Reductive Cyclodimerization of α,β-Unsaturated Ketones Promoted by $AlCl_3$/Sm System: A Facile Synthesis of 2-Aroyl-1,3,4-triaryl Cyclopentanol Derivatives

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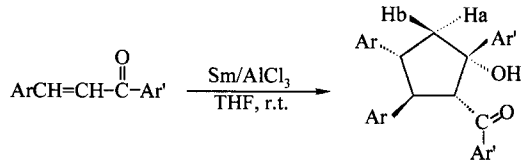
Promoted by $AlCl_3$/Sm bimetallic system, α,β-unsaturated ketones underwent reductive cyclodimerization to afford cyclopentanol derivatives under mild conditions. The reaction is stereocontrolled and regioselective over the competitive carbon-carbon double bond reduction.

Keywords Aluminum trichloride, metal samarium, α,β-unsaturated ketones, reductive cyclodimerization, cyclopentanol derivatives

Carbon-carbon bond formation is the essence of organic synthesis and the reductive dimerization of carbonyl derivatives by active metals is one of the most valuable methods for establishing carbon-carbon bonds. In general, the carbonyl derivatives are aldehydes, ketones, carboxylic esters, or acid chlorides. Recently, some reports on the reductive cyclodimerization of α,β-unsaturated carbonyl derivatives have also been reported, providing a novel access to functionalized five-membered ring products.[1]

The chemistry of aluminum has acquired renewed interest[2] and in recent years the versatility of aluminum chloride has been in rapid evolution. For examples, Dutta[3] has reported an efficient deoxygenation reaction of nitrones and heteroarenes *N*-oxides induced by Zn-$AlCl_3 \cdot 6H_2O$ bimetallic system. Similarly, this system has been used in the reductive cleavage of 2,1-benzisoxazole to give *ortho*-amino and *N*-alkylaminobenzophenones.[4] Most recently, a novel method for the reductive coupling of carbonyl compounds to olefins promoted by $AlCl_3$-Zn-CH_3CN system has also been reported.[5] Herein we wish to report our preliminary results on a novel utility of $AlCl_3$ with metal samarium as an efficient reagent for the reductive cyclodimerization of α,β-unsaturated ketones to give cyclopentanol derivatives (Scheme 1).

Scheme 1



1 2

As shown in Scheme 1, when α,β-unsaturated ketones **1** were treated with $AlCl_3$/Sm bimetallic system in anhydrous tetrahydrofuran, 2-aroyl-1, 3, 4-triaryl cyclopentanol derivatives **2** were obtained. The reductive cyclodimerization process was completed in two hours at room temperature to afford **2** in moderate to good yields with excellent regio- and stereo-selectivity. The relative stereochemistry of **2** was confirmed by the X-ray crystal structure of **2b**, which clearly illustrates the 1,2-*cis*-2, 3-*trans*-3, 4-*trans* relations.[6] Table 1 summarized the results on the reaction of a number of substrates. The

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Received January 12, 2001; revised March 2, 2001; accepted March 8, 2001.

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

chloro, bromo, alkoxyl groups of the substrates could not be reduced under the reaction conditions. In addition, it should be noted that no reaction took place with either metal samarium or aluminum trichloride alone (Table 1, Entry **2a**).

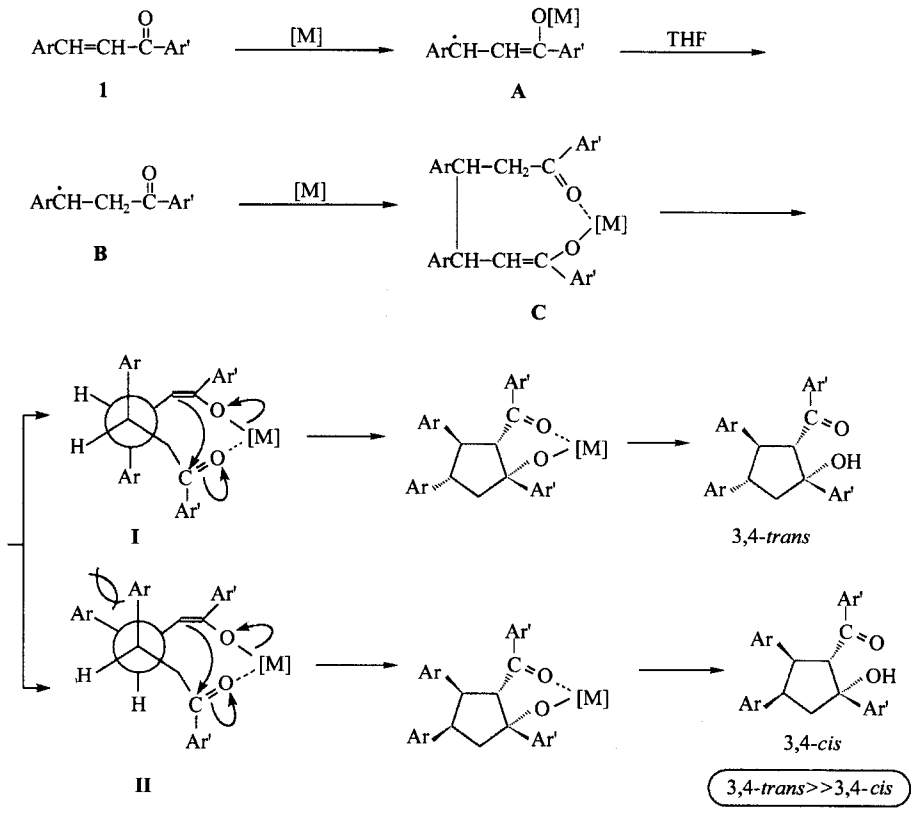
Although the detailed mechanism of the above reaction has not been clarified yet, it is proposed that the reaction may proceed *via* a single-electron transfer (SET) process (Scheme 2), with the Al(0),[5] which is generated *in situ* from the reaction of metal samarium and aluminum chloride, supplying the electrons to organic substrate **1** to generate the radical enolate **A**. The radical anion **A** then abstracts a proton from solvent (THF) to form a radical **B**. Promoted by Al(0), the radical **B** dimerizes with the substrate **1** to give a dimer enolate **C**, which undergoes ring closure through intramolecular attack of carbonion on the carbonyl group to form the final cyclopentanol derivative.

Table 1 Reaction of α,β-unsaturated ketones with $AlCl_3$/Sm system

Entry	Ar	Ar′	Yield (%)[a]
2a	C_6H_5	C_6H_5	81, 0[b]
2b	2-ClC_6H_4	C_6H_5	84
2c	4-ClC_6H_4	C_6H_5	79
2d	4-$CH_3C_6H_4$	C_6H_5	78
2e	3,4-$OCH_2OC_6H_3$	C_6H_5	72
2f	3-BrC_6H_4	C_6H_5	82
2g	C_6H_5	4-$CH_3C_6H_4$	77
2h	3,4-$OCH_2OC_6H_3$	4-$CH_3C_6H_4$	72

[a] Isolated yield of cyclopentanol derivatives. [b] In the presence of Sm powder or $AlCl_3$ alone.

Scheme 2



Based on the mechanism depicted in Scheme 2, the observed selectivity of the reaction can be explained by the existence of two different conformations for the dimer enolate **C**. Form **I**, which is a non-eclipsed conformation, may be favored since the steric interactions are minimized (the two aryl groups being in *anti*-positions) and when the cycle is generated, the 3,4-*trans* conformation product is obtained. However, the eclipsed conformation **II**, a less favored one since the steric interactions are maximized (the two aryl groups being in *syn*-

positions), forms the 3,4-*cis* configuration product with much more difficulty. In fact, no 3,4-*cis* product has been obtained in our experiments.

There appear to be only a few reports on the metal-promoted cyclodimerization of α,β-unsaturated ketones. For instance, the Yb-THF-HMPA,[8] $NdCl_3$-lithium naphthalide,[9] tributyltin hydride[10] and SmI_2-THF-HMPA,[7] as well as some electro-assisted systems[11] have been used. As shown in Table 1, compared with the above methods, $AlCl_3$/Sm bimetallic system induced the intermolecular cyclo-reductive coupling of α,β-unsaturated ketones to give cyclopentanol derivatives in higher yields and shorter time without using HMPA, a toxic and expensive reagent, as a co-solvent.

In conclusion, we have provided a new route to cyclopentanol derivatives, the advantages are high yielding, simple and mild reaction conditions, and high chemo- and stereo-selectivity. Further studies to develop other new uses of $AlCl_3$ and Sm bimetallic system are now in progress in our laboratory.

Experimental

General

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points were obtained on an electrothermal melting point apparatus and were uncorrected. Infrared spectra were recorded on a Shimadzu IR-408 spectrometer using KBr pellets with maximum absorption indicated in cm^{-1}. ^1H NMR spectra were recorded on a Bruker AC-400 (400 MHz) spectrometer using $CDCl_3$ solutions. J values are in Hz. Chemical shifts are expressed in δ downfield from internal tetramethylsilane. Mass spectra were recorded on a HP 5989B MS spectrometer. Elemental analyses were carried out on a Carlo Erba EA 1110 instrument.

General procedure for the reductive cyclodimerization of α,β-unsaturated ketones

A dry 100 mL flask was charged with powdered Sm (0.3 g, 2 mmol), $AlCl_3$ (0.2 g, 1.5 mmol) and THF (20 mL). The mixture was refluxed for 2 h under nitrogen atmosphere, then cooled to room temperature. A black slurry was formed. Then a solution of α,β-unsaturated ketone (1 mmol) in THF was added dropwise to the reaction mixture in five minutes. After being stirred for 2 h, 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_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:6) as eluent. All the cyclopentanol products have physical data (m.p.) and spectral characteristics (IR, MS and ^1H NMR) in agreement with the literature data.[6]

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1,3,4-*triphenylcyclopentanol* (**2a**) Colorless crystal, m.p. 191—192℃ (Lit.[6] 192—194℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.60 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 2.99 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 3.78 (ddd, J = 10.7, 10.2, 6.1 Hz, 1H, C_4-H), 4.12 (dd, J = 11.7, 10.2 Hz, 1H, C_3-H), 4.60 (d, J = 11.7 Hz, 1H, C_2-H), 5.24 (s, 1H, OH), 7.02—7.58 (m, 20H, ArH); IR (KBr) ν: 3440 (OH), 1645 (C=O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1-*phenyl*-3,4-*di*(2-*chlorophenyl*)*cyclopentanol* (**2b**) Colorless crystal, m.p. 191—192℃ (Lit.[6] 192—193℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.37 (dd, J = 14.4, 5.1 Hz, 1H, C_5-H_a), 3.11 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 4.68—4.82 (m, 3H, C_4-H, C_3-H, C_2-H), 5.61 (s, 1H, OH), 7.01—8.16 (m, 18H, ArH); IR (KBr) ν: 3445 (OH), 1645 (C=O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1-*phenyl*-3,4-*di*(4-*chlorophenyl*)*cyclopentanol* (**2c**) Colorless crystal, m.p. 191—192℃ (Lit.[6] 192—194℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.54 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 3.00 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 3.71 (ddd, J = 10.7, 10.1, 6.1 Hz, 1H, C_4-H), 4.06 (dd, J = 11.7, 10.1 Hz, 1H, C_3-H), 4.53 (d, J = 11.7 Hz, 1H, C_2-H), 5.08 (s, 1H, OH), 6.93—7.77 (m, 18H, ArH); IR (KBr) ν: 3445 (OH), 1640 (C=O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1-*phenyl*-3,4-*di*(4-*methylphenyl*)*cyclopentanol* (**2d**) Colorless crystal, m.p. 187—188℃ (Lit.[6] 188—190℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.16 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.54 (dd, J = 14.4, 6.3 Hz,

1H, C_5-H_a), 3.00 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 3.71 (ddd, J = 10.7, 10.2, 6.6 Hz, 1H, C_4-H), 4.13 (dd, J = 11.7, 10.2 Hz, 1H, C_3-H), 4.52 (d, J = 11.7 Hz, 1H, C_2-H), 5.22 (s, 1H, OH), 6.89—7.66 (m, 18H, ArH); IR (KBr) ν: 3440 (OH), 1640 (C = O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1-*phenyl*-3,4-*di*(3,4-*methylenedioxylphenyl*) *cyclopentanol* (**2e**)

Colorless crystal, m.p. 181—183℃ (Lit.[6] 183—184℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.56 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 3.01 (dd, J = 14.4, 10.6 Hz, 1H, C_5-H_b), 3.73 (ddd, J = 10.6, 10.0, 6.1 Hz, 1H, C_4-H), 4.07 (dd, J = 11.6, 10.1 Hz, 1H, C_3-H), 4.45 (d, J = 11.5 Hz, 1H, C_2-H), 5.24 (s, 1H, OH), 5.76 (s, 2H, OCH_2O), 5.90 (s, 2H, OCH_2O), 6.61—7.63 (m, 16H, ArH); IR (KBr) ν: 3460 (OH), 1645 (C = O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-*Benzoyl*-1-*phenyl*-3,4-*di*(3-*bromophenyl*) *cyclopentanol* (**2f**) Colorless crystal, m.p. 170—172℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.57 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 2.98 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 3.70 (ddd, J = 10.7, 10.1, 6.1 Hz, 1H, C_4-H), 4.03 (dd, J = 11.7, 10.2 Hz, 1H, C_3-H), 4.58 (d, J = 11.7 Hz, 1H, C_2-H), 5.19 (s, 1H, OH), 7.16—7.74 (m, 18H, ArH); IR (KBr) ν: 3445 (OH), 1650 (C = O) cm^{-1}; MS (70 eV) m/z (%): 574 (M^+, 0.4), 456(5), 287(10), 289(9), 105 (100), 77(27); Anal. Calcd. for $C_{30}H_{24}Br_2O_2$: C 62.50; H 4.15; Found: C 62.31, H 4.03.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-(4-*Methylbenzoyl*)-1-(4-*methylphenyl*)-3,4-*diphenylcyclopentanol* (**2g**) Colorless crystal, m. p. 168—170℃ (Lit.[6] 170—171.5℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.27 (s, 3H, CH_3), 2,28 (s, 3H, CH_3), 2.60 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 2.95 (dd, J = 14.4, 10.6 Hz, 1H, C_5-H_b), 3.78 (ddd, J = 10.6, 9.5, 6.1 Hz, 1H, C_4-H), 4.09 (dd, J = 11.6, 9.6 Hz, 1H, C_3-H), 4.52 (d, J = 11.6 Hz, 1H, C_2-H), 5.25 (s, 1H, OH), 6.92—7.80 (m, 18H, ArH); IR (KBr) ν: 3450 (OH), 1640 (C = O) cm^{-1}.

1,2-*cis*-2,3-*trans*-3,4-*trans*-2-(4-*Methylbenzoyl*)-1-(4-*methylphenyl*)-3,4-*di*(3,4-*methylenedioxyphenyl*) *cyclopentanol* (**2h**) Colorless crystal, m.p. 170—171℃ (Lit.[6] 171—172℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.25 (s, 3H, CH_3), 2.46 (dd, J = 14.4, 6.1 Hz, 1H, C_5-H_a), 3.02 (dd, J = 14.4, 10.7 Hz, 1H, C_5-H_b), 3.68 (ddd, J = 10.7, 10.1, 6.1 Hz, 1H, C_4-H), 4.00 (dd, J = 11.7, 10.1 Hz, 1H, C_3-H), 4.42 (d, J = 11.7 Hz, 1H, C_2-H), 5.22 (s, 1H, OH), 5.80 (s, 2H, OCH_2O), 5.83 (s, 2H, OCH_2O), 6.58—7.56 (m, 14H, ArH); IR (KBr) ν: 3440 (OH), 1640 (C = O) cm^{-1}.

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(E0101122 SONG, J.P.; LING, J.)