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dl-Selective Reductive Coupling/Dieckmann Condensation Sequence of α,β-Unsaturated Amides with Samarium(II) Iodide/HMPA. Synthesis of a New Ligand, *trans*-1,2-Cyclopentanediyl-2,2'-biphenol

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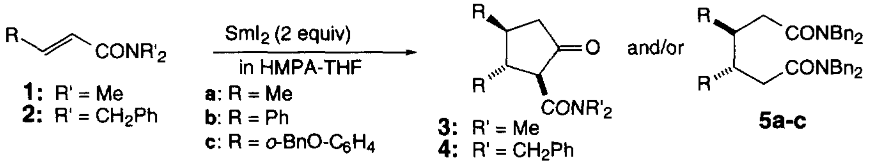
Abstract: By action of SmI_2-HMPA in THF, the *N,N*-dimethyl derivatives of (*E*)-α,β-unsaturated amides produce the 1,2-*trans*-2,3-*trans* stereoisomers of 2,3-disubstituted 5-oxo-1-cyclopentanecarboxamides via a highly *dl*-selective reductive coupling followed by Dieckmann condensation. Water-d_2 is an effective quenching agent. This reaction is successfully applied to the synthesis of *trans*-1,2-cyclopentanediyl-2,2'-biphenol, which is a new C_2-symmetric chiral ligand.

In our synthetic study of a new C_2-symmetric chiral ligand, *trans*-1,2-cyclopentanediyl-2,2'-biphenol, we synthesized its oxygen analog for simplification of synthesis, but the resulting *trans*-2,2-dimethyl-4,5-bis(*o*-hydroxyphenyl)dioxolane was so labile against Lewis acids that the acetal moiety underwent ring opening on treatment with titanium salts.[1] To avoid this undesired liability, we planned to replace the dioxolane ring by a cyclopentane ring. However, synthesis of the cyclopentane ligand from the easily available 1,2-bis(*o*-hydroxyphenyl)cyclopentene was unsuccessful.[2] The present communication describes its synthesis based on the reductive coupling of *N,N*-dimethyl derivatives of α,β-unsaturated amides with SmI_2.

When SmI_2 (2-3 equiv relative to **1**)[3] in HMPA/THF (1/10 v/v) was treated with α,β-unsaturated *N,N*-dimethylamides **1a-c** under dry nitrogen at room temperature, in the presence or absence of *tert*-BuOH (1 equiv if employed), 1,2-*trans*-2,3-*trans* isomers of 2,3-disubstituted 5-oxo-1-cyclopentanecarboxyamides **3a-c** were produced as single isomers (entries 1-4). Use of excess SmI_2 is important for the completion of reactions. Although *tert*-BuOH was essential as internal proton quencher in the reaction of the crotonamide substrate **1a**,[4,5] its presence lowered the yield of coupling products **3** for aryl derivatives of α,β-unsaturated amides **1b,c**. In contrast, use of *N,N*-dibenzylamides **2** only gave the *dl*-isomers of coupling products **5a-c**.[4]

Table 1. Reaction of α,β-Unsaturated Amides with SmI_2

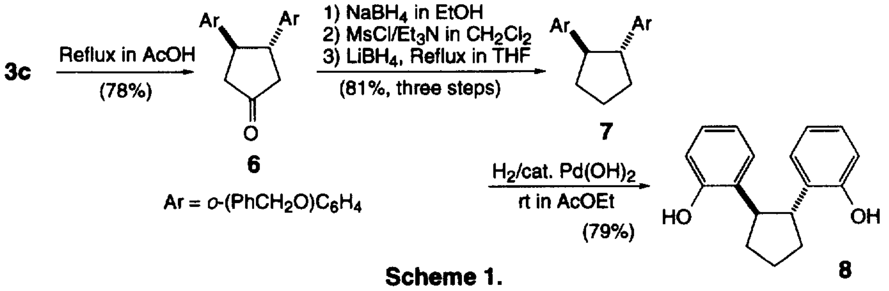


Entry	Amide	SmI_2/equiv	*tert*-BuOH/equiv[a]	Time/min	Product	Yield/%[b]
1	**1a**	3	1	150	**3a**	46
2	**1b**	2.5	–	40	**3b**	39
3	**1c**	2	–	30	**3c**	43
4	**1c**	2	–	120	**3c**	52

[a] Equivalent to the substrate. [b] Yield of isolated products.

The 5-oxo-1-cyclopentanecarboxyamide **3c**, obtained by the *dl*-selective reductive coupling/Dieckmann condensation[6,7] of (*E*)-3-(*o*-benzyloxyphenyl)-*N,N*-dimethylpropenamide (**1c**), was readily transformed to the target molecule **8** (Scheme 1). Thus, **3c** was hydrolyzed by simple heating in wet AcOH under reflux to produce cyclopentanone **6** in 78% yield. Reduction of the carbonyl function of **6** with $NaBH_4$ in EtOH was followed by a sequence of *O*-mesylation ($MeSO_2Cl/Et_3N$) and reduction with $LiBH_4$ in THF to give **7** (81%

in three steps). The benzylic protecting groups of **7** were removed by a catalytic hydrogenation over $Pd(OH)_2$ under an atmospheric pressure of hydrogen to give the final target molecule of **8** in 79% yield. Optical resolution of **8** is now under way.



Scheme 1.

According to mechanistic considerations, the reductive coupling requires one equivalent of SmI_2. We therefore investigated the reactions of *N,N*-dibenzylamide **2b** with an equimolar amount of SmI_2 and found that the proper choice of quenching agent was critical.[7] Poor quenchers such as dilute acid, water or bulky alcohols resulted in the recovery of **2b**, while D_2O and less bulky alcohols gave better combined yields of **4b** and **5b**. However, yield of **4b** was relatively low even under the best quenching conditions (entry 3). It should be emphasized that the cyclized product **4b** is formed from *N,N*-dibenzylamide **2b** only in the reaction employing one equivalent of SmI_2.

Table 2. Effect of Quenching Agent in Reaction of 2b with SmI_2 (1 equiv)[a]

$$\mathbf{2b} \xrightarrow[\text{in HMPA-THF}]{SmI_2\text{ (1 equiv)}} \xrightarrow{\text{Quenching agent}} \mathbf{4b} \text{ and/or } \mathbf{5b}$$

Entry	Quencher	Time/h[b]	4b	5b	Entry	Quencher	Time/h[b]	4b	5b
1	0.1 M HCl aq	1+3	0	15	5	*i*-PrOH	1+3	0	5
2	H_2O	1+3	0	10	6	*tert*-BuOH	1+3	0	6
3	D_2O	1+10[c]	32	62[d]	7	NH_4Cl (solid)	1+3	14	31
4	MeOH	1+3	10	39					

[a] **2b** (0.3 mmol), SmI_2 (0.3 mmol), HMPA (0.3 ml) in THF (3 ml) at room temperature. Recovered **2b**: 73, 72, 0, 35, 74, 67, and 44% for entries 1-7, respectively. [b] Times for reaction + quenching. [c] In min. [d] D-Content at H-2 and H-5 of **5b**: 21% .

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