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Synthesis of a Water-Stable 2,4-Bis(trifluoromethyl)phenyl-Substituted Phosphonous Acid Palladium Complex and its Catalytic Activity in Cross-Coupling Reactions

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Dedicated to Professor Helge Willner on the Occasion of His 65th Birthday

Keywords: Phosphinic acid; Phosphonous acid metal complex; Platinum; Palladium; Phosphorus

Abstract. This manuscript describes the selective synthesis of 2,4-bis(trifluoromethyl)phenylphosphinic acid, $(R_f)P(O)(H)OH$. Reaction of chlorobis(diethylamino)phosphane with a mixture of 2,4-$(CF_3)_2C_6H_3Li$ and 2,6-$(CF_3)_2C_6H_3Li$ results in the formation of 2,4-bis(trifluoromethyl)phenylbis(diethylamino)phosphane, $(R_f)P(NEt_2)_2$. The following in situ reaction with gaseous HBr leads to the cleavage of the phosphorus nitrogen bonds resulting in the selective formation of the corresponding dibromophosphane $(R_f)PBr_2$.

2,4-Bis(trifluoromethyl)phenylphosphinic acid is available via two different synthetic strategies starting from the dibromophosphane $(R_f)PBr_2$. Reduction of the dibromophosphane with tributyltin hydride affords selectively the phosphane $(R_f)PH_2$. The following oxidation to the phosphinic acid $(R_f)P(O)(H)OH$, however, only proceeds in moderate yields. A more efficient synthesis is achieved via the hydrolysis of the dibromophosphane $(R_f)PBr_2$ in dichloromethane solution. 2,4-bis(trifluoromethyl)phenylphosphinic acid, $(R_f)P(O)(H)OH$, is surprisingly stable towards air and water. The water soluble phosphinic acid reacts sluggishly with a 30% H_2O_2 solution, yielding only 23% of the corresponding phosphonic acid $(R_f)P(O)(OH)_2$ after seven days at ambient temperature.

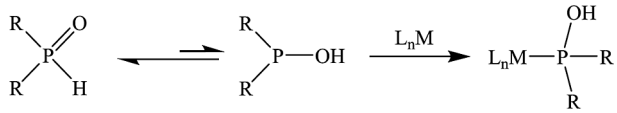
In principle a tautomerization of the phosphinic acid $(R_f)P(O)(H)OH$ to the corresponding phosphonous acid $(R_f)P(OH)_2$ – analogously to the phosphane oxide $(R_f)_2P(O)H$ and the phosphinous acid $(R_f)_2POH$ – is conceivable. However, the phosphonous acid could not be detected with spectroscopic methods. The energy difference between the phosphinic acid and the phosphonous acid is calculated by quantum chemical calculations at the B3LYP/6-311+G(2df,p) level of theory to 30.1 kJ·mol^{-1}. This high value explains why the phosphonous acid tautomer could not be detected by spectroscopic methods so far.

As transition metal complexes featuring phosphonous acid ligands are of significant interest for the application as homogeneous catalysts we studied the coordination chemistry of the related phosphinic acid in more detail. The preligand 2,4-bis(trifluoromethyl)phenylphosphinic acid reacts smoothly with palladium dichloride in THF to the dinuclear complex $[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}_2]$, featuring a phosphonous acid phosphonato unit, with a strong hydrogen bridge substantiated by an O···O distance of 247.7(3) pm. The dinuclear phosphonous acid palladium complex exhibits a high catalytic activity in the Suzuki cross-coupling. Alternatively, the phosphinic acid can be used as preligand for the in situ formation of a phosphonous acid palladium complex. These compounds combine catalytic activity with a very high stability towards air and water.

Dedicated Cluster

Introduction

Although there is a variety of phosphorus ligands available,[1,2] the motivation to generate new ligands strongly depend on the industrial demand for economical and robust ligands with a high catalytic activity and a high stability towards ambient air and moisture. In contrast, common complexes, such as $[Pd(PPh_3)_4]$, are highly air and moisture sensitive. The phosphane ligands, like tri-*tert*-butylphosphane, $P(tBu)_3$, show as the corresponding transition metal complex a amazing catalytic activity in many cross-coupling reactions, despite their air sensitivity.[1,3] Due to the sensitivity of phosphane ligands, the employment of secondary phosphane oxides (SPO), so called preligands,[2] is getting more and more popular. Pentavalent phosphane oxides are involved in tautomerization processes with the corresponding trivalent phosphinous acid form. For electron donating aryl- and alkyl substituents, this tautomeric equilibrium (cf. Equation (1)) is completely shifted to the side of the phosphane oxide tautomer.



R = alkyl, aryl (1)

Introducing electron withdrawing substituents, such as trifluoromethyl- and pentafluoroethyl-groups, allows the isolation of the corresponding phosphinous acids.[4,5] The less electron withdrawing *p*-tetrafluoropyridyl-, pentafluorophenyl-, 2,4-bis(trifluoromethyl)phenyl- and 2,6-bis(trifluoromethyl)-

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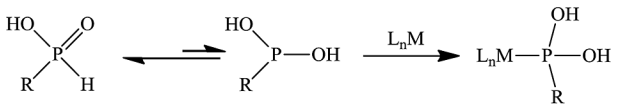
phenyl groups favor the phosphane oxide tautomer in the solid state, while in solution a solvent-dependent equilibrium is observed. An increasing donor number[6] of the chosen solvent leads to an increasing value of the corresponding phosphinous acid tautomer.[7–10]

Chatt and *Heaton* demonstrated in 1968 that phosphinous acids can be trapped by coordination to transition metals (cf. Equation (1)).[11] In the recent years the development of new secondary phosphane oxides has progressed rapidly, exhibiting catalytic activity in many cross-coupling reactions.[2,7]

Phosphinic acids RP(O)(H)OH and phosphonous acids $RP(OH)_2$ are related by an equilibrium. However, free phosphonous acids could not be detected by spectroscopic methods so far. But like phosphinous acids, they can be stabilized in the coordination sphere of suitable transition metals (cf. Equation (2)).[12]



R = alkyl, aryl (2)

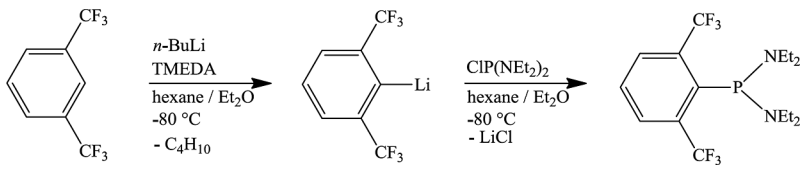
To investigate the influence of electron withdrawing groups on the catalytic activity of phosphonous acids palladium complexes, this paper describes the selective synthesis of 2,4-bis(trifluoromethyl)phenylphosphinic acid, 2,4-$(CF_3)_2C_6H_3$-P(O)(H)OH, and the thorough study of the coordination properties of the corresponding phosphonous acid 2,4-$(CF_3)_2C_6H_3P(OH)_2$ towards catalytically relevant metals, such as palladium.

Results and Discussion

Metalation of commercially available 1,3-bis(trifluoromethyl)benzene at 0 °C with n-butyllithium in the presence of TMEDA (tetramethylethylenediamine) leads to the selective formation of 2,6-bis(trifluoromethyl)phenyllithium.[13,14] Quenching the mixture with chlorobis(diethylamino)phosphane, $ClP(NEt_2)_2$, afforded the corresponding bis(diethylamino)phosphane in a 30% yield (cf. Equation (3)).[13]

In the absence of an auxiliary ligand such as TMEDA, the reaction of n-butyllithium and 1,3-$(CF_3)_2C_6H_4$ results in the formation of a mixture of 2,4- and 2,6-bis(trifluoromethyl)-phenyllithium (cf. Scheme 1).[15–19] Treatment of PCl_3 with an excess of the lithiated species leads to the formation of a complex product mixture (cf. Scheme 1). The study of the chemistry of mono-substituted 2,4-bis(trifluoromethyl)phenylphosphane derivatives, however, requires a more selective synthesis.

For a selective synthesis of bis[2,4-bis(trifluoromethyl)-phenyl]phosphane derivatives we utilized the steric demand of the diethylamino group to discriminate between the two lithium aryls.[19] As a consequence the reaction of chlorobis(diethylamino)phosphane with an excess (1:2,6) of 2,4-and 2,6-bis(trifluoromethyl)phenyllithium leads to a selective formation of 2,4-bis(trifluoromethyl)phenylbis(diethylamino)phosphane (**1**). The ^{31}P NMR spectrum of the aminophosphane **1** reveals a multiplet at $\delta = 92.7$ with a $^4J(P,F)$ coupling of 55 Hz. The subsequent treatment of the aminophosphane **1** with gaseous HBr at –80 °C results in a cleavage of the two phosphorus nitrogen bonds and in the selective formation of the corresponding dibromophosphane **2** (Scheme 2). Product **2** is ob-



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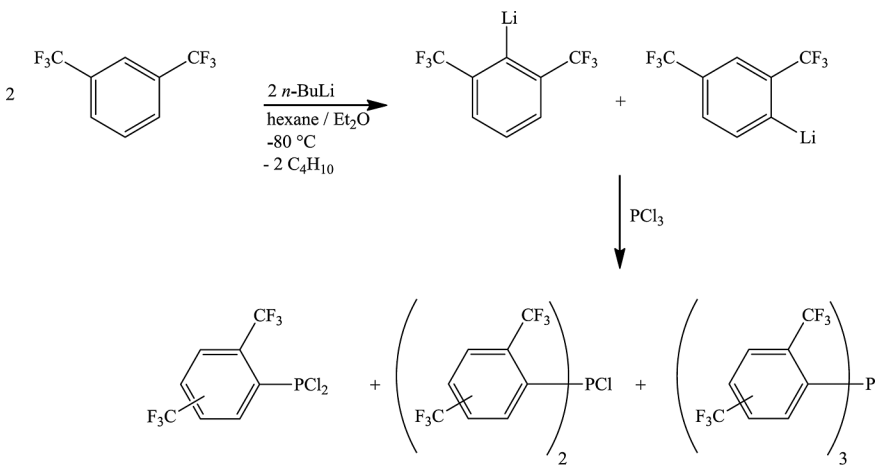
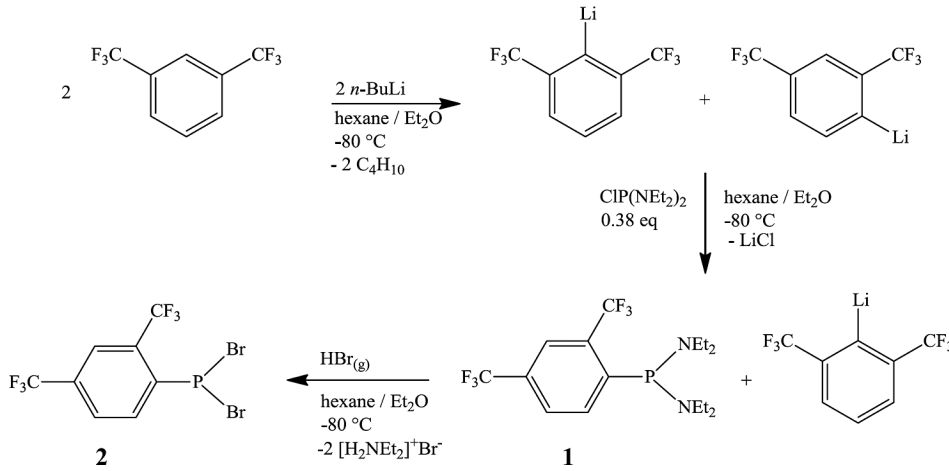


Scheme 1. Reaction of PCl_3 with lithiated 1,3-bis(trifluoromethyl)benzene.



Scheme 2. Reaction of chlorobis(diethyl)aminophosphane with lithiated 1,3-bis(trifluoro-methyl)benzene.

tained by distillation as a colorless liquid in an overall yield of 59 %.

The synthesis of 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) is realized by two different methods starting from the dibromophosphane **2**. In the low-volatile solvent 1,6-dibromohexane the reduction of **2** with a slight excess of tributyltin hydride selectively affords 2,4-$(CF_3)_2C_6H_3PH_2$ (**3**), which can be separated from the reaction mixture via a fractional condensation in a 80 % yield. In the ^{31}P NMR spectrum the product reveals a triplet of quartets at δ = –121.0 with characteristic ^1J(P,H) and ^4J(P,F) couplings of 208 Hz and 85 Hz, respectively (cf. Table 1 and Table 2). The subsequent oxidation to the phosphinic acid **4** proceeds through contact with ambient air or with an excess of NO_2 gas in CH_2Cl_2.

A more efficient access to the phosphinic acid **4** is the hydrolysis of the dibromophosphane **2** in CH_2Cl_2 within 30 minutes at room temperature (cf. Scheme 3). Removal of all volatiles in vacuo yielded 95 % of 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) as a colorless solid, which melts in the range of 77–79 °C. The ^{31}P NMR spectrum of Phosphinic acid

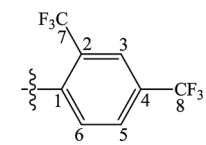
Table 1. Compilation of selected ^{31}P and ^{19}F NMR spectroscopic data of 2,4-bis(trifluoromethyl)phenyl derivatives.[a].

	No.	$\delta(^{31}P)$	^4J(P,F)	$\delta(^{19}F_o)$	$\delta(^{19}F_p)$
2,4-$(CF_3)_2C_6H_3P(NEt_2)_2$	**1**	92.7	55	–	–
2,4-$(CF_3)_2C_6H_3PH_2$[b]	**3**	–121.0	29	–61.7	–63.0
2,4-$(CF_3)_2C_6H_3PBr_2$	**2**	140.6	85	–56.5	–63.5
2,4-$(CF_3)_2C_6H_3P(O)(H)OH$[c]	**4**	17.5	8	–57.6	–63.3
2,4-$(CF_3)_2C_6H_3P(O)(OH)_2$ [d]	**5**	7.8	n. r.	–58.6	–63.3
$[PdCl_2\{(2,4\text{-}(CF_3)_2C_6H_3P(OH)_2\}_2]$	**7**	94.6	n. r.	–	–
$[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}]$	**8**	77.4	n. r.	–56.2	–63.7

a) Coupling constants in Hz. $CDCl_3$; room temp.; n. r. = not resolved; b) C_6D_6, $\delta(^{31}P)$ –121.0 (t, q, ^1J(P,H) 208 Hz); c): δ = (^{31}P) 17.5 (d, ^1J(P,H) 615 Hz); d) D_2O, (d, ^3J(P,H) 14.3 Hz, ArH).

Table 2. $^{13}C\{^1H\}$ NMR spectroscopic data of 2,4-bis(trifluoromethyl)phenyl derivatives (R = 2,4-$(CF_3)_2C_6H_3$)[a] Chemical Shifts.

	$\delta(^{13}C1)$	$\delta(^{13}C2)$	$\delta(^{13}C3)$	$\delta(^{13}C4)$	$\delta(^{13}C5)$	$\delta(^{13}C6)$	$\delta(^{13}C7)$	$\delta(^{13}C8)$
RPH_2 (**3**)[b]	135.8	133.8	122.9	130.2	n. r.[b]	136.8	123.8	122.9
$RPBr_2$ (**2**)	141.4	131.1	121.8	133.6	129.4	137.2	123.1	122.8
RP(O)(H)OH (**4**)	133.3	132.9	123.9	134.9	128.7	134.0	123.0	122.6
$RP(O)(OH)_2$ (**6**)[c]	136.7	132.4	123.1	132.7	128.2	136.6	123.0	123.4



Coupling Const.	^1J(P,C1)	^2J(F,C2)	^2J(P,C2)	^3J(F,C3)	^2J(F,C4)	^4J(P,C4)	^3J(F,C5)	^3J(P,C5)	^2J(P,C6)	^1J(F,C7)	^3J(P,C7)	^1J(F,C8)
RPH_2 (**3**)	24.7	31.7	10.4	5.3	33.5	n. r.	n. r.	n. r.	8.8	274.4	n. r.	272.3
$RPBr_2$ (**2**)	82.3	32.5	32.4	n. r.	33.7	n. r.	3.5	n. r.	1.6	275.6	2.3	270.1
RP(O)(H)OH (**4**)	124.0	34.2	9.9	n. r.	33.5	1.0	n. r.	n. r.	7.4	275.5	3.0	273.1
$RP(O)(OH)_2$ (**6**)	179.0	33.4	7.2	n. r.	33.1	3.1	13.2	3.5	7.6	273.6	4.5	272.2

a) Coupling constants in Hz. $CDCl_3$; room temp.; n. r. = not resolved; b) C_6D_6; resonance overlaid with [D_6]benzene; c) solvent [D_8]THF.

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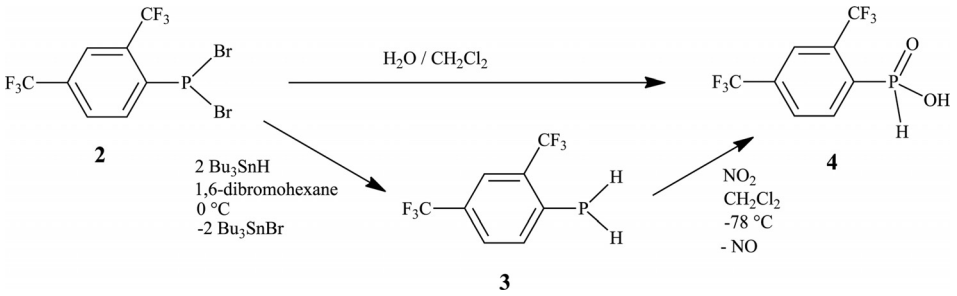
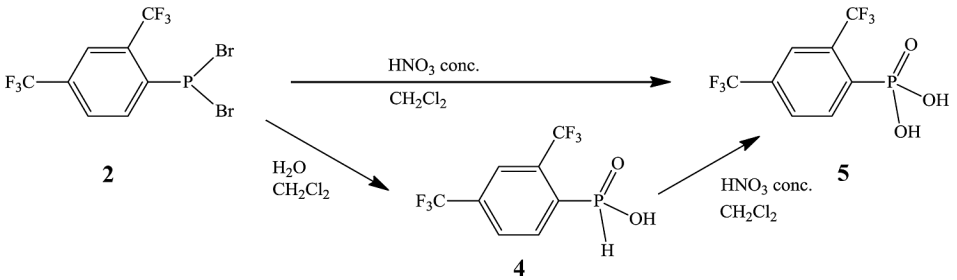


Scheme 3. Synthesis of 2,4-bis(trifluoromethyl)phenylphosphane (**3**) and 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**).

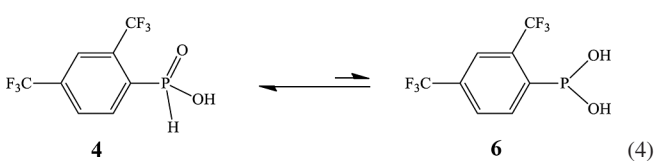


Scheme 4. Syntheses of 2,4-bis(trifluoromethyl)phenylphosphonic acid (**5**).

4 is characterized by a multiplet signal at $\delta = 17.5$ with characteristic couplings of $^1J(P,H) = 615$ Hz, $^3J(P,H) = 14$ Hz and $^4J(P,F) = 8$ Hz (cf. Table 1 and Table 2). The phosphinic acid **4** is stable towards hydrolysis and not easy to oxidize. A solution of **4** in a 30 % hydrogen peroxide solution shows a conversion of only 23 % to the corresponding phosphonic acid **5** after 7 days.

A more efficient way to oxidize **4** to **5** is the reaction with conc. HNO_3 (Scheme 4). Alternatively 2,4-$(CF_3)_2C_6H_3P(O)(OH)_2$ (**5**) is synthesized by in situ hydrolysis and oxidation of the dibromophosphane **3** with conc. HNO_3. The ^{31}P NMR spectrum of 2,4-$(CF_3)_2C_6H_3P(O)(OH)_2$ (**5**) is characterized by a singlet signal at $\delta = 7.8$.

Similar to the tautomerization between a phosphinous acid and a phosphane oxide (cf. Equation (1)), for the phosphinic acid **4** an equilibrium with the corresponding phosphonous acid, 2,4-$(CF_3)_2C_6H_3P(OH)_2$ (**6**) (cf. Equation (4)) can be postulated.

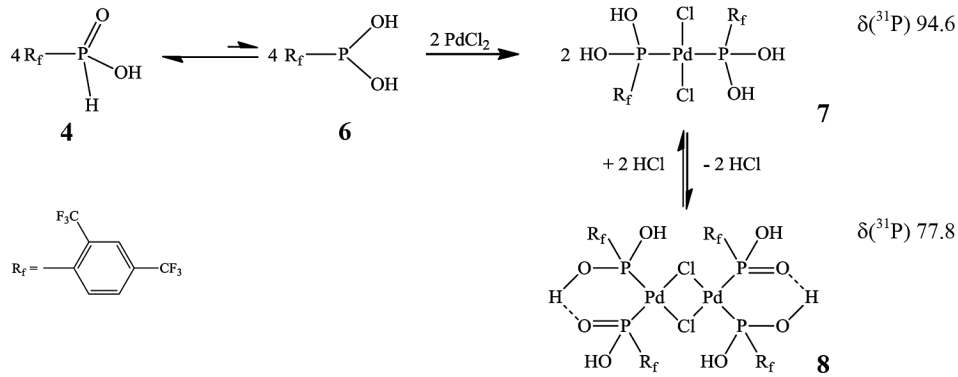


(4)

To the best of our knowledge there is no example of a free phosphonous acid described in the literature so far and the postulated equilibrium between phosphinic acids and their corresponding phosphonous acids could not be substantiated by spectroscopic evidence. However, the existence of the parent phosphonous acid $HP(OH)_2$ is postulated from kinetic studies and it is estimated that the ratio $HP(OH)_2/H_2P(O)(OH)$ in the equilibrium mixture does not exceed 10^{-12} in an aqueous solution.[20] The tautomer 2,4-$(CF_3)_2C_6H_3P(OH)_2$ (**6**) could not be detected even in highly donating solvents, such as DMA (dimethylacetamide), DMF (dimethylformamide) or HMPA (hexamethylphosphoric acid triamide). The energy difference between the phosphinic acid **4** and the phosphonous acid **6** is calculated by quantum chemical calculation at the B3LYP/6-311+G(2df,p) level of theory to 30.1 kJ·mol^{-1}. This large value may rationalize why the phosphonous acid tautomer is still elusive.

Like phosphinous acids, phosphonous acids also can be stabilized or trapped in the coordination sphere of suitable transition metals (cf. Equation (1) and (2), respectively). However, only few examples of phosphonous acid transition metal complexes are known so far.[12] With regard to a possible application in cross-coupling reactions, we investigated the coordination properties of 2,4-bis(trifluoromethyl)phenylphosphonous acid (**6**) in more detail.

The addition of solid palladium dichloride to a THF solution of 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) leads to a mixture of a mononuclear (**7**) and a dinuclear palladium complex (**8**) (cf. Scheme 5) after six days of stirring at room temperature. The reversible transformation between the mono- and the dinuclear complex mirrors the equilibrium observed for phosphinous acid derivatives bearing 2,4-bis(trifluoromethyl)-phenyl groups.[7] In keeping with this, exposure of a THF solution of the dinuclear complex **8** in an atmosphere of HCl selectively furnished the mononuclear complex **7** (cf. Scheme 5). The reverse reaction occurs in the presence of a base, such as pyridine, or by the removal of all volatiles in vacuo. The constitution and configuration of complex **8** in the solid state was elucidated by a single crystal structure analysis. Colorless crystals of **8** were obtained from a THF solution. Complex **8** crystallizes with two disordered solvent molecules (thf) in the



Scheme 5. Coordination of the phosphonous acid **6** and equilibrium between the mononuclear **7** and dinuclear palladium complex **8**.

monoclinic space group $P2_1/c$ (no. 14) (a = 1359.0(1) pm, b = 1120.7(1) pm, c = 1842.0(1) pm, β = 109.87(1)°) and reveals a quasi-chelating phosphonous acid phosphonato unit with an O1···O3 separation of 247.7(2) pm, indicating a strong intramolecular hydrogen bridge. The oxygen-bonded hydrogen atoms were refined isotropically revealing an O1–H1 distance of 108(4) pm and a H1···O3 distance of 1.41(4) pm, hence the P1–O1 distance is significantly longer than the P2–O3 distance (155.6(2) pm resp. 153.4(2) pm). The oxygen atoms O2 and O4 build intermolecular hydrogen bridges (Figure 1).

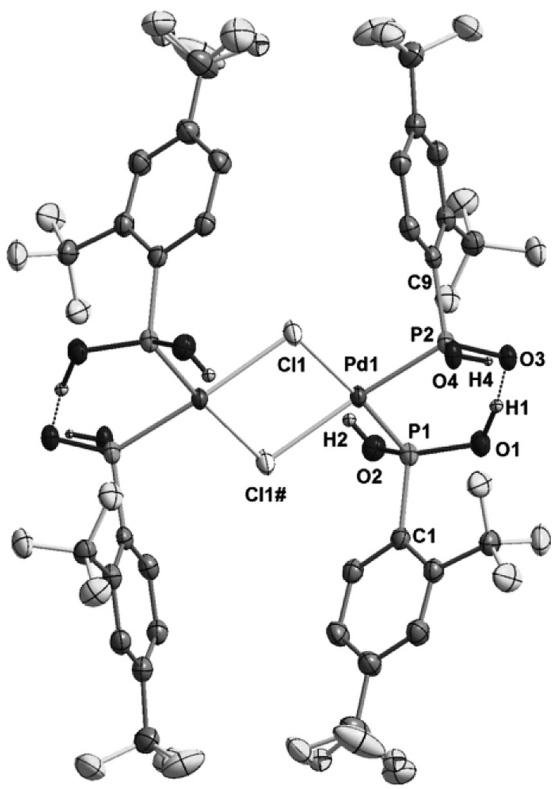


Figure 1. Molecular structure and numbering scheme of $[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}_2]\cdot 2THF$ (**8**); the solvent molecules (thf) and all carbon-bonded hydrogen atoms are omitted for clarity; 50 % probability amplitude displacement ellipsoids are shown; selected bond lengths /pm: P1–Pd1 221.8(1), P2–Pd1 223.9(1), P1–C1 182.6(2), P2–C9 183.0(2), P1–O1 155.6(2), P2–O3 153.4(2), O1–O3 247.7(3), Pd1–Cl1 239.9(1), Pd–Cl1# 243.6(1).

The successful synthesis of 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) and the corresponding phosphonous acid palladium complex **8** are the basis for the investigations in terms of a possible catalytic activity in Heck cross-coupling reactions between n-butyl acrylate and 1-bromo-2-fluorobenzene (cf. Table 3). The advantage of the fluorinated benzene is the possibility to determine the conversion rate by ^{19}F NMR spectroscopy. Using a catalyst loading of 0.01 mol-% palladium, which parallels 0.005 mol-% of the dinuclear complex **8**, leads to a conversion of 61.5 % after 48 hours at 135 °C. This underlines the high catalytic activity of the air stable complex **8**. The known[1a–e] air sensitive catalyst designed from $Pd_2(dba)_3$ (dba = dibenzylideneacetone) and tri-*tert*-butylphosphane gave a slightly higher conversion rate of 69.0 % under the same conditions.

The phosphinic acid **4** can be successfully used as a so called preligand for the in situ formation of catalytically active phosphonous acid complexes. The catalytic system $Pd_2(dba)_3$ / $2,4\text{-}(CF_3)_2C_6H_3P(O)(H)OH$ (**4**) (Pd atom ligand ratio 1:2) results within the chosen test system in a conversion rate of 51.0 % (cf. Table 3). Using $Pd_2(dba)_3$ without the preligand **4** leads to a conversion rate of only 23.5 %, which proves the beneficial influence of the phosphinic acid **4** to the catalytic activity.

The Suzuki cross-coupling is one of the most popular and industrially used reactions and therefore a widely used benchmark for new synthesized catalysts.[1,2] According to a former study of the catalytic activity of the phosphinous acid palladium complex $[Pd_2(\mu\text{-}Cl)_2\{\{[2,4\text{-}(CF_3)_2C_6H_3]_2PO\}_2H\}_2]$ in the reaction of 1-bromo-3-fluorobenzene with phenyl boronic acid clearly proves 2-propanole as solvent and potassium phosphate as the most efficient base.[7] Based on these observations, the catalytic activity of the phosphonous acid palladium complex **8** and the phosphinic acid **4** as a preligand in combination with $Pd_2(dba)_3$ are investigated under identical conditions (cf. Table 4).

Using a catalyst loading of 0.01 mol-% palladium (0.005 mol-% of the dinuclear complex **8**) leads after 20 hours at room temperature to a conversion rate of 80.0 %. The competition with the air sensitive catalyst[1a–e] $Pd_2(dba)_3$ / $P(t\text{Bu})_3$ results under identical conditions in a conversion of only 55.0 %. Using three equivalents of the phosphinic acid **4** as a preligand

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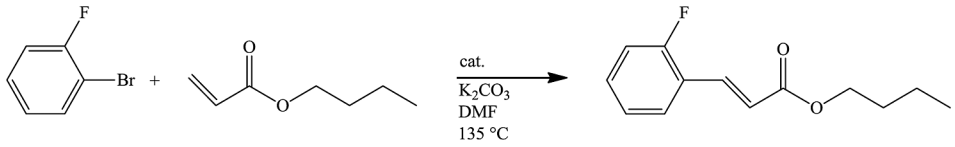
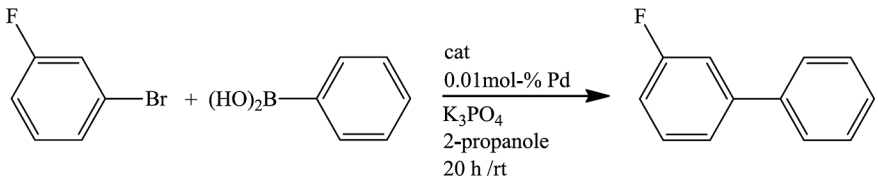
Table 3. Results of the Heck cross-coupling reactions.



Catalyst /0.01 mol-% palladium	M:L[a)]	t /h	Yield /%[b)]	TON	TOF
$Pd_2(dba)_3$ / 2,4-$(CF_3)_2C_6H_3P(O)(H)OH$ (**4**)	1:2	24	42.0	4200	175
		48	51.0	5100	106
$[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}_2]$ (**8**)		24	45.0	4500	187
		48	61.5	6150	128
$Pd_2(dba)_3$ / P(*t*Bu)$_3$	1:2	24	58.0	5800	241
		48	69.0	6900	143
$Pd_2(dba)_3$		24	13.0	1300	54
		48	23.5	2350	49
$PdCl_2$		24	19.5	1950	81
		48	24.5	2450	51

a) M:L = palladium ligand ratio. b) Determined via integration of the ^{19}F NMR resonances.

Table 4. Results of the Suzuki cross-coupling reaction.



Catalyst /0.01 mol-% palladium	M:L[a)]	Yield /%[b)]	TON	TOF
$Pd_2(dba)_3$ / 2,4-$(CF_3)_2C_6H_3P(O)(H)OH$ (**4**)	1:1	88.0	8800	440
$Pd_2(dba)_3$ / 2,4-$(CF_3)_2C_6H_3P(O)(H)OH$ (**4**)	1:2	90.5	9050	452
$Pd_2(dba)_3$ / 2,4-$(CF_3)_2C_6H_3P(O)(H)OH$ (**4**)	1:3	73.1	7310	365
$[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}_2]$ (**8**)		80.0	8000	400
$Pd_2(dba)_3$ / P(*t*Bu)$_3$	1:2	55.0	5500	229
$Pd_2(dba)_3$		78.0	7800	325
$PdCl_2$		7.5	750	31

a) M:L = palladium ligand ratio. b) Determined via integration of the ^{19}F NMR resonances.

(palladium ligand ratio 1:3) leads to a decreased catalytic activity (cf. Table 2). Test reactions without any palladium species show no conversion at all.

Conclusion

The selective synthesis of 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) was achieved by the reaction of chlorobis(diethylamino)phosphane with a mixture of 2,4-$(CF_3)_2C_6H_3Li$ and 2,6-$(CF_3)_2C_6H_3Li$, resulting in the formation of 2,4-bis(trifluoromethyl)phenylbis(diethylamino)-phosphane (**1**). The subsequent in situ reaction with gaseous HBr leads to the cleavage of the two phosphorus nitrogen bonds yielding the corresponding dibromophosphane **2**. The target product 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) can be synthesized by two different routes. Reduction of the dibromophosphane **2** with tributyltin hydride yields 2,4-$(CF_3)_2C_6H_3PH_2$ (**3**). The following air oxidation to the phosphinic acid **4** gave only moderate yields. A more efficient synthesis is achieved by hydrolysis of the dibromophosphane **2** in dichloromethane solution at room temperature. 2,4-Bis(trifluoromethyl)phenylphosphinic acid (**4**) is surprisingly stable towards air and water. The water soluble acid **4** is extremely resistant vs. oxidation. Dissolved in a 30 % H_2O_2 solution after seven days at room temperature the corresponding phosphonic acid **5** is detected in only 23 %.

Analogously to the phosphinous acid and phosphane oxide tautomerization, an equilibrium between the phosphinic acid **4** and the corresponding phosphonous acid **6** may be possible. In contrast to the phosphinous acid derivative, however, there is no spectroscopic evidence of the phosphonous acid **6** even in strongly donating solvents such as HMPA.

The preligand 2,4-bis(trifluoromethyl)phenylphosphinic acid (**4**) reacts smoothly with palladium dichloride in THF to the dinuclear complex $[Pd_2(\mu\text{-}Cl)_2\{[2,4\text{-}(CF_3)_2C_6H_3P(OH)O]_2H\}_2]$ (**8**) featuring a phosphonous acid phosphonato unit. The strong hydrogen bridge is identified by an O···O distance of 247.7(3) pm.

The phosphonous acid palladium complex **8** combines catalytic activity with a remarkably high stability towards air and water. The phosphinic acid **4** also proved useful for catalysis as a preligand for the in situ formation of a transition metal

complex enhancing the catalytic activity of the palladium source, $Pd_2(dba)_3$. These remarkable attributes enable the possibility for the employment in green chemistry.

Experimental Section

Materials and Apparatus

Chlorobis(diethylamino)phosphane was prepared according to the procedure of *Burg* and *Slota* treating PCl_3 with two equivalents of $HNEt_2$ in a hexane solution.[21] All other chemicals were obtained from commercial sources and used without further purification. Standard high-vacuum techniques were employed throughout all preparative procedures. Non-volatile compounds were handled under dry nitrogen by using Schlenk techniques.

The NMR spectra were recorded with a Bruker Model Avance III 300 spectrometer (^{31}P 111.92 MHz; ^{19}F 282.40 MHz; ^{13}C 75.47 MHz, ^{1}H 300.13 MHz) with positive shifts being downfield from the external standards (85 % orthophosphoric acid (^{31}P), CCl_3F (^{19}F) and TMS (^{1}H)). EI mass spectra were recorded with a Finnigan MAT 95 spectrometer (20 eV). Intensities are referenced to the most intense peak of a group. Isotope patterns for comparison were calculated with the program Isopro.[22] ESI mass spectra were recorded using an Esquire 3000 ion trap mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a standard ESI/APCI source. Samples were introduced by direct infusion with a yringe pump. Nitrogen served both as nebulizer gas and dry gas. Nitrogen was generated by a Bruker nitrogen generator NGM 11. Helium served as cooling gas for the ion trap and collision gas for MS^n experiments. The spectra were recorded with the Bruker Daltonik esquireNT 5.2 esquireControl software by the accumulation and averaging of several single spectra. DataAnalysis™ software 3.4 was used for processing the spectra.

Melting and visible decomposition points were determined using a HWS Mainz 2000 apparatus. C, H and N analyses were carried out with a HEKAtech Euro EA 3000 apparatus.

Single-crystal X-ray diffraction data of **8** were determined with a Bruker Nonius Kappa CCD diffractometer (Mo-K_α radiation). The crystal details and refinement characteristics are shown in Table 5.

Table 5. Crystal data and refinement characteristics for **8**.

8	
Crystallographic Section	
empirical formula	$C_{32}H_{18}Cl_2F_{24}O_8P_4Pd_2$, 2·($C_4H_8O$)
F(000)	1512
a /pm	1359.0(2)
b /pm	1120.7(1)
c /pm	1842.0(1)
θ /°	109.87(1)
V /10^6·pm^3	2638.5(1)
Z	2
D_x /g·cm^{-3}	1.936
crystal system	monoclinic
space group	$P2_1/c$ (no. 14)
shape / color	colorless fragment
crystal size /mm	0.20 × 0.16 × 0.10
Data collection	
diffractometer	Bruker Nonius Kappa CCD
radiation	Mo-K_α (graphite monochromator, λ = 71.073 pm)
T /K	100(2)
theta range	2.92–30.00
index range	$-19 \le h \le 19$
	$-15 \le k \le 15$
	$-25 \le l \le 25$
total data collected	79079
unique data	7673
observed data ($I > 2\ \sigma$)	6406
parameters	417
μ /mm^{-1} (numerical)	1.043
absorption correction	multi scan
T min / max	0.8186 / 0.9029
SHELX-97[24]	
$R1$ / $wR2$ [$I > 2\sigma(I)$]	0.031 / 0.077
$R1$ / $wR2$ (all data)	0.042 / 0.081
goodness of fit	1.042
R(int) / R(σ)	0.052
$\Delta\rho_{max/min}$ / 10^6 e·pm^{-3}	0.931 / –0.671
CCDC number	833102

2,4-Bis(trifluoromethyl)phenyldibromophosphane (2)

A 1.6 M n-butyllithium solution in hexane (100 mL, 160.0 mmol) was added to a solution of 1,3-bis(trifluoromethyl)benzene (35.0 g, 163.0 mmol) in diethyl ether (200 mL) at –78 °C. The temperature was slowly raised to room temperature. Stirring the mixture overnight gave a black solution. After the addition of chlorobis(diethylamino)phosphane, $ClP(NEt_2)_2$ (12.6 g, 59.9 mmol) at –78 °C, the mixture was warmed to room temperature and stirred overnight. The diethyl ether was removed under reduced pressure, n-hexane (700 mL) was added and the solution was stirred for 60 minutes at –60 °C in an atmosphere of HBr (248 mmol, 4.1 equiv.). The temperature was slowly raised to room temperature and stirring was continued for 60 minutes. The precipitate was filtered off. After evaporation of the solvent, compound **2** was obtained by vacuum distillation at 33–36 °C as colorless liquid in 59 % yield (14.4 g, 35.6 mmol).

2,4-Bis(trifluoromethyl)phenylphosphane (3)

A degassed solution of 2,4-bis(trifluoromethyl)phenyldibromophosphane (**2**) (1.96 g, 4.85 mmol) in 1,6-dibromohexane (25 mL) was cooled to 0 °C and tributyltin hydride (4.59 g, 15.8 mmol) was added within 2 hours. After 30 minutes of stirring at 0 °C, the temperature was slowly raised to room temperature. The colorless liquid **3** was isolated by fractional condensation in a yield of 0.95 g (3.86 mmol).

MS (EI; 20 eV) {*m*/*z* (%) [assignment]}: 490 (20) [2,4-$(CF_3)_2C_6H_3P(H)$-P(H)2,4-$(CF_3)_2C_6H_3]^+$; 246 (100) $[M]^+$; 195 (35); 175 (20) $[M\text{-}CF_3\text{-}2H]^+$; 157 (35) $[M\text{-}CF_3\text{-}HF]^+$.

2,4-Bis(trifluoromethyl)phenylphosphinic Acid (4)

A solution of 2,4-bis(trifluoromethyl)phenyldibromophosphane (**2**) (1.65 g, 4.10 mmol) in CH_2Cl_2 (15 mL) was combined with H_2O (0.5 mL) and stirred for 30 minutes at room temperature. After removal of all volatiles in vacuo and recrystallization from CH_2Cl_2 the phosphinic acid **4** was obtained in 95 % yield (1.08 g, 3.88 mmol) as a colorless solid (mp. 77–79 °C).

Elemental analysis calcd. (%) for $C_8H_5F_6PO_2$ (MW = 277.9 g·mol^{-1}): C 34.53, H 1.81; found: C 33.73, H 1.79. **MS** (EI; 20 eV) {*m*/*z* (%)

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[assignment]}: 474 (8) [{2,4-$(CF_3)_2C_6H_3$}$_2$PHO]$^+$; 278 (100) [M]$^+$; 259 (10) [M-F]$^+$; 230 (56) [M-2F]$^+$; 214 (14); 194 (30).

2,4-Bis(trifluoromethyl)phenylphosphonic Acid (5) (Route 1)

A solution of 2,4-bis(trifluoromethyl)phenyldibromophosphane (**2**) (0.66 g, 1.63 mmol) in CH_2Cl_2 (30 mL) was treated with conc. HNO_3 (2 mL) and stirred for one day at room temperature. The aqueous layer was separated and the organic phase was extracted twice with water (5 mL). The aqueous layers were combined and all volatiles were removed in vacuo. The product was recrystallized from a CH_2Cl_2/THF solution at –28 °C to give **5** as a colorless solid in 50 % yield (0.24 g, 0.81 mmol).

2,4-Bis(trifluoromethyl)phenylphosphonic Acid (5) (Route 2)

A sample of 2,4-bis(trifluoromethyl)phenylphosphinic acid (0.25 g, 0.89 mmol) was solved in conc. HNO_3 (6 mL) and the mixture was stirred for one day at room temperature. After removal of all volatiles in vacuo, 2,4-bis(trifluoromethyl)phenylphosphonic acid was obtained in 98 % yield (0.26 g, 0.88 mmol) as a colorless solid.

Elemental analysis calcd. (%) for $C_8H_5F_6PO_3$ (MW = 293.9 g•mol^{-1}): C 32.65, H 1.71; found: C 32.50, H 1.74. **MS** (EI; 70 eV) {*m/z* (%) [assignment]}: 294 (100) [M]$^+$; 275 (28) [M-F]$^+$; 255 (16) [M – HF_2]$^+$; 230 (60); 226 (35) [M-CF_2–OH_2]$^+$; 210 (82) [M-CF_2_2OH]$^+$; 194 (37); 182 (34); 144 (45).

[Pd_2(μ-Cl)$_2${[2,4-$(CF_3)_2C_6H_3$P(OH)O]$_2$H}$_2$] (8)

Solid palladium dichloride (49 mg, 0.278 mmol, 1.0 equiv.) was added to a solution of 2,4-bis(trifluoromethyl)phenylphosphinic acid (155 mg, 0.557 mmol, 2.0 equiv.) in THF (15 mL)and the mixture was stirred for six days at room temperature. The solid components were filtered off and all volatiles were removed from the filtrate in vacuo. The palladium(II) complex **8** was obtained in 85 % yield (200 mg, 0.119 mmol) as a light yellow solid.

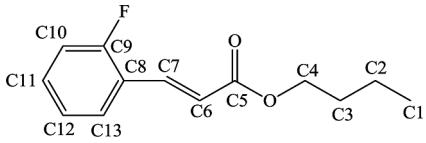
ESI MS in the negative range (neg.) {*m/z* (%) [assignment]}: 1394 (24) [M-H]$^-$; 1356 (12) [M-2F]$^-$; 880 (14); 852 (27); 696 (100) [M-2H]$^{2-}$.

General Procedure for Heck Cross-Coupling Reactions (e.g. for [Pd_2(μ-Cl)$_2${[2,4-$(CF_3)_2C_6H_3$P(OH)O]$_2$H}$_2$] (8))

A 150 mL Schlenk tube was charged with n-butyl acrylate (2.33 g, 18.18 mmol, 1.5 equiv.), bromo-2-fluorobenzene (2.08 g, 11.89 mmol, 1.0 equiv.), potassium carbonate (2.47 g, 17.87 mmol, 1.5 equiv.), and DMF (20 mL). After stirring the mixture for 10 minutes at room temperature, the catalyst (1 mg, e.g. **8**, 0.595 μmol, 0.01 mol-% palladium) was added. The reaction mixture was stirred for 24 hours at 135 °C. After cooling to room temperature the conversion was analyzed by ^{19}F NMR spectroscopy. The amounts of n-butyl acrylate, benzene, and bases were calculated for 1 mg catalyst.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.77 (d, ^2J(H,H) = 16.2 Hz, 1 H, C7-*H*), 7.48–7.03 (m, 4 H,

ArH), 6.49 (d, ^2J(H,H) = 16.0 Hz, 1 H, C6-*H*), 4.18 (t, ^3J(H,H) = 6.7 Hz, 2 H, C4-*H*), 1.65 (tt, ^3J(H,H) = 6.8, 6.8 Hz, 2 H, C3-*H*), 1.40 (qt, ^3J(H,H) = 7.3, ^3J(H,H) = 6.8 Hz, 2 H, C2-*H*), 0.92 (t, ^3J(H,H) = 7.3 Hz, 3 H, C1-*H*).



^{13}C{^{1}H} NMR (75.47 MHz $CDCl_3$): δ = 166.7 (s, C5), 161.3 (d, ^1J(C,F) = 254.3 Hz, C9), 137.1 (d, ^3J(C,F) = 3.0 Hz, C7), 131.5 (d, ^1J(C,F) = 8.8 Hz) 128.9 (d, ^1J(C,F) = 3.0 Hz), 124.3 (d, ^1J(C,F) = 3.6 Hz), 122.5 (d, ^2J(C,F) = 11.6 Hz, C8), 120.8 (d, ^4J(C,F) = 6.5 Hz, C6), 116.1 (d, ^2J(C,F) = 22.9 Hz, C10), 64.5 (s, C4), 30.7 (s, C3), 19.1 (s, C2), 13.9 (s, C1); an unambiguous assignment for ^{13}C atoms (C11, C12, C13) could not be given. **^{19}F NMR** (282.40 MHz, $CDCl_3$): δ = –116.5 (s).

General Procedure for Suzuki Cross-Coupling Reaction (e.g. for [Pd_2(μ-Cl)$_2${[2,4-$(CF_3)_2C_6H_3$P(OH)O]$_2$H}$_2$] (8))

A 50 mL Schlenk flask was charged with phenylboronic acid (2.18 g, 17.88 mmol, 1.5 equiv.), bromo-3-fluorobenzene (2.06 g, 11.77 mmol, 1.0 equiv.), potassium phosphate (3.79 g, 17.85 mmol, 1.5 equiv.), and 2-propanole (20 mL). After stirring the mixture for three hours at room temperature, the catalyst (1 mg, e.g. **8**, 0.595 μmol, 0.01 mol-% palladium) was added. The reaction mixture was stirred for 20 hours at room temperature and the conversion was analyzed by ^{19}F NMR spectroscopy. The amount of boronic acid, benzene and bases were calculated for 1 mg catalyst.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.67–7.61 (m, 2 H, CH), 7.55–7.40 (m, 5 H, CH), 7.40–7.35 (m, 1 H, CH), 7.15–7.06 (m, 1 H, CH). **^{13}C{^{1}H} NMR** (75.47 MHz, $CDCl_3$): δ = 163.2 (d, ^1J(C,F) = 245.4 Hz), 143.5 (d, ^3J(C,F) = 7.6 Hz), 139.9 (d, ^4J(C,F) = 2.2 Hz), 130.2 (d, ^3J(C,F) = 8.3 Hz), 128.9 (s), 127.9 (s), 127.1 (s), 122.8 (d, ^4J(C,F) = 3.4 Hz), 114.07 (d, ^2J(C,F) = 21.8 Hz), 114.05 (d, ^2J(C,F) = 20.9 Hz). **^{19}F NMR** (282.40 MHz, $CDCl_3$): δ = –113.1 (s). Comparison with literature gave identical ^{13}C and ^{19}F NMR spectroscopic data.[23] **MS** (EI; 70 eV) {*m/z* (%) [assignment]}: 172 (100) [M]$^+$; 154 (32) [$C_{12}H_{10}$]$^+$; 152 (12) [M – HF]$^+$.

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