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Effects of Linker Length on the Rate and Selectivity of Platinum-Catalyzed Asymmetric Alkylation of the Bis(isitylphosphino)alkanes IsHP$(CH_2)_n$PHIs (Is = 2,4,6-(*i*-Pr)$_3C_6H_2$, *n* = 1−5)

Timothy W. Chapp, Adam J. Schoenfeld, and David S. Glueck*

6128 Burke Laboratory, Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755

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Catalytic asymmetric alkylation of the bis(secondary phosphines) IsHP$(CH_2)_n$PHIs (**1a**−**e**, *n* = 1−5, Is = isityl = 2,4,6-(*i*-Pr)$_3C_6H_2$) with benzyl bromide using the base $NaOSiMe_3$ and the catalyst precursor Pt((*R,R*)-Me-DuPhos)(Ph)(Cl) gave the bis(tertiary phosphines) Is(PhCH$_2$)P$(CH_2)_n$P(CH$_2$Ph)Is (**2a**−**e**, *n* = 1−5) via the intermediates Is(PhCH$_2$)P$(CH_2)_n$PHIs (**4a**−**e**, *n* = 1−5). The rates of these reactions depended strongly on *n*, in the order **1a** < **1b** < **1c** ≈ **1d** ≈ **1e**. The bulkier bis(secondary phosphine) Mes*HP$(CH_2)_2$PHMes* (**5**, Mes* = 2,4,6-(*t*-Bu)$_3C_6H_2$) did not undergo catalytic alkylation under these conditions. The alkylation selectivity also depended on *n*. Alkylation of **1b** was *meso*-selective, while alkylation of **1a**,**c**−**e** was *rac*-selective, occurring with similar diastereoselectivity and enantioselectivity for the longer linkers (**1c**−**e**). The product ratios suggested that the catalyst controlled the selectivity for **1d**,**e**, while substrate control operated for ethano-bridged **1b**, with negative cooperativity. Substrate control also likely occurred for **1a**, for which competition from the background alkylation was significant. Analysis of the observed diastereo- and enantioselectivity for Pt-catalyzed alkylation of **1c** and the mixed secondary/tertiary phosphine IsHP$(CH_2)_3$P(CH$_2$Ph)Is (**4c**) yielded quantitative information on the selectivity of both P−C bond-forming steps, which was consistent with predominant catalyst control, altered slightly by the influence of the substrate.

Introduction

P-stereogenic bidentate diphosphines such as Knowles' DiPAMP[1] are important ligands in catalytic asymmetric reactions.[2] We recently developed a new method for synthesis of this class of compounds by Pt-catalyzed asymmetric alkylation of bis(secondary phosphines).[3] With these symmetrical bifunctional substrates, after formation of one chiral center, the selectivity of the second alkylation may be the same (catalyst control) or different (substrate control).[4] Catalyst control may lead to asymmetric amplification and increased enantiomeric ratio (er) for the *rac* product; this process is presumably important in the alkylation of PhHP$(CH_2)_2$PHPh (**A**), which enabled isolation of enantiomerically pure **B** (Scheme 1).[5]

Substrate control may occur with positive or negative cooperativity. We recently characterized the latter in the Pt-catalyzed alkylation of IsHP$(CH_2)_2$PHIs (**1b**; Is = isityl = 2,4,6-(*i*-Pr)$_3C_6H_2$) with 2-(bromomethyl)naphthalene, which was *meso*-selective. Although the catalyst controlled the selectivity of the first alkylation (**1b** → **C**), its preference was overridden in the second alkylation (**C** → **D**) by substrate control. In particular, the absolute configuration of the tertiary phosphine in intermediate **C** controlled the selectivity of the second alkylation with *alternation* of stereochemistry ((*R*$_P$)-**C** → (*R*,*S*)-**D**; (*S*$_P$)-**C** → (*S*,*R*)-**D**), selectively yielding *meso*-**D** (Scheme 1).[6]

This negative cooperativity (formation of *meso*-**D** instead of one enantiomer of *rac*-**D**) presumably occurred because one P stereocenter in **1b** and **C** was close enough to the other to influence its reactivity. Such effects are expected to depend on the linker connecting the two reactive centers in bifunctional

*To whom correspondence should be addressed. E-mail: glueck@dartmouth.edu.

(1) Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998–2007.

(2) (a) *Phosphorus Ligands in Asymmetric Catalysis. Synthesis and Applications*; Börner, A., Ed.; Wiley-VCH: Weinheim, Germany, 2008. (b) *Asymmetric Catalysis on Industrial Scale. Challenges, Approaches, and Solutions*; Blaser, H.-U., Schmidt, E., Eds.; Wiley-VCH: Weinheim, Germany, 2004.

(3) (a) Scriban, C.; Glueck, D. S. *J. Am. Chem. Soc.* **2006**, *128*, 2788–2789. (b) Scriban, C.; Glueck, D. S.; Golen, J. A.; Rheingold, A. L. *Organometallics* **2007**, *26*, 1788−1800, 5124 (addition/correction). For related syntheses using secondary phosphines and bifunctional alkyl halides, see: (c) Chan, V. S.; Chiu, M.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 6021–6032.

(4) (a) Takahata, H.; Takahashi, S.; Kouno, S.; Momose, T. *J. Org. Chem.* **1998**, *63*, 2224–2231. (b) El Baba, S.; Sartor, K.; Poulin, J.-C.; Kagan, H. B. *Bull. Soc. Chim. Fr.* **1994**, *131*, 525–533. (c) Rautenstrauch, V. *Bull. Soc. Chim. Fr.* **1994**, *131*, 515–524. (d) Tai, A.; Ito, K.; Harada, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 223–227. (e) Muramatsu, H.; Kawano, H.; Ishii, Y.; Saburi, M.; Uchida, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 769–770. (f) Aggarwal, V. K.; Evans, G.; Moya, E.; Dowden, J. *J. Org. Chem.* **1992**, *57*, 6390–6391. (g) Hoye, T. R.; Mayer, M. J.; Vos, T. J.; Ye, Z. *J. Org. Chem.* **1998**, *63*, 8554–8557. (h) Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. *Tetrahedron Lett.* **1995**, *36*, 5239–5242. (i) Hayashi, T.; Hayashizaki, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 215–218. (j) Kalck, P.; Urrutigoïty, M. *Coord. Chem. Rev.* **2004**, *248*, 2193–2200. (k) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed.* **1985**, *24*, 1–30. (l) Lagasse, F.; Tsukamoto, M.; Welch, C. J.; Kagan, H. B. *J. Am. Chem. Soc.* **2003**, *125*, 7490–7491. (m) Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629–631.

(5) Anderson, B. J.; Glueck, D. S.; DiPasquale, A. G.; Rheingold, A. L. *Organometallics* **2008**, *27*, 4992−5001; **2009**, *28*, 386 (addition/correction).

(6) Chapp, T. W.; Glueck, D. S.; Golen, J. A.; Moore, C. E.; Rheingold, A. L. *Organometallics* **2010**, *29*, 378–388.

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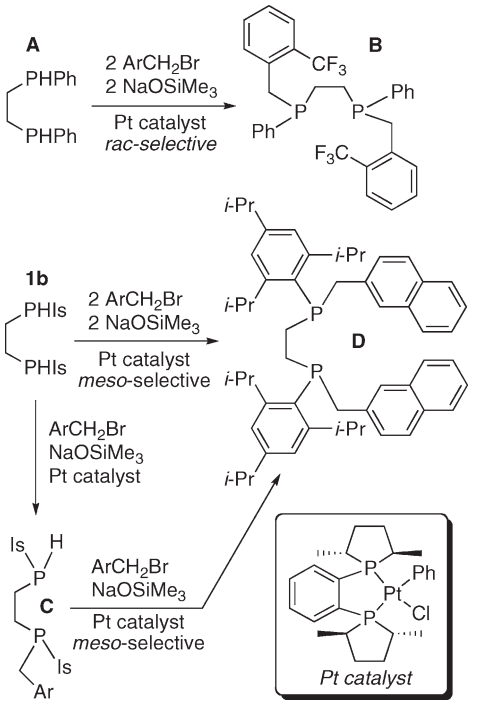
Scheme 1. Pt-Catalyzed Asymmetric Alkylation of Bis(secondary phosphines)



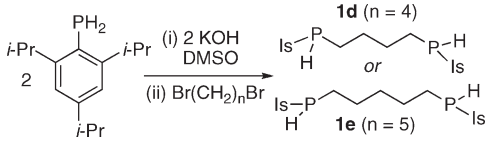
substrates; they should vanish at sufficiently long separations (catalyst control). Understanding these structure/reactivity/selectivity relationships is potentially useful for developing improved catalytic processes for the synthesis of chiral ligands. With this goal in mind, we report here studies of the effects of the linker in the bis(secondary phosphines) $IsHP(CH_2)_nPHIs$ (**1a**−**e**, $n = 1-5$) on rate and selectivity in their Pt-catalyzed asymmetric alkylation with benzyl bromide.

Results and Discussion

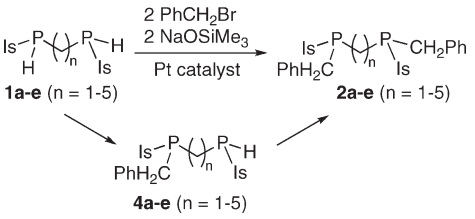
Preparation of Bis(secondary phosphines). The bis(secondary phosphines) $IsHP(CH_2)_nPHIs$ (**1a**,**b**; $n = 1-2$) are known,[7] and we prepared the longer chain substrates by alkylation of PH_2Is with dibromoalkanes in the superbasic medium[8] KOH/DMSO (Scheme 2), as we recently reported for **1c**.[9,7c] Under these conditions, **1c** was formed more slowly than the less hindered $MesHP(CH_2)_3PHMes$[9] (Mes = 2,4,6-$Me_3C_6H_2$).[7c] The rates of formation of **1d**,**e** were similar to that of **1c**; these compounds were relatively insoluble in DMSO, which simplified their purification.

Catalytic Alkylation. Catalytic alkylation of bis(secondary) phosphines **1a**−**e** with benzyl bromide and $NaOSiMe_3$ using 10 mol % of the catalyst precursor Pt((*R*,*R*)-Me-DuPhos)(Ph)(Cl) (see Scheme 1) gave bis(tertiary phosphines) **2a**−**e** (Scheme 3).

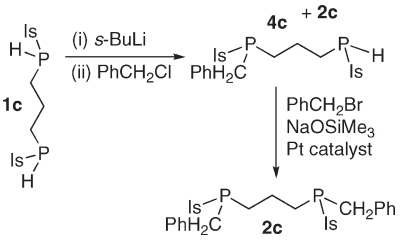
Scheme 2. Synthesis of Bis(secondary phosphines) 1d,e



Scheme 3. Pt-Catalyzed Asymmetric Alkylation of Bis(secondary isitylphosphines) 1a−e



Scheme 4. Synthesis and Pt-Catalyzed Alkylation of 4c



The mixed secondary/tertiary phosphines $Is(PhCH_2)P(CH_2)_n$-PHIs (**4a**−**e**, $n = 1-5$) were intermediates in these reactions; their ^{31}P NMR data are reported in the Experimental Section (Table 4). Control experiments showed that the background reactions (Pt-free alkylation of **1a**−**e**) were much slower than the catalytic processes for substrates **1b**−**e** but about as fast as the catalytic reaction of **1a** (see the Supporting Information for details).

Deprotonation/alkylation of **1c** with 1 equiv of *s*-BuLi/$PhCH_2Cl$ gave the mixed tertiary/secondary bis(phosphine) **4c** as the major component of an inseparable mixture containing unreacted **1c** and overalkylated **2c** (Scheme 4). However, adding additional *s*-BuLi and monitoring the deprotonation of **1c** by ^{31}P NMR spectroscopy enabled isolation of a 63/37 mixture of **4c** (1/1 mixture of diastereomers) and **2c** (0.65/1 *rac*/*meso* ratio). Pt-catalyzed alkylation of this mixture converted **4c** to **2c**, which was not further alkylated under these conditions (Scheme 4).

The observed times for completion of the Pt-catalyzed double alkylations (Scheme 3) suggested that their rates depended strongly on *n*, in the order **1a** < **1b** < **1c** ≈ **1d** ≈ **1e**. (We did not measure the reaction rates, but catalyst decomposition was not observed; therefore, we assume that the reaction times correlate with rates.) These observations can be explained most simply by steric effects, in which the presence of another bulky isitylphosphino group near the reactive center slows alkylation or another step in the catalytic cycle. A similar trend occurred in substrates which differed only in the P substituent; the rate of catalytic alkylation of the bis(secondary phosphines) $ArHP(CH_2)_n$-PHAr depended on the aryl group (for $n = 3$, Ph > Mes ≈ Is; for $n = 2$, Ph > Is).[5] For comparison, we prepared the even bulkier bis(secondary phosphine) Mes*$HP(CH_2)_2PHMes$* (**5**; Mes* = 2,4,6-(t-Bu)$_3C_6H_2$; see the Experimental Section),

(7) $n = 1$: (a) Bitterer, F.; Kucken, S.; Langhans, K. P.; Stelzer, O. *Z. Naturforsch., B* **1994**, *49*, 1223–1238. Bitterer, F.; Brauer, D. J.; Dorrenbach, F.; Fischer, J.; Stelzer, O. *Z. Naturforsch., B* **1992**, *47*, 1529–1540. n = 2: (b) Reference 6. n = 3: (c) Lane, E. M.; Chapp, T. W.; Hughes, R. P.; Glueck, D. S.; Feland, B. C.; Bernard, G. M.; Wasylishen, R. E.; Rheingold, A. L. *Inorg. Chem.* **2010**, *49*, 3950–3957.

(8) (a) Tsvetkov, E. N.; Bondarenko, N. A.; Malakhova, I. G.; Kabachnik, M. I. *Synthesis* **1986**, 198–208. (b) Terekhova, M. I.; Bondarenko, N. A.; Malakhova, I. G.; Tsvetkov, E. N.; Petrov, E. S.; Shatenshtein, A. I. *J. Gen. Chem. U.S.S.R.* **1982**, *52*, 452–455.

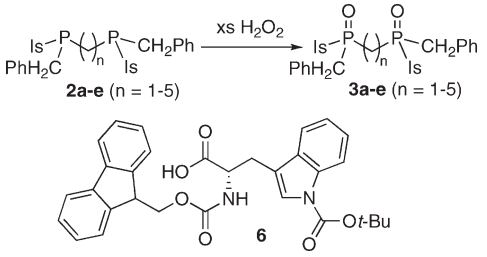
(9) Karasik, A. A.; Naumov, R. N.; Spiridonova, Y. S.; Sinyashin, O. G.; Lonnecke, P.; Hey-Hawkins, E. *Z. Anorg. Allg. Chem.* **2007**, *633*, 205–210.

Table 1. ^{31}P NMR Data for Diphosphines 2a−e and Their Derivatives, with Product Ratios from Schemes 3 and 4[a]

n (No.)	δ (diphosphine **2**)[b]	δ (oxide **3**)[b]	δ (**3**/**6** adduct)[c]	dr[d]	er[e]
1 (**a**)	−30.9, −33.9	40.4, 38.4	41.9, 41.8, 40.2 (AB, J = 14)	1.4(3)	1.2(1)
2 (**b**)	−22.0, −22.1	43.8, 44.3	47.9, 47.8, 47.6 (AB, J = 53)	0.33(1)	3.9(1)
3 (**c**)	−26.9, −27.0	43.7, 43.5	48.1, 47.9, 47.5, 47.4	1.8(1)	4.6(3)
4 (**d**)	−26.0, −25.9	43.6, 43.4	47.7, 47.6, 47.5, 47.4	1.4(1)	4.7(4)
5 (**e**)	−25.9[f]	44.6, 44.3	49.2, 49.1, 48.8, 48.7	1.3(1)	4.8(5)
3 (**c**)[g]				1.5(1)	2.1(1)

[a] The external standard for ^{31}P NMR chemical shifts was 85% H_3PO_4. Coupling constants are reported in Hz. Solvents: $CDCl_3$ for **2a**,**c**−**e**, **3a**−**e**, and adducts of **3b**,**c**; C_6D_6 for **2b** and the adduct of **3e**; CD_2Cl_2 for adducts of **3a**,**d**. [b] The chemical shift of the *rac* diastereomer (which was the major one for all but **b**) is listed first, followed by that for the *meso* isomer. [c] Chemical shifts are reported in the order minor *rac*, major *rac*, *meso*, for products formed using the Pt((*R*,*R*)-Me-DuPhos)(Ph)(Cl) catalyst precursor. [d] dr = diastereomer ratio, *rac*/*meso*. [e] er = enantiomer ratio. The dr and er values reported are the average of two or more separate experiments, with the standard deviation reported as the error (see the Supporting Information). [f] Only one peak was observed [g] Data for alkylation of **4c** (Scheme 4), corrected for the presence of **2c** in the starting material

Scheme 5. Formation of 3a−e by Oxidation of 2a−e and Structure of the Shift Reagent 6

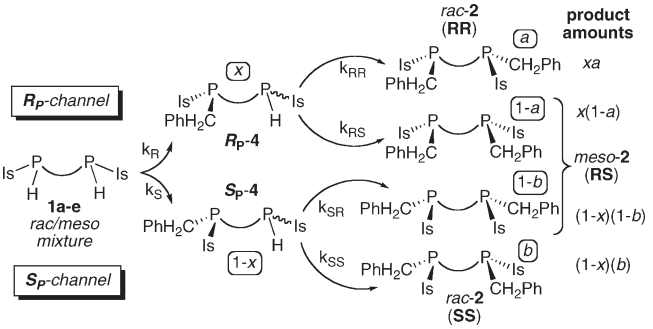


which did not undergo catalytic alkylation under these conditions.

The selectivity of alkylation of **1a−e** also depended on linker length *n*. In most cases (n = 1−4; **2a−d**), the diastereoselectivity could be ascertained directly from ^{31}P NMR spectra, since the *rac* and *meso* isomers had distinct chemical shifts.[5] Bis(tertiary phosphines) **2a−e** were then treated with H_2O_2 to yield phosphine oxides **3a−e** in high yields (Scheme 5); such oxidations proceed with retention of configuration at phosphorus.[10] The improved ^{31}P NMR chemical shift dispersion in **3a−e** provided another opportunity to measure the diastereomeric ratio (dr).[11] Treatment of **3a−e** with the chiral amino acid shift reagent Fmoc-Trp(Boc)-OH (**6**) gave diastereomeric mixtures of hydrogen-bonded adducts with distinct singlet ^{31}P NMR chemical shifts for the *R,R* and *S,S* diphosphine oxides, while the *meso R,S* isomers gave rise to two peaks, for which AB patterns with P−P couplings were observed for shorter chain lengths (n = 1, 2).[12] Integration of these spectra provided the product ratios shown in Table 1, which also contains results for the Pt-catalyzed alkylation of **4c** (Scheme 4, corrected for the presence of **2c** in the starting material; see the Supporting Information for details). Consistent dr values were obtained from spectra of **2a−e**, **3a−e**, and the adducts with **6** (see the Supporting Information). We have previously validated this approach by comparing ^{31}P NMR and chiral HPLC assays of product ratios for closely related diphosphine oxides.[6]

Selectivity of Catalytic Alkylation. These data showed that the linker length had a strong influence on the selectivity of the double alkylation (Scheme 3). Most strikingly, formation of ethano-bridged **2b** was *meso*-selective, as observed previously with the same substrate (**1b**) and 2-(bromomethyl)naphthalene (Scheme 1).[6] Diastereoselectivity and enantioselectivity were similar for substrates **1c−e**, with linkers of three to five methylenes, while **1a**,**b** gave anomalous results.

Scheme 6. Stereoselectivity of Pt-Catalyzed Alkylation of 1 (To Yield 4) and of 4 (To Yield 2), Defined by the Mole Fractions *x*, *a*, and *b*[a]



[a] The mole fraction x is defined by the relative amounts of intermediates **4**; $x = [R]/([R] + [S])$.

The simplest hypothesis to explain the observed selectivity is that alkylation of the short-linker substrates **1a**,**b** was under substrate control, while catalyst control prevailed for longer linkers in **1c−e**. As described previously, alkylation selectivity may be described quantitatively using parameters shown in Scheme 6 and eqs 1−4.[6]

$$\text{substrate control}: \text{dr} = \frac{xa + (1-x)(b)}{(x)(1-a) + (1-x)(1-b)} \quad (1)$$

$$\text{er} = \frac{xa}{(1-x)(b)} \quad (2)$$

$$\text{catalyst control}: \text{dr} = \frac{x^2 + (1-x)^2}{2x(1-x)} \quad (3)$$

$$\text{er} = \frac{x^2}{(1-x)^2} \quad (4)$$

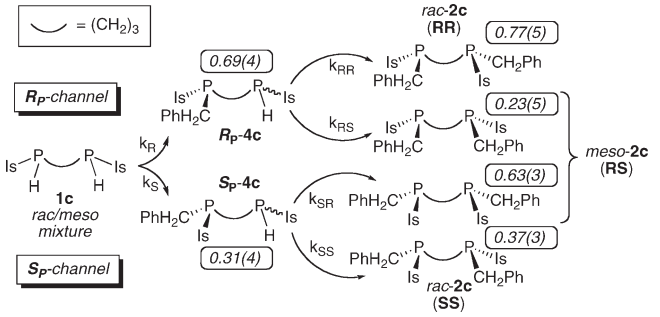
Considering the two alkylations of **1** separately, the mole fractions x and $1 - x$ define the amounts of diastereomeric intermediates **4** (for example, R_P-**4** refers to (*R*,*R*)-**4** plus (*R*,*S*)-**4**; the labels are for the tertiary and secondary phosphine stereocenters, respectively). Note that the absolute configuration of the diphosphines has not been established; therefore, we have arbitrarily assigned the major *rac* diastereomers of **2** to be *R*,*R*,

(10) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley-Interscience: New York, 2000; pp 300−303.
(11) Gawley, R. E. *J. Org. Chem.* **2006**, *71*, 2411–2416.
(12) Li, Y.; Raushel, F. M. *Tetrahedron: Asymmetry* **2007**, *18*, 1391–1397.

Table 2. Predicted and Experimental Selectivities for Pt-Catalyzed Alkylation of 1c−e

entry	*n* (no.)	*x*	dr	dr (calcd)	er	er (calcd)
1	3 (**c**)	0.77	1.8(1)	1.82	4.6(3)	11
2	3 (**c**)	0.73		1.54		7.3
3	3 (**c**)	0.68		1.30		4.5
4	4 (**d**)	0.69	1.4(1)	1.34	4.7(4)	4.9
5	5 (**e**)	0.68	1.3(1)	1.30	4.8(5)	4.5

Scheme 7. Stereoselectivity in Pt-Catalyzed Alkylation of 1c (To Yield 4c) and of 4c (To Yield 2c)



by analogy to the (R_P)-PMe(Is)(CH_2Ph) formed in Pt-catalyzed alkylation of PHMe(Is) with the same catalyst precursor.[3b,13] Conversion of **4** to **2** then occurs in two parallel channels, which differ only in the configuration of the tertiary phosphine in substrate **4**[6,14] and are defined by the mole fractions *a* and *b*. If the selectivities of alkylation of the two phosphorus sites in substrates **1** differ ($x \neq a \neq 1 - b$), then the product ratios are given by eqs 1 and 2 (substrate control). If they are the same ($x = a = 1 - b$), eqs 3 and 4 give dr and er values (catalyst control).[6,15]

If catalyst control is operative in a given reaction, there must be an *x* value which yields product ratios from eqs 3 and 4 that match the experimental observations. For example, approximately the same *x* predicts dr and er values for alkylation of **1d**,**e** in reasonable agreement with the experimental data (Table 2, entries 4 and 5; results are included for two different values of *x* to show how sensitive the predictions are to small changes in this parameter). In contrast to this catalyst control, the selectivity of the two alkylation steps for **1b** must be different (substrate control), as characterized quantitatively with a different benzyl bromide (Scheme 1).[6] Because the background reaction competes with the Pt-catalyzed alkylation of **1a**, we did not attempt such analyses for this substrate, but the observed product distribution is most consistent with substrate control. Substrate **1c** is an intermediate case, where a choice of *x* to match the experimental dr (entry 1) predicts too large an er, but reducing *x* to fit the experimental enantioselectivity (entry 3) leads to a too-small dr, and an intermediate value (entry 2) gets them both wrong. These observations suggested a low degree of substrate control, which was investigated in more detail.

(13) It is plausible that the major *rac* diastereomer has the same configuration in each case; this would be consistent with the ^{31}P NMR chemical shift trends for adducts of **3a**−**e** with **6**, in which the major *rac* signal appears upfield of the minor one, but there is no direct evidence for this assumption.

(14) As described in ref 6 (see Scheme 5 and accompanying discussion), the selectivity of alkylation of the diastereomers in a given channel (such as (*R,R*)-**4** and (*R,S*)-**4**) is expected to be identical, since both will form the same mixture of Pt−phosphido intermediates.

(15) Fleming, I.; Ghosh, S. K. *J. Chem. Soc., Chem. Commun.* **1994**, 99–100.

Table 3. Experimental and Calculated Product Ratios in Pt-Catalyzed Formation of 2c from 1c and from 4c under Substrate Control (SC) or Catalyst Control (CC)[a]

	(*R,R*)-**2c**	*meso*-**2c**	(*S,S*)-**2c**	dr	er
from **1c** (exptl)	0.525[b]	0.36	0.115[b]	1.8(1)	4.6(3)
from **1c** (calcd (SC))[c]	0.53	0.35	0.11	1.8	4.8
from **1c** (calcd (CC))	0.49	0.42	0.09	1.4	5.4
from **4c** (exptl)	0.41	0.40	0.19	1.5(1)	2.1(2)
from **4c** (calcd (SC))	0.39	0.43	0.18	1.3	2.2
from **4c** (calcd (CC))	0.35	0.50	0.15	1.0	2.3

[a] The major enantiomer of **2c** was arbitrarily assumed to have an *R,R* configuration. For SC, $x = 0.69$, $a = 0.77$, $b = 0.37$ ($1 - b = 0.63$). For CC, $x = a = 1 - b = 0.70$. [b] The third digit is included to avoid rounding errors. [c] These product ratios do not sum to 1.0 because of rounding errors.

Table 4. ^{31}P NMR Data for the Intermediates IsHP(CH_2)$_n$-P(CH_2Ph)(Is) (4a−e)[a]

n (no.)	δ(PH)	δ(PCH_2Ph)	*J*
1 (**a**)	−97.2	−28.0	119
	−97.1	−28.6	125
2 (**b**)	−90.6	−22.8	31
	−89.3	−23.1	30
3 (**c**)	−95.9	−27.8	
	−95.8	−27.7	
4 (**d**)	−94.9	−26.7	
	−95.0	−26.8	
5 (**e**)[b]	−94.90	−26.75	
	−94.91	−26.77	

[a] ^{31}P NMR chemical shift standard: 85% H_3PO_4. Coupling constants are reported in Hz. Solvent: THF. Intermediates **4** were generated during Pt-catalyzed conversion of bis(secondary phosphines) **1a**−**e** to bis(tertiary phosphines) **2a**−**e**. In most cases, the ratio of diastereomers of **4** was close to 1/1; data for the major isomers are given first. [b] Overlapping signals.

Values of *x*, *a*, and *b* (Scheme 6), and hence quantitative characterization of catalyst vs substrate control, may be obtained by comparing the product ratios in separate Pt-catalyzed alkylations of substrate **1c** and intermediate **4c**.[6] Substituting these data from Table 1 (rows 3 and 6) into eqs 1 and 2 gave $x = 0.69(4)$, $a = 0.77(5)$, and $b = 0.37(3)$ ($1 - b = 0.63(3)$), as shown in Scheme 7.[16] As anticipated from the discussion of the data in Table 2, these values are close to, but not identical with, those required for catalyst control ($x = a = 1 - b$). The predicted product ratios are in good agreement with experimental dr and er values for Pt-catalyzed formation of **2c** from either **1c** or **4c** (Table 3) and significantly better than the catalyst-control predictions made by using an average value, $x = a = 1 - b = 0.70$ (see Tables 2 and 3).[16]

Therefore, alkylation of **1c** appears to be mainly catalyst-controlled, with a minor contribution from substrate control; the selectivities of alkylation of R_P-**4c**, S_P-**4c**, and **1c** are slightly different.[17] Note that the value $x = 0.69$ is similar to those deduced for catalyst-controlled alkylation of the longer-chain substrates **1d**,**e**, suggesting that the selectivity of the first alkylation of **1c** may be unaffected by the pendant

(16) See the Supporting Information for estimates of the errors in determination of the parameters *x*, *a*, and *b*; note that they are not independent. Rounding errors in calculations of product ratios and dr and er values in Table 3 also affect those numbers; see the Supporting Information for more discussion.

(17) It is plausible that the selectivity of alkylation of R_P-**1c** also differs from that of S_P-**1c**, but as discussed previously,[6] we cannot determine these parameters independently.

$(CH_2)_3$PHIs group, and only in the second alkylation does the larger $(CH_2)_3P(CH_2Ph)$(Is) moiety affect the selectivity.

Conclusion

In catalytic asymmetric reactions of symmetrical bifunctional substrates, the selectivity of a transformation at one site may affect the selectivity of the same transformation at the nominally identical second site (substrate control). This effect should depend on the separation between the reactive centers, vanishing at sufficiently long distances (catalyst control). In Pt-catalyzed alkylation of the bis(secondary phosphine) substrates **1a**−**e**, four or five methylene groups provided a long enough linker to insulate the two P-nucleophiles and ensure catalyst-controlled *rac*-selective alkylation for **1d**,**e**. In contrast, a two-carbon linker in **1b** resulted in substrate control with negative cooperativity (*meso*-selective alkylation), and substrate control also appeared to be operative for **1a**. The three-carbon linker in **1c** resulted in intermediate behavior, where the catalyst control was only slightly affected by the substrate.

The linker also affected the rate of catalysis, which was slower for **1a**,**b**, presumably due to steric effects of the large isityl groups, which is also the likely origin of the substrate-controlled selectivity.[6] Logical future steps in establishing such structure/reactivity/selectivity relationships include varying the size of the P substituent and using more rigid linkers; both are currently under investigation.

Experimental Section

General Experimental Details. Unless otherwise noted, all reactions and manipulations were performed in dry glassware under a nitrogen atmosphere at 20 °C in a drybox or using standard Schlenk techniques. Petroleum ether (bp 38−53 °C), CH_2Cl_2, ether, THF, and toluene were dried over alumina columns similar to those described by Grubbs.[18] NMR spectra were recorded using Varian 300 or 500 MHz spectrometers. ^{1}H or ^{13}C NMR chemical shifts are reported vs Me_4Si and were determined by reference to the residual ^{1}H or ^{13}C solvent peaks. ^{31}P NMR chemical shifts are reported vs H_3PO_4 (85%) used as an external reference. Coupling constants are reported in Hz, as absolute values unless noted otherwise. Unless indicated, peaks in NMR spectra are singlets. Elemental analyses were provided by Quantitative Technologies Inc. Mass spectra were recorded at the University of Illinois, Urbana−Champaign (http://www.scs.uiuc.edu/~msweb).

Reagents were from commercial suppliers, except for these compounds, which were made by the literature procedures: Pt((*R,R*)-Me-DuPhos)(Ph)(Cl),[19] PH_2Is,[20] Mes*Br,[21] IsHP(CH_2)-PHIs (**1a**),[7a] IsHP$(CH_2)_2$PHIs (**1b**),[7b] and IsHP$(CH_2)_3$PHIs (**1c**).[7c]

IsHP$(CH_2)_4$PHIs (1d). To a mixture of PH_2Is (1.18 g, 79% purity by ^{1}H NMR spectroscopy, containing 21% 1,3,5-triisopropylbenzene, 4.23 mmol, 2 equiv) and anhydrous K_2CO_3 (691 mg, 5 mmol, 2.4 equiv) in DMSO (ca. 40 mL) under N_2 was added freshly ground KOH (238 mg, 4.23 mmol, 2 equiv) to produce a yellow solution. (Note: reactions with added K_2CO_3, as reported in ref 8a, were no faster than those in its absence.) The solution was stirred for 1 h, and then 1,4-dibromobutane (253 μL, 2.12 mmol, 1 equiv) was injected via microliter syringe. The solution turned clear and then cloudy. The mixture was stirred for 62 h, over which time a white solid precipitated. The reaction was quenched with 30 mL of degassed H_2O, and then the mixture was extracted with three 30 mL portions of petroleum ether. The ^{31}P NMR spectrum of the crude reaction mixture showed mainly the desired bis(phosphine) (δ −101.3, −101.4), the starting material PH_2Is (δ −166.6), an unidentified peak (δ −39.0), and some phosphine oxide (δ 59.0). The petroleum ether solution was dried over $MgSO_4$ and filtered, and the solvent was removed to leave an oily white residue. PH_2Is was removed from the crude product by Kugelrohr distillation. The residue melted completely at 100−110 °C, and PH_2Is was distilled away from the product at 151 °C under vacuum. Upon cooling, the solid bis(phosphine) was further purified to remove the phosphine oxide by eluting over a silica column (0.5 cm wide × 3.5 cm high) with 15 mL of petroleum ether and then washing the solid with three 10 mL portions of DMSO to leave 383 mg (34% yield) of white solid.

The mass spectrum was consistent with oxidation of the air-sensitive phosphine: calcd HRMS (ES+) for $C_{34}H_{57}O_2P_2$ (MO_2H+) m/z 559.3834, found m/z 559.3829. ^{31}P{^{1}H} NMR ($CDCl_3$): δ −94.28, −94.29 (overlapping, ~1:1); plus traces of unidentified impurities:, δ −32.6, −112.2, −116.6. ^{1}H NMR ($CDCl_3$): δ 7.03 (d, J = 2, 4H, Ar), 4.25 (dm, J_{PH} = 215, 2H, P−H), 3.67−3.60 (m, 4H, *i*-Pr CH), 2.88 (sep, J = 7, 2H, *i*-Pr CH), 1.82 (broad, 2H, P−CH_2), 1.58 (broad m, 6H, CH_2), 1.30 (d, J = 7, 12H, *i*-Pr CH_3), 1.27 (d, J = 7, 12H, *i*-Pr CH_3), 1.23 (d, J = 7, 12H, *i*-Pr CH_3). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 152.7 (d, J = 11, quat, Ar), 149.3 (quat, Ar), 128.1 (d, J = 14, quat, Ar), 121.3 (d, J = 3, CH, Ar), 34.2 (*i*-Pr CH), 32.6 (d, J = 14, *i*-Pr CH), 29.8 (t, J = 11, P−CH_2), 24.9 (*i*-Pr CH_3), 24.3 (*i*-Pr CH_3), 23.8 (d, J = 2, *i*-Pr CH_3), 23.7 (d, J = 11, CH_2).

IsHP$(CH_2)_5$PHIs (1e). To a mixture of PH_2Is (1.03 g, 79% purity by ^{1}H NMR spectroscopy, containing 21% 1,3,5-triisopropylbenzene, 3.67 mmol, 2 equiv) and anhydrous K_2CO_3 (553 mg, 4 mmol, 2.2 equiv) in DMSO (ca. 40 mL) under N_2, was added freshly ground KOH (216 mg, 3.85 mmol, 2 equiv) to produce a yellow solution. The solution was stirred for 1 h, and then 1,5-dibromobutane (251 μL, 1.83 mmol, 1 equiv) was injected via microliter syringe. The solution turned clear and then cloudy. The mixture was stirred for 62 h, over which time a white solid precipitated. The mixture was quenched with 25 mL of degassed H_2O and then extracted with three 30 mL portions of ether. The ^{31}P NMR spectrum of the crude reaction mixture showed mainly the desired bis(phosphine) (δ −100.9), the starting material PH_2Is (δ −166.4), and an unidentified peak (δ −51.0). The ether solution was dried over $MgSO_4$ and filtered, and the solvent was removed to leave an oily white residue. PH_2Is was removed from the crude product by Kugelrohr distillation under vacuum at 140 °C. When the distillation pot was cooled, a white solid was recovered, which was further purified by washing with three 10 mL portions of DMSO to give 514 mg (52% yield) of the desired product.

Anal. Calcd for $C_{35}H_{58}P_2$: C, 77.73; H, 10.81. Anal. Calcd for $C_{35}H_{58}O_2P_2$: C, 73.39; H, 10.21. Found: C, 71.16; H, 9.88. The mass spectrum was consistent with oxidation of the air-sensitive phosphine: calcd HRMS (ES+) for $C_{35}H_{59}O_2P_2$ (MO_2H^+) m/z 573.3990, found m/z 573.3976. ^{31}P{^{1}H} NMR ($CDCl_3$): δ −94.06, −94.07 (~1:1 mixture of diastereomers). ^{1}H NMR ($CDCl_3$): δ 7.02 (d, J = 2, 4H, Ar), 4.23 (d of apparent t, J_{PH} = 215, J = 8, 2H, P−H), 3.70−3.61 (m, 4H, *i*-Pr CH), 2.88 (sep, J = 7, 2H, *i*-Pr CH), 1.84−1.76 (broad m, 2H, P−CH_2), 1.61−1.44 (broad m, 8H, CH_2), 1.29 (d, J = 7, 12H, *i*-Pr CH_3), 1.26 (d, J = 7, 12H, *i*-Pr CH_3), 1.22 (d, J = 7, 12H, *i*-Pr CH_3). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 152.7 (d, J = 11, quat, Ar), 149.3 (quat, Ar), 128.2 (d, J = 15, quat, Ar), 121.3 (d, J = 4, CH, Ar), 34.2 (*i*-Pr CH), 32.6 (d, J = 14, *i*-Pr CH), 32.4 (t, J = 10,

(18) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.
(19) Brunker, T. J.; Blank, N. F.; Moncarz, J. R.; Scriban, C.; Anderson, B. J.; Glueck, D. S.; Zakharov, L. N.; Golen, J. A.; Sommer, R. D.; Incarvito, C. D.; Rheingold, A. L. *Organometallics* **2005**, *24*, 2730–2746.
(20) van der Winkel, Y.; Bastiaans, H. M. M.; Bickelhaupt, F. *J. Organomet. Chem.* **1991**, *405*, 183–194.
(21) Cowley, A. H.; Norman, N. C.; Pakulski, M. *Inorg. Synth.* **1990**, *27*, 235–240.

P−CH_2), 28.1 (d, J = 12, CH_2), 24.9 (*i*-Pr CH_3), 24.3 (*i*-Pr CH_3), 23.86 (d, J = 2, *i*-Pr CH_3), 23.8 (d, J = 11, CH_2).

Pt-Catalyzed Alkylation of 1a−e. General Procedure for Synthesis of Is(PhCH$_2$)P(CH$_2$)$_n$P(CH$_2$Ph)Is (2a−e). A solution of Pt((*R,R*)-Me-DuPhos)(Ph)(Cl) (3 mg, 0.005 mmol, 10 mol %) in 1 mL of THF was added to the bis(secondary phosphine) (0.05 mmol; for example, 25 mg of **1b**) followed by $NaOSiMe_3$ (12 mg, 0.1 mmol, 2 equiv), and the solution turned yellow. The mixture was transferred to an NMR tube, and benzyl bromide (12 μL, 0.1 mmol, 2 equiv) was added neat via syringe. Once the reaction was complete, as monitored by ^{31}P NMR spectroscopy, the solvent was removed under reduced pressure to leave an oily white residue, which was eluted over a silica column (0.6 cm width × 3.0 cm height) with three 1 mL portions of 9/1 petroleum ether/THF. The catalyst and the NaBr did not elute. The eluted solvent was removed under reduced pressure to leave an oily residue of **2a−e**. See the individual compounds for the amounts of **1a−e**, reaction times, and yields of **2a−e**.

Is(PhCH$_2$)PCH$_2$P(CH$_2$Ph)Is (2a). A 24 mg amount of **1a** was used; 4 days, 66% yield (22 mg of **2a**). The time for completion of this slow reaction varied in duplicate experiments from ca. 2−4 days. Despite standard precautions to exclude oxygen, an additional product tentatively assigned as Is(CH_2Ph)P(O)CH_2P(CH_2Ph)Is (**2a-O**, ^{31}P{^{1}H} NMR (THF) δ 40.7 (d, J = 83), 40.2 (d, J = 68), −39.3 (d, J = 68), −42.4 (d, J = 83); dr ranged from 1.6/1 to 1.3/1) was also observed in varying amounts (from ca. 10 to 20%). Oxidation of a sample of **2a** containing this material with H_2O_2 (see below) gave the bis(phosphine oxide) **3a**, consistent with the proposed structure of **2a-O**. The er of **2a** did not depend on the amount of this impurity, but the dr of **2a** was higher in samples which contained more of it. See the Supporting Information for more details and information on the Pt-free background alkylation, which occurred at a similar rate.

HRMS (ES+): calcd for $C_{45}H_{63}P_2$ (MH^+) m/z 665.4405, found m/z 665.4399. ^{31}P{^{1}H} NMR (C_6D_6): δ −31.6 (*rac*), −34.1 (*meso*), ∼1.4/1 (*rac*/*meso*). ^{1}H NMR (C_6D_6): δ 7.18−7.13 (m, 4H, Ar, *rac*/*meso*), 7.10 (2H, Ar, *rac*/*meso*), 7.05−6.92 (m, 8H, Ar, *rac*/*meso*), 3.98 (broad, 4H, *i*-Pr CH, *rac*/*meso*), 3.47 (AB pattern, J = 13, 4H, CH_2Ph, *rac*), 3.30 (AB pattern, J = 13, 4H, CH_2Ph, *meso*), 2.80−2.73 (m, 2H, CH_2, *rac*/*meso*), 2.72−2.60 (m, 2H, *i*-Pr CH, *rac*/*meso*), 1.30 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.20 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.17−1.04 (m, 24H, *i*-Pr CH_3, *rac*/*meso*). ^{13}C{^{1}H} NMR (C_6D_6): δ 150.9 (quat, Ar, *rac*/*meso*), 150.6 (quat, Ar, *rac*/*meso*), 139.9−139.7 (m, quat, Ar, *rac*/*meso*), 129.6−129.5 (m, CH, Ar, *rac*/*meso*), 128.53 (CH, Ar, *meso*), 128.49 (CH, Ar, *rac*), 128.3−127.7 (m, Ar, *rac*/*meso*, overlapping C_6D_6 peaks), 125.9 (CH, Ar, *rac*/*meso*), 122.3−122.2 (m, CH, Ar, *rac*/*meso*), 36.3 (t, J = 6, CH_2, *meso*), 35.88 (t, J = 7, CH_2, *rac*), 34.6 (*i*-Pr CH, *rac*), 34.5 (*i*-Pr CH, *meso*), 31.8−31.5 (m, P−CH_2−P, *rac*/*meso*), 25.2 (broad, *i*-Pr CH, *rac*/*meso*), 24.84 (*i*-Pr CH_3, *meso*), 24.80 (*i*-Pr CH_3, *rac*), 23.99 (*i*-Pr CH_3, *rac*), 23.97 (*i*-Pr CH_3, *meso*).

Is(PhCH$_2$)P(CH$_2$)$_2$P(CH$_2$Ph)Is (2b). A 25 mg amount of **1b** was used; 10 h, 85% yield (29 mg). HRMS (ES+): calcd for $C_{46}H_{65}P_2$ (MH^+) m/z 679.4562, found m/z 679.4580. ^{31}P{^{1}H} NMR (C_6D_6): δ −22.0 (*rac*), −22.1 (*meso*), ∼2.9/1 *meso*/*rac* (overlapping peaks). ^{1}H NMR (C_6D_6): δ 7.16−6.91 (m, 14H, Ar), 4.04 (broad, 4H, *i*-Pr CH), 3.22 (AB pattern, J = 13, 2H, CH_2Ph, *meso*), 3.21 (AB pattern, J = 13, 2H, CH_2Ph, *rac*), 3.14 (AB pattern, J = 13, 2H, CH_2Ph, *rac*), 3.06 (AB pattern, J = 13, 2H, CH_2Ph, *meso*), 2.70 (m, 2H, *i*-Pr CH, overlapping *rac*/*meso*), 2.26 (broad m, 1.5H, P−CH_2, overlapping *rac*/*meso*), 2.09 (broad m, 2.5H, P−CH_2, overlapping *rac*/*meso*), 1.28 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.27 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.18−1.13 (m, 24H, *i*-Pr CH_3, *meso*, m, 12H, *i*-Pr CH_3, *rac*), 1.03 (d, J = 7, 12H, *i*-Pr CH_3, *rac*). ^{13}C{^{1}H} NMR (C_6D_6): δ 156.1 (broad, quat, Is), 150.6 (quat, Is, *meso*), 150.5 (quat Is, *rac*), 140.2 (t, J = 6, Ar, *rac*), 140.0 (t, J = 6, Ar, *meso*), 129.4 (m, Ar, *rac*/*meso*), 128.6 (m, Ar, *rac*), 128.5 (Ar, *meso*), 125.9 (Ar, *rac*), 125.8 (Ar, *meso*), 122.3 (CH, Is, overlapping *rac*/*meso*), 36.0 (dd, J = 8, 12, CH_2Ph, *rac*), 35.8 (dd, J = 8, 12, CH_2Ph, *meso*), 34.6 (CH, *i*-Pr, *meso*), 34.5 (CH, *i*-Pr, *rac*), 31.7 (apparent t, J = 10, CH, *i*-Pr, *rac*/*meso*), 26.8 (d, J = 6, P−CH_2, *rac*/*meso*), 25.1 (*i*-Pr CH_3, *rac*/*meso*), 25.0 (*i*-Pr CH_3, *meso*), 24.8 (*i*-Pr CH_3, *rac*), 24.0 (*i*-Pr CH_3, *meso*), 23.9 (*i*-Pr CH_3, *rac*). One quaternary carbon signal was not found.

Is(PhCH$_2$)P(CH$_2$)$_3$P(CH$_2$Ph)Is (2c). A 25 mg amount of **1c** was used; 1 h, 84% yield (29 mg of **2c**). HRMS (ES+): calcd for $C_{47}H_{67}P_2$ (MH^+) m/z 693.4718, found m/z 693.4713. ^{31}P{^{1}H} NMR (C_6D_6): δ −27.3 (*rac*), −27.4 (*meso*), ∼1.8/1 (*rac*/*meso*). ^{1}H NMR (C_6D_6): δ 7.13−7.11 (m, 4H, Ar, *rac*/*meso*), 7.10 (d, J = 2, 4H, Ar, *rac*), 7.09 (d, J = 2, 4H, Ar, *meso*), 7.07−7.03 (m, 4H, Ar, *rac*/*meso*), 6.99−6.96 (m, 2H, Ar, *rac*/*meso*), 4.04 (broad, 4H, *i*-Pr CH, *rac*/*meso*), 3.19 (AB pattern, J = 14, 4H, CH_2Ph, *rac*), 3.18 (AB pattern, J = 13, 4H, CH_2Ph, *meso*), 2.76−2.70 (m, 2H, *i*-Pr CH, *rac*/*meso*), 2.08−1.98 (m, 4H, P−CH_2, *rac*/*meso*), 1.65−1.56 (m, 2H, P−CH_2, *rac*/*meso*), 1.28 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.27 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.19−1.16 (m, 24H, *i*-Pr CH_3, *rac*/*meso*). ^{13}C{^{1}H} NMR (C_6D_6): δ 156.0 (broad, quat, Ar, *meso*), 155.9 (broad, quat, Ar, *rac*), 150.5 (quat, Ar, *rac*/*meso*), 140.19 (d, J = 12, quat, Ar, *meso*), 140.17 (d, J = 12, quat, Ar, *rac*), 130.0 (d, J = 26, quat, Ar, *rac*), 129.9 (d, J = 26, quat, Ar, *meso*), 129.41 (d, J = 7, CH, Ar, *rac*), 129.40 (d, J = 7, CH, Ar, *meso*), 128.54 (m, CH, Ar), 125.9 (d, J = 3, CH, Ar, *rac*/*meso*), 122.3 (broad, CH, Ar, *rac*/*meso*), 36.1 (d, J = 19, CH_2, *rac*/*meso*), 34.57 (*i*-Pr CH, *rac*), 34.56 (*i*-Pr CH, *meso*), 31.8 (*i*-Pr CH, *meso*), 31.6 (*i*-Pr CH, *rac*), 29.7−29.4 (m, CH_2, *rac*/*meso*), 27.8 (apparent t, J = 27, P−CH_2CH_2, *rac*), 27.7 (apparent t, J = 27, P−CH_2CH_2, *meso*), 25.1 (*i*-Pr CH_3, *rac*), 25.03 (*i*-Pr CH_3, *meso*), 25.00 (*i*-Pr CH_3, *rac*/*meso*), 24.0 (*i*-Pr CH_3, *rac*/*meso*).

Is(PhCH$_2$)P(CH$_2$)$_4$P(CH$_2$Ph)Is (2d). A 26 mg amount of **1d** was used; 2 h, 97% yield of **2d** (34 mg). HRMS (ES+): calcd for $C_{48}H_{69}P_2$ (MH^+) m/z 707.4875, found m/z 707.4881. ^{31}P{^{1}H} NMR (C_6D_6): δ −26.30 (*meso*), −26.33 (*rac*), ∼1.3/1 (*rac*/*meso*, overlapping signals). ^{1}H NMR (C_6D_6): δ 7.15−7.13 (m, 4H, Ar, *rac*/*meso*), 7.11−7.09 (m, 4H, Ar, *rac*/*meso*), 7.07−7.02 (m, 4H, Ar, *rac*/*meso*), 6.99−6.95 (m, 2H, Ar, *rac*), 4.05 (broad, 4H, *i*-Pr CH, *rac*/*meso*), 3.17 (overlapping AB patterns, J = 14, 4H, P−CH_2Ph, *rac*/*meso*), 2.78−2.68 (m, 2H, *i*-Pr CH, *rac*/*meso*), 1.90−1.84 (m, 2H, CH_2, *rac*/*meso*), 1.82−1.76 (m, 2H, CH_2, *rac*/*meso*), 1.42−1.38 (broad m, 4H, CH_2, *rac*/*meso*), 1.31 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.30 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.18−1.15 (m, 24H, *i*-Pr CH_3, *rac*/*meso*). ^{13}C{^{1}H} NMR (C_6D_6): δ 156.0 (broad, quat, Ar, *meso*), overlapping 155.9 (broad, quat, Ar, *rac*), 150.5 (quat, Ar, *rac*/*meso*), 140.2 (d, J = 12, quat, Ar, *rac*/*meso*), 129.9 (d, J = 27, quat, Ar, *meso*), 129.8 (d, J = 27, quat, Ar, *rac*), 129.4−129.3 (m, CH, Ar, *rac*/*meso*), 128.55 (CH, Ar, *rac*), 128.54 (CH, Ar, *meso*), 125.9−125.8 (m, CH, Ar, *rac*/*meso*), 122.3 (broad, CH, Ar, *rac*/*meso*), 36.1 (d, J = 19, CH_2Ph, *meso*), 36.0 (d, J = 20, PCH_2Ph, *rac*), 34.6 (*i*-Pr CH, *rac*/*meso*), 31.63 (d, J = 21, *i*-Pr CH, *meso*), 31.60 (d, J = 21, *i*-Pr CH, *rac*), 30.5−29.9 (m, CH_2, *rac*/*meso*), 27.9 (d, J = 18, CH_2, *meso*), 27.8 (d, J = 18, CH_2, *rac*), 25.1 (*i*-Pr CH_3, overlapping *rac*/*meso*), 25.0 (*i*-Pr CH_3, overlapping *rac*/*meso*), 24.02 (*i*-Pr CH_3, *rac*), 24.00 (*i*-Pr CH_3, *meso*).

Is(PhCH$_2$)P(CH$_2$)$_5$P(CH$_2$Ph)Is (2e). A 27 mg amount of **1e** was used; 2 h, 97% yield of **2e** (35 mg). HRMS (ES+): calcd for $C_{49}H_{71}P_2$ (MH^+) m/z 721.5031, found m/z 721.5022. ^{31}P{^{1}H} NMR (C_6D_6): δ −26.3 (*meso*), −26.4 (*rac*), ∼1.2/1 (overlapping, *rac*/*meso*). ^{1}H NMR (C_6D_6): δ 7.17−7.13 (m, 4H, Ar, *rac*/*meso*), 7.12−7.10 (m, 4H, Ar, *rac*/*meso*), 7.08−7.03 (m, 4H, Ar, *rac*/*meso*), 6.99−6.96 (m, 2H, Ar, *rac*/*meso*), 4.09 (broad, 4H, *i*-Pr CH, *rac*/*meso*), 3.29−3.24 (m, 2H, CH_2Ph, *rac*/*meso*), 3.16−3.11 (m, 2H, CH_2Ph, *rac*/*meso*), 2.73 (sep, 2H, *i*-Pr CH, *rac*/*meso*), 1.92−1.87 (m, 2H, P−CH_2, *rac*/*meso*), 1.84−1.79 (m, 2H, P−CH_2, *rac*/*meso*), 1.32 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.31 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.29 (broad, 6H, CH_2, *rac*/*meso*), 1.20 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.19 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.18 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.17 (d, J = 7,

12H, *i*-Pr CH_3, *meso*). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 156.1 (broad, quat, Ar, *meso*), 155.9 (broad, quat, Ar, *rac*), 150.52 (quat, Ar, *meso*), 150.51 (quat, Ar, *rac*), 140.26 (d, J = 12, quat, Ar, *rac*), 140.25 (d, J = 12, quat, Ar, *meso*), 130.1 (d, J = 26, quat, Ar, *rac*), 130.0 (d, J = 26, quat, Ar, *meso*), 129.4 (d, J = 7, CH, Ar, *rac*/*meso*), 128.57−128.56 (m, CH, Ar, *rac*/*meso*), 125.91−125.88 (m, CH, Ar, *rac*/*meso*), 122.3 (broad, CH, Ar, *rac*/*meso*), 36.11 (d, J = 19, CH_2, *meso*), 36.08 (d, J = 19, CH_2, *rac*), 34.6 (*i*-Pr CH, *rac*/*meso*), 32.9 (t, J = 14, CH_2, *rac*), 32.8 (t, J = 14, CH_2, *meso*), 31.66 (d, J = 21, *i*-Pr CH, *meso*), 31.65 (d, J = 21, *i*-Pr CH, *rac*), 28.40 (d, J = 26, CH_2, *meso*), 28.37 (d, J = 25, CH_2, *rac*), 28.05 (d, J = 18, CH_2, *meso*), 28.01 (d, J = 18, CH_2, *rac*), 25.12 (*i*-Pr CH_3, *meso*), 25.11 (*i*-Pr CH_3, *rac*), 25.03 (*i*-Pr CH_3, *rac*/*meso*), 24.0 (d, J = 3, *i*-Pr CH_3, *rac*/*meso*).

Is(PhCH$_2$)P(CH$_2$)$_3$PHIs (4c). To a solution of $IsHP(CH_2)_3$PHIs (**1c**; 100 mg, 0.20 mmol, 1 equiv) in 5 mL of THF at −78 °C was added *s*-BuLi (210 μL, 0.21 mmol, 1 equiv, 1.0 M in cyclohexane) dropwise with stirring, and the solution turned yellow. The solution was stirred at −78 °C for 10 min, at which point the ^{31}P NMR spectrum showed a mixture of the starting $IsHP(CH_2)_3PHIs$ (δ −99.4, −99.5, 28%), the desired $IsLiP(CH_2)_3PHIs$ (−98.0 (broad), −98.4, 64%), and $IsLiP(CH_2)_3PLiIs$ (−108, very broad, 8%). Additional *s*-BuLi was added in small portions (155 μL added, 365 μL (1.9 equiv) total) until the mixture contained 2% of the starting $IsHP(CH_2)_3PHIs$, 58% of the desired $IsLiP(CH_2)_3PHIs$, and 40% of $IsLiP(CH_2)_3PLiIs$. To this solution was added dry degassed benzyl chloride (54 μL, 0.39 mmol, 1.9 equiv) via microliter syringe, and the solution turned pale yellow and slightly cloudy. The solution was stirred an additional 1 h at −78 °C and was then warmed to room temperature and stirred overnight. The THF was removed under reduced pressure, and the residue was redissolved in 20 mL of Et_2O. To this solution was added 10 mL of a degassed saturated aqueous NH_4Cl solution, and the two layers were stirred vigorously until both layers were clear. The organic layer was removed via cannula, and the aqueous layer was extracted with two additional 20 mL portions of Et_2O. The combined extracts were dried over $MgSO_4$, the solid was filtered off, and the solvent was removed under reduced pressure. The oily white residue was eluted over a silica pipet column (0.5 cm wide by 3.0 cm high) with four 1 mL fractions of 9/1 petroleum ether/THF. The solvent was removed under reduced pressure to yield 125 mg of a white residue containing 62% of the desired $(Is)(CH_2Ph)P(CH_2)_3PHIs$ (**4c**; δ −27.29, −27.30, −95.05, −95.36 ($CDCl_3$), ∼1/1 mixture of diastereomers), 37% $(Is)(CH_2Ph)P(CH_2)_3P(CH_2Ph)(Is)$ (**2c**; δ −26.9, −27.0 ($CDCl_3$), ∼0.65/1 *rac*/*meso*), and 1% unidentified impurities (δ −30.1) by ^{31}P NMR spectroscopy in $CDCl_3$. This is a quantitative yield based on the starting bis(secondary phosphine) **1c** (theoretical yield of **4c** 120 mg).

HRMS (ES+): calcd for $C_{40}H_{61}P_2$ (MH^+) m/z 603.4249, found m/z 603.4252. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −27.29, −27.30, −95.05, −95.36 (∼1/1). ^1H NMR ($CDCl_3$): δ 7.23−7.19 (m, 2H, Ar), 7.13−7.11 (m, 3H, Ar), 6.98 (d, J = 2, 2H, Ar), 6.97 (d, J = 2, 2H, Ar), 4.16 (dq, J_{PH} = 216, J_{HH} = 7, 1H, Ar), 3.87 (broad, 2H, *i*-Pr CH), 3.57−3.50 (m, 2H, *i*-Pr CH), 3.26−3.15 (m, 2H, PCH_2Ph), 2.91−2.82 (m, 2H, *i*-Pr CH), 2.08−1.94 (broad m, 2H, CH_2), 1.81−1.75 (broad m, 1H, CH_2), 1.61−1.53 (broad m, 1H, P−CH_2), 1.53−1.42 (broad m, 2H, CH_2), 1.29−1.21 (m, 24H, *i*-Pr CH_3), 1.15 (overlapping d, J = 7, 6H, *i*-Pr CH_3), 1.11 (d, J = 7, 6H, *i*-Pr CH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 155.4 (quat, Ar), 155.3 (quat, Ar), 152.7 (quat, Ar), 152.5 (d, J = 4, quat, Ar), 150.1 (quat, Ar), 149.3 (d, J = 16, quat, Ar), 139.6 (quat, Ar), 128.9 (d, J = 7, CH, Ar), 128.3 (d, J = 2, CH, Ar), 128.1−127.8 (m, overlapping quat, Ar), 125.6 (CH, Ar), 122.0 (quat, Ar), 121.3 (d, J = 4, CH, Ar), 121.2 (d, J = 4, CH, Ar), 35.6 (d, J = 18, PCH_2Ph), 34.2 (*i*-Pr CH), 34.1 (*i*-Pr CH), 32.7−32.5 (m, *i*-Pr CH), 31.5 (*i*-Pr CH), 31.3 (*i*-Pr CH), 29.3−29.1 (m, CH_2), 27.1 (m, CH_2), 25.6−25.4 (m, CH_2), 24.8−24.7 (m, *i*-Pr CH_3), 23.9−23.8 (m, *i*-Pr CH_3), 24.3−24.2 (m, *i*-Pr CH_3).

^{31}P NMR data for **4a**−**e** are given in Table 4.

Pt-Catalyzed Alkylation of 4c To Yield 2c. A solution of Pt((*R*,*R*)-Me-DuPhos)(Ph)(Cl) (3 mg, 0.005 mmol, 10 mol %) in 1 mL of THF was added to $Is(CH_2Ph)P(CH_2)_3PHIs$ (**4c**; 0.05 mmol total, containing 0.031 mmol of **4c** and 0.019 mmol of **2c**, 32 mg total) followed by $NaOSiMe_3$ (4 mg, 0.03 mmol), and the solution turned yellow. The mixture was transferred to an NMR tube, and benzyl bromide (4 μL, 0.03 mmol) was added neat via syringe. The reaction was complete in < 30 min by ^{31}P NMR spectroscopy. The solvent was removed under reduced pressure to leave an oily white residue, which was eluted over a silica column (0.5 cm width × 3.0 cm height) with three 1 mL portions of 9/1 petroleum ether/THF. The catalyst and the NaBr did not elute. The eluted solvent was removed under reduced pressure to leave 27 mg (79% yield) of an oily residue. The product ratios were determined after oxidation, as described below.

General Procedure for Oxidation of 2a−e: Synthesis of Is(PhCH$_2$)P(O)(CH$_2$)$_n$P(O)(CH$_2$Ph)Is (3a−e) and Assay of Alkylation Selectivity Using Fmoc(Trp)Boc-OH (6). To a solution of $Is(PhCH_2)P(CH_2)_nP(CH_2Ph)Is$ (**2a**−**e**; 0.03−0.05 mmol) in 1 mL of THF was added excess H_2O_2 (0.1 mL of a 30% solution in H_2O). The solution was stirred for 1 h, and the solvent was removed under reduced pressure. Drying in a vacuum desiccator gave a quantitative yield of the desired phosphine oxide. See below for the amounts of **2a**−**e** used. The er and dr were measured using ^{31}P NMR spectroscopy by dissolving either all or a portion of phosphine oxides **3a**−**e** in 1 mL of a deuterated solvent with Fmoc(Trp)Boc-OH (**6**; 2.5 equiv). See below for the amounts of **3a**−**e** and **6** used and the solvents, Table 2 for ^{31}P NMR data, and the Supporting Information for a table of data from multiple er and dr determinations.

Is(PhCH$_2$)(O)PCH$_2$P(O)(CH$_2$Ph)Is (3a). Amounts: 22 mg (0.03 mmol) of **2a**; all of **3a** was used in the assay with 39 mg (0.075 mmol, 2.5 equiv) of **6** in CD_2Cl_2. HRMS (ES+): calcd for $C_{45}H_{63}O_2P_2$ (MH^+) m/z 697.4303, found m/z 697.4297. $^{31}P\{^1H\}$ NMR (C_6D_6): δ 40.8 (*rac*), 38.7 (*meso*), ∼1.7/1 *rac*/*meso*. ^1H NMR (C_6D_6): δ 7.20−7.13 (m, 8H, Ar, *rac*/*meso*), 7.10−7.06 (m, 6H, Ar, *rac*/*meso*), 4.27−4.20 (m, part of an ABXX′ pattern, 2H, P−CH_2Ph, *rac*), 3.92−3.82 (broad m, 4H, *i*-Pr CH, *rac*/*meso*), 3.81−3.68 (m, 4H, P−CH_2Ph, *rac*/*meso*), 3.68−3.52 (m, part of an ABXX′ pattern, 2H, P−CH_2Ph, *meso*), 3.29 (filled-in d,[22] J = 13, 2H, P−CH_2−P, *rac*), 3.00−2.93 (m, 2H, P−CH_2−P, *meso*), 2.88 (sep, J = 7, *i*-Pr CH, *rac*/*meso*), 1.26−1.22 (m, 24H, *i*-Pr CH_3), 0.97−0.94 (m, 12H, *i*-Pr CH_3). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 153.8 (broad, quat, Ar, *rac*/*meso*), 152.4 (quat, Ar, *rac*/*meso*), 132.0−131.9 (m, quat, Ar, *rac*/*meso*), 130.6 (t, J = 3, CH, Ar, *rac*), 130.3 (t, J = 3, CH, Ar, *meso*), 128.4 (CH, Ar, *meso*), 128.2 (CH, Ar, *rac*), 126.8 (quat, Ar, *meso*), 126.3 (quat, Ar, *rac*), 123.3−123.1 (m, CH, Ar, *rac*/*meso*), 42.8 (d, J = 66, P−CH_2Ph, *rac*), 41.7 (d, J = 62, P−CH_2Ph, *meso*), 40.1 (t, J = 53, P−CH_2−P, *rac*), 38.5 (t, J = 53, P−CH_2−P, *meso*), 34.0 (*i*-Pr CH, *rac*/*meso*), 29.8 (*i*-Pr CH, *rac*), 29.5 (*i*-Pr CH, *meso*), 25.0 (*i*-Pr CH_3, *rac*/*meso*), 24.7 (*i*-Pr CH_3, *rac*), 24.6 (*i*-Pr CH_3, *meso*), 23.6 (*i*-Pr CH_3, *rac*), 23.5 (*i*-Pr CH_3, *meso*).

Is(PhCH$_2$)(O)P(CH$_2$)$_2$P(O)(CH$_2$Ph)Is (3b). Amounts: 29 mg (0.04 mmol) of **2b**; 21 mg (0.03 mmol) of **3b**, 39 mg (0.075 mmol, 2.5 equiv) of **6** in $CDCl_3$. HRMS (ES+): calcd for $C_{46}H_{65}O_2P_2$ (MH^+) m/z 711.4460, found m/z 711.4441. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 44.3 (*meso*), 43.8 (*rac*), ∼3.1/1 *meso*/*rac*. ^1H NMR ($CDCl_3$): δ 7.27−7.21 (m, 2H, Ar, *rac*/*meso*), 7.16−7.08 (m, 8H, Ar, *rac*/*meso*), 7.07 (t, J = 2, 4H, Is, *meso*), 7.01 (t, J = 2, 4H, Is, *rac*), 3.81−3.76 (m, 4H, *i*-Pr CH, *rac*/*meso*), 3.43−3.34 (m, 4H, CH_2Ph, *rac*/*meso*), 2.93−2.80 (m, 2H, *i*-Pr CH, overlapping *rac*/*meso*), 2.32−2.26 (m, 2H, P−CH_2, *rac*/*meso*), 2.16−2.10 (m, 2H, P−CH_2, *rac*), 2.06−2.00 (m, 2H, overlapping *rac*/*meso*), 1.27 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.21 (d, J = 7, 12H, *i*-Pr CH_3, *rac*/*meso*), 1.18 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.06 (d, J = 7, 12H,

(22) Redfield, D. A.; Cary, L. W.; Nelson, J. H. *Inorg. Chem.* **1975**, *14*, 50–59.

i-Pr CH_3, *meso*), 0.92 (d, J = 7, 12H, *i*-Pr CH_3, *rac*). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 154.1 (broad, quat, Ar), 152.2 (quat, Ar), 132.0 (t, J = 4, Ar), 130.0 (t, J = 2, Ar, *rac*), 129.8 (t, J = 2, Ar, *meso*), 128.44 (Ar, *rac*), 128.38 (Ar, *meso*), 126.75 (Ar, *rac*), 126.66 (Ar, *meso*), 123.0 (t, J = 6, CH, Is), 122.6−121.3 (m, quat, Ar), 41.8−40.9 (m, CH_2Ph), 34.1 (*i*-Pr CH, *meso*), 34.0 (*i*-Pr CH, *rac*), 29.8 (*i*-Pr CH, *meso*), 29.7 (*i*-Pr CH, *rac*), 25.8−25.5 (m, P−CH_2, *rac*), 25.2 (*i*-Pr CH_3, *meso*), 25.09 (*i*-Pr CH_3, *rac*), 25.3−24.8 (m, P−CH_2, *meso*), 24.7 (*i*-Pr CH_3, *meso*), 24.6 (*i*-Pr CH_3, *rac*), 23.6 (d, J = 1, *i*-Pr CH_3, *meso*), 23.5 (d, J = 5, *i*-Pr CH_3, *rac*).

Is(PhCH$_2$)(O)P(CH$_2$)$_3$P(O)(CH$_2$Ph)Is (3c). Amounts: 29 mg (0.05 mmol) of **2c**; 21 mg (0.03 mmol) of **3c**, 39 mg (0.075 mmol, 2.5 equiv) of **6** in $CDCl_3$. HRMS (ES+): calcd for $C_{47}H_{67}O_2P_2$ (MO_2H^+) m/z 725.4616, found m/z 725.4623. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 43.7 (*rac*), 43.5 (*meso*), ∼1.8/1 *rac*/*meso*. ^1H NMR ($CDCl_3$): δ 7.24−7.13 (m, 10H, Ar, *rac*/*meso*), 7.05−7.04 (m, 4H, Ar, *rac*/*meso*), 3.82−3.75 (m, 4H, *i*-Pr CH, *rac*/*meso*), 3.40−3.30 (m, 4H, CH_2Ph, *rac*/*meso*), 2.86 (sep, J = 7, 2H, *i*-Pr CH, *rac*/*meso*), 2.11−2.04 (m, 2H, CH_2, *rac*/*meso*), 2.01−1.94 (m, 2H, CH_2, *rac*/*meso*), 1.91−1.84 (m, 2H, CH_2, *rac*/*meso*), 1.244 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.238 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.20 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.17 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.04 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.03 (d, J = 7, 12H, *i*-Pr CH_3, *meso*). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 154.0 (broad, quat, Ar, *rac*), 153.9 (broad, quat, Ar, *rac*), 152.0 (quat, Ar, *rac*/*meso*), 132.3−132.2 (m, quat, Ar, *rac*/*meso*), 129.94−129.91 (m, CH, Ar, *rac*/*meso*), 128.4 (CH, Ar, *rac*/*meso*), 126.7 (CH, Ar, *rac*/*meso*), 123.0−122.9 (m, CH, Ar, *rac*/*meso*), 122.2 (quat, Ar, *rac*/*meso*), 41.3 (d, J = 60, P−CH_2Ph, *rac*/*meso*), 34.0 (*i*-Pr CH, *rac*/*meso*), 33.6 (dd, J = 67, 12, P-CH_2CH_2, *rac*/*meso*), 29.7 (*i*-Pr CH, *rac*/*meso*), 25.0 (*i*-Pr CH_3, *rac*/*meso*), 24.8 (*i*-Pr CH_3, *meso*), 24.7 (*i*-Pr CH_3, *rac*), 23.6−23.5 (*i*-Pr CH_3, *rac*/*meso*), 16.04−16.01 (m, PCH_2CH_2, *rac*/*meso*).

Is(PhCH$_2$)(O)P(CH$_2$)$_4$P(O)(CH$_2$Ph)Is (3d). Amounts: 34 mg (0.05 mmol) of **2d**; 21 mg (0.03 mmol) of **3d**, 39 mg (0.075 mmol, 2.5 equiv) of **6** in $CDCl_3$. HRMS (ES+): calcd for $C_{48}H_{69}O_2P_2$ (MH^+) m/z 739.4773, found m/z 739.4755. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 43.6 (*rac*), 43.4 (*meso*), ∼1.4/1 (*rac*/*meso*). ^1H NMR ($CDCl_3$): δ 7.26−7.16 (m, 10H, Ar, *rac*/*meso*), 7.08 (d, J = 4, 4H, Ar, *meso*), 7.06 (d, J = 4, 4H, Ar, *rac*), 3.86 (sep, J = 7, 4H, *i*-Pr CH, *rac*/*meso*), 3.47−3.30 (m, 4H, CH_2Ph, *rac*/*meso*), 2.90−2.82 (m, 2H, *i*-Pr CH, *rac*/*meso*), 1.87−1.81 (broad m, 4H, CH_2, *rac*/*meso*), 1.58−1.49 (m, 2H, CH_2, *rac*/*meso*), 1.48−1.40 (m, 2H, CH_2, *rac*/*meso*), 1.26 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.24 (d, J = 7, 12H, *i*-Pr CH_3, *rac*/*meso*), 1.22 (d, J = 7, 12H, *i*-Pr CH_3, *rac*), 1.09 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.07 (d, J = 7, 12H, *i*-Pr CH_3, *rac*). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 154.2 (d, J = 11, quat, Ar, *rac*/*meso*), 152.26−152.20 (m, quat, Ar, *rac*/*meso*), 132.8 (d, J = 6, quat, Ar, *rac*/*meso*), 130.15−130.09 (m, CH, Ar, *rac*/*meso*), 128.73−128.70 (apparent t, J = 3, CH, Ar, *rac*/*meso*), 127.00−126.96 (apparent t, J = 3, CH, Ar, *rac*/*meso*), 123.27 (d, J = 88, quat, Ar, *meso*), 123.21 (d, J = 11, CH, Ar, *meso*), 123.18 (d, J = 11, CH, Ar, *rac*), 123.12 (d, J = 88, quat, Ar, *rac*), 41.76 (d, J = 61, PCH_2Ph, *meso*), 41.73 (d, J = 61, P−CH_2Ph, *rac*), 34.3 (*i*-Pr CH, *rac*/*meso*), 32.50 (d, J = 69, P−CH_2, *meso*), 32.47 (d, J = 68, P−CH_2, *rac*), 30.10−30.01 (m, *i*-Pr CH, *rac*/*meso*), 25.36 (d, J = 13, P−CH_2CH_2, *rac*), 25.34 (*i*-Pr CH_3, *meso*), 25.33 (*i*-Pr CH_3, *rac*), 25.17 (*i*-Pr CH_3, *meso*), 25.12 (*i*-Pr CH_3, *rac*), 24.9 (d, J = 15, P−CH_2CH_2, *meso*), 23.9 (*i*-Pr CH_3, *rac*/*meso*).

Is(PhCH$_2$)(O)P(CH$_2$)$_5$P(O)(CH$_2$Ph)Is (3e). Amounts: 35 mg (0.05 mmol) of **2e**; 22 mg (0.03 mmol) of **3e**, 39 mg (0.075 mmol, 2.5 equiv) of **6** in C_6D_6. HRMS (ES+): calcd for $C_{49}H_{71}O_2P_2$ (MH^+) m/z 753.4929, found m/z 753.4912. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 44.6 (*rac*), 44.3 (*meso*), ∼1.3/1 (*rac*/*meso*). ^1H NMR (C_6D_6): δ 7.25−7.17 (m, 10H, Ar, *rac*/*meso*), 7.09 (d, J = 4, 4H, Ar, *meso*), 7.07 (d, J = 4, 4H, Ar, *rac*), 3.88 (sep, J = 7, 4H, *i*-Pr CH, *rac*/*meso*), 3.47−3.32 (m, 4H, CH_2Ph, *rac*/*meso*), 2.88 (sep, J = 7, 2H, *i*-Pr CH, *rac*/*meso*), 1.87−1.78 (broad m, 4H, CH_2, *rac*/*meso*), 1.58−1.42 (broad m, 2H, CH_2, *rac*/*meso*), 1.40−1.24 (broad m, 4H, CH_2, *rac*/*meso*), 1.27−1.23 (m, 24H, *i*-Pr CH_3, *rac*/*meso*), 1.10 (d, J = 7, 12H, *i*-Pr CH_3, *meso*), 1.08 (d, J = 7, 12H, *i*-Pr CH_3, *rac*). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 153.95 (d, J = 12, quat, Ar, *rac*), 153.92 (d, J = 11, quat, Ar, *meso*), 151.9 (apparent t, J = 2, quat, Ar, *rac*/*meso*), 132.5 (d, J = 8, Ar, *rac*/*meso*), 129.8 (apparent t, J = 6, CH, Ar, *rac*/*meso*), 128.43 (CH, Ar, *meso*), 128.42 (CH, Ar, *rac*), 126.7 (d, J = 3, Ar, *rac*/*meso*), 122.9 (d, J = 3, CH, Ar, *meso*), 122.8 (d, J = 3, CH, Ar, *rac*), 122.3 (d, J = 27, quat, Ar, *rac*/*meso*), 41.5 (d, J = 60, P−CH_2Ph, *rac*/*meso*), 34.05 (*i*-Pr CH, *meso*), 34.03 (*i*-Pr CH, *rac*), 32.6 (d, J = 14, CH_2, *rac*/*meso*), 32.1 (apparent t, J = 13, CH_2, *meso*), 32.0 (apparent t, J = 13, CH_2, *rac*), 29.74−29.67 (m, *i*-Pr CH, *rac*/*meso*), 25.08 (*i*-Pr CH_3, *meso*), 25.05 (*i*-Pr CH_3, *rac*), 24.8 (*i*-Pr CH_3, *rac*/*meso*), 23.6 (*i*-Pr CH_3, *rac*/*meso*), 21.71 (d, J = 15, CH_2, *rac*/*meso*), 21.69 (d, J = 14, CH_2, *rac*/*meso*).

Mes*HP(CH$_2$)$_2$PHMes* (5). A solution of Mes*Br (3.13 g, 9.6 mmol) in 20 mL of THF was cooled to −78 °C, and then *n*-BuLi (4.8 mL of a 2.0 M solution in cyclohexane, 9.6 mmol) was added dropwise via cannula over 2 h to give a yellow solution, which was added via cannula to a solution of $Cl_2P(CH_2)_2PCl_2$ (1.1 g, 4.8 mmol, 0.5 equiv) in 20 mL of THF, and this mixture was cooled to −78 °C. After 2 h at −78 °C, the $^{31}P\{^1H\}$ NMR spectrum of a sample of the reaction mixture ($CDCl_3$) showed that the reaction was incomplete, with signals assigned to Mes*ClP$(CH_2)_2$PClMes* (δ 80.0, 77.5), $Cl_2P(CH_2)_2PCl_2$ (δ 191.0), and Mes*ClP$(CH_2)_2PCl_2$ (δ 191.2 (d, J = 23), 75.9 (d, J = 23)), in a 6/1/3 ratio. Another 1 equiv (9.6 mmol) of *n*-BuLi/Mes*Br was added as above, and the mixture was stirred overnight, which improved the ratio to 8/1/1. The reaction mixture was then added to a solution of $LiAlH_4$ (368 mg, 9.7 mmol) in 20 mL of THF at −78 °C. The mixture was warmed to room temperature and then stirred overnight to give a gray slurry. Triethanolamine (1.3 mL, 9.7 mmol) was added via syringe to give a white solid and a clear solution.[23] Bubbling was observed. The mixture was stirred for 2 h, and then 10 mL of distilled H_2O was added dropwise over 1 h. H_2 evolution was observed. The clear solution was filtered and washed with 50 mL of ether. The solution was extracted with H_2O (3 × 75 mL); the organic layer was separated, dried over $MgSO_4$, and then filtered. The solvent was removed from the filtrate to give a white solid, whose $^{31}P\{^1H\}$ NMR spectrum in $CDCl_3$ revealed a 3/2 mixture of the desired product, Mes*HP$(CH_2)_2$PHMes* (**5**: δ −67.8, −68.2; 1/1 ratio) and Mes*HP$(CH_2)_2PH_2$ (δ −69.1 (d, J = 12), −127.4 (d, J = 12)).[24] This mixture was dissolved in warm isopropyl alcohol (50 mL). Cooling this solution to −15 °C overnight gave a white solid, which was one diastereomer of **5** ($^{31}P\{^1H\}$ NMR ($CDCl_3$) δ −68; 330 mg, 12% yield), which could be washed with Et_2O to remove impurities, which were observed in some cases by $^{31}P\{^1H\}$ NMR in $CDCl_3$ (δ 25.7, 25.4, 2.8). When the material was purified by filtration through silica, with 40/60 CH_2Cl_2/petroleum ether as eluent, **5** appeared to isomerize to yield a 1/1 mixture of diastereomers ($^{31}P\{^1H\}$ NMR ($CDCl_3$) δ −67.7, −68.3).

Anal. Calcd for $C_{38}H_{64}P_2$: C, 78.30; H, 11.07. Found: C, 78.07; H, 11.15. HRMS: calcd for $C_{38}H_{63}P_2$ $(M - H)^+$ m/z 581.4405, found m/z 581.4403. NMR data for one diastereomer are as follows. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −68.0. ^1H NMR ($CDCl_3$): δ 7.35 (4H, Ar), 4.8 (broad d, J_{PH} = 240, 2H, P−H), 1.53 (36H, *t*-Bu CH_3), 1.48 (m, 4H, CH_2), 1.30 (18H, *t*-Bu CH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 154.2 (quat, Ar), 149.0 (quat, Ar), 132.9 (m, quat Ar), 122.0

(23) Powell, J.; James, N.; Smith, S. J. *Synthesis* **1986**, 338–340.

(24) More of the mixed tertiary/primary phosphine Mes*HP$(CH_2)_2PH_2$ was formed than expected from the observed ratio of intermediate chlorophosphines. It is possible that P−C cleavage occurred during the $LiAlH_4$ reduction step. Such processes have been observed previously: Reiter, S. A.; Nogai, S. D.; Schmidbaur, H. *Z. Anorg. Allg. Chem.* **2005**, *631*, 2595–2600. Kyba, E. P.; Liu, S. T. *Inorg. Chem.* **1985**, *24*, 1613–1616.

(CH, Ar), 38.2 (quat, CMe_3), 34.9 (quat CMe_3), 33.5 (apparent t, $J = 7$, *o*-CMe_3), 31.3 (*p*-CMe_3), 25.5 (CH_2). IR (KBr): 2959, 2868, 2390 (P−H), 1594, 1361, 1261, 1100, 806, 661, 467 cm^{-1}.

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Supporting Information Available: Text, tables, and figures giving additional experimental details and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.