

## Chiral Hypervalent Iodine: Asymmetric Synthesis of Indanes

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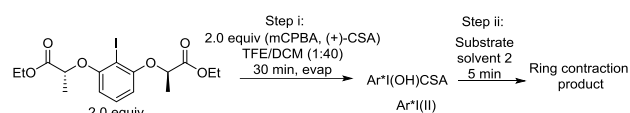
## Introduction

Hypervalent iodine reagents play a substantial role in chemical synthesis.<sup>1,2</sup> In last decade the development of *in situ* generated chiral hypervalent iodine reagents for asymmetric reactions have received a lot of attention.<sup>3-5</sup> Rearrangement reactions are one of the important reactions promoted by I(III).<sup>1,6,7</sup> Herein we report an efficient protocol for asymmetric ring contraction reactions in variety of cyclic alkenes giving functionalized indanes in good yield and enantiomeric ratio (*e.r.*).

## Results and Discussion

The reactivity of several chiral aryl iodine(III) with 1,2-dihydronaphthalene (**6**) was examined. After the optimization of condition for asymmetric oxidative rearrangement of alkene **6**,<sup>8</sup> we planned to explore the scope of asymmetric ring contraction in variety of cyclic alkenes containing nitrogen, oxygen, methyl and aryl substituted substrates. Results obtained demonstrate protecting groups tolerance in nitrogenous substrate as well as the successful oxidative rearrangement in oxygenated and 4-substituted alkenes (Table 1).

Table 1. Scope for asymmetric ring contraction

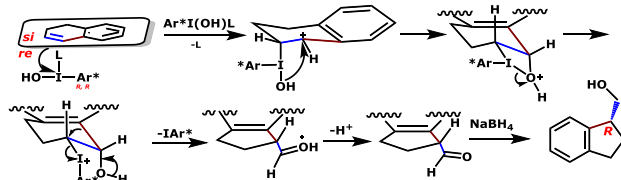


Entry	Substrate	Step ii	Product <sup>a</sup>
1	<b>1a</b>	TFE/DCM (1:4), -78 °C	<b>R-2a</b> 60%, <i>e.r.</i> 79:21
2	<b>1a</b>	HFIP/DCM (1:40), -78 °C	<b>3b</b> 34%, <i>e.r.</i> 80:20
3	<b>1a</b>	TFE/DCM (1:4), -78 °C	<b>S-2a</b> 57%, <i>e.r.</i> 22:78 <sup>b</sup> 56%, <i>e.r.</i> 23:77 <sup>b,c</sup> 56%, <i>e.r.</i> 23:77 <sup>b,d</sup>
3	<b>1b</b>	TFE:DCM (1:1), -40 °C	<b>2b</b> 61%, <i>e.r.</i> 78:22
4	<b>1c</b>	TFE:DCM (1:1), -40 °C	<b>2c</b> 58%, 82:18
6	<b>1d</b>	TFE:DCM (1:1), -40 °C	<b>2d</b> 41%, <i>e.r.</i> 89:11

7	<b>1e</b>	TFE:DCM (1:1), -40 °C	<b>2e</b> 53%, <i>e.r.</i> 23:77
8	<b>1f</b>	DCM, 50 equiv MeOH -78 °C	<b>4f</b> 60%, <i>e.r.</i> 18:82
9	<b>1g</b>	DCM, 50 equiv MeOH -78 °C	<b>4g</b> 71%, <i>e.r.</i> 21:79
10	<b>1h</b>	DCM, 50 equiv MeOH -78 °C	<b>4h</b> 75%, <i>e.r.</i> 21:79
11	<b>1i</b>	TFE/DCM (1:1), -40 °C NaBH <sub>4</sub> , 2 h	<b>2i</b> + <b>3i</b> 44%, <i>trans, e.r.</i> 70:30 44%, <i>trans, e.r.</i> 67:33
12	<b>1j</b>	TFE/DCM (1:1), -78 °C NaBH <sub>4</sub> , 2 h	<b>2j</b> + <b>3j</b> 43%, <i>trans, e.r.</i> 69:31 34%, <i>trans, e.r.</i> 67:33

a) Isolated yield, *e.r.* determined by chiral HPLC and GC. b) Ar\*<sup>1</sup> derived from (+)-ethyl-D-lactate c) Ar\*<sup>1</sup> recovered and reused. d) (-)-CSA

Based on the absolute configuration of alcohol **3b**<sup>9</sup> the electrophilic attack of chiral hypervalent iodine(III) occurred selectively on the *re*-face of double bond to have desired *R*-configured indane.

Scheme 1. Asymmetric ring contraction mechanism in (CF<sub>3</sub>)<sub>2</sub>CHOH.

## Conclusion

Ring contraction of 1,2-dihydronaphthalenes with chiral hypervalent iodine in nitrogen (protected with Ac, Bz and Fmoc) and oxygen containing substrates gave desired indanes in good yields and *e.r.* In the case of 4-substituted alkenes high yields, moderate *e.r.* and higher *d.r.* were observed.

## Acknowledgement

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<sup>1</sup> Silva, L. F., Jr.; Olofsson, B. *Nat. Prod. Rep.* **2011**, *28*, 1722. <sup>2</sup> Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. <sup>3</sup> Farid, U.; Malmady, F.; Claveau, R.; Albers, L.; Wirth, T. *Angew. Chem. Int. Ed.* **2013**, *52*, 7018. <sup>4</sup> Uyanik, M.; Okamoto, H.; Yasui, T.; Ishihara, K. *Science* **2010**, *328*, 1376. <sup>5</sup> Liang, H.; Ciufolini, M. A. *Angew. Chem. Int. Ed.* **2011**, *50*, 11849. <sup>6</sup> Silva, L. F., Jr.; Siqueira, F. A.; Pedrozo, E. C.; Vieira, F. Y. M.; Doriguetto, A. C. *Org. Lett.* **2007**, *9*, 1433. <sup>7</sup> Ahmad, A.; Scarasatti, P.; Jalalian, N.; Olofsson, B.; Silva, L. F., Jr. *Tetrahedron Lett.* **2013**, *54*, 5818. <sup>8</sup> Ahmad, A.; Silva, L. F., Jr. 10<sup>th</sup>-13<sup>th</sup> Nov., 15<sup>th</sup> BMOS, **2013**. <sup>9</sup> Caro, Y.; Torrado, M.; Masaguer, C. F.; Ravina, E. *Tetrahedron: Asymmetry* **2003**, *14*, 3689.