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Synthesis of *o*-Diorganylphosphino-substituted Benzoic Acids and Their Derivatives

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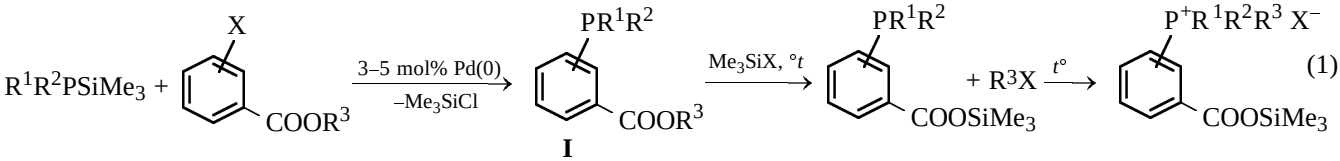
Abstract — *o*-Substituted dialkyl- and alkylphenylphosphinobenzoic acids, as well as their esters, nitriles, and amides, including those containing three different substituents on the phosphorus atom, were prepared for the first time by two different synthetic procedures. The most general procedure involves metal–halogen exchange in bromo- and iodoarenes, followed by phosphorylation of the resulting lithium derivatives.

Reactions catalyzed by metal complexes have recently taken on great significance [1, 2]. In this connection the search for new organophosphorus ligands, especially those containing hydrophilic substituents that render complexes on their basis water-soluble, has become urgent. Water-soluble phosphine ligands, including P- and C-chiral, are attracting growing researcher's attention [3–6].

The aim of this work was to develop methods for synthesis of phosphines of the general formula 2-(R^1R^1P)-C_6H_4Y **I** (R = *s*- and *t*-Alk, Ar; Y = COOH, COOR, CN, $CONR_2$), that is derivatives of *o*-phosphino-substituted benzoic acids, potentially chiral and water-soluble.

Historically, the first method of synthesis of tertiary aromatic phosphines containing functional groups sensitive to organometalllic reagents and, therefore, excluding the application of organolithium and organomagnesium reagents, is the Stille reaction [7]. It involves cross coupling of (trimethylsilyl)diphenylphosphine with functionally-substituted aryl halides, catalyzed by Pd(0) complexes. This reaction was successfully extended to secondary functionalyzed alkylarylphosphines [8] and vinylphosphines [9]. Later on the same cross-coupling reaction was performed with phenyl- and diphenylphosphines (or their complexes with BH_3) instead of silylphosphines [10–14], which allowed iodine-substituted arylcarboxylic and arylsulfonic acids and phenols to be included in the range of electrophilic reagents [15–17]. Just recently the first short communication concerning the synthesis of tertiary diphenylarylphosphines with the acetyl and methoxycarbonyl groups in the aryl substituent by the cross coupling of diphenylphosphine with iodoarenes, catalyzed by copper iodide, appeared [18].

In [19], we found that the conditions of the synthesis by the Stille reaction of tertiary phosphines **I** with Y = COOR, even with one secondary or tertiary alkyl radical on phosphorus, become, in view of the steric hindrances, so rigid that the major cross-coupling products in this case are not phosphines **I** but teriary phosphonium salts formed by the side reactions presented in scheme (1).



(1)

R^1 = *i*-Pr, *t*-Bu; R^2 = Ph; R^3 = Me, Et; X = Br, I.

These results prompted us to investigate the cross coupling of dialkyl- or alkylarylphosphines with bromo- and iodobenzoic acids, as well as their derivatives (esters, amides, nitriles), under the conditions described in [15, 16]. The greatest interest presented the synthesis of hardly available *o*-phosphino-substituted benzoic acids that, like our chosen secondary phosphines, were not studied in the cited works.

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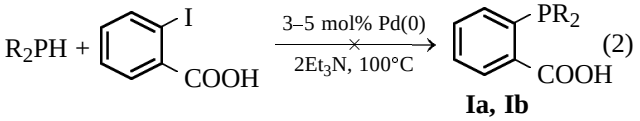
First of all we have studied as a model the cross coupling of diphenylphosphine with *o*-iodobenzoic acid and found that this reaction, unlike the previously reported reaction of *m*-bromobenzoic acid, yielding corresponding phosphine **I** [17], gave no phosphine **Ia**.



(2)

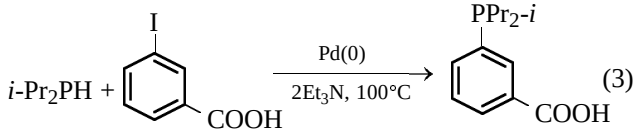
Ia, Ib

I, R = Ph (**a**), *i*-Pr (**b**).

As judged from the ^{31}P NMR spectra, after 12 h of heating of the reaction mixture in a sealed ampule diphenylphosphine is consumed completely, but, instead of phosphine **Ia**, a mixture of phosphino-substituted compounds is formed. The mixture contains one major product (δ_P 14.4 ppm) and four compounds (δ_P 27–32 ppm) that, by tabulated δ_P values [20], are suggested to involve a $Ph_2P(O)$ group. No of these signals is attributable to phosphine **Ia**, since the δ_P values of triarylphosphines (for Ph_3P, δ_P –6 ppm) substituted in the *o*-position span the range –5 to –20 ppm [17]. Actually, phosphine **Ia** prepared by another procedure had δ_P –4.05 ppm. Probably, under the conditions of reaction (2), oxidation of trivalent phosphorus compounds takes place, and the source of oxygen is the carboxy group that is oxidized in fairly rigid conditions. Analogous processes, especially facile with aldehydes and ketones, are well known in the chemistry of organophosphorus compounds [21].

Reaction (2) with diisopropylphosphine, a more nucleophilic but stronger sterically congested reagent, occurs much slower: After 25 h at 100°C more than one third of the phosphine remains unreacted. In other aspects, the reaction pattern is similar to that described above for diphenylphosphine, viz. the reaction gives no phosphine **Ib** and provides a mixture of a compound with δ_P 27 ppm and four compounds with δ_P 54–57 ppm, that contain, according to tabulated data [20], an *i*-$Pr_2P(O)$ fragment.

At the same time, the reaction of diisopropylphosphine with *m*-iodobenzoic acid is complete within 10–12 h at 100°C to form phosphine **Ic** (δ_P 11.5 ppm) in a nearly quantitative yield.

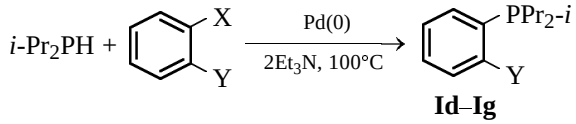


(3)

Ic

The thermal stability data for phosphine **Ic** suggest that phosphines **Ia** and **Ib** are most probably not primary products of reaction (2), and the whole set of compounds that appear in the downfield region of the ^{31}P NMR spectra results from intricate reactions of secondary phosphines with the carboxy group of *o*-iodobenzoic acid. Nevertheless, it should be mentioned that the successful synthesis of phosphine **Ic** by reaction (3) is the first example of cross coupling of dialkylphosphines with halobenzoic acids, that opens the way to dialkylphosphino-substituted benzoic acids. The enhanced steric hindrances on replacement of diisipropylphospihe by *tert*-butyl(isopropyl)-phosphine revealed themselves in that cross coupling with *m*-iodobenzoic acid failed to occur even on heating at 100°C for 20 h. At the same time, the ^{31}P NMR spectrum of the reaction mixture contained no new signals but that of the starting phosphine. These data provide further evidence to show that cross coupling is sensitive to the steric structure of both reagents.

With derivatives of *o*-bromo- and *o*-iodobenzoic acids, the situation in the cross-coupling reactions was each time different but predictable and controlled primarily by the steric properties of the phosphine and the electrophilicity of the *o*-halobenzoic acid derivative [reaction (4)].



(4)

Id–**Ig**

I, Y = $CONMe_2$ (**d**), $COOCH_3$ (**e**), $COOSiMe_3$ (**f**), CN (**g**); X = = I, Br.

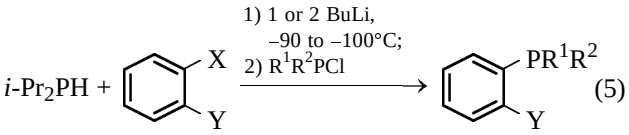
With the least electrophilic *N*,*N*-dimethyl-*o*-iodobenzamide, reaction (4) did not take place even for 20 h at 100°C. Even after 50 h at that temperature, in the ^{31}P NMR spectrum of the reaction mixture we could detect ca. 15% of phosphine **Id** (δ_P –0.28 ppm). The major reaction products were tetraisopropyldiphosphine (50%, δ_P –13 ppm) [22] and compounds with δ_P 56 and 62 ppm, that is those containing *i*-$Pr_2P(O)$ and *i*-$Pr_2P(O)O$ groups (the analog of phosphine **Id** with Y = $CONEt_2$ we prepared in high yield by another procedure). The more electrophilic *o*-halobenzoic acid esters slightly faster react with diisopropylphosphine. Hence, after 12 h at 100°C, ca. 20% of phosphine **Ie** (δ_P 3.5 ppm) and ca. 10% of phosphine **If** (δ_P 2.9 ppm) were detected. Note that in the first case we used methyl *o*-bromobenzoate and in the second case, trimethylsilyl *o*-iodobenzoate. After 30 h at 100°C, the mixture contained ca. 40% of phosphine **Ie**, but longer heating at 100°C (higher temperatures are still less favorable) caused decomposition of phosphine **Ie** and formation of several

compounds with δ_P 40–60 ppm. These findings suggest that the *o*-alkoxycarbonyl group, like *o*-carboxyl, effects oxidation of P(III), though to a lesser extent. As a result, phosphines **Ie** and **If** containing an ester group can be synthesized in 30–40% yields by reaction (4).

Finally, *o*-bromobenzonitile reacts with diisopropylphosphine faster than *o*-halobenzoic acid esters. Therewith, the synthesis of phosphine **Ig** is not complicated by side processes (which is most probably associated with the absence of the oxygen atom in the C≡N group), and the content of the target product in the reaction mixture after 45-h heating at 100°C was 82%. Phosphine **Ig** is thermally stable and was isolated in high yield by vacuum distillation.

Sterically more hindered phosphines, such as *tert*-butyl(isopropyl)- and *tert*-butyl(phenyl)phosphines, fail to react even with *o*-bromobenzonitrile. Hence, cross coupling with the first phosphine did not begin even after heating at 100°C for 25 h. In the ^{31}P NMR spectrum, the signal of the starting phosphine remained unchanged. With the second phosphine, several unidentified organophosphorus compouns were formed, but the target product, that is phosphine **I**, was absent.

Analysis of the resulting data on the cross coupling of secondary phosphines with *o*-halo-substituted benzoic acids and their derivatives allows us to conclude that reactions (2) and (4) are of low preparative significance for a broad range of phosphines sterically more hindered than diisopropylphosphine. This result prompted us to focus on another synthetic route to 2-phosphino-substituted benzoic acids and their derivatives, based on the reaction of *o*-lithiated derivatives of the latter with chlorophosphines.



(5)

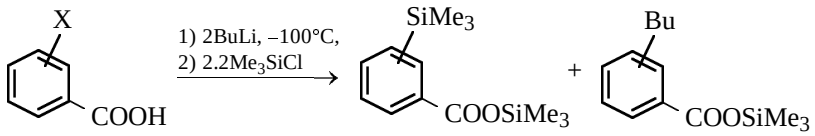
X = H, Br; Y = COOH, COOR, $CONR_2$, CN.

By changing the polarity of the reagents in reaction (5) as compared to the previous cases we might expect that it would require much milder conditions to occur (phenyllithium fast reacts at reduced temperatures even with di-*tert*-butylchlorophosphine. The main complication was that, even though the syntheses of *o*-lithiated benzoic acid both by direct metalation [23–25] and by halogen–lithium exchange [26–30], as well as the syntheses of *o*-lithiated benzoic acid derivatives by the first [31–33] or second [26–28, 34–37] methods are well-documented, comparative and systematic analysis of the results obtained by different methods and with different derivatives was lacking from the literature. Moreover, all subsequent reactions of *o*-lithiated derivatives were performed with electrophiles other than P(III) chlorides (mainly D_2O, alkyl and acyl halides, and carbonyl compounds).

Analysis of published data permitted us to conclude that the most suitable starting compounds for preparing *o*-lithiated derivatives of benzoic acid both by direct metalation and by exchange reactions are amides and nitriles, whereas free acids and their esters (except for the strongly shielded *tert*-butyl esters) are less suitable. As to the synthetic procedures, then, even though they both have certain disadvantages, halogen–metal exchange reactions are more facile (15–45 min at –100°C) and provide higher yields of aryllithium compounds (70–90%). Direct metalation of the cheaper and available benzoic acid and its esters proceeds much slower (up to 1.5–2 h at –100°C) with 50–65% converion. Therewith, even at such a low temperature *o*-lithiated *n*-alkyl esters noticeably decompose.

In view of the above findings, we have chosen halogen–lithium exchange as the most universal and experimentally convenient method for preparing not only *o*-, but also *m*- and *p*-lithiated benzoic acid derivatives (as shown in [29, 30], *m*- and *p*-lithiated salts of benzoic acid prepared in 60–85% yield by this reaction are thermally stable at –78°C for 1.5–2 h).

Before investigation of the synthesis of phosphine **I** by reaction (5), we tried to reproduce the halogen–lithium exchange reaction of *o*-, *m*, and *p*-iodobenzoic acids under the action of butyllithium and subsequent reaction of the resulting aryllithium salts with chlorotrimethylsilane [reaction (6)], presented in [29, 30].



(6)

IIa, IIb **IIIb, IIIc**

X = Br (*o*-, *m*-), I (*p*-); **IIa**, **IIb**, *o*- (**a**), *m*- (**b**); **III**, *m*- (**b**), *p*- (**c**).

Table 1. Constants, yields, and elemental analyses of phosphines $R^1R^2PC_6H_4Y$ **Ia**–**Ic** and **If**–**Il**

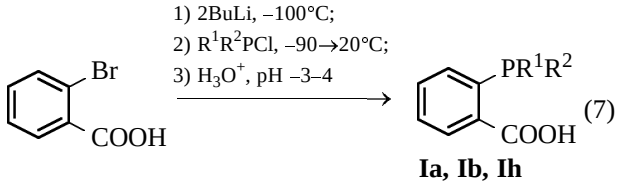
Comp. no.	R^1	R^2	Y	Method[a]	Yield, % (by ^{31}P data)	bp, °C (*p*, mm Hg)	Found, %			Formula	Calculated, %		
							C	H	N		C	H	N
Ia	Ph	Ph	2-COOH	B	60 (87)	159	74.05	4.61	–	$C_{19}H_{15}O_2P$	74.50	4.94	–
Ib	*i*-Pr	*i*-Pr	2-COOH	B	50 (70)	107–112 (1)	65.15	7.92	–	$C_{13}H_{19}O_2P$	65.53	8.04	–
Ic	*i*-Pr	*i*-Pr	3-COOH	A	70 (90)	120–124 (1)	65.08	7.85	–	$C_{13}H_{19}O_2P$	65.53	8.04	–
If	*i*-Pr	*i*-Pr	2-$COOSiMe_3$	B	70 (86)	86–88 (1)	61.56	8.61	–	$C_{16}H_{27}O_2PSi$	61.90	8.77	–
Ig	*i*-Pr	*i*-Pr	2-CN	B	58 (80)	90–92 (1)	79.78	7.95	5.90	$C_{13}H_{18}NP$	71.21	8.27	4.77
Ig	*i*-Pr	*i*-Pr	2-CN	A	70 (90)	90–92 (1)							
Ih	*t*-Bu	Ph	2-COOH	B	58 (90)	[b]	71.05	6.65	–	$C_{17}H_{19}O_2P$	71.32	6.79	–
Ii	Ph	Ph	3-COOH	B	30	128	74.12	4.68	–	$C_{19}H_{15}O_2P$	74.50	4.94	–
Ij	*i*-Pr	*i*-Pr	3-$COOSiMe_3$	B	28	90–95 (1)	61.62	8.55	–	$C_{16}H_{27}O_2PSi$	61.90	8.77	–
Ik	*i*-Pr	*i*-Pr	2-$C(O)NEt_2$	B	79 (97)	132–135 (1)	69.05	9.15	4.35	$C_{17}H_{28}NOP$	69.60	9.62	4.77
Il	*i*-Pr	*t*-Bu	2-$C(O)NEt_2$	B	72 (95)	138–140 (1)	69.98	9.62	4.32	$C_{18}H_{30}NOP$	70.33	9.84	4.56

[a] (A) Cross coupling of secondary phosphines with aryl halides and (B) reaction of *o*- or *m*-lithiated benzoic acids or their derivatives with chlorodiorganylphosphines. [b] Oil.

The results of reaction (6) occurred to be quite unexpected. With *o*-bromobenzoic acid, we obtained nothing more than the expected product, trimethylsilyl *o*-(trimethylsilyl)benzoate (**IIa**). With *m*-bromobenzoic acid, a mixture of silyl esters of *m*-(trimethylsilyl)benzoic **IIb** and *m*-butylbenzoic acids **IIIb** was obtained. Ester **IIIb** was the major product (>80%) when we used the conditions described in [29, 30] to prepare the *m*-lithiated salt (1.5 h at –95°C before addition of the electrophilic agent). Even if the lithium salt had been kept for a short time (5–10 min at –100°C) before chlorotrimethylsilane was added, the fraction of expected product **IIb**, according to ^1H NMR, was no more than 35%, and ester **IIIb** still remained the preferred product. In the case of *p*-iodobenzoic acid, the substitution product of *p*-lithiated lithium benzoate with chlorotrimethylsilane, ester **IIc**, was not detected even spectrally. Instead, trimethylsilyl *p*-butylbenzoate (**IIIc**) formed, implying that the *p*-aryllithium salt completely reacts with butyl iodide even at –100°C for 10–20 min (i.e. the time of addition of butyllithium). These results we could repeatedly reproduce. They disagree with the results in [29, 30] and suggest that with *m*- and *p*-bromo(iodo)-benzoic acids and their derivatives one should use bases sterically more hindered than butyllithium.

Since *o*-diorganylphosphino-substituted benzoic acids **Ia** and **Ib** could not be synthesized by cross-coupling reaction (2), we synthesized them by a scheme analogous to scheme (5).

The time of handling of the reaction mixture after a solution of butyllithium in hexane has been added



(7)

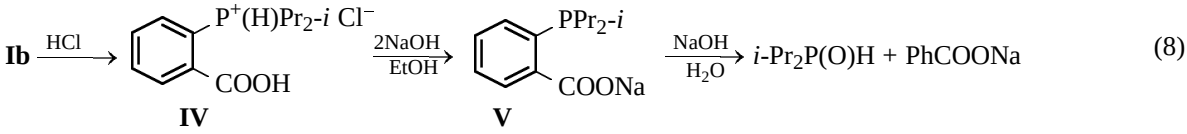
Ia, Ib, Ih

I, $R^1 = R^2$ = Ph (**a**); $R^1 = R^2$ = *i*-Pr (b); R^1 = *t*-Bu, R^2 = Ph (**h**).

to a solution of *o*-bromobenzoic acid in ether (with THF, the yield of compounds **I** is not better) is 30–40 min. The optimal amount of diorganylphosphine is 0.7–0.8 mol/mol benzoic acid, because the yields of the aryllithium salts do not exceed 80%. The spectral yield of phosphines **I** is 85–90%, and the isolable yield, 60–70% (Table 1). With equimolar amounts of chlorophosphines, by-products appear in the reaction mixtures, the most abundant of them being $R^1R^2 \cdot POBu$, $R^1R^2P(O)Bu$, and compounds with $R^1R^2P(O)O$ fragments. The presence of by-products makes phosphines **I** much more difficult to isolate pure.

Phosphino-substituted benzoic acids **Ia, Ib**, and **Ih** should be isolated with certain precautions: After the reaction mixtures had been decomposed with water, and the organic layer separated, the aqueous layer containing lithium salts of acids **Ia, Ib,** and **Ih** should be treated with 5% HCl very carefully, so that the pH of the solution is no higher than 3–4 units, because in a more acidic medium the products are protonated by the phosphorus atom, the easiest protonated being

the most basic dialkylphosphino-substituted derivative **Ib**. Treatment phosphonium salt **IV** (δ_P 34 ppm) with equimolar amount of aqueousethanolic NaOH gives rise to sodium salt **V** (δ_P 5 ppm). With excess alkali, however, facile cleavage of the phosphorus–aryl bond takes place to form diisopropylphosphinous acid (δ_P 54 ppm, $^1J_{PH}$ 430 Hz [20]) [scheme (8)].

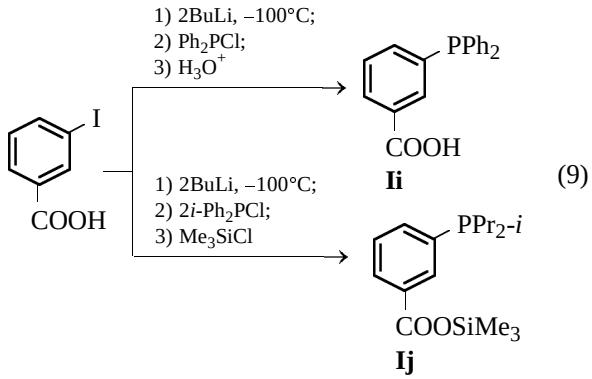


(8)

Replacement of hydrochloric acid with a concentrated solution of ammonium chloride results in slower neutralization and requires longer contact with lithium salt of acid **Ib** and does not improve the yield of acid **Ib** significantly (by ^{31}P NMR, ca. 60%). The main difficultly is isolation of phosphino-substituted acids **Ia, Ib**, and **Ih** is associated that the ester and and diorganylphosphino groups in them are very close to each other in basicity (pK_a values of the conjugate acids differ by 1–2), and, consequently, suitable acids for neutralization of lithium salts of theses acids should not protonate the P(III) atom.

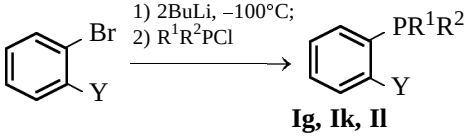
Isolation of compounds **Ia** and **Ih** with less basic R^1R^2P fragments is not associated with the above difficulties. Nevertheless, to simplify this process, we developed a procedure that excludes aquoeus-acidic treatment of the reaction mixtures and involving treatment of lithium salts of compounds **I** with excess chlorotrimethylsilane followed by vacuum distillation of trimethylsilyl esters of acids **I**. The spectral yields of the silyl esters reach 85–90% (phosphine **If** was isolated in 70% yield, whereas its yield by cross coupling (4) was no higher than 30%). If necessary, silyl esters of acids **I** can be easily hydrolyzed to give the corresponding acids under mild conditions [8].

On attempted synthesis of *m*-diorganylphosphino-substituted benzoic acid **Ii** or trimethylsilyl ester **Ij** from *m*-iodobenzoic acid by reaction (7) the yields of phosphines did not exceed 30%, which agrees with the yield of silyl ester of *m*-trimethylsilylbenzoic acid **IIb** and is explained by the same reasons.



(9)

The halogen–lithium exchange for preparing phosphines **I** was studied with nitriles and *N*,*N*-diethylamides of *o*-bromobenzoic acid [reaction (10)].



(10)

I, $R^1 = R^2 = i$-Pr, Y = CN (**g**); $R^1 = R^2 = i$-Pr, Y = $CONEt_2$ (**k**); $R^1 = i$-Pr, $R^2 = t$-Bu, Y = $CONEt_2$ (**l**).

Especially good results in reaction (10) were obtained with phosphines **Ik** and **Il** (by ^{31}P NMR, 95–98%) that could not be prepared by cross coupling (4).

To conclude, the cross-coupling reactions of dialkyl(trimethylsilyl)phosphines and secondary phosphines with *o*-halosubstituted benzoic acids and their derivatives failed to provide sterically congested *o*-dialkylphosphino-substituted compounds (nitrile **Ig**, $R^1 = R^2 = i$-Pr, was the only exception). At the same time, in the reactions of *o*-lithiated benzoic acid and its derivatives with diorganylchlorophosphines steric hindrances did not play the decisive role, which allowed us to prepare by this procedure a series of previously unavailable phosphines **I**. Their yields, constants, and spectral characteristics are listed Tables 1 and 2.

EXPERIMENTAL

The ^{1}H and ^{31}P NMR spectra were obtained on a Varian VXR-400 spectrometer against internal TMS (^{1}H) and external 85% phosphoric acid (^{31}P).

All manipulations with phosphines were carried out under dry argon. The solvents were purified by standard procedures and degassed in a vacuum under cooling and them purged with argon (2–3 times).

Table 2. ^{1}H and ^{31}P NMR spectra of phosphines **I**

Comp. no.	^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz)	^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm
Ia	6.9–8.2 (m)	–4.05
Ib	0.93 d.d (6H, 8.0), 1.25 d.d (6H, 8.0), 1.79 m (1H), 2.17 m (1H), 7.32–7.9 m (4H)	7.1
Ic	0.99 d.d (6H, 8.0), 1.16 d.d (6H, 8.0), 2.15 m (1H), 2.52 m (1H), 7.51 t (1H, 7.6), 7.76 t (1H, 7.6), 8.15 d (1H, 7.6), 8.27 s (1H), 10.7 s (1H)	11.5
Id[a]	–	–0.28
Ie[a]	–	3.5
If	0.34 s (9H), 0.9 d.d (6H, 7.0), 1.05 d.d (6H, 7.0), 1.6 m (1H), 2.05 septet (1H, 7.0), 7.29 t (1H, 6.6), 7.35 t (1H, 6.0), 7.47 d (1H, 7.4), 7.71 d (1H, 7.4)	3.5
Ig	0.93 d.d (6H, 8.0), 1.16 d.d (6H, 8.0), 2.23 m (2H, 7.0), 7.45 m (1H), 7.58 br.d (2H, 4.0), 7.72 m (1H)	5.91
Ih	1.43 d (9H, 20), 7.0–8.3 m (9H)	–13
Ii	7.3–8.1 m	–5.6
Ij	0.41 s (9H), 0.93 d.d (6H, 8.0), 1.1 d.d (6H, 8.0), 1.7 m (1H), 2.14 m (1H), 7.4–8.2 m (4H)	10.8
Ik	0.85–1.2 m (12H), 1.28 m (6H), 1.97 m (1H), 2.27 m (1H), 3.1 m (2H), 3.43 m (1H), 3.7 m (1H), 7.21 m (1H), 7.33 m (2H), 7.51 m (1H)	–0.91
Il	0.84 d.d (3H, 7.0), 1.06 d (9H, 12.0), 1.0–1.3 m (9H), 2.37 septet (1H, 7.0), 3.06 m (2H), 3.45 m (1H), 7.22 m (1H), 7.35 m (2H), 7.55 m (1H)	9.26

[a] Compounds **Id** and **If** were not isolated pure and characterized by the ^{31}P NMR spectrum only.

Synthesis of phosphines Ic–Ie and Ig by cross coupling of diisopropylphosphine with 3-iodobenzoic acid and 2-bromobenzoic acid derivatives (method A). Diisopropyl(3-carboxyphenyl)phosphine (Ic). An evacuated and argon-filled ampule was charged with 0.7 g of *m*-iodobenzoic acid, 2 ml of acetonitrile, 0.57 g of triethylamine, 0.4 g of diisopropylphosphine, 0.045 g of palladium dichloride, and 0.08 g of 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, after which it was sealed and thermostated at 100°C for 10 h with intermittent shaking. By ^{31}P NMR, this time is enough for complete reaction (spectral yield 75%). The ampule was unsealed, volatile products were removed in a vacuum, and the residue was dissolved in 10 ml of benzene and washed with 1 ml of water. The solvent was then removed in a vacuum, and the residue was distilled to give 0.4 g of phosphine **Ic** as a very viscous oil that quickly solidified at 20°C.

(2-Cyanophenyl)diisopropylphosphine (Ig). An evacuated and argon-filled ampule was charged with 0.36 g of diisopropylphosphine, 0.46 g of *o*-bromobenzonitrile, 0.44 ml of triethylamine, 0.5 ml of benzonitrile, and 177 mg of $PdCl_2(CH_3CN)_2$. The ampule was sealed and thermostated at 100°C for 45 h. By ^{31}P NMR, this time is enough for complete reaction (spectral yield 80%). The ampule was opened, volatile products were removed in a vacuum, and the residue was distilled to give 0.5 g of phosphine **Ig**.

Synthesis of phosphines Ia, Ib, If, and Ig–Il by eaction of *o*- and *m*-lithiated benzoic acids or their derivatives with diorganylchlorophosphines (method B). (2-Carboxyphenyl)diphenylphosphine (Ia). A two-necked flask equipped with a dropping funnel and a reflux condenser was evacuated, filled with argon, charged with a solution of 1 g of *o*-bromobenzoic acid in 20 ml of diethyl ether, and cooled to –95°C. After that 4.75 ml of a 2.1 N solution of butyllithium in hexane was added dropwise over the course of 40 min. The reaction mixture was stirred for an additional 30 min at –95°C, and then 0.66 g of diphenylchlorophosphine was added dropwise for 20 min. The reaction mixture was stirred for 30 min at –78°C, heated to room temperature, and left overnight, after which it was treated with 10 ml of argon-purged water to dissove the precipitate. The aqueous layer was separated, treated with 2% HCl until pH 3–24 (under these conditions, a colorless precipitate formed) and extracted with 20 ml of benzene. The organic layer was separated, and the aqueous layer was treated with 5 ml of 2% HCl and extracted with 10 ml of benzene. The combined benzene layers were dried over sodium sulfate, the solvent was removed in a vacuum, and the residue was crystallized from a 2 : 1 acetic acid–water mixture to give 0.6 g of phosphine **Ia**.

(2-Carboxyphenyl)diisopropylphosphine (Ib). A mixture of diisopropyl[2-(trimethylsiloxycarbonyl)-phenyl]phosphine (**If**) prepared from 1.2 g of *o*-bromobenzoic acid, 8.26 ml of a 1.44 N solution of butyllithium, 0.68 g of chlorodiisopropylphosphine, and 0.97 g of chlorotrimethylsilane was treated with 3 ml of methanol and refluxed for 1 h. Volatile products were removed, and the residue was subjected to a vacuum (1 mm Hg) to obtain phosphine **Ib** as a yellow oil partially crystallizing at room temperature. When distilled in a vacuum (1 mm Hg), phosphine **Ib** underwent partial decomposition.

Diisopropyl[2-(trimethylsiloxycarbonyl)phenyl]-phosphine (If). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 0.5 g of *o*-bromobenzoic acid in 10 ml of diethyl ether, and cooled to –95°C. After that 2.37 ml of a 2.1 N solution of butyllithium in hexane was added dropwise with stirring for 25 min. The reaction mixture was kept at –95°C for 30 min and then a solution of 0.29 g of diisopropylchlorophosphine in 5 ml of diethyl ether was added dropwise for 30 min. The reaction mixture was stirred at –78°C for 30 min, heated to room temperature, and, after addition of 0.46 ml of chlorotrimethylsilane, was left overnight. The colorless precipitate was filtered off on a glass filter, the solvent was removed in a vacuum, and the residue was distilled to give 0.32 g of phosphine **If**.

(2-Cyanophenyl)diisopropylphosphine (Ig). A two-necked flask equipped with a dropping funnel and a reflux codenser, and an argon inlet was evacuated, filled with argon, charged with 2.1 ml of *o*-bromobenzonitrile in 40 ml of diethyl ether, and cooled to –95°C. After that 7.23 ml of a 1.44 N solution of butyllithium in hexane was added over the course of 15 min. The reaction mixture was stirred for an additional 20 min at –95°C, and 1.26 g of diisopropylphosphine was added over the course of 10 min. The mixture was stirred for 15 min at –78°C, heated to room temperature, and left overnight. The colorless precipitate was filtered off on a glass filter, the solvent was removed, and the residue was distilled in a vacuum to give 1.05 g of phosphine **Ig** as a viscous oil.

***tert*-Butyl(2-carboxyphenyl)phenylphosphine (Ih)**. A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 2 g of *o*-bromobenzoic acid in 20 ml of diethyl ether, and cooled to –95°C. After that 9.48 ml of a 2.1 N solution of butyllithuim in hexane was added dropwise with stirring for 45 min. The reaction mixture was stirred for an additional 30 min, and 1.5 g of *tert*-butyl(chloro)phenylphosphine was added dropwise with stirring over the course of 30 nim. The mixture was stirred for 30 min at –78°C, heated to room temperature, and left overnight. Argon-purged water, 30 ml, was then added, and the aqueous layer was separated, treated with 2% HCl to pH 4, and extracted with ether (2×20 ml). The ethereal fractions were combined and dried over sodium sulfate. The solvent was removed in a vacuum, and the residual oil was washed with petroleum ether and subjected to a vacuum (1 mm Hg) for 20 min to give 1.25 of phosphine **Ih** as a viscous colorless oil.

(3-Carboxyphenyl)diphenylphosphine (Ii). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 1 g of *m*-iodobenzoic acid in 20 ml of diethyl ether, and cooled to –95°C. After that 3.84 ml of a 2.1 N solution of butyllithium in hexane was added dropwise over the course of 30 min. The reaction mixture was stirred at –95°C for 30 min, and 0.53 g of chlorodiphenylphosphine was added dropwise with stirring over the course of 20 min. The mixture was stirred for 30 min at –78°C, heated to room temperature, and left overnight. Argon-purged water, 30 ml, was then added (the precipitate that formed completely dissolved), and the aqueous layer was separated, treated with 2% HCl to pH 4 (a colorless precipitate formed), and extracted with benzene (2×20 ml). The benzene fractions were combined and dried over sodium sulfate. The solvent was removed in a vacuum, and the residue crystallized from 2 : 1 acetic acid–water to give 0.33 g of phosphine **Ii**.

Diisopropyl[3-(trimethylsiloxycarbonyl)phenyl]-phosphine (Ij). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 1 g of *m*-iodobenzoic acid in 20 ml of diethyl ether, and cooled to –95°C. After that 3.84 ml of a 2.1 N solution of butyllithium in hexane were added dropwise with stirring over the course of 30 min. The reaction nixture was stirred for 30 min at –95°C, and a solution of 0.43 g of diisipropylchlorophosphine in 5 ml of diethyl ether was added dropwise with stirring over the course of 20 min. The mixture was stirred for 30 min at –78°C, heated to room temperature, and, after addition of 0.75 ml of chlorotrimethylsilane, was left overnight. The colorless precipitate was filtered off on a glass filter, the solvent was removed in a vacuum, and the residue was distilled to give 0.35 g of phosphine **Ij**.

[2-(Diethylaminocarbonyl)phenyl]diisopropyl-phosphine (Ik). A two-necked flask equipped with a

dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 2 g of *N*,*N*-diethyl-*o*-bromobenzamide in 40 ml of diethyl ether, and cooled to –95°C. After that 5.43 ml of a 1.44 N solution of butyllithium in hexane were added dropwise with stirring for 20 min. The reaction mixture was stirred for 40 min, and a solution of 0.9 g of chlorodiisipropylphosphine in 5 ml of diethyl ether was added dropwise. The mixture was stirred for 20 min at –78°C, heated to room temperature, and left overnight. The precipitate was filtered on a glass filter under argon, the filtrate was washed with 2–3 ml of argon-purged water, and dried over sodium sulfate. The solvents were removed in a vacuum, and the residue was distilled to give 1.35 g of phosphine **Ik** as a viscous oil.

Phosphine **Il** was obtained analogously.

Trimethylsilyl *o*-(trimethylsilyl)benzoate (IIa). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 2 g of *o*-bromobenzoic acid in 40 ml of diethyl ether, and cooled to –95°C. After that 9.48 ml of a 2.1 N solution of butyllithium in hexane was added dropwise over the course of 40 min. The reaction mixture was stirred for 1.5 h at –95°C, and a solution of 2.7 ml of trimethylchlorosilane in 5 ml of diethyl ether was added dropwise with stirring over the course of 30 min. The mixture was stirred for 20 min at –78°C, heated to room temperature, and left overnight. The colorless precipitate was filtered off on a glass filter, the solvents were removed in a vacuum, and the residue was distilled to give 1.9 g (72%) of ester **IIa**, bp 125–126°C (10 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.35 s (9H), 0.42 s (9H), 7.43 t (1H, J_{HH} 8.0), 7.5 t (1H, J_{HH} 8.0), 7.7 d (1H, J_{HH} 8.0), 8.05 d (1H, J_{HH} 8.0). Found, %: C 58.11; H 8.12. $C_{13}H_{22}O_2Si_2$. Calculated, %: C 58.59; H 8.32.

Trimethylsilyl *m*-butylbenzoate (IIIb). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 2 g of *m*-bromobenzoic acid in 40 ml of diethyl ether, and cooled to –95°C. After that 9.48 ml of a 2.1 N solution of butyllithium in hexane was added dropwise with stirring over the course of 40 min. The reaction mixture was stirred for 1.5 h, and a solution of 2.7 ml of chlorotrimethylsilane in 5 ml of diethyl ether was added dropwise with stirring over the course of 30 min. The mixture was stirred for 20 min at –78°C, heated to room temperature, and left overnight. The colorless precipitate was filtered on a glass filter, the solvents were removed in a vacuum, and the residue was distilled to give 1.75 g of ester **IIIb**, bp 153–155°C (15 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.3 s (9H), 0.94 t (3H, J_{HH} 8.0), 1.39 sexet (2H, J_{HH} 8.0), 1.7 quintet (2H, J_{HH} 8.0), 2.92 t (2H, J_{HH} 8.0), 7.31 t (1H, J_{HH} 8.0), 7.63 t (1H, J_{HH} 8.0), 7.85 d (1H, J_{HH} 8.0), 8.06 s (1H). Found, %: C 67.02; H 8.71. $C_{14}H_{22}O_2Si$. Calculated, %: C 67.15; H 8.86.

At a shorter mlation time and keeping the reaction mixture for 5–10 min at –95°C, a mixture of trimethylsilyl *m*-butylbenzoate (**IIIb**) and trimethylsilyl *m*-(trimethylsilyl)benzoate (**IIb**) was obtained, spectral yields 65 and 35%, respectively.

Trimethylsilyl *p*-butylbenzoate (IIIb). A two-necked flask equipped with a dropping funnel and a reflux condenser with an argon inlet was evacuated, filled with argon, charged with a solution of 0.8 g of *p*-iodobenzoic acid in 20 ml of diethyl ether, and cooled to –95°C. After that 4.88 ml of a 1.44 N solution of butyllithium in hexane was added dropwise with stirring for 15 min, and the reaction mixture was kept at –95°C for 30 min. A solution of 0.9 ml of chlorotrimethylsilane in 5 ml of diethyl ether was added dropwise with stirring for 15 min, and the mixture was stirred for 20 min at –78°C, heated to room temperature, and left overnight. The colorless precipitate was filtered off on a glass filter, the solvents were removed in a vacuum, and the residue was distilled to give 0.5 g (60%) of ester **IIIc**, bp 145–148°C (10 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.29 s (9H), 0.95 t (3H, 8.0), 1.41 sextet (2H, 8.0), 1.72 quintet (2H, 8.0). 2.96 t (2H, 8.0), 7.61 d (2H, 8.0), 7.92 d (2H, 8.0).

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