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Resolution of 1-substituted-3-methyl-3-phospholene 1-oxides by molecular complex formation with TADDOL derivatives☆

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Dedicated to Professor Dr. Lajos Novák (Budapest University of Technology and Economics) on the occasion of his 70th birthday

Abstract—The antipodes of 1-aryl-, 1-alkyl- and 1-alkoxy-3-methyl-3-phospholene 1-oxides **1a**–**h** and 1-phenyl-3-methyl-3-phospholene 1-sulfide **1i** were separated in good yields and high enantiomeric excesses (up to >99% ee) by resolution via formation of diastereomeric complexes with either (−)-(4*R*,5*R*)-4,5-bis(diphenylhydroxymethyl)-2,2-dimethyldioxolane **2** (TADDOL) or (−)-(2*R*,3*R*)-α,α,α′,α′-tetraphenyl-1,4-dioxaspiro[4.5]decan-2,3-dimethanol **3**. The stereostructure of the supramolecular formations and the absolute configurations of the 3-phospholene oxides **1a**, **1e** and **1f** were elucidated by single crystal X-ray crystallography. CD spectroscopy was also useful in determining the absolute configurations of some phospholene oxides **1b**, **1c**, **1g** and **1h**.

1. Introduction

Chiral phosphine oxides have been valuable targets for synthetic chemists since they provide the corresponding phosphines after deoxygenation, which can be used as ligands in transition metal catalysts.[2,3] Since P-chiral organophosphorus compounds cannot be found in enantiomeric forms in the natural pool of chirality,[4] resolution and asymmetric synthesis form the primary source of such compounds.[2,5] Despite the large number of enantioselective syntheses for the preparation of a single enantiomer to achieve industrial and scientific goals, the separation and splitting of racemates into pure enantiomers will always require efforts from organic chemists.[6,7] The methods described in the literature on the resolution of P(III) and P(V) phosphorus compounds are based on the formation of separable covalent diastereomers, diastereomeric salts, diastereomeric transition metal complexes and molecular complexes, as well as chemical and enzymatic kinetic resolution.[2] Direct acid–base resolutions of *O*-alkyl-phenylphosphonothioic acid,[8,9] thiophosphinic acid,[10] as well as a carboxylic acid derivative of a phosphine sulfide,[11] with (+)- or (−)-1-phenylethylamine are known. According to a new procedure, the resolution of ^{t}BuPhP(OH)(BH$_3$) using a combination of ephedrine and cinchonine can lead to enantiopure ^{t}BuPhP(O)H after suitable derivatizations.[12] The resolution of phosphonium salts can be accomplished by combining the racemate with the silver salt of a chiral acid.[13,2] In this relatively general method, the silver cation does not participate in the formation of diastereomeric salts. Several chiral transition metal complexes, such as Pd, Pt, Ni and Fe complexes were found to be useful in the separation of racemic phosphines.[2,14,15] Although the resolution via transition metal complexes was found to be reasonably general and efficient, the cost of these reagents limited its usefulness. Enantiomeric separation of P=O derivatives via inclusion complex formation with a chiral acid, such as (+)-bromocamphorsulfonic acid,[16] camphorsulfonic acid,[17] (−)-dibenzoyltartaric acid[2,18,19] and (+)-mandelic acid[20] or with 2,2′-dihydroxy-1,1′-binaphthalene[20,21] was reported before. Although these methods proved to be

☆See Ref. 1.
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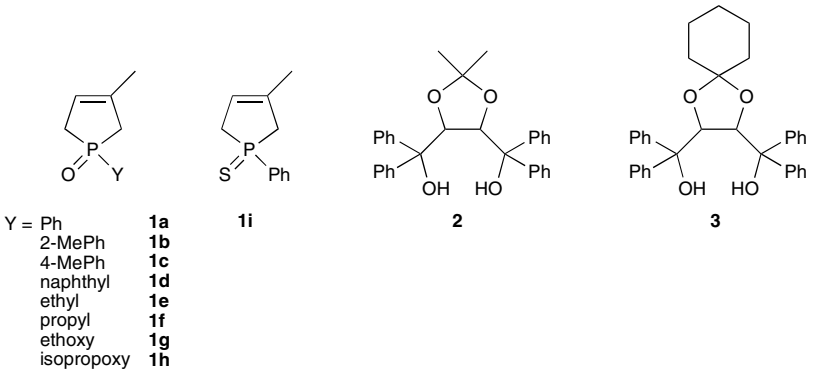


Figure 1.

useful in some special cases, they did not turn out to be general.

Five-membered P-heterocycles, such as 1-aryl-, 1-alkyl- and 1-alkoxy-3-phospholene 1-oxides (or 2,5-dihydro-1*H*-phosphole 1-oxides), for example, **1**, form a representative class of ring P-compounds as they can be the starting materials for a variety of five-, six-, seven- and eight-membered P-heterocycles including bridged derivatives.[22–25] Pietrusiewicz et al. developed several methods for the resolution of 1-phenyl-2- or 1-phenyl-3-phospholene 1-oxides and their epoxide derivatives based on dipolar cycloaddition,[26] enantioselective desymmetrization,[27–29] and quaternization of the respective phosphines with a chiral reactant.[29] These methods were not, however, generalized probably because of their substrate specificity.

Recently, we have shown that the 1-phenyl-3-methyl-3-phospholene 1-oxide **1a** can be resolved via molecular complex formation.[1] As an extension and generalization, we now report the resolution of 1-aryl-, 1-alkyl- and 1-alkoxy-3-methyl-3-phospholene 1-oxides **1a**–**h** and that of 1-phenyl-3-methyl-3-phospholene 1-sulfide **1i** by molecular complex formation with the chiral hosts TADDOL[30] **2** or the TADDOL analogue **3**[30] (Fig. 1).

2. Results and discussion

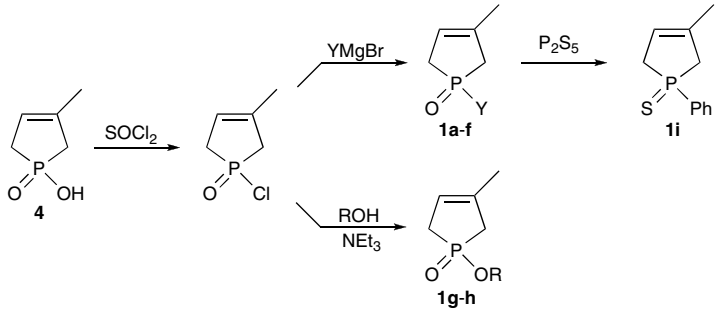
2.1. Resolution of racemic 3-phospholene 1-oxides

Racemic 1-aryl-, 1-alkyl- and 1-alkoxy-3-methyl-3-phospholene 1-oxides **1a**–**h** and 1-phenyl-3-methyl-3-phospholene 1-sulfide **1i** were synthesized from 1-hydroxy-3-phosphole oxide **4** (Scheme 1) as described in the literature[23–25] (for specific references, see Section 4). Compound **1d** is new amongst the P-cycles applied.

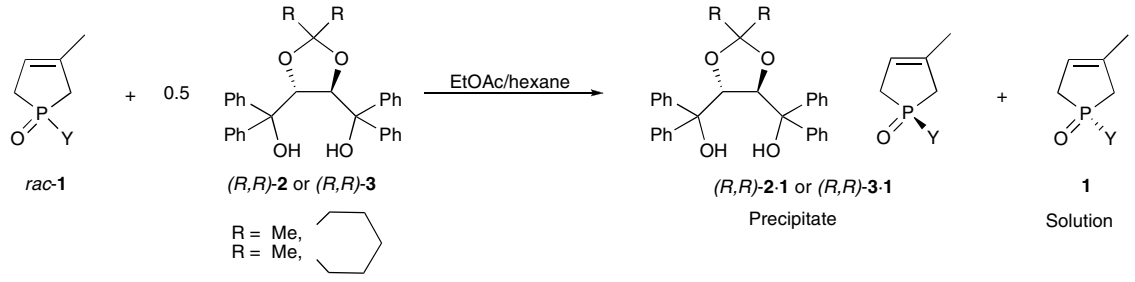
Enantiomerically pure 1-substituted-3-methyl-3-phospholene derivatives **1** were prepared by molecular complex formation with chiral hosts **2** and **3** (Scheme 2 and Table 1). To a solution of racemic phospholene 1-oxides **1a**–**h** and half equivalent of (−)-TADDOL **2** or its analogue (−)-**3** in hot ethyl acetate was added hexane, whereupon a **1**·(−)-**2** or a **1**·(−)-**3** crystalline complex precipitated.

Complexes **1a**–**d**·(−)-**2** and **1a**–**d**·(−)-**3** were analyzed by chiral HPLC (Chiralpack AD) directly, while species **1e**–**h**·(−)-**2** and **1e**–**h**·(−)-**3** by chiral GC (BetaDEC™) after regenerating the phospholene oxides **1e**–**h** by passing the primary **1e**–**h**·(−)-**2** or **1e**–**h**·(−)-**3** species through a short silica gel layer using 3% methanol in chloroform as the eluant. The enantiomeric purity of (−)-**1a**–**h** obtained in this way was 10–96% ee (Table 1). Recrystallization of these complexes from a mixture of ethyl acetate–hexane significantly improved the enantiomeric excesses of complexes **1**·(−)-**2** and **1**·(−)-**3**, up to >99% ee in most cases (Table 1). After flash column chromatography, 3-phospholene 1-oxides **1a**–**h** were recovered quantitatively without the loss of chirality.

In most cases, the 1:1 complexes of **1**·(−)-**2** or **1**·(−)-**3** were formed. In the instance of 1-propyl-3-phospholene oxide **1f** and resolving agent **3**, a 1:2 complex of (+)-**1f**·(−)-**3** was obtained as shown by the ^{1}H NMR spectrum. For this, the resolution of **1f** was achieved with the use of 1 equiv



Scheme 1.



Scheme 2.

Table 1. Resolution of 1-aryl-, 1-alkyl- and 1-alkoxy-3-methyl-3-phospholene 1-oxides **1a**–**h** with chiral host **2** and **3**

Subst.	Complex forming agents							
	(*R*,*R*)-**2**				(*R*,*R*)-**3**			
	Enantiomeric purity[a] (% ee)	Yield (%)	*S*[b]	$[\alpha]_D$[c]	Enantiomeric purity[a] (% ee)	Yield (%)	*S*[b]	$[\alpha]_D$[c]
1a	97 (71) (*S*)[d]	44	0.43		>99 (53) [*S*]	29	0.29	−37.0 (*S*)
1b	57 (31) (*S*)	49	0.28		>99 (48) [*S*][e]	41	0.41	−28.6
1c	69 (29) (*S*)	42	0.29		>99 (11) [*S*][e]	30	0.30	−39.1
1d	70 (25)	42	0.29		>99 (27)	55	0.55	−40.9
1e	24 (10) (*R*)	36	0.09		58 (23) [*R*][d]	45	0.26	+8.7 (*R*)
1f	95 (68) (*R*)[d]	35	0.33	+13.4 [*R*]	89 (29)[f] [*S*]	30	0.27	
1g	44 (20) (*S*)	25	0.11		95 (58) [*R*][e]	50	0.48	−10.6
1h	>99 (89) (*R*)	5	0.05		>99 (96) [*R*][e]	37	0.37	−15.6

[a] The enantiomeric purities were determined by chiral HPLC (Chiralpack AD) or chiral GC (BetaDEC™) after two recrystallizations (and after crystallization).
[b] Resolving capability, also known as the Fogassy parameter.[31]
[c] Specific rotation of the regenerated enantiomer (*c* 1, $CHCl_3$).
[d] Absolute configuration was determined by X-ray analyses (see later).
[e] Absolute configuration was determined by CD spectroscopy (see later).
[f] One equivalent of **3** was used.

of **3**. Interestingly, in all but two cases, the resolving agents **2** and **3** preferred complex formation with the same enantiomer of the given 3-phospholene oxides **1a**–**e**,**h**. In case of **1f** and **1g**, **2** and **3** formed complexes with opposite antipodes.

To clarify the absolute configuration of (−)-**1a**, (+)-**1e** and (+)-**1f**, the supramolecular formations (−)-**1a**·(−)-**2**·acetone, (+)-**1e**·(−)-**3** and (+)-**1f**·(−)-**2** were subjected to single crystal X-ray analysis. The absolute configuration of the P-atom in (−)-**1a**, (+)-**1e** (Fig. 2) and (+)-**1f** (Fig. 3) was found to be (*S*),[1] (*R*) and (*R*), respectively.

Conventional resolution methods based on diastereomeric salt formation are usually controlled thermodynamically. However, sometimes kinetic effects have also been observed and simultaneous detection of both phenomena in an induced crystallization process has been reported.[32] A kinetic study on the resolution of the 1-phenyl-3-methyl-3-phospholene 1-oxide **1a** with TADDOL derivative **3** showed that the diastereomer purity of the complex formed decreased considerably over time. The diastereomeric selectivity of the resolution after 1 h of crystallization was 60%, which decreased to 38% after a week. These results showed that at the onset of crystallization, crystals form under kinetic control, which subsequently recrystallize slowly to give a thermodynamically controlled product mixture. The isomeric composition of the complex of 1-phenyl-phospholene **1a** oxide with TADDOL **2** showed no changes after a week's time.

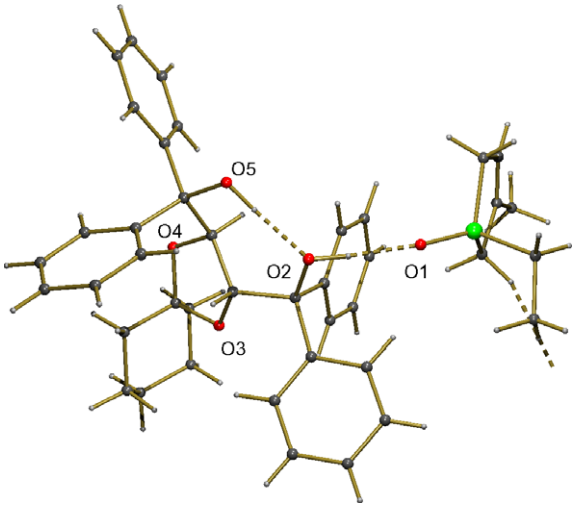


Figure 2. Asymmetric unit structures with the basic H-bridge interactions indicated by dotted lines for **1e**·**3** with O atom numbering used in the text.

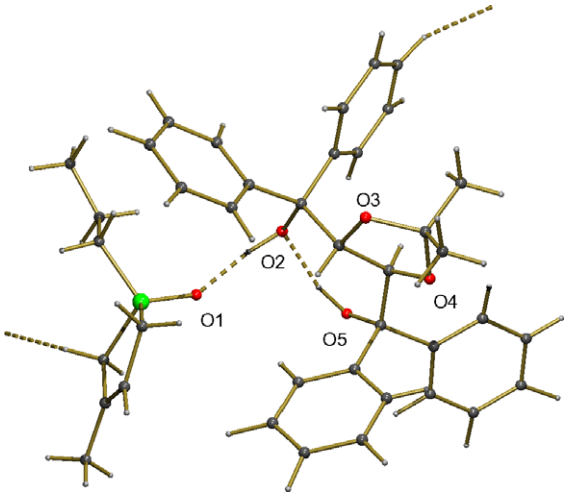


Figure 3. Asymmetric unit structures with the basic H-bridge interactions indicated by dotted lines for **1f·2** with O atom numbering used in the text.

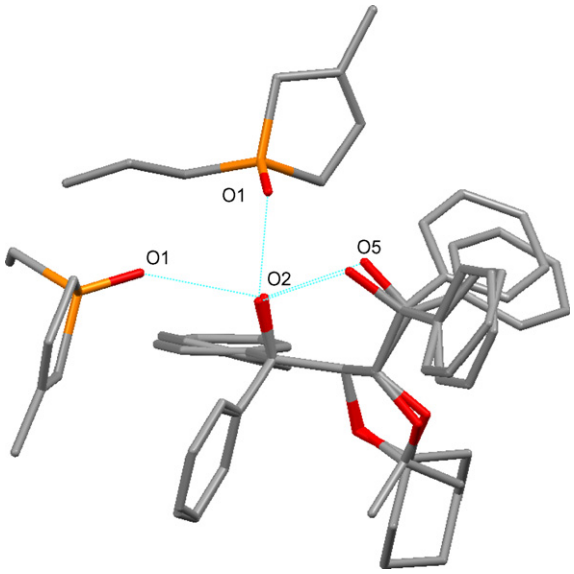


Figure 4. Structure overlays on the C8–C9–C10 atoms of **1e·3** and **1f·2** with the guest anchoring H-bonds also indicated, also showing O atom numbering (for O2–C8–C9–C10 and for C8–C9–C10–C11 torsion angles see text).

2.2. Single crystal X-ray analysis of 1e·3 and 1f·2

Final structure models are shown in Figures 2 and 3 with the basic H-bridges indicated. The resulting crystal structure models are well ordered and contain in both cases, with 1:1 stoichiometry, the associated forms of the resolving agents with either one of the phospholene target guest molecules as in **1e·3** and in **1f·2**. The resolving machinery is affected by the interplay of the anchoring and identical primary O–H···O hydrogen bridges to the guest P═O functions, as well as by a series of weaker C–H···O and C–H···π interactions. In spite of the similarity of the way crystal structures for **1e·3** and **1f·2** are built and of the same space group, the large differences in the *b* and *c* axes indicate that these crystals are not isometric.

Alike conformations of the TADDOL host molecules in **1e·3** and in **1f·2** are shown by some selected torsion angles. The host backbone is stiffened by an internal O–H···O hydrogen bridge between O2 and O5. Thus, the central host region appears to be fairly conserved as attested by two selected torsion angles (O2–C8–C9–C10 torsion angles are 61.8(4)°, 56.0(2)° and 62.8(1)° for **1e·3**, **1f·2** and **1a·2**,[1] respectively, while C8–C9–C10–C11 torsion angles are −102.7(4)°, −92.9(2)° and 90.6(1)° in that order). These torsion angles vary little and even the phenyl wings, mainly contributing to the bulk of the hosts, seem to adopt similar positions in these crystals. A least-squares fit of the two hosts central molecular portions (atoms C8, C9 and C10) from **1e·3** and from **1f·2** is shown in Figure 4, illustrating the similarity in the host conformations and guests anchoring. Guest molecules in **1e·3** and in **1f·2** have comparable dimensions as expected on the basis of their normal covalent bonding. The intra-associate metrics in **1e·3** and **1f·2**, represented by the primary (O–H···O) H-bridges (see Table 2), also for a comparison with **1a·2**[1] keep hosts and guests anchored (Figs. 2 and 3). The O5–H···O2 H-bridge keeps the TADDOL host frame fixed, while the O2–H2O···O1═P H-bridge establishes the primary host–guest interaction. Figures 2 and 3 also clearly show how the donor H-position alternative at O2 is made use of in **1e·3** and in **1f·2**. The H-bridge acceptor positions are as dictated by the immediate environment surrounding O2 and the respective guests. Steric fit and C–H···π interactions also seem to play a role in maintaining these assemblies. Together with the secondary (C–H···O) H-bridges and C–H···π interactions, these weak, albeit numerous interactions, further affect the initially loose association of molecules into the making of macroscopic crystals.

Table 2. Dimensions [Å, °], with their s.u.'s where applicable, of the principal O–H···O hydrogen bridges in **1e·3** and in **1f·2** as compared for **1a·2**[1]

	D–H···A	D–H [Å]	H···A C	D···A [Å]	D–H···A [°]
1e·3	O2–H2O···O1	0.95(5)	1.77(5)	2.714(4)	169(4)
1f·2	O2–H2O···O1	0.97	1.66	2.618(2)	168
1a·2	O2–H2O···O1	0.83(2)	1.86(2)	2.653(1)	161(2)
1e·3	O5–H5O···O2	0.94(6)	1.78(6)	2.713(4)	176(4)
1f·2	O5–H5O···O2	1.00	1.71	2.690(2)	167
1a·2	O5–H5O···O2	0.81(2)	1.83(2)	2.636(1)	175(2)

2.3. CD spectra of phospholene oxides

Following the determination of the absolute configurations of (−)-**1a**, (+)-**1e** and (+)-**1f** by X-ray diffraction, the UV absorption and CD spectra of all the phospholene oxides were recorded and analyzed on the basis of theoretical chemical calculations. The latter involved a conformational analysis and the determination of the equilibrium geometries of the most stable conformers by density functional theory (DFT) method, and the computation of the characteristics of their UV and CD spectra (excitation energies, oscillatory strengths, rotatory strengths) by time-dependent DFT (TD-DFT) method. This way the configurations

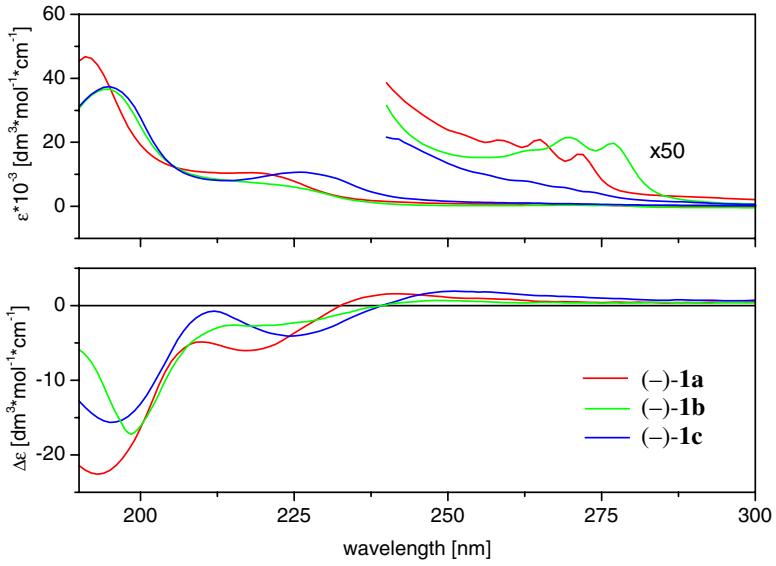


Figure 5. UV absorption and CD spectra of aryl substituted phospholene oxides **1a**, **1b**, **1c**.

of the further four derivatives, (−)-**1b**, (−)-**1c**, (−)-**1g** and (−)-**1h** could be assigned.

The experimentally obtained UV and CD spectra of the phospholene oxides with aryl substituents, (−)-**1a**, (−)-**1b** and (−)-**1c** are displayed in Figure 5. As can be seen, the three UV spectra, as well as the three CD spectra show close similarities, the latter suggesting that (−)-**1b** and (−)-**1c** have the same (*S*)-configuration as (−)-**1a**. The absolute configurations of α,α-disubstituted toluene derivatives are often determined from the sign of their CD bands belonging to their ^1L_b (lowest energy $\pi\rightarrow\pi^*$) excitations.[33,34] These transitions appear in the UV spectra of **1a**, **1b** and **1c** as vibronically structured, weak bands around 270 nm, but they cannot be clearly identified in the CD spectra. The calculations predict negative ^1L_b CE-s for the (*S*)-isomers. The sign of the bands at 240–250 nm in the CD spectra of these compounds can, however, be correlated with their absolute configurations. The calculations indicate that in these CD bands the dominant contributions arise from two charge transfer type (CT) transitions, one of $\pi_{C=C}\rightarrow\pi^*_{Ph}$, the other of $n_O\rightarrow\pi^*_{Ph}$ character, and they both have relatively large rotatory powers, with positive sign in case of the (*S*)-enantiomers.

The experimental spectra of the alkyl substituted derivative (+)-**1f** and of the alkoxy substituted ones (−)-**1g** and (−)-**1h** are shown in Figure 6. As can be seen, the CD spectra of (−)-**1g** and (−)-**1h** are in close resemblance to the mirror image of the CD spectrum of (+)-**1f**, as well as the UV, where the CD bands of these chemically closely related compounds exhibit a similar pattern. This suggests that (−)-**1g** and (−)-**1h** have an (*S*)-configuration. The calculations indicate that these molecules have low energy Ryd-

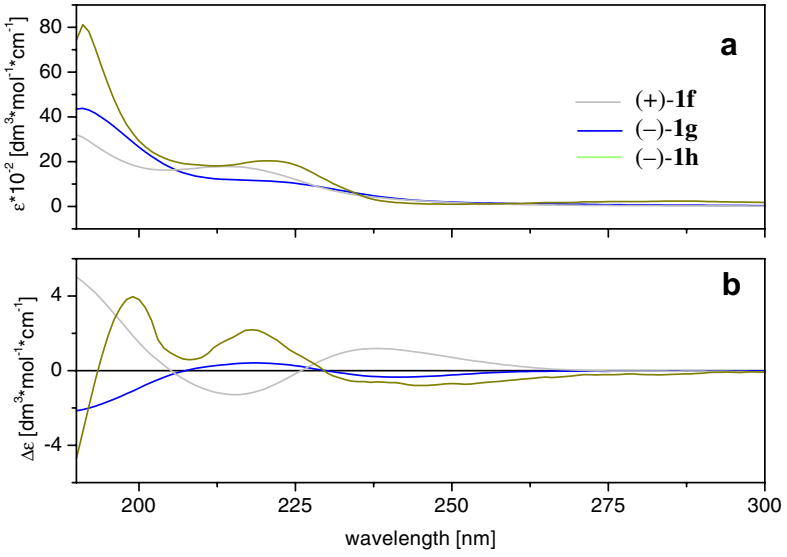


Figure 6. UV absorption and CD spectra of alkyl and alkoxy substituted phospholene oxides, **1f**, **1g**, **1h**.

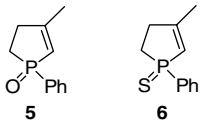
berg orbitals (RO-s), and their highest wavelength CD bands around 240 nm arise primarily from a $\pi_{C=C} \rightarrow RO$ excitation, whereas the bands around 215 nm can be assigned to two closely lying $n_{C=O} \rightarrow RO$ type transitions. Since the TD-DFT method does not describe the excitations to RO-s suitably,[35] the results of the calculations are not reliable for these transitions. For the assignment of the absolute configuration by comparing the CD bands in the experimental and theoretically simulated spectra, the CE-s around 190 nm seem to be more relevant (only a part of these bands can be seen in Fig. 6). By the calculations they belong to localized $\pi_{C=C} \rightarrow \pi^*_{C=C}$ transitions with high oscillatory strength and rotatory power, the respective CD-bands are negative in the spectra of the (*S*) isomers of **1f**, **1g** and **1h**.

2.4. Nonlinear effect of the impurities on the resolution of 3-methyl-1-phenyl-3-phospholene chalcogenides

As previously reported, the efficiency of a resolution can be improved in the presence of a chiral or achiral structurally similar derivative of the substrate or the resolving agent (e.g., Dutch resolution).[36–38] We found that the result of the resolution of 1-phenyl-3-methyl-3-phospholene oxide **1a** with chiral host **3** was improved in the presence of impurities. The resolution of pure **1a** with **3** led to the corresponding complex **1a**·(−)-**3** of 53% diastereomeric excess in 87% yield. When substrate **1a** contained 5% of 1-phenyl-3-methyl-2-phospholene oxide **5,** the crystals were formed in a de of 60%, in 75% yield. We obtained the best results when we used crude **1a** (containing 5% of 1-phenyl-3-methyl-2-phospholene oxide and ca. 3% of unidentified impurities). In this case the diastereomeric excess of complex **1a**·(−)-**3** formed was 79% with 71% yield.

It was also interesting that the resolution of 1-phenyl-3-methyl-3-phospholene oxide **1a** with 0.25 equiv of **2** and 0.25 equiv of **3** proved to be more efficient than with either 0.5 equiv of **2** or with 0.5 equiv of **3**. Diastereomeric excesses of complexes **1a**·(−)-**2**·(−)-**3**, **1a**·(−)-**2** and **1a**·(−)-**3**, were 77%, 71% and 53% de, respectively. Complex **1a**·(−)-**2**·(−)-**3** incorporated 40% of **2** and 60% of **3** based on ^{1}H NMR.

The experiments for the separation of the enantiomers of 1-phenyl-3-methyl-3-phospholene sulfide **1i** with TADDOL **2** were unsuccessful while with its analogue **3** were puzzling at first. The resolution of the pure racemic compound **1i** with (−)-**3** was not too efficient (24% de). When substrate **1i** contained 4% of 1-phenyl-3-methyl-2-phospholene sulfide **6**, the enantiomeric purity of complex (+)-**1i**·(−)-**3** was quite similar (20% de). The efficiency of the resolution was, however, improved significantly by using the crude product of the synthesis of **1i**. In this case, the diastereomeric excess of the complex formed (+)-**1i**·(−)-2*3 was 65% after crystallization and >99% after recrystallization $\{[\alpha]_D^{20} = -65.2$ (c 1, $CHCl_3$)$\}$. In this case, the ^{1}H NMR spectrum suggested a 1:2 stoichiometry of **1i** and **3**. The 1-phenyl-3-methyl-2-phospholene sulfide was regenerated by column chromatography $\{[\alpha]_D^{20} = +7.8$ (c 1, $CHCl_3$)$\}$.



5 **6**

3. Conclusion

An efficient resolution process of 1-substituted-3-methyl-3-phospholene 1-oxides **1a**–**h** has been developed. The enantiomeric separation is based on the crystallization of the phospholene oxides **1a**–**h** and phospholene sulfide **1i** with TADDOL **2** or its modified derivative **3** (1), the recrystallization of the molecular complexes (2) and the regeneration of the substrates (3). The method suggested seems to be of general value for phospholene chalcogenides **1a**–**i**, with it being simple and efficient, providing the optically active form of phospholene chalcogenides in ⩾95% ee after two recrystallizations in eight instances from among the nine cases studied. X-ray crystal structures also attest the persistent acceptor···donor relationship of the resolving host **2** or **3** to guests **1f** and **1e**. Key motifs in these crystals are the alike host conformations fixed by the internal O5–H···O2 H-bridge and the identical way of guest binding via the O2–H2O···O=P H-bridge. The size and interaction matching affect the resolving power via crystallization. Alkyl P-substituted guests are successful contestants in **1e**·**3** and **1f**·**2** in the same enantiomeric form towards the modified host **3** and TADDOL **2**, respectively. It is interesting to note that both possible H-donor positions from atom O2 are utilized in **1e**·**3** and **1f**·**2**, thus indicating that a certain amount of flexibility might be beneficial at resolution via associate formation.

The absolute configurations of four additional phospholene oxides **1b**, **1c**, **1g** and **1h** were assigned by CD spectroscopy, using TD-DFT quantum chemical calculations for the analysis of the spectra.

4. Experimental

The ^{31}P, ^{13}C and ^{1}H NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4, 125.7 and 500 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4 and TMS. The couplings are given in Hertz. The enantiomeric excesses were determined by chiral HPLC (Daicel Chem. Ind., Chiralpack AD) or by chiral GC (BetaDEC™). Optical rotations were determined on a Perkin–Elmer 241 polarimeter. The UV absorption and CD spectra of phospholene oxides were measured in acetonitrile solution. The UV–vis spectra were recorded on an Agilent 8453 diode array spectrometer, the CD spectra were obtained with a Jasco J-810 spectropolarimeter.

The 3-phospholene 1-oxides **1a**–**c**, **e**–**h** and the phospholene sulfide **1i** were synthesized as described earlier.[39–44] (−)-(4*R*,5*R*)-4,5-Bis(diphenylhydroxymethyl)-2,2-dimethyldioxolane **2** was purchased from Aldrich Chemical Co. (−)-(2*R*,3*R*)-α,α,α′,α′-Tetraphenyl-1,4-dioxaspiro[4.5]decan-2,3-dimethanol **3** was synthesized as described before.[28]

4.1. Synthesis of 1-naphthyl-3-methyl-2,5-dihydro-1*H*-phospholene oxide 4

To 13.2 g (0.10 mol) of phosphinic acid **4** in 40 mL of chloroform was added 8.9 mL (0.12 mmol) of thionyl chloride and the solution was stirred overnight. After the volatiles were removed in vacuo, the residue was dissolved in 60 mL of THF. To the solution thus obtained was added 110 mL (0.11 mmol) of a 1 M solution of naphthylmagnesium bromide in THF at 0 °C and the mixture was stirred overnight. The reaction was quenched with a saturated solution of NH_4Cl at 0 °C, washed with $NaHCO_3$, brine and then dried. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, 3% methanol in chloroform) to give 12.1 g (50%) of the title compound as a dense oil. ^{31}P NMR ($CDCl_3$) δ 56.6; ^1H NMR ($CDCl_3$) δ 1.95 (s, 3H, CH_3), 2.8–3.0 (m, 4H, $2 \times CH_2$), 5.75 (d, $^3J_{PH} = 31.0$, 1H, CH), 7.5–7.6 (m, 3H, Ar-H), 7.9–8.0 (m, 2H, Ar-H), 8.03 (d, $J = 8.5$, 1H, Ar-H), 8.19 (dd, $J = 7.03, 14.3$, 1H, Ar-H); ^{13}C NMR ($CDCl_3$) δ 20.0 ($^3J = 6.72$, Me), 35.4 ($^1J = 39.6$, C_5), 38.5 ($^1J = 41.4$, C_2), 121.2 ($^2J = 4.5$, C_4), 124.3 ($^3J = 3.1$, C_{Ar}), 124.6 ($^2J = 7.6$, C_{Ar}), 126.1 (C_{Ar}), 127.4 (C_{Ar}), 128.7 ($^1J = 74.5$, C_{Ar}), 129.3 (C_{Ar}), 132.2 ($^2J = 6.1$, C_{Ar}), 132.4 ($^3J = 4.7$, C_{Ar}), 132.9 ($^4J = 1.7$, C_{Ar}), 133.5 ($^3J = 5.6$, C_{Ar}), 137.2 ($^2J = 7.4$, C_3); MS 243 (M+H); HRMS $(M+H)^+_{found} =$ 243.0926, $C_{15}H_{15}OP$ required 243.0939.

4.2. Resolution of 1-phenyl-3-methyl-3-phospholene 1-oxide 1a with TADDOL 2 in a mixture of ethyl acetate and hexane. Representative procedure

To 0.48 g (2.49 mmol) of racemic 1-phenyl-3-methylphosphol-3-ene 1-oxide **1a** and 0.58 g (1.245 mmol) of (−)-TADDOL **2** in 1 mL of hot ethyl acetate was added 5 mL of hexane. After the addition, colourless crystals of the complex started to appear immediately. After 2 h, the crystals were separated by filtration to give 0.59 g (72%) of complex (−)-**1a**·(−)-**2**; enantiomeric purity (determined by HPLC), 71% ee. The complex was further purified by two recrystallizations from ethyl acetate–hexane (1 mL/5 mL) to afford complex (−)-**1a**·(−)-**2** in 54% yield with 87% ee and in 43% yield with 97% ee, respectively. Column chromatography (silica gel, chloroform) of the complex regenerated 96 mg (40%) of the enantiomerically pure (−)-(*S*)-1-phenyl-3-methyl-3-phospholene 1-oxide (−)-**1a**; enantiomeric purity, 97% ee, $[\alpha]_D^{25} = -37.0$ (*c* 1, $CHCl_3$).

4.3. Resolution of 1-substituted-3-methyl-3-phospholene 1-oxide 1 with resolving agent 2 or 3

Compounds **1a**–**i** were resolved with resolving agent **2** or **3** according to the general procedure except the complexes were crystallized and recrystallized from a mixture of ethyl acetate–hexane with the ratio of 2:10 in case of **1a**, **b**, **d**, **f**–**i** or 1:10 in case of **1c**, **e**.

4.4. X-ray measurements

Crystal structure determinations of **1e**·**3** and **1f**·**2**. Crystals were taken from their crystallization vials directly and mounted in loops in high viscosity oil droplet, all X-ray diffraction experiments were carried out on a Rigaku R-AXIS Rapid IP diffractometer at low temperatures using an X-Stream 2000 unit.

Crystal data for **1e**·**3** were collected using standard ω-scan procedures, with monochrome (graphite) Mo-Kα radiation: $C_{34}H_{34}O_4 \cdot C_7H_{13}OP$, Fwt.: 650.76, colourless block, size: $0.21 \times 0.31 \times 0.36$ mm, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 9.614(2)$ Å, $b = 10.101(2)$ Å, $c = 35.558(9)$ Å, $V = 3453.1(13)$ Å^3, $T = 95(2)$ K, $Z = 4$, $D_C = 1.252$ Mg/m^3, numerical absorption correction ($T_{max}/T_{min} = 0.985/0.964$). 33,474 reflections, 6072 unique [$R_{int} = 0.155$, completeness 99.6%]; and $3748 > 2\sigma(I)$, initial structure model by direct methods, hydrogen atoms either calculated from assumed geometries or located from difference density maps and kept riding, model refined by least-squares, final $R_1 = 0.0627$ and $wR_2 = 0.1288$ for all (6072) intensity data, number of parameters = 474, goodness-of-fit = 0.97, absolute structure parameter Flack $x = 0.13(16)$.

Crystal data for **1f**·**2** were collected via standard ω-scan procedures, with monochrome (graphite) Mo-Kα radiation: $C_{31}H_{30}O_4 \cdot C_8H_{15}OP$, Fwt.: 624.72, colourless block, size: $0.55 \times 0.49 \times 0.48$ mm, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 9.5257(14)$ Å, $b = 16.696(3)$ Å, $c = 21.355(4)$ Å, $V = 3396.3(10)$ Å^3, $T = 93(2)$ K, $Z = 4$, $D_C = 1.222$ Mg/m^3, numerical absorption correction ($T_{max}/T_{min} = 0.974/0.952$). 74,174 reflections, 5984 unique [$R_{int} = 0.134$, completeness 99.7%]; and $5613 > 2\sigma$ (I), initial structure model by direct methods, hydrogen atoms either calculated from assumed geometries or located from difference density maps and kept riding, model refined by least-squares, final $R_1 = 0.0396$ and $wR_2 = 0.0973$ for all (5984) intensity data, number of parameters = 457, goodness-of-fit = 1.02, absolute structure parameter Flack $x = 0.01(9)$. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication Number CCDC 661592 and 661593. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.5. Calculations

The conformational analysis was performed and the geometries were optimized with the aid of DFT using B3LYP functional[44] and 6-31++G** basis set.[45] The excitation energies, the oscillatory strengths and the rotatory powers (velocity gauge) of the molecules were then calculated with time-dependent DFT (TD-DFT) method[46] at the optimized geometries, using the above functional and basis set. For the quantum chemical calculations the GAUSSIAN 03 package was used.[47] For the qualitative description of the excitations figures showing the various MO-s were prepared by a recently proposed algorithm based on the singular value decomposition method.[48] Simulated CD spectra were obtained by forming weighed sums of the spectra of the conformers, and fitting Gaussians of width $\sigma = 0.2$ eV

with centres at the wavelengths of the theoretically calculated transitions.[49]

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