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SYNTHESIS OF ENANTIOMERICALLY PURE (Z)-2-HALOALKENYL SULFOXIDES

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Summary: Efficient procedures to prepare enantiomerically pure (Z)-2-haloalkenyl sulfoxides from alkynyl sulfoxides are described.

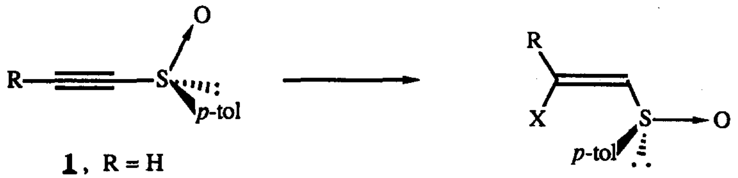
Enantiomerically pure vinyl sulfoxides are useful synthetic intermediates[1] and, accordingly, their chemistry is receiving a great deal of attention in recent years.[2] In connection with our interest in sulfur chemistry[3] we sought efficient stereo- and enantiocontrolled routes to (Z)-2-haloalkenyl sulfoxides. We considered that these compounds should allow for the preparation of a variety of (Z)-vinylsulfoxides (e.g., dienyl sulfoxides) via transition metal mediated couplings and would thus complement their corresponding (*E*) isomers.[4,5] Recent disclosures from several laboratories[6] prompt us to report our preliminary results concerning the first synthesis of enantiomerically pure (Z)-2-haloalkenyl sulfoxides.

We envisioned that the readily available enantiomerically pure α,β-acetylenic sulfoxides[7] could be adequate precursors for the title compounds. Therefore, we tested several mild halogenated Lewis acids[8], expecting that coordination of the sulfinyl oxygen with the metal center of the acid would facilitate transfer of a halide atom to the β-position of the alkynyl sulfoxide. After several fruitless attempts[9], we found that treatment of (+)-(*R*)-ethynyl *p*-tolylsulfoxide with 3.0 equivalents of ZnI_2 in anhydrous benzene (room temp., 15 hr.; then dil. $NaHCO_3$, followed by standard work-up and flash chromatography) resulted in an excellent yield of the pure (Z)-iodovinyl sulfoxide 3 (J_{cis} = 7.3 Hz). The enantiomeric purity of the product was judged to be 100% after analysis of the ^{1}H NMR spectrum in the presence of Eu(hfc)$_3$. Furthermore, none of the (*E*) isomer was detected in the ^{1}H NMR spectrum of the crude reaction mixture.

The corresponding bromo and chloro analogs were prepared similarly in good yields; reaction times of 30 and 72 hr., respectively, were required to effect the transformations (Table 1; entries 2, 3). Encouraged by these results, we examined a more substituted substrate, (+)-(*S*)-1-hexynyl *p*-tolylsulfoxide **2**; unfortunately we found no reaction with ZnI_2 at ambient temperature and decomposition under harsher conditions. However, at this stage we became aware of Marek's procedure for effecting a related transformation on propargyl esters[10] and, indeed, (Z)-iodovinyl sulfoxide 6 was obtained in good yield under these conditions (NaI, AcOH, reflux, 5 min.). This procedure could also be applied to the unsubstituted substrate **1** (NaI, AcOH, room temp., 90 min.) with comparable yield and optical purity to the ZnI_2 method (Table 1; entry 5).

In conclusion, efficient routes to enantiomerically pure (Z)-2-haloalkenyl sulfoxides have been developed. The use of these synthons in stereocontrolled transition metal mediated couplings is currently being explored in our laboratories.

Table 1. Synthesis of (Z)-2-Haloalkenyl Sulfoxides



1, R = H

2, R = *n*-Bu

3 - **6**

Entry	Substrate	Reagent[a]	Product (X)	Yield[b] ($[\alpha]_D$)[c]
1	**1**	ZnI_2	**3** (I)	87 % (-483.3)
2	**1**	$ZnBr_2$	**4** (Br)	75 % (-473.5)
3	**1**	$ZnCl_2$	**5** (Cl)	83 % (-453.9)
4	**2**	NaI / AcOH	**6** (I)	82 % (-294.5)
5	**1**	NaI / AcOH	**3** (I)	87 % (-477.4)

[a] Recently purchased reagents were used, without further purification.

[b] Yields of pure products, isolated by flash chromatography.

[c] In $CHCl_3$ at 25°C.

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