Frustrated Lewis pairs

DOI: 10.1002/anie.201101051

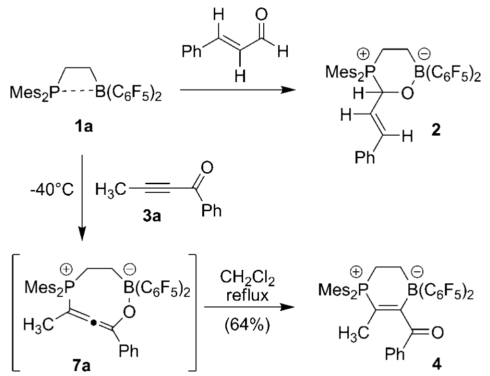
Reaction of Frustrated Lewis Pairs with Conjugated Ynones-Selective Hydrogenation of the Carbon–Carbon Triple Bond

*Bao-Hua Xu, Gerald Kehr, Roland Fröhlich, Birgit Wibbeling, Birgitta Schirmer, Stefan Grimme, and Gerhard Erker**

Dedicated to Professor Siegfried Hünig on the occasion of his 90th birthday

Frustrated Lewis pairs (FLPs), comprised of sterically encumbered strong Lewis acids and Lewis bases, undergo a variety of remarkable reactions.[1] They add to alkenes and alkynes,[2] add to various carbonyl compounds, including carbon dioxide,[3] and undergo unique 1,4-addition reactions to conjugated enynes and diynes to yield zwitterionic cumulene derivatives.[4] Most notably many FLPs split dihydrogen heterolytically, some reversibly, and are able to transfer the resulting P/B or N/B bonded H^+/H^- pair to selected unsaturated substrates.[5] This ability has resulted in the development of a small series of metal-free catalytic hydrogenation processes; some frustrated Lewis pairs are able to serve as hydrogenation catalysts for bulky imines, enamines, or silylenolethers.[6] We have now found a significant extension to the scope of FLPs in the metal-free hydrogenation of organic substrates. This new development is based on observations made upon treating phosphine/borane FLPs with various conjugated ynones.

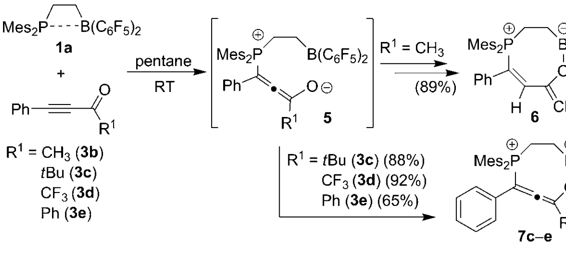
We had shown that the ethylene-bridged intramolecular frustrated P/B Lewis pair **1a**[7] underwent a clean 1,2-addition reaction to the carbonyl group of *trans*-cinnamic aldehyde (to give **2**).[8] The reaction of **1a** with the ynone **3a** takes a different course. At low temperature we observe the formation of the zwitterionic 1,4-addition product **7a**, which upon heating is converted into the isomer **4**, the 1,2-addition product of the FLP **1a** to the carbon–carbon triple bond of **3a** (see Scheme 1). Compound **4** is characterized by typical spectroscopic data [$\delta(^{31}P\{^1H\}) = 7.8$ ppm, $\delta(^{11}B\{^1H\}) = -13.8$ ppm, $\delta(^{13}C(C{=}O)) = 200.9$ ppm (d, $^3J_{PC} = 22.7$ Hz), IR $\tilde{\nu}(C{=}O) = 1643\ cm^{-1}$] and it was characterized by X-ray diffraction (for details see the Supporting Information).



Scheme 1.

The reaction takes a slightly different course when **1a** was treated with the ynone **3b** that formally has the CH_3 and Ph substituents exchanged. The reaction with this enolizable acetylenic ketone gives a product that is derived from 1,4-FLP-addition to the ynone framework coupled with an enolate tautomerization reaction. The eight-membered heterocyclic product **6** shows NMR signals at $\delta = 22.5$ ppm ($^{31}P\{^1H\}$), $\delta = -2.6$ ppm ($^{11}B\{^1H\}$), and $\delta = 4.35, 4.27$ ppm (^1H, $=CH_2$). It was also characterized by X-ray diffraction (for details see the Supporting Information).

The reactions of **1a** with the non-enolizable ynones **3c**–**3e** proceeded with preferential formation of the eight-membered ring products. In these cases 1,4-addition results in the formation of the cyclic allene derivatives **7c**–**7e**, which were isolated in good yields (see Scheme 2). These compounds were characterized by C,H elemental analysis, spectroscopy, and X-ray crystal structure analysis (see Figure 1 for a representative example; for further details see the Supporting Information). Compound **7c** ($R^1 = t$Bu) as a typical example exhibits a non-planar eight-membered core structure (B1–O3 1.501(3) Å, P1–C6 1.835(2) Å) that contains a close to linear allene substructure (C4–C5 1.324(3), C5–C6 1.311(3) Å; angle C4-C5-C6 172.7(2)°). Compound **7c** features a typical allene



Scheme 2.

---

[*] Dr. B.-H. Xu, Dr. G. Kehr, Dr. R. Fröhlich,[+] B. Wibbeling,[+] B. Schirmer,[++] Prof. Dr. S. Grimme,[++] Prof. Dr. G. Erker
Organisch-Chemisches Institut der Universität Münster
Corrensstrasse 40, 48149 Münster (Germany)
Fax: (+49) 251-8336503
E-mail: erker@uni-muenster.de

[+] X-ray crystal structure analyses.

[++] Quantum chemical calculations.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201101051.

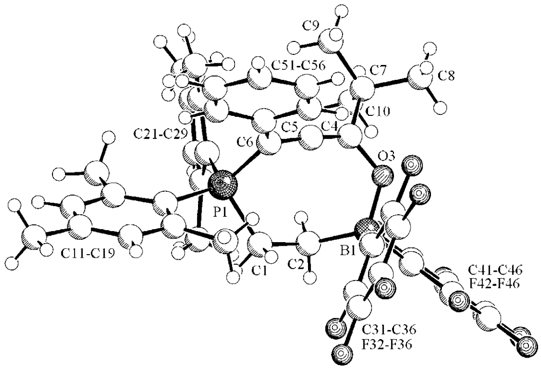


Figure 1. A view of the molecular structure of the cyclic allenic product **7c** ($R^1 = t$Bu).

$^{13}C\{^1H\}$ NMR resonance signals at $\delta = 216.4$ ppm (C5) and $\delta(^{31}P\{^1H\}) = 8.5$ ppm and $\delta(^{11}B\{^1H\}) = 0.7$ ppm.

The analogous reactions can also be carried out with the intermolecular frustrated Lewis pair P*t*Bu$_3$/B(C$_6$F$_5$)$_3$ (**1b**).[5b] Treatment of the FLP **1b** with the ynone **3a** in pentane at room temperature went to completion within 24 h and we isolated the acyclic 1,4-P/B addition product **8a** in over 80% yield. Its NMR spectra show resonance signals at $\delta(^{31}P\{^1H\}) = 46.0$ ppm and $\delta(^{11}B\{^1H\}) = -2.3$ ppm and it shows a typical allenic sp-hybridized C atom ^{13}C NMR resonance at $\delta = 224.9$ ppm. The X-ray crystal structure analysis features the linear central C=C=C moiety (C2–C3 1.322(3) Å, C3–C4 1.302(3) Å, angle C2-C3-C4 176.0 (2)°) to which the O-B(C$_6$F$_5$)$_3$ (C2–O1 1.359(3), O1–B1 1.490(3) Å; angle C2-O1-B1 123.8(2)°) and the P*t*Bu$_3$ units are attached (see Figure 2). The reaction of the FLP **1b** with the ynones **3c** and **3e** proceeded analogously to yield the 1,4-addition products (see Scheme 3), **8c** and **8e**, respectively. Compound **8c** was also characterized by X-ray diffraction (see the Supporting Information).

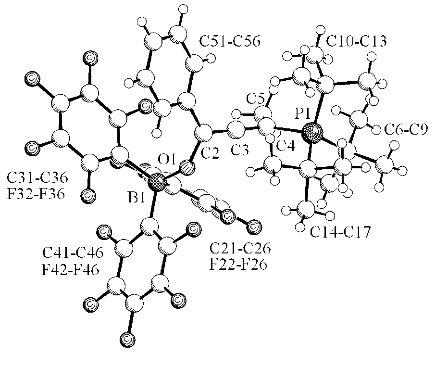
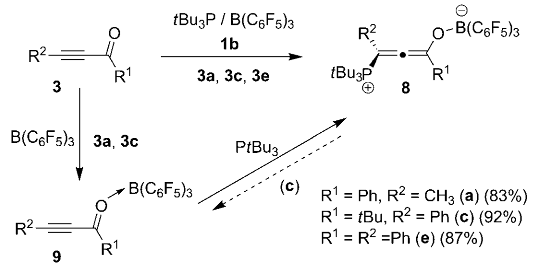


Figure 2. A projection of the molecular structure of compound **8a**.

Treatment of the ynones **3a** and **3c**, respectively, with B(C$_6$F$_5$)$_3$ gave the respective Lewis acid adducts (**9a**, **9c**). They show characteristic NMR signals [**9c**: $^{11}B\{^1H\}$ $\delta = 3.4$ ppm; $^{13}C\{^1H\}$ (C=O-[B]) $\delta = 208.7$ ppm, compared with $\delta = 194.1$ ppm for **3c**[9]]. Compound **9a** was characterized by X-ray diffraction (see Figure 3: B1–O1 1.570(3), O1–C2 1.271(3), C2–C3 1.416(3), C3–C4 1.202(3) Å; angle C2-C3-C4 176.3(3)°)



Scheme 3.

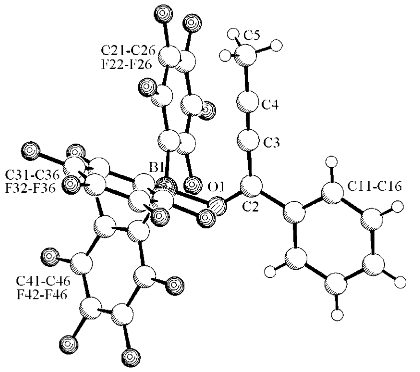


Figure 3. Molecular structure of the B(C$_6$F$_5$)$_3$/ynone adduct **9a**.

The B(C$_6$F$_5$)$_3$/ynone adducts **9a,c** were subsequently treated with P*t*Bu$_3$ to cleanly give the zwitterions **8a,c** in high yield. When brought back into solution (CD$_2$Cl$_2$, room temperature) the compounds **8a** and **8c** showed the expected NMR spectra, but the sterically congested system **8c** showed a pronounced equilibrium between the zwitterion and its precursor compounds **9c** and free *t*Bu$_3$P. This equilibrium is markedly temperature dependent, varying from an **8c**/(**9c**+*t*Bu$_3$P) ratio of approximately 1:1 at room temperature to approximately 10:1 at 233 K (for details see the Supporting Information).

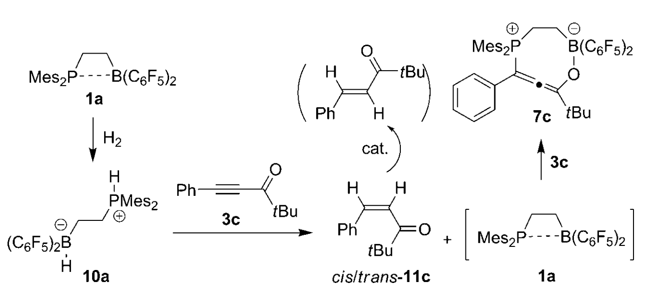
The reactions of the FLPs **1a** and **1b** with the ynones **3** were analyzed by state of the art DFT calculations.[10] Inclusion of solvent effects in the calculations were tested (for details see the Supporting Information) but led only to minor changes in relative reaction energies. These calculations revealed (see Table 1) that the six-membered ring product **4** and the eight-membered exocyclic boron-enolate system **6**, as well as the acyclic systems **8**, are the respective thermodynamically favored isomers, whereas the eight-membered heterocyclic 1,4-P/B addition products **7** are formed in kinetically controlled reactions.

We had shown that the FLP **1a** rapidly activates dihydrogen by heterolytic splitting at ambient conditions to yield the zwitterionic phosphonium/hydridoborate system **10a**.[7] This system then transfers the H$^+$/H$^-$ pair rapidly to the carbon–carbon triple bond of the ynone **3c** to yield the α,β-unsaturated ketone **11** (Scheme 4). Typically, we treated one molar equivalent of the FLP·H$_2$ reagent **10a** with two molar

Table 1: Reaction energies [kcal mol^{-1}] for the formation of products between the ynones **3** and the FLPs **1a** and **1b**, calculated with B2PLYP-D3/def2-TZVP//TPSS-D3/def2-TZVP.

FLP	product[a]	ynone **3a**	**3b**	**3c**	**3d**	**3e**
1a	**4**	*−40.8*	−37.8	−37.6	−38.8	−38.5
	6	–	*−40.5*	–	–	–
	7	−27.9	−28.6	*−31.1*	*−33.1*	*−31.9*
1b	**8**	*−34.2*	–	*−31.3*	–	*−34.9*
	16[b]	−7.5	–	12.5	–	−8.6

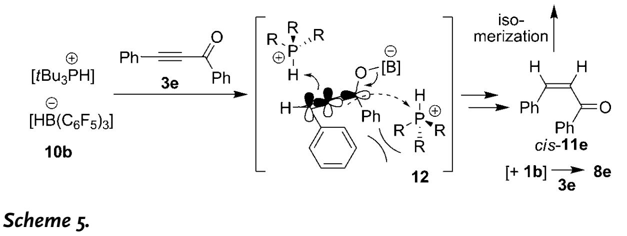
[a] The energy for the structure found in experiments is given in italics. [b] The structure of **16** used for the calculation is analogous to **4**, in which **1b** was added to the triple bond of the ynone substrate (see the Supporting Information).



Scheme 4.

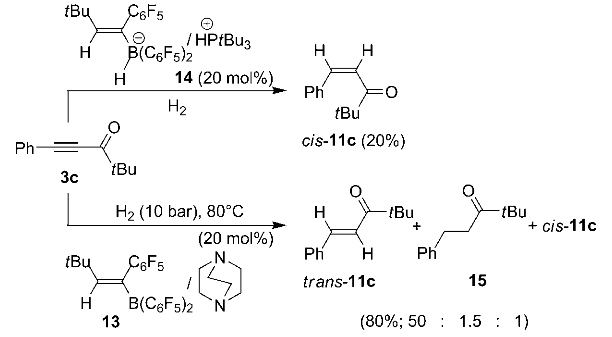
equivalents of the ynone **3c** to isolate a mixture of **11c** (45% yield out of a maximum 50% possible yield) and the eight-membered heterocycle **7c** (40%). Monitoring the progress of the reaction by NMR spectroscopy revealed that initially only the *cis*-enone isomer *cis*-**11c** [^{1}H NMR: $\delta = 6.77$ (=CH$^{\mathrm{Ph}}$), 6.48 (=CH$^{\mathrm{C=O}}$) ppm ($^3J_{\mathrm{HH}} = 13$ Hz)] was formed, which became then subsequently slowly isomerized to *trans*-**11c** [^{1}H NMR: $\delta = 7.64$ (=CH$^{\mathrm{Ph}}$), 7.17 (=CH$^{\mathrm{C=O}}$) ppm ($^3J_{\mathrm{HH}} = 16$ Hz)] under the Lewis acidic reaction conditions.

Treatment of the intermolecular FLP $t\mathrm{Bu_3P/B(C_6F_5)_3}$ with H_2 at ambient conditions gave the salt $[t\mathrm{Bu_3PH}]^+[\mathrm{HB(C_6F_5)_3}]^-$ (**10b**).[5b] This heterolytic hydrogen activation product cleanly transferred the $\mathrm{H^+/H^-}$ pair stoichiometrically to the ynone **3e** with formation of *cis*/*trans*-**11e**. The in situ liberated free FLP **1b** is efficiently trapped by the ynone to give the 1,4-adduct (in this case: **8e**). Again the *cis*-enone product is found initially, which can be explained by a reaction sequence of 1,4-hydridoborate addition to **3e** to give the allenic enolate intermediate (**12**) followed by preferred subsequent protonation by the very bulky $t\mathrm{Bu_3PH^+}$ from the less hindered side (Scheme 5).



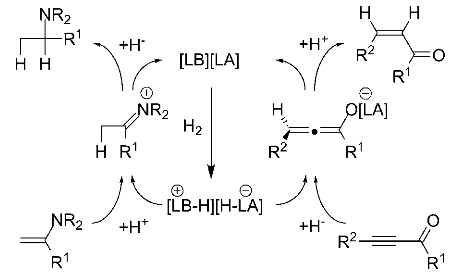
Scheme 5.

Variations of the Lewis acid and Lewis base components eventually led to a catalytic variant of the ynone hydrogenation reaction. Treatment of the FLP **13**/P*t*Bu$_3$ with H_2 gave the salt **14**. This reacted with the ynone **3c** to give the hydrogenation product *cis*-**11c** in a stoichiometric reaction, even under a hydrogen atmosphere. However, employing the FLP **13**/DABCO (20 mol%) resulted in catalytic hydrogenation of **3c** at elevated temperature (80 °C, 10 bar H_2, 48 h) to yield the enone *trans*-**11c** as the major product admixed with minor amounts of *cis*-**11c** and the saturated ketone **15** (for the result of a typical experiment see Scheme 6).[11]



Scheme 6.

Frustrated Lewis pairs have been known to be metal-free catalyst for the hydrogenation of enamines, dienamines, silylenolethers, bulky imines, and related compounds.[1,6] All of these reactions probably proceed by a reaction sequence characterized by initial protonation of the organic substrate followed by hydride transfer to the resulting reactive cationic species.[12] From this investigation and a related reaction studied by Soós et al,[13] there is now increasing evidence that FLP induced hydrogenation can also be carried out with α,β-unsaturated carbonyl compounds. The FLP reduction of the activated carbon–carbon triple bonds probably follows a reversed sequence which is initiated by hydride addition to the β position of the substrate with subsequent protonation of the resulting boron–enolate intermediate (see Scheme 7).



Scheme 7. LA: Lewis acid, LB: Lewis base.

These results indicate that the potential applications frustrated Lewis pair chemistry are increasing steadily. It is going beyond the mere activation of small molecules towards applications in a broad range of fields of chemistry.

Experimental Section

General procedure for **4**, **6**, and **7**: $Mes_2PCH{=}CH_2$ (100 mg, 0.34 mmol) and $HB(C_6F_5)_2$ (117 mg, 0.34 mmol) were dissolved in pentane (6 mL) and stirred for 15 min. A solution of ynone (**3**) (0.34 mmol) in CH_2Cl_2 (1 mL) was added at room temperature. After the reaction mixture had been stirred for 24 h, the solid was isolated by cannula filtration and washed with cold pentane. **4** (after reflux (CH_2Cl_2) for 4 h): yield 64%; elemental analysis (%) calcd for $C_{42}H_{34}BF_{10}OP{\cdot}0.5\,C_5H_{12}$: C 64.98, H 4.90; found: C 65.19, H 4.33; NMR $^{31}P\{^1H\}$: $\delta = 7.8$ ppm; $^{11}B\{^1H\}$: $\delta = -13.8$ ppm; $^{13}C\{^1H\}$ (C=O): $\delta = 200.9$ ppm. **6**: yield 89%; elemental analysis (%) calcd for $C_{42}H_{34}BF_{10}OP$: C 64.14, H 4.36; found: C 63.32, H 4.22; NMR $^{31}P\{^1H\}$: $\delta = 22.5$ ppm; $^{11}B\{^1H\}$: $\delta = -2.6$ ppm; $^{13}C\{^1H\}/^1H$ (=CH): $\delta = 153.1/6.55$, (=CH_2) 102.8/4.35, 4.27 ppm. **7c**: yield 88%; elemental analysis (%) calcd for $C_{45}H_{40}BF_{10}OP$: C 65.23, H 4.87; found: C 64.53, H 4.80; NMR $^{31}P\{^1H\}$: $\delta = 8.5$ ppm; $^{11}B\{^1H\}$: $\delta = 0.7$ ppm; $^{13}C\{^1H\}$ (=C=): $\delta = 216.4$ ppm.

General procedure for **8**: A pentane (3 mL) solution of $PtBu_3$ (40 mg, 0.20 mmol) was added to a mixture of $B(C_6F_5)_3$ (100 mg, 0.20 mmol) and the respective ynone **3** (0.20 mmol) in CH_2Cl_2 (4 mL). After stirring the reaction mixture for 24 h, the solid was isolated by cannula filtration and washed with cold CH_2Cl_2. **8e**: yield 87%, HRMS (ESI) exact mass for $[M+Na]^+$ ($C_{45}H_{37}BF_{15}PONa$): calcd m/z 943.2329, found 943.2311; NMR $^{31}P\{^1H\}$: $\delta = 41.5$ ppm; $^{11}B\{^1H\}$: $\delta = -2.3$ pm; $^{13}C\{^1H\}$ (=C=): $\delta = 226.5$ ppm.

General procedure for **11**: **10** (0.2 mmol) and ynone **3** (0.4 mmol, 2 equiv) were dissolved in CH_2Cl_2 (10 mL). The solution was stirred 2 h at room temperature. Afterwards, the solvent (CH_2Cl_2) was removed under vacuum and the residue was extracted with pentane (3 × 20 mL) to give the P/B products as white solids. The organic phase was separated and the solvent was removed under reduced pressure. Purification by chromatography on silica gel provided enone **11**. Reaction of **10a** with **3c** afforded **7c**: (40%) and *cis*-**11c** (45%); Reaction of **10b** with **3e** afforded after heating to 50 °C for 30 min **8e** (36%) and **11e** (40%, the ratio of *cis*/*trans* is 1.3:1).

For additional experimental details see the Supporting Information.

Received: February 11, 2011
Revised: April 5, 2011

Keywords: 1,4-additions · allenes · frustrated Lewis pairs · hydrogenations · ynones

---

[1] D. W. Stephan, G. Erker, *Angew. Chem.* **2010**, *122*, 50–81; *Angew. Chem. Int. Ed.* **2010**, *49*, 46–76.

[2] a) C. M. Mömming, S. Frömel, G. Kehr, R. Fröhlich, S. Grimme, G. Erker, *J. Am. Chem. Soc.* **2009**, *131*, 12280–12289; b) T. Voss, C. Chen, G. Kehr, E. Nauha, G. Erker, D. W. Stephan, *Chem. Eur. J.* **2010**, *16*, 3005–3008.

[3] a) C. M. Mömming, E. Otten, G. Kehr, R. Fröhlich, S. Grimme, D. W. Stephan, G. Erker, *Angew. Chem.* **2009**, *121*, 6770–6773; *Angew. Chem. Int. Ed.* **2009**, *48*, 6643–6646; b) A. E. Ashley, A. L. Thompson, D. O'Hare, *Angew. Chem.* **2009**, *121*, 10023–10027; *Angew. Chem. Int. Ed.* **2009**, *48*, 9839–9843; c) A. Berkefeld, W. E. Piers, M. Parvez, *J. Am. Chem. Soc.* **2010**, *132*, 10660–10661.

[4] C. M. Mömming, G. Kehr, B. Wibbeling, R. Fröhlich, B. Schirmer, S. Grimme, G. Erker, *Angew. Chem.* **2010**, *122*, 2464–2467; *Angew. Chem. Int. Ed.* **2010**, *49*, 2414–2417.

[5] a) G. C. Welch, R. R. S. Juan, J. D. Masuda, D. W. Stephan, *Science* **2006**, *314*, 1124–1126; b) G. C. Welch, D. W. Stephan, *J. Am. Chem. Soc.* **2007**, *129*, 1880–1881; c) V. Sumerin, F. Schulz, M. Atsumi, C. Wang, M. Nieger, M. Leskelä, T. Repo, P. Pyykkö, B. Rieger, *J. Am. Chem. Soc.* **2008**, *130*, 14117–14119.

[6] a) P. A. Chase, G. C. Welch, T. Jurca, D. W. Stephan, *Angew. Chem.* **2007**, *119*, 8196–8199; *Angew. Chem. Int. Ed.* **2007**, *46*, 8050–8053; b) P. Spies, S. Schwendemann, S. Lange, G. Kehr, R. Fröhlich, G. Erker, *Angew. Chem.* **2008**, *120*, 7654–7657; *Angew. Chem. Int. Ed.* **2008**, *47*, 7543–7546; c) H.-D. Wang, R. Fröhlich, G. Kehr, G. Erker, *Chem. Commun.* **2008**, 5966–5968; d) D. Chen, J. Klankermayer, *Chem. Commun.* **2008**, 2130–2131; e) D. Chen, Y.-T. Wang, J. Klankermayer, *Angew. Chem.* **2010**, *122*, 9665–9668; *Angew. Chem. Int. Ed.* **2010**, *49*, 9475–9478.

[7] P. Spies, G. Erker, G. Kehr, K. Bergander, R. Fröhlich, S. Grimme, D. W. Stephan, *Chem. Commun.* **2007**, 5072–5074.

[8] P. Spies, G. Kehr, K. Bergander, B. Wibbeling, R. Fröhlich, G. Erker, *Dalton Trans.* **2009**, 1534–1541.

[9] R. J. Cox, D. J. Ritson, T. A. Dane, J. Berge, J. Charmant, A. Kantacha, *Chem. Commun.* **2005**, 1037–1039.

[10] a) B2PLYP: S. Grimme, *J. Chem. Phys.* **2006**, *124*, 034108; b) def2-TZVP: F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305; c) TPSS: J. Tao, J. P. Perdew, V. N. Staroverov; G. E. Scuseria, *Phys. Rev. Lett.* **2003**, *91*, 146401; d) D3 dispersion correction: S. Grimme, J. Antony, S. Ehrlich; H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; e) TURBOMOLE, version 6.0: R. Ahlrichs et al., Universität Karlsruhe **2009**, see http://www.turbomole.com.

[11] Compound **13** is readily available by a simple 1,1-carboboration of *tert*-butylacetylene with $B(C_6F_5)_3$ as recently described by us: a) C. Chen, F. Eweiner, B. Wibbeling, R. Fröhlich, S. Senda, Y. Ohki, K. Tatsumi, S. Grimme, G. Kehr, G. Erker, *Chem. Asian J.* **2010**, *5*, 2199–2208; b) C. Chen, G. Kehr, R. Fröhlich, G. Erker, *J. Am. Chem. Soc.* **2010**, *132*, 13594–13595; c) C. Chen, T. Voss, R. Fröhlich, G. Kehr, G. Erker, *Org. Lett.* **2011**, *13*, 62–65; see also: d) C. Jiang, O. Blacque, H. Berke, *Organometallics* **2010**, *29*, 125–133.

[12] S. Schwendemann, T. A. Tumay, K. V. Axenov, I. Peuser, G. Kehr, R. Fröhlich, G. Erker, *Organometallics* **2010**, *29*, 1067–1069.

[13] G. Erös, H. Mehdi, I. Pápai, T. A. Rokob, P. Király, G. Tárkányi, T. Soós, *Angew. Chem.* **2010**, *122*, 6709–6713; *Angew. Chem. Int. Ed.* **2010**, *49*, 6559–6563.