Synthesis of Selenium-containing Binaphthyls and their Application to the Asymmetric Ring-opening of Cyclohexene Oxide

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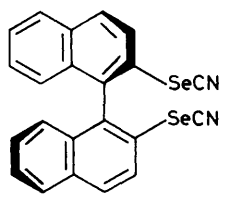
Three novel selenium-containing binaphthyl compounds (**1**—**3**) have been synthesized in optically active form and applied to the asymmetric ring-opening reaction of cyclohexene oxide (**4**), resulting in enantiomeric excesses of between 16 and 50%.

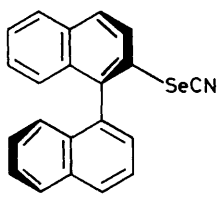
While the importance of organoselenium reagents in selective organic synthesis is well-documented,[1] little attention has been directed to their application to asymmetric synthesis.[2] We now report the first synthesis of three optically active organoselenium reagents possessing axial dissymmetry which are potentially useful for asymmetric reactions such as asymmetric ring-opening of prochiral symmetric epoxides.

The design of asymmetric organoselenium reagents has required some consideration not only because the carbon–selenium bond is relatively weak but also because removal of the selenium moiety by oxidative *syn*-elimination of the selenoxide is not generally regioselective when the organic residue on the selenium atom is not an aromatic ring. As the optimum compromise between dissymmetry and the problem associated with selenoxide elimination, we have concluded that the binaphthyl skeleton[3] would be the best choice of organic residue.

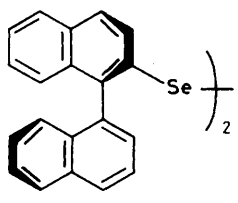
The synthesis of the three selenium-containing binaphthyl compounds (**1**—**3**) has been achieved as follows after several unsuccessful attempts. Optically active *R*-2,2′-diselenocyanato-1,1′-binaphthyl *R*-(**1**)† and *R*-2-selenocyanato-1,1′-binaphthyl *R*-(**2**)† were synthesized from the corresponding diamine[4] and monoamine[5] in 24 and 33% overall yields respectively, by diazotization followed by the reaction with potassium selenocyanate according to the method described previously for the preparation of aryl selenocyanate.[6] Treatment of *R*-(**2**) with sodium hydroxide in ethanol quantitatively yielded bis[*R*-(1,1′-binaphthalene)-2-yl] diselenide *R*-(**3**).†



(**1**)



(**2**)



(**3**)

† *Selected spectroscopic data.* *R*-(**1**), m.p. 153—156 °C, $[\alpha]_D^{25}$ +920° (*c* 0.0012, MeCN), ^{13}C n.m.r. δ 100.7 (SeCN), ^{77}Se n.m.r. 324.9 p.p.m., i.r. 2155 cm^{-1} (CN), mass spec.(*m/z*) 464, u.v. (max) 225 nm (ε 3.4 × 10^4).

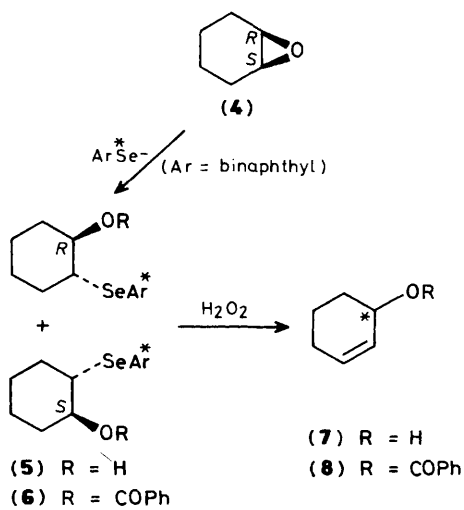
R-(**2**), m.p. 149—151 °C, $[\alpha]_D^{25}$ −61 ° (*c* 0.033, MeCN), ^{13}C n.m.r. δ 102.3 (SeCN), ^{77}Se n.m.r. 310.4 p.p.m., i.r. 2158 cm^{-1} (CN), mass spec.(*m/z*) 459, u.v. (max.) 220 nm (ε 9.2 × 10^4).

R-(**3**), m.p. 156—158 °C, $[\alpha]_D^{25}$ −80 ° (*c* 0.075, MeCN), ^{77}Se n.m.r. 410.2 p.p.m., mass spec. (*m/z*) 666, u.v. (max) 220 nm (ε 1.7 × 10^5).

The ability of the selenobinaps (**1**—**3**) thus prepared to act as chiral inducers was tested by using the prochiral symmetric epoxide, cyclohexane oxide (**4**). It should be noted here that although asymmetric ring-opening reactions of (**4**) have been well-documented and have achieved a useful level of asymmetric induction in many cases when chiral catalysts are used,[7] asymmetric reactions which proceed purely *via* an S_N2 mechanism in the absence of catalysts with more than 10% enantiometric excess (e.e.) have not been reported to date.[8] The reactions reported herein are the first examples of this class which give decent optical yields.

To a mixture of *R*-(**1**) and cyclohexene oxide (**4**) in methanol was added *ca.* 10 fold excess of sodium borohydride. After quenching the reaction mixture with an aqueous solution of ammonium choride, the *trans*-hydroxyselenides (**5**) containing three diastereoisomeric isomers were quantitatively obtained. In order to determine the optical yield of this reaction, benzoylation of (**5**) and oxidative elimination of the seleno-moiety of (**6**) using hydrogen peroxide were successively carried out. 2-Cyclohexenyl benzoate (**8**) was formed in 62% overall yield. Because of difficulty in determining the absolute configuration and the e.e. of (**7**), benzoylation had to be performed. The absolute configuration of (**8**) was determined by the first Cotton effect of its c.d. spectra.[9] H.p.l.c. analysis using an optically active column [CHIRALPAK OT(+), Daicel; methanol as eluent] gave the e.e. of (**8**).

The optical yields obtained under various reaction conditions are listed in Table 1. When the selenolate anion from *R*-(**1**) was used (entries 1—12), *R*-(**8**) was predominantly obtained in all cases. The maximum asymmetric induction was 34% e.e. (entries 3 and 9) and this value was hardly decreased on changing the solvent or metal (Li or Na) of hydride sources, and by the addition of water to the reaction mixture. However, an effect of reaction temperature was observed; the optical yields were higher at room temperature than those obtained at low temperatures.



(**5**) R = H
(**6**) R = COPh
(**7**) R = H
(**8**) R = COPh

Table 1. Asymmetric ring-opening of cyclohexene oxide (**4**) using selenobinaps as chiral inducers.[a]

Entry	Selenide	Solvent	MBH_4[b] M =	Temperature (°C)	e.e.[c] (%)	Selectivity[d]
1	*R*-(**1**)	MeOH	Na	r.t.	33	*R*
2	*R*-(**1**)	1%H_2O/MeOH	Na	r.t.	32	*R*
3	*R*-(**1**)	5%H_2O/MeOH	Na	r.t.	34	*R*
4	*R*-(**1**)	MeOH	Li	r.t.	28	*R*
5	*R*-(**1**)	MeOH	Li	0	18	*R*
6	*R*-(**1**)	5%H_2O/MeOH	Li	0	26	*R*
7	*R*-(**1**)	EtOH	Na	−78	23	*R*
8	*R*-(**1**)	1%H_2O/EtOH	Na	r.t.	28	*R*
9	*R*-(**1**)	EtOH	Li	r.t.	34	*R*
10	*R*-(**1**)	Pr^iOH	Na	−78	16	*R*
11	*R*-(**1**)	Bu^nOH	Na	r.t.	29	*R*
12	*R*-(**1**)	Et_2O	Na	0	17	*R*
13	*R*-(**2**)	MeOH	Na	r.t.	45	*S*
14	*R*-(**2**)	MeOH	Li	r.t.	47	*S*
15	*R*-(**3**)	EtOH	Na	r.t.	50	*S*

[a] See text for reaction conditions. [b] Metal hydride (M = metal) employed for reduction of the selenides. [c] Enantiomeric excess (e.e.) was determined by liquid chromatography (see text for details). Chemical yields of these reactions were quantitative in all cases. [d] Absolute configuration of excess enantiomer of (**8**) produced.

When the selenolate anions generated from *R*-(**2**) or *R*-(**3**) (entries 13—15) were employed, *S*-(**8**) was predominantly obtained with increased asymmetric induction of up to *ca.* 50% e.e. Although *R*-(**2**) and *R*-(**3**) exhibited similar values of asymmetric recognition, it should be noted that the *S* enantioselectivity shown by these selenides is opposite to the enantioselectivity shown by *R*-(**1**). Such reversal of enantioselectivity between (**1**) and (**2**) [or (**3**)] cannot be explained at the moment.

We are now making efforts to enhance the enantiomeric excess of this reaction and to apply these reagents (**1**—**3**) to new types of asymmetric reactions.

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