Double Differentiation in Asymmetric Methoxyselenenylation of *trans*-β-Methylstyrene

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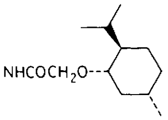
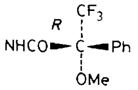
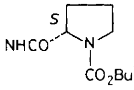
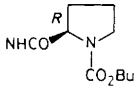
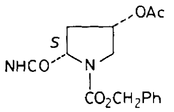
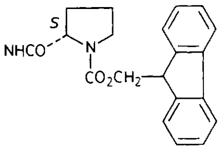
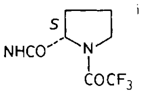
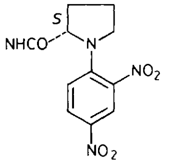
The effect of double differentiation in the reaction between chirally modified optically active di(2′-*N*-substituted amido-2-binaphthyl) diselenide and *trans*-β-methylstyrene has been examined.

The useful asymmetric addition reactions across carbon–carbon double bonds are mechanistically classified exclusively as *cis*- (or *syn*-) addition. Representative examples are: (i) hydrogenation of dehydroamino acid in the presence of a Rh complex,[1] (ii) Brown's hydroboration,[2] (iii) Katsuki and Sharpless epoxidation,[3] and (iv) osmium tetroxide-catalysed bis-hydroxylation.[4] The other mechanistic alternative, the *trans*-addition, has been little investigated to date with much less success.[5]

We have reported previously[6] on the first asymmetric methoxyselenenylation of various alkenes, for which the chirality-inducing agents employed were optically active binaphthyl compounds containing one selenium atom. The highest optical yield (49%) was achieved when styrene was employed as the substrate. Variation of reaction conditions, such as temperature and solvent (ethanol, propan-2-ol), did not improve the optical yield. Asymmetric induction in the *trans*-addition across the C=C bond is, in principle, much less effective than that in the corresponding *cis*-addition. This is because the attack of a nucleophile takes place from the opposite side of the optically modified electrophile (selenenyl cation in this case), far distant from chiral moiety, which may cause significant reduction in optical induction. It was nevertheless expected that the creation of a confined transition state would be a useful approach to improve the optical yield. A possible solution to this would be the introduction of a co-ordinating group, such as an amide group, at the 2′-position in the binaphthyl skeleton. In addition, it was expected that modification of the amide group with a chiral reagent might further enhance optical induction. Described herein is the first example of double differentiation of selenobinaps having the chirally modified amide group in asymmetric *trans*-addition to alkenes.

To examine whether or not attachment of an amide group would indeed enhance the optical yield, (*R*)-di-2-(2′-acetylamino-1,1′-binaphthyl) diselenide (**1b**) was synthesized from (*R*)-2-amino-2′-acetylamino-1,1′-binaphthyl[7] according to a procedure similar to that described previously.[6] When (**1b**) was subjected to the methoxyselenenylation sequence shown in Scheme 1 [namely, addition of an equimolar amount of bromine to a dichloromethane solution of (**1b**), followed by replacement of dichloromethane by methanol, and then addition of an excess amount of *trans*-β-methylstyrene], the methoxyselenide (**3b**) was obtained in 63% isolated yield as

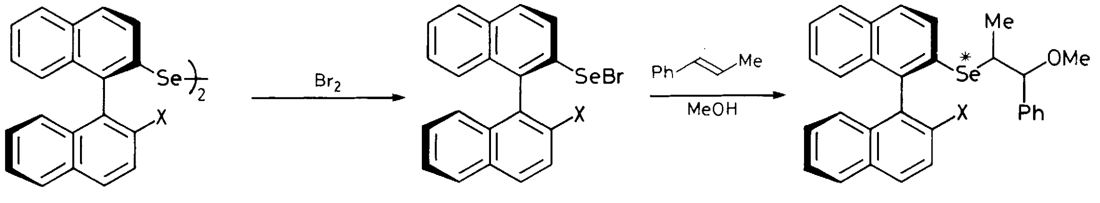
Table 1. Asymmetric methoxyselenenylation of *trans*-β-methylstyrene using 2′-amido derivatives of (*R*)-2-seleno-1,1′-binaphthyl.

		Yield of (**3**)[a]	d.e.[b]	^{1}H NMR[c]/δ	
(**1**)	X	/%	/%	Major	Minor
a[d]	H[d]	49	24	3.15	3.01[e]
b	NHCOMe	63	54	3.17	3.05[f]
c		90	8	3.15	3.09[g]
d		79	8	3.18	3.10[e]
e		90	59	3.16	3.02[g]
f		77	32	3.12	3.00[e]
g		78	43[h]	3.18	2.99[g]
h		83	57	3.13	2.96[e]
i[i]	 [i]	100	67	3.16	3.03[g]
j		87	79	3.23	3.07[g]

[a] Isolated yield of (**3**) after purification by silica gel column chromatography. [b] Diastereoisomeric excess determined by integration of ^{1}H NMR[c] absorptions due to methoxy group. [c] Measured in $CDCl_3$ using tetramethylsilane as internal standard. [d] From ref. 6. [e] Measured at 90 MHz. [f] Measured at 270 MHz. [g] Measured at 500 MHz. [h] Determined by integration of the absorptions at about δ 4.6 due to -C*H*OMe. [i] Commercially available reagent, which is claimed to be optically pure [actually containing about 20% of the (*R*)-isomer], was used without purification.

the only product with a diastereoisomeric excess (d.e.) of 54% after column chromatographic purification on silica gel. The d.e. is substantially enhanced compared with that of an unsubstituted case (**1a**) (24% d.e.: see Table 1). The presence of an amide group was thought to be effective to obtain a high optical yield.

Encouraged by these results, we then proceeded to use a chirally modified amide group as the X group. Compounds (**1c**—**j**) were easily synthesized from (**1b**) by hydrolysis with dioxane-concentrated hydrochloric acid (1 : 1) at reflux temperature followed by reaction with the corresponding chiral acid chlorides. When open-chain chiral amide groups such as (**1c**) and (**1d**) were employed, the d.e. was significantly reduced (8%), contrary to expectation. However, when chiral proline derivatives (**1e**) and (**1f**) were used, the d.e. values were much greater (59 and 32%, respectively) than those for (**1c**) or (**1d**). The chiral reagent (*S*)-(**1e**) gave a better d.e. than (*R*)-(**1f**). The introduction of a second chiral centre in the proline ring did not improve the d.e. (**1g**) (43% d.e.). We then examined the effects of *N*-substituents in the proline ring



(1) (2) (3)

Scheme 1

having the (*S*)-configuration (**1h**, **1i**, and **1j**). In all these cases, the d.e. values were much higher than in the unsubstituted case (**1a**). Among these, (**1j**), which has a 2,4-dinitrophenyl group on the proline nitrogen, gave 79% d.e., which is the highest optical yield ever achieved in the asymmetric *trans*-addition to alkenes and is considered to be a practical level of asymmetric induction. Although we have no definitive explanation at the moment for the high asymmetric induction in the case of (**1j**), the presence of a 2,4-dinitrophenyl group, a quite bulky substituent, could be responsible.

Finally it should be mentioned that these methoxyselenenylation products (**3**) could be readily converted into allyl methyl ethers by oxidation with an excess amount of hydrogen peroxide. For example, (**3b**) or (**3j**), when allowed to react with hydrogen peroxide in dichloromethane at room temperature, provided the selenoxide elimination product, 3-methoxy-3-phenylprop-1-ene, in nearly quantitative yields.

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