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# Highly efficient Barbier allylation from allyl alcohol using iridium(I)/tin(II): Unusual and indirect roles of allyl alcohol and tin

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**Abstract**

A reagent combination of $SnCl_2$ and catalytic $[Ir(COD)Cl]_2$ (1 mol%) in THF–$H_2O$ promotes the reaction of allyl alcohol and aldehyde leading to homoallyl alcohols in good to excellent yields. Control studies suggest the plausible participation of π-allyl-iridium intermediate(s) from which direct allyl transfer takes place to aldehyde.


*Keywords:* Barbier allylation; Homoallylic alcohol; Diallyl ether; Allyl transfer; π-Allyl-iridium

## 1. Introduction

Barbier allylation of carbonyl compounds using in situ generated allyl-metal offers a straightforward access to synthetically useful homoallyl alcohols, for which a plethora of metal reagents are available today [1–3]. Furthermore, various allyl electrophiles including halides, carbonates, tosylates, mesylates and acetates have been employed, which are synthesized most often from respective allyl alcohols. Not surprisingly, the scope and utility of Barbier allylation increases tremendously when the allyl-metal is generated in situ directly from readily available allyl alcohols. Such a transformation, is very attractive as it obviates customary pre-functionalization to reactive allyl electrophile. However, there are only few reports in this direction [4–12]. Also note that umpolung of a C–OH bond is considerably difficult than a C–X bond. Our continuing interest in the organic reactivity of transition metal/tin reagents, including "Rh–Sn" and "Ir–Sn" combinations [13–16], prompted us to look into carbonyl allylation using allyl alcohol. Herein, we delineate a highly efficient carbonyl allylation reaction from allyl alcohol using tin(II) chloride and catalytic iridium(I) [17]. Control experiments clearly suggested that the reactive allyl electrophile is diallyl ether, and that the reaction does not proceed via usual allyltin intermediate instead involves a direct allyl transfer from π-allyl-iridium.

## 2. Results and discussion

Taking allyl alcohol **2a** and 4-chlorobenzaldehyde **1a** as model substrates, optimization studies were carried out varying the transition metal catalyst, solvent and $SnCl_2$:alcohol molar ratio. For reactions conducted using $SnCl_2$:**2a** ratio of 0.75 in THF–$H_2O$, and judged by the isolated yield of homoallyl alcohol **3a**, $[IrCl(COD)]_2$ is found to be the best catalyst over Rh(I), Pd(0) and Pd(II), while $d^8$-complexes of Ni, Co and Pt failed to react (Table 1).

For example, while 1 mol% of $[IrCl(COD)]_2$ afforded 95% of **3a** after 4 h, the corresponding rhodium catalyst provided only 47% of the product (entry 1 versus entry 4). The influence of water is noteworthy [18–20]. Screening of solvents with varying dielectric constant and donor ability establish that allylation is favored in organic–aqueous medium compared to only organic or aqueous medium; THF–$H_2O$ (9:1) being the best (Table 2).

Control studies were also carried out varying $SnCl_2$:alcohol and alcohol:aldehyde molar ratio, and the yield of homoallylic alcohol **3a** was determined after 1 h (Fig. 1). Note that when Sn(II):aldehyde ratio is 1:1, only 32% of **3a** was obtained (Fig. 1A). The yield of **3a** sharply increased with increasing amount of Sn(II), and at a Sn(II):aldehyde ratio of 1.5:1, the yield of **3a** was 83%. Further increase in the amount of Sn(II)

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Table 1
Reaction of allyl alcohol **2a** with 4-chlorobenzaldehyde **1a** in the presence of $SnCl_2$ and transition metal catalyst[a]

| Entry | Catalyst | Yield (%)[b] |
|---|---|---|
| 1 | $[Ir(COD)Cl]_2$ | 95 |
| 2 | $IrCl(CO)(PPh_3)_2$ | 69 |
| 3 | $Ir(SnCl_3)(CO)_2(PPh_3)_2$ | 64 |
| 4 | $[Rh(COD)Cl]_2$ | 47 |
| 5 | $RhCl(PPh_3)_3$ | 11 |
| 6 | $Pd_2(dba)_3$ | 27 |
| 7 | $PdCl_2(PhCN)_2$ | 25 |
| 8 | $PdCl_2(PPh_3)_2$ | 19 |
| 9 | $PtCl_2(PPh_3)_2$ | Nil |
| 10 | $CoCl(PPh_3)_2$ | Nil |
| 11 | $NiCl_2(PPh_3)_2$ | Nil |

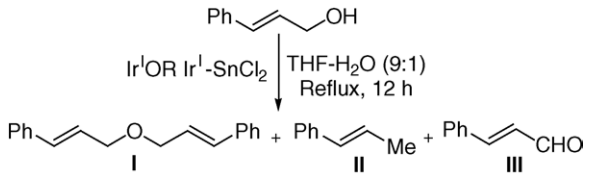
[a] Condition: alcohol (2 mmol), aldehyde (1 mmol), $SnCl_2{\cdot}2H_2O$ (1.5 mmol), catalyst (0.01 mmol), THF–$H_2O$ (5 mL, 9:1, v/v), reflux, 4 h.
[b] Refers to isolated yield of homoallylic alcohol **3a**.

Table 2
Reaction of allyl alcohol **2a** with aldehyde **1a** in the presence of $SnCl_2$ and catalytic $[Ir(COD)Cl]_2$ in various solvents[a]

| Entry | Solvent | $\varepsilon$ | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | THF–$H_2O$ (9:1) | – | 4 | 95 |
| 2 | THF | 7.6 | 10 | 34 |
| 3 | $H_2O$ | 80.2 | 10 | 9 |
| 4 | $CH_2Cl_2$ | 8.9 | 10 | 20 |
| 5 | $CH_2Cl_2$–$H_2O$ (9:1) | – | 10 | 87 |
| 6 | NMP | 32.2 | 10 | 62 |
| 7 | NMP–$H_2O$ (9:1) | – | 10 | 64 |
| 8 | MeOH | 32.7 | 10 | 10 |
| 9 | MeOH–$H_2O$ (9:1) | – | 10 | 42 |

[a] Condition: alcohol (2 mmol), aldehyde (1 mmol), $SnCl_2{\cdot}2H_2O$ (1.5 mmol), catalyst (0.01 mmol), solvent 5 mL, reflux.
[b] Refers to isolated yield of homoallylic alcohol **3a**.

did not cause major change in the yield of **3a**. Therefore, the optimized ratio of Sn(II):aldehyde was kept at 1.5:1. The data for the variation in the ratio of alcohol:aldehyde from 1:1 to 2:1 was collected at a fixed concentration of $SnCl_2$ (Fig. 1B). The yield of **3a** did not vary when the alcohol:aldehyde ratio was




Scheme 1.

above 1.5:1. However, for substituted allyl alcohols a ratio of 2:1 was adjudged as best.

Motivated by the above results, we tested the general applicability of the iridium(I) catalyzed allylation reaction varying both alcohol and aldehyde (Table 3). Gratifyingly, in the majority of cases the corresponding homoallyl alcohols were obtained in good to excellent yields. Gamma-substituted alcohols **2b** and **2d** gave the corresponding homoallyl alcohols, which are γ-regioselective (entries 4, 5, 9 and 10). The *syn*/*anti*-diastereoselectivity varied depending on the alcohol and aldehyde. However in case of 1-substituted alcohols **2c** and **2e** apparent α-regioselective products were obtained (entries 6, 7, 8 and 11). Control studies revealed that this is due to in situ transformation of 1-substituted alcohols to their 3-substituted isomers and corresponding diallyl ethers (see later). In the case of geraniol, alcohol **3l** was obtained in 25% yield (entry 12) while formylferrocene resulted in diene **3i** in 42% yield due to dehydration of the initially formed homoallyl alcohol (entry 8).

Taking cinnamyl alcohol, various control experiments were carried out to ascertain the primary mechanistic steps in the present allylation reaction. An initial surprise had been our failure to isolate or detect by NMR an allyltin intermediate from the reaction of alcohol and $Ir^I$–$SnCl_2$ reagent. On a preparative scale, the reaction of cinnamyl alcohol (1 mmol) and catalytic $[IrCl(COD)]_2$ (1 mol%) in refluxing THF–$H_2O$ afforded dicinnamyl ether **I**, 3-phenylpropene **II** and cinnamaldehyde **III** in about 1:2:1 ratio. Under identical condition but with $[IrCl(COD)]_2$ (1 mol%) and $SnCl_2$ (0.75 mmol) dicinnamyl ether was the major product, the ratio of **I**, **II** and **III** being 5:1:2 (Scheme 1) [21,22]. Treatment of 1-phenyl-2-

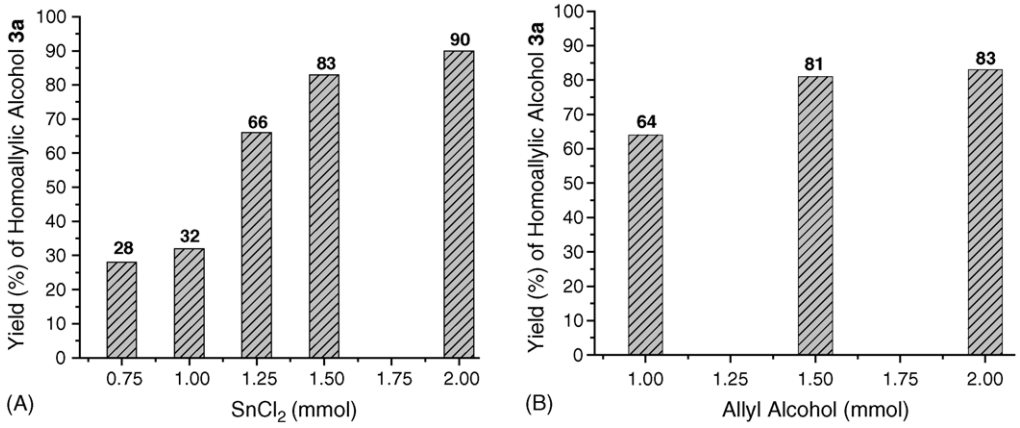
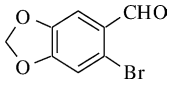
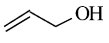
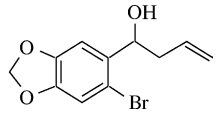
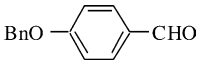
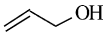
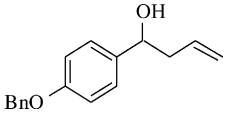
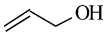
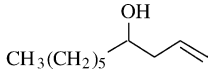
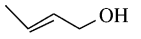
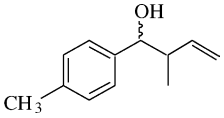
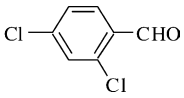
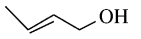
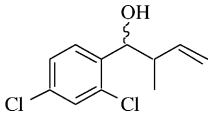
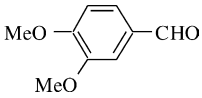
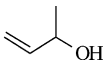
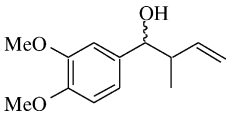
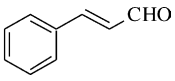
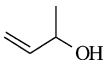
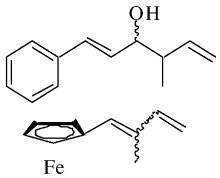
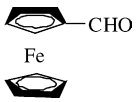
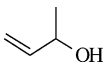
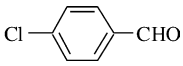
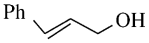
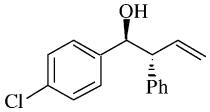
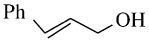
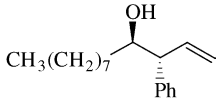
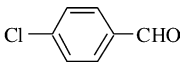
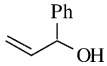
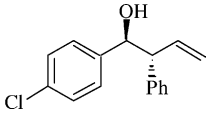
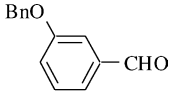
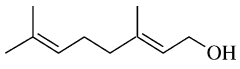
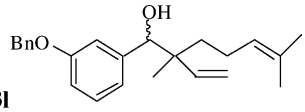



Fig. 1. Yield optimization in the $[Ir(COD)Cl]_2$ catalyzed reaction of allyl alcohol **2a** with aldehyde **1a**. All data after 1 h. (A) Data for the reaction of aldehyde (1 mmol), allyl alcohol (2 mmol) and varying amounts of $SnCl_2$. (B) Data for the reaction of aldehyde (1 mmol), $SnCl_2$ (1.5 mmol) and varying amounts of allyl alcohol.

Table 3
Ir(I) catalyzed carbonyl allylation using allylic alcohols[a]

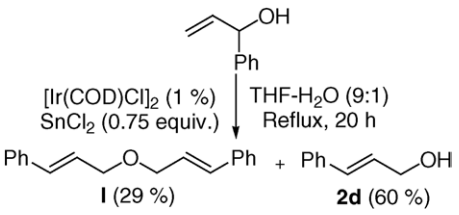
| Entry | Aldehyde | Allylic alcohol | Homoallylic alcohol | Time (h) | Yield (%)/*syn*:*anti* |
|---|---|---|---|---|---|
| 1 | **1b**  | **2a**  | **3b**  | 12 | 97 |
| 2 | **1c**  | **2a**  | **3c**  | 10 | 99 |
| 3 | **1d** $CH_3(CH_2)_5CHO$ | **2a**  | **3d**  | 8 | 93 |
| 4 | **1e**  | **2b**  | **3e**  | 50 | 89/46:54 |
| 5 | **1f**  | **2b**  | **3f**  | 48 | 81/73:27 |
| 6 | **1g**  | **2c**  | **3g**  | 14 | 73/39:61 |
| 7 | **1h**  | **2c**  | **3h**  | 16 | 77/52:48 |
| 8 | **1i**  | **2c**  | **3i**  | 12 | 42[b] |
| 9 | **1a**  | **2d**  | **3j**  | 72 | 99/0:100 |
| 10 | **1j** $CH_3(CH_2)_7CHO$ | **2d**  | **3k**  | 16 | 72/0:100 |
| 11 | **1a**  | **2e**  | **3j**  | 72 | 88/0:100 |
| 12 | **1k**  | **2f**  | **3l**  | 64 | 25/23:77 |

[a] Condition: alcohol (2 mmol), aldehyde (1 mmol), $SnCl_2{\cdot}2H_2O$ (1.5 mmol), $[Ir(COD)Cl]_2$ (0.01 mmol), THF–$H_2O$ (5 mL, 9:1, v/v), reflux.
[b] *E*:*Z* = 64:36.

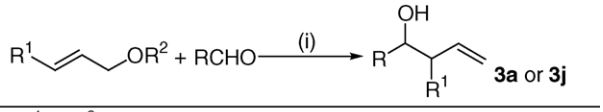
propenyl alcohol **2e** with $Ir^I$–$SnCl_2$ also led to the formation of dicinnamyl ether **I** along with isomeric cinnamyl alcohol (Scheme 2).

We further noted that the carbonyl allylation reaction could be carried out using diallyl ether as the allyl electrophile. Thus, in the presence of $Ir^I$–$SnCl_2$ as reagent, allylation of aldehyde with dicinnamyl ether was six-fold faster than with cinnamyl alcohol (Scheme 3). Similar reaction of allyl phenyl ether with aldehyde gave rise to homoallyl alcohol along with phenol.

While detailed understanding on the mechanistic course of the reaction must await further studies, a preliminary suggestion is outlined in Schemes 4–7. While suggesting these pathways, we aimed to look into a common organoiridium intermediate,




Scheme 2.




| $R^1$ | $R^2$ | mmol | Time (h) | Pdt No. (%) | Other (%) |
|---|---|---|---|---|---|
| H | Ph | 2 | 6 | **3a** (98) | PhOH (67) |
| Ph | H | 2 | 72 | **3j** (99) | nil |
| Ph | Cinnamyl | 1 | 12 | **3j** (95) | nil |

(i) R = 4-$ClC_6H_4$, aldehyde (1 mmol), $[Ir(COD)Cl]_2$ (0.01 mmol), $SnCl_2.2H_2O$ (1.5 mmol), THF-$H_2O$ (9:1 v/v), reflux

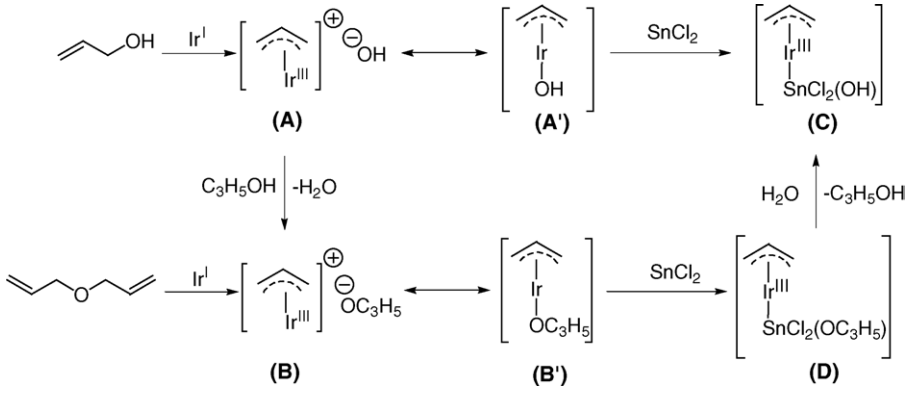
Scheme 3.

which could conform to the major experimental observations, namely (i) formation of dicinnamyl ether **I**, 3-phenylpropene **II** and cinnamaldehyde **III** from cinnamyl alcohol; (ii) formation of cinnamyl alcohol and dicinnamyl ether **I** from 1-phenyl-2-propenyl alcohol; (iii) formation of homoallylic alcohol from allyl alcohol or diallyl ether; (iv) absence of allyltin intermediate as suggested by NMR.

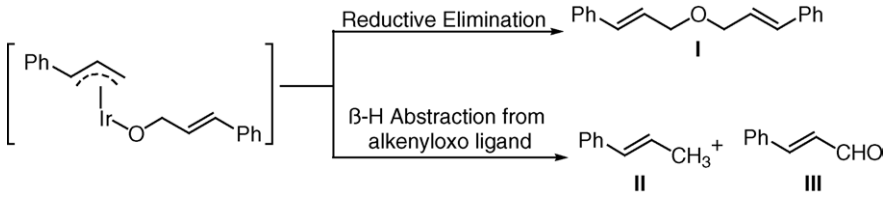
Central to our hypothesis are the two π-allyl-iridium intermediates A and B, which could be generated by the oxidative addition of allyl alcohol or diallyl ether (Scheme 4). The two intermediates are shown in both outer-sphere and inner-sphere coordination modes (A, A′ and B, B′). Note that the cleavage of the C–O to obtain intermediate B will be easier from diallyl ether than allyl alcohol. Facile oxidative addition of allyl phenyl ether and diallyl ether across $Ni(COD)_2$, $Pd(PCy_3)_4$, $[PtH(PPh_3)_2]^{2+}$ and $Pd(^tBu_3)_4$ to generate the corresponding π-allyl-metal is well known [23–26]. Moreover, since the carbonyl allylation does not proceed without Sn(II), we invoke the formation of Ir–Sn intermediates as in **C** and **D**; the allyl transfer step being discussed later (Scheme 7).

The formation of dicinnamyl ether **I**, 3-phenylpropene **II** and cinnamaldehyde **III** from cinnamyl alcohol can be easily explained taking the cinnamyl analogue of intermediate B′, involving reductive elimination and β-hydrogen transfer steps (Scheme 5). The cinnamyl analogue of intermediate **A** could also account for the isomerization of 1-phenyl-2-propenyl alcohol to cinnamyl alcohol (Scheme 6).

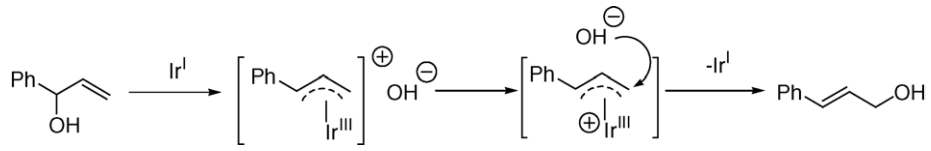
Regarding the mechanism of allyl transfer to aldehyde, we rule out the formation of an allyltin species from intermediates **C** or **D** since no organotin species could be detected in control studies. Accordingly we suggest an allyl-transfer directly from π-allyl-Ir (**C** or **D**) to aldehyde via a seven-member transition state **E** (Scheme 7). While this remains highly speculative at the moment, further studies are warranted to resolve the mechanistic issue.



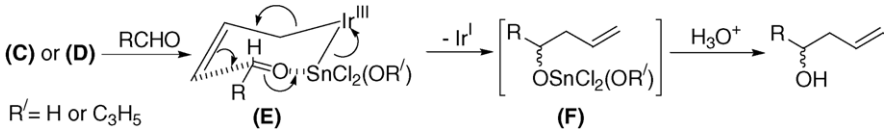

Scheme 4.




Scheme 5.



Scheme 6.



Scheme 7.

## 3. Conclusion

In summary, we presented here an efficient Barbier allylation directly from allyl alcohol. Three noteworthy features of the reaction are: (a) that the reaction also proceeds smoothly with diallyl ether, (b) that isomeric 3-substituted allyl alcohol and 1-substituted allyl alcohol leads to the same homoallyl alcohol and (c) that the reaction might not proceed via usual allyltin, instead follow a direct allyl transfer from π-allyl-iridium.

## 4. Experimental

$^{1}$H (200 MHz) and $^{13}$C{H} (50.6 MHz) NMR spectra were recorded on a BRUKER-AC 200 MHz. Spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: $\delta$ 7.27 ppm). Data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, br: broad and m: multiplet), coupling constant (Hz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: $\delta$ 77.0 ppm). ESI-MS and HRMS were taken using a Waters LCT mass spectrometer. Elemental analyses were carried out using a CHNS/O Analyzer Perkin-Elmer 2400 Series II instrument.

### *4.1. Typical procedure for the reaction of allylic alcohols with aldehydes in presence of $SnCl_2{\cdot}2H_2O$ and catalytic Ir(I)*

A mixture of 4-chlorobenzaldehyde **1a** (140.5 mg, 1 mmol) and allyl alcohol **2a** (116 mg, 2 mmol) in peroxide free freshly distilled THF (2 mL) was slowly added to a stirred solution containing $SnCl_2{\cdot}2H_2O$ (338.5 mg, 1.5 mmol) and $[Ir(COD)Cl]_2$ (6.7 mg, 0.01 mmol) in peroxide free freshly distilled THF (2.5 mL) and $H_2O$ (0.5 mL) which was previously refluxed for 30 min. The suspension was refluxed at 70 °C under $N_2$ atmosphere for 4 h (TLC monitoring on silica gel, eluent: ethyl acetate/hexane, 1/9, v/v). An aqueous solution of $NH_4F$ (15%, 10 mL) was added to the reaction mixture and the organic layer was extracted with diethyl ether (3 × 10 mL), washed with water (2 × 10 mL), brine (2 × 10 mL) and dried over magnesium sulfate. Solvent removal followed by column chromatography (eluent: *n*-hexane:ethyl acetate, 97:3) afforded pure 1-(4-chlorophenyl)-but-3-en-1-ol **3a** (174 mg, 95% w.r.t. aldehyde).

$^{1}$H NMR ($CDCl_3$): $\delta$ 2.17 (brs, 1H, –CHO*H*), 2.42–2.540 (m, 2H, –C*H*$_2$–), 4.69 (t, 1H, $J$ = 6.38 Hz, –C*H*OH), 5.10–5.18 (m, 2H, =C*H*$_2$), 5.66–5.87 (m, 1H, –C*H*=CH$_2$), 7.24–7.34 (m, 4H, aryl).

$^{13}$C NMR ($CDCl_3$): $\delta$ 43.71, 72.50, 118.67, 127.13, 128.43, 133.06, 133.89, 142.23.

ESI-MS: for $C_{10}H_{11}ClO$ [M], $[M-OH]^+$ = 165.05($^{35}$Cl) and 167.05($^{37}$Cl). HRMS calculated for the fragment ion $C_{10}H_{10}Cl$ $[M-OH]^+$ = 165.0471 found 165.0475($^{35}$Cl) and 167.0441 found 167.0452($^{37}$Cl).

Anal. ($C_{10}H_{11}ClO$) calcd, C: 65.76, H: 6.07; found, C: 65.39, H: 6.22.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2005.11.009.

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