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A convenient application of the NMR and CD methodologies for the determination of enantiomeric ratio and absolute configuration of chiral atropoisomeric phosphine oxides

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ABSTRACT

Certain commercial carboxylic acids appear to be powerful chiral solvating agents, which allow for a rapid determination of enantiomeric purity and, subject to some limitations, the absolute configuration of common classes of phosphine oxides by means of ^{1}H and/or ^{31}P NMR spectroscopy. The complementary application of CD spectroscopic measurement enables the determination of their absolute configuration. Herein, we report a convenient, inexpensive, and straightforward approach to the complete determination of the enantiomeric ratio of mono-phosphine oxides and bis-phosphine dioxides.

1. Introduction

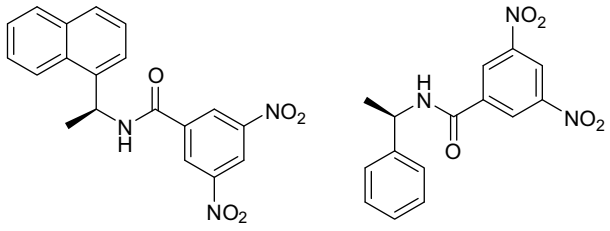
The determination of enantiomeric purity is a central problem in the analytical chemistry of chiral compounds. This issue was largely resolved for the most common classes of organic compounds, such as chiral amines or acids etc., but it remains only partially resolved for chiral phosphine oxides.[1] In the case of organophosphorus compounds, NMR spectroscopy became one of the most important methods for analyzing chiral molecules due to an added possibility to observe a large chemical dispersion of ^{31}P nuclei in the simple ^{1}H-decoupled ^{31}P NMR spectra.[2] A wide variety of chiral discriminating agents applicable to the NMR spectroscopy were developed to facilitate the determination of the enantiomeric ratio (er) and/or the assignment of the absolute configuration. The discrimination is achieved either by the use of a chiral derivatizing agent (CDA) or by a chiral solvating agent (CSA).[3] The determination of the enantiomeric ratio using CDA, by analysis of a diastereoisomeric mixture, is a widely used NMR technique. Its usefulness is due to the fact that the discrete diastereomers display their chemical shifts as non-equivalences that are usually larger than those observed while using the analogous CSAs.[4] Nevertheless, there are some limitations of using CDA, for example, the usual inability of the oxides of chiral phosphorus ligands to produce covalent adducts with chiral reagents.[2a] Therefore, the most advantageous and simple approach for determination of the enantiomeric ratio of phosphine oxides is based on the use of CSAs, which form in situ a pair of diastereoisomeric complexes that can be distinguished by their non-equivalent NMR spectra.[5]

Herein, we report a simple method to determine the enantiomeric purity of phosphine oxides.

2. Results and discussion

2.1. Chiral solvating agents used for the determination of er of phosphine oxides

It has already been shown that the Kagan's amides[6] **1** and **2** are convenient and efficient CSAs, which may be recommended for the determination of the enantiomeric ratio of a wide range of non-racemic unsaturated phosphine oxides. Compounds **1** and **2** are especially effective for the analysis of the phospholene oxide derivatives (Fig. 1). Our attempts to apply these CSAs for the er determination of chiral non-racemic atropoisomeric bis-phosphine



(*S*)-(+)- **1** (*R*)-(+)- **2**

Figure 1. Kagan's amides.

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dioxides were unsuccessful: only a low enantiodiscrimination in both ^{31}P and ^{1}H NMR experiments has been observed.[1] In all the bis-phosphine dioxides tested, the separation of signals was not sufficient enough to achieve an accurate integration. This observation prompted us to look for other CSAs, suitable to analysis of dioxides of atropoisomeric bis-phosphine ligands.

Among commonly used CSAs, the commercially available carboxylic acids such as (*S*)-Naproxen® **3**[7] and (*S*)-mandelic acid **4**[8] are of interest as NMR shift reagents for determination of the enantiomeric composition of sulfoxides as well as of phosphine oxides because of their simple structure and attractive prices (Fig. 2). The dibenzoyltartaric acid **5** and its mono-dimethylamide **6** have often been used as reagents for the separation of racemic mixtures of phosphine oxides into the individual enantiomers. Surprisingly, we did not find any reports concerning the enantiomeric discrimination observed in the NMR spectra of the pertinent racemic mixtures in the presence of those acids. We therefore decided to fill in the gap and to check the possibility of the application of compounds **3**–**6** as potential CSAs for atropoisomeric phosphine oxides.

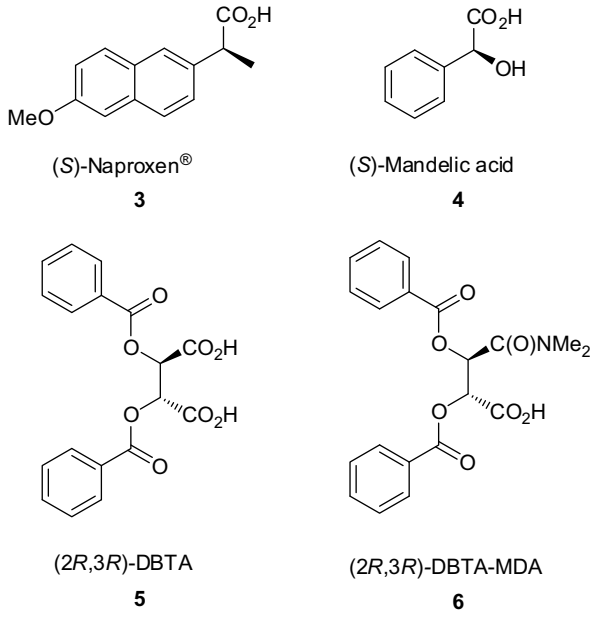

Figure 2. Chiral carboxylic acids used as CSAs.

2.2. Determination of the optimal ratio of CSA to phosphine oxides

As model compounds for the er determination, we have used several racemic as well as enantiomerically enriched bis-phosphine dioxides of chiral atropoisomeric ligands **7**–**14**, which were either commercially available or synthesized by us previously[9] (Fig. 3). In the first model experiment with (*S*)-Naproxen® **3** and racemic **7** in a 1:1 molecular ratio, we observed a weak effect of CSA on the chemical shifts of the two enantiomers in both ^{31}P and ^{1}H NMR spectra recorded in $CDCl_3$. However, most signals appeared progressively better differentiated when **3** was used in higher molecular ratios (see Table 1).

The observed experimental dependence could be fitted using the saturated function of Langmuir's type $y = a * (b * x/(1 + b * x))$.

The best-fitting parameters are presented in Table 2, and the corresponding graphical representation is shown in Figure 4.

The extrapolated curve, representing the dependence between the number of equivalents of **3** and the separation of the signals of the corresponding enantiomers in the ^{31}P NMR spectra, was quickly saturated near a $\Delta\delta$ of 40 Hz. The optimal quantity of **3** was defined as 3 equiv for each phosphorus group. This dependence was significantly weaker for all proton groups in the corresponding ^{1}H NMR spectra. For this reason, our further studies were focused first on the ^{31}P NMR measurements (see Tables 3 and 4).

2.3. ^{31}P NMR measurements

The influence of the nature of chiral carboxylic acids **3**–**6** on the separation of the signals in ^{31}P NMR and in ^{1}H NMR of C_2-symmetric atropoisomeric bis-phosphine dioxides **7**–**14** was studied next. Analysis of the collected ^{31}P NMR data indicates that in most cases those simple chiral acids are very efficient CSAs for the determination of the enantiomeric purity of atropoisomeric bis-phosphine dioxides. The observed values of $\Delta\delta$ are usually found between 20 and 40 Hz but in some instances amount to more than 70 Hz. In all the cases examined, the signals in the ^{31}P NMR spectra were shifted by about 6 ppm toward the lower field as compared to signals of the free phosphine oxides. The results were also compared with respective NMR data obtained with (*S*)-**1** (2 equiv used) to examine phosphineoxides. The respective observed shifts in the latter cases were insignificant (see Table 3).

It is interesting to note that the chiral acids tested can also be considered as promising reagents for the determination of the absolute configuration of bis-phosphine dioxides. In all tested cases where the discrimination was observed, compounds **3** and **6** caused shift of signals of the (*R*)-enatiomers of phosphine dioxides toward a lower field. The (2*R*,3*R*)-**5** and (*S*)-**4** usually caused the shifts toward the higher field. The Kagan's amide **1** did not exhibit any appreciable dependence of that type.

2.4. ^{1}H NMR measurements

The data obtained from the ^{1}H NMR measurements were less informative. The values of $\Delta\delta$ were found between 5 and 55 Hz (for **5**), but no clear dependence of the sign of the observed shifts and the absolute configuration of the tested compounds was found. Often, analysis of the NMR data was complicated because of significant overlapping of different signals or their excessive width. Nevertheless, in many cases, the data from the ^{1}H NMR measurements were helpful for the determination of er of atropoisomeric bis-phosphine dioxides. The use of **4** produced satisfactory resolutions of signals of the two enantiomers, but its utility is limited due to its low solubility in chloroform (see Table 4).

The addition of tetrachloromethane as a co-solvent to improve the signal splitting did not produce the expected results. In contrast to the Kagan's CSAs, where the resolution increases along with the dielectric constant of the solvent,[1] in our case the values of $\Delta\delta$ slowly decreased when $CDCl_3$ was diluted with CCl_4. Surprisingly, the use of pure, dry $CDCl_3$ allowed us to reach a somewhat higher degree of signal separation in both ^{31}P and ^{1}H NMR spectra.

2.5. Monophosphine oxides

We have also found that the studied chiral acids **3**–**6**, which can also be successfully used are convenient CSAs for the determination of the er's of a wide range of mono phosphine oxides **16**–**19** (Fig. 5). In those cases, however, Kagan's amide **1** was a more efficient CSA than any of the chiral acids (Table 5, **1**).

We speculate that the better discrimination observed for bis-phosphine dioxides could be explained by the intramolecular interaction between the two phosphine oxide groups and two molecules of chiral acid bound in a single complex. The PM3 computer optimization of such a complex (Fig. 6) shows that the most stable complexes of this type have 3 pairs of intramolecular hydrogen

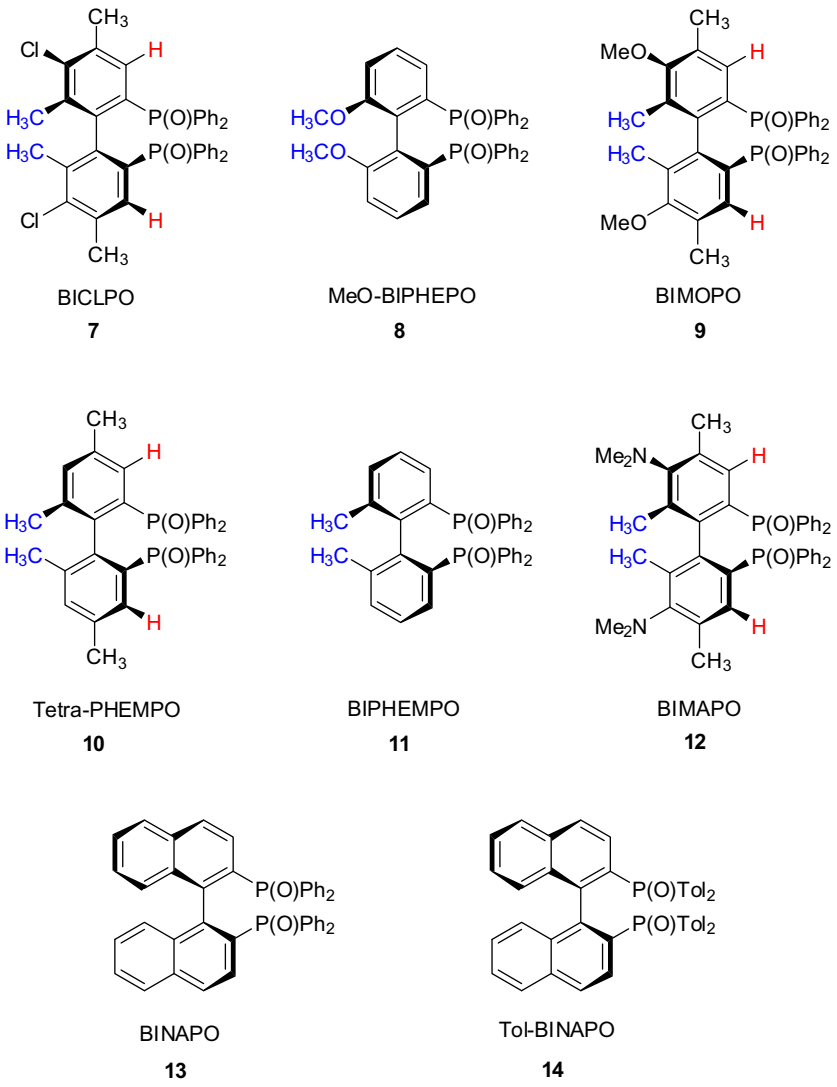

Figure 3. Bis-phosphine dioxides tested.

Table 1
Dependence of $\Delta\delta$ (Hz) in the NMR (500 MHz) spectra of **7** in the presence of different amounts of **3**

Number of equiv of **3**	^{31}P NMR $\Delta\delta$ (Hz)	^{1}H NMR $\Delta\delta$ (Hz)	
		CH	CH_3
1	12.9	0	0
2	16.9	0	2.0
3	21.3	0	3.1
4	23.5	1.5	3.7
6	28.4	3.7	5.1
8	30.5	4.0	5.8
10	32.4	4.6	6.7
20	36.7	5.6	8.6

Table 2
Parameters of extrapolated curves

Equilibrium parameters	For ^{31}P NMR data	From ^{1}H NMR data	
		CH	CH_3
a	41.16 ± 1.109	13.54 ± 1.70	11.45 ± 6.54
b	0.37 ± 0.03	0.09 ± 0.02	0.06 ± 0.05

bonds: PO–H_{acid} (0.99 Å), CO–*ortho*H–C_6H_4–PO (1.78 Å), (CO)′–*ortho*H–C_6H_4–(PO)′ (1.84 Å). In this way, the chiral acid can strongly influence both phosphorus groups at the same time.

2.6. The assignment of the enantiomeric composition and absolute configuration by the analysis of electronic circular dichroism spectra (ECD)

To prove the accuracy of the NMR methodology discussed above for the absolute configuration assignment of bis-phosphine dioxides, we decided to apply electronic circular dichroism spectroscopy (ECD) for this purpose.

The electronic absorptions and chiroptical data for bis-phosphine dioxides **7**, **8**, and **10**–**14** are presented in Table 6. The experimental data demonstrate that the investigated compounds display two UV bands and up to six distinct Cotton effects (CEs) in the 200–350 nm spectral range. From Table 6, it can be seen that the investigated bis-phosphine dioxides can be divided into two separate classes with respect to their CEs signs. In the first class, consisting of compounds (*R*)-**7**, (*R*)-**8**, (*R*)-**10,** (*R*)-**11,** (*R*)-**13,** and (*R*)-**14**, the signs of the CD bands at around 200, 226, 240, and 255 nm are positive, negative, negative, and positive, respectively. In the second class, represented by compounds (*S*)-**7**, (*S*)-**8,** (*S*)-**10,** (*S*)-**11,** and (*S*)-**12**, the signs of the same bands are negative,

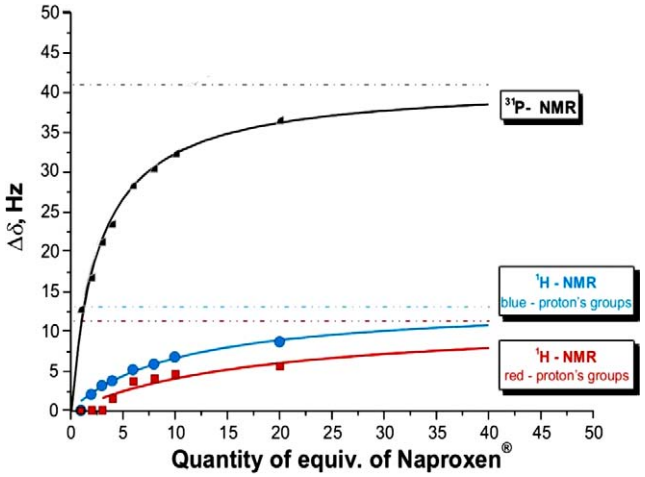

Figure 4. A graph of the dependence of $\Delta\delta$ on the quantity of **3**.

Table 3
The comparison of ^{31}P NMR $\Delta\delta$ values of **7**–**14** induced by different CSAs

CSA	Phosphine oxide							
	7	**8**	**9**	**10**	**11**	**12**	**13**	**14**
1	+6	−3	0	+8	+7	−3	+3	0
3	+29	+19	0	+27	+18	—[a]	+52	+76
4	−41	0	0	—[a]	0	—[a]	−23	0
5	0	−29	−25	−12	+12	−30	0	−36
6	+16	+15	+41	+9	+16	+44	+16	+11

All measurements were carried out in a 0.006 M solution of phosphorus compounds (racemic or about 40% ee) in $CDCl_3$ with 3 equiv of CSA (or 2 equiv of Kagan's amide) to one phosphine oxide group at rt. The sign '+' before $\Delta\delta$ means that the signal of the (*R*)-enantiomer is at a lower field.

[a] The width of signal does not allow to determine the value of $\Delta\delta$.

Table 4
The comparison of ^{1}H NMR $\Delta\delta$ values of **7**–**12** induced by different CSAs

CSA	Phosphine oxide									
	7		**8**		**9**	**10**		**11**	**12**	
1	0	−2	0	−6	+4	0	−4	−3	−4	−5
3	+4	+5	+3	0	+4	+4	0	0	+6	+3
4	+11	+31	−25	+20	+43	+14	+13	+28	−15	−13
5	+46	+5	−55	+41	+11	+34	−3	+34	−28	−4
6	+9	−9	—	−15	+5	+13	−8	+22	−9	+6

positive, positive, and negative, respectively (Fig. 7). The sign of the long-wavelength CD band, associated with the electronic absorption arising at around 290 nm, does not reveal such a regularity.

According to the literature, the CD spectra of axially dissymmetric biphenyl diphosphines are characterized by the presence of two CD bands occurring at around 235–240 and 280 nm.[10] It was also reported that the strong negative CE at 235–240 nm and a weaker positive CE at 280–290 nm are indicative of the (*R*)-configuration of the biphenyl chromophore. Among the investigated compounds, however, only the enantiomers of biphenyl **8** fulfil the above mentioned rule by displaying a negative/positive and a positive/negative CEs at around 230 and 290 nm, respectively. This discrepancy could be explained by the fact that the sign of the long-wavelength CD band depends strongly on the substitution pattern. Therefore, this band cannot serve as a diagnostic tool in our case, because compound **8** differs from other investigated compounds in the substitution at the *ortho*-position (methoxy groups *versus* methyl group). Thus, the CE within the so-called

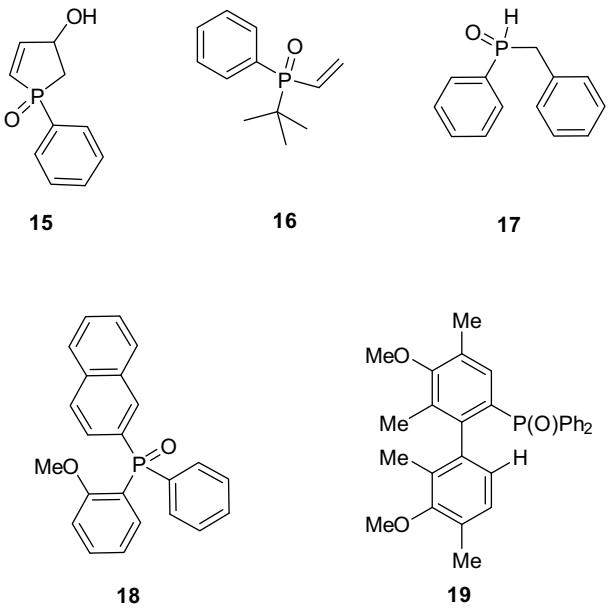

Figure 5. Monophosphine oxides tested.

Table 5
The comparison of ^{31}P NMR $\Delta\delta$ values of **15–19** induced by different CSAs

CSA	Phosphine oxide				
	15	**16**	**17**	**18**	**19**
1	9	4	35	19	38
3	0	0	0	1	5
4	0	0	11	2	3
5	4	19	34	1	8
6	0	9	18	2	0

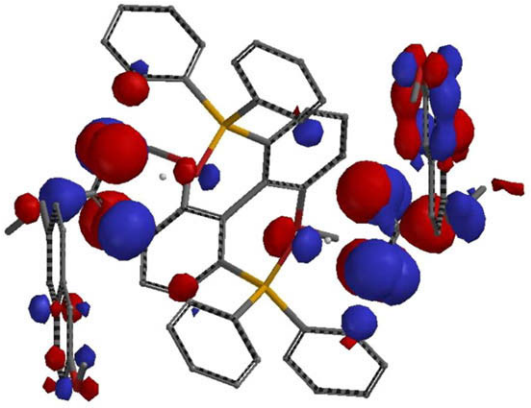

Figure 6. The computer model of complex of MeO-BIPHEPO with Naproxen®. The HOMO orbitals involved in formation of hydrogen bonds are presented.

'conjugation band' around 230 nm should be the most indicative because it is determined by the helicity of the biphenyl system only.[11] Later studies showed that 'a negative maximum corresponding to the A band (ca. 252 nm) is related to a *P* torsion of the C_{Ar}–C_{Ar} bond'.[12] Under the assumption that a similar behavior is also valid in the case of bis-phosphine dioxides, the first class of investigated compounds could be recognized as the (*M*)-series. Thus, compounds from the second class, that is, exhibiting the opposite sign pattern for the same CD band, should belong to the (*P*)-series. In our case, *P*/*M* configuration corresponds to the (*S*)/

Table 6
UV and CD data of compounds **7**, **8**, and **10**–**14** recorded in acetonitrile

Comp.	UV ε (λ/nm)		CD $\Delta\varepsilon$ (λ/nm)					
(*R*)-**7**	1700 (280)	20,000 (242)	+52.72 (208.5)	−10.45 (227.5)	−6.46 (246.0)	+0.72 (255.5)	−0.83 (288.0)	
(*S*)-**7**			−86.73 (208.8)	+19.86 (229.5)	+10.56 (245.6)	−1.07 (255.6)	+1.53 (288.5)	
(*R*)-**8**	5100 (298)	766,000 (220)	+75.24 (205.0)	−27.20 (231.5)		+2.48 (259.5)	+6.32 (289.0)	−1.13 (311.0)
(*S*)-**8**			−88.07 (204.5)	+32.33 (231.0)		−3.58 (258.0)	−9.16 (288.5)	+1.56 (309.5)
(*R*)-**10**	3400 (282)	11,200 (240)	+20.43 (202.8)	−6.30 (227.2)	−4.32 (238.0)	+0.60 (252.5)	−0.26 (288.0)	
(*S*)-**10**			−82.00 (201.0)	+23.87 (225.0)	+21.29 (237.0)	−2.77 (252.5)	+0.95 (290.5)	
(*R*)-**11**	4400 (284)	19,600 (242)	+82.16 (202.5)	−30.76 (226.0)	−25.50 (235.0)	+0.61 (252.2)	−0.91 (285.5)	
(*S*)-**11**			−24.14 201.5	+9.07 (226.0)	+5.89 (233.0)	−0.59 (251.0)	+0.20 (282.5)	
(*S*)-**12**			−59.81 (201.0)		+11.40 (232.0)	−2.91 (262.5)	−6.01 (300.0)	
(*R*)-**13**	9000 (286)	66,000 (231)	+40.81 (206.5)	−24.18 (227.5)	+51.70 (239.0)	+3.95 (268.5)	−5.42 (301.0)	−1.97 (332.0)
(*R*)-**14**	12000 (286)	19,600 (242)	+53.74 (207.4)	−20.20 (224.4)	+67.67 (240.5)	+8.87 (262.5)	−9.59 (301.0)	−2.64 (332.0)

Data are given as ε (nm) and $\Delta\varepsilon$ (λ/nm), respectively.

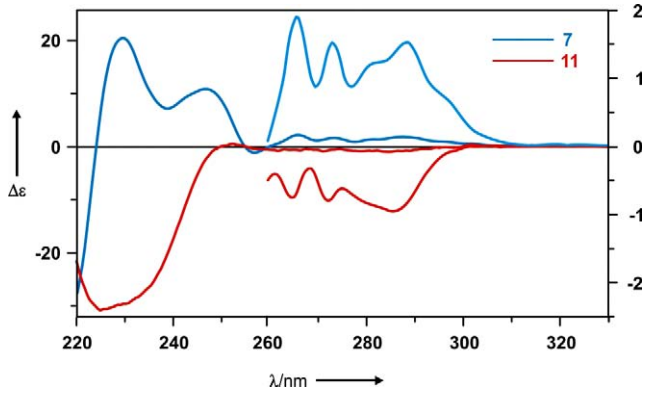

Figure 7. CD spectra of bis-phosphineoxides (*S*)-**7** and (*R*)-**11** in the range 330–220 nm recorded in acetonitrile.

(*R*) absolute configuration in the CIP notation, respectively. Additional evidence in support of such assignment is given by the comparison of the CD data obtained for (+)-**8** and (−)-**8** with the respective CD data for (*R*)-(+)- and (*S*)-(−)-MeO-BIPHEPO previously reported.[10] Since the CD spectra perfectly match each other, we were able to assign the (*R*)-configuration to the (+)-**8** enantiomer and the (*S*)-configuration to (−)-**8** enantiomer.

The difference in the amplitude of particular CEs in the case of enantiomeric bis-phosphineoxides **7**, **10**, and **11** is likely due to the different enantiomeric purities of the counterpart enantiomers (Table 6). In the case of compounds (*R*)-**7,** (*R*)-**10**, and (*S*)-**11**, their CD spectra were measured using a sample of the same enantiomeric purity as used for the NMR measurements**.** It means that the enantiomeric excess (ee) was approximately equal to 60%, 40%, and 60%, respectively. Accordingly, the amplitude of CEs tracks well the enantiomeric purity, as expected.

The determination of the absolute configuration of compound (*S*)-**8** was additionally corroborated by X-ray structure analysis (Fig. 8).

The X-ray data unambiguously confirm the assignment made using the CD data. In addition, the solid-state CD curve for compound (*S*)-**8** is in a good agreement with the data recorded in solution (Fig. 9), thus providing an additional proof that the same molecular species are present in the solid state as well as in solution. This indicates that the solute–solvent interactions, which may affect the CD spectra considerably due to both the conformational and the vicinal effects, are negligible in this case and points out that the CD observed is largely a molecular property.

In an effort to corroborate the conclusions made on the basis of the experimental results, TDDFT calculations for (*S*)-**8** were attempted. Since for a given conformation TDDFT calculations provide a detailed picture of the electronic structure, a comparison of the computed CD spectra with the experimental ones allows one to infer conclusions about the stereochemistry of the phosphine dioxides studied. As can be seen in Figure 9, the agreement between the simulated and the experimental CD spectra is very satisfactory, and confirms the absolute configuration and conformation of (*S*)-**8**. On the basis of this result an unequivocal assignment of the absolute configuration to remaining phosphine dioxides is possible.

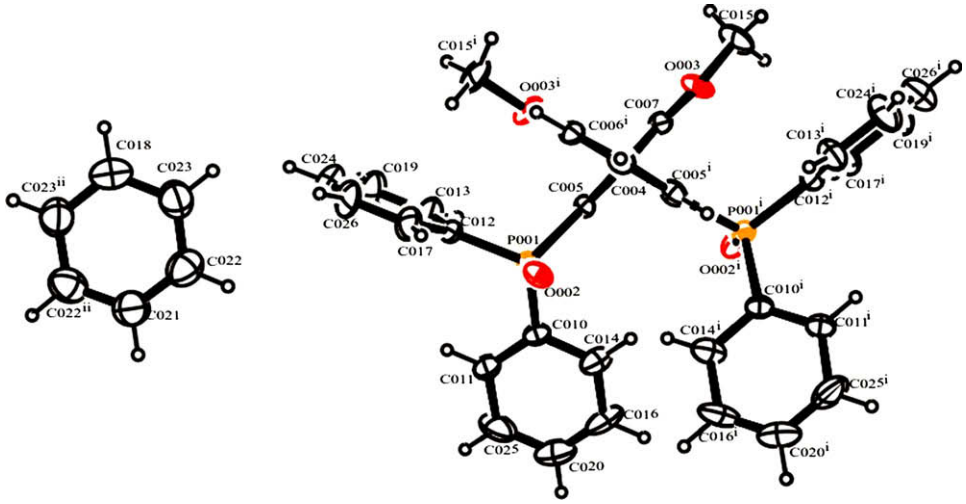

Figure 8. ORTEP diagram of compound **8** with the crystallographic numbering scheme. Thermal ellipsoids are shown at 30% probability level.

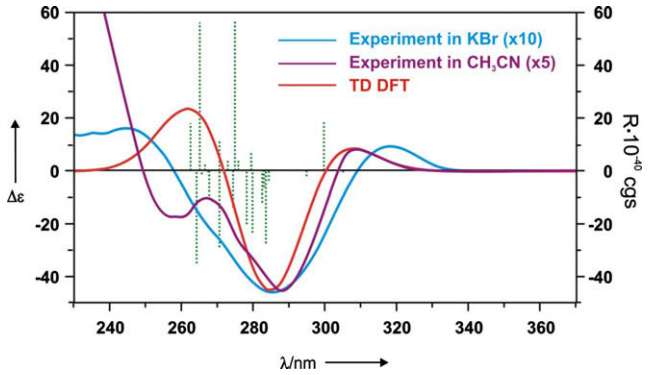

Figure 9. Experimental and computed CD spectra of bis-phosphineoxide (*S*)-**8** in the range 230–360 nm. Experimental CD curve recorded as KBr mull is tenfold and the one measured in acetonitrile is fivefold enhanced.

We can thus conclude that such a combined experimental and theoretical treatment provides a basis for the determination of the absolute configuration with a high degree of confidence.

3. Conclusions

In conclusion, we have proposed a simple method for determination of the er of C_2-symmetric atropoisomeric bis-phosphine dioxides using set of CSAs in ^{1}H and ^{31}P NMR measurements. The most reliable determination of the absolute configuration was possible by comparison of experimental data from several ^{31}P NMR experiments or by utilization of CD spectroscopy. Based on the combined theoretical and experimental treatment of chiroptical properties, the assignment of the absolute configuration to phosphineoxides studied could be performed with a high degree of confidence.

4. Experimental

4.1. General

All commercially available compounds were used as received. Compounds **1**,[12] **2**,[6,13] **9**,[14] **10**,[15] **15**,[16] **16**,[17] **17**,[18] and **18**[19] were prepared according to the published literature procedures. Compounds **7**, **12**, and **19** were available from other current research projects.[9] The NMR spectra were recorded on Bruker AVANCE 500, Varian Gemini 200, and 400 spectrometers in $CDCl_3$; the chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hertz. The UV spectra were measured using Cary 100 spectrophotometer in acetonitrile solutions. The CD spectra were recorded between 185 and 380 nm at room temperature with a JASCO J-715 spectropolarimeter in acetonitrile solutions. The solutions with concentrations in the range of 0.8×10^{-4} to 1.2×10^{-3} mol dm^{-3} were examined in cells with the path length of 0.1 or 1 cm. For CD spectra measurements in solid state, the KBr discs were prepared as for IR measurements. In general, 200–210 mg of dried KBr and an appropriate amount of a sample (0.6–0.09 mg) were ground in an agate mortar, and the mixture was pressed as usual to form a disk. During the entire measurement, the disc was rotated around the optical axis using original JASCO equipment for this purpose.

4.2. Procedure of sample preparation for the NMR measurements

The phosphorus compound (3–5 mg) was weighed directly into the NMR tube followed by the calculated amount of CSA and 0.7 mL of deuterated solvent. The NMR tube was closed with PP cap and heated at about 100 °C until the complete dissolution of all components. The NMR spectra were recorded as soon as the sample solution was cooled down to rt.

4.3. X-ray crystallographic data and structure determination

Intensity data for (*S*)-**8** were collected on a Nonius MACH3 diffractometer using Cu Kα radiation ($\lambda = 1.54178$ Å) with an ω–2θ scan at 293 K. The unit cell parameters were determined by least-squares refinement on diffractometer angles $20.92° \leqslant \theta \leqslant 42.95°$ for 10 automatically centered reflections.

Data were corrected by ψ-scan[20] based absorption. The structure was solved by direct method using SHELXS-97,[21] and refined anisotropically (non-hydrogen atoms) by full-matrix least-squares on F^2 using the SHELXL-97[21] program. The program ROTAX[22] was used for obtaining the twining matrix. The data relating to the single crystal X-ray structure of (6,6′-dimethoxybiphenyl-2,2′-diyl)-bis(diphenylphosphine oxide) **8** have been deposited at the Cambridge Crystallographic Database (CCDC: 689485).

$C_{38}H_{32}O_4P_2{\cdot}C_6H_6$, M_r 614.61, monoclinic, space group $C2$, $a = 14.877(5)$, $b = 8.997(5)$, $c = 14.422(5)$, $\beta = 107.868(5)°$, $V = 1837.3(1)$ Å^3, $Z = 4$, $D_{ca} = 1.252$ Mg m^{-3}, $\mu = 1.410$ mm^{-1}, $F(000) = 728$, data were collected using a crystal of size $0.50 \times 0.40 \times 0.20$ mm^3. A total of 2041 reflections were collected for $1.48° \leqslant \theta \leqslant 26.33°$, $-18 \leqslant h \leqslant 0$, $-11 \leqslant k \leqslant 0$, $-17 \leqslant l \leqslant 17$. There were 1963 independent reflections [$R_{int} = 0.0672$]. There were determined twining matrices with 180.0° rotation about [0 1 0] direction. The final R indices were [$I > 4\sigma(I)$] $R_1 = 0.0647$, $wR_2 = 0.1653$. The largest difference peak and hole were 0.310 and −0.410 e Å^{-3}.

4.4. Computational method

The theoretical calculations of the CD spectrum were carried out for phosphineoxide (*S*)-**8**. The conformational analysis was carried out with the CACHE program package. (CaChe. Ws Pro 5.0 Fujitsu Ltd) In the first step, using CONFLEX® software, the lowest-energy conformer was found which, in the second step, was re-optimized at B3LYP/6-31 G++(d,p) level in GAUSSIAN software.[23] The CD and UV spectra were simulated by overlapping Gaussian functions for each transition according to the procedure described by Grimme et al.[24] To reduce the calculation time only 25 transition states in the range 290–250 nm were used for simulation of the theoretical CD spectrum. The rotatory strength was calculated at the B3LYP/6-31 G(d,p) and B3LYP/6-31 G++(d,p) levels using both the length and the velocity representations. The differences between the length and the velocity calculated values of the rotatory strengths were quite small and for this reason only the velocity rotatory strengths were taken into further consideration. The wavelength scaling by UV correction was done before the experimental and theoretical CD spectra were compared.[25] No correlation for the medium dielectric constant was implemented. Better agreement with the experimental CD spectra recorded in solution and in solid state was achieved for the simulated CD spectrum determined at the B3LYP/6-31 G(d,p) level.

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