The First Example of Enantioselective Carbenoid Addition to Organochalcogen Atoms: Application to [2,3]Sigmatropic Rearrangement of Allylic Chalcogen Ylides

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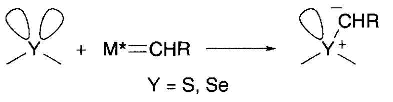
In the presence of a catalytic amount of chiral copper(I) or rhodium(II) compounds the enantioselective addition of a carbenoid, derived from ethyl diazoacetate, to chalcogen atoms of aryl cinnamyl chalcogenides affords a diastereoisomeric mixture of ethyl 2-arylchalcogeno-3-phenylpent-4-enoates *via* [2,3]sigmatropic rearrangement of the intermediate chalcogen ylide with up to 41% ee.

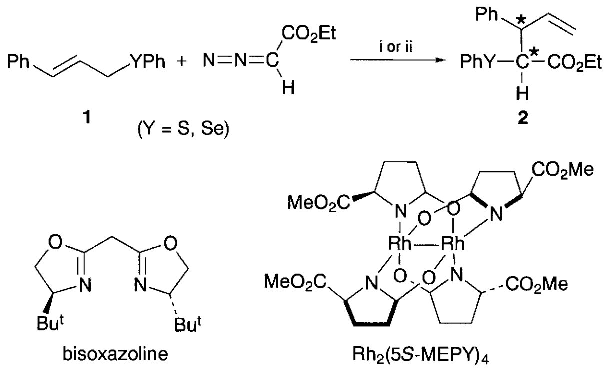
We have been interested in the application of optically active organochalcogen compounds having a chiral centre on a chalcogen atom such as chiral sulfoxide,[1] selenoxide,[2] telluroxide[3] and selenimide[4] to organic synthesis. Next, attention was paid to the chiral chalcogen ylides which have been widely used for the preparation of epoxides[5] and cyclopropanes.[6] The method for the preparation of chiral chalcogen ylides, however, has so far been limited only to a diastereoselective reaction for obtaining sulfur ylides.[7] Recently, a direct diastereoselective formation of sulfur ylides by the rhodium-catalysed decomposition of diazo compounds in the presence of sulfides was also reported.[8] Since the chiral copper-[9] or rhodium-catalysed[10] enantioselective cyclopropanation of alkenes with diazo compounds has been studied extensively and high selectivities obtained, we chose this asymmetric catalytic system as a carbenoid source for the enantioselective preparation of a chiral chalcogen ylide (Scheme 1), the results of which are reported here.[11]

First, (*E*)-cinnamyl phenyl sulfide was treated with ethyl diazoacetate in a variety of solvents at 0–15 °C for 20–24 h in the presence of a catalytic amount of copper(I) salt and bisoxazoline (5 mol%).[9] A diastereoisomeric mixture (*ca.* 3 : 2–2 : 1) of ethyl 2-phenylsulfanyl-3-phenylpent-4-enoates (**2**; Y = S) having a new carbon–carbon bond was produced (Scheme 2), but only in moderate enantioselectivity (Table 1, runs 1–3).† At higher temperatures the reaction proceeded more smoothly, but the product **2** was racemic. When (*E*)-cinnamyl phenyl selenide was used in place of the sulfide, a slightly better enantioselectivity was obtained in **2** (Y = Se, Table 1, run 4). The introduction of an electron-withdrawing group such as *o*-nitro or *o*-trifluoromethyl into the phenylselenium moiety improved the enantioselectivity of the corresponding products (Table 1, runs 5 and 6),[12] while the introduction of an electron-donating group such as *o*-methoxy and the use of a ferrocenylselenium moiety instead of phenylselenium inhibited the reaction completely. Next, similar reactions were carried out by employing the Doyle catalyst, $Rh_2(5S\text{-MEPY})_4$,[10] (1 mol%) in place of the chiral copper(I) catalyst. At 15 °C the reaction was quite slow, but at 40 °C it proceeded smoothly and a slightly better enantioselectivity (up to 41% ee) was observed compared with that obtained using the copper catalyst (up to 34% ee; Table 1, runs 7 and 8).

The plausible reaction pathway of this catalytic reaction is shown in Scheme 3. Since it is known that the chirality transfer from sulfur to carbon in a sulfur ylide *via* [2,3]sigmatropic rearrangement proceeds without loss of optical purity[13] and also that racemization does not occur at a chiral selenium ylide,[14] the observed enantioselectivity of the products might depend on the initial step of carbenoid addition to the chalcogen atoms. To our knowledge, this is the first example of enantioselective carbenoid addition to chalcogen atoms of prochiral organic chalcogenides. The chirality transfer from the produced chiral chalcogen ylide *via* [2,3]sigmatropic rearrangement provides a new methodology for carbon–carbon bond formation with chiral induction at both carbon centres.



Scheme 1 Enantioselective carbenoid addition to chalcogen atoms

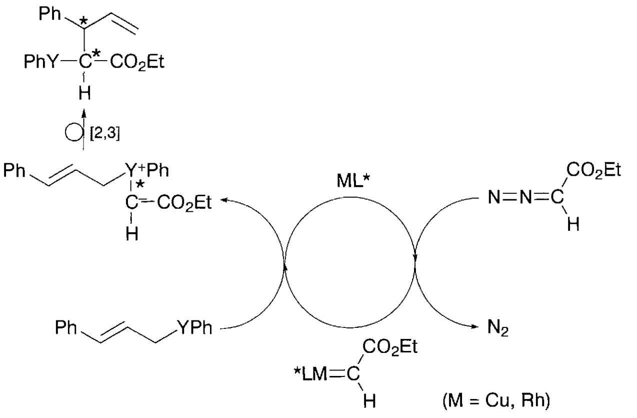


Scheme 2 *Reagents and conditions*: i, cat. Cu^I: CuOTf (5 mol%) + bisoxazoline (5 mol%); ii, cat. Rh^{II}: $Rh_2(5S\text{-MEPY})_4$ (1 mol%). Tf = SO_2CF_3.

Table 1 Enantioselective carbenoid addition to organochalcogen atoms

Run[a]	Y	Catalyst[b]	Solvent	T/°C (t/h)	Yield (%)[c]	Diastereoisomeric ratio of **2**[d] (ee, %[e])
1	S	Cu	$CHCl_3$	15 (20)	45	60:40 (6, 15)
2	S	Cu	Benzene	15 (24)	68	66:34 (13, 11)
3	S	Cu	Toluene	0 (24)	41	65:35 (20, 14)
4	Se	Cu	$CHCl_3$	0 (24)	71	66:34 (22, 32)
5[f]	Se	Cu	$CHCl_3$	0 (24)	55	53:47 (13, 34)
6[g]	Se	Cu	$CHCl_3$	0 (24)	35	69:31 (8, 30)
7	S	Rh	CH_2Cl_2	40 (20)	49	60:40 (18, 17)
8	Se	Rh	CH_2Cl_2	40 (20)	65	58:42 (25, 41)
9	Se	Rh	CH_2Cl_2	15 (20)	10	—[h]

[a] All the reactions were carried out with cinnamyl phenyl chalcogenide (0.22 mmol) and ethyl diazoacetate (0.35 mmol). [b] Cu: CuOTf (5 mol%) and bisoxazoline (5 mol%) were used. Rh: $Rh_2(5S\text{-MEPY})_4$ (1 mol%) was used. [c] Isolated yield. [d] Determined by ^1H NMR. [e] Determined by ^1H NMR using $Eu(hfc)_3$. [f] (*E*)-Cinnamyl *o*-nitrophenyl selenide was used. [g] (*E*)-Cinnamyl *o*-trifluoromethyl- phenyl selenide was used. [h] Not determined.



Scheme 3 Plausible reaction pathway

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Footnote

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† General procedure: A mixture of CuOTf (0.01 mmol) and bisoxazoline (0.01 mmol) in $CHCl_3$ (2 cm^3) was stirred for 1 h at room temp. under N_2 and then cinnamyl phenyl sulfide (0.22 mmol) was added. A solution of ethyl diazoacetate (0.35 mmol) in $CHCl_3$ (2 cm^3) was then added to the reaction mixture at 0 °C *via* syringe pump over 12–15 h. After the addition, the reaction mixture was stirred for several hours, quenched with brine and then extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$) and evaporated to dryness. The oily residue obtained was purified by preparative TLC on SiO_2 with ethyl acetate–hexane (10%) as eluent to afford compound **2** (Y = S). The ratio of the two diastereoisomers of **2** (Y = S) was determined by ^{1}H NMR by comparing the integral ratio of the methyl protons of an ethyl group, and each ee value of the diastereoisomers was similarly determined by ^{1}H NMR in the presence of Eu(hfc)$_3$.

Satisfactory spectral data was obtained for **2** (Y = S). *Selected spectroscopic data*: ^{1}H NMR (270 MHz, $CDCl_3$) (major isomer) δ 0.87 (3 H, t, J = 7.29 Hz), 3.80 (2 H, q, J = 7.29 Hz), 4.00 (1 H, d, J = 11.3 Hz), 4.2 (1 H, m), 5.1–5.2 (2 H, m), 5.9–6.2 (1 H, m) and 7.2–7.6 (10 H, m); (minor isomer) δ 1.15 (3 H, t, J = 7.29 Hz), 4.00 (1 H, d, J = 11.0 Hz) and 4.08 (2 H, q, J = 7.29 Hz).

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