Published on 01 January 1989. Downloaded by University of Chicago on 26/10/2014 14:41:15.

P-Chiral Thioxaphosphoranesulphenyl Chlorides [RR¹P(S)SCI]. Unique Stereochemical Probe for the Nucleophilic Displacements at the Dico-ordinate Sulphur

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P-Chiral thioxaphosphoranesulphenyl chlorides [RR¹P(S)SCI] (R = L-menthoxy, R¹ = EtO) are synthesized in high yield and with optical purity, they are shown to undergo nucleophilic attack at the dico-ordinate sulphur centre by a synchronous mechanism.

Phosphoranesulphenyl halides of the general formula $RR^{1}P(Y)SX$ and their selenium analogues $RR^{1}P(Y)SeX$ (X = Cl, Br; Y = O, S) have been shown to be useful intermediates for access to many new classes of compounds containing phosphorus, sulphur, or selenium centres. Sulphenyl chlorides of type (3) are very reactive towards C, N, O, and P nucleophiles. Their chemical behaviour is similar to other compounds of dico-ordinate sulphur with the general formula R-S-X where X is a good leaving group.¹

Previous mechanistic studies on the nucleophilic displacement at a dico-ordinate sulphur atom, based on kinetics and free energy correlations, have led to the general belief that such substitutions normally entail a trigonal bipyramidal intermediate (or transition state) in which the entering and leaving groups occupy two apical positions.² In this communication, we demonstrate that important mechanistic information about the nature of bond breaking and bond formation at the dico-ordinate sulphur can be disclosed using P-chiral thioxaphosphoranesulphenyl chlorides RR¹P(S)SCl (3).

The achiral chlorides (3) ($R = R^1$) recently became readily available from the corresponding bromides *via* thioxaphosphoranealkylsulphenates $R_2P(S)SOR'$ in reaction with trimethylsilylchloride³ or chlorination of mixed anhydrides of phosphorodithioic and carboxylic acids.⁴ Neither of these methods was found suitable for the synthesis of their chiral analogues. The strategy shown in Scheme 1 was employed for the stereoselective synthesis of the ethoxy-L-menthoxythioxaphosphoranesulphenyl chlorides (R)_P- and (S)_P-(3).

The morpholidate (2), which is a 1:1 mixture of diastereoisomers $(R)_P$ and $(S)_P$, was readily separated by crystallization into pure components.[†] The crucial step in the synthesis of chiral $(R)_P$ -(3) is the conversion of the morpholidate $(R)_P$ -(2) into the sulphenyl chloride $(R)_P$ -(3), by action of hydrogen chloride [equation (1)].⁵ Our numerous attempts to convert (2) or similar compounds into (3) ended with relatively low chemical yields and 1:1 mixtures of $(R)_P$ and $(S)_P$ diastereoisomers. Chlorides (3) have been obtained in excellent yield in this laboratory⁶ when sulphenamides of type (2) were allowed



[†] The absolute configuration of diastereoisomeric sulphenamides $(R)_{P}$ and $(S)_{P}$ -(2) was established in collaboration with Dr. G. Palenik and Dr. A. Kozioł by X-ray crystallography (to be published).

to react with the hydrogen chloride produced in situ from trimethylsilyl chloride and ethanol. Following this procedure the sulphenamides $(R)_{P}$ and $(S)_{P}$ -(2) form the desired thioxaphosphoranesulphenyl chlorides $(R)_{P}$ and $(S)_{P}$ -(3) in high stereoselectivity (Scheme 2).

$$R_2P(S)S-NR'_2 + 2HCl \rightarrow R_2P(S)S-Cl + R'_2NH \cdot HCl (1)$$

Successful stereoselective synthesis of configurationally stable sulphenyl chlorides $(R)_{P}$ - and $(S)_{P}$ -(3) demonstrates an absence of halotropy; a symmetrical structure in which the chloride atom is bonded to both sulphur atoms is not involved, since in this type of structure the phosphorus atom is achiral.









P-Chiral sulphenyl chlorides (3) serve as a stereochemical probe for displacement reactions occurring at dico-ordinate sulphur in this type of compound. Only synchronous processes of bond breaking and bond formation at the S centre will be accompanied by retention of configuration at the chiral P-centre; in contrast, a dissociative process, either ionic or radical, should result in the loss of stereoselectivity in the course of nucleophilic displacement.

To illustrate this, the P-chiral chlorides (3) were allowed to react with secondary amines such as morpholine (Scheme 3).‡

All these displacements reactions proceed with almost complete stereochemical integrity at the phosphorus atom. These observations speak for a synchronous mechanism of bond breaking and bond formation during the nucleophilic displacement at the dico-ordinate sulphur atom. This statement is also valid for the reaction of sulphenamides (2) with hydrogen chloride. Even though the achiral nature of dicoordinate sulphur precludes any direct investigations of the stereochemistry of nucleophilic substitution at sulphenyl sulphur, our stereochemical results corroborate with mechanistic views derived from the kinetic studies.²

 \ddagger Similar behaviour was observed in the case of $(R)_P$ chloride R(Ph)P(S)SCl in reactions with morpholine and dicyclohexylamine.

This work was supported by the Polish Academy of Sciences (project CPBP 01.13).

Received, 17th May 1989; Com. 9/02080B

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