ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2014, **50**, 10038

Received 14th March 2014,
Accepted 15th July 2014

DOI: 10.1039/c4cc01922a

www.rsc.org/chemcomm

Frustrated Lewis pair-mediated C–O or C–H bond activation of ethers†

Michael H. Holthausen,[a] Tayseer Mahdi,[a] Christoph Schlepphorst,[b] Lindsay J. Hounjet,[a] Jan J. Weigand*[b] and Douglas W. Stephan*[ac]

Protocols for the FLP-mediated transformation of ethers are presented. Distinct reaction pathways involving either C–O or C–H bond activation occur depending on the application of oxophilic $B(C_6F_5)_3$ or hydridophilic tritylium ions as the Lewis acid.

The recent renaissance of main-group chemistry has been driven by the discovery that main-group compounds can be used in transformations that are typically the purview of transition metal complexes.[1] In this context, frustrated Lewis pairs (FLPs), which are sterically encumbered Lewis acids and bases, have garnered considerable interest due to their propensity to bind and activate a plethora of small molecules.[2]

A variety of O-based substrates including CO_2, CO, aldehydes, ketones, isocyanates, enones and ynones have been shown to react stoichiometrically with intermolecular P/B FLPs resulting in cooperative addition to the C–O multiple bonds.[2] Similarly, intramolecular P/B FLPs have been shown to bind carbonyl fragments of ketones and aldehydes.[2] The reactions of endiones with intermolecular P/B systems were shown to result in a 1,4 addition product while the corresponding reaction of intramolecular FLPs results in cyclization to give an acetal derivative.[3] Furthermore, such FLP combinations have also been shown to deprotonate alcohols yielding phosphonium-alkoxyborates.[4] While the $(Et_2O)B(C_6F_5)_3$ adduct has been shown to act as an FLP activating H_2,[5] P/B FLPs react with THF to effect C–O bond cleavage resulting in its ring-opening.[6] Such FLP ring-openings have also been applied to a number of other ethers including dioxane, thioxane, and lactides.[7] Gagné and co-workers have exploited related C–O bond cleavage and ring-opening reactions, using the Lewis acid $B(C_6F_5)_3$ in the presence of silanes, to catalytically deoxygenate carbohydrates.[8]

Reactions of a variety of FLPs with cyclic ethers, THF in particular, are well documented.[6,7] The ring-opening of THF was first described by Wittig and Rückert in 1950,[9] who showed C–O bond scission by combination of the anion $[Ph_3C]^-$ and $THF(BPh_3)$ affording $[Ph_3C(CH_2)_4OBPh_3]^-$. Subsequent reports have shown similar THF ring-opening reactions by phosphine/$ZrCl_4(THF)_4$,[10] and other transition metal Lewis acids based on U,[11] Sm,[12] Ti[13] Zr[14] and Mn,[15] as well as other main group systems, like Al Lewis acids[16] and Te nucleophiles.[17] Nonetheless, reactions of acyclic ethers with combinations of Lewis acids and bases have drawn less attention.

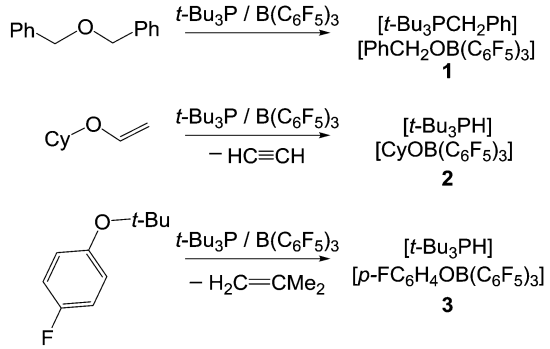
In the present manuscript, we describe the stoichiometric reactions of differing FLPs with ethers. We demonstrate that judicious choice of the components of the FLP altered the chemistry observed. Selective routes to C–O bond activation and unprecedented avenues to α-C–H bond activation in these substrates are described.

The intermolecular FLP, t-Bu_3P and $B(C_6F_5)_3$ reacts with an equivalent of dibenzyl ether, $(PhCH_2)_2O$ to effect heterolytic C–O bond cleavage yielding the salt (**1**) isolated in 86% yield (Scheme 1). The ^1H NMR spectrum reveals two distinct methylene resonances, a singlet at 4.30 ppm assignable to a benzyloxyborate anion and a doublet at 3.71 ppm with two-bond PH coupling of 13 Hz attributable to the benzyl-phosphonium moiety. Collectively, the heteronuclear NMR spectroscopy, elemental analysis and X-ray crystallography are consistent with the formulation of **1** as $[t\text{-}Bu_3PCH_2Ph][PhCH_2OB(C_6F_5)_3]$. The new B–O and P–C bond distances of 1.457(4) and 1.896(3) Å in **1** are typical (Fig. 1).

The corresponding reaction of cyclohexyl-vinyl ether with the P/B FLP gives the salt (**2**) which was isolated in 80% yield. The formation of the phosphonium cation $[t\text{-}Bu_3PH]^+$ was confirmed by the diagnostic doublet in the ^1H NMR spectrum at 5.05 ppm ($^1J_{PH}$ = 427 Hz). Furthermore, the ^{11}B NMR spectrum showed a sharp singlet at −3.45 ppm. These data, together with the resonances in the ^{19}F NMR spectrum, support the presence of

[a] *Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario, Canada M5S 3H6. E-mail: dstephan@chem.utoronto.ca*
[b] *Institut für Anorganische Koordinationschemie, TU Dresden, 01062 Dresden, Germany. E-mail: jan.weigand@tu-dresden.de; Fax: +49-351-83-33126*
[c] *Chemistry Department, Faculty of Science, King Abdulaziz University (KAU), Jeddah 21589, Saudi Arabia*

† Electronic supplementary information (ESI) available: Synthetic and spectroscopic details. CCDC 991775–991782. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc01922a



Scheme 1 Reaction of ethers with the FLP t-$Bu_3P/B(C_6F_5)_3$.

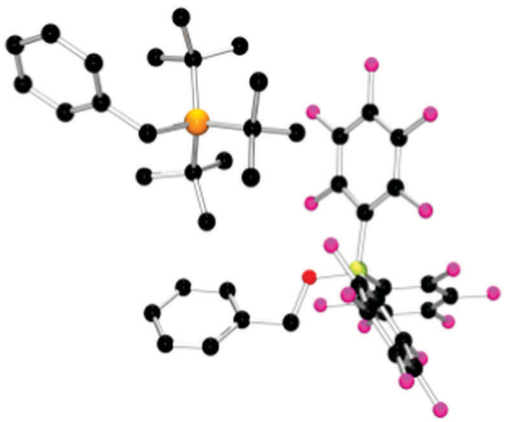


Fig. 1 POV-ray depiction of **1**. C: black, P: orange, O: red, F: pink, B: yellow-green, hydrogen atoms have been omitted for clarity.

the $[C_6H_{11}OB(C_6F_5)_3]^-$ anion and thus the formulation of **2** as $[t\text{-}Bu_3PH][C_6H_{11}OB(C_6F_5)_3]$ with the concurrent loss of acetylene (Scheme 1). The analogous product $[t\text{-}Bu_3PH]$ $[(p\text{-}C_6H_4F)OB(C_6F_5)_3]$ (**3**) was obtained in 88% isolated yield from the reaction of 4-fluorophenyl *tert*-butyl ether with t-Bu_3P and $B(C_6F_5)_3$ (Scheme 1). In this case, the reaction proceeds with the liberation of isobutylene (see ESI†).

The formation of compounds **1–3** is thought to proceed by initial coordination of the ether to the oxophilic Lewis acid $B(C_6F_5)_3$. This is followed by subsequent nucleophilic attack of the Lewis base at the α-carbon leading to alkylation of P or alternatively deprotonation of the β-carbon atom (Scheme 1). In either case this is accompanied by the heterolytic cleavage of a C–O bond.

We were interested in probing the impact of less oxophilic Lewis acids on the reactivity of FLPs with ethers. To that end, we first considered the combination of the Lewis acid $[Ph_3C][X]$ ($X = OSO_2CF_3$ or $B(C_6F_5)_4$) and the Lewis base t-Bu_2PH. Initial combination of these reagents gave the salt $[t\text{-}Bu_2PH\text{-}(C_6H_5)CPh_2][X]$ **4** which was isolated in almost quantitative yield (96% for $X = OSO_2CF_3$).

While the NMR data for **4** is consistent with the formulation of a phosphonium ion featuring a cyclohexadienyl-substituent (see ESI†), this was further confirmed by X-ray crystallography (Fig. 2). The cyclohexadienyl-moiety of **4** is evidenced by the

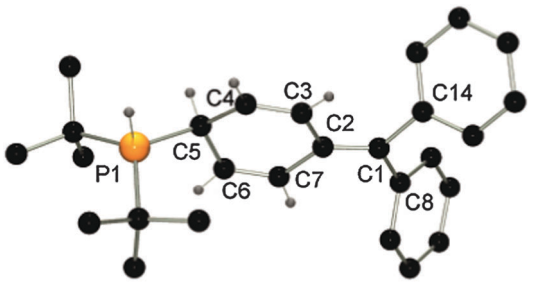


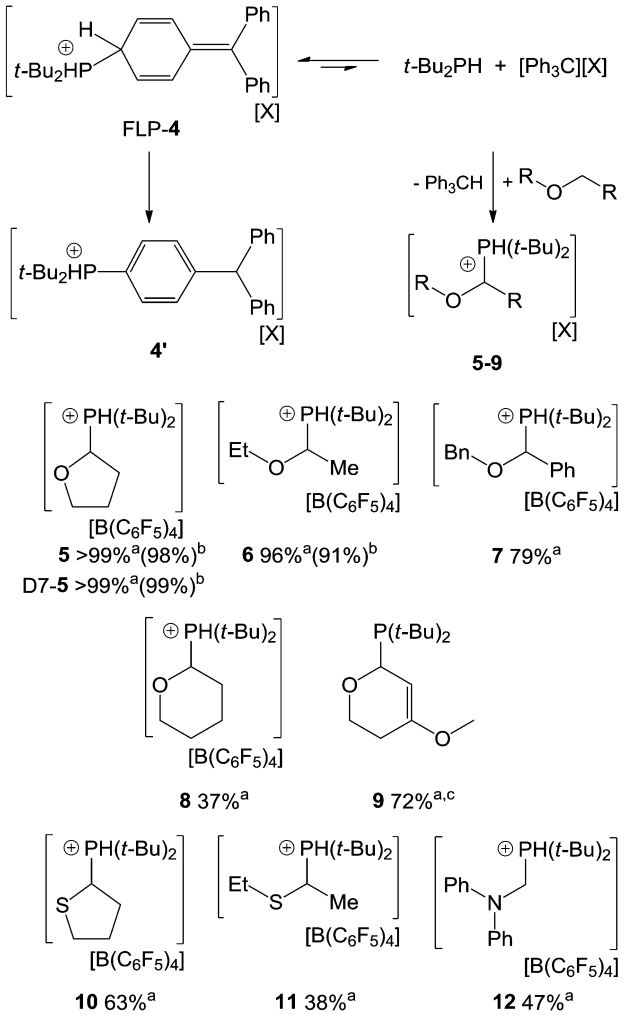
Fig. 2 POV-ray depiction of the cation of **4**. C: black, P: orange, hydrogen atoms on phenyl and t-Bu groups are omitted for clarity.

short C6–C7 and C4–C3 bond distances of 1.332(3) Å and 1.329(3) Å, the C1–C2 bond length of 1.364(3) Å and the sum of angles at C1 of 359.9(6)°. The P–C5 bond distance of 1.837(2) Å is shorter than the $P\text{–}C_{trityl}$ bond length in phosphonium ions of the type $[R_3PCPh_3]^+$ (av. 1.876(4) Å, see ESI†),[18] consistent with the diminished steric crowding in **4**. It is noteworthy that the corresponding reactions of R_2PH (R = Ph, Cy) led to the formation of cations of type $R_2PHCPh_3^+$ (see ESI†), illustrating the impact of steric demand of the phosphine. These latter species are unreactive with ethers. Analogues of **4** have been spectroscopically observed, however, to the best of our knowledge, compound **4** represents the first structurally characterized cyclohexadienyl-phosphonium cation.[19]

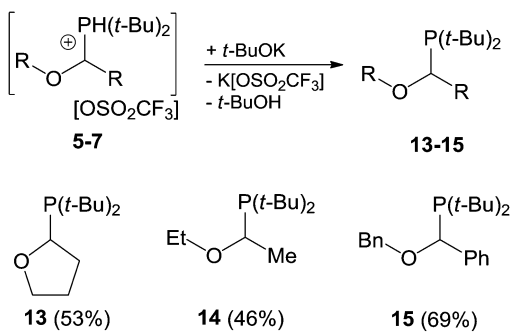
Despite the formation of this phosphonium-cyclohexadienyl cation in **4**, this species behaves as an FLP which reacts with a range of ethers (Scheme 2).

Reacting **4** with THF or THF-d^8 yielded the 2-tetrahydrofuranyl-substituted phosphonium ions **5** or **5**-d^7 in quantitative yield. An additional competition reaction containing THF and THF-d^8 indicates that the dissociation of FLP **4** to $[Ph_3C]^+$ and t-Bu_2PH is the rate determining step in the reaction sequence with ethers (see ESI† for additional information). Subsequently, abstraction of hydride by $[Ph_3C]^+$ from the α-carbon atom of the respective ether generates a transient oxonium ion which is intercepted by t-Bu_2PH. The FLP **4** slowly isomerizes in solution to compound **4′** (see ESI† for details on the mechanism of the isomerization and full characterization of **4′**). Reacting **4** with varying amounts of Et_2O showed that large ether concentrations favour the C–H bond activation pathway. The respective phosphonium ion salt **6** was obtained almost quantitatively when 20 equivalents of Et_2O were employed. Although Bn_2O and tetrahydropyran derivatives were successfully converted to compounds **7–9**, these reactions were accompanied by the formation of considerable amounts of **4′**. Finally, tetrahydrothiophene, diethyl sulfide and *N*-methyldiphenylamine are converted to phosphonium ion salts **10–12** in moderate yields showing that the scope of this synthetic protocol also includes thioethers and amines.

It was of interest to investigate if this method is suitable for the preparation of functionalized phosphines. Thus mixtures containing the OSO_2CF_3-salts of **5–7** were prepared and treated with t-BuOK (Scheme 3). This resulted in deprotonation of the phosphonium ions and afforded the respective phosphines **13–15** which could be isolated by distillation in satisfying yields on a multi-gram scale.



Scheme 2 Isomerization of FLP **4** to **4′**; equilibrium dissociation of **4** to $[Ph_3C][X]$ and *t*-Bu_2PH and compounds **5–12** obtained in the reaction of FLP **4** with (thio)ethers. X = OSO_2CF_3 or $B(C_6F_5)_4$. [a] Yield determined by integration of all resonances in the ^1H and ^{31}P NMR spectra of the reaction mixture. [b] Isolated yield. [c] Obtained as the free phosphine.



Scheme 3 Synthetic route to phosphines **13–15**.

In conclusion, we have uncovered distinct reaction pathways for the FLP-mediated transformation of ethers. Oxophilic $B(C_6F_5)_3$ reacts *via* coordination to the oxygen donor and initiates reaction sequences which involve heterolytic C–O bond cleavage. In contrast, the FLP system **4**, which is based on a hydridophilic tritylium ion, reacts with ethers *via* hydride abstraction and instalment of a phosphoniumyl-substituent on an α-carbon atom. This reaction constitutes a rare example of FLP-mediated C–H bond activation.[20] While previous studies have illustrated the ability of FLPs to effect both ether C–O and aromatic[20b] or allylic[20a] C–H activations, the present results are the first to demonstrate that judicious selection of the Lewis acid/base composition of an FLP provides an avenue for selective reactivity of one class of substrates. We are currently exploring the impact of varying the Lewis acid in the reactivity of FLPs with other substrates and on catalysis.

NSERC of Canada, the German Science Foundation (DFG, WE 4621/2-1) and the ERC (SynPhos 307616) is thanked for financial support. DWS is grateful for the award of a Canada Research Chair. TM is grateful for an NSERC CGS-D. MHH is grateful for a scholarship by the Fonds der Chemischen Industrie.

Notes and references

1 J. G. de Vries and C. J. Elsevier, *The Handbook of homogeneous Hydrogenation*, Wiley-VCH, Weinheim, 2007.
2 (*a*) G. Erker and D. W. Stephan, *Frustrated Lewis Pairs I: Uncovering and Understanding*, Topics in Current Chemistry, 332, Springer Verlag, 2013; (*b*) G. Erker and D. W. Stephan, *Frustrated Lewis Pairs II: Expanding the Scope*, Topics in Current Chemistry 334, Springer Verlag, 2013.
3 B. H. Xu, R. A. A. Yanez, H. Nakatsuka, M. Kitamura, R. Frohlich, G. Kehr and G. Erker, *Chem. – Asian J.*, 2012, **7**, 1347–1356.
4 R. C. Neu, *The Activation of Small Molecules Employing Main Group and Transition Metal Frustrated Lewis Pairs*, thesis dissertation, 2012, pp. 27–28.
5 L. J. Hounjet, C. Bannwarth, C. N. Garon, C. B. Caputo, S. Grimme and D. W. Stephan, *Angew. Chem., Int. Ed.*, 2013, **52**, 7492–7495.
6 G. C. Welch, J. D. Masuda and D. W. Stephan, *Inorg. Chem.*, 2006, **45**, 478–480.
7 B. Birkmann, T. Voss, S. J. Geier, M. Ullrich, G. Kehr, G. Erker and D. W. Stephan, *Organometallics*, 2010, **29**, 5310–5319.
8 L. L. Adduci, M. P. McLaughlin, T. A. Bender, J. J. Becker and M. R. Gagné, *Angew. Chem., Int. Ed.*, 2014, **53**, 1646–1649.
9 G. Wittig and A. Rückert, *Liebigs Ann. Chem.*, 1950, **566**, 101–113.
10 T. L. Breen and D. W. Stephan, *Inorg. Chem.*, 1992, **31**, 4019–4022.
11 (*a*) L. R. Avens, D. M. Barnhart, C. J. Burns and S. D. McKee, *Inorg. Chem.*, 1996, **35**, 537–539; (*b*) M. P. C. Campello, A. Domingos and I. Santos, *J. Organomet. Chem.*, 1994, **484**, 37–46.
12 W. J. Evans, J. T. Leman, J. W. Ziller and S. I. Khan, *Inorg. Chem.*, 1996, **35**, 4283–4291.
13 A. Mommertz, R. Leo, W. Massa, K. Harms and K. Z. Dehnicke, *Z. Anorg. Allg. Chem.*, 1998, **624**, 1647–1652.
14 (*a*) Z. Y. Guo, P. K. Bradley and R. F. Jordan, *Organometallics*, 1992, **11**, 2690–2693; (*b*) M. Polamo, I. Mutikainen and M. Leskelä, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1997, **53**, 1036–1037.
15 M. Gomez-Saso, D. F. Mullica, E. Sappenfield and F. G. A. Stone, *Polyhedron*, 1996, **15**, 793–801.
16 J. P. Campbell and W. L. Gladfelter, *Inorg. Chem.*, 1997, **36**, 4094–4098.
17 (*a*) T. Chivers and G. Schatte, *Eur. J. Inorg. Chem.*, 2003, 3314–3317; (*b*) S. M. Kunnari, R. Oilunkaniemi, R. S. Laitinen and M. Ahlgren, *Dalton Trans.*, 2001, 3417–3418.
18 (*a*) H. Hoffmann and P. Schellenbeck, *Chem. Ber.*, 1966, **99**, 1134–1142; (*b*) J. R. Sanders, *J. Chem. Soc., Dalton Trans.*, 1973, 743–747; (*c*) J. B. Lambert and J.-H. So, *J. Org. Chem.*, 1991, **56**, 5960–5962; (*d*) X. Fang, B. L. Scott, K. D. John, G. J. Kubas and J. G. Watkin, *New J. Chem.*, 2000, **24**, 831–833.
19 (*a*) G. Bidan and M. Genies, *Tetrahedron Lett.*, 1978, **28**, 2499–2502; (*b*) L. Cabrera, G. C. Welch, J. D. Masuda, P. Wei and D. W. Stephan, *Inorg. Chim. Acta*, 2006, **359**, 3066–3071.
20 (*a*) G. Menard and D. W. Stephan, *Angew. Chem., Int. Ed.*, 2012, **51**, 4409–4412; (*b*) K. Groll, S. M. Manolikakes, X. Mollat du Jourdin, M. Jaric, A. Bredihhin, K. Karaghiosoff, T. Carell and P. Knochel, *Angew. Chem., Int. Ed.*, 2013, **52**, 6776–6780 and references therein.

