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# Novel synthesis of pinacols and sulfones promoted by Sm–$NiCl_2$ bimetallic system

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**Sm–$NiCl_2$ as a reductive system promoted reductive coupling of aryl adehydes and aryl ketone into pinacols in good yields and also promoted coupling reaction of aryl sulfonyl chlorides and active halides into sulfones in good yields. Copyright © 2011 John Wiley & Sons, Ltd.**

**Keywords:** Sm-$NiCl_2$; reductive coupling; pinacols; sulfones; bimetallic system

## Introduction

Pinacols are useful synthons in organic synthesis. Recently, novel calixarene hemisphere were synthesized via pinacol rearrangement of [2.1.2.1]metacyclophane.[1] Pinacol rearrangement generated the pinacolone products.[2] Pinacol–pinacolone rearrangement of various pinacols was efficiently performed using $ZnCl_2$ supported on silica.[3] (+)-Austrodoral and (+)-austrodoric acid were synthesized via diastereoselective routes toward the austrodorane skeleton based on pinacol rearrangement.[4] Isoxazole-directed pinacol rearrangement was a stereocontrolled approach to angular stereogenic centers.[5] Asymmetric addition of cycloalkenyl boronic pinacol esters to aldehyde with *ortho*-cycloalkyl substituted diol as a chiral ligand fabricated chiral alcohol.[6] The (*R*,*R*)-diol diphosphane worked more efficiently in the rhodium-catalyzed asymmetric hydrogenation of $\alpha$-acetamidocinnamic acid.[7] $SmI_2$-mediated pinacol macrocyclization was the key step for the synthesis of the polyfused medium-sized CDE ring system of lancifodilactone G.[8] The prins–pinacol annulation method was applied in the synthesis of oxaspirobicycles which exist in many natural products.[9] Pinacol coupling, which was described in 1859, is still a versatile method to construct carbon–carbon bonds.[10–25]

Sulfones are also useful synthons in organic synthesis.[26] Vinyl sulfone-modified pyranoses and furanoses were unlimited and versatile source of chiral building blocks.[27] Both allylic sulfones and the disulfone intermediates were the key synthons for carotenoid synthesis.[28,29] C15–C25 fragment of sulfone was the key synthon for total synthesis of (+)-lasonolide.[30] Asymmetric Aza–Michael addition of chiral hydrazines to alkenyl sulfones followed by N–N bond cleavage and *N* protection and then $\alpha$-alkylation generated $\alpha$-alkylated $\beta$-amino sulfones.[31] Solid-phase supported sulfones as traceless linkers were efficient tools to synthesize target molecules or natural products.[32] Yao developed a novel strategy for solid-phase synthesis of a small-molecule library based on the vinyl sulfone scaffolds.[33]

The classic method to synthesis of sulfone is oxidation of thioether or sulfoxide.[34] Other main methods include nucleophilic substitution of sulfinate with haloalkane,[35] Friedel–Crafts reaction of sulfonyl chloride with benzene,[36] rearrangement of sulfinate[37] and radical addition of sulfonyl chloride to unsaturated hydrocarbon compounds.[38] Suzuki[39] and Huang[40] reported tellurium anion promoted coupling reaction of arylsulfonyl chloride and haloalkane. Fry reported synthesis of sulfones with alkylmagnesium and alkylcopper reagents.[41] Recently, Huang reported solid-phase synthesis of $\beta$-keto sulfones.[42]

Samarium metal is very active in organic synthesis. Recently Zhang reported many organic reactions promoted by samarium.[43–49] Banik reported that Samarium induced reductive dimerization of methyl cinnamate to synthesize 2,8-diamino chrysene[50] and that samarium–NBS induced reductive dimerization of carbonyl compounds to fabricate pinacols.[51,52] Jia reported that samarium promoted acylation of primary, secondary, allyl and benzyl alcohols with acid chlorides to give esters,[53] that samarium promoted C-acetylation of Baylis–Hillman adducts in the presence of $FeCl_3$ and iodine[54] and that samarium-promoted reduction of nitroarenes with arylaldehydes formed C,N-diarylnitrones.[55] Zhang reported samarium-promoted coupling-cyclization of chalcones.[56] In this work, we developed a novel Sm–$NiCl_2$ bimetallic system to promote reductive coupling of aryl aldehydes/aryl ketone into pinacols and to promote coupling reaction of aryl sulfonyl chlorides and active halides into sulfones.

## Experimental

### General Procedure for the Synthesis of Pinacols

Aryl aldehydes or aryl ketone (1 mmol) were added to a suspension of Sm powder (0.15 g, 1 mmol) and $NiCl_2$ powder (0.13 g, 1 mmol) in anhydrous THF was distilled from sodium (10 ml) under nitrogen atmosphere. The mixture was stirred at room temperature for 10 h. Then water (10 ml) was added. The mixture was extracted with ether (20 ml × 3). The organic phase was washed with brine and dried over anhydrous $Na_2SO_4$. After distillation of the solvent, the mixture was subjected to preparative TLC. The known compounds (**2a**–**2g**) were similarly characterized by comparing their NMR and IR spectra with those found in the literature.

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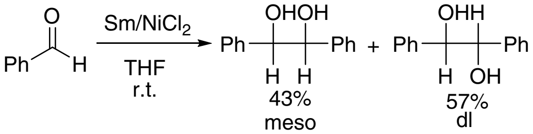
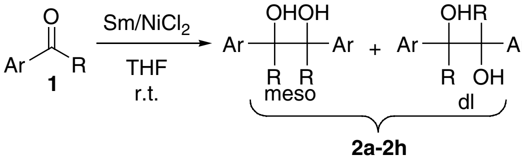


**Scheme 1.** Reductive coupling of benzyl aldehyde.



**Scheme 2.** Synthesis of various kinds of pinacols from arylketones using Sm/NiCl$_2$.

**Table 1.** Reductive coupling of aromatic aldehydes and ketone with Sm–NiCl$_2$ bimetallic system

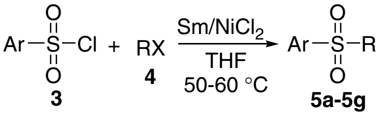
| Entry | Ar | R | Product | Yield (%)[a] | DL:meso[b] |
|---|---|---|---|---|---|
| 1 | $C_6H_5$ | H | **2a** | 71 | 57 : 43 |
| 2 | *p*-Cl$C_6H_4$ | H | **2b** | 78 | 55 : 45 |
| 3 | *m*-Cl$C_6H_4$ | H | **2c** | 73 | 54 : 46 |
| 4 | *p*-Br$C_6H_4$ | H | **2d** | 77 | 52 : 48 |
| 5 | *p*-$CH_3C_6H_4$ | H | **2e** | 67 | 50 : 50 |
| 6 | *o*-Br$C_6H_4$ | H | **2f** | 75 | 53 : 47 |
| 7 | $C_6H_5$ | $CH_3$ | **2g** | 70 | 55 : 45 |

[a] Isolated yield. [b] Ratios determined from the intensities of benzylic protons in $^1$H NMR spectra (entries 1–6), in which the protons of DL isomer appeared at a higher magnetic field compared with that of meso isomer, and from the intensities of methyl protons in $^1$H NMR spectra (entry 7), in which the methyl protons of DL isomer appeared at higher magnetic field, compared with that of meso isomer.

**2a**, lit.[57]; **2b**, lit.[58]; **2c**, lit.[59]; **2d**, lit.[60]; **2e**, lit.[58]; **2f**, lit.[61]; **2g**, lit.[57]

### General Procedure for the Synthesis of Sulfones

Active halides (1.2 mmol) were added into a suspension of Sm powder (0.17 g, 1.1 mmol), NiCl$_2$ powder (0.143 g, 1.1 mmol) and aryl sulfonyl chloride (1.0 mmol) in anhydrous THF (10 ml) under nitrogen atmosphere. The mixture was stirred at 50–60 °C for 2–3 h. Then water (10 ml) was added. The mixture was extracted with ether (20 ml × 3). The organic phase was washed with brine and dried over anhydrous Na$_2$SO$_4$. After distillation of the solvent, the mixture was subjected to preparative TLC. The known compounds (**5a**–**5g**) were similarly characterized by comparing their NMR and IR spectra with those found in the literature



**Scheme 3.** Synthesis of various kinds of sulfones from aryl sulfonyl chlorides and active halides using Sm/NiCl$_2$.

**5a**, m.p. 145–146 °C (lit.,[62] 146–146.5 °C); **5b**, m.p. 41–42 °C (lit.,[63] 42–43 °C); **5c**, m.p. 93–94 °C (lit.,[64] 93–95 °C); **5d**, m.p. 208–210 °C (lit.,[65] 209–211 °C); **5e**, m.p. 143–144 °C (lit.,[66] 143–145 °C); **5f**, m.p. 50–51 °C (lit.,[67] 50–52 °C); **5g**, m.p. 109–110 °C (lit.,[67] 108–109.5 °C).

## Results and Discussion

We reported the reductive cleavage of S–S bond promoted by the Sm–NiCl$_2$ system.[68] Can this system be used in the reductive coupling of aryl aldehydes or ketone? Benzyl aldehyde was added into a suspension of Sm powder and NiCl$_2$ powder in anhydrous THF under nitrogen atmosphere. After the mixture was stirred at room temperature for 10 h, Sm powder disappeared. Then water was added. We found that a new spot appeared on TLC. We were pleased to obtain the new product in 71% yield with preparative TLC. According to $^1$H NMR, the DL:meso ratio of the pinacols is 57 : 43 (see Scheme 1). With the above method, we synthesized several kinds of pinacols (see Scheme 2 and Table 1).

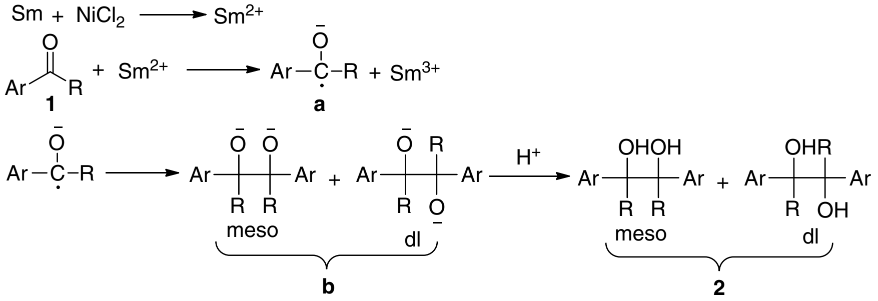
Aryl aldehydes or aryl ketone afforded pinacols in good yields. Can this system be used in the coupling of aryl sulfonyl chlorides with active halides? Fortunately, we synthesized several kinds of sulfones from aryl sulfonyl chlorides with active halides promoted by Sm–NiCl$_2$ with the above-mentioned method (see Scheme 3 and Table 2).

All active halides (entries 1–7) reacted with aryl sulfonyl halides afforded sulfones in good yields except butylbromide (entry 8) in 0 yield, although Zhang reported synthesis of sulfones with Sm–HgCl$_2$ bimetallic system from arylsulfonyl chlorides and alkyl halides.[69] Hg and HgCl$_2$ are prohibited in industry as they are very poisonous and cause severe environmental pollution. NiCl$_2$

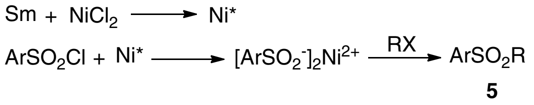
**Table 2.** Coupling of aryl sulfonyl chlorides and active halides with Sm–NiCl$_2$ system

| Entry | Ar | RX | Time (h) | Temperature (°C) | Product | Yield (%)[a] |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_5CH_2Br$ | 2 | 50 | **5a** | 74 |
| 2 | $C_6H_5$ | $BrCH_2COOC_2H_5$ | 2 | 50 | **5b** | 71 |
| 3 | $C_6H_5$ | $C_6H_5COCH_2Br$ | 2 | 50 | **5c** | 75 |
| 4 | $C_6H_5$ | *p*-$NO_2C_6H_5CH_2Br$ | 3 | 60 | **5d** | 67 |
| 5 | *p*-$CH_3C_6H_4$ | $C_6H_5CH_2Br$ | 2 | 60 | **5e** | 71 |
| 6 | *p*-$CH_3C_6H_4$ | $CH_2{=}CHCH_2Br$ | 2 | 50 | **5f** | 68 |
| 7 | *p*-$CH_3C_6H_4$ | $C_6H_5COCH_2Br$ | 3 | 50 | **5g** | 73 |
| 8 | *p*-$CH_3C_6H_4$ | $CH_3(CH_2)_2CH_2Br$ | 5 | 60 | | 0 |

[a] Isolated yield.



**Scheme 4.** Possible reaction mechanism of reductive coupling of aryl aldehydes and aryl ketone promoted by Sm–$NiCl_2$ bimetallic system.



**Scheme 5.** Possible reaction mechanism of coupling of aryl sulfonyl chlorides and active halides promoted by Sm–$NiCl_2$ bimetallic system.

and Ni are widely used in industry and are less poisonous. The use of Sm–$NiCl_2$ offers advantages over the Sm–$HgCl_2$ previously reported.

The possible reaction mechanism of reductive coupling of aryl aldehydes and aryl ketone mediated by Sm–$NiCl_2$ are given in Scheme 4. $NiCl_2$ oxidized Sm to $Sm^{2+}$. *In situ*-generated $Sm^{2+}$ reacted with aryl aldehydes or aryl ketone to form radical carbon anion **a** and $Sm^{3+}$. Then radical carbon anion **a** dimerized into **b** followed by protonation to form pinacol **2** in meso and DL form (see Scheme 4).

The possible reaction mechanism of coupling of aryl sulfonyl chlorides and active halides mediated by Sm–$NiCl_2$ is explained in Scheme 5. Sm reduced $NiCl_2$ to active Ni*. *In situ*-generated active Ni* reacted with aryl sulfonyl chlorides to form aryl sulfonyl anion. Then aryl sulfonyl anion attacked active halides to form sulfones **5** (see Scheme 5).

## Conclusions

In summary, we developed novel methods to synthesize pinacols from aryl aldehydes and aryl ketone in good yields and synthesize sulfones from aryl sulfonyl chlorides and active halides in good yields with an Sm–$NiCl_2$ bimetallic system. The main advantages of the present procedure are the milder reaction conditions and simple operation. The further utility of the Sm–$NiCl_2$ bimetallic system in organic synthesis was under study.

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