anhydrous THF (3 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was then reacted at 60°C according to the reaction time in Table 2 and quenched with dilute hydrochloric acid (5% HCl, 2 mL). After usual work-up, the crude product was purified by preparative thin layer chromatography on silica gel using ethyl acetate–cyclohexane (1:3) as the eluent.

1-Amino-2-cyano-3,5-diphenylcyclopentene 11a. 11a (201 mg) was obtained from ketonitrile **8a** (275 mg) as colorless crystals in 77% yield, mp 185–186°C; ν_{max} (KBr)/cm^{-1} 3490, 3360, 3280, 2200, 1660, 1610, 1500, 1460, 1400, 1070, 750, 695; δ_H ($CDCl_3$) 1.78–2.39 (1H, m, H-4), 2.43–2.88 (1H, m, H-4), 3.88–4.24 (2H, m, H-3, H-5), 4.41 (2H, br s, NH_2), 7.19–7.41 (10H, m, ArH); *m/z* 261 (M+1, 24%), 260 (M^+, 83), 259 (M−1, 100), 183 (36), 91 (9), 77 (12); Anal. for $C_{18}H_{16}N_2$: Calcd (Found) C, 83.04 (83.25); H, 6.19 (6.24); N, 10.76 (10.45)%.

1-Amino-2-cyano-3-(*p*-chlorophenyl)-5-(*p*-methylphenyl) cyclopentene 11b. 11b (230 mg) was obtained from ketonitrile **8b** (320 mg) as colorless crystals in 74% yield, mp 145–147°C; ν_{max} (KBr)/cm^{-1}; 3480, 3320, 2190, 1655, 1600, 1515, 1495, 1085, 810; δ_H ($CDCl_3$) 1.69–2.30 (1H, m, H-4), 2.36 (3H, s, CH_3), 2.34–2.88 (1H, m, H-4), 3.84–4.18 (2H, m, H-3, H-5), 4.43 (2H, br s, NH_2), 7.06–7.74 (8H, m, ArH); *m/z* 310 (5.6%), 308 (M^+, 32), 306 (46), 272 (100), 215 (10) 197 (26), 181 (18); Anal. for $C_{19}H_{17}N_2Cl$: Calcd (Found) C, 73.90 (74.06); H, 5.55 (5.78); N, 9.07 (9.23)%.

1-Amino-2-cyano-3-(*p*-chlorophenyl)-5-phenylcyclopentene 11c. 11c (210 mg) was obtained from ketonitrile **8c** (209 mg) as colorless crystals in 74% yield, mp 157–159°C; ν_{max} (KBr)/cm^{-1}; 3490, 3360, 2220, 1660, 1615, 1500, 1460, 755, 695; δ_H ($CDCl_3$) 1.73–2.25 (1H, m, H-4), 2.39–2.88 (1H, m, H-4), 3.88–4.20 (2H, m, H-3, H-5), 4.43 (2H, br s, NH_2), 7.14–7.40 (9H, m, ArH); *m/z* 296 (12%), 294 (50), 293 (44), 292 (49), 259 (100) 183 (31); Anal. for $C_{18}H_{15}N_2Cl$: Calcd (Found) C, 73.34 (73.21); H, 5.13 (5.02); N, 9.50 (9.62)%.

1-Amino-2-cyano-3-(3,4-methylenedioxyphenyl) cyclopentene 11d. 11d (221 mg) was obtained from ketonitrile **8d** (320 mg) as colorless crystals in 72% yield, mp 198–200°C; ν_{max} (KBr)/cm^{-1}; 3470, 3315, 2200, 1655, 1600, 1490, 1240, 1030, 920, 810, 775, 695; δ_H ($CDCl_3$) 1.72–2.32 (1H, m, H-4), 2.35–2.83 (1H, m, H-4), 3.86–4.15 (2H, m, H-3, H-5), 1.41 (2H, br s, NH_2), 5.93 (2H, s, OCH_2O), 6.62–6.82 (3H, m, ArH), 7.16–7.40 (5H, m, ArH); *m/z* 304 (M^+, 31%), 303 (100), 273 (25), 245 (13) 183 (34); Anal. for $C_{19}H_{16}N_2O_2$: Calcd (Found) C, 74.98 (74.83); H, 5.30 (5.41); N, 9.20 (9.31)%.

1-Amino-2-cyano-3-(*o*-chlorophenyl)-5-phenylcyclopentene 11e. 11e (237 mg) was obtained from ketonitrile **8e** (311 mg) as colorless crystals in 81% yield, mp 169–171°C; ν_{max} (KBr)/cm^{-1}; 3470, 3350, 3280, 3240, 2190, 1655, 1605, 1450, 1400, 1340, 1035, 745, 715, 695; δ_H ($CDCl_3$) 1.60–2.32 (1H, m, H-4), 2.48–3.08 (1H, m, H-4), 3.87–4.00 (1H, m, H-3), 4.50 (2H, br s, NH_2), 4.58–4.68 (1H, H-5), 7.15–7.50 (9H, m, ArH); *m/z* 296 (22%), 295 (45), 294 (M^+,79), 293 (100), 292 (52), 259 (20), 258 (88), 183 (70), 155 (13), 91 (15), 77 (15); Anal. for $C_{18}H_{15}N_2Cl$: Calcd (Found) C, 73.34 (73.55); H, 5.13 (5.26); N, 9.50 (9.41)%.

1-Amino-2-cyano-3-(*p*-methylphenyl)-5-phenyl-1-cyclopentene 11f. 11f (205 mg) was obtained from ketonitrile **8f** (280 mg) as colorless crystals in 77% yield, mp 190–192°C; ν_{max} (KBr)/cm^{-1}; 3500, 3360, 3280, 2195, 1665, 1610, 1460, 815, 760, 705; δ_H ($CDCl_3$) 1.77–2.34 (1H, m, H-4), 2.35 (3H, s, CH_3), 2.38–2.84 (1H, m, H-4), 3.87–4.18 (2H, m, H-3, H-5), 4.38 (2H, br s NH_2), 7.15–7.40 (9H, m, ArH); *m/z* 274 (M^+, 49%), 273 (M−1, 59), 259 (100), 195 (13), 183 (52), 182 (27), 181 (43), 168 (23), 154 (21), 140 (19), 128 (26), 105 (20), 91 (42), 77 (42); Anal. for $C_{19}H_{18}N_2$: Calcd (Found) C, 83.18 (83.01); H, 6.61 (6.69); N, 10.21 (10.30)%.

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