Catalytic Double Addition of Diazo Compounds to Alkynes: Synthesis of Functional Conjugated Dienes

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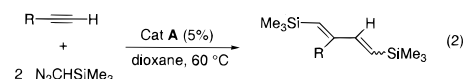
A major challenge in organic synthesis deals with the discovery of one-pot, several-step reactions selectively leading to the formation of several carbon–carbon bonds under mild conditions. Metal-catalyzed reactions of diazo compounds have shown an important contribution in this area, and still offer a strong potential in synthesis.[1] Catalytic additions of diazo compounds to alkynes, especially with $Rh_2(OAc)_4$ catalyst, afford either cyclopropene intermediates[2] or reactive vinylcarbenoid species promoting C–C bond formations in cascade.[3–5] On the other hand, ruthenium precatalysts have recently shown efficiency in the activation of diazoalkane derivatives for their dimerization,[6] cyclopropanation,[7] or ring-opening metathesis,[8] but to our knowledge, no example of ruthenium-catalyzed addition of diazo compounds to alkynes has been reported yet. As ruthenium–carbene species are well known to easily generate, on reaction with an alkyne, alkenyl-carbene–ruthenium species,[9] and as it was recently shown that two cis carbene ligands can be accommodated on a Cp*(Cl)Ru moiety (Cp* = C_5Me_5),[10,11] we have investigated the possibility of coupling alkenylcarbene–ruthenium, in situ generated from diazoalkane derivative and alkyne, with a second equivalent of carbene species arising from diazoalkane in order to produce dienes and thus to show the formal bis-carbene character of alkynes R–C≡C–R ↔ R–C(:)–C(:)–R.

Now we report a novel, selective catalytic synthesis of new substituted 1,4-bistrimethylsilylbuta-1,3-dienes, by the combination of two molecules of trimethylsilyldiazomethane and one of alkyne, catalyzed by $RuCl(cod)C_5Me_5$ (eq 1). The stereoselective formation of these functional conjugated dienes results from the ruthenium-catalyzed selective creation of two carbon–carbon double bonds via double dimerization of a 1,2 bis-carbene precursor with another carbene source.

$$R\!\!=\!\!\!=\!\!R' + 2\ N_2CHY \longrightarrow \underset{R}{\overset{Y}{\diagdown}}\!\!=\!\!=\!\!\underset{Y}{\overset{R'}{\diagup}} + 2\ N_2 \quad (1)$$
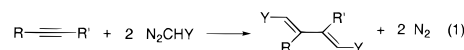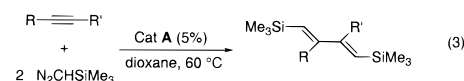
The reaction of 1.25 mmol of phenylacetylene with 2.4 equiv of trimethylsilyldiazomethane (2 M in hexane), in the presence of 5 mol % of catalyst precursor $RuCl(cod)C_5Me_5$[12] (**A**) in 2 mL of dioxane, affords the 1,4-bistrimethylsilylbutadiene **1** after 6 h at 60 °C in 72% yield (eq 2). ^1H NMR and NOE experiments

$$\begin{array}{c} R\!\!=\!\!\!=\!\!H \\ + \\ 2\ N_2CHSiMe_3 \end{array} \xrightarrow[\text{dioxane, 60 °C}]{\text{Cat A (5%)}} \begin{array}{c} Me_3Si \diagdown H \\ \diagup\!\!=\!\!=\!\!\diagdown \\ R \diagdown SiMe_3 \end{array} \quad (2)$$

1 R = Ph (72%, *E/Z* = 70/30)
2 R = cyclohex-1-enyl
(80%, *E/Z* = 89/11)

showed *Z* stereoselectivity for the trisubstituted double bond, whereas the disubstituted double bond is formed with an *E/Z* stereoselectivity in the ratio 70/30. The bulky, electron-rich precursor **A** appears to be a selective catalyst for this reaction, whereas $RuCl_3 \cdot xH_2O$, $(PPh_3)_3RuCl_2$, $[(p\text{-cymene})RuCl_2]_2$, $(p\text{-cymene})RuCl_2(PCy_3)$, and $Cp*RuBr_2(\eta^3\text{-}C_4H_7)$ do not catalyze it at all.

Consequently, the catalyst precursor **A** and the above reaction conditions (dioxane, 60 °C) have been selected to study the activation of a variety of alkynes.[13] 1-Ethynylcyclohexene affords after 5 h the 1,4-bistrimethylsilylbutadiene derivative **2** in 80% yield (*E/Z* = 89/11) (eq 2). The reaction has also been extended to various disubstituted alkynes, and the 1,4-bistrimethylsilyl-butadienes **3** and **4** have been obtained in 56 and 30% yield, respectively (eq 3). Only one isomer has been observed by NMR

$$\begin{array}{c} R\!\!=\!\!\!=\!\!R' \\ + \\ 2\ N_2CHSiMe_3 \end{array} \xrightarrow[\text{dioxane, 60 °C}]{\text{Cat A (5%)}} \begin{array}{c} Me_3Si \diagdown R' \\ \diagup\!\!=\!\!=\!\!\diagdown \\ R \diagdown SiMe_3 \end{array} \quad (3)$$

	R	R'	
3	Ph	Me	(56%)
4	Ph	Ph	(30%)
5	Et	Et	(72%)
6	CH₂OH	Me	(95%)

for these tetrasubstituted dienes. NOE experiments and selective ^{13}C NMR decoupling show that this isomer has both substituents in the cis position on each double bond. Hex-3-yne affords the (*E,E*)-1,4-bistrimethylsilylbutadiene **5** (R = R′ = Et) in 72% yield.

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(1) (a) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (b) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797. (c) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

(2) (a) Petiniot, N.; Anciaux, A. J.; Noels, A. F.; Hubert, A. J.; Teyssié, P. *Tetrahedron Lett.* **1978**, *14*, 1239. (b) Dowd, P.; Garner, P.; Schappert, R.; Irngartinger, H.; Goldman, A. *J. Org. Chem.* **1982**, *47*, 4240. (c) Conde-Petiniot, N.; Hubert, A. J.; Noels, A. F.; Warin, R.; Teyssié, P. *Bull. Soc. Chim. Belg.* **1986**, *95*, 649.

(3) (a) Padwa, A.; Xu, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 5881. (b) Müller, P.; Pautex, N.; Doyle, M. P.; Bagheri, V. *Helv. Chim. Acta* **1990**, *73*, 1233.

(4) (a) Mueller, P. H.; Kassir, J. M.; Semones, M. A.; Weingarten, M. D.; Padwa, A. *Tetrahedron Lett.* **1993**, *34*, 4285. (b) Padwa, A.; Krumpe, K. E.; Kassir, J. M. *J. Org. Chem.* **1992**, *57*, 4940. (c) Padwa, A.; Austin, D. J.; Xu, S. L. *Tetrahedron Lett.* **1991**, *32*, 4103. (d) Padwa, A.; Austin, D. J.; Xu, S. L. *J. Org. Chem.* **1992**, *57*, 1330.

(5) (a) Hoye, T. R.; Dinsmore, C. J.; Johnson, D. S.; Korkowski, P. F. *J. Org. Chem.* **1990**, *55*, 4518. (b) Hoye, T. R.; Dinsmore, C. J. *Tetrahedron Lett.* **1991**, *32*, 3755. (c) Hoye, T. R.; Dinsmore, C. J. *J. Am. Chem. Soc.* **1991**, *113*, 4343.

(6) (a) Collman, J. P.; Rose, E.; Venburg, G. D. *J. Chem. Soc., Chem. Commun.* **1993**, 934. (b) Baratta, W.; Del Zotto, A.; Rigo, P. *J. Chem. Soc., Chem. Commun.* **1997**, 2163.

(7) (a) Simal, F.; Demonceau, A.; Noels, A. F.; Knowles, D. R. T.; O'Leary, S.; Maitlis, P. M.; Gusev, O. *J. Organomet. Chem.* **1998**, *558*, 163. (b) Doyle, M. P.; Peterson, C. S.; Zhou, Q.; Nishiyama, H. *J. Chem. Soc., Chem. Commun.* **1997**, 211. (c) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223.

(8) (a) Stumpf, A. W.; Saive, E.; Demonceau, A.; Noels, A. F. *J. Chem. Soc., Chem. Commun.* **1995**, 1127. (b) Demonceau, A.; Stumpf, A. W.; Saive, E.; Noels, A. F. *Macromolecules* **1997**, *30*, 3128.

(9) (a) Kinoshita, A.; Mori, M. *J. Org. Chem.* **1996**, *61*, 8356. (b) Stragies, R.; Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2518. (c) Picquet, M.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1998**, 2249. (d) Zuercher, W. J.; Scholl, M.; Grubbs, R. H. *J. Org. Chem.* **1998**, *63*, 4291.

(10) Le Paih, J.; Dérien, S.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1999**, 1437.

(11) Gemel, C.; La Pensée, A.; Mauthner, K.; Mereiter, K.; Schmid, R.; Kirshner, K. *Monatsh. Chem.* **1997**, *128*, 1189.

(12) Fagan, P. J.; Mahoney, W. S.; Calabrese, J. C.; Williams, I. D. *Organometallics* **1990**, *9*, 1843–1852.

(13) The alkyne (2.5 mmol) and trimethylsilyldiazomethane (2.4 equiv) are stirred in dioxane (2–4 mL) in the presence of catalyst **A** (0.125 mmol) at 60 °C for 5–6 h. The solvent is evaporated under vacuum, and the products are isolated by column chromatography over silica gel. The isolated yields are based on the alkyne. All compounds were fully characterized by spectroscopic methods. Selected data for **1**: isomer *Z,E*, ^1H NMR (200 MHz, CDCl₃) δ −0.16 (9H, s), 0.09 (9H, s), 5.44 (1H, d, *J* = 18 Hz), 5.88 (1H, d, *J* = 1 Hz), 6.75 (1H, dd, *J* = 18 Hz, *J* = 1 Hz), 7.10–7.13 (2H, m), 7.28–7.35 (3H, m); isomer *Z,Z*, ^1H NMR (200 MHz, CDCl₃) δ −0.09 (9H, s), 0.13 (9H, s), 5.59 (1H, d, *J* = 14 Hz), 5.88 (1H, d, *J* = 1 Hz), 6.87 (1H, dd, *J* = 14 Hz, *J* = 1 Hz), 7.19–7.24 (2H, m), 7.28–7.35 (3H, m). Selected data for **3**: ^1H NMR (200 MHz, CDCl₃) δ −0.2 (9H, s), 0.05 (9H, s), 2.04 (3H, s), 5.24 (1H, s), 5.93 (1H, s), 7.02–7.14 (2H, m), 7.26–7.38 (3H, m).

Communications to the Editor

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Methyl propargyl alcohol also reacts in the presence of 2.4 equiv of trimethylsilyldiazomethane to give the 1,4-bistrimethylsilyl-butadiene **6** (R = CH₂OH, R′ = Me) in very good yield (95%), thus showing that the reaction tolerates a hydroxy functional group. The reactivity of a conjugated diyne such as bistrimethylsilylbutadiyne has been examined to clear up the regioselectivity of the addition (1,2; 1,4 or 1,2 plus 3,4). In the presence of 4.8 equiv of trimethylsilyldiazomethane, this 1,3-diyne reacts as a monoalkyne, and only one C≡C bond was transformed to give the tetrasilylated dienyne **7** (48%) (eq 4), a useful molecule for the search of functional unsaturated carbon-rich molecules and networks.[14] This catalytic reaction offers a new route to selectively build functional 1,3-dienes useful in synthesis as the vinylsilane moiety can be easily converted into a variety of functionalities.[15]
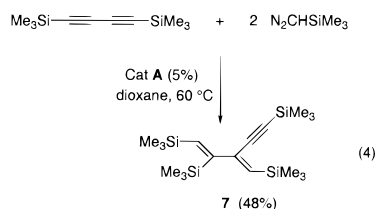
The efficiency of the reaction depends on the nature of the solvent, despite the presence of hexane in the reaction mixture, and the temperature. After 6 h at 60 °C the reaction of phenylacetylene carried out in dichloromethane, dimethylformamide, hexane, tetrahydrofuran, and dioxane leads to the diene **1** in 15, 40, 52, 64, and 72% yield, respectively. The reaction performed in dioxane at room temperature for 20 h affords only 25% of the corresponding diene. This low yield could be explained by the observation that, at room temperature, RuCl(cod)C₅Me₅ dimerizes phenylacetylene and leads to a biscarbene derivative[10,11] which is not a catalyst for this reaction.

Ethyldiazoacetate is less reactive than trimethylsilyldiazomethane and requires more drastic reaction conditions. After 20 h at 100 °C in dioxane (4 mL), in the presence of 5 mol % of catalyst precursor **A**, phenylacetylene with 2.4 equiv of ethyldiazoacetate affords the butadiene **8** in 64% yield as a mixture of isomers (eq 5).
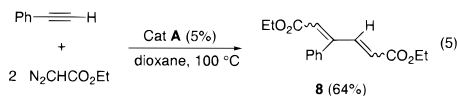

A possible mechanism for this selective formation of 1,4-bistrimethylsilylbutadiene derivatives **1**–**7** from simple alkynes

(14) (a) Touchard, D.; Haquette, P.; Daridor, A.; Toupet, L.; Dixneuf, P. H. *J. Am. Chem. Soc.* **1994**, *116*, 11157. (b) Diederich, F.; Rubin, Y. *Angew. Chem., Int. Ed. Engl.* **1992**, *9*, 1101. (c) Bunz, U. H. F.; Enkelmann, V. *Organometallics* **1994**, *13*, 3823.

(15) (a) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857 and references therein. (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic: London, 1988; Chapter 3. (c) Armitage, D. A. In *Comprehensive Organometallic Chemistry*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995; Vol. 2, Chapter 1. (d) Farinola, G. M.; Fiandanese, V.; Mazzone, L.; Naso, F. *J. Chem. Soc., Chem. Commun.* **1995**, 2523. (e) Babudri, F.; Cicciomessere, A. R.; Farinola, G. M.; Fiandanese, V.; Marchese, G.; Musio, R.; Naso, F.; Sciacovelli, O. *J. Org. Chem.* **1997**, *62*, 3291. (f) Babudri, F.; Farinola, G. M.; Fiandanese, V.; Mazzone, L.; Naso, F. *Tetrahedron* **1998**, *54*, 1085.

Scheme 1
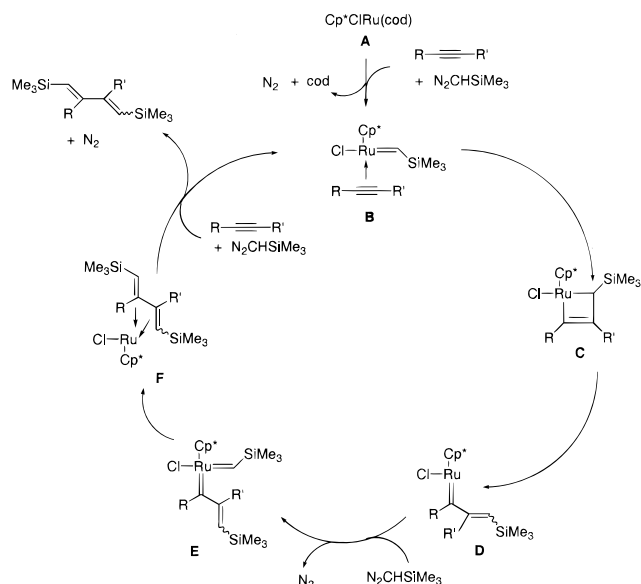
is shown in Scheme 1. As trimethylsilyldiazomethane is known to give a Ru=CHSiMe₃ species with a coordinatively unsaturated ruthenium complex,[8] the coordination of the alkyne and one molecule of trimethylsilyldiazomethane to the ruthenium center is expected, on displacement of the cod ligand, to give the ruthenium–carbene intermediate **B**. Classical coupling of the carbene and triple bond should afford the intermediate **C** and then the unsaturated ruthenium vinyl carbene derivative **D**. Addition of a second molecule of N₂CHSiMe₃ on **D** may lead to species **E**, and then to the coordinated diene **F** by coupling of both carbene species, or directly via addition on species **D**.

This formation of 1,4-bisfunctional buta-1,3-dienes constitutes an alternative route, with the advantageous presence of reactive vinylsilane moieties, to terminal 1,3-dienes from alkynes and ethene via catalytic ene/yne metathesis.[16]

The above catalytic reaction constitutes an unusual crossover 2:1 coupling between diazoalkanes and a substantial wide range of alkynes. It represents a novel example of a one-pot, mild, ruthenium-catalyzed reaction combining three substrates into only one, with release of only two molecules of dinitrogen, via selective C=C coupling. Moreover, we have shown that it was possible to selectively create two C–C double bonds and to produce only one stereoisomer of 2,3-disubstituted 1,4-trimethylsilyl-1,3-dienes from disubstituted alkynes.

Supporting Information Available: Spectroscopic data for compounds **1**–**7** and ¹H and ¹³C NMR spectra for the selected compound **4** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

(16) (a) Kinoshita, A.; Sakakibara, N.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 12388. (b) Smulik, J. A.; Diver, S. T. *J. Org. Chem.* **2000**, *65*, 1788.