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Full Papers

Efficient Large-Scale Synthesis of 9-Alkylfluorenyl Phosphines for Pd-Catalyzed Cross-Coupling Reactions

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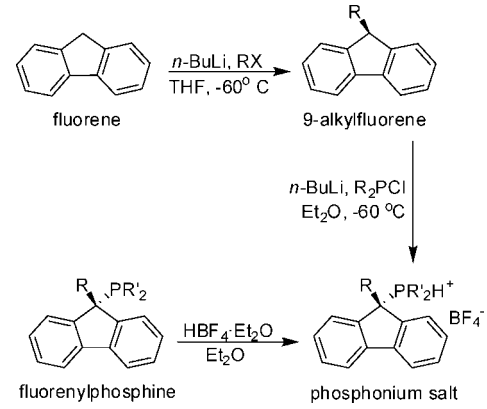
Abstract:

The reactions of aliphatic alcohols with fluorene coupled with a transfer hydrogenation result in the facile formation of 9-alkylfluorenes, whose deprotonation with *n*BuLi and quenching of the fluorenyl anion with Cy_2PCl in MTBE gave 9-alkylfluorenyldicyclohexyl phosphines, which are conveniently isolated as the respective phosphonium tetrafluoroborates after treatment with aqueous HBF_4. This route enables the facile large-scale (kilogram) synthesis of new ligands highly effective in Pd-catalyzed cross-coupling reactions.

Introduction

Pd-catalyzed cross-coupling reactions have become valuable tools in the production of fine chemicals.[1–5] The significant interest in this chemistry for industrial applications is documented in a large number of patents, which were recently compiled and reviewed by Corbet and Mignani.[6] Selected examples for applications of cross-coupling reactions include the Sonogashira reaction for the synthesis of an antimitotic agent (Novartis)[7] or tazarotene,[8] the Buchwald−Hartwig coupling in the hydrazonation of aromatic chlorides (Rhodia),[9] the Negishi coupling for a pyrimidine-based PDE-V inhibitor (Johnson & Johnson),[10] and the synthesis of the oncology candidate CP-724,714 (Pfizer).[11]

Scheme 1. **Small-scale synthesis of 9-alkylfluorenyl phosphines**



Usually, high activity catalysts for Pd-mediated coupling reactions require sterically demanding and electron-rich phosphines,[12] which need to be available in sufficient amounts to allow the production of commercial products.[13] We have recently reported the synthesis of 9-fluorenyl based phosphines, which are versatile ligands for various cross-coupling reactions.[14,15]

The published small-scale synthesis of 9-alkyl-fluorenyldialkylphosphines and their respective phosphonium salts is depicted in Scheme 1. Starting from commercially available fluorene, deprotonation with *n*BuLi in THF at −60 °C and subsequent quenching of the fluorenide with alkyl halides afforded the respective 9-alkylfluorene. In the second step the 9-alkylated fluorene was deprotonated with *n*BuLi in diethylether at −60 °C and quenched with Cy_2PCl to result in the formation of the respective fluorenyl phosphine, which was conveniently isolated as the phosphonium salt after treatment of the free phosphine with $HBF_4 \cdot Et_2O$. This route is useful for the small-scale synthesis of such phosphines and renders up to 10 g of various 9-alkylfluorenylphosphines, which were isolated as phosphonium salts in yields of 70– 90%. For the large-scale synthesis (several hundred grams to kilograms) of such phosphines, the present setup is inconvenient. First of all the yields of the overall reactions need to be improved, and additional problems such as the use of less favourable solvents (diethyl-

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ether), the application of highly flammable $HBF_4 \cdot Et_2O$, and the need for low temperatures (−60 °C) for the *n*BuLi reactions need to be dealt with.

We describe herein an optimized, large-scale synthesis of various 9-alkyl-fluorenyl phosphonium salts.[16]

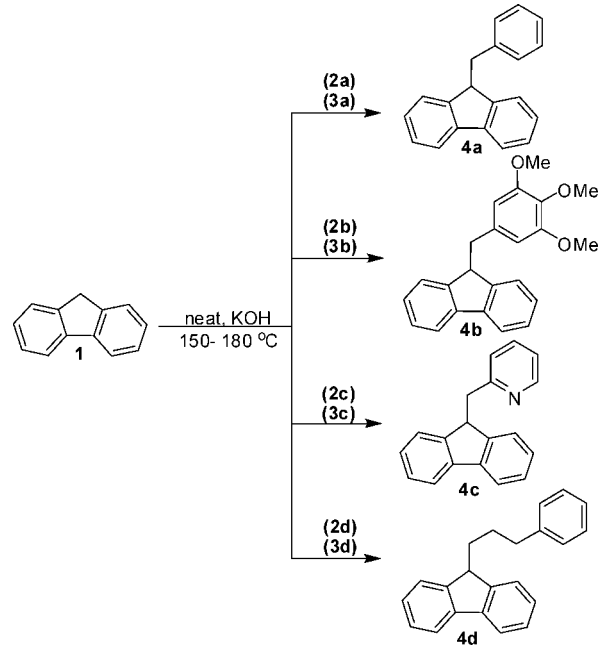
Improved Synthesis of 9-Alkylated Fluorenes

The decisive observation that forced us to look for improvements in the synthesis of 9-alkylated fluorenes was the unexpected formation of significant amounts of 9,9-dialkylated fluorenes (up to 30%) on quenching the fluorenyl anion with alkyl halides in large-scale reactions (>50 g). This is in stark contrast to the results of the small-scale synthesis (<5 g) which produces virtually quantitative yields of the 9-alkylated fluorenes. These problems partially originate from the increased concentration of reactants in the reaction mixture. In combination with the relatively faster addition of the alkyl halide to the metalated fluorene and the small differences in the CH-acidity of fluorene and 9-alkylated fluorene, the irreversible formation of the dialkylated product (up to 30% yield) becomes a major problem in the upscaling of this reaction. Furthermore, the separation of the resulting mixture of fluorene and mono- and dialkylated fluorenes by recrystallisation was impracticable owing to similar solubility properties. In conclusion, we were forced to look for alternative pathways, as the small-scale route is not feasible for the synthesis of bulk amounts.

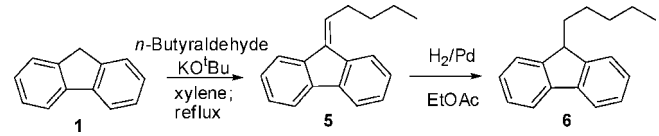
The literature offers other synthetic pathways for the preparation of 9-alkylfluorenes, such as the condensation of fluorene and alcohols with sodium metal at elevated temperatures[17–19] or the formation of alkylidenefluorenes via condensation of fluorene and aldehydes and their subsequent hydrogenation.[20–22] According to Sprinzak[23] the direct benzylation of fluorene with benzylalcohol containing small amounts of benzaldehyde initially leads to the formation of benzylidenefluorene, which at elevated temperatures (ca. 230 °C) undergoes transfer hydrogenation with benzylalcohol. This route was used by Sprinzak, affording 5–10 g of 9-benzylfluorene.

We decided to test the Sprinzak approach for the large-scale synthesis of 9-benzylfluorenes and to generalize this method. Accordingly, 9-benzylfluorene (**4a**) was synthesized on a 300 g scale in benzylalcohol (**2a**) without additional solvent. By deliberate addition of a substoichiometric amount (ca. 10%) of benzaldehyde (**3a**), the reaction temperature was lowered to 150 °C.[24] The white crystalline product thus formed in near quantitative yield and excellent purity does not require additional purification. This method could be generalized for the synthesis of various 9-benzylated fluorenes, whose Pd complexes turn out to be highly active catalysts for various carbonylation

Scheme 2. **Synthesis of 9-alkylated fluorenes**



Scheme 3. **Two-step synthesis of 9-alkylated fluorene via alkylidenes**



reactions:[25] Benzylalcohols bearing electron-rich substituents such as 3,4,5-trimethoxybenzylalcohol (**2b**) were reacted with fluorene in the same manner as electron-deficient building blocks such as 2-pyridinemethanol (**2c**) (Scheme 2). The resulting 2-(9*H*-fluoren-9-ylmethyl)-pyridine (**4c**) is an interesting building block for potential N,P bidentate ligands; the facile multigram synthesis reported here provides easy access to this compound.

The value of this synthetic approach could be extended significantly with the successful transformation of aliphatic alcohols other than benzylic alcohols. Fluorene was reacted with 3-phenyl-propan-1-ol (**2d**) employing the improved Sprinzak conditions. Raising the reaction temperature to 185 °C resulted in the formation of the respective 9-alkylated flourene **4d** in near quantitative yield on 400 g scale. Obviously, this method is suitable for the bulk production of a broad variety of 9-monoalkylated fluorenes and easily extendable to multikilogram production.

A modified approach was, however, needed for short chain aliphatic alcohols and aldehydes having low boiling points. Such aldehydes were reacted directly with fluorene to produce the respective alkylidene using the method of Bachmann and Polansky.[21] For safety reasons elemental potassium was successfully replaced by KO^{t}Bu.

In this manner 9-butylidenefluorene (**5**) was isolated in 63% yield and >99% purity as a white solid, which was directly introduced into the next step (Scheme 3). The following hydrogenation of **5** to the respective 9-*n*-butylfluorene (**6**) has

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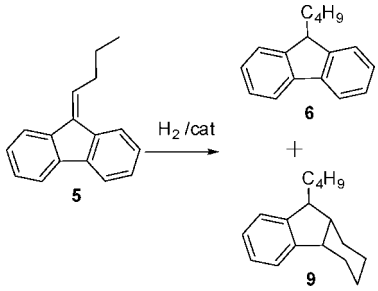
Scheme 4. **Synthesis of 9-alkylated fluorenederivatives via hydrogenation**



already been reported using Pd on charcoal or PtO_2 as catalysts.[17,22] The reported yields of only 75–90% and the need for distillative workup required improvements. However, initial hydrogenation experiments utilizing 10% Pd on activated charcoal (10 bar H_2 pressure, room temperature) produced an impurity of **9** in 10% yield, in which one aromatic ring was hydrogenated (Scheme 4). Changing the catalyst to PtO_2 and applying only 5 bars of H_2 at 25 °C reduced the amount of **9** to 3%. The use of 5% Pd on activated charcoal, 2 bar H_2 in technical grade ethyl acetate gave **6** in >99% yield without detectable impurities.

9-Alkylfluorenyl Phosphonium Tetrafluoroborates

Improved conditions were also developed for the phosphination of 9-alkylfluorenes. The deprotonation of the 9-alkylfluorene is now performed in MTBE instead of diethylether with a stoichiometric amount of *n*BuLi at 0 °C instead of −60 °C as previously reported. Addition of Cy_2PCl (**7**) leads to smooth carbon-phosphorous bond formation at room temperature. The removal of the formed LiCl was easily achieved by a simple washing of the MTBE-LiCl suspension with deaerated water. The formation and the precipitation of the phosphonium salt were accomplished by addition of 48% aqueous HBF_4 to the MTBE solution. Again the use of hazardous diethylether was avoided. Other ethereal solvents are not suitable as the respective phosphonium salts do not precipitate from THF or dioxane. The resulting 9-alkylfluorenyl phosphonium tetrafluoroborates were isolated as white crystals following a simple filtration. The phosphonium salts are air-stable and storable equivalents of the desired phosphines, which are liberated under the basic conditions of the cross-coupling experiment.[26,27]

Applying this improved synthetic route the phosphonium salts **8a**, **8b**, and **8c** (Scheme 5) were produced on a 200–250 g scale in >95% overall yield and ≫99% purity.

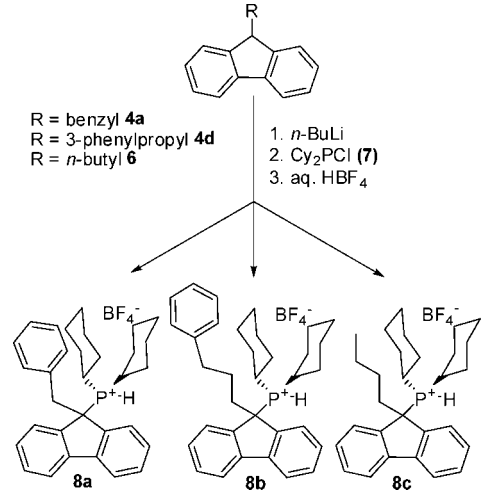
Summary

We have reported a significantly improved large-scale synthesis of 9-alkylfluorenylphosphines. Following an in situ deprotonation of the respective phosphonium salts, the obtained phosphines are useful as ligands for a variety of palladium-catalyzed coupling reactions.

Experimental Section

General Experimental. All chemicals were purchased as reagent grade from commercial suppliers and used without further purification, unless otherwise noted. Fluorene was purchased from Fluka (purity >99%). For the hydrogenation of *n*-butylidenefluorene Pd on carbon (5%) from Aldrich was used. *n*-Butyllithium (2.5 M in hexane) was purchased from Acros. MTBE was purchased from Fluka as crown cap-quality and used without any further deaeration treatment for the phosphine syntheses. Water used in phosphine syntheses for extraction of LiCl was deaerated with argon (20 min). Proton (^{1}H NMR), carbon (^{13}C NMR), nitrogen (^{15}N NMR), and phosphorus (^{31}P NMR) nuclear magnetic resonance spectra were recorded on a Bruker DRX 500 instrument at 500, 125.75, 50.69, and 202.46 MHz, respectively at 293 K. The chemical shifts are given in parts per million (ppm) on the delta scale (δ) and are referenced to tetramethylsilane (δ = 0 ppm), ^{1}H NMR and 65% aqueous H_3PO_4, (δ = 0 ppm), ^{31}P NMR nitromethane (δ = 0 ppm), ^{15}N NMR. Abbreviations for NMR data: s = singlet; d = doublet; t = triplet; q = quartet; qi = quintet; dd = doublet of doublets; dt = doublet of triplets; dq = doublet of quartets; tt = triplet of triplets; m = multiplet. Mass spectra were recorded on a Finigan MAT 95 magnetic sector spectrometer. GC experiments were run on a Clarus 500 GC with autosampler and FID detector. Column: Varian CP-Sil 8 CB (l = 15 m, d_i = 0.25 mm, d_F = 1.0 μm), N_2 (flow 17 cm/s; split 1:50); injector temperature 270 °C, detector temperature 350 °C. Temperature program: isotherm 150 °C for 5 min, heating to 300 °C with 25 °C/min, isotherm for 15 min.

Scheme 5. **Formation of 9-alkylfluorenyl phosphonium salts**



9-Benzyl-9*H*-fluorene (4a). In a 1-L 2-necked round-bottomed flask was suspended fluorene (**1**) (200 g, 1.20 mol) in benzyl alcohol (**2a**) (480 mL, 4.64 mol) and benzaldehyde (**3a**) (72 mL, 0.71 mol). KOH pellets (96 g, 1.71 mol) were added, and the mixture was stirred at 150 °C for 2.5 h. During the reaction the color changed from yellow to red, then to yellow, and finally to off white. The stirred reaction mixture was cooled to 95 °C, water (400 mL) was added, and the mixture was cooled to room temperature and stirred for another 0.5 h to obtain a white suspension. The product was separated via filtration (glass frit G3), washed with water (3 × 200 mL), recrystallized from EtOH/*i*-propanol and dried at 50 °C in vacuo to afford 9-benzyl-9*H*-fluorene (**4a**) (285 g, 93%) as white

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crystals. Purity (GC/NMR): >99%. ^{1}H and ^{13}C NMR spectra were identical with the literature.[14,28]

9-(3,4,5-Trimethoxybenzyl)-9*H*-fluorene (4b). In a 250-mL 2-necked round-bottomed flask was suspended fluorene (**1**) (20 g, 0.120 mol) in 3,4,5 trimethoxybenzyl alcohol (**2b**) (50 mL, 0.311 mol) and 3,4,5-trimethoxybenzaldehyde (**3b**) (5.0 g, 0.025 mol). KOH pellets (10 g, 0.178 mol) were added, and the mixture was stirred at 185 °C for 3 h. During the reaction the mixture changed its colour from yellow to dark brown and finally to cream (after 20 min). The stirred reaction mixture was cooled to 95 °C, water (125 mL) was added, and the mixture was cooled to room temperature and stirred for another 0.5 h to get a suspension. The product was separated via filtration (glass frit G3) and washed with water (3 × 75 mL), giving a beige crude product. This crude product was recrystallized from hot EtOH using 1 g of charcoal to decolorize affording 9-(3,4,5-trimethoxybenzyl)-9*H*-fluorene (**4b**) (36.8 g, 89%) as off-white crystals. Purity (GC/NMR): > 99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, ^3J = 7.5 Hz, 2 H, *CH*, ar), 7.33 (ddt, J = 0.5 Hz, ^4J = 1.5 Hz, ^3J = 7.5 Hz, 2 H, *CH*, ar), 7.27–7.20 (m, 4 H, C*H*, ar), 6.34 (s, 2 H, *CH*, ar), 4.20 (t, ^3J = 7.0 Hz, 1 H, 9-Flu *H*), 3.83 (s, 3 H, OCH_3), 3.73 (s, 6 H, OCH_3), 3.07 (d, ^3J = 7.0 Hz, 2 H, CH_2); ^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$) δ 153.3, 147.0, 141.4, 136.9, 135.4, 127.6, 127.0, 125.3, 120.3, 106.9, 61.3, 56.5, 49.1, 40.6; HRMS calcd for $C_{23}H_{22}O_3$ 346.1568, found 346.15881.

2-(9*H*-Fluoren-9-ylmethyl)-pyridine (4c). In a 500-mL 2-necked round-bottomed flask was suspended fluorene (**1**) (37.4 g, 0.225 mol) in 2-pyridinemethanol (**2c**) (90 mL, 0.926 mol) and 2-pyridinecarbaldehyde (**3c**) (12.8 g, 0.141 mol). KOH pellets (18 g, 0.321 mol) were added, and the mixture was stirred at 185 °C for 2 h. The stirred reaction mixture was cooled to 100 °C, water (125 mL) was added, and the mixture was cooled to room temperature and stirred for another 0.5 h. The product was suspended as slightly turquoise pellets in the reaction mixture. The crude product was separated via filtration (glass frit G3) and washed with water (3 × 75 mL). The crude product was dissolved in a mixture of ice (700 g) and concentrated HCl (200 mL). The solution was extracted with methylene chloride (400 mL) to remove remaining **2c** and **3c** (**4c**·HCl is to be found in the organic phase). The organic layer was brought to pH 9 with NaOH, washed with water (2 × 200 mL), and dried over $MgSO_4$. The volatiles were stripped off from the clear colourless filtrate at 50 °C in vacuo to afford **4c** (55 g, 95%) as white crystals. Purity (GC/NMR): >99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (dq, ^3J = 5.0 Hz, J = 1.0 Hz, 1 H, *CH*, ar), 7.74 (dt, ^3J = 7.5 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.59 (td, ^3J = 7.5 Hz, J = 2.0 Hz, 1 H, *CH*, ar), 7.33 (tt, ^3J = 7.5 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.22–7.17 (m, 3 H, C*H*, ar), 7.07 (dq, ^3J = 7.5 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.01 (dt, ^3J = 7.5 Hz, J = 1.0 Hz, 1 H, *CH*, ar), 4.63 (t, ^3J = 7.5 Hz, 1 H, 9-Flu *H*), 3.22 (d, ^3J = 7.5 Hz, 2 H, C H_2); ^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$) δ 160.3, 150.0, 147.5, 141.2, 136.6, 127.5, 127.1, 125.1, 124.8, 122.1, 120.2, 47.6, 43.0; ^{15}N NMR (50.69 MHz, $CDCl_3$) δ −68.4; HRMS calcd for $C_{19}H_{15}N$ 257.1205, found 257.12060.

9-(3-Phenyl-propyl)-9*H*-fluorene (4d). In a 1-L 2-necked round-bottomed flask was suspended fluorene (**1**) (250 g, 1.50 mol) in 3-phenyl-1-propanol (**2d**) (450 mL, 3.30 mol) and 3-phenylpropionaldehyde (**3d**) (39 g, 0.29 mol). KOH pellets (120 g, 2.14 mol) were added, and the mixture was stirred at 185 °C for 4 h. During the reaction the mixture changed its colour from yellow to orange, red, and brown and turned yellow in the end again. The stirred reaction mixture was cooled to ambient temperature and neutralized with concentrated HCl. Toluene (1 L) and water (1 L) were added, and the organic phase separated, washed with water (1 × 1 L) and dried over $MgSO_4$. After removal of the volatiles at 50 °C in vacuo, methanol (500 mL, technical grade) was added to the warm oily product. The solution was cooled to 4 °C under stirring, and after 10 min crystallisation of product started. The suspension was stirred for additional 1 h at that temperature, and then the product was separated via filtration with suction (glass frit G3), washed with ice-cold MeOH (3 × 200 mL), and dried at 50 °C in vacuo to afford the title compound **4d** (389 g, 91%) as off white crystals. Purity (GC/NMR): >99%. ^{1}H and ^{13}C NMR spectra were identical to those in the literature.[28]

9-Butylidene-9*H*-fluorene (5). In a 2-L 3-necked round-bottomed flask were suspended fluorene (**1**) (166 g, 1.0 mol) and KO*t*Bu (119 g, 1.06 mol) in xylene (1.5 L) under an argon atmosphere. The reaction mixture was refluxed for 5 min under stirring. The formed orange suspension was cooled to 25 °C, and under stirring *n*-butyraldehyde (**3e**) (300 mL, 3.33 mol) was added dropwise during 5 min. The colour changed to greenish. The reaction mixture was refluxed for 5 min again, cooled to 25 °C, and neutralized with concentrated HCl. The reaction mixture was transferred into a separation funnel and washed with water (1 × 1 L). The organic layer was dried over $MgSO_4$, and the volatiles of the clear colourless filtrate were removed at 80 °C in vacuo to afford a slightly yellowish oil. Methanol (70 mL) was added to the oily crude product, and the solution was stirred at 0 °C. After some minutes the title compound crystallized, and the suspension was stirred for an additional 1 h at 0 °C. The product is separated via suction filtration (glass frit G3) and dried in vacuo (the product melts at 50 °C) to afford **5** (138 g, 63%) as a white solid. Purity (GC/NMR): >99%. HRMS calcd for $C_{17}H_{16}$ 220.1252, found 220.12700. ^{1}H and ^{13}C NMR spectra were identical to those the literature.[29]

9-Butyl-9*H*-fluorene (6). 9-Butylidene-9*H*-fluorene (**5**) (80 g, 0.136 mmol) was dissolved in EtOAc (120 mL, technical grade). Five percent Pd on carbon (2.0 g) was added, and the mixture was hydrogenated at 20–25 °C (external cooling with ice), 2 bar H_2 for 1.5 h. The catalyst was filtered off via celite, and the filtrate was evaporated at 50 °C in vacuo to afford **6** (80 g, 100%) as a clear colorless oil that solidified at room temperature. Purity (GC/NMR): >99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dq, ^3J = 7.5 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.49 (ddt, ^3J = 7.5 Hz, J = 2.0 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.34 (tddd, ^3J = 7.5 Hz, J = 1.0 Hz, J = 1.0 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 7.28 (td, ^3J = 7.5 Hz, J = 1.0 Hz, 2 H, *CH*, ar), 3.96 (t, ^3J = 6.0 Hz, 1 H, 9-Flu *H*), 2.02–1.96 (m, 2 H, CH_2), 1.31–1.23 (m, 2 H, CH_2), 1.19–1.12 (m, 2 H, CH_2), 0.82 (t, ^3J

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= 7.5 Hz, 3 H, CH_3); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$) δ 148.1, 141.6, 127.3, 127.2, 124.8, 120.2, 47.9, 33.2, 28.2, 23.4, 14.3; HRMS calcd for $C_{17}H_{18}$ 222.1408, found 222.13953.

BnFluPCy$_2$·HBF$_4$ (8a). In a 6-L 3-necked round-bottomed flask was suspended 9-benzyl-9*H*-fluorene (**4a**) (90 g, 0.351 mol) in dry MTBE (3 L) under an argon atmosphere. At 0 °C *n*-BuLi (2.5 M in hexane, 139 mL, 0.348 mol) was added within 10 min. The reaction mixture was allowed to warm to 20 °C, a deep red, clear solution formed, and stirring was continued for an additional 2 h at ambient temperature. Then the mixture was cooled to −30 °C, and Cy_2PCl (**7**) (79.05 g, 0.340 mol) was added within 10 min. The red colour disappeared to form a yellow clear solution, which was stirred for an additional 1 h at 20 °C (after about 20 min precipitation of LiCl started). The suspension was extracted with degassed water (1 × 750 mL) to remove the LiCl. The clear, slightly yellowish organic layer was treated with aqueous HBF_4 (48%, 50.5 mL, 0.386 mol) under vigorous stirring within 2 min to precipitate the title compound as white crystals. Additional HBF_4 (2 M in water, 25 mL) was added, and the suspension was stirred for another 10 min. Product was separated via suction filtration (glass frit G3), washed with MTBE (2 × 100 mL), and dried at 60 °C in vacuo to afford **8a** (180 g, 98%) as white crystals. ^1H, ^{13}C, and ^{31}P NMR spectra were identical with the literature.[14]

PhenPropFluPCy$_2$·HBF$_4$ (8b). In a 6 L 3 necked round bottomed flask 9-(3-phenyl-propyl)-9H-fluorene (**4d**) (117 g, 0.410 mol) were suspended in dry MTBE (2.7 L) under an argon atmosphere. At 0 °C n-BuLi (2.5 M in hexane, 162 mL, 0.406 mol) were added within 10 min. The reaction mixture was warmed to 20 °C forming a deep red, clear solution which was stirred for additional 2 h at ambient temperature. Then the mixture was cooled to −30 °C, and Cy_2PCl (**7**) (92.75 g, 0.399 mol) was added within 10 min. The red colour disappeared to form a yellow clear solution, which was stirred for an additional 1 h at 20 °C (after about 20 min precipitation of LiCl started). The suspension was extracted with degassed water (1 × 750 mL) to remove the LiCl. The clear, slightly yellowish organic layer was treated with aqueous HBF_4 (48%, 59 mL, 0.451 mol) under vigorous stirring within 2 min to precipitate the title compound as white crystals. Additional HBF_4 (2 M in water, 25 mL) was added, the suspension stirred for another 10 min, and the precipitate was separated via suction filtration (glass frit G3) and washed with MTBE (2 × 100 mL). Drying of the product at 60 °C in vacuo afforded **8b** (208 g, 92%) as white crystals. ^1H, ^{13}C, and ^{31}P NMR spectra were identical to those the literature.[14]

BuFluPCy$_2$·HBF$_4$ (8c). In a 6-L 3-necked round-bottomed flask was suspended 9-butyl-9*H*-fluorene (**6**) (113.7 g, 0.511 mol) in dry MTBE (3.2 L) under an argon atmosphere. At 0 °C *n*-BuLi (2.5 M in hexane, 200 mL, 0.500 mol) was added within 15 min. The reaction mixture was warmed to 20 °C and formed a deep red, clear solution, which was stirred for an additional 2 h at ambient temperature. Then the mixture was cooled to −30 °C again, and Cy_2PCl (**7**) (113.8 g, 0.489 mol) was added within 15 min. The red colour disappeared to form a yellow clear solution, which was stirred for an additional 1 h at 20 °C (after about 20 min precipitation of LiCl started). The suspension was extracted with degassed water (1 × 750 mL) to remove the LiCl. The clear, slightly yellowish organic layer was treated with aqueous HBF_4 (48%, 67 mL, 0.511 mol) under vigorous stirring within 2 min to precipitate the title compound as white crystals. Additional HBF_4 (2 M in water, 25 mL) was added, the suspension was stirred for another 10 min, and the precipitate was separated via suction filtration (glass frit G3) and washed with MTBE (2 × 100 mL). Removal of the volatiles at 60 °C in vacuo afforded **8c** (234 g, 95%) as white crystals. ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, ^3J = 7.5 Hz, J = 0.5 Hz, 2 H, ar), 7.80 (d, ^3J = 7.5 Hz, 2 H, ar), 7.59 (tt, ^3J = 7.5 Hz, J = 1.3 Hz, 2 H, ar), 7.53 (td, ^3J = 7.5 Hz, J = 1.3 Hz, 2 H, ar), 6.51 (dt, ^1J = 479.52 Hz, J = 2.5 Hz, 1 H, P*H*), 2.70–2.64 (m, 2 H, CH_2 (butyl)), 2.23 (qq, J = 12.3 Hz, J = 2.7 Hz, 2 H, CH_2), 1.93–1.85 (m, 2 H, C*H*), 1.80–1.48 (m, 8 H, CH_2), 1.40 (qdd, J = 12.6 Hz, J = 4.5 Hz, J = 3.7 Hz, 2 H, CH_2), 1.27–1.06 (m, 10 H, CH_2), 0.66 (t, ^3J = 7.3 Hz, 3 H, CH_3), 0.59–0.51 (m, 12 H, CH_2 (butyl)); $^{13}C\{^1H\}$ NMR (125.75 MHz, $CDCl_3$) δ 141.8 (d, J_{PC} = 4.4 Hz), 140.5 (d, J_{PC} = 1.5 Hz), 130.6, 129.5, 125.4 (d, J_{PC} = 2.9 Hz), 121.5, 52.8 (d, J_{PC} = 32.2 Hz), 34.0, 31.6 (d, J_{PC} = 36.0 Hz), 29.8 (d, J_{PC} = 3.4 Hz), 28.4 (d, J_{PC} = 3.5 Hz), 27.1 (d, J_{PC} = 13.2 Hz), 26.9 (d, J_{PC} = 12.8 Hz), 25.3, 24.8 (d, J_{PC} = 9.9 Hz), 22.6, 14.0; $^{31}P\{^1H\}$ NMR (202.45 MHz, $CDCl_3$) δ 35.3; ^{31}P NMR (202.45 MHz, $CDCl_3$) δ 35.3 (d, ^{PH}J = 479 Hz).

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Supporting Information Available

NMR spectra (^1H, ^{13}C, ^{15}N, ^{31}P) of the previously unknown compounds. This information is available free of charge via the Internet at http://pubs.acs.org.

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