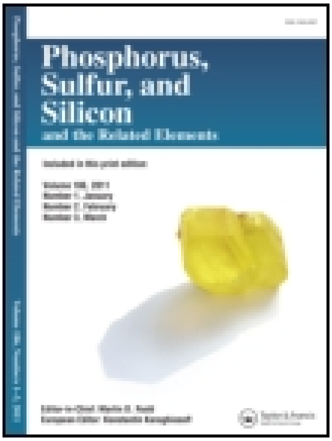

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Chiral P-Heterocycles: Efficient Method for the Resolution of 3-Methyl-3-phospholene 1-Oxides

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Chiral P-Heterocycles: Efficient Method for the Resolution of 3-Methyl-3-phospholene 1-Oxides

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The enantiomers of 1-aryl-, 1-alkyl- and 1-alkoxy-3-methyl-3-phospholene 1-oxides were separated in good yields and in high enantiomeric excesses (up to >99% ee) by resolution via formation of diastereomeric complexes with (–)-(4R,5R)-4,5-bis(diphenylhydroxymethyl)-2,2-dimethyldioxolane (TADDOL) or (–)-(2R,3R)-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-1,4-dioxaspiro[4.5]decan-2,3-dimethanol.

Keywords Chiral P-heterocycles; diastereomeric complex formation; resolution; TADDOL

INTRODUCTION

Phosphine oxides form an important class of phosphorus compounds, since they are precursors of the corresponding phosphines which, in turn, may serve as ligands in transition metal complexes that can be applied in several highly efficient homogenous catalytic processes.[1,2] Five-membered P-heterocycles, such as 1-substituted-3-phospholene 1-oxides (e.g., **1**) are of synthetic importance, as they can be used as starting materials in the preparation of a variety

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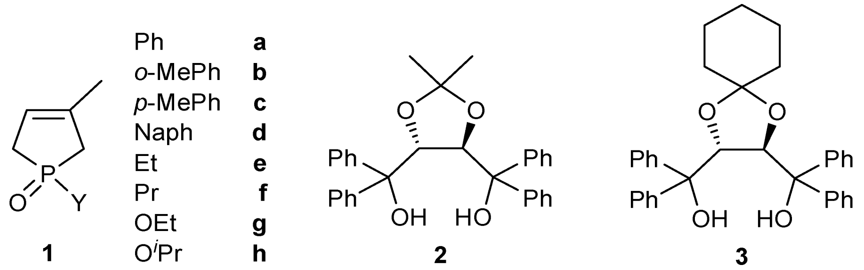

FIGURE 1 Racemic phospholene oxides (**1**) and the resolving agents (**2** and **3**).

of five-, six-, seven-, and eight-membered P-heterocycles including bridged derivatives.[3–6] Pietrusiewicz and coworkers reported several methods for the preparation of optically pure 1-phenyl-2- or 1-phenyl-3-phospholene 1-oxides and their epoxide derivatives based on dipolar cycloaddition,[7]enantioselective desymmetrization,[8–10] and quaternerization of their deoxigenated derivatives with a chiral reactant.[10]A simple procedure for the resolution of 1-substituted-3-methyl-3-phospholene 1-oxides (**1**) by separation of the diastereomeric complexes formed by the interaction of (*R*)-**1** or (*S*)-**1** with chiral hosts, such as TADDOL **2** or TADDOL analogue **3**[11] is described (Figure 1).[12]

Racemic 1-substituted-3-methyl-3-phospholene 1-oxides (**1**) were resolved by adding half equivalent of (–)-TADDOL (**2**) or its derivatives (**3**) to their hot ethyl acetate solution and precipitating an 1:1 crystalline complexes (+ or −)-**1**·(–)-**2** by the addition of hexane. After two recrystallizations from a mixture of ethyl acetate–hexane and flash chromatography on a silica gel, complexes (+ or −)-**1a–h** were regenerated and analyzed on a chiral HPLC column (Chiralpack AD) or on a chiral GC column (BETA DEC$^{\text{TM}}$). The optical purities of (+ or −)-**1a–h** are shown in Table I. As it can be seen, in all cases resolution took place and quite often we could separate the optically pure compound.

The complete resolution procedure is shown for **1a** with TADDOL **2** in Figure 2.

TABLE I Optical Purities of P-Heterocycles (1a–h) After Resolution with 2 or 3

	Optical purity of the products [ee %]							
Resolving agent	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**
2	97	57	69	70	24	95	44	>99
3	>99	>99	>99	>99	58	89*	95	>99

*for the 1:2 complex formed by the use of one equivalent of **3**.

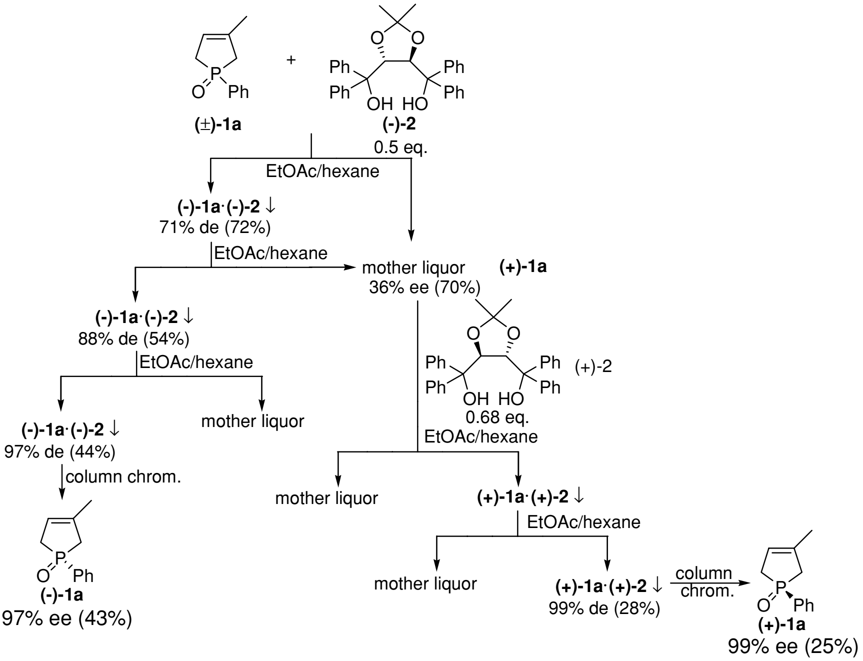

FIGURE 2 The complete resolution procedure of **1a** with TADDOL **2**.

To clarify the absolute configuration of **1a**, **1e**, and **1f**, (−)-**1a**·(−)-**2**·acetone, (+)-**1e**·(−)-**3** and (+)-**1f**·(−)-**2** were subjected to single crystal X-ray analysis. The absolute configuration of (−)-**1a**, (+)-**1e**, and (+)-**1f**, was found to be *S*, *R*, and *R*, respectively. X-ray structure showed inter- and intramolecular H-bridges which held the supramolecular formation together. These short contacts are shown for the case of (−)-**1a**·(−)-**2**·acetone on Figure 3.

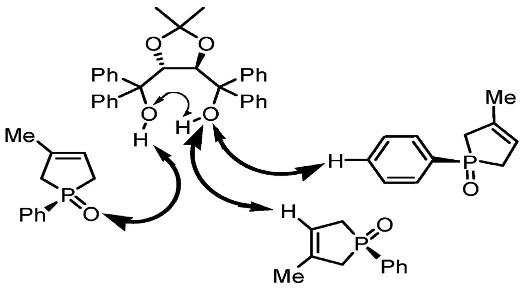

FIGURE 3 Inter- and intramolecular H-bridges in the crystall structure of (−)-**1a**·(−)-**2**·acetone.

The resolution procedure described above is the first example for the resolution of a cyclic phosphine oxide or a phosphinate via inclusion complex formation. The method comprises crystallization with TADDOL **2** or its analogue **3**, recrystallization of the supramolecular formation and the regeneration of **1**. Our procedure form a simple and convenient method for the preparation of both enantiomers with high enantiomeric purity. The method introduced may be suitable for the resolution of other P-heterocycles or acyclic P-compounds with P = O function, as well.

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