Synthesis of an oxygen-linked germinal frustrated Lewis pair and its application in small molecule activation†

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Reaction of Mes2P(O)Li with (C6F5)2BCl gave access to an oxygen-linked germinal intramolecular frustrated Lewis pair Mes2P(O)B(C6F5)2 (1). Compound 1 is stable at room temperature and only decomposes when heated to 90 °C. NMR analysis and theoretical analysis revealed the frustrated nature between the boron and phosphorus centers. Compound 1 shows typical frustrated Lewis pair reactivity when treated with dihydrogen, carbon dioxide, alkyne and alken e. The reaction of 1 with isoprene resulted in selective formation of 3,4-phosphoryl/boryl addition product 8.

Introduction

Ever since the groundbreaking discovery by Stephan et al. that an unquenched phosphine/borane pair can activate dihydrogen under ambient conditions, the concept of a “frustrated Lewis pair” (FLP) has been successfully applied in small-molecule activation, organic synthesis and catalysis.7 Mechanism investigations revealed that one of the most prominent features of FLP mediated reactions is that substrates are usually synergistically activated by both the Lewis acid and base centers.7 To enhance such a synergistic effect, the most often employed strategy is to pre-organize Lewis acid and base functionalities through a linker.8 Among a variety of intramolecular FLPs, germinal FLPs in which donor and acceptor sites are separated by one atom have attracted substantial attention because the proximity of their Lewis acid and base centers can facilitate their synergistic reactivities against small molecules. Furthermore, despite such proximity, intramolecular interaction between Lewis acid and base centers in germinal FLPs is largely excluded because of the high constrain of formation of a three-membered ring. Attempts to introduce frequently applied Lewis pair and its application in small molecule catalyst.

Additionally, a few alkylidene-bridged FLPs based on Ga/P,11 B/P12 and Zr/P13 functionalities were reported by Uhl and Erker groups. In spite of the progress in the study of germinal FLPs, the linker is almost exclusively based on carbon. Only very recently, Streubel and coworkers synthesized an anionic oxygen-linked germinal FLP (VI) and investigated its reactivity against CO2.14 Since the nucleophilicity of phosphinite is markedly lower than alkyl- or alkenyl-substituted phosphine, we reasoned that an oxygen-linked germinal FLP containing −B(C6F5)2 and −PMes2 functionalities (1) would be less susceptible to intramolecular nucleophilic substitution, which could render this FLP stable enough for isolation. Herein, we report the synthesis of oxygen-linked germinal FLP 1 and its reactivity against small molecules (Fig. 1).

Results and discussion

Synthesis of 1 was achieved by treatment of Mes2P(O)H with nBuLi and subsequently (C6F5)2BCl in hexane and it can be isolated as a pale yellow oil with 83% yield after workup (Scheme 1). Compound 1 was characterized by multinuclear NMR analysis. The 31P NMR spectrum of 1 showed a resonance at δ 126.4 ppm, similar to that observed for phosphinite Ph2P(O)Me (117 ppm).15 In the 11B NMR spectrum of 1 a broad
A singlet was observed at $\delta$ 42.4 ppm, indicating the existence of a tri-coordinated boron center. This was corroborated by the appearance of signals at $\delta$ 131.4, 148.8, 161.2 ppm in the $^{19}\text{F}$ NMR spectrum of $\text{I}$. The identity of $\text{I}$ was further confirmed by derivatization. Addition of equimolar of pyridine to $\text{I}$ in hexane resulted in quantitative formation of adduct $\text{II}$, which was characterized by X-ray crystal structure analysis. Compound $\text{I}$ is stable at room temperature both in solution and neat form. Upon heating to 90 °C in a toluene solution, $\text{I}$ undergoes intramolecular nucleophilic substitution to a third compound $\text{III}$ (Scheme 1), which was isolated in 36% yield and fully characterized by NMR spectroscopy and X-ray analysis.

To understand the electronic structure of $\text{I}$, DFT (M06-2X) calculation was carried out. In the calculated structure, the P–O–B bond angle is 114° and the distance between the P and B atoms is 2.57 Å (Fig. 2a), which is shorter than the observed intramolecular P–B distance in $\text{tBu}_2\text{PCH}_2\text{B(Fxy1)}_2$ (2.90 Å).

Population analysis suggested that the interaction between the P and B atoms is very weak and the covalent P–B Wiberg bond order is only 0.02. The HOMO of $\text{I}$ mainly corresponds to the lone pair on phosphorus, with some contribution from π orbital of the mesityl substituent (Fig. 2b). The LUMO is largely distributed over the boron center as well as one C$_6$F$_5$ ring and the oxygen linker, indicative of π electron donation from the oxygen atom to the empty p orbital of the boron center (Fig. 2c).

While $\text{I}$ does not react with H$_2$ under 6 bar at room temperature, it reacts with H$_2$ under harsher conditions (60 bar, 50 °C) to afford compound $\text{IV}$ with 58% yield after workup (Scheme 2). Compound $\text{IV}$ can be also independently synthesized from Mes$_2\text{P(O)}\text{H}$ and HB(C$_6$F$_5$)$_2$. Existence of a P–H moiety was confirmed by the appearance of a doublet at $\delta$ 31.5 ppm ($^3$J$_{\text{P–H}}$ = 514 Hz) in the $^{31}\text{P}$ NMR spectrum, with a corresponding doublet at $\delta$ 8.02 ppm ($^3$J$_{\text{P–H}}$ = 514 Hz) observed in the $^1\text{H}$ NMR spectrum. However, both the $^{11}\text{B}$ and $^{11}\text{B}$$^1$H NMR spectra displayed a broad signal at -4.79 ppm, excluding study of the coupling constant with the adjacent H atom. The $^1\text{H}$ NMR spectrum displayed a broad singlet at $\delta$ 4.59 ppm with integration of 1, which was assigned to the BH moiety. The identity of $\text{IV}$ was further validated by X-ray crystal structure analysis (Fig. 3).

Treatment of $\text{I}$ with CO$_2$ (1.8 bar) at room temperature in hexane resulted in formation of a CO$_2$ adduct $\text{V}$, in an analogous way with other germinal FLPs (Scheme 3).$^{15a,b,c,d,e,11,12,13,14}$ $\text{V}$ was characterized by both NMR spectroscopy and X-ray analysis (Fig. 4). $\text{V}$ is stable in nitrobenzene as solid. But unlike germinal B/P FLPs $\text{II}$ and $\text{III}$, the solution of $\text{V}$ in C$_6$D$_6$ slowly released CO$_2$ under N$_2$ atmosphere at room temperature. In a sealed
NMR tube at room temperature, equilibrium was reached after 24 hours and about 25% of 5 was converted to 1.

Reaction of 1 with phenylacetylene in hexane led to addition of both phosphoryl and boryl moieties to the C≡C bond to give 6 in 73% yield (Scheme 4). This is in line with the discovery by Stephan and Erker that FLPs with phosphine moiety of low basicity tend to afford addition products. In the solid structure of 6 (Fig. 5), the distances of B–O and P–O are similar to those observed in tBu3P(μ-O)(μ-C6H4)B(C6F5)2 (P–O 1.546, B–O 1.550 Å) reported by Wagner.

Compound 1 reacted with equimolar of styrene in hexane at room temperature to yield a white precipitate, which was identified as 1,2-boryl/phosphoryl addition product 7 via NMR spectroscopy and X-ray analysis. When 1 was treated with isoprene in hexane, 3,4-phosphoryl/boryl addition product 8 was formed as the only regioisomer, which can be isolated as a white solid in 79% yield (Scheme 5). 8 was characterized by both NMR spectroscopy and X-ray analysis (Fig. 6). This observed regioselectivity is in contrast to previous reports by Stephan and Lerner that activation of dienes with intermolecular FLP tBu3P/B(C6F5)3 or intramolecular FLP di-t-butylphosphaboradibenzofulvene affords predominately 1,4-addition products. It is likely that in the case of intramolecular FLP 1, the favored formation of a five-member ring dictates the observed 3,4-selectivity.

Conclusions

By employing an oxygen atom as the linker, a germinal FLP containing both electrophilic B(C6F5)2 and nucleophilic PMes2 moieties was synthesized for the first time. This intramolecular FLP readily reacts with a series of small molecules, such as H2, CO2, phenylacetylene, styrene and isoprene. Among them, regioselective 3,4-addition to a diene is unprecedented. Current research is focusing on deoxygenation of addition adducts, which might provide a novel way for the synthesis of intramolecular FLPs.
Experimental section

General experimental methods

Solvents were dried by reflux under N2 over sodium or CaH2 and freshly distilled prior to use. Air-sensitive compounds were handled under a N2 atmosphere using standard Schlenk and glovebox techniques. NMR spectra were recorded on Bruker SPECT NMR (400 MHz for 1H, 376 MHz for 19F, 100 MHz for 13C) and Bruker DMAX500 NMR (500 MHz for 1H, 160 MHz for 13C) spectrometers. Most assignments were based on a series of 2D NMR experiments. HRMS analyses were performed at Bruker microTOF II. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre: CCDC 1843771-1843777 (compound 2-8) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif. Mes2P(O)H (Mes = 2,4,6-trimethylphenyl)11 and C12B(C6F3)2 (ref. 22) were prepared as reported.

Synthesis of compound 1

A solution of n-BuLi (2.5 M, 0.80 mL, 2.0 mol) was added to a suspension of Mes2P(O)H (0.57 g, 2.0 mmol) in hexane (8 mL) at 0 °C, affording a pale yellow solution. After stirring for 4 h at room temperature, a solution of C12B(C6F3)2 (0.76 g, 2.0 mmol) in hexane (6 mL) was added at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 12 h. The resulting white slurry was filtered and the filtrate was dried under vacuum affording 1 as a white yellow oil (1.05 g, 81%). 1H NMR (400 MHz, C6D6): δ [ppm] = 6.62 (d, J = 2 Hz, meta-Mes), 2.28 (s, 12H, ortho-CH3), 2.02 (s, 6H, para-CH3). 13C NMR (101 MHz, C6D6): δ [ppm] = 147.9 (dm, J = 248 Hz, ortho-C6F3), 143.2 (dm, J = 257 Hz, meta-C6F3), 137.6 (dm, J = 253 Hz, para-C6F3), 141.3 (d, J = 17 Hz, ortho-Mes), 140.2 (para-Mes), 133.3 (d, J = 28 Hz, ipso-Mes), 130.6 (d, J = 3 Hz, meta-Mes), 22.2 (d, J = 4 Hz, ortho-CH3), 20.9 (para-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = -131.4 (m, ortho-C6F3), -148.8 (t, para-C6F3), -161.2 (m, meta-C6F3). 31P NMR (162 MHz, C6D6): δ [ppm] = 126.4. 11B NMR (160 MHz, C6D6): δ [ppm] = 42.4. HRMS (m/z): calcd for C30H22OPBF10 [M + Na]+: 653.1239, found: 653.1258.

Synthesis of compound 3

A solution of 1 (132 mg, 0.206 mmol) in toluene (1 mL) was heated to 90 °C for 15 h. Then, all volatiles were removed under vacuum. The resulting oil residue was extracted with hexane (2 mL). Afterwards hexane was removed under vacuum affording an oily solid. Another portion of hexane (1 mL) was introduced and an insoluble oil was formed which became crystals after standing at room temperature for 30 min. The supernatant was removed and the crystals were dried under vacuum affording 3 as a white crystalline solid (47 mg, 36%). 1H NMR (400 MHz, C6D6): δ [ppm] = 6.43, 6.27 (each d, J = 2 Hz, para-H), 2.19, 2.05 (each s, 6H, ortho-CH3), 1.84, 1.71 (each s, 3H, para-CH3). 13C NMR (101 MHz, C6D6): δ [ppm] = 145.2, 144.6 (d, J = 3 Hz, meta-Mes), 143.5, 141.8 (d, J = 12 Hz, ortho-Mes), 132.4, 131.5 (d, J = 13 Hz, meta-Mes), 23.1, 21.8 (d, J = 5 Hz, ortho-CH3), 20.9, 20.7 (d, J = 1 Hz, p-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = -129.5 (m, 2F, C6F3), -134.5 (m, 2F, ortho-C6F3), -144.1 (m, 1F, C6F3), -149.5 (br s, 1F, BF), -153.6 (m, 1F, para-C6F3), -158.0 (t, 1F, para-C6F3), -164.6 (m, 2F, meta-C6F3). 31P NMR (162 MHz, C6D6): δ [ppm] = 58.3. 11B NMR (160 MHz, C6D6): δ [ppm] = 8.87. HRMS (m/z): calcd for C60H32OPBF10Na [M + Na]+: 653.1239, found: 653.1258.

Synthesis of compound 4

H2 (60 bar) was introduced to a solution of 1 (324 mg, 0.515 mmol) in hexane (2.5 mL) in an autoclave. The reaction mixture was stirred for 40 h at 50 °C, affording a white precipitate. The supernatant was removed by filtration and the solid was dried under vacuum affording 4 as a white powder (188 mg, 58%). Crystals suitable for X-ray diffraction were grown by slow diffusion of hexane into a solution of 4 in toluene. 1H NMR (400 MHz, C6D6): δ [ppm] = 8.02 (d, 1H, J = 514 Hz, PfH), 6.34 (d, J = 7 Hz, J = 5 Hz, para-Mes), 4.59 (br s, 1H, BF), 2.07 (s, 12H, ortho-CH3), 1.86 (s, 6H, para-CH3). 13C NMR (101 MHz, C6D6): δ [ppm] = 148.4 (dm, J = 240 Hz, ortho-C6F3), 139.9 (dm, J = 247 Hz, meta-C6F3), 137.4 (dm, J = 256 Hz, para-C6F3), 145.0 (d, J = 3 Hz, meta-Mes), 143.1 (d, J = 11 Hz, ortho-Mes), 131.2 (d, J = 12 Hz, meta-Mes), 117.8 (d, J = 107 Hz, ipso-Mes), 21.0 (d, J = 6 Hz, ortho-CH3), 20.9 (d, J = 2 Hz, para-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = -133.9 (m, ortho-C6F3), -159.8 (t, para-C6F3), -165.1 (m, meta-C6F3). 31P NMR (162 MHz, C6D6): δ [ppm] = 31.5. 11B NMR (160 MHz, C6D6): δ [ppm] = -4.79.

Synthesis of compound 5

CO2 (1.8 bar) was introduced to a degassed solution of 1 (551 mg, 0.875 mmol) in hexane (2.5 mL) at room temperature...
and the reaction mixture was stirred for 24 h, affording a white precipitate. The supernatant was removed by filtration and the residue was dried under vacuum affording 5 as a white powder (430 mg, 73%). Crystals suitable for X-ray diffraction were grown from toluene at −30 °C. 1H NMR (400 MHz, C6D6): δ [ppm] = 6.30 (s, 4H, meta-C6F5), 2.19 (s, 12H, ortho-C6H5), 1.79 (s, 6H, para-C6H3). 13C NMR (101 MHz, C6D6): δ [ppm] = 165.9 (d, Jpp-C = 108 Hz, C=C-O), 148.4 (d, Jpp-C = 243 Hz, ortho-C6F5), 141.0 (d, Jpp-C = 253 Hz, meta-C6F5) C6D6, 137.6 (d, Jpp-C = 251 Hz, para-C6F5), 145.7 (para-C6D6) 143.3 (d, Jpp-C = 12 Hz, ortho-Mes), 131.7 (d, Jpp-C = 13 Hz, meta-Mes), 118.0 (d, Jpp-C = 92 Hz, ipso-C6H5) C6D6, 21.8 (d, Jpp-C = 6 Hz, ortho-CH3), 20.9 (para-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = −133.9 (ortho-C6F5), −155.9 (para-C6F5), −163.5 (meta-C6F5). 31P NMR (162 MHz, C6D6): δ [ppm] = 35.0. 11B NMR (160 MHz, C6D6): δ [ppm] = 7.94. HRMS (m/z): calcd for C31H22O3PBF10Na [M + Na]$: 697.1138, found: 697.1123.

Synthesis of compound 6

PhC=CH (120 mg, 1.18 mmol) was added to a solution of 1 (567 mg, 0.900 mmol) in hexane (3 mL) at room temperature, affording a white precipitate. After the reaction mixture was stirred for 17 h, the supernatant was removed by filtration and the solid was dried under vacuum affording 6 as a white powder (480 mg, 73%). Crystals suitable for X-ray diffraction were grown by slow diffusion of hexane into a solution of 6 in toluene. 1H NMR (400 MHz, C6D6): δ [ppm] = 9.01 (d, 1H, Jpp-C = 46 Hz, C=C-H), 7.17 (m, 2H, PhHf), 7.00 (m, 3H, PhHf), 6.40 (d, 4H, Jpp-C = 4 Hz, meta-Mes), 2.10 (s, 12H, ortho-CH3), 1.85 (s, 6H, para-CH3). 13C NMR (101 MHz, C6D6): δ [ppm] = 176.7 (br s, BCF), 147.8 (d, Jpp-C = 241 Hz, ortho-C6F5), 139.9 (d, Jpp-C = 250 Hz, meta-C6F5), 137.1 (d, Jpp-C = 254 Hz, para-C6F5), 144.0 (d, Jpp-C = 3 Hz, para-Mes), 142.7 (d, Jpp-C = 11 Hz, ortho-Mes), 136.7 (d, Jpp-C = 21 Hz, ipso-Ph), 135.2 (d, Jpp-C = 81 Hz, PC=C), 131.5 (d, Jpp-C = 12 Hz, meta-Mes), 129.2 (Ph), 127.5 (d, Jpp-C = 5 Hz, ortho-Ph), 124.9 (d, Jpp-C = 97 Hz, ipso-Mes), 23.0 (d, Jpp-C = 5 Hz, ortho-CH3), 20.8 (d, Jpp-C = 1 Hz, meta-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = −163.5 (m, ortho-C6F5) −159.2 (h, para-C6F5), −164.5 (m, meta-C6F5). 31P NMR (162 MHz, C6D6): δ [ppm] = 68.4 (d, Jpp-C = 46 Hz). 11B NMR (160 MHz, C6D6): δ [ppm] = 2.65. HRMS (m/z): calcd for C31H22O3PBF10Na [M + Na]$: 755.1709, found: 755.1706.

Synthesis of compound 7

PhC≡CH (220 mg, 2.12 mmol) was added to a solution of 1 (1.00 g, 1.59 mmol) in hexane (6 mL) at room temperature, affording a white precipitate. After the reaction mixture was stirred for 15 h, the supernatant was removed by filtration and the solid was dried under vacuum affording 7 as a white powder (890 mg, 76%). Crystals suitable for X-ray diffraction were grown by slow diffusion of hexane into a solution of 7 in CH2Cl2. 1H NMR (400 MHz, C6D6): δ [ppm] = 6.92–6.74 (5H, Ph), 6.42 (d, 2H, Jpp-C = 3 Hz, meta-Mes), 6.32 (br s, 2H, meta-C6H5), 4.76 (dt, 1H, Jpp-C = 13 Hz, Jpp-H = 6 Hz, CH3), 2.96, 1.95 (each m, each 1H, BCF), 2.38–1.84 (18H, Mes-CH3). 13C NMR (101 MHz, C6D6): δ [ppm] = 148.1 (d, Jpp-C = 241 Hz, ortho-C6F5), 139.7 (dm, Jpp-C = 248 Hz, meta-C6F5), 137.5 (dm, Jpp-C = 249 Hz, para-C6F5), 143.8, 143.4, 138.2 (ortho-Mes and para-Mes), 131.7, 131.4 (meta-Mes), 129.1, 128.5, 127.6 (Ph), 51.3 (d, Jpp-C = 46 Hz, PCH), 35.6 (BCH3), 23.5, 22.4, 20.7 (Mes-CH3). 19F NMR (376 MHz, C6D6): δ [ppm] = −133.0 (ortho-C6F5), −159.4 (t, para-C6F5), −164.4 (meta, m-C6F5). 31P NMR (162 MHz, C6D6): δ [ppm] = 82.4 (d, Jpp-H = 39 Hz). 11B NMR (160 MHz, C6D6): δ [ppm] = 3.16. HRMS (m/z): calcd for C33H18OPBF10Na [M + Na]$: 757.1856, found: 757.1865.

Conflicts of interest

There are no conflicts to declare.

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