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Highly regioselective iridium-catalyzed and samariumpromoted coupling of allylic carbonates with ketones: a new approach towards homoallylic alcohols[†]

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A highly regioselective Ir-catalyzed and Sm-promoted coupling of allylic carbonates with ketones has been realized, which provides the homoallylic alcohols in up to 89% yields. This strategy gives a convenient method for the synthesis of liquid crystals with a monofluorinated quaternary carbon chain.

The iridium (Ir)-catalyzed allylation reaction has become an important synthetic approach in organic synthesis during the last decade, regioselectively providing branched allylic products.1 In this reaction, allylic carbonate or acetate can be employed as an allyl electrophile and combined with an iridium catalyst to form a $(\pi$ -allyl)-iridium complex, which can be rendered nucleophilic by means of an umpolung process.² The umpolung of the allylic fragment can be induced by reduction with a salt (SnCl₂)³ or alcoholic reductant.⁴ Samarium diiodide (SmI₂) serves as a one-electron reductant⁵ and has been utilized in palladium (Pd)-catalyzed coupling of carbonyl compounds with allylic acetates.6 To date, an Ir-catalyzed and Sm-promoted allylation of carbonyl compounds with allylic carbonates has not been reported. This method may afford both branched allylic alcohols and homoallylic alcohols, in which a hydroxyl group (OH) is an equivalent of a fluorine atom. These tertiary homoallylic alcohols can undergo a fluorination with diethylaminosulfur trifluoride (DAST) to produce the corresponding products with a mono-fluorinated quaternary carbon. Here, we present the first example of the Ir-catalyzed and Sm-promoted coupling of allylic carbonates with ketones, which regioselectively gives the homoallylic alcohols.

At the outset, our efforts were focused on the investigation of an Ir-catalyzed and Sm-promoted coupling reaction between (E)-cinnamyl acetate **1a** and cyclohexanone **2a**. Initially, when we carried out this coupling reaction in the presence of [Ir(COD)Cl]₂ (2 mol%) in tetrahydrofuran (THF) at room temperature under argon, no coupling product was observed (entry 1). When SmI₂ (2 equiv.) was added as a reducing reagent, the formation of the homoallylic alcohol 3a and the branched allylic alcohol 4a, with the ratio of 3a/4a being 99/1, was unexpectedly observed (entry 2). Such high regioselectivity with respect to the linear allylic product is not in agreement with what is seen in Ir-catalyzed and SnCl2-mediated carbonyl allylations. In contrast, the same allylation reaction with a Pd-Sm catalyst system gave the corresponding allylic products (3a + 4a) with low regioselectivity (3a/4a = 2.44/1).^{6a} When (E)-cinnamyl methyl carbonate 1b was used in place of (E)-cinnamyl acetate 1a, the yield of 3a was improved from 68% to 75% (entry 2 vs. entry 3). Increasing the amount of SmI_2 in this reaction to 2.5 equiv. produced 3a in a superior yield of 83% (entry 4).

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Screening a diverse range of solvents such as THF, dimethoxyethane (DME), MeCN, dichloromethane (DCM), and toluene showed THF to be the optimum solvent choice, while other solvents such as MeCN and DME resulted in poor results (entries 6 and 7). DCM and toluene were also both ineffective in this reaction, presumably due to the poor solubility of SmI₂ (entries 8 and 9). Changing the reaction temperature revealed that although the reaction proceeded smoothly at room temperature, good yields were also obtained at 10 °C and 40 °C (entries 4, 10 and 11). SnCl₂ (ref. 3a) was also examined as a reducing agent and it failed to promote this coupling reaction (entry 12). It is noteworthy that the formation of 4a was successfully suppressed in the course of this reaction. Therefore, the conditions presented in entry 4 of Table 1 were chosen for further experimentation. Under the optimized conditions, the [Ir(COD)Cl]₂-SmI₂ catalytic system was used to explore the scope of the coupling of various allylic carbonates with cyclic or acyclic ketones (Table 2). For example, either cyclohexanone 2a or acetone 2b reacted with the allylic carbonates 1a-e to produce the tertiary homoallylic alcohols 3a-j in moderate to high yields (Table 2, entries 1-10). Varying the substituents on the phenyl ring of the allylic carbonates 1a-e had a great

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influence on the coupling reactions. (*E*)-Cinnamyl methyl carbonate **1b** and the allylic carbonates **1c**–**e** with electrondonating groups (*e.g.*, *m*-MeO, *p*-Me, *p*-MeO) on the phenyl ring gave the corresponding products in good to high yields (entries 1–3 and 6–8). In the case of the allylic carbonate **1e** with an electron-withdrawing group (*e.g.*, *o*-Cl) on the phenyl ring, 3 equiv. of SmI₂ and a longer reaction time were required, and this gave only a 50% yield of **3d** (entry 4). The bulky aryl (*e.g.*, biphenyl and naphthyl)-substituted allylic carbonates **1h** and **1f** gave **3e**, **3i** and **3j** in moderate yields (entries 5, 9 and 10). Notably, the formation of **4a–j** was suppressed in all cases (entries 1–10).

In contrast, the Grignard reagent (*E*)-cinnamylmagnesium chloride¹⁰ reacted with 2a in THF at room temperature to afford the corresponding product 3a in a 46% yield; 4a was not observed in this case. A representative example of the synthetic utility of this method is illustrated in Scheme 1. Hydrogenation of 3e or 3j, followed by fluorination with diethylaminosulfur trifluoride (DAST)⁷ gave the mono-fluorinated compounds 3eb or 3jb in a two-step 74% and 53% yield, respectively. Compound 3jb may exhibit good liquid crystalline properties in comparison with a known liquid crystal, 4-(4,4-dimethylpentyl)-1,1'-biphenyl.⁸ The introduction of fluorine enhances the dipole moment and reduces the viscosity of the liquid crystal, thereby improving its performance.⁹

Conclusions

We have developed a practical method for the synthesis of tertiary homoallylic alcohols *via* Ir-catalyzed and Sm-promoted coupling of allylic carbonates with ketones, which

 Table 1
 Optimization of the reaction conditions for an Ir-catalyzed and Smpromoted coupling of (E)-cinnamyl acetate 1a with cyclohexanone 2a^a



Entry	MX ₂ (eq.)	R	Solvent	Т (°С)	3a/4a	Yield ^b (%)
1	_	Ac	THF	25	_	N.R. ^c
2	$SmI_{2}(2.0)$	Ac	THF	25	99/1	68
3	SmI_2 (2.0)	CO ₂ Me	THF	25	99/1	75
4	$SmI_{2}(2.5)$	CO_2Me	THF	25	99/1	83
5	$SmI_2(3.0)$	CO_2Me	THF	25	_	79
6	$SmI_2(2.5)$	CO ₂ Me	DME	25	_	10
7	$SmI_2(2.5)$	CO ₂ Me	MeCN	25	_	Trace
8	$SmI_2(2.5)$	CO ₂ Me	DCM	25	_	N.R.
9	SmI_2 (2.5)	CO ₂ Me	Toluene	25	_	N.R.
10	$SmI_2(2.5)$	CO ₂ Me	THF	10	99/1	78
11	$SmI_2(2.5)$	CO ₂ Me	THF	40	99/1	70
12	$SnCl_2$ (2.5)	CO ₂ Me	THF	25	_	N.R.

^{*a*} Reagents and conditions: **1a** and **1b** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 1.5 equiv.), $[Ir(COD)Cl]_2$ (2 mol%), SmI_2 (2–3 mol%, 0.1 M in THF) in solvent (2 mL) under argon. ^{*b*} Isolated yield. ^{*c*} N.R. = no reaction.

 $\textbf{Table 2} \quad \mbox{Ir-catalyzed and Sm-promoted coupling of allylic carbonates with ketones^a$

$R^{1} \xrightarrow{OCO_{2}Me} + \frac{1}{R^{2}} \xrightarrow{R^{2}}{R^{2}} \frac{2 \operatorname{mol}\% [Ir(COD)C]_{2}}{2a R^{2} = -(CH_{2})_{5^{-}}} \xrightarrow{THF, rt, 6 h} R^{1} \xrightarrow{R^{2}}{R^{2}} + R^{1} \xrightarrow{R^{2}}{R^{2}} \xrightarrow{H^{2}}{R^{2}} \xrightarrow{H^{2}}{4a \cdot j}$										
Entry	R ¹		R^2	3/4	Product	$\operatorname{Yield}^{b}(\%)$				
1	Ph	1b	-(CH ₂) ₅ -	99/1	3a	83				
2	$3-MeOC_6H_4$	1c	-(CH ₂) ₅ -	99/1	3b	76				
3	4-MeC ₆ H ₄	1d	-(CH ₂) ₅ -	99/1	3c	72				
4^c	$2-ClC_6H_4$	1e	-(CH ₂) ₅ -	99/1	3d	50				
5 ^c	4-PhC ₆ H ₄	1f	-(CH ₂) ₅ -	99/1	3e	49				
6	Ph	1b	CH ₃	99/1	3f	89				
7	$4-MeC_6H_4$	1d	CH_3	99/1	3g	78				
8	4-MeOC ₆ H ₄	1g	CH_3	99/1	3ĥ	75				
9 ^c	1-Naphthyl	1ĥ	CH_3	99/1	3i	54				
10^c	$4\text{-PhC}_6\text{H}_4$	1f	CH_3	99/1	3ј	43				

^{*a*} Reaction conditions: **1b-f** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 1.5 equiv.) or **2b** (0.4 mmol, 2.0 equiv.), SmI_2 (2.5 equiv., 5 mL, 0.1 M in THF), and $[Ir(COD)Cl]_2$ (2 mol%) in THF (2 mL) under argon. ^{*b*} Isolated yield. ^{*c*} 3.0 equiv. of SmI_2 , 10 h.

regioselectively provides the tertiary homoallylic alcohols in moderate to high yields. This method can be applied to the synthesis of liquid crystals containing a mono-fluorinated quaternary carbon chain.

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Notes and references

1 (a) B. Bartels, C. Garcia-Yebra, F. Rominger and G. Helmchen, *Eur. J. Inorg. Chem.*, 2002, 2569; (b) H. Miyabe and Y. Takemoto, *Synlett*, 2005, 1641; (c) R. Takeuchi and S. Kezuka, *Synthesis*, 2006, 20, 3349; (d) C. Gnamm, K. Broedner, C. M. Krauter and G. Helmchen, *Chem.-Eur. J.*, 2009, 15, 10514; (e) J. F. Hartwig and L. M. Stanley, *Acc. Chem. Res.*, 2010, 43, 1461; (f) J. F. Hartwig and M. J. Pouy, *Top. Organomet. Chem.*, 2011, 34, 169; (g) P. Tosatti, A. Nelson and S. P. Marsden, *Org.*



 $\ensuremath{\textbf{Scheme 1}}$ Synthesis of a liquid crystal with a mono-fluorinated quaternary carbon chain.

Biomol. Chem., 2012, 10, 3147; (h) W. B. Liu, J. B. Xia and
S. L. You, *Top. Organomet. Chem.*, 2012, 38, 155; (i) H. He,
K. Y. Ye, Q. F. Wu, L. X. Dai and S. L. You, *Adv. Synth. Catal.*, 2012, 354, 1084.

- 2 (a) J. F. Bower and M. J. Krische, in *Iridium Catalysis*, ed. P. G. Andersson, 2011, p. 107; (b) S. B. Han, I. S. Kim and M. J. Krische, *Chem. Commun.*, 2009, 7278.
- 3 (a) Iridium-catalyzed and tin-mediated allylation of (E)-but-2en-1-ol with a range of aldehydes has been reported, giving the branched products (46–80% with b/l 64/36-99/1) as the major, see: Y. Masuyama, T. Chiyo and Y. Kurusu, *Synlett*, 2005, 2251; (b) M. Banerjee and S. Roy, *J. Mol. Catal. A: Chem.*, 2006, **246**, 231; (c) Y. Masuyama and M. Marukawa, *Tetrahedron Lett.*, 2007, **48**, 5963.
- 4 (a) I. S. Kim, M.-Y. Ngai and M. J. Krische, J. Am. Chem. Soc., 2008, 130, 14891; (b) Y. Lu, I. S. Kim, A. Hassan, D. J. Del Valle and M. J. Krische, Angew. Chem., Int. Ed., 2009, 48, 5018; (c) I. S. Kim, S. B. Han and M. J. Krische, J. Am. Chem. Soc., 2009, 131, 2514; (d) Y. J. Zhang, J. H. Yang, S. H. Kim and M. J. Krische, J. Am. Chem. Soc., 2010, 132, 4562; (e) S. B. Han, X. Gao and M. J. Krische, J. Am. Chem. Soc., 2010, 132, 9153; (f) X. Gao, I. A. Townsend and M. J. Krische, J. Org. Chem., 2011, 76, 2350.
- 5 (a) A. Krief and A. M. Laval, *Chem. Rev.*, 1999, 99, 745; (b)
 G. A. Molander and C. R. Harris, *Chem. Rev.*, 1996, 96, 307;
 (c) H. B. Kagan, *Tetrahedron*, 2003, 59, 10351; (d)

D. J. Edmonds, D. Johnston and D. J. Procter, *Chem. Rev.*, 2004, **104**, 3371; (e) K. C. Nicolaou, S. P. Ellery and J. S. Chen, *Angew. Chem., Int. Ed.*, 2009, **48**, 7140.

- 6 (a) The dependence of branched allylic product/linear allylic product ratios on reaction conditions was investigated in Pd-catalyzed and Sm-promoted allylations, see: S. Medegan, F. Helion and J. L. Namy, *Eur. J. Org. Chem.*, 2005, 4715; (b) O. Jacquet, T. Bergholz, C. Magnier-Bouvier, M. Mellah, R. Guillot and J.-C. Fiaud, *Tetrahedron*, 2010, 66, 222; (c) T. Tabuchi, J. Inanaga and M. Yamaguchi, *Tetrahedron Lett.*, 1986, 27, 601; (d) T. Tabuchi, J. Inanaga and M. Yamaguchi, *Tetrahedron Lett.*, 1986, 27, 1195; (e) T. Tabuchi, J. Inanaga and M. Yamaguchi, J. Tabuchi, J. Inanaga and M. Yamaguchi, J. Inanaga and M. Yamaguchi, J. Tabuchi, J. Inanaga and M. Yamaguchi, J. Tabuchi, J. Inanaga and M. Yamaguchi, *Chem. Lett.*, 1987, 2275.
- 7 L. N. Markovskii, V. E. Pashinnik and A. V. Kirsanov, *Synthesis*, 1973, 787.
- 8 T. Inukai, H. Sato and T. Ishibe, *Liquid crystal composite*, 1975, JP51078793A.
- 9 R. Berger, G. Resnati, P. Metrangolo, E. Weber and J. Hulliger, *Chem. Soc. Rev.*, 2011, **40**, 3496.
- 10 (E)-Cinnamylmagnesium chloride is generated from a reaction of (E)-(3-chloroprop-1-enyl)benzene with Mg in THF at 60 °C, see: (a) G. Courtois, M. Harama and P. Miginiac, J. Organomet. Chem., 1981, 218, 275; (b) G. Cahiez, A. Moyeux, J. Buendia and C. Duplais, J. Am. Chem. Soc., 2007, 129, 13788.