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COMMUNICATION

Fluorinative Hydrolysis of Phosphorothioic Acid Esters with a Binaphthyl Group Through Axis-to-Center Chirality Transfer Leading to the Formation of *P*-Chiral Phosphorothioic Monofluoridic Acid Salts[†]

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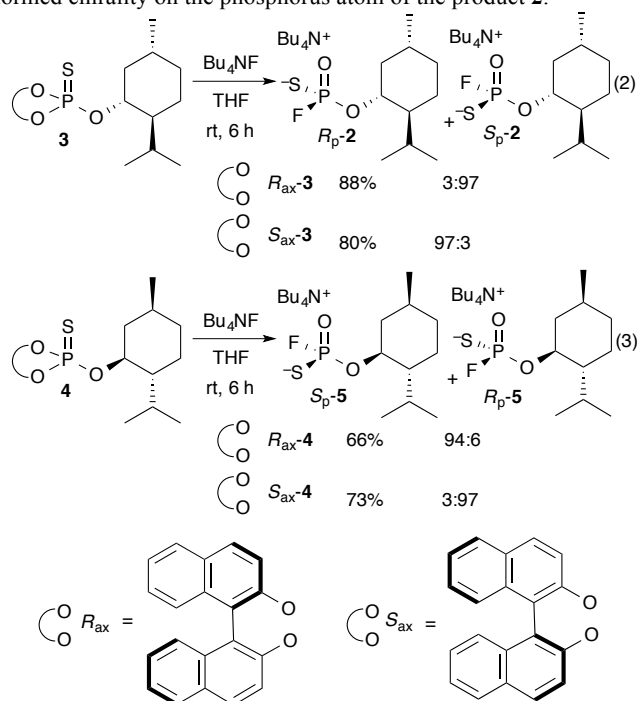
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Asymmetric synthesis of *P*-chiral phosphorothioic monofluoridic acid ammonium salts was achieved via axis-to-center chirality transfer reactions by using phosphorothioic acid *O*-esters with a binaphthyl group, and the absolute stereochemistry of the salts was determined by X-ray analyses and by comparison of their CD spectra.

P-Chiral organophosphorus compounds are important because their skeletons are found in biologically active compounds¹ and because they can be used as optically active ligands and chiral auxiliaries.² Many types of reactions have been reported for their synthesis, including diastereoselective substitution reactions at the phosphorus carbon atoms and the enantioselective deprotonation of achiral organophosphorus compounds.³ Meanwhile, reactions involving the transfer of stereochemical information from chiral centers and axes to prochiral moieties are efficient methods for the synthesis of enantioenriched compounds. In particular, axial chirality transfer reactions of allenes have been developed in great depth.⁴ Binaphthyl groups having axial chirality are also potentially useful as a chiral origin for the transfer of chirality to prochiral moieties. In our recent studies on organochalcogen compounds,⁵ we found that fluoride ion shows high affinity toward the phosphorus atom of phosphoric acid esters and their selenium isologues.⁶ Herein we report axis-to-center chirality transfer reactions of phosphorothioic acid *O*-esters with a binaphthyl group leading to the formation of optically active *P*-chiral phosphorothioic monofluoridic acid ammonium salts.

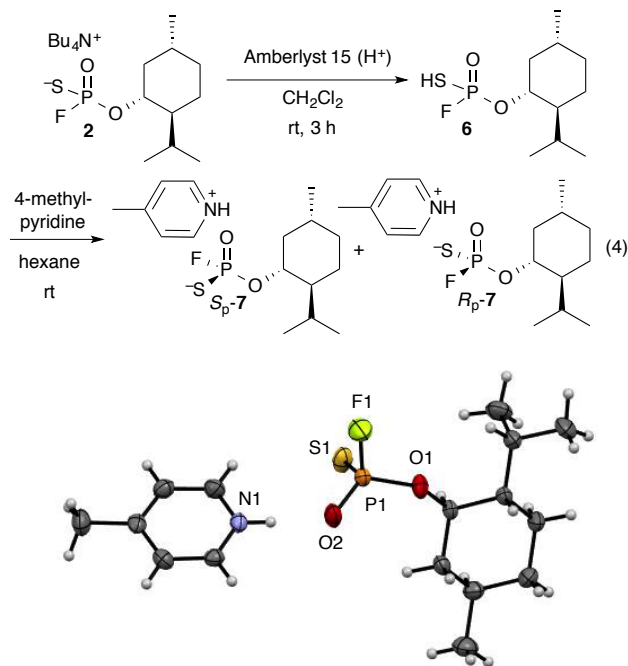
First, we reacted phosphorothioic acid *O,O*-diphenyl, *O*-alkyl ester **1** with a THF solution of Bu₄NF (eqn (1)),⁵ in a series of studies on organochalcogen compounds.⁶ Aqueous workup gave a mixture of two diastereomers of phosphorothioic monofluoridic acid ammonium salts *R_p*-**2** and *S_p*-**2**⁷ in a nearly equal ratio in low yields. In this case, fluorinative hydrolysis of **1** took place, but the chirality on a menthyloxy group of **1** had very little influence on the newly formed chirality on the phosphorus atom of the product **2**.



Phosphorothioic acid esters with a binaphthyl group were then used in fluorinative hydrolysis (eqns (2) and (3)). A similar fluorinative hydrolysis of **3**⁸ and **4** with Bu₄NF proceeded highly

efficiently to give the corresponding salts **2** and **5** with high diastereoselectivity. The stereochemistry of **2** and **5** was controlled by the axial chirality of binaphthyl groups in the starting materials **3** and **4**, and the reaction was noted to be stereospecific, e.g., S_{ax} -**4**, which was the enantiomer of R_{ax} -**3**, gave R_p -**5**, which was the enantiomer of S_p -**2**.

Salt **2** was converted to acid **6** upon treatment with Amberlyst 15 (H^+), but **6** was labile and was treated with tertiary amines to give ammonium salts (eqn (4)). Among them, the use of 4-methylpyridine gave salts S_p -**7** and R_p -**7** as fine crystals. During the acid hydrolysis of **2** and neutralization of acid **6**, the diastereomeric ratio of **2**, **6**, and **7** was retained.



The absolute configuration at the phosphorus center of salt S_p -**7** was unequivocally determined by X-ray analyses (Figure 1). Structurally, the phosphorus atom in S_p -**7** adopts a slightly deviated tetrahedral geometry. The bond length of P(1)–O(2) is clearly shorter than that of P(1)–O(1) and is close to the reported bond length for a formal P=O double bond (~ 1.49 Å).⁹ This implied that the negative charge on the S–P–O moiety is localized on the sulfur atom. Nevertheless, the bond length of the P(1)–S(1) bond is the nearly midway between those of formal P–S single bonds (~ 2.1 Å)¹⁰ and P=S double bonds (~ 1.9 Å).¹¹ In fluorinative hydrolysis (eqns (2) and (3)), the R_{ax} and S_{ax} configurations in **3** and **4** were transferred to S_p and R_p configurations in the products, respectively. CD spectra of salts S_p -**7** and R_p -**7** and of S_p -**2**, R_p -**2**, S_p -**5**, and R_p -**5** are shown in Figures 2 and 3, respectively.

Compound S_p -**7** gave a CD curve with a maximum positive peak at 220 nm, whereas its diastereomer R_p -**7** gave a maximum positive peak at 235 nm. These peaks were clearly due to the chirality at the phosphorus atoms in **7**, since diastereomers S_p -**7** and R_p -**7** possessed an identical menthylloxy group. Additionally, the reported CD spectra of optically active menthols show peaks only at greater than

250 nm.¹² These trends in the CD spectra were identical to those of S_p -**2** and R_p -**2** and to those of their enantiomers R_p -**5** and S_p -**5**.

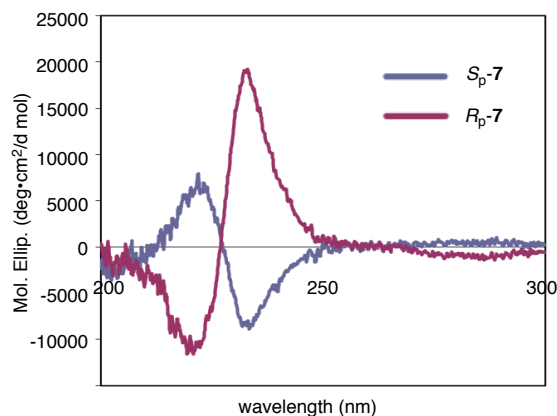


Figure 2. CD spectra of S_p -**7** and R_p -**7**

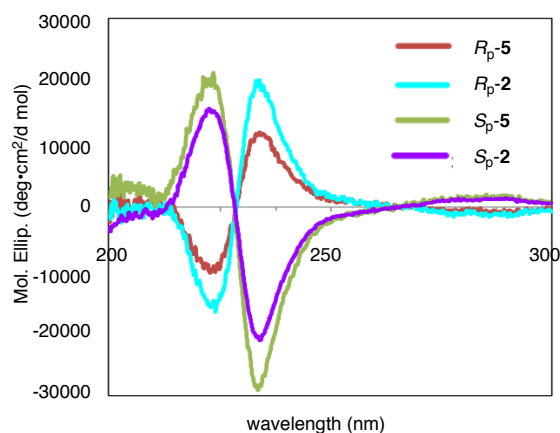
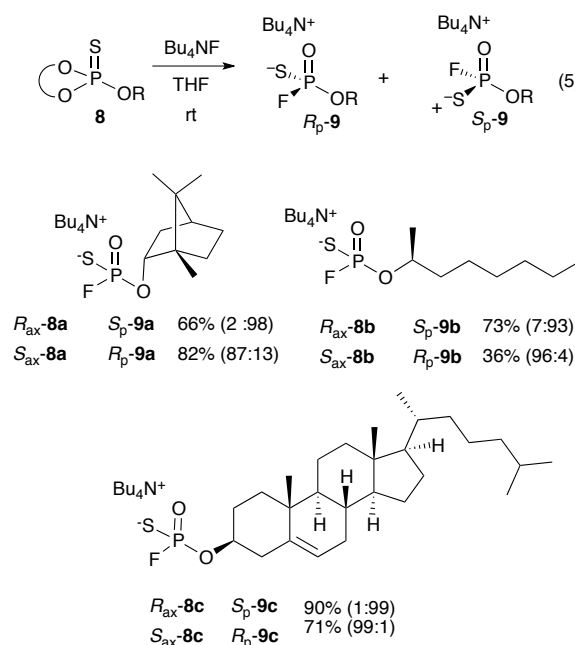


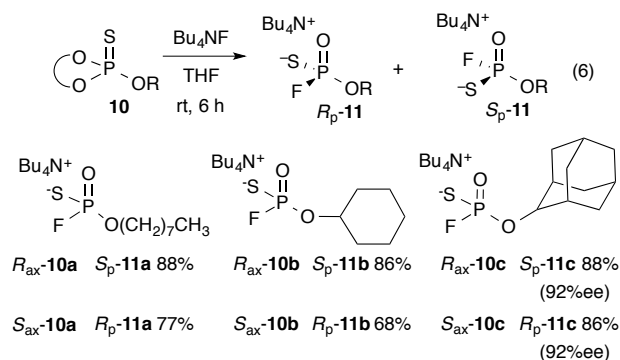
Figure 3. CD spectra of S_p -**2**, R_p -**2**, S_p -**5**, and R_p -**5**



To better understand the efficiency of the axis-to-central chirality transfer reaction, phosphorothioic acid esters **8** derived from chiral optically active alcohols such as (–)-borneol, *S*-2-octanol,

and cholesterol were reacted with Bu_4NF (eqn (5)). In all cases, fluorinative hydrolysis proceeded with high efficiency to give the corresponding products **9** with high diastereoselectivity. A slight difference in diastereoselectivity was observed, and cholesteryl esters showed the highest selectivity. This implied that the central chirality in the alkoxy groups may also affect the selectivity, at least to some extent. The absolute configuration at the phosphorus atom was analogized based on a comparison of their CD spectra (details, see electronic Supporting Information).

Finally, to evaluate the applicability of this highly diastereoselective chirality transfer reaction to an enantioselective version, phosphorothioic acid esters **10** derived from achiral alcohols such as 1-octanol, cyclohexanol and 2-adamantanol were subjected to the fluorinative hydrolysis (eqn (6)). The products **11** derived from opposite enantiomers showed mirror-image of CD spectra (Figures S1–S6), indicating that the reaction of **10** with Bu_4NF proceeded in an enantioselective fashion. To determine the enantiomeric excess of **11c**, several Daicel Chiralcel columns were used. As a result, Chiralcel OZ-H was found to discriminate the enantiomers of **11c**, as shown in Figure S7 and S8. The analytical results showed that the reaction in eqn (6) proceeded with relatively high enantioselectivity.



Conclusions

In summary, we have demonstrated the first example of the fluorinative hydrolysis of phosphorothioic acid esters with a binaphthyl group. The reaction proceeded in a stereospecific manner, and the axial chirality of the binaphthyl group was highly efficiently transferred to the newly formed central chirality in the phosphorothioic monofluoridic acid salts. Although further studies are necessary to determine the mechanistic details, an *R* configuration on the binaphthyl group was transferred to an *S* configuration at the phosphorus atom, and vice versa.

Notes and references

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† Electronic supplementary information (ESI) available: Materials including experimental procedures, NMR spectra of all new products and X-ray data for $S_{\text{p}}\text{-7}$. CCDC-1012135. For ESI and crystallographic data in CIF or other electronic formats see DOI:

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