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Synthesis of fluorous trialkyl phosphines with the complete exclusion of PH_3

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Abstract—A novel synthetic protocol has been developed for the synthesis of fluorous tertiary phosphines excluding the use of hazardous PH_3 and with control over the number of methylene spacers and the length of fluorous ponytails.

Fluorous catalysts could offer easy product separation for numerous homogeneous catalytic reactions by temperature dependent liquid–liquid[1a,b] or solid–liquid[2] phase separation. One of the most effective ways to make a homogeneous catalyst soluble in the fluorous phase is the incorporation of fluorous ponytail(s) into the catalyst design.[3,4] Since tertiary phosphines could be used as organocatalysts[2,5] or as ligands in homogeneous catalysis,[1b] a large number of methods have been developed for the preparation of fluorous phosphines.[6] Fluorous mono- and polydentate tertiary alkyl phosphines are attractive ligands, since they coordinate very strongly to metals, a key factor in designing robust and recyclable catalysts. It is important to recognize, that the direct attachment of perfluoroalkyl groups to a phosphorus atom leads to phosphines,[6a,b,7] in which the strong electron-withdrawing effect of the fluorous ponytails limits the coordination capability.[8] Therefore, the insertion of two or more methylene spacers between the phosphorus atom and the perfluoroalkyl groups is necessary to insulate the phosphorus from the electron-withdrawing effects.[4,6f,9]

Although there are several procedures for the synthesis of fluorous trialkyl phosphines utilizing the coupling of $R_{FX}(CH_2)_AI$ with PCl_3 in the presence of the appropriate Rieke-[10a,b] or Grignard-reagents,[10c] the much more efficient routes still require the use of the highly toxic PH_3 either directly[4,6e,f] or indirectly.[6f,11] Furthermore, pure PH_3 ignites in air at about 150 °C and is often contaminated with traces of P_2H_4 that promotes its spontaneous combustion, representing significant hazards even in small scale preparations. Hence, we developed a new procedure avoiding either the direct or indirect use of PH_3, which also allows partial control of the number of the methylene spacers and the length of the fluorous ponytails and combinations of these.

Our new approach is based on the radical addition of 2 equiv of perfluoroalkyl-alkene to 1 equiv of phenylphosphine, which can be prepared by the reduction of phenylphosphonic dichloride with lithium aluminum hydride,[12] resulting in a bis(perfluoroalkyl-alkyl)phenylphosphine. The alkylation of this phosphine with a perfluoroalkyl-alkyl iodide yields a phosphonium salt, which can be converted into a phosphine oxide by selective removal of the phenyl group using sodium hydroxide. The final product fluorous trialkylphosphines can be obtained by reduction of the phosphine oxides with trichlorosilane (Scheme 1). For example, the radical addition of 3-perfluorooctyl-1-propene ($R_{F8}CH_2$–$CH{=}CH_2$) to phenylphosphine in the presence of AIBN at 78–80 °C was carried out by mixing the two compounds without any solvent under nitrogen. The pure bis(perfluorooctyl-propyl)phenylphosphine, $PPh[R_{F8}(CH_2)_3]_2$, was obtained by removing all volatile side products and excess alkene in vacuo. The radical addition of

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Keywords: Fluorous; Phosphines; Phosphonium salts; Phosphine oxides; Radical addition.

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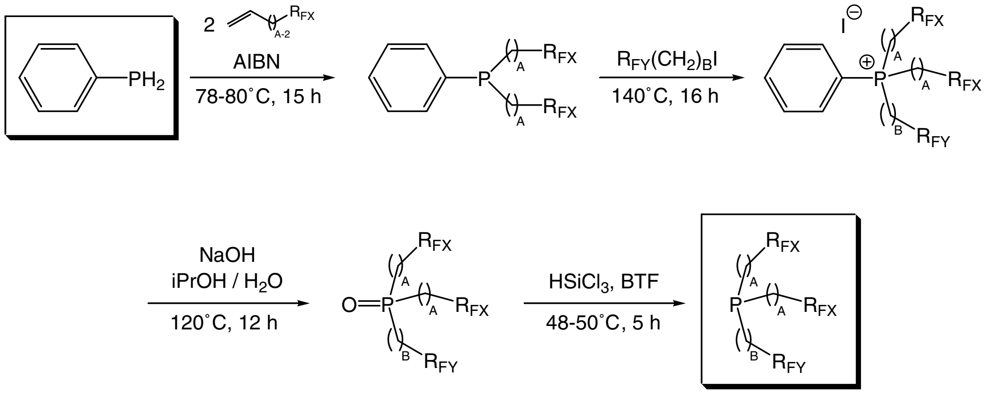


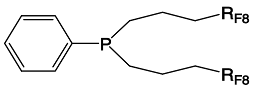
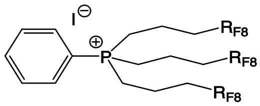
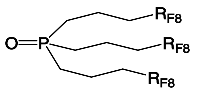
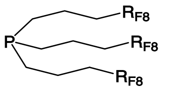
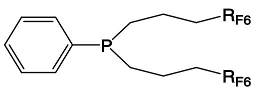
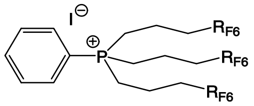
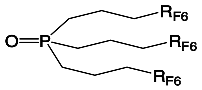
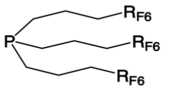
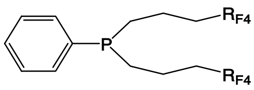
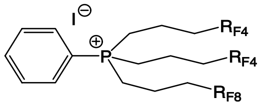
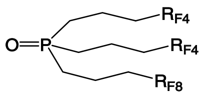
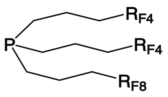
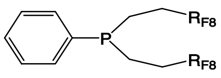
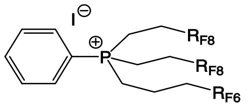
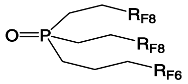
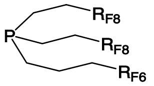
Scheme 1. Synthetic protocol leading to fluorous tertiary phosphines; $A = 2$ and 3; $B = 3$; X, $Y = 4$, 6, and 8.

$PhPH_2$ to fluorous olefins $R_{F6}CH_2–CH{=}CH_2$, $R_{F4}CH_2–CH{=}CH_2$, and $R_{F8}CH{=}CH_2$ resulted in the corresponding fluorous dialkyl-phenylphosphine in 87–93% yield (Table 1). These phosphines are air-sensitive white solids ($R_{F6}(CH_2)_3$-, $R_{F8}(CH_2)_3$-, and $R_{F8}(CH_2)_2$- ponytail) or slightly yellow viscous oils ($R_{F4}(CH_2)_3$-ponytail) and all are soluble in dichloromethane, isooctane, and fluorous solvents.[13]

The third fluorous ponytail was introduced by the alkylation of $Ph[R_{FX}(CH_2)_A]_2P$ with 1-iodo-3-perfluoroalkylpropane ($R_{FY}(CH_2)_3I$) at 140 °C. After 16 h of reaction time, the isolated yield for phosphines with three or two methylene spacers was typically 95–97% and 90%, respectively. The $Ph[R_{FX}(CH_2)_A]_2[R_{FY}(CH_2)_3]P^+I^-$ compounds are air-stable white or slightly yellow powders and their melting points increase with the length of the fluorous ponytails, as expected.[11] They are insoluble in apolar organic solvents and fluorous solvents, but soluble in acetone and with three $R_{F6}(CH_2)_3$-groups or two $R_{F4}(CH_2)_3$-groups and one $R_{F8}(CH_2)_3$-groups are slightly soluble in dichloromethane.[14]

Selective removal of the phenyl group from the phosphonium salts was effected by treatment with sodium hydroxide in a 1:3 mixture of 2-propanol and water resulting in the formation of benzene and the corresponding $[R_{FX}(CH_2)_A]_2[R_{FY}(CH_2)_3]P{=}O$ compounds in 78–83% yields.[15] It should be noted that in the case of a phosphine containing $R_{F8}(CH_2)_2$-groups, the isolated yield of the corresponding phosphine oxide was only 55%. However, we could isolate a phosphine oxide containing two fluorous chains and one phenyl group from the reaction mixture indicating that the selectivity of the removal of the phenyl group decreases when strong electron-withdrawing groups are attached to the phosphorus atom. These phosphine oxides are air-stable white powders and are soluble in acetone and FC-72 (except for $[R_{F8}(CH_2)_3]_3P{=}O$), and with three $R_{F6}(CH_2)_3$-groups or two $R_{F4}(CH_2)_3$-groups and one $R_{F8}(CH_2)_3$-

Table 1. Syntheses of fluorous tertiary phosphines

Entry	$(Ph)R^1_2P$; yield[a]	$(Ph)R^1_2R^2P^+I^-$; yield	$R^1_2R^2P{=}O$; yield	$R^1_2R^2P$; yield
1	 93	 89	 70	 62
2	 90	 85	 71	 62
3	 93	 91	 74	 65
4	 87	 78	 43	 37

[a] Isolated overall yields, based on phenylphosphine.

groups are soluble in dichloromethane, and insoluble in diethyl ether and apolar organic solvents.[16]

The fluorous tertiary phosphines were obtained in 86–89% yield by reduction of the $[R_{FX}(CH_2)_A]_2$-$[R_{FY}(CH_2)_3]P{=}O$ derivatives, as reported by Gladysz and co-workers,[6e] using trichlorosilane ($HSiCl_3$) in trifluoromethyl-benzene (BTF). Since the resulting phosphines were expected to be soluble in fluorous solvents, we used fluorous extraction during the work-up procedure. The product phosphines are colorless or slightly yellow viscous oils ($[R_{F4}(CH_2)_3]_2[R_{F8}(CH_2)_3]P$, $[R_{F8}(CH_2)_2]_2[R_{F6}(CH_2)_3]P$, $[R_{F6}(CH_2)_3]_3P$) or a white solid ($[R_{F8}(CH_2)_3]_3P$).[17]

In conclusion, a new synthetic protocol was developed for the synthesis of fluorous tertiary phosphines. Our procedure offers a safer approach by avoiding the use of the highly toxic and hazardous PH_3. Furthermore, the synthetic protocol allows variation of the number of methylene spacers and the length of the fluorous ponytails providing a library of fluorous tertiary phosphines with fine tuning of the basicity of the phosphorus atom and the partition coefficients of the phosphines or their transition metal complexes.

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Supplementary data

Supplementary data containing the NMR data of the compounds is available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.09.166.

References and notes

1. (a) Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72–75; (b) Gladysz, J. A.; Curran, D. P.; Horváth, I. T. *Handbook of Fluorous Chemistry*; Wiley/VCH: Weinheim, 2004.
2. Wende, M.; Gladysz, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 5861–5872.
3. Horváth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641–650.
4. Horváth, I. T.; Kiss, G.; Cook, R. A.; Bond, J. E.; Stevens, P. A.; Rábai, J.; Mozeleski, E. J. *J. Am. Chem. Soc.* **1998**, *120*, 3133–3143.
5. Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138–5175.
6. (a) Parshall, G. W.; England, D. C.; Lindsey, R. V., Jr. *J. Am. Chem. Soc.* **1959**, *81*, 4801–4802; (b) Lavrent'ev, A. N.; Maslennikov, I. G.; Sochilin, E. G. *Zh. Obshch. Khim.* **1973**, *43*, 2663–2665; (c) Gopal, H.; Snyder, C. E., Jr.; Tamborski, C. *J. Fluorine Chem.* **1979**, *14*, 511–518; (d) Nixon, J. F. *Adv. Inorg. Chem. Radiochem.* **1985**, *29*, 41–42; (e) Alvey, L. J.; Rutherford, D.; Juliette, J. J. J.; Gladysz, J. A. *J. Org. Chem.* **1998**, *63*, 6302–6308; (f) Alvey, L. J.; Meier, R.; Soós, T.; Bernatis, P.; Gladysz, J. A. *Eur. J. Inorg. Chem.* **2000**, 1975–1983.
7. Kampa, J. J.; Nail, J. W.; Lagow, R. J. *Angew. Chem.* **1995**, *107*, 1361–1364.
8. Battle, S. L. Ph.D. Thesis, University of Texas, Austin, TX, 1993.
9. (a) Jiao, H.; Le Stang, S.; Soós, T.; Meier, R.; Kowski, K.; Rademacher, P.; Jafarpour, L.; Hamard, J.-B.; Nolan, S. P.; Gladysz, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 1516–1523; (b) Bhattacharyya, P.; Croxtall, B.; Fawcett, J.; Fawcett, J.; Gudmunsen, D.; Hope, E. G.; Kemmitt, R. D. W.; Paige, D. R.; Russell, D. R.; Stuart, A. M.; Wood, D. R. W. *J. Fluorine Chem.* **2000**, *101*, 247–255; (c) Stibrany, R.; Gorun, S. M. *J. Organomet. Chem.* **1999**, *579*, 217–221.
10. (a) Benefice-Malouet, S.; Blancou, H.; Commeyras, A. *J. Fluorine Chem.* **1985**, *30*, 171–187; (b) Langer, F.; Püntener, K.; Stürmer, R.; Knochel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 715–738; (c) Bhattacharyya, P.; Gudmunsen, D.; Hope, E. G.; Kemmitt, R. D. W.; Paige, D. R.; Stuart, A. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3609–3612.
11. Vlád, G.; Richter, F.; Horváth, I. T. *Org. Lett.* **2004**, *6*, 4559–4561.
12. Freedman, L. D.; Doak, G. O. *J. Am. Chem. Soc.* **1952**, *74*, 3414–3415.
13. General procedure for the radical additions of fluorous olefins to phenylphosphine: A 20 mL Fischer–Porter bottle was charged with the appropriate fluorous olefin (18.25 mmol, 25% excess), $PhPH_2$ (7.30 mmol), and AIBN (100 mg, 8 mol %) under nitrogen. The bottle was closed and the biphasic mixture was stirred at 78–80 °C for 2 h. AIBN (100 mg) was added after every 2 h (four times), and finally the homogeneous mixture was stirred for 7 h. The resulting slightly yellow oil/solid was placed under vacuum (0.05 mbar) at 80 °C in order to remove the excess fluorous olefin and the tetramethyl-succinonitrile giving the corresponding bis(perfluoroalkyl-alkyl)phenylphosphine. This phosphine could be recrystallized from isooctane at low temperature, if needed.
14. General procedure for the alkylation of fluorous phenylphosphine derivatives: The appropriate bis(perfluoroalkyl-alkyl)phenylphosphine (6.80 mmol) and perfluoroalkyl-alkyl iodide (13.6 mmol, 100% excess) were placed in a 20 mL heavy-walled vial under nitrogen. The vial was closed and the mixture was stirred at 140 °C for 16 h. After cooling to room temperature, 40 mL of FC-72 or CH_2Cl_2 was added to the yellowish solid, the mixture was finely powdered in a mortar, and filtered through a Büchner funnel. Washing with 2×10 mL of FC-72 and drying in vacuo resulted in the corresponding phosphonium salt as a white or slightly yellow powder.
15. Fenton, G. W.; Ingold, C. K. *J. Chem. Soc.* **1929**, 2342–2357.
16. General procedure for the dephenylation of phosphonium salts: The appropriate phosphonium salt (4.33 mmol) was placed into a heavy-walled round-bottomed flask and treated with NaOH (17.3 mmol) and with 1:3 mixture of 2-propanol/water (9 mL). The flask was closed and heated to 120 °C with vigorous stirring. After 12 h the reaction mixture was cooled to room temperature and treated with FC-72 (40 mL) and water (30 mL). The biphasic mixture was stirred for 2 min, the fluorous phase was filtered through a layer of $MgSO_4$, and evaporated in vacuo to give the corresponding phosphine oxide as a white powder. For further purification, the solid could be recrystallized from perfluoro-2-butyl-tetrahydrofuran. According to its low solubility in FC-72,

$[R_{F8}(CH_2)_3]_3P{=}O$ was isolated by filtration of the biphasic mixture through a Büchner funnel and drying in vacuum.

17. General procedure for the reduction of phosphine oxides: A heavy-walled 200 mL Schlenk-flask was charged with trichlorosilane (52.6 mmol), trifluoromethyl-benzene (17 mL), and the appropriate phosphine oxide (1.4 mmol) under nitrogen and then closed. The solution was stirred at 48–50 °C for 5 h, evaporated in vacuum, treated with 20 mL of O_2-free FC-72, filtered under nitrogen, and evaporated again. The resulting solid or oil was dissolved in 10 mL of FC-72, filtered, and evaporated in vacuo (0.05 mbar) to give the corresponding phosphine.