Phosphanes

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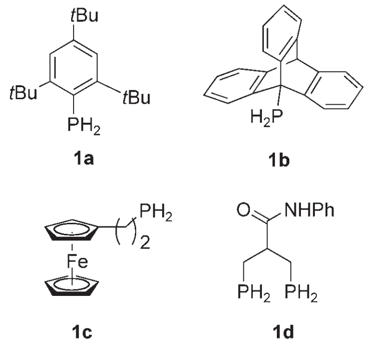
Taming a Functional Group: Creating Air-Stable, Chiral Primary Phosphanes**

Rachel M. Hiney, Lee J. Higham, Helge Müller-Bunz, and Declan G. Gilheany**

Primary phosphanes, unlike their nitrogen counterparts, have a reputation as being toxic, volatile compounds that often spontaneously ignite in air.[1] Accordingly, despite an impressive range of applications as asymmetric ligand precursors,[2] biomedicines,[3] polymers,[4] carbohydrates,[5] and macrocycles,[6] as well as possessing two reactive P–H bonds for functionalization, they remain under-used. Some of the few primary phosphanes reported to be air stable[7] are shown in Scheme 1. There appears to be more than one factor that can confer stability. Thus supermesitylphosphane (**1a**),[8]-triptycylphosphane (**1b**),[9] and various related compounds[7] undoubtedly owe their stability to steric factors. More puzzling is **1c**, which is stable in air indefinitely, whereas $FcPH_2$ and 1,1′-$Fc'(PH_2)_2$ ($Fc = [(\eta^5\text{-}C_5H_4)Fe^{II}(\eta^5\text{-}C_5H_5)]$, $Fc' = [Fe^{II}(\eta^5\text{-}C_5H_4)_2)]$) are oxidized in three–five days.[10a] Clearly the alkyl spacer groups are important, but their significance is not currently understood. The reasons for the air-stability of the compounds $[R^2R^1N(CH_2)_nPH_2]I$,[11] $S(CH_2SCH_2CH_2PH_2)_2$,[3] and the related **1d**[12a] are also unclear; the authors suggested that the remote heteroatom might confer stability through negative hyperconjugation.[11,12] Herein we report a potentially larger class of air-stable phosphanes, which possess extended π conjugation, and we suggest that stability may be more the norm than the exception.



Scheme 1. Phosphanes possessing a high degree of air stability.

As part of our research into P-stereogenic 2-methoxy-2′-diphenylphosphanyl-1,1′-binaphthyl (mop) ligands,[13] we required precursor chiral primary phosphanes, which have rarely been used in the design of asymmetric ligands.[14,2c] Our initial target was (*R*)-2-phosphanyl-2′-methoxy-1,1′-binaphthyl (**4**). We also recognized that **4** might provide a test of whether the local heteroatom conferred air stability.

Compound (*R*)-**4** was prepared in a straightforward manner (Scheme 2) in high yield as a white powder, and its ^{31}P NMR ($\delta = -126.3$ ppm, average $^{1}J_{\text{P-H}} = 202.6$ Hz) and IR data ($\nu(\text{P-H}) = 2291\ \text{cm}^{-1}$) were as expected.

More gratifying was that (*R*)-**4** did indeed show remarkable stability towards air oxidation: no oxidation was observed for (*R*)-**4** after seven-days exposure to air. Suitable crystals of (*R*)-**4** for X-ray crystallography[15] were obtained from acetonitrile, and the resulting structure (Figure 1) represents, to the best of our knowledge, the first such characterization of an optically pure primary phosphane. The P–C bond length (1.811(6) Å) correlates with the few other crystal structures reported for uncoordinated primary-phosphanes.[9,10b,11,12a,16,17]

On closer examination of the solid-state molecular structure we noted that the environment around the P atom is not crowded, nor does there appear to be any interaction between the P atom and the O atom of the methoxy substituent, apparently ruling out the ether group as being a

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[*] R. M. Hiney, Dr. L. J. Higham,[+] Dr. H. Müller-Bunz,
Dr. D. G. Gilheany
School of Chemistry and Chemical Biology
Centre for Synthesis and Chemical Biology
Conway Institute for Biomolecular and Biomedical Research
University College Dublin, Belfield, Dublin 4 (Ireland)
Fax: (+353) 1-716-2127
E-mail: lee.higham@ucd.ie
declan.gilheany@ucd.ie

[+] Current address:
School of Natural Sciences-Chemistry, Bedson Building
Newcastle University, Newcastle upon Tyne, NE1 7RU (UK)

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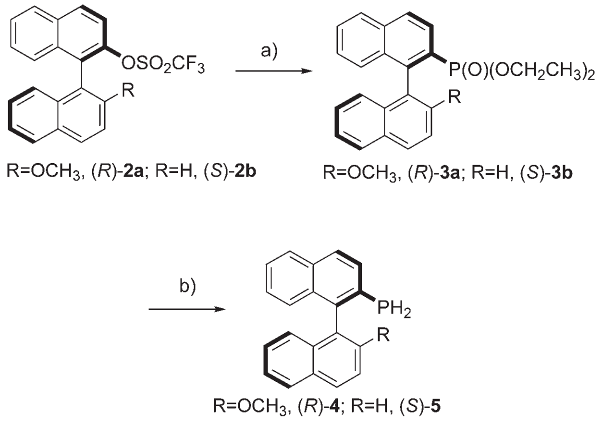
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author (detailed preparations of (*R*)-**2a**, (*S*)-**2b** , (*R*)-**3a**, (*S*)-**3b**, (*R*)-**4**, (*S*)-**5**, **6**, **7** and **8** are included, together with the method for preparing the *cis*-$[Mo(RPH_2)_2(CO)_4]$ complexes. Further details of the electrochemical experiments, oxidation protocols and safety precautions may also be found therein).



R=OCH$_3$, (*R*)-**2a**; R=H, (*S*)-**2b**

R=OCH$_3$, (*R*)-**3a**; R=H, (*S*)-**3b**

R=OCH$_3$, (*R*)-**4**; R=H, (*S*)-**5**

Scheme 2. Synthesis of (*R*)-**4** and (*S*)-**5**. a) Pd(OAc)$_2$, 1,4-bis(diphenylphosphanyl)butane, ((CH$_3$)$_2$CH)$_2$N(CH$_2$CH$_3$), NaCOOH, HP(O)(OCH$_2$CH$_3$)$_2$, DMSO, 100°C; b) LiAlH$_4$, (CH$_3$)$_3$SiCl, THF, −78→−40°C.

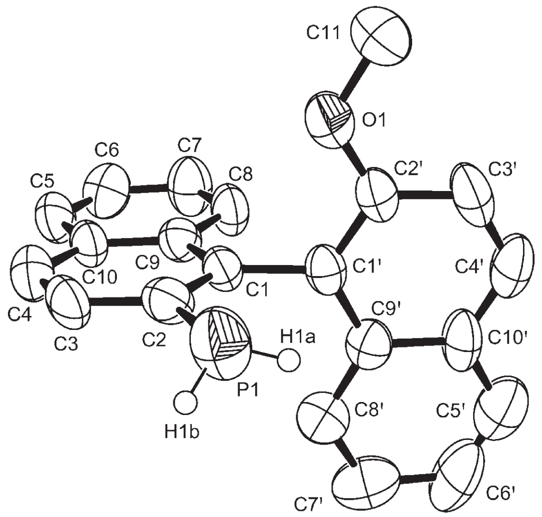


Figure 1. The X-ray crystal structure of (*R*)-**4**. Hydrogen atoms attached to carbon atoms are omitted for clarity.

contributor to the air stability. To confirm this latter point, we prepared the analogous phosphane lacking the 2′-methoxy substituent, (*S*)-2-phosphanyl-1,1′-binaphthyl (**5**, Scheme 2), again as a white solid in high yield (^{31}P NMR: $\delta = -126.7$ ppm, $^1J_{\text{P-H}} = 203.8$ Hz; IR: ν(P-H) = 2297 cm^{-1}). Remarkably, samples of (*S*)-**5** in the solid state were also stable over the same timeframe (Figure 2). Additionally, (*S*)-**5** is a novel chiral ligand precursor.[18]

Having discounted the relevance of the ether group, we sought to simplify the structure even further and we found that 2-naphthylphosphane (**6**), a white solid prepared by using a similar route, exhibited good air stability (88% phosphane remained after seven days, Figure 2). For comparison, the regioisomer of **6**, 1-naphthylphosphane (**7**) showed significantly more oxidation than **6** (Figure 2), but we attribute this result to the fact that it is an oil under ambient conditions. We also prepared the related compound 5,6,7,8-tetrahydro-2-naphthylphosphane (**8**) where the ring without the phosphorus substituent is hydrogenated and conjugation thereby reduced. Compound **8**, also an oil, had very low air stability commensurate with that of PhPH$_2$.

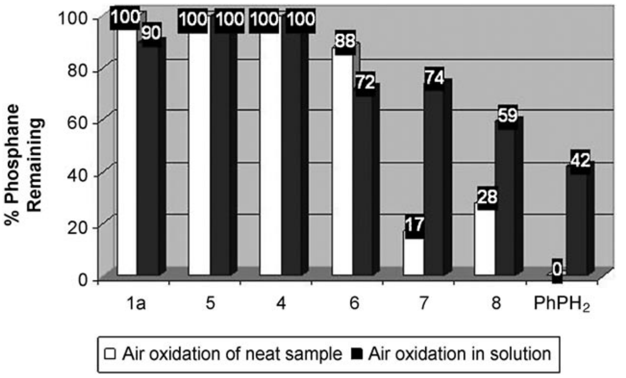


Figure 2. Oxidation profiles of RPH$_2$ of neat (left bar) and in CDCl$_3$ solution (right bar) after seven days.

It is important to note that in previous reports the air stability of primary phosphanes often only referred to the neat samples. We were concerned that the nature of the sample (crystalline solid or oil) would influence the rate of oxidation. Therefore, we examined the solution behavior of our primary phosphanes in CDCl$_3$ on exposure to air over seven days in uncapped NMR tubes (a method rarely performed[10b,11]; Figure 2).

Under these conditions, there was a small quantity of oxidation in the case of supermesitylphosphane (**1a**), but remarkably even without the steric stabilization of **1a**, **4** and **5** exhibited no oxidation. Thus their stability in air is not simply a result of the slow rate of solid-state reactions. Even when the solution of **5** was enriched with dioxygen, we observed no oxidation after 24 h. In solution, the naphthylphosphanes **6** and **7** showed similar levels of oxidation, with notable quantities of the oxides and H-phosphinic acids produced.[19]

This observation indicates that the sensitivity of neat **7** relates to it being an oil at ambient temperature. The monoarenes **8** and PhPH$_2$ had oxidized to a large extent by the end of the seven days in solution, but were still more stable than in their neat state as oils.

As steric factors do not appear significant in the stabilization of **4** and **5** to oxidation, we wished to examine their electronic nature. Unfortunately, the low basicity of the phosphanes (**5** was unprotonated with 6 M HCl) and solubility difficulties precluded the measurement of pK$_a$ values. Some insight into their basicity was obtained from IR studies following the protocol of Henderson and Alley,[10a] in which two equivalents of FcCH$_2$PH$_2$ were treated with *cis*-[Mo(C$_5$H$_{10}$N)$_2$(CO)$_4$] to give *cis*-[Mo(FcCH$_2$PH$_2$)$_2$(CO)$_4$] (Table 1).

Comparison of entries 3, 4, and 7 in Table 1 shows there is no apparent correlation between the oxidative stability of the primary phosphanes and the $\nu_{(\text{CO})}$ (A_1) stretching frequency. This routine method to assess the basicity of the phosphanes cannot therefore be extrapolated to predict their stability in air.

We turned next to the electrochemical behavior of the phosphanes, which was examined by voltammetry using a Pt-disk electrode. We believe that this is the first report of such

Table 1: The oxidation potentials of the phosphanes and their $\nu_{(CO)}$ (A_1) vibrations in *cis*-$[Mo(RPH_2)_2(CO)_4]$.

	RPH_2	$E_{s,max}$ [mV[a]]	$\nu_{(CO)}$ [cm^{-1}]
1	$FcCH_2PH_2$	–	2020[b]
2	**1a**	960	–[c]
3	(*R*)-**4**	1005[d]	2023
4	(*S*)-**5**	1170	2025
5	**6**	850	2027
6	**7**	845	2027
7	**8**	770[e]	2025
8	$PhPH_2$	795	2025

[a] Tetrabutylammonium tetrafluoroborate (0.1 M) as the supporting electrolyte, scan rate 100 $mV s^{-1}$, 20 °C; potential in mV, measured with a Pt disk working electrode in degassed dichloromethane solution; the values are referenced to ferrocene/ferrocinium. [b] See Ref. [10b]. [c] The *cis* compound was not formed. [d] This value is attributable to the ether group, as (*R*)-2,2′-dimethoxy-1,1′-binaphthylene gave a value of 1030 mV. [e] Partially masked by the wave of the oxidation product at 1160 mV.

studies on uncomplexed primary phosphanes. We have used the potential of maximum slope $E_{s,max}$[20] to quantify the position of the waves on the potential axis because of the irreversibility of the phosphane oxidation under these experimental conditions. In this case the values obtained do appear to indicate a trend with oxidative stability (Table 1). The lowest potentials are observed for the most readily oxidized compounds **8** and $PhPH_2$. Intermediate in value and very similar in magnitude are the naphthylphosphanes **6** and **7**, again emphasizing that the difference observed in the oxidation of the neat samples is directed by kinetic factors (a solid versus an oil), but also confirming that the position of substitution has little effect. Finally, the oxidation-resistant **5** and **1a** show high $E_{s,max}$ values. These results indicate a correlation between the ease of generation of a radical such as $[RPH_2]^{+\bullet}$ and air stability.[21] This finding is consistent with the reported[22] mechanism of phosphorus oxidation by triplet oxygen having a radical nature.[23]

Our results show that the simple addition of a benzene ring to phenylphosphane imparts stability towards oxidation. In discussing the source of this remarkable stability, we note that there are no steric factors and no remote heteroatom. Therefore the source of this stabilization must be a type of conjugative effect. This is confirmed by the fact that when the additional ring is saturated, the stability was not affected.[24] The conjugative effect could be between the phosphorus lone pair of electrons and the aromatic system, simply within the aromatic system itself, or both. In considering this, we take into account the following: 1) conjugation of phosphanyl groups and aromatic rings has been a most contentious issue in the literature;[25] 2) both 1-naphthyl and 2-naphthyl substitution lead to a similar stabilization, whereas a conjugative effect to the lone pair of electrons might be expected to show a difference; 3) there appears to be no relation between the stabilization and the basicity of the phosphane, which would again imply that the lone pair of electrons is not involved in imparting stability; 4) a lower oxidation potential of the phosphane seems to correlate with the stability observed; and 5) studies from photoelectron spectroscopy (PES)[25a–c] have established that the highest occupied molecular orbital (HOMO) of phenylphosphane is a perturbed π orbital of the benzene ring. We believe therefore that the conjugative effect is related to the aromatic system and that the greater conjugation in (*R*)-**4** and (*S*)-**5** either raises the energy required to form a $[RPH_2]^{+\bullet}$-type radical cation, or conversely stabilizes it, thereby rendering it less reactive in the next stage of the oxidation. However, the manner in which the conjugation operates in exerting such effects is unclear and indeed this still may not be the critical factor controlling the oxidation. We will report in due course on theoretical, PES, and microwave studies of this intriguing system which we hope will allow us to elucidate the origin of the air stability.

In conclusion, we have synthesized the first air-stable chiral primary phosphanes and have attributed their stability to conjugation in their aryl backbones. Our findings suggest that many, perhaps most, primary phosphanes have no greater air sensitivity than moderately reactive aldehydes.[26] We hope that this will prompt a renaissance in the use of primary phosphanes as synthetic precursors; for example, (*R*)-**4** and (*S*)-**5** are convenient starting materials for previously inaccessible asymmetric phosphanes, such as phospholane–mop hybrids. More generally we note that 2-naphthylphosphane (**6**) could be used as a safe and convenient replacement for phenylphosphane.

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