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Cyclobutene formation by borane catalyzed [2+2] cycloaddition of a vinylphosphane with conjugated ynones

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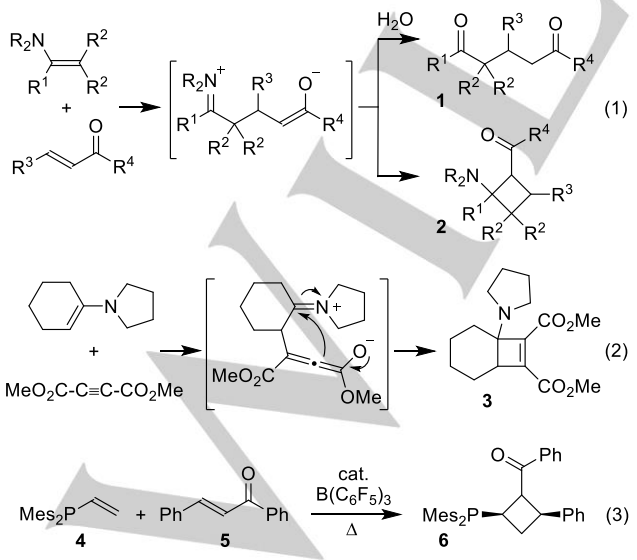
Supporting information for this article is given via a link at the end of the document.

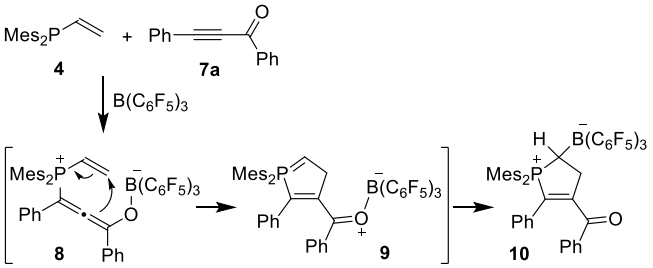
Abstract: Dimesityl(vinyl)phosphane reacts with benzoyl(phenyl)-acetylene under $B(C_6F_5)_3$ catalysis to give the formal [2+2] cyclo-addition product 1-benzoyl-3-dimesitylphosphino-2-phenylcyclo-butene **11a**.

Enamines are important reagents in organic synthesis. They undergo carbon-carbon coupling reactions with a variety of organic carbonyl compounds and related systems (Stork reaction).[1,2] Enamine carbon nucleophiles add to the Michael position of α,β-unsaturated ketones.[1b] Ultimately, this leads either to 1,5-dicarbonyl products or to substituted cyclobutane derivatives, depending on the substituent pattern of the system.[3] There are also a few reports about the reaction of enamines with electron deficient acetylenes.[4] The reaction of pyrrolidino-cyclo-hexene with dimethyl acetylenedicarboxylate is a typical example. It yields the cyclobutene derivative **3**, which undergoes subsequent ring opening upon heating to give the isomeric cyclooctadiene derivative.[5]



Scheme 1. Variants of the Stork reaction.

We had recently described a phosphane analogue of the enamine Stork reaction: treatment of the "enphosphane" **4** with chalcone (**5**) gave the respective cyclobutane derivative **6** in a $B(C_6F_5)_3$ catalyzed reaction (10 mol% cat., 50 °C) [eqn. (3) in Scheme 1].[6] In view of the reported variants of the enamine Stork reaction with acetylenic esters [eqn. (2) in Scheme 1],[4,5] it was tempting to also react the enphosphane **4** with carbonyl substituted alkynes. In this sense we had reacted the bulky vinylphosphane **4** with a small series of conjugated ynones. We reported that in the presence of a stoichiometric quantity of the strong borane Lewis acid $B(C_6F_5)_3$ this formally resulted in the generation of a [3+2] cycloaddition product **9** that had become trapped by $B(C_6F_5)_3$ to form the stable derivative **10**, which we isolated (Scheme 2).[7] We have now carried out the reaction of the Mes_2P-vinyl phosphane (**4**) with a small series of conjugated ynones in the presence of a *catalytic* amount of $B(C_6F_5)_3$ and found a different preferred product formation, namely of substituted cyclobutene derivatives. This will be described in this account.



Scheme 2. Formal enephosphane plus ynone [3+2] cycloaddition in the presence of stoichiometric $B(C_6F_5)_3$.

Thermolysis of a mixture of the compounds **4** and **7a** (in CD_2Cl_2 solution, 60 °C, 24 h) in an autoclave did not result in any reaction. The compound mixture remained unchanged under these conditions. However, in the presence of 10 mol% of $B(C_6F_5)_3$ a catalyzed reaction between the bulky vinylphosphane **4** and the conjugated ynone **7a** took place under otherwise the same conditions. Workup gave the cyclobutene derivative **11a** that we isolated as a solid in 85% yield. The product **11a** was

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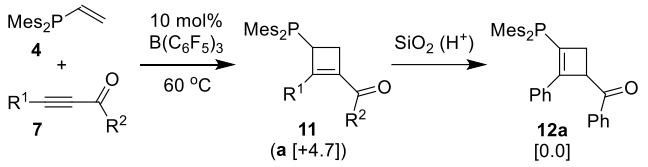
characterized by spectroscopy and by X-ray diffraction. Single crystals suited for the X-ray crystal structure analysis were obtained from dichloromethane/pentane at -35 °C by the diffusion method. The structure (Figure 1) shows the close to planar cyclobutene core. The carbon-carbon double bond bears the benzoyl substituent at its carbon atom C3 and the phenyl substituent at C4. This phenyl substituent is oriented close to coplanar with the four-membered ring plane. The C5=O1 carbonyl group in compound **11a** is markedly rotated away from conjugation with the adjacent C3=C4 carbon-carbon double bond (θ C4-C3-C5-O1: 38.1(4)°). Carbon atom C1 has the -$PMes_2$ substituent bonded. The coordination geometry at the phosphorus atom is trigonal pyramidal.



a: $R^1 = R^2$ = Ph; **b**: R^1 = p-tolyl, R^2 = Ph; **c**: R^1 = Ph, R^2 = *p*-C_6H_4-^{t}Bu

Scheme 3. $B(C_6F_5)_3$ catalyzed cyclobutene formation [with DFT calculated relative Gibbs energies $\Delta G(298)_{solv}$ in dichloromethane solution in kcal mol^{-1}].

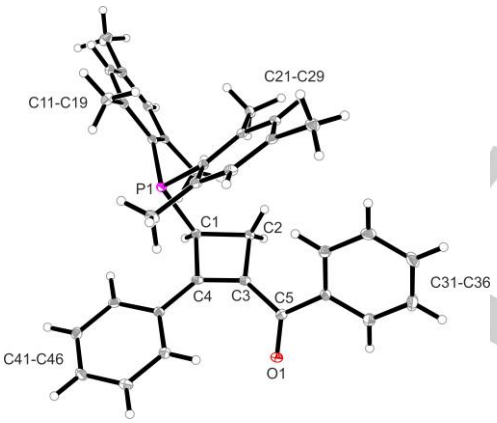


Figure 1. A view of the molecular structure of the cyclobutene derivative **11a** in the crystal. (with unsystematic atom numbering scheme, thermal ellipsoids shown at 30% probability). Selected bond lengths (Å) and angles (°): C1-C2 1.571(3), C2-C3 1.522(3), C3-C4 1.352(3), C4-C1 1.528(3), C3-C5 1.484(3), C5-O1 1.230(3), P1-C1 1.869(2), P1-C11 1.847(2), P1-C21 1.852(2), $\Sigma P1^{CCC}$ 319.3, C3-C4-C41-C46 13.0(4).

In solution compound **11a** shows the single [P]-CH ^{1}H NMR signal at δ 4.74 and the respective resonances of the adjacent pair of methylene hydrogen atoms at δ 3.38 and 3.00. The ^{13}C NMR spectrum shows the signals of the olefinic ring carbon atoms at δ 157.1 and δ 136.1 [CH at δ 38.2 ($^1J_{PC}$ = 26.7 Hz), CH_2 at δ 37.1 ($^2J_{PC}$ = 16.4 Hz)]. The carbonyl carbon resonance was located at δ 190.6. There are the ^{1}H/^{13}C NMR signals of the pair of phenyl groups. Compound **11a** features a ^{31}P NMR signal at δ −12.3.

The substituted ynones **7b** (R^1 = p-tolyl, R^2 = phenyl) and **7c** (R^1 = phenyl, R^2 = p-^{t}butylphenyl) reacted with dimesityl(vinyl)-phosphane (**4**) under analogous conditions to give the substituted cyclobutene derivatives **11b** and **11c**, respectively (Scheme 3). Both were isolated in ca. 70% yield after removal of the solvent and washing with pentane. We found for the example **11c** that the isolated amorphous solid contained small amounts of as yet unidentified fluoro-containing impurities. Both the compounds **11b** and **11c** were characterized spectroscopically and by X-ray crystal structure analysis (see the Supporting Information for the respective data and the depicted NMR spectra and molecular structures).

In an attempt to further purify the cyclobutene derivative **11a** ($R^1 = R^2$ = phenyl) by column chromatography (silica gel, dichloro-methane/pentane ca. 1:2) we isolated its isomer **12a** in 80% yield. We assume an acid catalyzed isomerization of compound **11a** to **12a** on the column.

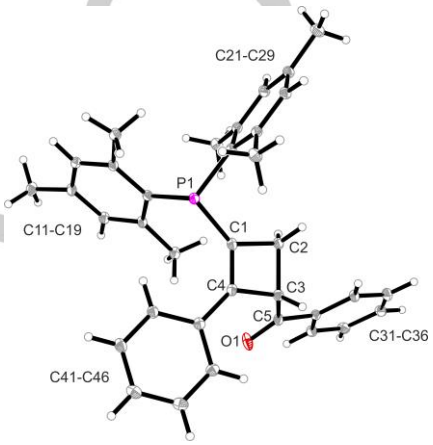


Figure 2. Molecular structure of compound **12a** (with unsystematic atom numbering scheme, thermal ellipsoids are shown at 15% probability). Selected bond lengths (Å) and angles (°): C1–C2 1.523(4), C2-C3 1.568(4), C3-C4 1.522(4), C4-C1 1.359(4), C3-C5 1.513(4), C5-O1 1.223(3), P1-C1 1.803(3), P1-C11 1.843(3), P1-C21 1.846(3), $\Sigma P1^{CCC}$ 320.0, C4-C1-P1-C11 -82.2(3), C4-C1-P1-C21 163.2(3), C1-C4-C41-C42 9.8(5), C1-C2-C3-C4 -0.5(2).

Compound **12a** was characterized by an X-ray crystal structure analysis. In the solid state compound **12a** shows a central four-membered carbocycle (Figure 2). It contains a carbon-carbon double bond that has the phosphanyl group and the phenyl substituent attached. Consequently, now a sp^3-carbon atom of the ring bears the benzoyl substituent. The Mes_2P-substituent has the P1–C21 vector oriented close to in plane with the four-membered ring, whereas the other (P1–C11) is oriented toward an orthogonal arrangement. The coordination geometry at phosphorus is trigonal-pyramidal. The phenyl substituent at the sp^2-C ring carbon atom is oriented close to in conjugation with the C1=C4 π system.

In solution (CD_2Cl_2, 299 K) compound **12a** shows a ^{31}P NMR resonance at δ −43.4. It features ^{13}C NMR signals of the four-membered core at δ 154.1 ($^2J_{PC}$ = 27.6 Hz), δ 139.4 ($^1J_{PC}$ = 32.6 Hz), δ 47.4 ($^3J_{PC}$ = 12.9 Hz) and δ 37.1 ($^2J_{PC}$ = 4.8 Hz) and the carbonyl carbon resonance at δ 198.1. The P-coupled ABX pattern of the ring -CH_2-CHCO unit is found at δ 2.88/2.50 (CH_2) and δ 4.89. A DFT analysis (PW6B95-D3/def2-TZVP+COSMO-RS)[8] has confirmed that compound **12a** is thermodynamically favored over its precursor **11a** by ΔG(298K) = 4.7 kcal/mol in CH_2Cl_2 (see the Supporting Information for details of the computational analysis).

We note that the phospha-Stork reaction between a bulky vinylphosphane and a conjugated enone yields cyclobutane derivatives that have the carbonyl functionality and the

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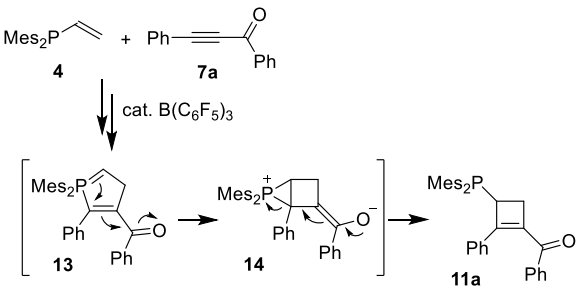
phosphanyl substituent 1,2-positioned at the four-membered carbocyclic framework. In contrast, the here described borane catalyzed carbon-carbon coupling reactions between vinylphosphane Mes_2P-CH=CH_2 and the conjugated ynones **7** give rise to the formation of cyclobutene derivatives with the Mes_2P- and the -COAr substituents being 1,3-positioned at the central ring system.[6a] The products **11** were, consequently, not formed by means of a variant of the phospha-Stork reaction.



Scheme 4. Mechanistic rationalization of the $B(C_6F_5)_3$ catalyzed formation of the cyclobutene derivatives **11**.

We assume a pathway that is initiated by a reaction sequence as it is taking place in the reaction between **4** and **7** with stoichiometric $B(C_6F_5)_3$, namely by a reaction that is governed by attack of the phosphane nucleophile at the "Michael" position of the ynone.[9] Subsequent ring closure will then lead to the ylidic[10] intermediate **13**. In the stoichiometric reaction (Scheme 2) this is then trapped by addition of the $B(C_6F_5)_3$ electrophile to the nucleophilic ylide carbon atom to form **10**. In the catalytic reaction this pathway is apparently precluded. The P-ylide nucleophile may then attack the adjacent enone moiety intramolecularly. Ring opening in the resulting reactive intermediate **14** by cleavage of the proximal P-C bond directly leads to the observed products **11** (Scheme 4). It seems that under the influence of a strongly electrophilic borane vinylphosphanes can react either as carbon or as phosphorus nucleophiles, depending on the detailed overall conditions. In any case these reactions are taking place under frustrated Lewis pair conditions which precludes deactivating P/B Lewis pair adduct formation.

Keywords: phosphorus • boron • cyclobutene • ynone • catalysis

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[1] a) G. Stork, R. Terrell, J. Szmuszkovicz, *J. Am. Chem. Soc.* **1954**, *76*, 2029; b) G. Stork, S. R. Dowd, *J. Am. Chem. Soc.* **1963**, *85*, 207.

[2] a) P. W. Hickmott, *Tetrahedron* **1982**, *38*, 1975; b) P. W. Hickmott, *Tetrahedron* **1982**, *38*, 3363.

[3] K. C. Brannock, A. Bell, R. D. Burpitt, C. A. Kelly, *J. Org. Chem.* **1961**, *26*, 625.

[4] a) C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, P. Strachan, *J. Org. Chem.* **1963**, *28*, 3134; b) G. A. Berchtold, G. F. Uhlig, *J. Org. Chem.* **1963**, *28*, 1459; c) D. Becker, L. R. Hughes, R. A. Raphael, *J. Chem. Soc., Chem. Commun.* **1974**, 430; d) N. Tunoglu, N. Uludag, *Org. Prep. Proced. Int.* **1997**, *29*, 541; e) N. Uludag, O. Asutay, M. Yakup, *Asian J. Chem.* **2014**, *26*, 971.

[5] K. C. Brannock, R. D. Burpitt, V. W. Goodlett, J. G. Thweatt, *J. Org. Chem.* **1963**, *28*, 1464.

[6] a) Y. Hasegawa, C. G. Daniliuc, G. Kehr, G. Erker, *Angew, Chem. Int. Ed.* **2014**, *53*, 12168; b) Y. Hasegawa, G. Kehr, S. Ehrlich, S. Grimme, C. G. Daniliuc, G. Erker, *Chem. Sci.* **2014**, *5*, 797.

[7] J. Li, C. G. Daniliuc, G. Kehr, G. Erker, *Eur. J. Inorg. Chem.* **2020**, 1096.

[8] a) A. Klamt, *J. Phys. Chem.* **1995**, *99*, 2224 (COSMO-RS); b) F. Weigend, R. Ahlrichs. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297 (def2-TZVP basis set); c) Y. Zhao, D. G. Truhlar, *J. Phys. Chem. A* **2005**, *109*, 5656 (PW6B95); d) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; e) S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456 (D3 dispersion correction).

[9] A. W. Johnson and J. C. Tebby, *J. Chem. Soc.* **1961**, 2126.

[10] See for a comparison: a) I. F. Wilson, J. C. Tebby, *J. Chem. Soc., Perkin Trans. 1* **1972**, 2830; b) I. Yavari, M. Adib, L. Hojabri, *Tetrahedron* **2002**, *58*, 7213; c) R. A. Aitken, S. J. Costello, A. M. Z. Slawin, N. J. Wilson, *Eur. J. Org. Chem.* **2003**, 623; d) M. R. Islami, Z. Hassani, K. Saidi, *Synth. Commun.* **2003**, *33*, 65; e) V. Nair, A. Deepthi, P. B. Beneesh, S. Eringathodi, *Synthesis* **2006**, 1443; f) M. Adib, E. Sheibani, A. Abbasi, H. R. Bijanzadeh, *Tetrahedron Lett.* **2007**, *48*, 1179; h) K. Nagao, H. Ohmiya, M. Sawamura, *J. Am. Chem. Soc.* **2014**, *136*, 10605; i) A. Ramazani, F. Z. Nasrabadi, K. Ślepokura, T. Lis, S. W. Joo, *J. Heterocycl. Chem.* **2017**, *54*, 55.

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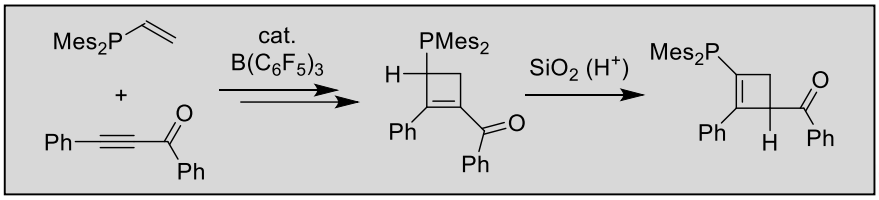

The tris(pentafluorophenyl)borane catalyzed reactions of the bulky dimesityl(vinyl)phosphane with conjugated ynones yield cyclobutene derivatives. The reaction is probably initiated by phosphane attack at the activated carbon-carbon triple bond followed by ring-closure and rearrangement to give the conjugated acyl-cyclobutene products. Isomerization to the non-conjugated isomer takes place during chromatography.

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