ChemComm

COMMUNICATION

View Article Online
View Journal

Cite this: DOI: 10.1039/c5cc03572d

Received 29th April 2015,
Accepted 12th June 2015

DOI: 10.1039/c5cc03572d

www.rsc.org/chemcomm

Electrophilic phosphonium cations catalyze hydroarylation and hydrothiolation of olefins†

Manuel Pérez, Tayseer Mahdi, Lindsay J. Hounjet and Douglas W. Stephan*

Electrophilic phosphonium cations (EPCs) are efficient main group catalysts for the hydroarylation of olefins under mild conditions, providing a facile route to substituted aniline, bis-arylamine, phenol, furan, thiophene, pyrrole, and indole derivatives. Similarly, EPCs catalyze the hydrothiolation of aryl olefins with thiophenol affording a series of alkyl aryl thioethers. Experimental data support a mechanism for these reactions that involves initial activation of the olefin.

Main group chemistry is an area from which a variety of new catalysts are emerging.[1] While classical group 13 Lewis acids are well established with a variety of applications,[2] recent interest has focused on group 15 reagents. The Lewis acidity of P(III) phosphenium cations has been explored by the groups of Gudat,[3] Burford,[4] Yoshifuji,[5] and Bertrand[6] among others. Gabbaï *et al.*[7] have demonstrated the utility of Lewis acidic group 15 centers in sensor technology, while others have applied P(V) compounds for catalytic additions to polar unsaturates and Diels–Alder reactions.[8] Recently, Radosevich *et al.* have exploited P(III)/P(V) redox chemistry for transfer hydrogenation catalysis and for the activation of alcohols, amines and ammonia.[9] We have recently described electrophilic phosphonium cations (EPCs), such as $[(C_6F_5)_3PF]^+$, which are more Lewis acidic than $B(C_6F_5)_3$ as a result of the positive charge and a low lying σ* orbital which is directed under the umbrella of the arene rings, opposite from the P–F bond.[10] These Lewis acids have proven to be quite versatile, effecting hydrodefluorinations of fluoralkanes,[17] isomerizations and polymerizations of olefins, hydrosilylation of olefins, alkynes,[11] ketones, amines and nitriles,[12] and dehydrocoupling of silanes with anilines, phenols, thiophenols and acids (Fig. 1).[13] The latter dehydrocouplings can also be accompanied by hydrogen transfer to olefins.[13] Herein, we exploit $[(C_6F_5)_3PF][B(C_6F_5)_4]$ (**1a**) as a catalyst for hydroarylation and hydrothiolation reactions involving a variety of aromatic substrates and olefins. While other Lewis acids can mediate Friedel–Crafts reactions,[14] the present report described the first examples of phosphonium-catalyzed hydroarylation and hydrothiolation reactions.

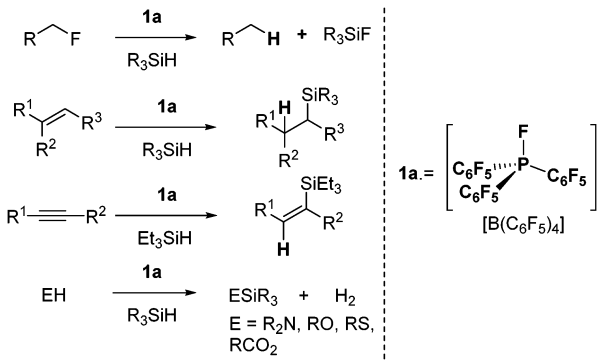


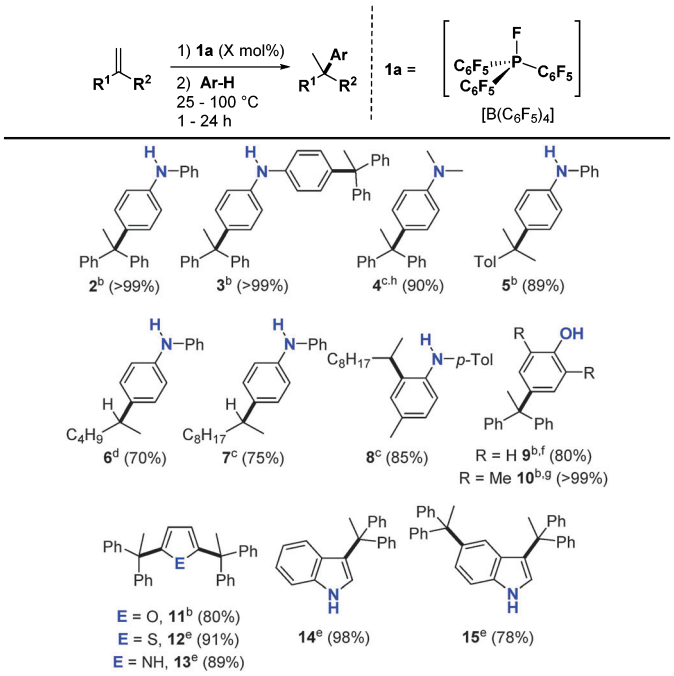
Fig. 1 EPC-catalyzed reactions.

We initially probed the reaction of Ph_2NH with 1.0 equiv. of $Ph_2C{=}CH_2$ in the presence of 1.0 mol% **1a**. The ensuing olefin hydroarylation yielded *p*-$(Ph_2CMe)C_6H_4NHPh$ (**2**) quantitatively after 16 h at 25 °C (Table 1). Under the same mild conditions, Ph_2NH reacted with 2.0 equiv. of $Ph_2C{=}CH_2$ in the presence of **1a** to give the doubly alkylated product, $(p\text{-}(Ph_2CMe)C_6H_4)_2NH$ (**3**) in quantitative yield. A similar reaction using $[(C_6F_5)Ph_2PF][CF_3SO_3]$ **1b** as the catalyst was noticeably slower, with only 75% conversion being achieved after 5 d at 100 °C despite increasing catalyst loading to 12 mol% (see ESI†). The reaction of $PhNMe_2$ with $Ph_2C{=}CH_2$ produced *p*-$(Ph_2CMe)C_6H_4NMe_2$ (**4**) in 90% yield after 24 h at 100 °C in the presence of catalytic **1a**. In a similar fashion, Ph_2NH reacts with styrene, affording mixtures of *p*-alkylated and polymeric products, while the reaction of Ph_2NH and *p*,α-dimethylstyrene yielded exclusively *p*-$(TolCMe_2)C_6H_4NHPh$ (**5**) in 89% isolated yield after 16 h at 25 °C. The unactivated olefins 1-hexene and 1-decene also reacted with Ph_2NH using 3.0 and 5.5 mol% of **1a**, at 100 °C for 24 and 16 h, affording *p*-$(Bu(Me)CH)C_6H_4NHPh$ (**6**) and *p*-$(C_8H_{17}(Me)CH)C_6H_4NHPh$ (**7**) in 70% and 75% yields, respectively. In the case of the hexene reaction,

Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario M5S 3H6, Canada. E-mail: dstephan@chem.utoronto.ca

† Electronic supplementary information (ESI) available: Preparative and spectroscopic characterization. CCDC 1046673 (**9**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5cc03572d

Table 1 EPC-catalyzed Friedel–Crafts-type reactions[a]



[a] Reaction conditions: **1a** in CH_2Cl_2 or C_6H_5Br (10 mL $mmol^{-1}$), aromatic moiety (1.0–2.0 equiv.) and olefin (1.0–5.0 equiv.). [b] X = 1.0 mol%. [c] X = 5.5 mol%. [d] X = 3.0 mol%. [e] X = 1.5 mmol. [f] 5.0 equiv. of PhOH. [g] 2.0 equiv. of 2,6-$Me_2(C_6H_3)OH$. [h] 2.0 equiv. of $PhNMe_2$.

GC-MS analysis of the mixture revealed the presence of minor by-products (5.5%) resulting from alkylation of both arene rings, at either the *ortho* or *para* positions.

Alkylation of *p*-Tol_2NH with 1-decene proceeded more slowly, but selectively generated singly *ortho*-alkylated product, *o*-(C_8H_{17}(Me)CH)-*p*-(Me)C_6H_3NH(*p*-Tol) (**8**), in 50% yield after 4 d at 100 °C while complete conversion was achieved after 12 d. The slower reaction is attributed to steric congestion at the *ortho* position. This notion is further supported by the analogous reaction with $Ph_2C{=}CH_2$, where steric effects preclude hydroarylation at the *ortho* position giving instead 1,1-diphenylethane in 40% yield after 2 d at 100 °C (see ESI†).

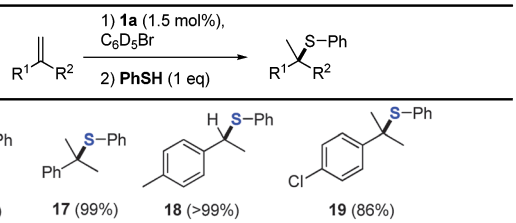
Reaction of phenol (2.0 equiv.) with $Ph_2C{=}CH_2$ affording a 2 : 3 mixture of the cyclodimerized olefin and *p*-(Ph_2CMe)C_6H_4OH (**9**) after 16 h at 25 °C. Nonetheless, the species **9** was isolated in 55% yield and the formulation of **9** was confirmed by X-ray structural analysis (see ESI†). Increasing the amount of PhOH to 5.0 equiv. resulted in an increase in the yield of **9** to 80%. In a similar fashion, the reaction of $Ph_2C{=}CH_2$ with the comparatively electron-rich phenol derivative, 2,6-$Me_2(C_6H_3)OH$ (2.0 equiv.), afforded 90% yield of *p*-(Ph_2CMe)-*o*-$(Me)_2C_6H_2OH$ (**10**). This reactivity was also extended to include furan, thiophene, and pyrrole derivatives, each of which reacted with $Ph_2C{=}CH_2$ over 16 h at 60 °C using 1.5 mol% of **1a** to give the doubly alkylated products, 2,5-$(Ph_2CMe)_2C_4H_2O$ (**11**), 2,5-$(Ph_2CMe)_2C_4H_2S$ (**12**), and 2,5-$(Ph_2CMe)_2C_4H_2NH$ (**13**), respectively, in 78–90% yields. Attempts to obtain mono-alkylated furan analogues were unsuccessful. Nonetheless, the corresponding reaction of indole with 1.0 or 2.0 equiv. of $Ph_2C{=}CH_2$ at 60 °C in the presence of **1a** furnished either the mono-alkylated 3-(Ph_2CMe)$C_4H_2NC_4H_4$ (**14**) or the dialkylated 3,6-$(Ph_2CMe)_2$-$C_4H_2NC_4H_3$ (**15**) in 98 and 78% yields, respectively (Table 1).

To further put this reactivity in perspective, it is important to note that Friedel and Crafts described the electrophilic aromatic substitution between benzene and amyl chloride in the presence of $AlCl_3$,[14a] in 1877. Since then, the methodology has been used extensively both in academic laboratories and in industrial processes.[14b] Despite this long history, modern renditions are motivated by efforts to achieve lower catalyst loadings, milder conditions and eliminate leaving groups, thus providing atom economic catalysis. Compatibility with different functional groups as alkyl anilines remains an issue.[15] In recent highlights, Ingleson *et al.* described the borylation of an extensive scope of arene substrates using borenium reagents to generate pinacol boronate esters.[16] In 2013, the groups of Yamaguchi and Erker reported $B(C_6F_5)_3$-catalyzed cyclization of 1,2-bis(phenylethynyl) benzenes to form dibenzopentalenes,[17] while Bertrand *et al.* recently reported the hydroarylation of alkenes with basic *N*,*N*-dialkylanilines employing a CAAC–gold catalyst[18] although this required 5.0 mol% of the gold species at 145 °C in 24 h to give 84% of **4**.[6] Similarly, using 5.5 mol% $B(C_6F_5)_3$ produced only 22% yield of **4** after 48 h at 100 °C (see ESI†) whereas **1a** afforded the product **4** in 90% yield after 24 h at 100 °C.

Efforts to extend this catalytic procedure to thiophenol resulted exclusively in the Markovnikov hydrothiolation[19] of the olefin. A catalytic amount of *p*-Tol_2NH was observed to prevent the dimerization of $Ph_2C{=}CH_2$. Thus reaction of $Ph_2C{=}CH_2$ with PhSH in the presence of a catalytic amount of **1a** and *p*-Tol_2NH furnished 83% of the product, $Ph_2MeCSPh$ (**16**). In a similar fashion, reaction of α-methylstyrene with PhSH gave the product, $PhMe_2CSPh$ (**17**) in 99% isolated yield. Similarly, the olefins, *m*,α-dimethylstyrene and *p*-chloro-α-methylstyrene reacted with thiophenol in the presence of **1a** to give *p*-TolMe(H)CSPh (**18**, 70%) and *p*-$ClC_6H_4Me_2CSPh$ (**19**, 86%), respectively in 1 h. In these latter two instances, *p*-Tol_2NH was not required (Table 2). Despite this divergent reactivity of thiophenol, the present results provide a mild, metal-free catalytic approach to thioether linkages; a class of compounds of interest as intermediates in Julia-type couplings and S_N2 reactions, as well as their presence in natural products.[20]

The reaction mechanism for both hydroarylation and hydrothiolation processes is thought to proceed by initial activation of the olefin by the EPC catalyst, generating a transient carbocation. Interaction of the nucleophilic *p*-C atom of the aryl group with the incipient carbocation prompts C–C bond formation (Fig. 2). Subsequent proton transfer from the *p*-C atom to the olefinic unit yields the Friedel–Crafts product and liberates the catalyst. This

Table 2 Olefin hydrothiolation



Reaction conditions: 1 h, 25 °C. For **16** and **17**, *p*-Tol_2NH (20 mol%) was added to each reaction to inhibit dimerization of $Ph_2C{=}CH_2$.

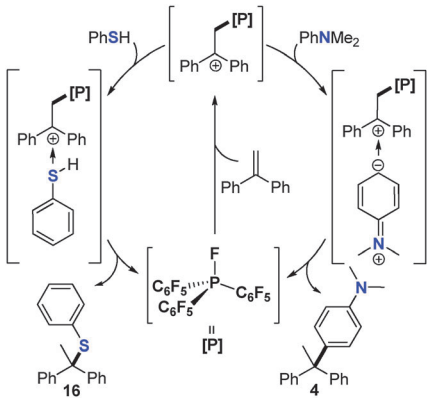


Fig. 2 Proposed mechanisms for EPC-catalyzed hydroarylation and hydrothiolation reactions.

proposition is consistent with our previous observation that **1a** mediates terminal olefin isomerizations in CH_2Cl_2, which was also probed by computational analysis.[18] Further, the observation of trace amounts of the cyclodimerized $Ph_2C{=}CH_2$ further supports the notion that olefin activation initiates C–C coupling. The proposed mechanism is consistent with the regioselective alkylation of 5-membered ring substrates at the 2 and 5 positions. It is also noteworthy that monitoring the reactions by ^{11}B and ^{19}F NMR spectroscopy showed no evidence of degradation of the $[B(C_6F_5)_4]^-$ anion, thus eliminating any role of borane in the Lewis acid catalysis. Further, attempts to monitor the reaction by ^{31}P-NMR spectroscopy were challenged by the low solubility and low loading of **1a**. However, the analogous species $[(C_6F_5)_2(C_6H_5)PF]^+$, was observed to persist during catalysis. In both cases, prolonged heating ultimately affords the corresponding phosphine-oxides, presumably arising from catalyst degradation of the fluorphosphonium cations *via* reaction with the glassware and trace water.

An alternate mechanistic possibility worth considering involves **1a** initiating Brønsted acid-catalysis.[21] However, the reactions are highly selective for *para*-substituted products and there is a dramatic slowing of the reaction when the substantially less Lewis acidic **1b** is used as the catalyst instead of **1a**. Further, the kinetically impeded *ortho*-substitution at *p*-Tol_2NH affording **9** demonstrates the impact of steric factors. Attempts to bring about the reactions of *p*-Tol_2NH with $Ph_2C{=}CH_2$ or 1-decene in the presence of as much as 20 mol% of $(CF_3SO_2)_2NH$ gave less than 5% or 15% of the corresponding products after 1 week at 100 °C (see ESI†). Collectively, these results are contrary to those expected were Brønsted acid-catalysis operative.

Notably, this main group element-catalyzed Friedel–Crafts reaction can be used in conjunction with frustrated Lewis pair-mediated reductions of aniline derivatives.[22] To this end, the Friedel–Crafts product **7** was treated with 1.0 equiv. of $B(C_6F_5)_3$ and 4 atm of H_2, then heated at 100 °C for 2 d, resulting in the concurrent reduction of both *N*-bound aryl groups to produce $[4\text{-}(C_8H_{17}(Me)CH)(C_6H_{10})NH_2Cy][HB(C_6F_5)_3]$ (**20**) as a mixture of stereoisomers in 40% yield (Fig. 3). Although the yield is modest, this reaction exemplifies the potential viability of a completely metal-free process for the substitution and reduction of aniline derivatives to produce substituted cyclohexylamines.[23]

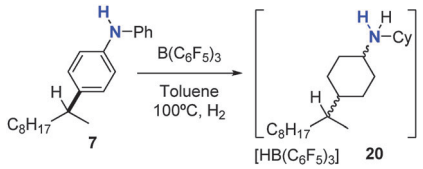


Fig. 3 Hydrogenation of a *p*-substituted aniline.

In summary, the fluorophosphonium salt **1a** catalyzes the hydroarylation of olefins with a variety of aromatic substrates including aromatic amines, phenols, furans, thiophenes, pyrroles, and indoles. In addition, hydrothiolation of olefins is also catalyzed by **1a**. These reactions proceed at moderate temperatures giving products in respectable to high yields. Activation of the olefin by the EPC prompts nucleophilic attack thus providing effective P-based Lewis acid catalysis of these hydroarylation and hydrothiolation reactions. Such EPC catalyzed reactions offer metal-free, atom economical processes that require relatively mild reaction conditions. Continuing work targets the use of phosphonium catalysts in the development of new methodologies in synthesis. In addition, the development of related EPC Lewis acid catalysts for stereoselective protocols are ongoing.

The authors gratefully acknowledge financial support from NSERC of Canada. DWS is grateful for the award of a Canada Research Chair and TM is grateful for an NSERC CGS-D2 postgraduate scholarship.

Notes and references

1 E. M. Leitao, T. Jurca and I. Manners, *Nat. Chem.*, 2013, **5**, 817–829.
2 (*a*) O. Sereda, S. Tabassum and R. Wilhelm, *Top. Curr. Chem.*, 2010, 349–393; (*b*) D. W. Stephan, *Acc. Chem. Res.*, 2015, **48**, 306–316; (*c*) D. W. Stephan and G. Erker, *Chem. Sci.*, 2014, **5**, 2625–2641; (*d*) D. W. Stephan and G. Erker, *Angew. Chem., Int. Ed.*, 2010, **49**, 46–76; (*e*) M. Oestreich, J. Hermeke and J. Mohr, *Chem. Soc. Rev.*, 2015, **44**, 2202–2220.
3 D. Gudat, *Acc. Chem. Res.*, 2010, **43**, 1307–1316.
4 N. Burford and P. J. Ragogna, *ACS Symp. Ser.*, 2006, **917**, 280–292.
5 S. Sasaki, K. Sutoh, F. Murakami and M. Yoshifuji, *J. Am. Chem. Soc.*, 2002, **124**, 14830–14831.
6 O. Guerret and G. Bertrand, *Acc. Chem. Res.*, 1997, **30**, 486–493.
7 (*a*) T. W. Hudnall, Y. M. Kim, M. W. P. Bebbington, D. Bourissou and F. P. Gabbaï, *J. Am. Chem. Soc.*, 2008, **130**, 10890–10891; (*b*) C. R. Wade, I. S. Ke and F. P. Gabbai, *Angew. Chem., Int. Ed.*, 2012, **51**, 478–481.
8 (*a*) O. Sereda, S. Tabassum and R. Wilhelm, *Lewis Acid Organocatalysts*, 2010; (*b*) M. Terada and M. Kouchi, *Tetrahedron*, 2006, **62**, 401–409; (*c*) T. Werner, *Adv. Synth. Catal.*, 2009, **351**, 1469–1481.
9 (*a*) N. Dunn, M. Ha and A. Radosevich, *J. Am. Chem. Soc.*, 2012, **134**, 11330–11333; (*b*) S. M. McCarthy, Y. C. Lin, D. Devarajan, J. W. Chang, H. P. Yennawar, R. M. Rioux, D. H. Ess and A. T. Radosevich, *J. Am. Chem. Soc.*, 2014, **136**, 4640–4650; (*c*) W. Zhao, S. M. McCarthy, T. Y. Lai, H. P. Yennawar and A. T. Radosevich, *J. Am. Chem. Soc.*, 2014, **136**, 17634–17644; (*d*) K. D. Reichl, N. L. Dunn, N. J. Fastuca and A. T. Radosevich, *J. Am. Chem. Soc.*, 2015, **137**, 5292–5295.
10 C. B. Caputo, L. J. Hounjet, R. Dobrovetsky and D. W. Stephan, *Science*, 2013, **341**, 1374–1377.
11 M. Perez, L. J. Hounjet, C. B. Caputo, R. Dobrovetsky and D. W. Stephan, *J. Am. Chem. Soc.*, 2013, **135**, 18308–18310.
12 M. Pérez, Z.-W. Qu, C. B. Caputo, V. Podgorny, L. J. Hounjet, A. Hansen, S. Grimme and D. W. Stephan, *Chem. – Eur. J.*, 2015, **21**, 6491–6500.
13 M. Perez, C. B. Caputo, R. Dobrovetsky and D. W. Stephan, *Proc. Natl. Acad. Sci. U. S. A.*, 2014, **111**, 10917–10921.
14 (*a*) C. Friedel and J. M. Crafts, *J. Chem. Soc.*, 1877, **32**, 725–791; (*b*) V. A. Welch, K. J. Fallon and H.-P. Gelbke, Ethylbenzene, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, 2005.

15 M. Rueping and B. J. Nachtsheim, *Beilstein J. Org. Chem.*, 2010, **6**, 6.
16 A. Del Grosso, P. J. Singleton, C. A. Muryn and M. J. Ingleson, *Angew. Chem., Int. Ed.*, 2011, **50**, 2102–2106.
17 C. Chen, M. Harhausen, R. Liedtke, K. Bussmann, A. Fukazawa, S. Yamaguchi, J. L. Petersen, C. G. Daniliuc, R. Frçhlich, G. Kehr and G. Erker, *Angew. Chem., Int. Ed.*, 2013, **52**, 5992–5996.
18 X. Hu, D. Martin, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2014, **136**, 13594–13597.
19 J. R. Cabrero-Antonino, A. Leyva-Pérez and A. Corma, *Adv. Synth. Catal.*, 2012, **354**, 678–687.
20 (*a*) A. Daemmrich and M. E. Bowden, *Chem. Eng. News*, 2005, 83; (*b*) P. C. B. Page, *Organo-Sulfur Chemistry I & II*, Springer, Berlin, 1999; (*c*) M. E. Peach, in *The Chemistry of the Thiol Group*, ed. S. Patai, John Wiley & Sons, London, 1979; (*d*) *Organic Sulfur Chemistry: Structure and Mechanism*, ed. S. Oae, CRC Press, Boca Raton, 1991.
21 (*a*) G. Kostrab, M. Lovič, A. Turan, P. Hudec, A. Kaszonyi, M. Bajus, J. Uhlár, P. Lehocký and D. Mravec, *Catal. Commun.*, 2012, **18**, 176–181; (*b*) L. L. Anderson, J. Arnold and R. G. Bergman, *J. Am. Chem. Soc.*, 2005, **127**, 14542–14543; (*c*) B. Das, M. Krishnaiah, K. Laxminarayana, K. Damodar and D. N. Kumar, *Chem. Lett.*, 2009, **38**, 42–43.
22 T. Mahdi, Z. M. Heiden, S. Grimme and D. W. Stephan, *J. Am. Chem. Soc.*, 2012, **134**, 4088–4091.
23 K. Eller, E. Henkes, R. Rossbacher and H. Höke, Amines, Aliphatic, *Ullmann's Encyclopedia of Indus-trial Chemistry*, Wiley-VCH, Weinheim, 2005.

