

Reactions of (*tert*-Butyldimethylsilyl)alkynes with IPy₂BF₄: Selective Synthesis of Novel Head-to-Head Dimers

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The straightforward elaboration of enynes by transition-metal-mediated linear dimerization of terminal alkynes is, in many cases, of limited synthetic value, mainly due to the formation of dimers as mixtures of regio- and stereoisomers with products arising from competitive further oligomerization reactions.¹ Thus, although remarkable examples of successful preparation of enynes using this approach had been reported,² alternative sp²–sp coupling reactions are commonly the choice to assemble this organic frame.³ The considerable current interest in acetylene chemistry,⁴ recent efforts focusing on selective dimerization of alkynes,⁵ and our finding of IPy₂BF₄-catalyzed head-to-tail dimerization of iodoalkynes⁶ prompted us to explore the reactivity of (trialkylsilyl)alkynes toward this reagent that, eventually, might lead to highly functionalized enynes through a new "C–C" bond-forming reaction.⁷ Herein, we report an unprecedented coupling of (trialkylsilyl)acetylenes **1** upon reaction with IPy₂BF₄/HBF₄⁸ (Py = pyridine) furnishing the regio- and diastereoisomerically pure enynes **2**. Moreover, at higher temperature, the enynes **2** further react with IPy₂BF₄ affording enynes **4** in another selective and efficient process.

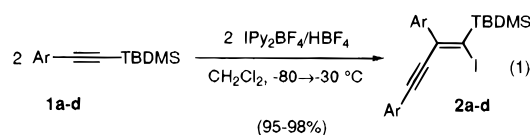
Alkynylsilanes easily give substitution products upon reaction with simple electrophiles,⁹ nevertheless, the reactivity of the "Si–C(sp)" σ-bond can be strongly modulated by the remainder substituents onto silicon.¹⁰ TMS-protected terminal acetylenes (TMS = Me₃Si) led only to iodoalkynes upon reaction with

Table 1. Dimers **2** and **4**^a

starting material	product	T (h)	yield (%) ^b	starting material	product	T (h)	yield (%) ^b
1a	2a	20	95	2c	4c	5	95
1b	2b	5	99	2d	4d	16	90
1c	2c	5	99	1a	4a	24	95
1d	2d	16	97 ^c	1b	4b	14	98
2a	4a	10	93	1c	4c	14	97
2b	4b	5	98	1d	4d	50	85 ^c

^a See eqs 1 and 3. ^b Isolated yield. ^c Excess of IPy₂BF₄/HBF₄ was used (1:2 molar ratio to the starting material).

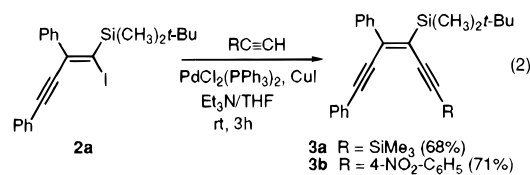
IPy₂BF₄/HBF₄; however, at low temperature, TBDMS-alkynes **1** (TBDMS = *t*-BuMe₂Si) react with IPy₂BF₄ furnishing 2,4-diaryl-1-iodo-1-(*tert*-butyldimethylsilyl)-1,3-enynes **2**, resulting in a new and selective method for the homocoupling of alkynylsilanes¹¹ (eq 1).



TBDMS: SiMe₂*t*-Bu
a: Ar = C₆H₅
b: Ar = 4-CH₃-C₆H₄
c: Ar = 4-(CH₃)₂C-C₆H₄
d: Ar = 4-Cl-C₆H₄

Head-to-tail dimers **2** were clean and efficiently obtained by mixing a 1:1:1 molar ratio of **1** to IPy₂BF₄ and HBF₄ (**1d** required 1:2 molar ratio of IPy₂BF₄/HBF₄) in CH₂Cl₂¹² and stirring the mixture for several hours (Table 1) at –80 to –30 °C (0 °C for **2a** and **2d**), followed by aqueous workup. Related aliphatic alkynylsilanes failed to couple under the same conditions. The proposed structure for **2** relies on spectroscopic (1D, 2D, and NOE NMR experiments) and analytical data.¹³

The above described homocoupling of alkynylsilanes yields enynes **2** functionalized in a way that makes them valuable for further synthetic transformations. Thus, for instance, it enables a short elaboration of enediyne cores from alkynes,¹⁴ as depicted for the synthesis of **3**¹⁵ (eq 2).



The rich chemistry of the I–C(sp²) bond adds synthetic potential to this coupling reaction and clearly establishes a significant difference with respect to methods relying upon transition-metal-catalyzed reaction of terminal alkynes, where a new C–H rather than a C–I bond is formed in the final product.

Moreover, dimers **2** were also unexpected starting materials for a new and selective process giving (*E*)-1,4-diaryl-1,2-diiodo-1,3-butadiynes **4** (eq 3). Pure samples of compounds **2** react

(11) (a) Ohshita, J.; Furumori, K.; Matsuguchi, A.; Ishikawa, M. *J. Org. Chem.* **1990**, *55*, 3277. (b) Heres, H. J.; Teuben, J. H. *Organometallics* **1991**, *10*, 1980. (c) Schaverien, C. J. *Ibid* **1994**, *13*, 69.

(12) Solutions of IPy₂BF₄ (5 × 10^{–2} M) were used.

(13) A full list of ¹³C and ¹H-MR data, together with representative IR stretching vibrations, MS data, and elemental analyses are provided in the Supporting Information.

(14) For a recent review on enediyne, see: Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453.

(15) X-ray analysis of **3b** proves its structure and, furthermore, confirms the proposed regio- and stereochemistry for the reaction of alkynylsilanes yielding the homocoupled compounds **2**. For crystal data of **3b** and a figure, see the Supporting Information.

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(1) Winter, M. J. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: Chichester, 1985; Vol. 3, p 261.

(2) (a) Trost, B. M.; Chan, C.; Ruther, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486. (b) Trost, B. M.; Sorum, M. T.; Chan, C.; Harms, A. E.; Rühter, G. *J. Am. Chem. Soc.* **1997**, *119*, 698.

(3) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 521–549.

(4) *Modern Acetylene Chemistry*; Stang, P., Diederich, F., Eds.; VCH: Weinheim, 1995.

(5) For recent examples, see: (a) Bianchini, C.; Frediani, P.; Masi, D.; Peruzzini, M.; Zanolini, F. *Organometallics* **1994**, *13*, 4616 and references cited therein. (b) Matsuzaka, H.; Takagi, Y.; Ishii, Y.; Nishio, M.; Hidai, M. *Organometallics* **1995**, *14*, 2153. (c) Straub, T.; Haskel, A.; Eisen, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 6364. (d) Yi, C. S.; Liu, N. *Organometallics* **1996**, *15*, 3968.

(6) Barluenga, J.; González, J. M.; Llorente, I.; Campos, P. *J. Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 893.

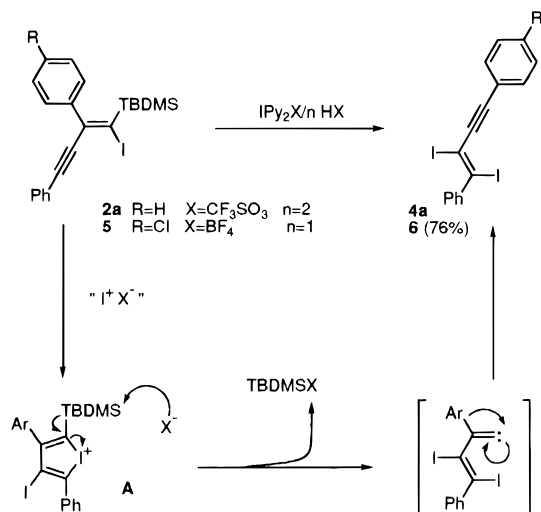
(7) This reaction would place an iodine atom attached to the functionality developed along the dimerization, adding synthetic interest to the final product.

(8) The acid protonates pyridine liberating the active iodine, see: Barluenga, J.; Campos, P. J.; González, J. M.; Suárez, J. L.; Asensio, G. *J. Org. Chem.* **1991**, *56*, 2234.

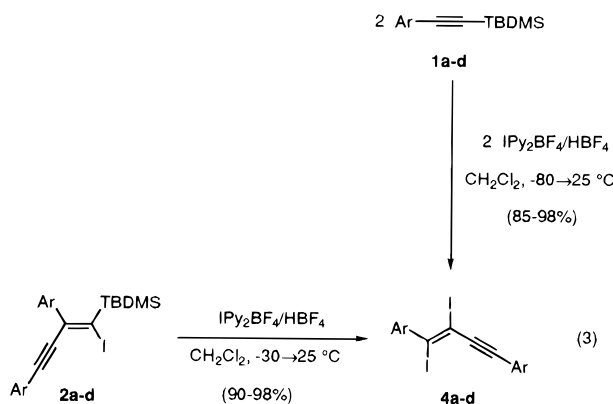
(9) Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organic Silicon Compounds, Part 2*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; p 929.

(10) See: (a) Schmidt-Radde, R. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1992**, *114*, 9713. (b) Boldi, A. M.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 468.

Scheme 1. Proposed Mechanism



(1:1 molar ratio) with $\text{IPy}_2\text{BF}_4/\text{HBF}_4$ affording enynes **4**, in excellent yield (Table 1, at -30°C to room temperature, IPy_2BF_4 2.5×10^{-2} M in CH_2Cl_2). Interestingly, compounds **4** can



also be prepared from the readily available alkynes **1**,¹⁶ using a 1:1:1 molar ratio of **1** to IPy_2BF_4 and HBF_4 ($\text{IPy}_2\text{BF}_4/\text{HBF}_4 = 1:2$, for **1d**), where the reaction time (see Table 1) and temperature (from -80 to 0°C for **4b,c**, and to room temperature for **4a,d**) represent the differences in the experimental conditions with respect to those furnishing dimers **2**. Spectroscopic and analytical data support the proposed structure for dimers **4**, which was confirmed by an X-ray analysis of **4c**.¹⁷

To gain further insights into the conversion of enynes **2** to **4**, the cross-coupled dimer **5** was prepared by linear dimerization of the parent-substituted alkynes using IPy_2BF_4 .¹⁸ Upon reaction with $\text{IPy}_2\text{BF}_4/\text{HBF}_4$ (1:1 molar ratio to **5**) from 0°C to room temperature for 16 h, only the enyne **6** was obtained, in 76% isolated yield, as depicted in Scheme 1. The reaction pathway includes several steps, namely, removal of the TBDMS group, migration of the aryl group labeled with chlorine from an internal to a terminal position, and migration of the already present iodine atom together with incorporation of an additional one. This transformation, resulting in the formation of three new σ -bonds and altering two π -bonds in the frame, is remarkably selective. A tentative mechanistic interpretation accounting for the conversion of dimers **2** into **4** is outlined in Scheme 1.

(16) Both 1,1-diiodo-2,4-disubstituted 1,3-butenynes (ref 6) and (*E*)-1,2-diiodo-1,4-disubstituted 1,3-butenynes can be selectively prepared upon reaction of the alkyne with IPy_2BF_4 , simply by prior substitution at the terminal position by iodine or TBDMS, respectively.

(17) For crystal data of **4c**, including interesting $-\text{C}-\text{I}\cdots\pi$ and $-\text{C}-\text{H}\cdots\pi$ bonding interactions and a figure, see the Supporting Information.

(18) Prepared in an unoptimized 35% isolated yield, adapting the synthesis above described for **2**, starting from **1d** and $\text{PhC}\equiv\text{CI}$ (2:1 molar ratio, respectively), at -60°C for 40 h, and 2:1 molar ratio of HBF_4 to IPy_2BF_4 .

Initial steps might comprise chemoselective attack of electrophilic iodine to the triple bond,¹⁹ followed by five-membered ring closure involving 1,4-neighboring iodine participation^{20,21} giving an iodolium ion²² which has been detected by low-temperature NMR experiments.²³ ^1H and ^{13}C NMR spectra at -30°C of the crude material obtained by reaction of **2a** with 1.0 equiv of $\text{IPy}_2\text{CF}_3\text{SO}_3$ and 2.0 equiv of $\text{CF}_3\text{SO}_3\text{H}$ in CDCl_3 showed a silylated intermediate that underwent rearrangement to the head-to-head dimer **4a** upon warming up to room temperature, whose NMR data are consistent with the cyclic iodolium ion **A** shown in Scheme 1 (Ar = Ph, X = CF_3SO_3). The assignment of the signals was based on 2D NMR heteronuclear and NOE difference experiments. Deshielding in the ^{13}C NMR spectrum of the Si,I-bearing carbon atom (from 118.0 ppm in **2a** to 144.5 ppm), the pair of acetylenic carbons (from 96.3 and 97.6 to 108.1 and 134.5 ppm for the C–I and C–I⁺, respectively), and the vinylic carbon bearing the aryl group (Ar = Ph, from 144.9 to 168.0 ppm) was observed and supports the existence of the cyclic iodolium ion.²⁴ A reasonable path for the evolution of this intermediate could involve counterion attack onto silicon²⁵ with concomitant loss of iodine that would migrate in a 1,4-sense affording an alkylidene carbene,²⁶ from which a 1,2-aryl rearrangement furnishing an alkyne is also well-documented in hypervalent iodonium chemistry.²⁷

In short, head-to-tail dimers **2** and head-to-head dimers **4** can be prepared from alkynes **1** upon reaction with IPy_2BF_4 . This manifold has not been reported in related coupling of alkynes mediated by transition metals. Other worthy features of this transformation include the yields and the noted regio- and stereoselectivity. The reactivity of the C–I bond formed in the reaction should enlarge the synthetic utility of this homocoupling process. Further work on the use of IPy_2BF_4 as a reagent simulating the outcome of transition-metal-based reactions of alkynes is in progress.

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Supporting Information Available: Characterization data for **2–7** and **A**, X-ray figures, and relevant features for **3b** and **4c**, NMR spectra for **A**, and X-ray crystallographic data for compounds **3b** and **4c** including tables of atomic coordinates, bond lengths and bond angles (40 pages). See any current masthead page for ordering and Internet access instructions.

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(20) For previous 1,4-halogen shifts, see: (a) Peterson, P. E.; Bopp, R. J.; Ajo, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 2834. (b) Reich, I. L.; Reich, H. J. *J. Am. Chem. Soc.* **1974**, *96*, 2654.

(21) The *cis*-relationship of iodine and the acetylene is crucial. Reaction of **2b** as a mixture of *E:Z* (2.6:1) gives **4b** and the product of I–Si exchange (2:1 ratio), proving its implication in the process.

(22) Iodolium ions: (a) Beringer, F. M.; Ganis, P.; Avitabile, G.; Jaffe, H. *J. Org. Chem.* **1972**, *37*, 879. (b) Yang, R.-Y.; Dai, L.-X.; Chen, C.-G. *J. Chem. Soc., Chem. Commun.* **1992**, 1487.

(23) We thank the referees for suggestions, particularly those about the stability of this iodolium intermediate that encouraged us to its detection and characterization.

(24) We have not found ^{13}C NMR data for cyclic iodolium ions; however, chemical shifts for **A** are concordant with these in alkynyl- and alkenyliodonium, see: Stang, P. J.; Arif, A. M.; Crittall, C. M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 287. Ochiai, M.; Sumi, K.; Takaoka, Y.; Kunishima, M.; Nagao, Y.; Shiro, M.; Fujita, E. *Tetrahedron* **1988**, *44*, 4095.

(25) The unique combination of silicon and positive iodine in one carbon and a mild source of F^- toward silicon provides a driving force to the formation of **4**. Related 2,4-diphenyl-1,1-diiodo-1,3-butenyne does not undergo this reaction, giving (*E*)-1,1,3,4-tetraiodo-2,4-diphenyl-1,3-butadiene **7**.

(26) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383. Stang, P. J. *Acc. Chem. Res.* **1982**, *15*, 348.

(27) Unsaturated carbenes are accepted as intermediates in 1,2-rearrangement on alkenyl and alkynyl(phenyl)iodonium compounds. For a review, see: Stang, P. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 274.