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Crafting chiral space. The synthesis of C_2-symmetric diphosphine ligands for an outer-sphere catalytic reaction[†]

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Summary — Because the mechanism of allylic alkylation involves the bond breaking or making events occurring outside the coordination sphere of palladium, an approach for asymmetric induction envisions chiral pockets to influence the events. A strategy to synthesize such chiral receptors is developed. A modular ligand design depends upon the employment of *trans*-1,2-diaminocyclohexane as a chiral scaffold which induces conformational chirality of an attached 2-(diarylphosphino)benzoic acid moiety. The synthesis of methyl[bis(3,5-dibromophenyl)phosphino]benzoate via a novel cross coupling reaction provides a convenient template for attachment of a variety of substituents, also using cross-coupling reactions.

chiral ligand / cross-coupling / phosphine

Résumé — Élaboration d'un espace chiral. Synthèse de ligands diphosphorés à symétrie C_2 pour une réaction catalytique à sphère externe. Étant donné que le mécanisme de l'alkylation allylique implique la coupure et la formation de liaisons à l'extérieur de la sphère de coordination du palladium, une des approches envisagées pour le contrôle de l'énantiosélectivité de cette réaction est la création d'une poche chirale. Une stratégie pour la synthèse de tels récepteurs chiraux est développée ici. La construction d'un ligand modulable est basée sur l'utilisation du *trans*-1,2-diaminocyclohexane comme squelette chiral, induisant la chiralité conformationnelle du groupe 2-(diarylphosphino)benzoyle qui lui est attaché. Le bis(3,5-dibromophényl)phosphinobenzoate de méthyle a été préparé par une nouvelle réaction de couplage croisé et représente un substrat approprié pour l'introduction d'une variété de substituants, via des réactions de couplage croisé.

ligand chiral / couplage / phosphine

Introduction

The development of enantioselective transition-metal catalyzed reactions is one of the major expanding fields [1] in organic chemistry. Some reactions like hydrogenation of certain olefins and ketones [1, 2], epoxidation [3], *cis*-dihydroxylation [4], hydrosilylation [5] of alkenes, and also cyclopropanation [6] give good to outstanding enantioselectivities and are rapidly being assimilated into the repertoire of organic synthesis. The reason for the success of all these examples lies in the design of the proper chiral ligands which are able to deliver high selectivities relatively independently of the nature of the substrate. A common feature in almost all these ligands is that they are bidentate and possess C_2-symmetry. As a result, a relatively rigid complex forms and, due to the symmetry, limits the number of possible reaction pathways.

A reaction which was rather resistant towards a general enantioselective approach was the palladium catalyzed allylic alkylation [7]. However, during the last few years, a number of different concepts have been examined to overcome the difficulties in an enantioselective allylic alkylation process. A brief comparison of the mechanisms of the allylation reaction and the asymmetric hydrogenation reveals some aspects of the nature of the problem (fig 1).

In the hydrogenation reaction, the hydrogen, which also serves as a ligand, transfers within the coordination sphere of the metal. In the alkylation reaction, the nucleophile attacks external to the metal and directly at an attached ligand, the η^3-allyl unit, ie, outside the coordination sphere of the metal. It is obvious that the chiral ligand in this case has much less ability to influence directly the event compared to the hydrogenation reaction. The nucleophile is insulated from any chiral environment by the allyl moiety.

This model clearly is very simplistic, nevertheless it shows that one has to look for different types of ligands for both reactions. A consequence of these considerations is that common C_2-symmetric bidentate ligands as Diop, Norphos and Chiraphos [1], which give good selectivities for the hydrogenation do not give good enantioselections in the allylation reaction. An approach to

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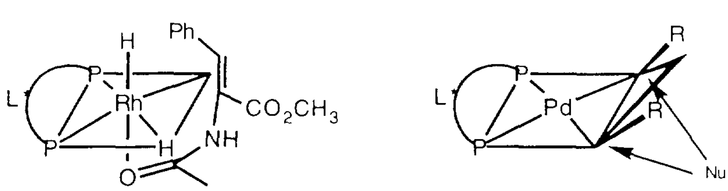
[†] Dedicated to Professor Henri Kagan with great admiration for his many scientific contributions, most notably for his pioneering studies in catalytic asymmetric induction with transition metal complexes.

[*] Correspondence and reprints



Enantioselective hydrogenation

Enantioselective allylic alkylation

Fig 1. Enantioselective hydrogenation vs allylic alkylation.

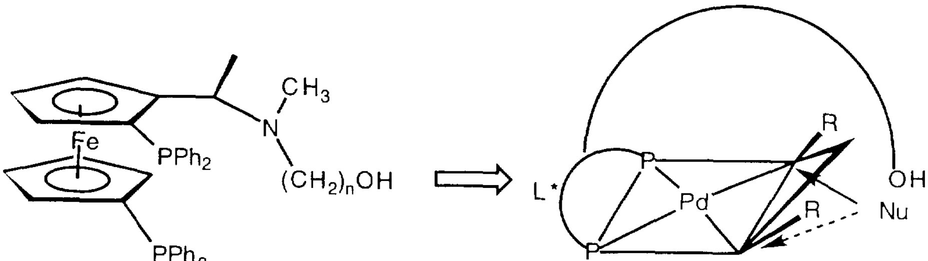


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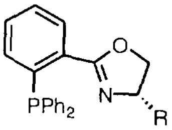
Fig 2. Ligand delivered nucleophile.

overcome this problem has been examined by Hayashi [7, 8] in his synthesis of a ferrocene based ligand **1** (fig 2) with a chiral side chain which is able to reach over the 'allyl barrier' and direct the attack of the nucleophile to preferentially only one carbon. An alternative approach envisioned electronic desymmetrization as in **2** [9] and **3** [10] which also involves a move away from C_2-symmetric compounds.



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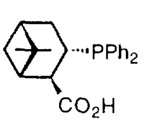

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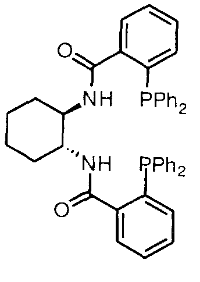
We have focused on a different design principle, chiral space, ie, a chiral environment by virtue of conformational chirality of the molecular environment constituting a chiral cleft or pocket into which the substrate resides [11]. Figure 3 depicts the projections of a η^3-cyclopentenylpalladium complex **5** derived from the chiral ligand **4**. So far, these modular ligands based upon 2-(diphenylphosphino)benzoic acid have given the broadest array of asymmetric induction in palladium catalyzed allylic alkylations. Figure 4 schematically raises questions regarding the impact of structural variations on the nature of the pocket.



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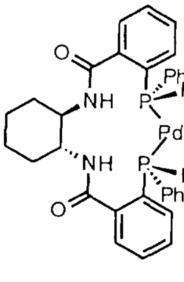


5

Envisioning the fact that the chiral space is largely defined by the triarylphosphine portion, variation of these aryl rings constitutes a high priority. Indeed, quite interesting insight into the role of the benzoic and aryl rings was gained in conjunction with the deracemization of a vinyl epoxide [12]. Initial molecular modeling studies suggest that the diarylphosphino fragments (diphenylphosphino in **4**) are situated quite close to the reactivity center. Earlier studies involving a Binapo (2,2′-[(diphenylphosphino)oxy]-1,1′-binaphthyl) ligand support this hypothesis [13]. Placing trimethylsilyl substituents in the 3,5 positions of the diphenylphosphino portion of Binapo had a significant effect on the enantioselectivity. Thus, we initiated a study to develop a synthetic protocol whereby our modular approach for ligand construction involving 2-(diarylphosphino)benzoic acids with various aryl groups are readily accessed.

Scheme 1 outlines the synthetic plan. We chose the 3,5-disubstituted positions since it should minimize interference with phosphorus–metal coordination and provide maximal interaction with the docked substrate (see fig 3). Other substitutions should be accessible by the same protocol. In order to explore the structure-function of these systems, introduction of the 3,5-substituents as late as possible becomes desirable. As a result, availability of **6** by cross-coupling chemistry from tetrabromo **7** is very attractive. Attaching the benzoic acid unit to **8** would allow variability of this linker at some later stage in our program. Mono-metal halo-

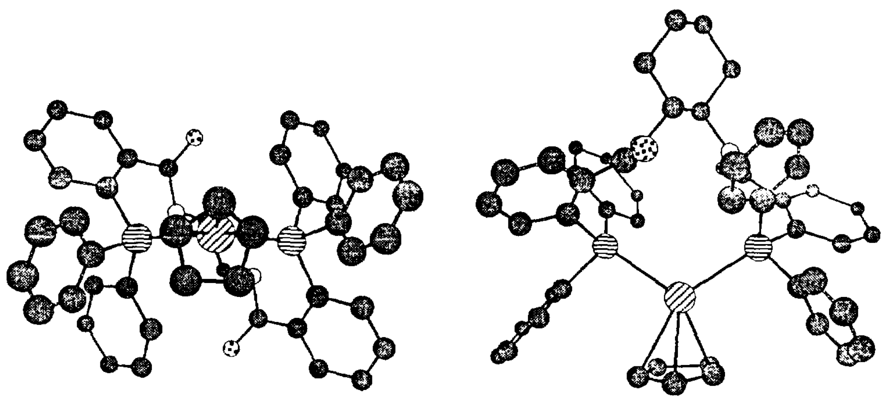


Fig 3. Projections of ligand-Pd-η^3-cyclopentenyl complex **5** (hydrogens deleted for clarity).

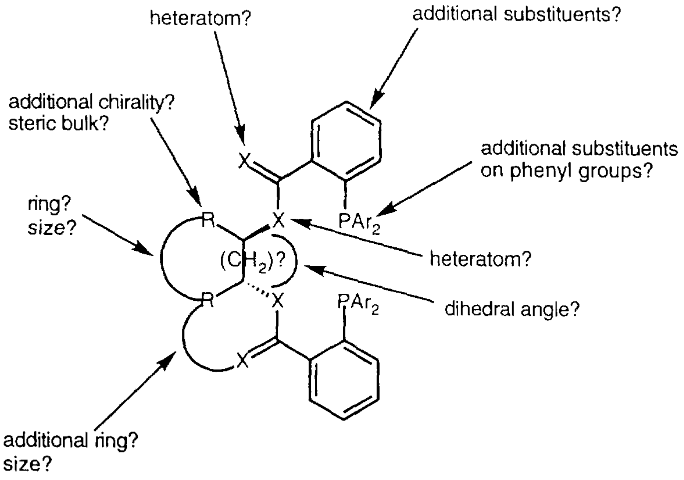
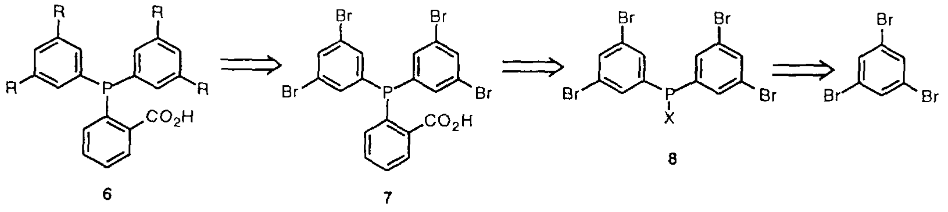


Fig 4. Parameters in modular ligand design.



Scheme 1. Retrosynthetic analysis of ligand precursor.

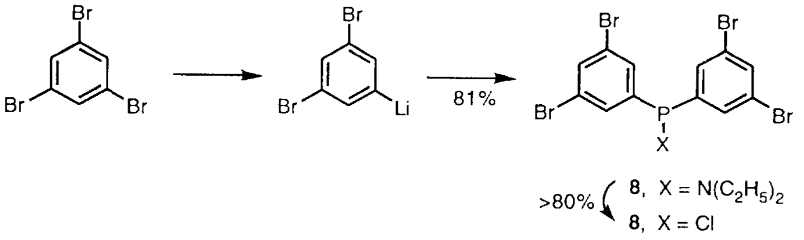
gen exchange from tribromobenzene [14] should provide access to **8**.

Initial studies

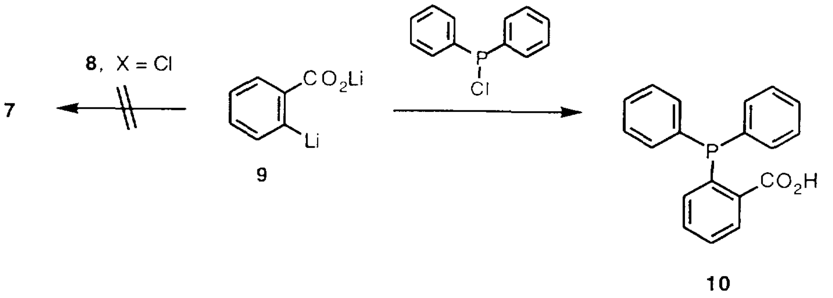
Equation 1 outlines the synthesis of **8**, X = Cl. In order to avoid uncontrolled substitution we decided to use (diethylamino)dichlorophosphine [15] rather than phosphorus trichloride.

Disproportionation of **8**, X = $N(C_2H_5)_2$, with phosphorus trichloride provides the desired chlorophosphine **8**, X = Cl [16]. Lithium 2- lithiobenzoate, **9** [17] generated at −120 °C, fails to combine with **8** to form the ligand precursor **7**. The viability of the concept is documented by the condensation of **9** with chlorodiphenylphosphine to form **10** in 50% unoptimized yield (eq 2).

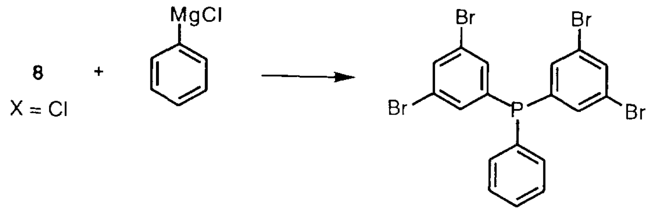
The presence of four aryl-bromide bonds and the facility of the metal halogen exchange may be the culprit in the failure of the desired coupling. Use of a less reactive metal may resolve the issue. Indeed, phenylmagnesium chloride does couple with **8**, X = Cl, as shown in equation 3. Unfortunately, attempts to transmetalate the lithium derivative **9** to magnesium and then couple still failed.



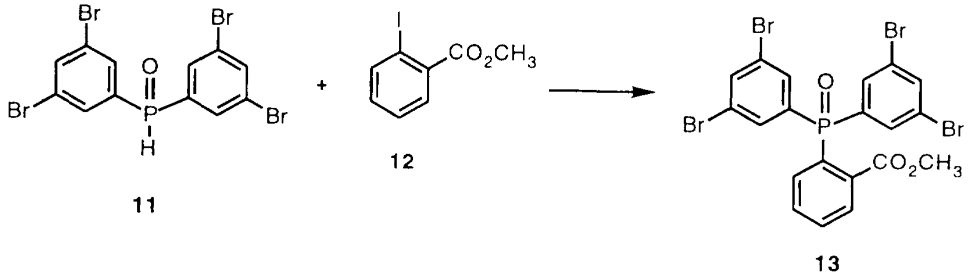
(1)



(2)



(3)



(4)

An alternative approach considers the possibility of a cross-coupling strategy as suggested in equation 4 [18]. The critical question posed by this strategy is the competition between self-coupling of **11** and the cross-coupling with **12** to form **13** considering the statistical superiority of quadruple bromines for the former reaction.

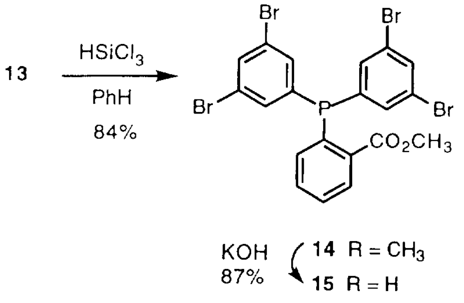
The *sec*-phosphine oxide **11** is available in 77% overall yield from **8**, X = $N(C_2H_5)_2$, first by conversion to the chloride, followed by simple hydrolysis or, more conveniently, by treatment with aqueous hydrochloric acid. A first experiment proved to be highly encouraging (table I, entry 1). Using *N*-methylmorpholine as base and palladium acetate and triphenylphosphine as catalyst, a 32% yield of the desired coupling product **13** is obtained. Increasing the ratio of iodide **12** to bromide **11** does not have a beneficial effect (entry 2). Increasing the polarity of the solvent decreases the effectiveness of the reaction (entries 3–5). Using ‘ligandless’ conditions (entry 6) or a bidentate ligand (entries 7 and 8) has little effect on the yield. Switching to a stibine ligand proves detrimental (entry 9). Changing the base has almost no (entry 10) to little (entry 11) effect. A more significant change occurs upon increasing the amount of catalyst (entries 12–14). The biggest increase arises by minimizing the concentration of *sec*-phosphine oxide **11** by slowly adding it to a mixture of iodide **12** and catalyst (entries 15–16). In this way, a 71% yield of the desired coupling product **13** is obtained.

The phosphine **14** is easily accessed by trichlorosilane reduction (eq 5) [19]. The acid **15** is also readily available by standard hydrolysis.

Table I. Cross-coupling variations[a].

Entry	*Ratio* **12**:**11**	*Pd (%)*	*Ligand*	*Solvent*	*Base*[b]	*Temperature (°C)*	*Yield (%)*
1	1:1	5	Ph_3P	$PhCH_3$	1 equiv NMM	reflux	32
2	3:1	5	Ph_3P	$PhCH_3$	3 equiv NMM	reflux	22
3	2:1	5	Ph_3P	THF	2 equiv NMM	reflux	NR
4	2:1	5	Ph_3P	CH_3CN	2 equiv NMM	reflux	NR
5	2:1	5	Ph_3P	DMF	2 equiv NMM	reflux	17
6	2:1	5	none	$PhCH_3$	2 equiv NMM	reflux	24
7	2:1	5	dppp	$PhCH_3$	2 equiv NMM	110	26
8	2:1	5	dppp	$PhCH_3$	2 equiv NMM	110	27
9	1.5:1	5	Ph_3Sb	$PhCH_3$	1.5 equiv NMM	110	14
10	1.5:1	5	Ph_3P	$PhCH_3$	1.5 equiv $(i\text{-}C_3H_7)_2NC_2H_5$	110	25
11[c]	1.1:1	5	Ph_3P	$PhCH_3$	propeneoxide	110	37
12	2:1	10	Ph_3P	$PhCH_3$	2 equiv NMM	110	46
13[d]	1.2:1	10	Ph_3P	$PhCH_3$	1.2 equiv NMM	110	>35
14[e]	1.2:1	15	Ph_3P	$PhCH_3$	1.2 equiv NMM	110	54
15[f]	1.2:1[h]	10	Ph_3P	$PhCH_3$	1.2 equiv NMM	110	71
16[g]	1.2:1[h]	15	Ph_3P	$PhCH_3$	1.2 equiv NMM	120	60

[a] All reactions run with a P/Pd ratio of ~ 4 using palladium acetate on a 0.3–0.5 mmol scale unless otherwise noted. [b] NMM = *N*-methylmorpholine. [c] Performed on 1.9 mmol scale. [d] Performed on 8.9 mmol scale. [e] Performed on 69.9 mmol scale. [f] Performed on 1.7 mmol scale. [g] Performed on 25.1 mmol scale. [h] Slow addition of **11**.



(5)

Substituent variation

The great facility of the cross-coupling of aryl-bromides with terminal alkynes [20, 21] led us to examine this process first. As shown in equation 6, standard cross-coupling protocols work with both phenylacetylene and (triphenylsilyl)acetylene to give the adducts **16** and **17** in 71% and 55% yields respectively. Base hydrolysis of **16** gives its acid **18** in 74% yield. On the other hand, similar hydrolysis of **17** produces not the acid **19** but its desilylated analogue **20**. To obviate this desilylation, the order of the two reactions was reversed. The tetrabrominated acid **15**, obtained by hydrolysis of the methyl ester, couples under the same conditions to give the desired acid **19** directly in 50% yield.

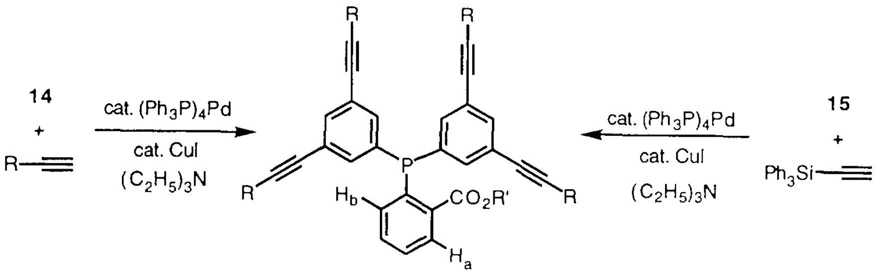
Coupling of **14** with phenylboronic acid (Suzuki coupling) [22, 23] to provide the tetraphenyl compound **21** proved to be more problematic (eq 7). Using benzene–water as solvent, coupling occurs sluggishly, stopping after the introduction of only two phenyl groups. Switching to DME improves the situation, but the reaction still falls short of completion. It is quite apparent that the reaction rate slows down as the per cent conversion increases. Assessing the problem as arising from the incorporation of an increasingly bulky phosphine in the coordination sphere of the palladium derived from the phenylated products, we examined the use of the phosphine oxide **13** rather than the phosphine **14** to ameliorate the 'automoderation' effect. Indeed, the Suzuki coupling of **13** proceeds in 68% yield to the tetraphenyl phosphine oxide **22**. Deoxygenation with trichlorosilane proceeds straightforwardly to the desired phosphine **21** which is also readily hydrolyzed to the acid **23**.

Derivatization of the lack of saturation of the alkynes also provides access to alternative analogues that modify the walls of the pocket. Converting a rigid rod into a flexible chain represents one interesting modification. Catalytic hydrogenation of the tetra-(phenylalkynyl) phosphine **16** is best followed by NMR spectroscopy to give the hexadecahydro adduct. Surprisingly, it is isolated as its phosphine oxide **24** in 56% yield. The source of the oxidation during or, more likely, after (upon work-up?) the reduction is not understood. Fortunately, trichlorosilane effects deoxygenation to the phosphine ester **25** which is readily hydrolyzed under standard conditions to the acid **26** (eq 8).

Coupling to a chiral scaffold

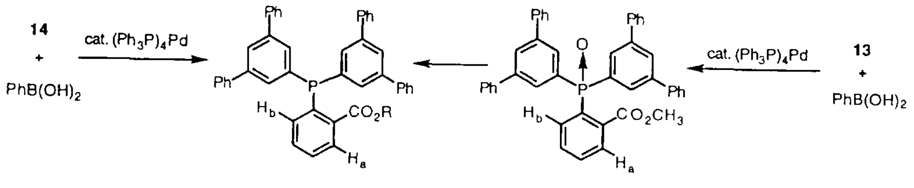
Completion of the sequence requires coupling these bulky phosphines to chiral scaffolds. We chose the *R,R*-1,2-diaminocyclohexane scaffold because of its availability and the widespread utility of **4** as preferred chiral ligand for many reactions. Our initial efforts take advantage of our earlier protocol using DCC (dicyclohexylcarbodiimide) according to equation 9. For the case of the tetrabromo derivative **15**, a 37% yield of the desired ligand **27** is obtained.

In the case of the tetra(phenylalkynyl)phosphine **18**, the same protocol gives a 51% yield. The modest yields in the DCC coupling method stem in part from the complications arising during work-up from the urea byproducts. As a result, alternative coupling procedures were examined. The difficulties with the (diarylphos-



(6)

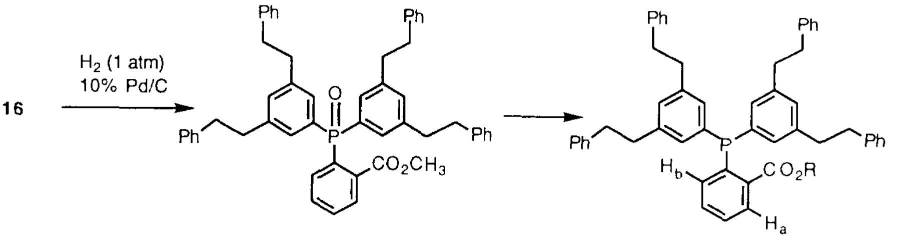
16 R = Ph, R' = CH_3
17 R = Ph_3Si, R' = CH_3
18 R = Ph, R' = H
19 R = Ph_3Si, R' = H
20 R = R' = H



(7)

21 R = CH_3
23 R = H

22



(8)

24

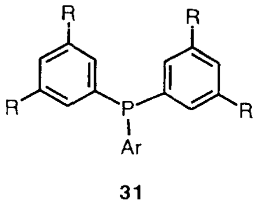
25 R = CH_3
26 R = H

phino)benzoic acids arise from the tendency of the activated acid to undergo an internal Friedel–Crafts acylation if the activation is too much. Diphenyl phosphorochloridate appears to be a good compromise and has the benefit that all the by-products of the coupling reagent are easily removed during the aqueous work-up. In this way, the yield of **28** increases to a more satisfactory 70%.

Initial attempts to couple the tetra(triphenylsilylalkynyl)phosphine **19** led to a mixture of products which were not pursued. On the other hand, the tetraphenyl analogue **23** couples well with this new protocol to give a 78% yield of **30**.

Discussion

The ability to utilize bis(3,5-dibromophenyl)phosphine oxide **11** as the nucleophilic partner in a palladium-catalyzed cross-coupling reaction with an external electrophile provides great flexibility for the synthesis of systematically varied phosphine ligands for transition metals of the style shown in **31**. It is a rather attractive core structure for a combinatorial approach to ligand construction. In the present case, it provides a powerful tool to craft the chiral pocket as depicted in figure 3 wherein the sides of the pocket can be extended by making R bigger than hydrogen. The phenyl substituents as in **30** tighten the pocket. On the other hand the phenyl-



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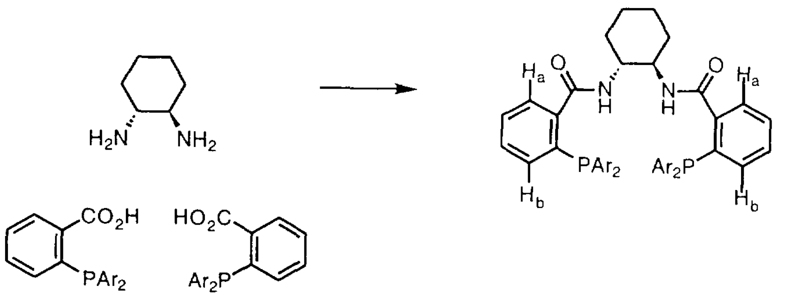
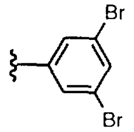
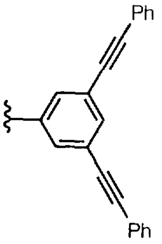


(9)

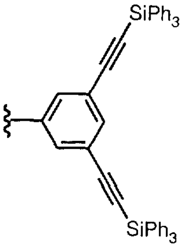
27 Ar =



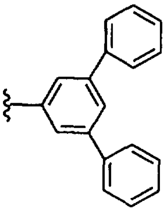
28 Ar =



29 Ar =



30 Ar =



alkynyl substituents as in **28** greatly extend the depth of the pocket without creating too much steric congestion. The bromines introduce polar substituents into a relatively non-polar environment. Obviously, many other modifications can be accessed in the same way.

The pockets being crafted are reaching a dimension that may make it appropriate to refer to them as receptors. For example, **30** has the formula $C_{92}H_{72}N_2O_2P_2$ which corresponds to a molecular weight of 1 300. Our largest receptor has the formula $C_{108}H_{72}N_2O_2P_2$ which corresponds to a molecular weight of 1 492. Thus, the methods reported herein provide a rather direct way to craft receptors of defined structure and shape with the aim of enhancing function.

The NMR spectra provide an interesting characterization of the phosphines and their related receptors. Table II summarizes some of the data. Among the phosphines, the most noteworthy ^1H shifts are those of the hydrogens *ortho* to the carboxyl (H_a) and *ortho* to the phosphine (H_b). There is remarkably little variation of the shifts for the protons *ortho* to the carboxyl function. On the other hand, a downfield shift of approximately 0.2 ppm occurs for H_b in the tetraphenyl phosphine **21**. This downfield shift correlates with the downfield shift in the ^{31}P spectrum compared to the other phosphines. Forming the chiral ligands causes a significant (~ 0.5 ppm) upfield shift of the protons *ortho* to the carbonyl group in every case (entries 1–3 and 5 versus entries 7–10). This shift suggests that the carbonyl group twists out-of-plane with respect to the adjacent aromatic ring in the ligands, thereby minimizing its conjugation. The poorer conjugation of the carbonyl group with the aromatic ring should be reflected in the coordinating ability of the phosphines, making them better donor ligands than they might be otherwise. There are no discernible trends in the ^{31}P shifts. The utility of these new phosphines as chiral receptors for molecular recognition in synthetic reactions will be the object of future work.

Table II. Selected NMR shifts.

Entry	*Compound*	^1H_a	^1H_b	^{31}P
1	**6**, R = H	8.16	6.96	–
2	**14**	8.15	6.91	−3.39
3	**16**	8.15	7.04	−4.18
4	**17**	8.16	6.97	−4.10
5	**21**	8.12	7.17	−1.90
6	**25**	8.05	6.85	–
7	**4**	7.57	6.91	−10.6
8	**27**	7.60	6.88	−6.2
9	**28**	7.56	6.96	−8.2
10	**30**	~7.58	7.16	−6.7

Experimental section

All reactions described in this experimental part were performed in a flame-dried flask or test tube with nitrogen as inert atmosphere. Solvents were distilled prior to use and transferred with syringe to the reaction vessel. ^1H and ^{13}C NMR spectra were recorded either on a Varian Gemini 200 or 300 or XL-400 spectrometer at the indicated frequencies. ^{31}P NMR spectra were recorded on a Varian XL-400 spectrometer at 161.92 MHz using 85% H_3PO_4 as an external standard. IR-spectra were recorded either neat or as a film on sodium chloride plates or as potassium bromide pellets. Combustion analyses were performed by M-H-W Laboratories, Phoenix, Arizona. Mass spectra were provided by the UC-SF-MS facility employing a Kratos MS-9 instrument with an ionization current of 98 mA and an ionizing voltage of 70 eV. For thin layer chromatography, Merck precoated glass plates were used and detection was carried out by either a UV-lamp, $KMnO_4$-solution, vanillin/sulfuric acid or ammonium molybdate/ceric sulfate in sulfuric acid. Flash chromatography employed E Merck silica gel, Kieselgel 60, 230–400 mesh.

bis(3,5-Dibromophenyl)diethylaminophosphine **8**

To a suspension of 80 g (254 mmol) of 1,3,5-tribromobenzene in 800 mL ether at −78 °C was added *n*-butyllithium (170 mL, 1.5 mol in hexanes, 254 mmol) over a period of 180 min followed by 18.2 mL (127 mmol) of dichloro(diethylamino)phosphine in 50 mL of ether during 5 min. The dark red solution was allowed to warm up to room temperature, filtered over celite and evaporated. The brown residue was dissolved in hexanes and filtered over silica gel to yield a slightly yellow solution. Evaporation yielded 58.8 g (80.9%) of **8** as slightly yellow crystals. An analytical sample, Mp 97 °C, was prepared by chromatography (hexanes) and drying in high vacuum.

IR (neat): 1 562, 1 540, 1 457, 1 387 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ 7.74 (dt, J = 0.6, 1.8 Hz, 2H), 7.41 (dd, J = 1.8, 6.1 Hz, 4H), 3.04 (dq, J = 10.1, 6.1 Hz, 4H), 0.98 (t, J = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.42 (d, J = 24.3 Hz), 134.49, 133.15 (d, J = 21.5 Hz), 123.64 (d, J = 5.5 Hz), 44.67 (d, J = 15.6 Hz), 14.70 (d, J = 3.0 Hz).

^{31}P NMR (161.92 MHz, $CDCl_3$): δ 60.57.

Anal calc for $C_{16}H_{16}Br_4NP$: C 33.54, H 2.81, N 2.44, P 5.41. Found: C 33.78, H 3.00, N 2.49, P 5.55.

bis(3,5-Dibromophenyl)phosphine oxide **11**

- *Method a*

bis(3,5-Dibromophenyl)diethylaminophosphine (55.0 g, 95.0 mmol) was dissolved in 120 mL of phosphorous trichloride and stirred at room temperature for 32 h. After distillation of the volatile reaction components, ice water (150 mL) was added and the solution extracted with dichloromethane. The organic layer was dried over magnesium sulfate and yielded upon evaporation in vacuo 42.0 g of white crystals (90% pure by NMR, 73.0 mmol, 77%). Chromatography (2:1 hexane/ethyl acetate) gave an analytical sample, Mp 186–187 °C.

- *Method b*

bis(3,5-Dibromophenyl)diethylaminophosphine (29.0 g, 50.6 mmol) was dissolved in 50 mL of chloroform and 60 mL of 1N aqueous hydrochloric acid were added. After stirring vigorously for 16 h, the organic layer was dried over $MgSO_4$ and evaporated. The residue was crystallized from 2:1 hexane/ethyl acetate to yield 15.5 g (58%) of **11**. Chromatography (2:1 hexane/ethyl acetate) of the mother liqueur provided another 4.6 g (18%) for a total yield of 76% of **11**.

IR (neat): 3 060, 1 551, 1 400, 1 366, 1 199, 1 134 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 500.8 Hz, 1H), 7.89 (m, 2H), 7.74 (dd, J = 1.7, 13.7 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.01 (d, J = 3.4 Hz), 134.60 (d, J = 97.4 Hz), 132.04 (d, J = 12.2 Hz), 124.53 (d, J = 17.5 Hz).

^{31}P NMR (161.92 MHz, $CDCl_3$): δ 14.27 (dquin, J = 500.6, 13.2 Hz).

Anal calc for $C_{12}H_7Br_4OP$: C 27.84, H 1.36, P 5.98. Found: C 27.68, H 1.17, P 5.81.

bis(3,5-Dibromophenyl)-2-(methoxycarbonyl)phenylphosphine oxide **13**

To a solution of 39 mg (0.17 mmol) of palladium acetate and 183 mg (0.70 mmol) of triphenylphosphine in 2 mL of toluene were added 287 μL (2.09 mmol) of methyl 2-iodobenzoate and 230 μL of 4-methylmorpholine. The reaction was heated to 110 °C (bath temperature) and 900 mg (1.74 mmol) of bis(3,5-dibromophenyl)phosphine oxide **11** were gradually added in portions of 50–100 mg over 90 min. The reaction became homogeneous shortly after the first addition and remained so for the rest of the reaction. After 10 min, TLC showed no remaining starting material. The solution was allowed to come to room temperature, methylene chloride was added and the solution washed with 1N aqueous hydrochloric acid and saturated aqueous sodium bicarbonate. After drying over $MgSO_4$ and evaporation, the residue was taken up in 1 mL of toluene and subjected to chromatography (4:1 to 2:1 hexane/ethyl acetate) which provided 800 mg (71%) of **13** as a white crystalline substance, Mp 200–202 °C.

IR (neat): 3 064, 1 729, 1 548, 1 397, 1 283, 1 203 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 1H), 7.85, (m, 2H), 7.69, (dd, J = 1.8, 12.1 Hz, 4H), 7.77–7.60 (m, 3H), 3.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.83, 137.84 (d, J = 3.4 Hz), 137.72 (d, J = 103.7 Hz), 135.22 (d, J = 9.1 Hz), 133.29, 132.99 (d, J = 9.8 Hz), 132.21 (d, J = 12.7 Hz), 131.52 (d, J = 8.9 Hz), 130.38 (d, J = 106.4 Hz), 123.92 (d, J = 16.6 Hz), 52.89.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ 27.35.

Anal calc for $C_{20}H_{13}Br_4O_3P$: C 36.86, H 2.01, P 4.75. Found: C 36.95, H 2.16, P 4.61.

Methyl 2-[bis(3,5-dibromophenyl)phosphino]benzoate **14**

To a solution of 24.0 g (36.8 mmol) of phosphine oxide **13** in 100 mL of benzene were added 8.54 mL (84.6 mmol) of trichlorosilane. After heating at reflux for 6 h, the reaction was stirred at room temperature for 16 h. Sodium hydroxide (150 mL, 40% in water) was added cautiously until two clear phases were obtained. The aqueous layer was extracted with three portions (3 × 100 mL) of toluene and the combined organic phases evaporated and subjected to silica gel chromatography (9:1 hexane/ethyl acetate) to give 19.7 g (84%) of **14** as white crystals. An analytical sample, Mp 107–109 °C, was obtained by recrystallization from 9:1 hexane/ethyl acetate.

IR (neat): 1 714, 1 561, 1 542, 1 391, 1 276, 1 109 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (m, 1H), 7.68 (t, J = 1.8 Hz, 2H), 7.51 (AB-system, 2H), 7.26 (dd, J = 1.8, 6.8 Hz, 4H), 6.91 (m, 1H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.01, 142.29 (d, J = 20.2 Hz), 137.66 (d, J = 25.7 Hz), 135.04, 135.01 (d, J = 22.2 Hz), 134.58, 134.09 (d, J = 18.9 Hz), 133.12, 131.45, 129.73, 123.87 (d, J = 7.3 Hz), 52.77.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −3.39.

Anal calc for $C_{20}H_{13}Br_4O_2P$: C 37.78, H 2.06, P 4.87. Found: C 38.05, H 1.84, P 4.61.

2-[bis(3,5-Dibromophenyl)phosphino]benzoic acid **15**

To a solution of 4.00 g (6.25 mmol) of the above ester **14** in 20 mL of THF were added 1.96 g (35 mmol) of potassium hydroxide in 20 mL of water. The reaction was heated at 75 °C (bath temperature) for 16 h. After cooling to room temperature, 1M aqueous sulfuric acid was added (pH 1). Extraction with dichloromethane, evaporation in vacuo, and flash chromatography (1:1 ethyl acetate/dichloromethane) yielded 3.39 g (86.7%) of **15** as a white foam. Crystallization from 9:1 hexane/ethyl acetate provided a crystalline sample, Mp 263–266 °C (decomp).

IR (KBr): 3 065, 2 618, 2 478, 1 696, 1 545, 1 397 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (ddd, J = 1.1, 4.1, 7.7 Hz, 1H), 7.84 (t, J = 2.0 Hz, 2H), 7.75 (tt, J = 1.5, 7.7 Hz, 1H), 7.60 (dd, J = 1.8, 12.4 Hz, 4H), 7.54 (tdd, J = 7.4, 1.2, 2.7 Hz, 1H), 7.10 (ddd, J = 0.9, 7.6, 15.5 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 167.70, 143.07 (d, J = 21.9 Hz), 136.96 (d, J = 26.8 Hz), 134.63, 134.42, 134.18, 133.78, 133.08, 131.04, 129.84, 123.28 (d, J = 7.7 Hz).

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −2.67.

Anal calc for $C_{19}H_{11}Br_4O_2P$: C 36.70, H 1.78, P 4.98. Found: C 36.86, H 1.62, P 5.12.

Methyl 2-{di[3,5-bis(phenylethynyl)phenyl]phosphino}-benzoate **16**

A solution of 1.50 g (2.34 mmol) of methyl ester **14**, 2.58 mL (23.4 mmol) of phenylacetylene, 135 mg (0.117 mmol) of $Pd(PPh_3)_4$ and 45 mg (0.234 mmol) of copper(I) iodide in 6.20 mL (46.8 mmol) of triethylamine was heated at reflux for 5 h. The reaction mixture was evaporated and chromatographed on silica gel (9:1 hexane/ethyl acetate) to yield 1.20 g (71%) of **16** as white crystals. An analytical sample, Mp 166–169 °C, was obtained by recrystallization from ether/hexanes.

IR (neat): 3 056, 1 715, 1 599, 1 579, 1 562, 1 490, 1 442, 1 274 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (m, 1H), 7.72 (t, J = 1.6 Hz, 2H), 7.50 (m, 10H), 7.41 (dd, J = 1.5, 7.5 Hz, 4H), 7.32 (m, 12H), 7.04 (m, 1H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.16, 138.74 (d, J = 27.8 Hz), 138.65 (d, J = 14.5 Hz), 136.45 (d, J = 21.5 Hz), 135.40, 134.95, 134.36 (d, J = 19.9 Hz), 132.82, 131.90, 131.31, 129.15, 128.77, 228.59, 124.31 (d, J = 8.3 Hz), 123.01, 90.85, 88.60, 52.55.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −4.18.

Anal calc for $C_{52}H_{33}O_2P$: C 86.65, H 4.61, P 4.30. Found: C 86.84, H 4.72, P 4.41.

Methyl 2-(di{3,5-bis[(triphenylsilyl)ethynyl]phenyl}-phosphino)benzoate **17**

A solution of 800 mg (1.26 mmol) of methyl ester **14**, 2.68 g (10.06 mmol) of (triphenylsilyl)acetylene, 73 mg (0.063 mmol) of $Pd(PPh_3)_4$ and 24 mg (0.126 mmol) of copper(I) iodide in 5.0 mL of triethylamine was heated at reflux for 48 h. Dichloromethane was added and the solution washed with 1N aqueous hydrochloric acid. After drying over $MgSO_4$ and evaporation, the product was subjected to chromatography (4:1 hexane/ethyl acetate) to yield 1.00 g (55%) of a crude product. A second chromatography yielded 710 mg of pure **17** (39%).

IR (KBr): 3 066, 3 050, 2 156, 1 715, 1 578, 1 429, 1 275 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (m, 1H), 7.82 (t, J = 1.5 Hz, 2H), 7.66 (m, 24H), 7.59 (m, 2H), 7.44 (dd, J = 1.5, 7.4 Hz, 4H), 7.37 (m, 36H), 6.97 (m, 1H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.34, 138.64 (d, J = 15.0 Hz), 137.75 (d, J = 21.8 Hz), 136.58, 135.83, 135.10, 133.35, 133.05, 131.36, 130.23, 129.31, 128.26, 123.83 (d, J = 8.3 Hz), 108.11, 91.25, 52.65.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −4.10.

Anal calc for $C_{100}H_{73}O_2PSi_4$: C 82.83, H 5.07, P 2.14. Found: C 83.00, H 5.14, P 2.30.

2-{bis[3,5-bis(Phenylethynyl)phenyl]phosphino}-benzoic acid **18**

To a solution of 1.00 g (1.39 mmol) of methyl ester **16** in 5 mL of THF was added a solution of 467 mg (8.32 mmol) of potassium hydroxide in 5 mL of water. The mixture was heated at 85 °C (bath temperature) for 16 h followed by heating for 120 min at 115 °C (bath temperature). Upon cooling to room temperature, it was brought to pH 2 using 1M aqueous hydrochloric acid and extracted with dichloromethane (2 × 10 mL). Evaporation gave 1.00 g of a yellow oil which yielded upon chromatography (2:1 to 1:1 hexane/ethyl acetate) 730 mg (74%) of **18** as white crystals. An analytical sample, Mp 260–265 °C (decomp), was obtained by recrystallization from 4:1 hexane/ethyl acetate.

IR (KBr): 3 060, 2 675, 2 580, 1 692, 1 598, 1 578, 1 561, 1 489, 1 442, 1 405, 1 298, 1 277 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.55 (bs, 1H), 8.24 (ddd, J = 1.7, 4.0, 7.5 Hz, 1H), 7.71 (t, J = 1.6 Hz, 2H), 7.49 (m, 8H), 7.42 (dd, J = 1.5, 7.5 Hz, 4H), 7.72 (m, 2H), 7.31 (m, 12H), 6.99 (ddd, J = 1.4, 4.0, 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.04, 139.49 (d, J = 26.1 Hz), 138.78 (d, J = 14.4 Hz), 136.54 (d, J = 21.6 Hz), 135.37, 134.71, 133.13, 132.25, 131.91, 129.12, 128.70, 128.56, 128.22 (d, J = 8.5 Hz), 123.05, 90.84, 88.70.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −3.64.

Anal calc for $C_{51}H_{31}O_2P$: C 86.67, H 4.42, P 4.38. Found: C 86.86, H 4.28, P 4.41.

2-(di{3,5-bis[(Triphenylsilyl)ethynyl]phenyl}-phosphino)benzoic acid **19**

A solution of 200 mg (0.322 mmol) of acid **15**, 732 mg (2.57 mmol) of triphenylsilylacetylene, 19 mg (0.016 mmol) of $Pd(PPh_3)_4$ and 6.2 mg (0.032 mmol) of copper(I) iodide in 2.0 mL of triethylamine was heated at reflux for 16 h. After cooling to room temperature, 10 mL of dichloromethane were added and the solution washed with 1N aqueous hydrochloric acid and brine. After drying over $MgSO_4$ and evaporation in vacuo the product was subjected to flash chromatography (4:1 to 1:1 hexane/ethyl acetate) to yield 231 mg (50%) of product **19**.

IR (KBr): 3 068, 3 032, 2 155, 1 668, 1 578, 1 428, 1 270 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (ddd, J = 1.4, 4.0, 7.8 Hz, 1H), 7.84 (t, J = 1.5 Hz, 2H), 7.64 (m, 25H), 7.57 (m, 2H), 7.52 (dt, J = 1.5, 7.5 Hz, 1H), 7.46 (dd, J = 1.5, 7.5 Hz, 2H), 7.40 (m, 36H), 7.00 (ddd, J = 1.2, 3.8, 7.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.92, 141.98, 139.38 (d, J = 27.7 Hz), 138.51 (d, J = 15.1 Hz), 137.83 (d, J = 22.0 Hz), 136.65, 136.24, 136.08, 135.82, 135.03, 133.73, 133.57, 133.35, 133.00 (d, J = 8.5 Hz), 132.42, 130.32, 129.37, 128.26, 127.44, 123.82 (d, J = 8.2 Hz), 108.09, 91.26.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −3.80.

bis(3,5-Diphenylphenyl)-2-(methoxycarbonyl)phenylphosphine oxide **22**

A mixture of 1.50 g (2.30 mmol) of methyl ester **13**, 2.81 g (23.0 mmol) of phenylboronic acid, 132 mg (0.114 mmol) of $(Ph_3P)_4Pd$ and 4.77 g (34.5 mmol) of potassium carbonate in 5 mL of benzene and 5 mL water was stirred vigorously and heated at reflux for 16 h. After cooling to room temperature, 15 mL of water were added and the aqueous phase was extracted with 3 portions of 10 mL of benzene. The combined organic layers were dried over $MgSO_4$, evaporated and subjected to flash chromatography (2:1 hexane/ethyl acetate to 1:1:1 hexane/ethyl acetate/dichloromethane). The resulting 1.20 g of slightly red oil were crystallized from hexane/ethyl acetate to give 0.97 g (66%) of **22** as white crystals, Mp 199–200 °C.

IR (KBr): 3 050, 3 035, 2 950, 2 925, 1 731, 1 592, 1 497, 1 414, 1 295 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (m, 7H), 7.75 (ddd, $J = 1.4, 7.6, 13.6$ Hz, 1H), 7.66 (tt, $J = 1.4, 7.6$ Hz, 1H), 7.62 (m, 8H), 7.58 (m, 1H), 7.44 (m, 8H), 7.37 (m, 4H), 3.53 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.92, 142.23 (d, $J = 12.9$ Hz), 140.25, 136.23 (d, $J = 6.3$ Hz), 135.09 (d, $J = 9.9$ Hz), 133.99, 132.40 (d, $J = 3.2$ Hz), 131.46 (d, $J = 11.7$ Hz), 130.86 (d, $J = 8.5$ Hz), 129.63 (d, $J = 3.6$ Hz), 129.43, 129.32, 129.16, 128.17, 127.53, 52.50.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −3.32.

Anal calc for $C_{44}H_{33}O_3P$: C 82.48, H 5.19, P 4.83. Found: C 82.28, H 5.33, P 4.77.

bis-(3,5-Diphenylphenyl)-2-(methoxycarbonyl)phenylphosphine **21**

To a suspension of 500 mg (0.780 mmol) of phosphine oxide **22** in 5 mL of benzene were added 790 μL of trichlorosilane. After heating the solution to reflux for 16 h, another 30 mL of benzene, and cautiously, 30 mL of 40% aqueous potassium hydroxide were added dropwise until the organic phase became clear. Drying over $MgSO_4$ was followed by evaporation in vacuo and flash chromatography (4:1 hexane/ethyl acetate) which gave 468 mg (96%) of **21** as a white foam. An analytical sample, Mp 118–125 °C, was crystallized from ethanol.

IR (neat): 3 059, 3 033, 1 717, 1 590, 1 568, 1 497, 1 407, 1 291, 1 273, 1 257 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, 1H), 7.82 (t, $J = 1.7$ Hz, 2H), 7.62 (dd, $J = 1.7, 7.8$ Hz, 4H), 7.57 (m, 8H), 7.44 (m, 10H), 7.34 (m, 4H), 7.17 (m, 1H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.60, 142.06 (d, $J = 7.1$ Hz), 141.35, 140.00 (d, $J = 23.9$ Hz), 139.09 (d, $J = 11.9$ Hz), 134.73, 134.55, 13.50, 131.84 (d, $J = 20.9$ Hz), 131.02, 129.05, 128.81, 127.76, 127.50, 127.03, 52.44.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −1.90.

Anal calc for $C_{44}H_{33}O_2P$: C 84.60, H 5.32, P 4.96. Found: C 84.39, H 5.42, P 4.75.

2-[bis(3,5-Diphenylphenyl)phosphino]benzoic acid **23**

A solution of 650 mg (1.04 mmol) of methyl ester **21** in 8 mL of THF and 2.0 mL of 40% aqueous potassium hydroxide was heated to reflux for 16 h. After cooling, acidification with 1N aqueous hydrochloric acid to pH 1, extraction with dichloromethane, and drying over $MgSO_4$, flash chromatography (2:1 hexane/ethyl acetate) gave 610 mg (96%) of a white foam, Mp 119–123 °C.

IR (neat): 3 032, 1 689, 1 497, 1 407, 1 270, 908, 756, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (m, 1H), 7.80 (t, $J = 1.8$ Hz, 2H), 7.64 (dd, $J = 1.7, 8.2$ Hz, 4H), 7.57 (m, 8H), 7.46 (m, 2H), 7.40 (m, 8H), 7.33 (m, 4H), 7.23 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.97, 142.13 (d, $J = 7$ Hz), 140.99, 134.63, 133.23, 132.04, 132.00 (d, $J = 11$ Hz), 129.05, 127.77, 127.53, 127.27.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −1.82.

Anal calc for $C_{43}H_{31}O_2P$: C 84.50, H 5.12, P 5.07. Found: C 84.51, H 5.35, P 4.89.

Di-[3,5-bis(2-phenylethyl)phenyl]-2-(methoxycarbonyl)-phenylphosphine oxide **24**

A solution of 300 mg (0.416 mmol) of alkyne **16** in a mixture of 1 mL of THF, 1 mL of ethanol and 50 μL of water was hydrogenated employing 30 mg of 10% Pd–C with 1 atm of hydrogen (balloon). The progress of the reaction was followed by NMR spectroscopy (disappearance of all olefinic protons) and it was complete after 180 h. The solution was filtered over a plug of celite, evaporated and flash chromatographed (1:1 hexane/ethyl acetate) to give 176 mg (56%) of **24** as a colorless oil.

IR (KBr): 3 026, 2 925, 2 857, 1 733, 1 600, 1 496, 1 454, 1 428, 1 296, 1 256, 1 193, 1 127, 1 069, 749, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (ddd, $J = 1.3, 3.8, 7.7$ Hz, 1H), 7.63 (tt, $J = 1.5, 7.6$ Hz, 1H), 7.49 (ddt, $J = 1.4, 2.1, 7.6$ Hz, 1H), 7.30 (dd, $J = 1.7, 12.5$ Hz, 4H), 7.28 (m, 1H), 7.26 (d, $J = 1.6$ Hz, 2H), 7.24 (m, 6H), 7.16 (m, 4H), 7.09 (m, 10H), 3.44 (s, 3H), 2.87 (m, 16H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.81, 141.82 (d, $J = 13$ Hz), 141.17, 134.63 (d, $J = 11$ Hz), 133.62, 132.56, 132.28, 131.65, 130.78 (d, $J = 11$ Hz), 130.44 (d, $J = 9$ Hz), 129.22 (d, $J = 10$ Hz), 128.43, 128.31, 125.97, 52.00, 37.60.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ 31.80.

HRMS: calc for $C_{52}H_{49}O_3P$: 752.3419. Found: 752.3405.

Methyl 2-{bis[3,5-bis(phenylethyl)phenyl]phosphino}-benzoate **25**

A solution of 70 mg (0.093 mmol) of phosphine oxide **24** in 5 mL of benzene was treated with 200 μL of trichlorosilane. After heating to reflux for 8 h, the solution was allowed to come to room temperature and 40% aqueous potassium hydroxide was added until a clear organic layer was formed. After drying over $MgSO_4$, evaporation gave 60 mg (87%) of **22** as a colorless oil.

IR (KBr): 3 026, 2 925, 1 721, 1 595, 1 583, 1 495, 1 453, 1 290, 1 271, 1 253 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 1H), 7.40 (m, 2H), 7.22 (m, 8H), 7.16 (m, 4H), 7.10 (m, 8H), 6.94 (dd, $J = 1.7, 7.9$ Hz, 4H), 6.91 (bs, 2H), 6.85 (m, 1H), 3.71 (s, 3H), 2.82 (bs, 16H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.60, 151.24, 141.93, 137.90 (d, $J = 10.3$ Hz), 134.56, 132.06, 131.94, 131.73, 130.79, 129.61, 128.68, 128.50, 128.23, 126.11, 52.14, 38.00, 37.92.

HRMS: calc for $C_{51}H_{46}O_2P$ ($M^+ - CH_3$): 721.3235. Found: 721.3235.

(R,R)-1,2-Di-{2-[bis(3,5-dibromophenyl)phosphino]-benzamido}cyclohexane ***27***

To a solution of 128 mg (1.12 mmol) of (*R*,*R*)-1,2-diaminocyclohexane, 1.40 g (2.23 mmol) of 2-[bis(3,5-dibromophenyl)phosphino]benzoic acid (**15**) and 14 mg (0.11 mmol) of DMAP in 10 mL of dichloromethane were added 485 mg (2.35 mmol) of DCC. After stirring for 16 h at room temperature, the suspension was filtered over celite, evaporated and subjected to flash chromatography (9:1 to 2:1 hexane/ethyl acetate) to give 800 mg of a slightly impure product. Crystallization from 9:1 hexane/ethyl acetate gave 550 mg (37%) of **27** as white crystals, Mp 226–229 °C.

$[\alpha]_D^{20}$ +50.8 (c = 0.82, CH_2Cl_2).

IR (neat): 3 326, 3 060, 2 935, 2 857, 1 635, 1 541, 1 390, 1 327, 1 115, 1 101, 908, 856, 737, 674 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (t, J = 1.7 Hz, 2H), 7.63 (t, J = 1.7 Hz, 2H), 7.60 (ddd, J = 1.8, 4.2, 7.6 Hz, 2H) 7.40 (dt, J = 1.7, 7.6 Hz), 7.34 (dt, J = 1.5, 7.5 Hz, 2H), 7.20 (dd, J = 1.7, 6.7 Hz, 2H), 7.09 (dd, J = 1.7, 6.6 Hz, 2H), 6.70 (bd, 2H), 3.96 (bs, 2H), 1.95 (bd, 2H), 1.79 (bs, 2H), 1.32 (bs, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.65, 142.72 (d, J = 20.2 Hz), 142.61 (d, J = 21.7 Hz), 139.36 (d, J = 21.7 Hz), 135.42, 135.02, 134.89, 134.82, 134.76, 134.56, 131.56, 130.03, 127.61, 123.80 (d, J = 8 Hz), 123.73 (d, J = 8 Hz), 54.23, 32.47, 25.01.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −6.20.

Anal calc for $C_{44}H_{32}Br_8N_2O_2P_2$: C 39.93, H 2.44, N 2.12, P 4.69. Found: C 40.19, H 2.26, N 2.13, P 4.46.

(R,R)-1,2-Di(2-{[3,5-bis(phenylethynyl)phenyl]-phosphino}benzamido)cyclohexane ***28***

- *Method a, DCC coupling*

To a solution of 45 mg (0.396 mmol) of (*R*,*R*)-1,2-diaminocyclohexane, 600 mg (0.849 mmol) of 2-{di[3,5-bis(phenylethynyl)phenyl]phosphino}benzoic acid **18** and 10 mg of DMAP in 10 mL of dichloromethane were added 172 mg (0.832 mmol) of DCC. After stirring for 16 h at room temperature, the suspension was filtered over celite, evaporated and subjected to flash chromatography (5:1 hexane/ethyl acetate) to give 300 mg (51%) of **28** as a white solid, Mp 186–187 °C (decomp).

- *Method b, Diphenyl phosphorochloridate coupling*

To a solution of 545 mg (0.773 mmol) of benzoic acid **18** in 3 mL of dichloromethane at 0 °C were added 170 μL of triethylamine and 177 μL (0.85 mmol) of diphenyl phosphorochloridate. After stirring for 60 min at room temperature, the solution was cooled to 0 °C again and treated with 42.5 mg (0.371 mmol) of (*R*,*R*)-1,2- diaminocyclohexane and 170 μL of triethylamine in 1 mL of dichloromethane. The reaction was allowed to stir at room temperature for 16 h and was then washed with 1N aqueous hydrochloric acid and saturated aqueous sodium bicarbonate. After drying over $MgSO_4$ and evaporation, the residue was subjected to flash chromatography (4:1 to 2:1 hexane/ethyl acetate) to yield 390 mg (70%) of **28** as a white foam.

$[\alpha]_D^{20}$ +70.6 (c 1.34, CH_2Cl_2).

IR (KBr): 3 320, 3 055, 2 930, 1 654, 1 578, 1 516, 1 442 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (t, J = 1.5 Hz, 2H), 7.68 (t, J = 1.5 Hz, 2H), 7.56 (ddd, J = 1.4, 4.1, 7.8 Hz, 2H), 7.52–7.45 (m, 16H), 7.36–7.29 (m, 34H), 7.21 (dt, J = 1.4, 7.6 Hz, 2H), 6.96 (ddd, J = 1.2, 4.0, 7.8 Hz, 2H), 6.42 (bd, 2H), 4.01 (bs, 2H), 2.00 (bd, 2H), 1.76 (bs, 2H), 1.28 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.08, 139.13 (d, J = 14.6 Hz), 138.91 (d, J = 14.7 Hz), 136.38 (d, J = 21.2 Hz), 136.29 (d, J = 21.0 Hz), 135.55, 135.21 (d, J = 8.8 Hz), 135.03, 133.37, 131.92, 131.25, 129.87, 129.04, 128.74, 128.67, 128.61, 127.49, 124.23 (d, J = 7.5 Hz), 123.08, 90.83, 88.79, 88.68, 54.20, 32.50, 25.07.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −8.21.

Anal calc for $C_{108}H_{72}N_2O_2P_2$: C 86.96, H 4.86, N 1.88, P 4.15. Found: C 87.01, H 4.66, N 1.82, P 4.33.

(R,R)-1,2-Di{2-[bis(3,5-diphenylphenyl)phosphino]-benzamido}cyclohexane ***30***

To a suspension of 520 mg (0.851 mmol) of 2-[bis(3,5-diphenylphenyl)phosphino]benzoic acid **23** in 4 mL of dichloromethane at 0 °C were added 195 μL (0.936 mmol) of diphenyl phosphorochloridate and 170 μL of triethylamine. After stirring for 30 min at room temperature, the reaction was cooled to 0 °C again and 46.6 mg (0.408 mmol) of (*R*,*R*)-1,2-diaminocyclohexane and another 170 μL of triethylamine in 1 mL of dichloromethane were added. Stirring for 16 h at room temperature was followed by washing with 1N aqueous hydrochloric acid, saturated aqueous sodium bicarbonate and brine. The solution was dried over $MgSO_4$, evaporated and subjected to flash chromatography (4:1 to 2:1 hexane/ethyl acetate) to yield 420 mg (78%) as a white foam. The sample was dissolved in 1 mL of dichloromethane and precipitated by addition of hexanes to give a solid, Mp 168–173 °C.

$[\alpha]_D^{20}$ +67.8 (c 1.41, $CDCl_3$).

IR (neat): 3 396, 3 330, 3 058, 3 032, 2 933, 2 857, 2 246, 1 647, 1 638, 1 588, 1 567, 1 526, 1 407 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (t, J = 1.8 Hz, 2H), 7.79 (t, J = 1.7 Hz, 2H), 7.62 (m, 1H), 7.59 (dd, J = 1.7, 7.8 Hz, 4H), 7.58 (dd, J = 1.2, 7.7 Hz, 4H), 7.55 (m, 17H), 7.42–7.28 (m, 27H), 7.19 (m, 1H), 7.08 (dt, J = 1.6, 7.4 Hz, 1H), 6.49 (bd, 2H), 3.90 (m, 2H), 1.83 (bd, 2H), 1.58 (bd, 2H), 1.15 (m, 2H), 1.08 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.47, 142.04, 141.96, 141.88, 140.98, 140.62 (d, J = 23 Hz), 139.25 (d, J = 16 Hz), 139.20 (d, J = 16 Hz), 136.71 (d, J = 22 Hz), 134.51, 131.95 (d, J = 21 Hz), 131.82 (d, J = 21 Hz), 130.64, 129.32, 129.00, 127.71, 127.44, 126.84 (d, J = 15 Hz), 54.10, 32.22, 24.87, 14.43.

^{31}P NMR (161.92 MHz, $CDCl_3$): δ −6.68.

Anal calc for $C_{92}H_{72}N_2O_2P_2$: C 85.03, H 5.85, N 2.16, P 4.77. Found: C 84.87, H 5.75, N 2.12, P 4.90.

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