Synthesis of Hemilabile Phosphine−Phosphine Oxide Ligands via the Highly Selective Pd-Catalyzed Mono-oxidation of Bidentate Phosphines: Scope, Limitations, and Mechanism

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The first simple and efficient, one-step catalytic method has been developed for the preparation of bis-phosphine monoxides, valuable hemilabile ligands that have proven usefulness in homogeneous catalysis, synthesis, analytical chemistry, cancer and AIDS research, chemistry of materials, etc. Readily available bidentate phosphines (dppm, dppe, dppp, dppb, dppbz, dppfc, and BINAP) are selectively oxidized to the corresponding monoxides in 65−90% isolated yield with 1,2-dibromoethane in the presence of alkali and catalytic quantities (0.15−2 mol %) of a Pd(II) salt. This anaerobic oxidation smoothly occurs under biphasic conditions at 20−80 °C and atmospheric pressure. In certain cases, the mono-oxidation is promoted by I^-. Stoichiometric studies of the novel process demonstrate that the catalytic loop involves (i) the formation of Pd(0) and a bis-phosphine monoxide (BPMO) upon reaction of a Pd(II) complex of the corresponding bis-phosphine with alkali, (ii) chelation-driven phosphine ligand exchange to displace the coordinated BPMO produced, and (iii) reoxidation of the Pd(0) complex with 1,2-dibromoethane via C−Br oxidative addition followed by β-bromide elimination.

Introduction

Bis-phosphine monoxides (BPMOs) of the general formula $R^1R^2P-Y-P(O)R^3R^4$, where Y is a divalent spacer, constitute one of the most important classes of hemilabile ligands.[1] Various BPMOs have already proven remarkable usefulness in inorganic/organometallic synthesis,[2] metal complex catalysis,[3−9] cancer[10] and AIDS[11] research, and analytical chemistry.[12] While the synthetic utility and potential of mixed phosphine−phosphoryl ligands have long been realized, the chemistry of BPMOs has been developing slowly due to the lack of a convenient general method to synthesize these ligands.

A few methods[2t,w,13−15] have been developed to prepare BPMOs from two P1 building blocks. These methods are specific to the synthesis of BPMOs with only one or two C atoms separating the P atoms. A two-step process has been developed[16] for the preparation of BPMOs via monobenzylation of a bidentate phosphine, followed by alkaline hydrolysis.

The simplest and most attractive way to prepare BPMOs would be direct selective mono-oxidation of readily available bidentate phosphines. However, the direct oxidation of bidentate phosphines with conventional oxidants (e.g., O_2, H_2O_2, Br_2/H_2O) is usually nonselective, leading to mixtures of the unreacted diphosphine and its monoxide and dioxide.[10,18−21] Mäding and Scheller[19] have reported that basic bidentate di*alkyl*phosphino substrates (e.g., dmpe) can be selectively mono-oxidized via monoprotonation followed by oxidation. Due to their poor basicity, the most readily available and attractive di*aryl*phosphino substrates cannot be mono-oxidized this way.

Here we report the first general, highly efficient and convenient method for selective catalytic mono-oxidation of aromatic diphosphines to the corresponding BPMOs.

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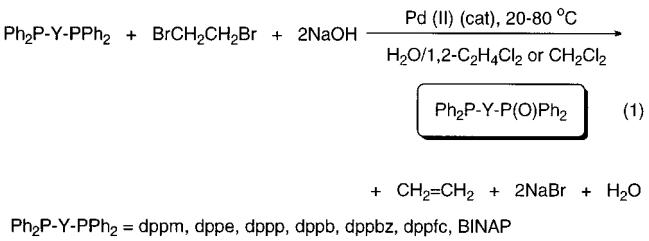
A preliminary communication of this novel method has been published.[22]

Results

Our research was focused exclusively on aromatic substrates containing PPh_2 moieties because they cannot be mono-oxidized selectively, using the simple Mäding−Scheller method.[19] The biphasic process developed (eq 1) readily occurred under mild conditions to produce the desired products in 50−90% isolated yield. The mono-oxidation was successfully performed for bis(diphenylphosphino)methane (dppm), 1,2-bis(diphenylphosphino)ethane (dppe), 1,3-bis(diphenylphosphino)propane (dppp), 1,4-bis(diphenylphosphino)butane (dppb), 1,2-bis(diphenylphosphino)benzene (dppbz), 1,1′-bis(diphenylphosphino)ferrocene (dppfc), and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) in its *R*, *S*, and racemic forms.



Catalytic Mono-oxidation of Bidentate Phosphines. As shown below, careful optimization of reaction conditions for each particular bis-phosphine substrate is needed to obtain the desired BPMO product in good yield. All catalytic reactions (Table 1) were run under nitrogen to protect Pd(0) catalytic intermediates from air and avoid noncatalytic, nonselective oxidation of the substrate.

$Ph_2P(CH_2)_2P(O)Ph_2$ (dppeO). The mono-oxidation of dppe to dppeO (eq 1) was successfully performed on a 0.5−50 g scale in 75−90% isolated yield. Although any palladium compound capable of forming $[(dppe)_2Pd]^{2+}$ or $[(dppe)_2Pd]$ upon mixing with dppe may be used as a catalyst for this reaction, $Pd(OAc)_2$ was the most convenient added catalyst to use due to its stability and solubility in organic solvents. Platinum complexes resulted in slower oxidation. The oxidation was conveniently performed in a 1,2-dichloroethane (DCE)−aqueous NaOH biphasic system under reflux. It took longer time (days) for the reaction to go to completion at room temperature. In the absence of a catalyst, a slow, nonselective oxidation reaction occurred, probably via the formation of a phosphonium salt from dppe and 1,2-dibromoethane, followed by alkaline hydrolysis.[16a] Because of this side-reaction, lower substrate-to-catalyst ratios resulted not only in longer reaction times but also in lower yields. For instance, an increase in the dppe to Pd molar ratio from 225 to 570 lowered the yield of dppeO from 87 to 82% (Table 1).

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(6) For hydroxycarbonylation of olefins, see: Terekhova, M. I.; Kron, T. E.; Bondarenko, N. A.; Petrov, E. S.; Tsvetkov, E. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1992**, 2003.

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(8) Enantioselective hydrosylylation,[8a] hydroformylation,[8b] and cycloaddition[8c−e] reactions catalyzed by transition metal complexes of optically active BPMO, e.g., BINAP mono-oxide (BINAP(O))[8a−c,e] have been recently reported. An attempt to use BINAP(O) for the hydrovinylation of 2-methoxy-6-vinylnaphthalene has been unsuccessful.[8f] Some BINAP(O) complexes of Rh have been reported[8g] to catalyze various hydrogenation, hydroboration, and hydroformylation reactions, albeit with low ee's. Nonenzymatic kinetic resolution of secondary alcohols in the presence of BINAP(O) has been recently described.[8h] See: (a) Gladiali, S.; Pulacchini, S.; Fabbri, D.; Manassero, M.; Sansoni, M. *Tetrahedron: Asymmetry* **1998**, *9*, 391. (b) Gladiali, S.; Alberico, E.; Pulacchini, S.; Kollár, L. *J. Mol. Catal. A* **1999**, *143*, 155. (c) Faller, J. W.; Parr, J. *Organometallics* **2000**, *19*, 1829. (d) Faller, J. W.; Liu, X.; Parr, J. *Chirality* **2000**, *12*, 325. Faller, J. W.; Parr, J. *Organometallics* **2001**, *20*, 697. (e) Faller, J. W. Grimmond, B. J.; D'Alliessi, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 2525. (f) Nandi, M.; Jin, J.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1999**, *121*, 9899. (g) Gladiali, S.; Medici, S.; Kegl, T.; Kollar, L. *Monatsh. Chem.* **2000**, *131*, 1351. (h) Sekar, G.; Nishiyama, H. *J. Am. Chem. Soc.* **2001**, *123*, 3603.

(9) (a) Olefin hydroformylation[3] and hydroxycarbonylation[6] reactions catalyzed by Rh and Pd BPMO complexes occur with unusually high selectivities to the desired linear products. In the presence of $Ph_2P(O)(CH_2)_2PPh_2$, the Rh-catalyzed Monsanto acetic acid process (MeOH + CO = AcOH; accounts for 55% of all acetic acid produced worldwide)[9b] is as efficient at 80 °C and 50 psi as the BPMO-free industrial process, which is conventionally run at 200 °C and 500 psi.[4a,d] (b) Weissermel, K.; Arpe, H.-J. *Industrial Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, 1997.

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(20) (a) The Staudinger-type reaction of 1,2-bis(diphenylphosphino)-benzene with Me_3SiN_3 results in the exclusive formation of the corresponding mono-iminophosphorane,[20b] which may be hydrolyzed to the oxide. This case is rather exceptional as diphosphines with a flexible backbone, such as dppm,[20c] always react with azides nonselectively. (b) Reed, R. W.; Santarsiero, B.; Cavell, R. G. *Inorg. Chem.* **1996**, *35*, 4292. (c) Katti, K. V.; Cavell, R. G. *Inorg. Chem.* **1989**, *28*, 413.

(21) It has been reported[21a,b] that some polydentate phosphines can be air-oxidized in the presence of cobalt catalysts. This way triphos has been oxidized to triphosO in 30−45% yield or to triphosO_2 in 80−95% yield.[21a] The cocatalyzed air-oxidation of dppm and dppe in the presence of excess sacrificial 3-methylbutanal has been claimed to produce dppmO and dppeO in ca. 55% yield at 88−100% conversion (GC; no isolation reported).[21b] See: (a) Heinze, K.; Huttner, G.; Zsolnai, L. *Chem. Ber./Recl.* **1997**, *130*, 1393. (b) Mastrorilli, P.; Muscio, F.; Nobile, C. F.; Suranna, G. P. *J. Mol. Catal. A* **1999**, *148*, 17.

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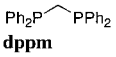
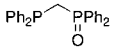
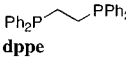
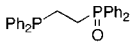
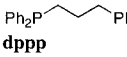
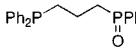
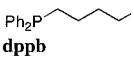
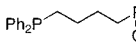
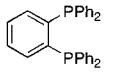
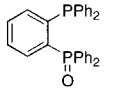
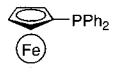
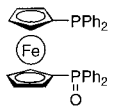
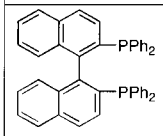
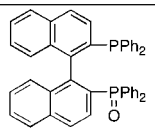
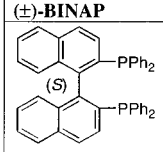
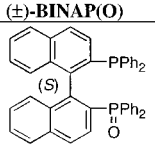
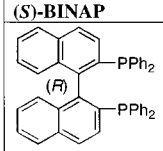
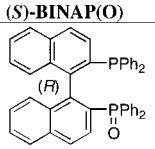
Table 1. Palladium-Catalyzed Mono-oxidation of Bidentate Phosphines with 1,2-Dibromoethane under Biphasic Conditions (Organic Solvent-Aqueous NaOH)

Substrate	Catalyst, mol % (promoter)	Org. phase[a]	T, °C	Time, h	BPMO product	Yield, %	^{31}P NMR δ, ppm ($J_{P,P}$, Hz)
 **dppm**	$Pd(OAc)_2$, 0.42 (NaI)	DCE	80	4		74	-26.5 +29.8 (50.5)
	$Pd(OAc)_2$, 0.55 (NaI)	DCE	80	3.7	 **dppmO**	80	
	$Pd(OAc)_2$, 1.18 (NaI)	DCE	80	4		84	
 **dppe**	$Pd(OAc)_2$, 0.44	DCE	80	7		87	-11.5 +32.3 (48.0)
	$Pd(OAc)_2$, 0.17	DCE	80	15	 **dppeO**	82	
	$Pd(OAc)_2$, 0.18	DCE	80	21.5		78	
 **dppp**	$Pd(OAc)_2$, 0.37	DCE	80	6	 **dpppO**	73	-17.2 +32.0
	$Pd(OAc)_2$, 0.46	DCE	80	6		76	
 **dppb**	$Pd(OAc)_2$, 0.47	DCM	20	72	 **dppbO**	80	-16.5 +32.2
	$Pd(OAc)_2$, 0.47	DCM	20	64		83	
 **dppbz**	$Pd(OAc)_2$, 1.00	DCE	80	7	 **dppbzO**	83	-12.8 +30.7 (14.8)
	$Pd(OAc)_2$, 1.00 (NaI)	DCE	80	7		81	
 **dppfc**	$Pd(OAc)_2$, 1.20 (NaI)	DCM	40	24		40-65	-16.7 +28.5
	PdI_2 1.72	DCM	40	23	 **dppfcO**	65	
	PdI_2 1.00	DCM	40	30		51	
 **(±)-BINAP**	PdI_2 1.00	DCM	40	34	 **(±)-BINAP(O)**	71	-14.5 +27.9
 **(*S*)-BINAP**	$Pd(OAc)_2$ 1.40	DCM	20[b] 40[b]	48[b] 24[b]	 **(*S*)-BINAP(O)**	80	-14.5 +27.9
	PdI_2 1.75	DCM	40	8		80-83	
 **(*R*)-BINAP**	$Pd(OAc)_2$ 1.40	DCM	20[b] 40[b]	48[b] 24[b]	 **(*R*)-BINAP(O)**	80	-14.5 +27.9
	PdI_2 2.25	DCM	40	10		81	

[a] DCE = 1,2-dichloroethane; DCM = dichloromethane.
[b] 48 hours at room temperature, then 24 h under reflux after addition of extra NaOH (see the Experimental Section).

The reaction was monitored by TLC (CH_2Cl_2−EtOAc, 2:1 by volume) and/or by ^{31}P NMR spectroscopy. The end of the reaction (ca. 100% conversion of dppe) was easily determined by a color change of the organic phase

from yellow ([(dppe)$_2$Pd]) to pale yellow ([(dppeO)$_2$PdBr$_2$]).[2e] At that point the reaction was stopped to avoid further, much slower oxidation of the dppeO product to dppeO$_2$. The oxidation of dppeO is considerably slower than dppe, providing the high selectivity for the catalytic process. This is due to the fact that in media of low polarity (1,2-dichloroethane) complexes of the type [(dppeO)$_2$PdX$_2$] are mostly trans,[2e] reacting with alkali more slowly than *cis*-[(dppe)PdX$_2$] (trans-effect) and water-soluble cationic [(dppe)$_2$Pd]$^{2+}$ (see below).

Ph$_2$P(CH$_2$)$_3$P(O)Ph$_2$ (dpppO). The above description of the dppe mono-oxidation reaction applies to the preparation of dpppO from dppp; except at room temperature the highest conversion of dppp ever observed was only ca. 70%. At 80 °C however, good yields of dpppO were obtained at virtually quantitative conversion (eq 1 and Table 1).

Ph$_2$P(CH$_2$)$_4$P(O)Ph$_2$ (dppbO). Due to the long −(CH$_2$)$_4$− spacer, dppb forms weaker metal chelates than dppe and dppp. Hence we had expected the mono-oxidation of dppb to be poorly selective. Indeed, poor selectivities and yields were observed when the oxidation was performed at 80 °C. At room temperature, however, good yields (>80%) of dppbO at a high conversion were obtained (eq 1 and Table 1). As the oxidation occurred, the poorly soluble dppbO formed precipitated out. Consequently, even at as high conversions of dppb to dppbO as 80−90% the concentration of dppbO in the reaction solution remained low, thus keeping the dppbO product from competing with the as yet unreacted dppb for coordination to Pd. This, in turn, provided the high selectivity for the reaction.

Ph$_2$PCH$_2$P(O)Ph$_2$ (dppmO). When the oxidation of dppm was carried out under the conditions developed for dppe (see above), only 60−70% conversions were obtained, at which point the reaction slowed considerably. Much higher conversions of 90−100% at 80−95% selectivity were reached when the oxidation was run in the presence of small quantities of NaI, ca. 5 mol % of the amount of dppm to be oxidized. The multifunctional role of the iodide promoter is discussed below. Because metal complexes of dppm and dppmO exhibit considerable C−H acidity of the methylene group (see for example, refs 2e and 23), highly concentrated alkali solutions (>20%) should not be used for the dppm oxidation, to avoid side-reactions due to deprotonation of the metal intermediates.

1,2-Ph$_2$PC$_6$H$_4$P(O)PPh$_2$ (dppbzO). Although 1,2-(Ph$_2$P)$_2$C$_6$H$_4$ (dppbz) has been mentioned in the literature twice[7,20b] its preparation has not been reported. We found that dppbz is selectively oxidized to dppbzO in over 80% isolated yield under conditions described above for the oxidation of dppe to dppeO. The oxidation of dppbz appeared to be equally selective and efficient in the absence and in the presence of NaI (Table 1). The ^{31}P NMR spectrum of dppbzO (see the Experimental Section) was in accord with that reported for a material tentatively formulated as dppbzO without isolation.[20b]

Ph$_2$PC$_5$H$_4$FeC$_5$H$_4$P(O)PPh$_2$ (dppfcO). Originally isolated as a minor side-product (11% yield) of the reaction between dppfc and [CpCo(CO)$_2$],[24] dppfcO is an attractive organometallic BPMO that cannot be prepared by conventional oxidations of dppfc. After careful optimization of reaction conditions the Pd-catalyzed oxidation afforded dppfcO in up to 65% isolated yield (eq 1 and Table 1). Higher selectivities were obtained when the mono-oxidation was run in dichloromethane under reflux. Like the analogous reaction of dppm, the Pd-catalyzed oxidation of dppfc is promoted by I$^-$. While the use of the Pd(OAc)$_2$/NaI system (see above) led to a relatively broad variation of yields of dppfcO in the range of ca. 40−65%, consistently good isolated yields of dppfcO (>60%) were obtained when PdI$_2$ was employed as added catalyst (see the Experimental Section). If necessary, the oxidation of dppfc can be driven to dppfcO$_2$ if run at a higher temperature (1,2-dichloroethane under reflux) for a longer time.

It has been reported[25] that [(dppfc)$_2$Pd] and some other dppfc Pd species undergo light-induced outer-sphere oxidation with organic halides. However, no significant difference in yields of dppfcO was noticed when the oxidation of dppfc was performed with or without protection from daylight.

Ph$_2$PC$_{10}$H$_6$C$_{10}$H$_6$P(O)PPh$_2$ (BINAP(O)). The one-step mono-oxidation of commercially available BINAP is a good alternative to the recently reported[8a] multistep synthesis of *racemic* BINAP(O). Both (*R*)- and (*S*)-BINAP(O) were obtained by the Pd(OAc)$_2$-catalyzed oxidation of (*R*)- and (*S*)-BINAP, respectively, with 1,2-dibromoethane/alkali in CH$_2$Cl$_2$ at room temperature. The reaction was very selective but slow, taking days to proceed to >80% conversion. Occasionally, early catalyst deactivation was observed under such conditions, accompanied by color change of the organic phase from red to yellow. The loss of catalytic activity was particularly fast when poorly soluble racemic (±)-BINAP was oxidized, with the conversions to (±)-BINAP(O) being as low as 5−15%. All these problems could be eliminated by using PdI$_2$ (ca. 2 mol %) instead of Pd(OAc)$_2$ and running the oxidation under reflux (eq 1 and Table 1). This way, conversions of 85−95% at 90−100% selectivity to BINAP(O) were achieved after 8−12 h. Isolated yields of spectroscopically (NMR) and chromatographically (TLC) pure (*R*)-, (*S*)-, and (±)-BINAP(O) were in the range 70−85%.

Ph$_2$P(CH$_2$)$_5$P(O)Ph$_2$ and Ph$_2$P(CH$_2$)$_6$P(O)Ph$_2$. Our numerous attempts to selectively mono-oxidize Ph$_2$P(CH$_2$)$_5$PPh$_2$ and Ph$_2$P(CH$_2$)$_6$PPh$_2$ using the above catalytic method failed.[26] The oxidations were nonselective, always producing mixtures of the mono- and dioxides.

Oxidation of Ph$_2$PCH$_2$P(Ph)CH$_2$PPh$_2$ (triphos). This substrate is easily oxidized with 1,2-dibromoethane and alkali in the presence of Pd(OAc)$_2$. At low conversions of 10−20%, Ph$_2$PCH$_2$P(Ph)CH$_2$P(O)Ph$_2$ and Ph$_2$PCH$_2$P(O)(Ph)CH$_2$PPh$_2$ were produced in ca. 2:1 statistical molar ratio (^{31}P NMR). An immediate interpretation of this ratio was comparable reactivity of both types of phosphine groups of the triphos molecule toward the

(23) Al-Jibori, S.; Shaw, B. L. *Inorg. Chim. Acta* **1982**, *65*, L 123; **1983**, *74*, 235.

(24) Kim, T.-J.; Lee, T.-H.; Kwon, S.-C.; Kwon, K.-H.; Uhm, J.-K.; Lee, H.; Byun, S.-I. *Bull. Korean Chem. Soc.* **1991**, *12*, 116.

(25) Kunkely, H.; Vogler, A. *J. Organomet. Chem.* **1998**, *559*, 215. See also: Tanase, T.; Matsuo, J.; Onaka, T.; Begum, R. A.; Hamaguchi, M.; Yano, S.; Yamamoto, Y. *J. Organomet. Chem.* **1999**, *592*, 103.

(26) (a) A different method has been developed for selective mono-oxidation of Ph$_2$P(CH$_2$)$_5$PPh$_2$ and Ph$_2$P(CH$_2$)$_6$PPh$_2$ to Ph$_2$P(CH$_2$)$_5$P(O)Ph$_2$ and Ph$_2$P(CH$_2$)$_6$P(O)Ph$_2$, respectively.[26b] This method also works well for other bis-phosphine substrates. (b) Grushin, V. V. Unpublished results, 1996.

Pd-catalyzed oxidation. As the reaction progressed, both monoxide products (still containing two phosphine functionalities and hence capable of forming *P*,*P*-chelates) began to compete with the triphos for vacant coordination sites on Pd. Because of that, the overall reaction was poorly selective, giving rise to triphosO (two isomers), triphosO_2 (two isomers), and triphosO_3.

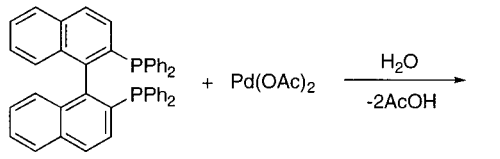
Reaction Mechanism: Step-by-Step Modeling of the Catalytic Loop. The starting point for the development of the catalytic process (eq 1) was a series of literature reports[27] describing the ability of hard ligands, such as O^{2-}, F^-, OH^-, and AcO^- to promote the remarkably clean inner-sphere red-ox transformation of phosphine complexes of Cu, Ni, Pd, and Pt (eq 2).

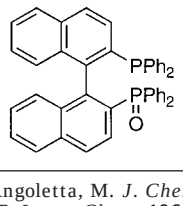
$$[L_nM^{m+}(PR_3)] + 2OH^- \longrightarrow [L_nM^{(m-2)+}] + R_3PO + H_2O \qquad (2)$$

Reaction 2 is most characteristic of Pd(II) complexes,[27d-s] likely involving coordination of a hard anionic base X^- to the metal center, followed by P−X reductive elimination. As a result, the Pd(II) is reduced to Pd(0), while the tertiary phosphine is oxidized to the corresponding P(V) derivative, such as phosphine oxide or difluorophosphorane if X = F.[27d] Importantly, Pd(II) complexes of bidentate phosphines undergo the Pd(II)/P(III) → Pd(0)/P(V) reduction−oxidation to give the corresponding BPMO or its difluoro derivative (eqs 3 and 4).[27d,h] In the presence of excess bis-phosphine the Pd remains in solution in the form of the corresponding zerovalent complex, $[(L-L)_2Pd]$ (L−L = diphosphine).

$$Ph_2P(CH_2)_nPPh_2 + PdCl_2 \xrightarrow[-2[Bu_4N]^+ Cl^-]{2[Bu_4N]^+ F^-,\ DMSO} Ph_2P(CH_2)_nP(F)_2Ph_2 + Pd(0) \qquad (3)^{27d}$$

n = 1-4





(4)[27h]

Rendering *stoichiometric* reactions 3 and 4 *catalytic* in Pd would be possible if the Pd(0) formed could be somehow oxidized back to Pd(II). The catalytic process would be selective and efficient only if there was an oxidant capable of rapidly oxidizing the Pd(0) back to Pd(II), while remaining unreactive toward the bidentate phosphine substrate. Since organic tertiary phosphines and their Pd(0) complexes are both strong reductants, finding such a selective oxidant was obviously the key problem to be solved. Practical requirements for the catalysis dictated that the oxidant must oxidize the Pd(0) rapidly, orders of magnitude faster than the phosphine substrate under conditions where the concentration of the palladium catalyst is orders of magnitude lower than that of the free phosphine substrate.

Original experiments with some polyhalogenated organic compounds (e.g., CCl_4) and certain metal ions (e.g., Cu^{2+} and Fe^{3+}) as potentially suitable oxidants failed. However, the most promising candidate, 1,2-dibromoethane, appeared to be an excellent, mild, and highly selective oxidant for Pd(0) in the presence of a large excess of bidentate phosphine substrates.

The suitability of 1,2-dibromoethane for reoxidation of the Pd(0) stemmed from the fact that tertiary phosphine complexes of zerovalent palladium are usually more reactive toward organic halides than free phosphines, especially in media of low polarity. Should the C−Br bond of 1,2-dibromoethane oxidatively add to a Pd(0) complex, the 2-bromoethylpalladium complex would undergo β-Br elimination[28] to produce Pd(II) and ethylene. Although the C−Br oxidative addition step had been expected to occur rather slowly,[29] the first tests of 1,2-dibromoethane for the Pd-catalyzed mono-oxidation of dppe were successful. A series of stoichiometric modeling studies is presented below in order to provide an illustration for the grounds on which the catalytic process was designed and developed.

Step 1. Reaction of Added Catalyst with dppe under Biphasic Conditions (Figure 1). Dissolving $Pd(OAc)_2$ and dppe (4-fold excess) in DCE resulted in the fast and clean formation of $[(dppe)_2Pd]^{2+}$ $(AcO^-)_2$ (Figure 1A; δ = 55.7 ppm).[31] Soon after the cationic complex began to precipitate out, the DCE solution was stirred with water for 5 min to produce two clear phases. Both layers were analyzed by ^{31}P NMR. Most of the cationic complex was found in the aqueous layer (Figure

(27) (a) Malatesta, L.; Angoletta, M. *J. Chem. Soc.* **1957**, 1186. (b) Vinal, R. S.; Reynolds, L. T. *Inorg. Chem.* **1964**, *3*, 1062. (c) Berners-Price, S. J.; Johnson, R. K.; Mirabelli, C. K.; Faucette, L. F.; McCabe, F. L.; Sadler, P. J. *Inorg. Chem.* **1987**, *26*, 3383. (d) Mason, M. R.; Verkade, J. G. *Organometallics* **1990**, *9*, 864; **1992**, *11*, 2212. (e) Ioele, M.; Ortaggi, G.; Scarsella, M.; Sleiter, G. *Polyhedron* **1991**, *10*, 2475. (f) Kozitsyna, N. Yu.; Ellern, A. M.; Antipin, M. Yu.; Struchkov, Yu. T.; Moiseev, I. I. *J. Chem. Soc., Mendeleev Commun.* **1991**, 92. (g) Amatore, C.; Jutand, A.; M'Barki, M. A. *Organometallics* **1992**, *11*, 3009. (h) Ozawa, F.; Kubo, A.; Hayashi, T. *Chem. Lett.* **1992**, 2177. (i) Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890; *J. Am. Chem. Soc.* **1995**, *117*, 4305. (j) Mandai, T.; Matsumoto, T.; Tsuji, J.; Saito, S. *Tetrahedron Lett.* **1993**, *34*, 2513. (k) Ozawa, F.; Kubo, A.; Matsumoto, Y.; Hayashi, T.; Nishioka, E.; Yanagi, K.; Moriguchi, K. *Organometallics* **1993**, *12*, 4188. (l) Grushin, V.V. Bensimon, C.; Alper, H. *Inorg. Chem.* **1994**, *33*, 4804. (m) Amatore, C.; Carré, E.; Jutand, A.; M'Barki, M. A. *Organometallics* **1995**, *14*, 1818. (n) Papadogianakis, G.; Peters, J. A.; Maat, L.; Sheldon, R. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1105. (o) Andrews, M. A.; Gould, G. L.; Voss, E. J. *Inorg. Chem.* **1996**, *35*, 5740. (p) Amatore, C.; Jutand, A.; Medeiros, M. J. *New J. Chem.* **1996**, *20*, 1143. (q) McLaughlin, P. A.; Verkade, J. G. *Organometallics* **1998**, *17*, 5937. (r) Csákai, Z.; Skoda-Földes, R.; Kollár, L. *Inorg. Chim. Acta* **1999**, *286*, 93. (s) Amatore, C.; Jutand, A.; Thuilliez, A. *Organometallics* **2001**, *20*, 3241.

(28) Friedrich, H. B.; Moss, J. R. *Adv. Organomet. Chem.* **1991**, *33*, 235.

(29) By the time our project was launched, Fitton and Rick[30a] had reported the lack of reaction between $[(dppe)_2Pd]$ and PhI. The report of Amatore et al.[30b] had not yet appeared in the literature, describing the lack of reaction between PhI and $[(L-L)_2Pd]$ (L−L = various bidentate phosphines). Had we been aware of that study[30b] we would have been considerably less encouraged to use 1,2-dibromoethane (which is presumably less reactive than PhI) as an oxidant for the Pd(0). Very recently, Alcazar-Roman et al.[30c] reported oxidative addition of aryl halides to $[(L-L)_2Pd]$ (L−L = dppfc, BINAP).

(30) (a) Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287. (b) Amatore, C.; Broeker, G.; Jutand, A.; Khalil, F. *J. Am. Chem. Soc.* **1997**, *119*, 5176. (c) Alcazar-Roman, L. M.; Hartwig, J. F.; Rheingold, A. L.; Liable-Sands, L. M.; Guzei, I. A. *J. Am. Chem. Soc.* **2000**, *122*, 4618.

(31) Lindsay, C. H.; Benner, L. S.; Balch, A. L. *Inorg. Chem.* **1980**, *19*, 3503.

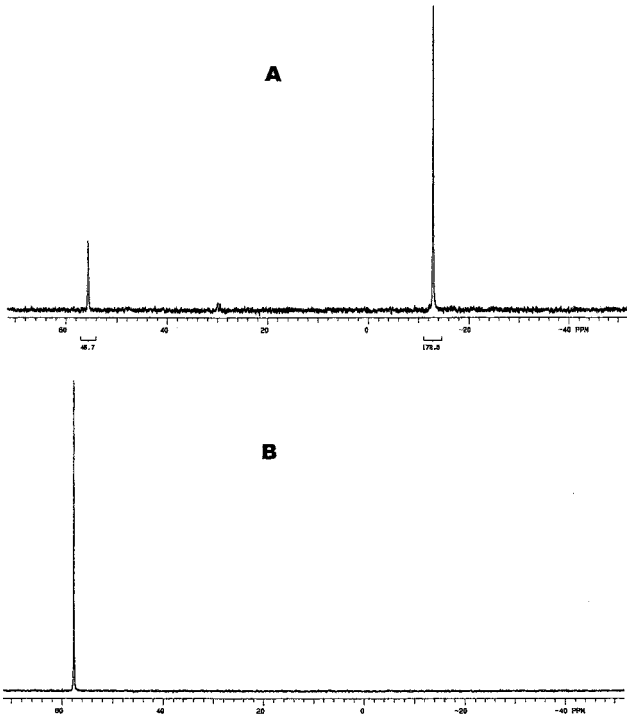
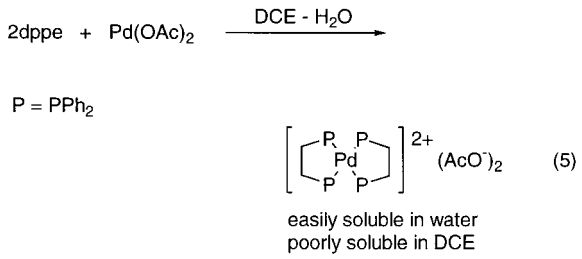


Figure 1. (A) ^{31}P NMR spectrum of the solution of Pd(OAc)$_2$ (30 mg) and dppe (213 mg; 4-fold excess) in DCE (5 mL) recorded immediately after the reagents were mixed. The singlet at −12.8 ppm is from free dppe; the singlet at 55.7 ppm is due to [(dppe)$_2$Pd]$^{2+}$(OAc$^-$)$_2$. (B) ^{31}P NMR spectrum of the aqueous phase after the mixture was stirred with water (5 mL) for 1 min. The singlet resonance at 57.8 ppm is from [(dppe)$_2$Pd]$^{2+}$(OAc$^-$)$_2$. For details, see text and the Experimental Section.

1B; δ = 57.8 ppm), and only trace amounts of [(dppe)$_2$Pd]$^{2+}$ remained in the organic phase (eq 5).



(5)

Step 2. Reaction of [(dppe)$_2$Pd]$^{2+}$ with Alkali (Figure 2). The organic layer of the biphasic system turned bright yellow immediately upon addition of aqueous NaOH. After 1 min of vigorous stirring both layers were analyzed by ^{31}P NMR spectroscopy. No signals were found in the spectrum of the colorless aqueous phase. The spectrum of the yellow organic phase (Figure 2) contained four resonances, i.e., a singlet at −12.8 ppm (excess dppe), two doublets at −12.4 and 30.8 ppm with J_{P-P} = 48.0 Hz (dppe monoxide, dppeO),[22,27c,d,r] and a singlet at 29.9 ppm from the zerovalent complex, [(dppe)$_2$Pd].[27d,30a,b] Thus, as anticipated, the alkali-induced redox reaction readily occurred to produce the desired product, dppeO, with 100% selectivity. It is believed that [(dppe)Pd(dppeO)] is

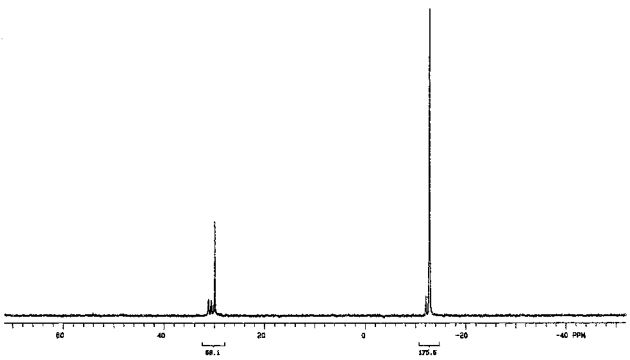
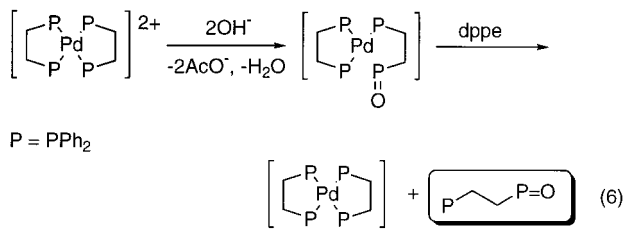


Figure 2. ^{31}P NMR spectrum of the organic phase after the DCE−H$_2$O biphasic system containing dppe and [(dppe)$_2$Pd]$^{2+}$(OAc$^-$)$_2$ (see Figure 1) was treated with NaOH. The singlets at −12.8 and 29.9 ppm are from dppe and [(dppe)$_2$Pd], respectively. The doublets at −12.4 and 30.8 ppm (J_{P-P} = 48 Hz) are from the dppeO produced. The upfield component of the doublet at −12.4 ppm overlaps with the singlet resonance from dppe at −12.8 ppm. For details, see text and the Experimental Section.

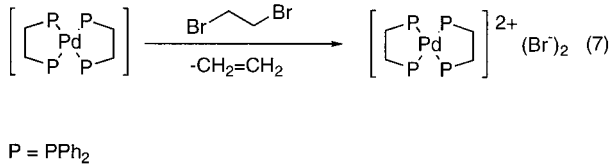
formed originally,[32] followed by chelation-driven ligand exchange (eq 6).



(6)

The mechanism of the reaction of tertiary phosphine complexes of Pd(II) with alkali likely involves nucleophilic attack of the OH$^-$ on the metal, followed by P−O reductive elimination.[27i]

Step 3. Oxidation of [(dppe)$_2$Pd] with 1,2-Dibromoethane (Figure 3). To the NMR sample containing the organic phase, 1,2-dibromoethane was added. The tube was placed back in the NMR probe, and ^{31}P NMR spectra of the sample were recorded every 10−15 min. The signal at 30.0 ppm from the [(dppe)$_2$Pd] gradually diminished in intensity while being replaced by a new singlet resonance at 54.3 ppm from [(dppe)$_2$Pd]Br$_2$[31] (Figure 3). After 2 h the resonance from [(dppe)$_2$Pd] disappeared altogether. No other changes in the original ^{31}P NMR pattern were observed, pointing to the high selectivity of the oxidation reaction (eq 7). At certain



(7)

(32) A clear colorless aqueous solution of [(dppe)$_2$Pd]$^{2+}$ (AcO$^-$)$_2$ turned yellow while growing turbid immediately upon addition of alkali. After 1.5 h a microcrystalline, highly air-sensitive orange precipitate formed, presumably [(dppe)Pd(dppeO)], which was extracted with O$_2$-free DCE and analyzed by ^{31}P NMR. The spectrum exhibited two broad resonances at ca. 30 and 22 ppm assigned to Ph$_2$PO and Ph$_2$P−Pd, respectively.

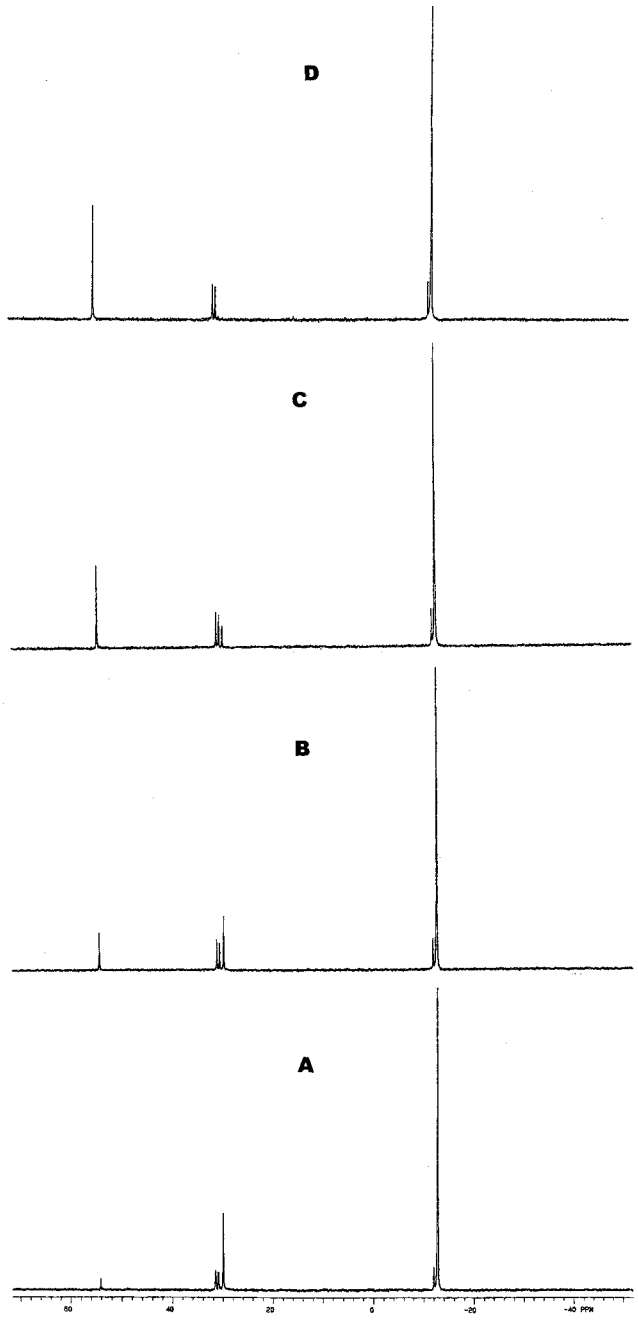
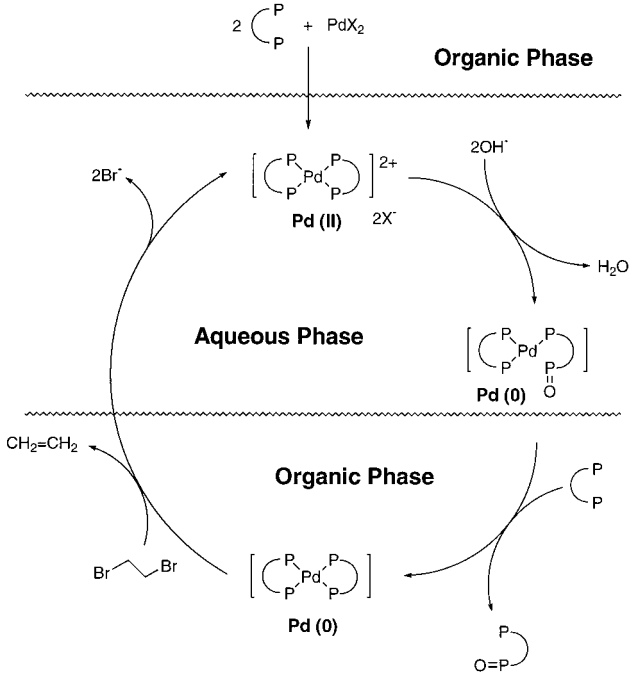


Figure 3. ^{31}P NMR spectra recorded 5 (A), 20 (B), 40 (C), and 120 (D) min after 1,2-dibromoethane was added to the NMR sample containing dppe, dppeO, and $[(dppe)_2Pd]$ (see Figure 2). The singlets at −12.8, 29.9, and 54.3 ppm are from dppe, $[(dppe)_2Pd]$, and $[(dppe)_2Pd]Br_2$, respectively. The doublets at −12.4 and 30.8 ppm (J_{P-P} = 48 Hz) are from dppeO. The upfield component of the doublet at −12.4 ppm overlaps with the singlet resonance from dppe at −12.8 ppm. For details, see text and the Experimental Section.

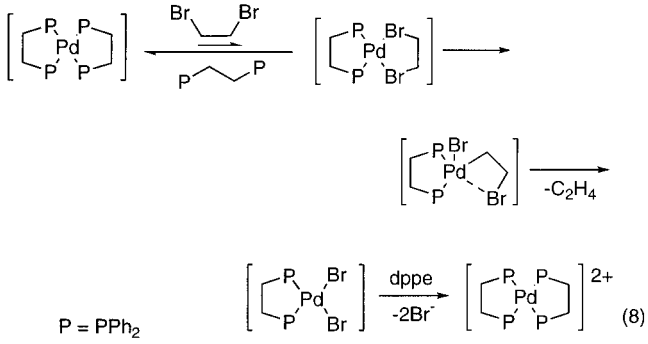
point, a weak signal at 5.3 ppm was observed in the ^1H NMR spectrum of the sample, indicating the formation of ethylene. When the sample was ejected from the probe after the reaction had gone to completion, a large amount of precipitate was found in the NMR tube. The well-shaped crystals were separated and found to be identical with an authentic sample of $[(dppe)_2Pd]Br_2$. The catalytic loop thus closed (Scheme 1).

Concerning the reaction of 1,2-dibromoethane with $[(dppe)_2Pd]$, two important observations merit special

Scheme 1



attention. First, unlike alkyl and benzyl bromides,[16] 1,2-dibromoethane is poorly reactive toward dppe and other tertiary phosphines. Neither phosphonium salts nor any other observable side-products were formed in step 3, in which $[(dppe)_2Pd]$ was oxidized with 1,2-dibromoethane *in the presence of free dppe*. Second, given the diminished reactivity of $[(L-L)_2Pd]$ toward PhI,[29,30] the oxidative addition reaction of 1,2-dibromoethane to $[(dppe)_2Pd]$ was surprisingly facile. This unexpectedly high reactivity may be accounted for by the formation of a mixed chelate $[(dppe)Pd(\eta^2\text{-}BrCH_2CH_2Br)]$, within which the oxidation addition occurred. The ability of organic halides to coordinate to transition metals via the halogen atom has been established.[33] A stable iridium η^2-1,2-diiodobenzene chelate has been isolated and characterized by single-crystal X-ray diffraction.[34] After oxidative addition of one of the two C−Br bonds to Pd, the bromine of the remaining C−Br bond is probably coordinated to the metal center,[35] facilitating halogen β-elimination (eq 13).[36] As the reaction between

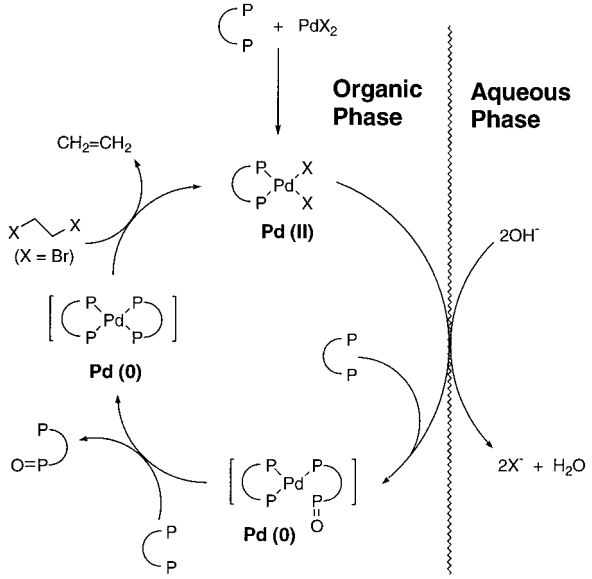


(8)

(33) For reviews, see: Kulawiec, R. J.; Crabtree, R. H. *Coord. Chem. Rev.* **1990**, *99*, 89. Plenio, H. *Chem. Rev.* **1997**, *97*, 3363. See also: Butts, M. D.; Scott, B. L.; Kubas, G. J. *J. Am. Chem. Soc.* **1996**, *118*, 11831, and references therein.

(34) Crabtree, R. H.; Faller, J. W.; Mellea, M. F.; Quirk, J. M. *Organometallics* **1982**, *1*, 1361.

Scheme 2



[(dppe)$_2$Pd] and 1,2-dibromoethane was monitored by ^{31}P NMR spectroscopy, no intermediates were observed.

The mechanism shown in Scheme 1 governs the mono-oxidation of dppe and other bidentate phosphine substrates, although some variations may take place. In certain cases, the structure and composition of the Pd(II) and Pd(0) bis(phosphine) intermediates may be different from [(η^2-L-L)$_2$Pd]$^{2+}$ and [(η^2-L-L)$_2$Pd]. For instance, neither Pd(0)[30b,c] nor Pd(II)[27h,37,38] forms stable bis-chelates with BINAP in *solution*. Reacting $PdBr_2$ and (*S*)-BINAP (1:1) in CH_2Cl_2 gave rise to yellow-orange [((*S*)-BINAP)$PdBr_2$] (^{31}P NMR: singlet, $\delta = 26.5$ ppm). The complex stayed intact and its ^{31}P NMR signal remained unaffected upon addition of 2 equiv of (*S*)-BINAP. Therefore, in sharp contrast with the above dppe experiments, no formation of cationic bis-chelate [((*S*)-BINAP)$_2$Pd]$^{2+}$ was observed. Nonetheless, when treated with alkali, the solution containing [((*S*)-BINAP)$PdBr_2$] and (*S*)-BINAP turned cherry-red due to the formation of Pd(0) species ($\delta = 27.4$ ppm) along with (*S*)-BINAP monoxide ((*S*)-BINAP(O); $\delta = -14.6$ and 28.4 ppm). Since neutral [((*S*)-BINAP)$PdBr_2$] (unlike salts of [(dppe)$_2$Pd]$^{2+}$) is insoluble in water, the reaction with alkali likely occurred at the interface rather than in the bulk of the aqueous phase.[38] The red zerovalent Pd complex readily reacted with 1,2-dibromoethane to produce [((*S*)-BINAP)$PdBr_2$] ($\delta = 26.5$ ppm), the starting point of the catalytic loop (Scheme 2).

Discussion

The generality of the catalytic method (eq 1) has been demonstrated by the high-yield (up to 90%) preparation of BPMOs, in which the phosphine and phosphoryl groups are separated by a variety of spacers, i.e., a saturated hydrocarbon chain of different length (dppmO, dppeO, dpppO, and dppbO), a benzene ring (dppbzO), the ferrocene framework (dppfcO), and a sequence of C−C bonds involved in a polyaromatic skeleton (BINAP(O)). Both high efficiency and selectivity of the mono-oxidation can be achieved for bis-phosphines with different bite angles, forming chelates of various strength, from weak (dppb) to very strong (dppe) and "super-strong" (dppbz).[39] A discussion below deals with different factors influencing the catalytic mono-oxidation of bis-phosphines to BPMOs.

Bis-Phosphine Substrates. The method is suitable only for bidentate phosphines capable of forming chelates with the metal catalyst (Pd). The oxidation may be selective only if the bis-phosphine chelates of Pd(II) are more stable than its complexes of the corresponding BPMOs.

Metal Complex Catalysts. Although Pt compounds may be used to catalyze the mono-oxidation, less costly palladium complexes exhibit higher catalytic activity and selectivity to BPMOs. For instance, under similar conditions, the oxidation of dppm catalyzed by $PtCl_2$ afforded dppmO in only 45% yield, whereas much higher yields (up to 84%) were obtained in the presence of Pd catalysts (see the Experimental Section). Likewise, the Pt- and Pd-catalyzed oxidations of dppfc afforded dppfcO in 32% and 65% yield, respectively.

Phase-Transfer Catalysts. We have examined the influence of various phase-transfer catalysts (5−10%) on the Pd-catalyzed oxidation of bis-phosphines. It has been found that all phase-transfer agents tested (Bu_4NHSO_4, Et_3NCH_2Ph Br, 18-crown-6) lowered the selectivity of the process, i.e., the yields of BPMOs decreased due to the formation of large quantities of bis-phosphine dioxides. The detrimental effect of the phase-transfer agents is explained by catalysis of X/OH ligand exchange in [(BPMO)$_2$PdX$_2$] (X = halogen), which results in oxidation of the BPMO to the dioxide (see above).

Cocatalysis with Iodide. The iodide cocatalyst is not required for reactions that proceed via the mechanism outlined in Scheme 1, i.e., for the bis-phosphine substrates that form cationic complexes of the type [(L−L)$_2$Pd]$^{2+}$ (e.g., L−L = dppe, dppbz, and dppp). These cationic complexes are water-soluble, readily reacting with OH^- in the aqueous phase of the biphasic system (see above).

In contrast, the beneficial effect of the iodide is well pronounced for the oxidation of bis-phosphines such as dppfc and BINAP, which are not prone to form water-soluble cationic complexes [(dppfc)$_2$Pd]$^{2+}$ and [(BINAP)$_2$Pd]$^{2+}$.[38] Neutral complexes [(L−L)PdX_2] are formed instead, which stay in the organic phase, reacting with aqueous alkali at the interface (Scheme 2). Under biphasic conditions, tertiary phosphine palladium(II) halides undergo facile ligand exchange with halide

(35) Garcia, M. P.; Jimenez, M. V.; Cuesta, A.; Siurana, C.; Oro, L. A.; Lahoz, F. J.; Lopez, J. A.; Catalan, M. P.; Tiripicchio, A.; Lanfranchi, M. *Organometallics* **1997**, *16*, 1026.

(36) (a) As the catalytic oxidation occurs, ethylene resulting from the β-halogen elimination may bind to Pd(0) intermediates to form unstable [(L-L)Pd(C_2H_4)], from which the olefin ligand is known[36b] to be easily displaced by excess diphosphine. (b) Broadwood-Strong, G. T. L.; Chaloner, P.; Hitchcock, P. B. *Polyhedron* **1993**, *12*, 721.

(37) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144.

(38) If it exists, the equilibrium between [(BINAP)$PdBr_2$] and [(η^2-BINAP)(η^1-BINAP)PdBr]$^+$Br$^-$ is shifted toward the former by >99%, as indicated by the ^{31}P NMR studies described above. It is conceivable that the reaction between [(BINAP)$PdBr_2$] and NaOH in the presence of BINAP may be driven by the reversible formation of a cationic complex, [(η^2-BINAP)(η^1-BINAP)PdBr]$^+$Br$^-$, which may be somewhat soluble in water.

(39) (a) Crumpton, D. M.; Goldberg, K. I. *J. Am. Chem. Soc.* **2000**, *122*, 962. (b) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205.

anions present in the aqueous phase.[40] As the iodide-promoted bis-phosphine oxidation occurs, two different halide anions are present in the biphasic system, i.e., the I^- and Br^- from 1,2-dibromoethane (eq 1). In accord with hydration/solvation energy considerations, the lighter, more strongly hydrated bromide would be preferentially located in the aqueous phase. Consequently, the heavier iodide would be bound to Pd in the organic phase of low polarity. In fact, after the PdI_2-catalyzed mono-oxidation of dppfc had gone to ca. 80% conversion, it is [(dppfc)PdI_2], not [(dppfc)$PdBr_2$] that was isolated from the organic phase by column chromatography.[41] Only trace amounts of the bromide [(dppfc)$PdBr_2$] were detected by TLC, indicating that the Pd(II) binds selectively to I^- rather than to Br^-, even at $Br^-:I^- \geq 45$ (see dppfc oxidation, experiment b of the Experimental Section). Similar observations were made when the oxidation of BINAP was performed in the presence of PdI_2.

The preferential formation of [(L−L)PdI_2] in the organic phase during the reaction has an important consequence. Because the Pd−X bond is more labile for X = I than for Br,[40] the iodo complexes [(L−L)PdI_2] undergo Pd−X ionization and ligand exchange reactions more readily than their bromide analogues [(L−L)-$PdBr_2$]. This way the displacement of X for OH in [(L−L)PdX_2] is facilitated for X = I, resulting in a faster Pd(II)/P(III) → Pd(0)/P(V) redox process. When dppm is ozidized, the presence of I^- favors the formation of more reactive Pd(II) complexes containing chelating rather than more common bridging dppm (A-frame).[42]

Because a vacant coordination site is required for β-elimination reactions,[43] the β-halogen elimination from [(L−L)Pd(X)(CH_2CH_2Br)] (Schemes 1 and 2) should occur more readily for the more labile iodo complex.

It has been demonstrated[44] that in the presence of I^- tertiary phosphine complexes of Pd(0) form electron-rich anionic complexes $[L_2PdI]^-$, which undergo oxidative addition of C−Hal bonds much faster than analogous neutral complexes of Pd(0) devoid of an anionic ligand. Therefore, the iodide may also facilitate oxidative addition of $BrCH_2CH_2Br$ to Pd(0) complexes involved in the catalytic cycle (Schemes 1 and 2).

Organic Solvent. Both dichloromethane and 1,2-dichloroethane are suitable for the biphasic reaction. The oxidation was sluggish when less polar benzene, toluene, and ether were used as the organic phase immiscible with water. No reaction occurred in hexane due to very low solubility of the substrate and catalyst.

Oxidant. The best results were obtained with 1,2-dibromoethane. Other 1,2-dihaloalkanes examined, i.e., 1-chloro-2-bromoethane, 1-chloro-2-iodoethane, and 1,2-diiodoethane gave lower yields and selectivities. The C−Cl bond of 1,2-dichloroethane (DCE) is not sufficiently reactive toward [$(L-L)_2Pd$]. In fact, DCE was successfully used as the organic phase.

Base. Most reactions were run in the presence of aqueous NaOH. Other bases, such as KOH, Na_2CO_3, and NaOAc, were also examined, mostly for dppfc oxidation. While comparable results were obtained with KOH, lower yields of dppfcO were obtained when Na_2CO_3 or NaOAc were employed.

Atmosphere. The reactions were run under N_2 to protect air-sensitive Pd(0) intermediates. An attempt to perform the otherwise selective Pd-catalyzed mono-oxidation of (*S*)-BINAP in air led to a sluggish and poorly selective reaction. Once formed in the anaerobic catalytic reaction, the air-stable BPMOs can be successfully isolated in air.

Experimental Section

A Varian VXR-200 instrument was used for measuring NMR spectra. Bidentate phosphines and other chemicals were purchased from Organometallics, Strem, Aldrich, and TCI chemical companies and used as received. All Pd-catalyzed oxidation reactions were conducted under nitrogen and monitored by TLC and/or ^{31}P NMR spectroscopy. Isolation and purification of the BPMOs were performed in air.

$Ph_2PCH_2P(O)PPh_2$, dppmO. (a) A mixture of palladium acetate (5 mg; 2.2×10^{-2} mmol), dppm (2.00 g; 5.21 mmol), 1,2-dibromoethane (2.0 g; 10.64 mmol), and 1,2-dichloroethane (10 mL) was stirred for 20 min. To this solution was added aqueous NaOH (20 wt %; 6 mL) containing NaI (40 mg; 0.27 mmol), and the mixture was vigorously stirred under reflux for 4 h. The organic phase was filtered through a silica plug, which was then washed (TLC control) with CH_2Cl_2/AcOEt (3:1 by volume). After the combined organic solutions were evaporated to dryness, the solid residue was dissolved in the minimum amount of boiling CH_2Cl_2 and the warm solution was treated with ether (100 mL; portionwise) and left at room temperature for 2 h. Slightly yellowish fluffy needles of spectroscopically and TLC pure dppmO were separated, washed with ether, and dried under vacuum. The yield was 1.53 g (74%). ^1H NMR ($CDCl_3$, 20 °C): δ 3.1 (d, 2H, J = 12.7 Hz, CH_2); 7.1−7.9 (m, 20H, Ph). ^{31}P NMR ($CDCl_3$, 20 °C): δ −26.5 (d, 1P, J_{P-P} = 50.5 Hz, PPh_2); 29.8 (d, 1P, J_{P-P} = 50.5 Hz, $P(O)Ph_2$).

(b) A mixture of $Pd(OAc)_2$ (19 mg; 8.5×10^{-2} mmol), dppm (6.00 g; 15.6 mmol), 1,2-dichloroethane (20 mL), and 1,2-dibromoethane (4.5 g; 23.9 mmol) was stirred for 20 min. After a solution of NaOH (2.5 g) and NaI (0.12 g; 0.8 mmol) in water (20 mL) was added the biphasic mixture was vigorously stirred under reflux for 3 h 40 min. ^{31}P NMR analysis of the organic layer indicated 95% conversion of dppm. After the mixture was kept under N_2 at 5 °C overnight the organic layer solidified. The aqueous layer was separated by a pipet and disposed of. The solidified organic phase was then stirred with dichloromethane (80 mL) until all solids dissolved. The solution was put on a silica column, which was washed with CH_2Cl_2/AcOEt (3:1 by volume). After the first fraction ($R_f \approx 1$) containing small amounts of unreacted dppm and dibromoethane was separated, the second orange fraction containing dppmO was collected and evaporated to dryness. The residue was thor-

(40) (a) Grushin, V. V. *Angew. Chem., Int. Ed.* **1998**, *37*, 994. (b) Flemming, J. P.; Pilon M. C.; Borbulevitch O. Ya.; Antipin M. Yu.; Grushin, V. V. *Inorg. Chim. Acta* **1998**, *280*, 87. (c) Grushin, V. V. *Organometallics* **2000**, *19*, 1888.

(41) (a) Due to considerably different R_f characteristics, brown-red [(dppfc)PdI_2] and orange-red [(dppfc)$PdBr_2$] can be easily separated by TLC or column chromatography. The dppfc Pd complex isolated from the reaction mixture was identical to an authentic sample of [(dppfc)-PdI_2].[41b] (b) Brown, J. M.; Cooley, N. A. *Organometallics* **1990**, *9*, 353. Colacot, T. J.; Fair, R. J., Jr.; Boyko, W. J. *Phosphorus, Sulfur Silicon Relat. Elem.* **1999**, *144−146*, 49.

(42) (a) Lindsay, C. H.; Balch, A. L. *Inorg. Chem.* **1981**, *20*, 2267. (b) Hunt, C. T.; Balch, A. L. *Inorg. Chem.* **1982**, *21*, 1641. (c) See also: Janka, M.; Anderson, G. K.; Rath, N. P. *Organometallics* **2000**, *19*, 5071.

(43) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*, 2nd ed.; John Wiley and Sons: New York, 1994. Spessard, G. O.; Miessler, G. L. *Organometallic Chemistry*; Prentice Hall: Upper Saddle River, NJ, 1996.

(44) (a) Negishi, E.; Takahashi, T.; Akiyoshi, K. *J. Chem. Soc. Chem. Commun.* **1986**, 1338. (b) Amatore, C.; Azzabi, M.; Jutand, A. *J. Am. Chem. Soc.* **1991**, *113*, 8375. (c) Amatore, C.; Jutand, A. *J. Organomet. Chem.* **1999**, *576*, 254, and references therein.

oughly washed with ether and then dried to give 4.97 g (80%) of TLC and spectroscopically pure (NMR), albeit yellowish dppmO. The dppmO was dissolved in ca. 20 mL of boiling CH_2Cl_2, treated with 200 mL of ether, and kept at −10 °C overnight. The precipitated dppmO was separated, washed with ether, and dried under vacuum. The yield after this recrystallization was 4.68 g (75%).

(c) A mixture of palladium acetate (4 mg; 2×10^{-2} mmol), dppm (0.65 g; 1.7 mmol), 1,2-dibromoethane (1.0 g; 5.3 mmol), and 1,2-dichloroethane (5 mL) was stirred for 1 h. To this solution was added aqueous NaOH (15 wt %; 4 mL) containing NaI (20 mg; 0.14 mmol), and the mixture was vigorously stirred under reflux for 4 h. After the standard workup (see above) the yield of spectroscopically and TLC pure, yellowish dppmO was 0.55 g (84%).

(d) A mixture of $PtCl_2$ (5 mg; 1.9×10^{-2} mmol), dppm (1.00 g; 2.6 mmol), 1,2-dibromoethane (0.75 g; 4.0 mmol), and 1,2-dichloroethane (6 mL) was stirred under reflux until the platinum salt dissolved. To this solution was added aqueous NaOH (15 wt %; 4 mL), and the mixture was vigorously stirred under reflux for 12 h. After the standard workup (see above) the yield of dppmO was 0.47 g (45%).

$Ph_2PCH_2CH_2P(O)PPh_2$, dppeO. (a) Palladium acetate (10 mg; 4.45×10^{-2} mmol), dppe (4.00 g; 10.05 mmol), and 1,2-dibromoethane (2.85 g; 15.2 mmol) were dissolved in 1,2-dichloroethane (30 mL). To this solution was added aqueous NaOH (10 wt %; 20 mL), and the biphasic mixture was vigorously stirred under reflux for 7 h until the originally yellow mixture turned pale yellow or almost colorless. The organic phase was filtered through a silica plug, which was then washed with 60 mL of CH_2Cl_2/AcOEt (5:3 by volume). The combined organic solutions were evaporated and treated with ether, causing precipitation of white crystals of dppeO, which were washed with ether and dried under vacuum. The yield was 3.62 g (87%). ^{1}H NMR ($CDCl_3$, 20 °C): δ 2.3 (m, 4H, CH_2); 7.2−7.7 (m, 20H, Ph). ^{31}P NMR ($CDCl_3$, 20 °C): δ −11.5 (d, 1P, $J_{P-P} = 48$ Hz, PPh_2); 32.3 (d, 1P, $J_{P-P} = 48$ Hz, $P(O)Ph_2$).

(b) Palladium acetate (5 mg; 2.2×10^{-2} mmol), dppe (5.00 g; 12.6 mmol), and 1,2-dibromoethane (3.6 g; 19.2 mmol) were dissolved in 1,2-dichloroethane (30 mL). To this solution was added aqueous NaOH (12 wt %; 20 mL), and the biphasic mixture was vigorously stirred under reflux for 15 h until the originally yellow mixture turned pale yellow or almost colorless. The product (4.29 g; 82%) was isolated as described above.

(c) Palladium acetate (50 mg; 22.3×10^{-2} mmol), dppe (50.00 g; 125.6 mmol), and 1,2-dibromoethane (36 g; 191.5 mmol) were dissolved in 1,2-dichloroethane (200 mL). To this solution was added aqueous NaOH (20 wt %; 125 mL) and the biphasic mixture was vigorously stirred under reflux for 21.5 h until the originally yellow mixture turned pale yellow. The product (40.75 g; 78.3%) was isolated as described above.

$Ph_2PCH_2CH_2CH_2P(O)PPh_2$, dpppO. (a) Palladium acetate (10 mg; 4.45×10^{-2} mmol), dppp (5.00 g; 12.1 mmol), and 1,2-dibromoethane (3.4 g; 18.9 mmol) were dissolved in 1,2-dichloroethane (15 mL). To this solution was added aqueous NaOH (20 wt %; 10 mL) and the biphasic mixture was vigorously stirred under reflux for 6 h until the originally yellow mixture turned pale yellow. The organic phase was filtered through a silica column, which was then washed with CH_2Cl_2/AcOEt (5:3 by volume) until the yellow band was about to come out. The combined organic solutions were evaporated to give a colorless oily residue. The oil was mixed with CH_2Cl_2 (2 mL) and ether (5 mL) and then treated with pentane (10 mL) and left for 1.5 h. More pentane (50 mL) was added, and in 2 h the fluffy white needles of dpppO were separated and dried under vacuum. The yield was 3.80 g (73%). ^{1}H NMR ($CDCl_3$, 20 °C): δ 1.8 (m, 2H, CH_2); 2.2 (m, 2H, CH_2); 2.4 (m, 2H, CH_2); 7.2−7.7 (m, 20H, Ph). ^{31}P NMR ($CDCl_3$, 20 °C): δ −17.2 (s, 1P, PPh_2); 32.0 (s, 1P, $P(O)Ph_2$).

(b) Palladium acetate (10 mg; 4.45×10^{-2} mmol), dppp (4.00 g; 9.7 mmol), and 1,2-dibromoethane (2.75 g; 14.6 mmol) were dissolved in 1,2-dichloroethane (15 mL). To this solution was added aqueous NaOH (25 wt %; 10 mL), and the biphasic mixture was vigorously stirred under reflux for 6 h until the originally yellow mixture turned pale yellow. The reaction mixture was worked up as described in the previous experiment. The yield of dpppO was 3.17 g (76%).

$Ph_2PCH_2CH_2CH_2CH_2P(O)PPh_2$, dppbO. (a) A mixture of palladium acetate (10 mg; 4.45×10^{-2} mmol), dppb (4.00 g; 9.4 mmol), 1,2-dibromoethane (3.6 g; 19.2 mmol), and dichloromethane (10 mL) was stirred for 30 min. To this suspension was added aqueous NaOH (20 wt %; 10 mL), and the mixture was vigorously stirred at room temperature for 3 days. Dichloromethane (30 mL) was added, and the organic phase was filtered through a silica plug, which was then washed with 80 mL of CH_2Cl_2/AcOEt (5:3 by volume). The combined organic solutions were evaporated to dryness. The solid residue was dissolved in boiling CH_2Cl_2 (ca. 30 mL), and the solution was treated with ether (100 mL; portionwise) and left at room temperature for 2 h. Well-shaped, colorless crystals were separated, washed with ether, and dried under vacuum. The yield of dppbO was 3.33 g (80%). ^{1}H NMR ($CDCl_3$, 20 °C): δ 1.5 (m, 2H, CH_2); 1.7 (m, 2H, CH_2); 2.0 (m, 2H, CH_2); 2.2 (m, 2H, CH_2); 7.2−7.8 (m, 20H, Ph). ^{31}P NMR ($CDCl_3$, 20 °C): δ −16.5 (s, 1P, PPh_2); 32.2 (s, 1P, $P(O)Ph_2$).

(b) A mixture of palladium acetate (10 mg; 4.45×10^{-2} mmol), dppb (4.00 g; 9.4 mmol), 1,2-dibromoethane (3.6 g; 19.2 mmol), and dichloromethane (10 mL) was stirred for 30 min. To this suspension was added aqueous NaOH (20 wt %; 10 mL), and the mixture was vigorously stirred at room temperature for 63 h. Water (5 mL) and dichloromethane (30 mL) were added, and the mixture was stirred for a few minutes until all solids dissolved. The organic phase was filtered through a silica column, which was then washed with 80 mL of CH_2Cl_2/AcOEt (5:3 by volume). The first portions of the eluants containing unreacted dppb (190 mg) were separated from the main fraction, which was collected and evaporated to dryness. This residue was dissolved in ca. 40 mL of warm CH_2Cl_2. Ether (100 mL) was added to the dichloromethane solution in four portions of 20−30 mL each. After 3 h the white crystals of dppbO were separated, wahsed with ether, and dried under vacuum. The yield was 3.44 g (83%).

1,2-$Ph_2PC_6H_4P(O)Ph_2$, dppbzO. (a) To a solution of dppbz (0.501 g; 1.1 mmol), $Pd(OAc)_2$ (2.5 mg; 1.1×10^{-2} mmol), and 1,2-dibromoethane (0.45 g; 2.4 mmol) in 1,2-dichloroethane (4 mL) was added a solution of NaOH (0.58 g; 14.5 mmol) in water (1.5 mL). The mixture was vigorously stirred under reflux for 7 h. Silica gel column separation of the organic phase with CH_2Cl_2/AcOEt (2:1 by volume) gave 0.43 g (83%) of spectroscopically pure dppbzO. ^{1}H NMR (CD_2Cl_2, 20 °C): δ 7.1 (m); 7.4 (m); 7.5 (m); 7.7 (m). ^{31}P NMR (CD_2Cl_2, 20 °C): δ −12.8 (d, $J_{P-P} = 14.8$ Hz, 1P, PPh_2); 30.7 (d, $J_{P-P} = 14.8$ Hz, 1P, $P(O)Ph_2$).

(b) Repeating the reaction in the presence of NaI (5 mg) produced, after 7 h, dppbzO in a similar yield of 81%. No effect of the iodide on the reaction was observed.

$Ph_2PC_5H_4FeC_5H_4P(O)PPh_2$, dppfcO. (a) A solution of NaOH (1.5 g; 37.5 mmol) and NaI (50 mg; 0.3 mmol) in water (6 mL) was added to a solution of dppfc (2.05 g; 3.7 mmol), $Pd(OAc)_2$ (10 mg; 4.45×10^{-2} mmol), and 1,2-dibromoethane (2.0 g; 10.6 mmol) in dichloromethane (8 mL). This mixture was vigorously stirred under reflux (N_2) for 23.5 h. At this point, the organic layer contained dppfcO as the main product and small amounts of dppfc, [(dppfc)PdI_2], $C_5H_5FeC_5H_4P(O)PPh_2$, and $dppfcO_2$. The organic phase was separated and evaporated. The dark residue was placed on a silica column, which was washed first with CH_2Cl_2 and then with CH_2Cl_2/AcOEt (5:3 by volume). Evaporation of the main orange fraction gave dppfcO, which was washed with cold ether (2 × 5 mL), pentane (2 × 5 mL), and dried under vacuum. The yield

was 1.36 g (65%). ^{1}H NMR ($CDCl_3$, 20 °C): δ 4.0 (m, 2H, Cp); 4.2 (m, 2H, Cp); 4.4 (m, 2H, Cp); 4.6 (m, 2H, Cp); 7.1−7.7 (m, 20H, Ph). ^{13}C NMR ($CDCl_3$, 20 °C): δ 72.9 (s, C_5H_4); 73.0 (s, C_5H_4); 73.1 (s, C_5H_4); 73.2 (s, C_5H_4); 73.3 (d, J_{P-C} = 1.7 Hz, C_5H_4); 73.5 (d, J_{P-C} = 1.7 Hz, C_5H_4); 128.2 (d, J_{P-C} = 11.0 Hz, m−C_6H_5PCp); 128.4 (d, J_{P-C} = 16.7 Hz, m-C_6H_5P(O)Cp); 131.3 (s, p-C_6H_5PCp); 131.4 (s, p-C_6H_5P(O)Cp); 131.4 (d, J_{P-C} = 9.7 Hz, o-C_6H_5PCp); 133.4 (d, J_{P-C} = 19.7 Hz, o-C_6H_5P(O)Cp); 134.5 (d, J_{P-C} = 105.6 Hz, q−C_6H_5PCp); 138.8 (d, J_{P-C} = 10.8 Hz, q-C_6H_5P(O)Cp). ^{31}P NMR ($CDCl_3$, 20 °C): δ −16.7 (s, 1P, CpPPh_2); 28.5 (s, 1P, CpP(O)Ph_2). Anal. Calcd for $C_{68}H_{58}Fe_2O_3P_4$ ($C_{34}H_{28}FeOP_2 \cdot 0.5H_2O$): C, 70.5; H, 5.0. Found: C, 70.7; H, 5.0. This procedure was repeated several times on a different scale to produce dppfcO in 35−63% yield. The use of PdI_2 instead of $Pd(OAc)_2$/NaI (see below) resulted in consistently better yields (51−65%).[45]

(b) A mixture of dppfc (1.00 g; 1.8 mmol), CH_2Cl_2 (6 mL), and PdI_2 (11 mg; 3.1×10^{-2} mmol) was stirred at room temperature until the Pd salt dissolved (2 h). To the resulting brown-red solution were added aqueous NaOH (25%; 4 g) and 1,2-dibromoethane (1.00 g; 5.32 mmol), and the mixture was stirred under reflux for 23 h. ^{31}P NMR analysis of the organic phase indicated ca. 80% conversion of dppfc to dppfcO (85%) and $dppfcO_2$ (15%). Silica gel column separation of the organic phase with first pure CH_2Cl_2 and then CH_2Cl_2/AcOEt (3:1 v/v) gave 0.23 g (23%) of unreacted dppfc and 0.67 g (65%; 85% on reacted dppfc) of spectroscopically pure dppfcO.

(c) A mixture of dppfc (0.12 g; 0.22 mmol), CH_2Cl_2 (6 mL), and PdI_2 (6.5 mg; 1.8×10^{-2} mmol) was stirred at room temperature until the Pd salt dissolved (3 h). To the resulting brown-red solution were added dppfc (0.88 g; 1.59 mmol) and aqueous NaOH (25%; 4 g). After 10 min of vigorous stirring, 1,2-dibromoethane (1.00 g; 5.32 mmol) was added, and the mixture was stirred under reflux for 30 h. ^{31}P NMR analysis of the organic phase indicated ca. 80% conversion of dppfc. Silica gel column separation of the organic phase with first pure CH_2Cl_2 and then CH_2Cl_2/AcOEt (3:1 v/v) gave 0.18 g (18%) of unreacted dppfc and 0.52 g (51%; 62% on reacted dppfc) of spectroscopically pure dppfcO.

$Ph_2P(O)C_5H_4FeC_5H_4P(O)PPh_2$, $dppfcO_2$. A solution of NaOH (2.2 g; 55 mmol) in water (8 mL) was added to a solution of dppfc (2.00 g; 3.6 mmol), $Pd(OAc)_2$ (10 mg; 4.45×10^{-2} mmol), and 1,2-dibromoethane (4.0 g; 21.3 mmol) in 1,2-dichloroethane (8 mL). After 9.5 h of vigorous stirring under reflux (N_2) 100% conversion of the dppfc was reached (^{31}P NMR). Dichloromethane (200 mL) was added, at stirring, to the mixture at room temperature. The organic phase was filtered through a short silica plug, then through Celite, and evaporated. The solid residue was recrystallized by addition of ether (20 mL) to its solution in 20 mL of warm 1,2-dichloroethane. Well-shaped orange crystals of $dppfcO_2$ were washed with ether and dried under vacuum. The yield of spectroscopically pure $dppfcO_2$ was 1.20 g (57%). ^{1}H NMR (CD_2Cl_2, 20 °C): δ 4.3 (dd, 4H, J = 3.8 and 1.9 Hz, 3,3′,4,4′-Cp); 4.7 (dd, 4H, J = 3.8 and 1.9 Hz, 2,2′,5,5′-Cp); 7.3−7.8 (m, 20H, Ph). ^{13}C NMR (CD_2Cl_2, 20 °C): δ 73.9 (d, J_{C-P} = 12.4 Hz, C_5H_4); 74.4 (d, J_{C-P} = 10.2 Hz, C_5H_4); 75.0 (d, J_{C-P} = 114.8 Hz, C_5H_4); 128.8 (d, J_{P-C} = 12.4 Hz, o-C_6H_5); 131.7 (d, J_{P-C} = 9.4 Hz, m-C_6H_5); 132.1 (d, J_{P-C} = 2.9 Hz, p-C_6H_5); 134.7 (d, J_{P-C} = 106.1 Hz, q−C_6H_5). ^{31}P NMR (CD_2Cl_2, 20 °C): δ 28.4 (s).

(±)-$Ph_2PC_{10}H_6C_{10}H_6P(O)PPh_2$, (±)-BINAP(O). A mixture of PdI_2 (3 mg; 8×10^{-3} mmol), (±)-BINAP (0.10 g; 0.16 mmol), and dichloromethane (6 mL) was stirred at room temperature for 0.5 h and then under reflux for 0.5 h until all PdI_2 dissolved to produce a purple-red solution. Additional (±)-BINAP (0.50 g; 0.81 mmol) was added, followed by a solution of NaOH (0.31 g; 7.8 mmol) in water (3 mL). After vigorous stirring for 30 min, 1,2-dibromoethane (0.60 g; 3.2 mmol) was added. The resulting mixture was stirred under reflux for 10 h. At that point, the mixture consisted of a yellow organic phase, colorless aqueous phase, and solid unreacted (±)-BINAP. ^{31}P NMR analysis of the organic phase indicated the presence of (±)-BINAP(O) and (±)-BINAP in ca. 7:3 ratio, and no (±)-BINAP-dioxide. The content of the NMR tube was shaken with more PdI_2 (finely ground; 3 mg; 0.8×10^{-3} mmol) until the latter dissolved. The resulting solution was added to the reaction flask along with 4 mL of dichloromethane. After stirring under reflux overnight, addition of extra 1,2-dibromoethane (0.60 g; 3.2 mmol) and then stirring under reflux for an additional 24 h, the (±)-BINAP had all dissolved. The ^{31}P NMR spectrum of the organic phase indicated ca. 85% conversion of (±)-BINAP to (±)-BINAP(O) at >95% selectivity. Silica column separation of the organic phase with first pure CH_2Cl_2 and then CH_2Cl_2/AcOEt (3:1 v/v) afforded 0.436 g (71%) of spectroscopically pure (±)-BINAP(O). ^{1}H NMR (CD_2Cl_2, 20 °C): δ 6.8−7.9 (m). ^{31}P NMR (CD_2Cl_2, 20 °C): δ −14.5 (s); 27.9 (s).[27h]

(*S*)-$Ph_2PC_{10}H_6C_{10}H_6P(O)PPh_2$, (*S*)-BINAP(O), and (*R*)-$Ph_2PC_{10}H_6C_{10}H_6P(O)PPh_2$, (*R*)-BINAP(O). (a) Palladium acetate (4 mg; 1.8×10^{-2} mmol), (*S*)- or (*R*)-BINAP (0.80 g; 1.29 mmol), and 1,2-dibromoethane (1.0 g; 5.3 mmol) were dissolved in dichloromethane (5 mL). Upon addition of aqueous NaOH (4.5 wt %; 6 mL) to this solution, the organic phase rapidly turned cherry-red. After stirring the mixture at room temperature for 2 days the conversion reached was ca. 60−70%. More aqueous alkali (0.4 g of NaOH in 1.5 mL of water) was added, and the mixture was stirred under reflux for 23 h. At this point, only small amounts of the unreacted BINAP were detected in the organic phase (TLC). The dichloromethane layer was filtered through a short silica plug, which was then washed with CH_2Cl_2/AcOEt (10:1 v/v). The combined organic solutions were evaporated. The remaining solid was redissolved in dichloromethane and reduced in volume until a thick oil was obtained. This oily residue was treated with ether (30 mL) and left at −17 °C overnight. Large, colorless crystals of BINAP(O) were separated, washed with ether, and dried under vacuum. The yield was 0.660 g (80%). This procedure is not applicable to (±)-BINAP and may be poorly efficient for the oxidation of enantiomerically impure samples of (*S*)-BINAP and (*R*)-BINAP. The use of PdI_2 instead of $Pd(OAc)_2$ (see below) gives consistently high yields of BINAP(O) independently of enantiomeric purity of BINAP used.[45]

(b) A mixture of PdI_2 (5 mg; 1.4×10^{-2} mmol), (*S*)-BINAP (0.50 g; 0.8 mmol), and dichloromethane (6 mL) was stirred at room temperature for 2 h until all PdI_2 dissolved to produce a purple-red solution. A solution of NaOH (0.47 g; 11.8 mmol) in water (3 mL) and 1,2-dibromoethane (1.00 g; 5.3 mmol) were added. The resulting mixture was stirred under reflux for 8 h, until the originally cherry-red solution turned light yellow. ^{31}P NMR analysis of the organic phase indicated 90% conversion of the BINAP to BINAP(O) at >95% selectivity. Silica column separation of the organic phase with first pure CH_2Cl_2 and then CH_2Cl_2/AcOEt (10:1 v/v) afforded 0.427 g (83%) of spectroscopically pure (*S*)-BINAP(O) as a yellow solid. The product was dissolved in 2 mL of dichloromethane, and the resulting solution was reduced in volume to ca. 0.5−1 mL by blowing nitrogen over its surface. Ether (ca. 3 mL) was added to the resulting viscous solution, followed by hexane (ca. 5 mL). After several hours, well-shaped pale yellow crystals of (*S*)-

(45) It is not clear why unsatisfactory reproducibility was occasionally observed when $Pd(OAc)_2$ (or $Pd(OAc)_2$/NaI) rather than PdI_2 was used as catalyst for the oxidation of dppfc and BINAP. The latter two do not form stable complexes of the type $[(L-L)_2Pd]^{2+}$ and hence undergo oxidation via the mechanism presented in Scheme 2 (see above). No reproducibility problem was encountered for the other bisphosphines whose oxidation is governed by a different mechanism (Scheme 1). We cautiously propose that AcO^- might have a negative effect on the catalytic oxidation of dppfc and BINAP. Some impurities in the materials used for the reaction might somehow scavenge the acetate anion from $Pd(OAc)_2$ catalyst. The $Pd(OAc)_2$-catalyzed oxidation reactions of dppfc and BINAP were highly reproducible when run in glass flasks that had been washed with $K_2Cr_2O_7/H_2SO_4$. Although the glassware was thoroughly rinsed with water after the washings, Cr^{3+} adsorbed on the glass surface may have trapped the AcO^- via chemisorption.

BINAP(O) were separated, washed with ether, and dried under vacuum. The yield of the recrystallized product was 0.408 g (80%).

(c) A mixture of PdI_2 (6.5 mg; 1.8×10^{-2} mmol), (*R*)-BINAP (0.505 g; 0.8 mmol), and dichloromethane (5 mL) was stirred at room temperature for 3 h until all PdI_2 dissolved to produce a purple-red solution. A solution of NaOH (0.45 g; 11.3 mmol) in water (3 mL) and 1,2-dibromoethane (1.00 g; 5.3 mmol) were added. The resulting mixture was stirred under reflux until the originally cherry-red solution turned light yellow (10 h). ^{31}P NMR analysis of the organic phase indicated 90% conversion of the BINAP to BINAP(O) at >95% selectivity. The mixture was treated with ca. 20% H_3PO_4 until the aqueous phase turned acidic (pH = 4). Then, dppe (20 mg) was added in order to convert the Pd(II) BINAP complexes present in the organic phase to more easily removable cationic $[(dppe)_2Pd]^{2+}$. After 5 min of stirring the organic phase was separated and placed on a silica column, which was then washed first with CH_2Cl_2 to remove the small amounts of unreacted BINAP and dppe and then with CH_2Cl_2/AcOEt (10:1 v/v) to isolate the monoxide. This separation afforded 0.419 g (81%) of spectroscopically (NMR) and chromatographically (TLC) pure (*R*)-BINAP(O) as a colorless crystalline solid. The product can be recrystallized from dichloromethane−ether−hexane as described above.

Stoichiometric Studies. (a) To a solution of $Pd(OAc)_2$ (30 mg) in 1,2-dichloroethane (5 mL) was added dppe (213 mg; 4-fold excess), and the resulting solution was immediately analyzed by ^{31}P NMR. The NMR spectrum indicated quantitative formation of $[(dppe)_2Pd]^{2+}$ $(AcO^-)_2$ (δ = 55.7 ppm).[31] After a few minutes the cationic complex $[(dppe)_2Pd]^{2+}$ $(AcO^-)_2$ began to precipitate out. Water (5 mL) was added, and the mixture was stirred for 5 min to produce two clear phases. ^{31}P NMR analysis of both layers indicated that most of the cationic complex was located in the aqueous layer (δ = 57.8 ppm) with only trace amounts of $[(dppe)_2Pd]^{2+}$ remaining in the organic phase. A solution of NaOH (100 mg) in water (2 mL) was added at stirring. The organic layer of the biphasic system turned bright yellow within the time of mixing, while the aqueous phase remained colorless. After 1 min of vigorous stirring both layers were analyzed by ^{31}P NMR spectroscopy. No signals were found in the spectrum of the colorless aqueous phase. The ^{31}P NMR spectrum of the yellow organic phase contained four resonances: a singlet at −12.8 ppm (excess dppe), two doublets at −12.4 and 30.8 ppm with J_{P-P} = 48.0 Hz (dppeO), and a singlet at 29.9 ppm ($[(dppe)_2Pd]$). No other signals were observed, indicating >99% selectivity of the reaction. A sample of the yellow organic phase (0.8 mL) was carefully separated by a pipet, filtered through cotton, and placed in a standard 5 mm NMR tube. To this sample was added 1,2-dibromoethane (ca. 50 mg). The tube was placed in the NMR probe, and ^{31}P NMR spectra of the sample were recorded every 10−15 min. As the reaction occurred, the signal at 30.0 ppm ($[(dppe)_2Pd]$) gradually diminished in intensity while being replaced by a singlet at 54.3 ppm ($[(dppe)_2Pd]^{2+}$). After 2 h full conversion of $[(dppe)_2Pd]$ to $[(dppe)_2Pd]Br_2$ with >99% selectivity was observed. The well-shaped crystals formed in the NMR tube were found to be identical with an authentic sample of $[(dppe)_2Pd]Br_2$.

(b) A mixture of $PdBr_2$ (21 mg), (*S*)-BINAP (50 mg; 1 equiv), and CH_2Cl_2 (2 mL) was stirred at room temperature for 2.5 h until the Pd complex dissolved to produce an orange solution. A ^{31}P NMR spectrum of this solution displayed only one singlet resonance at 26.5 ppm ($[((S)\text{-BINAP})PdBr_2]$). After an additional 2 equiv of (*S*)-BINAP (100 mg) was added, the solution was analyzed by ^{31}P NMR again. The spectrum contained only two sharp singlet resonances, at 26.5 ppm from $[((S)\text{-BINAP})PdBr_2]$ and −14.8 ppm from free (*S*)-BINAP, in a 1:2 intensity ratio. Therefore, no NMR-observable reaction between $[((S)\text{-BINAP})PdBr_2]$ and (*S*)-BINAP took place. The orange solution of $[((S)\text{-BINAP})PdBr_2]$ (1 equiv) and (*S*)-BINAP (2 equiv) was vigorously stirred with 10% aqueous NaOH for 30 min. The color of the organic phase changed to dark cherry-red due to the formation of a Pd(0) BINAP complex, while the aqueous layer remained colorless. The ^{31}P NMR spectrum of the dark red organic phase contained four singlet resonances at 28.8 (1P), 27.4 (2P), −14.5 (1P), and −14.6 (1P) ppm and an AB quartet with δ = 25.4 (0.5 P) and 28.6 (0.5P) ppm (J_{P-P} = 59 Hz). The singlet at −14.6 ppm was assigned to free (*S*)-BINAP, whereas singlets at −14.5 and 28.4 ppm were from the Ph_2P and Ph_2P(O) groups of (*S*)-BINAP(O) formed.[27h] Taking into account the solution behavior of $[(\eta^2\text{-BINAP})_2Pd]$,[30b,c,37] the singlet at 27.4 ppm and the two doublets are tentatively assigned to $[(\eta^2\text{-BINAP})(\eta^1\text{-BINAP})Pd]$ and $[(\eta^2\text{-BINAP})(\eta^1\text{-BINAP(O))Pd}]$. The former would give rise to the signal at 28.4 ppm appearing as a singlet[30c] due to fast η^2-BINAP/η^1-BINAP exchange, whereas the latter might exhibit two doublets from η^1-coordinated BINAP(O) and a singlet from η^2-BINAP, which overlaps with the resonance from $[(\eta^2\text{-BINAP})(\eta^1\text{-BINAP})Pd]$. The dichloromethane solution in the NMR tube was treated with excess 1,2-dibromoethane (30 mg) and left at room temperature for 2 h. This caused a color change from dark cherry-red to orange. ^{31}P NMR analysis of the sample indicated the presence of only BINAP(O) (−14.5 and 28.4 ppm), $[((S)\text{-BINAP})PdBr_2]$ (26.5 ppm), and (*S*)-BINAP (−14.6 ppm) (see Scheme 2).

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