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Synthesis of Simple Diynals, Diynones, Their Hydrazones, and Diazo Compounds: Precursors to a Family of Dialkynyl Carbenes (R^1—C≡C—C̈—C≡C—R^2)

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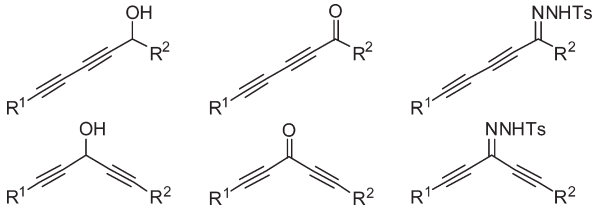

A variety of substituted pentadiynols, -diynals, and -diynones have been prepared en route to precursors to dialkynyl carbenes (R^1—C≡C—C̈—C≡C—R^2). In light of the marginal stability associated with these simple systems, several strategies were required to assemble the carbon backbones. The requisite five-carbon skeletons were prepared using 4 + 1, 3 + 2, 2 + 2 + 1, and 2 + 1 + 1 + 1 coupling methodologies. The Dess−Martin periodinane serves as an excellent method for the oxidation of pentadiynols to diynals and diynones, although many of the oxidized products are sufficiently reactive that they were not isolated; rather, they were generated in situ and intercepted with nucleophiles such as tosylhydrazide or trisylhydrazide. The hydrazone derivatives are generally reliable precursors to diazo compounds and carbenes, although cyclization of the hydrazone to afford a pyrazole can be a complicating factor in certain instances.

Introduction

Our studies of highly unsaturated carbon chain molecules HC_nH (n = odd) stem from an interest in fundamental issues of structure and bonding,[1−3] as well as an interest in the harsh chemical environments in which these species are known to exist. Many of these isomers represent important chemical intermediates in the combustion of fuel-rich hydrocarbon flames,[4,5] the chemistry of interstellar space,[6−8] and the atmospheric chemistry of Titan,[9] the largest moon of Saturn. Substituted propynylidene (propargylene) derivatives also find use as ligands in organometallic chemistry,[10,11] where these complexes exhibit interesting reactivity that has been exploited in organic synthesis.[12,13] Dialkynyl carbenes (pentadiynylidenes) serve as versatile reagents for the functionalization of fullerenes.[14−18] A detailed understanding of

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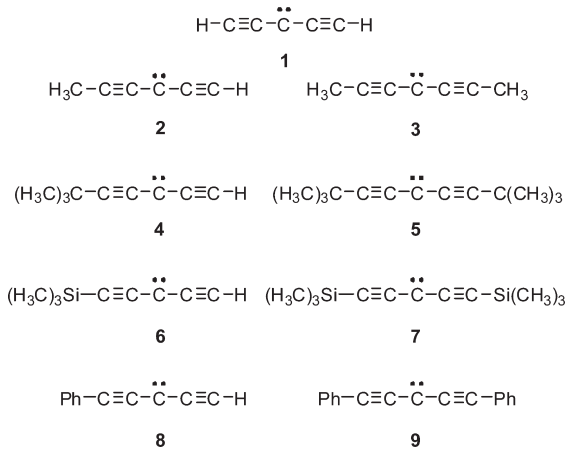


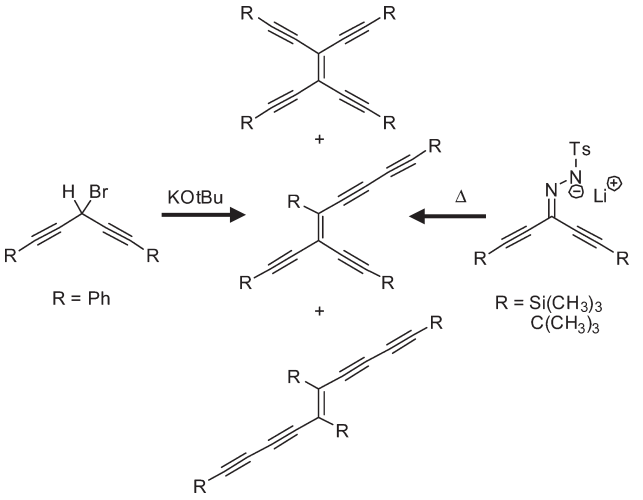
FIGURE 1. Dialkynyl carbenes that represent the targets of the current synthetic studies.

the electronic spectra of the HC_nH carbon chains is of particular importance in molecular spectroscopy and astrochemistry. An essential prerequisite for spectroscopic and mechanistic studies of dialkynyl carbenes (Figure 1) is the availability of suitable precursors to these reactive species. In the current article, we describe the synthesis and characterization of a variety of simple dialkynyl aldehydes and ketones, along with their hydrazone derivatives, which serve as chemical precursors to a family of dialkynyl carbenes (R^1—C≡C—C̈—C≡C—R^2).

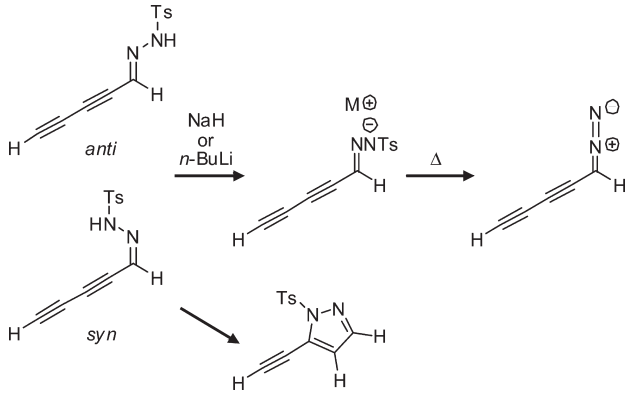
Background

Early efforts to generate dialkynyl carbenes involved base-induced α-elimination of a 3-halo-1,4-pentadiyne[19] or thermal decomposition of tosylhydrazone salts[20] (Scheme 1). In pioneering studies, Bernheim and Skell reported the direct detection of carbene intermediates by EPR spectroscopy.[21,22] The alkynyl carbenes were generated by photolysis of diazo compounds, which were, in turn, prepared from the corresponding *N*-nitrosourea precursors.[21,22] Detailed experimental procedures for the syntheses of these carbene precursors, unfortunately, were not published. The EPR data for these carbenes have long puzzled chemists and spectroscopists,[2] and, in more recent years, the electronic absorption spectrum of the parent dialkynyl carbene, triplet HC_5H (**1**), also became a matter of uncertainty.[23,24] The absence of synthetic procedures for the preparation of suitable carbene precursors limited progress toward resolving these lingering questions. Our successful preparation of 1-diazo-2,4- pentadiyne (**13a**) allowed us to begin to address some of these questions.[3] In light of the significance of HC_5H (**1**) to molecular spectroscopy and mechanistic chemistry, as well as the difficulties encountered by eminent researchers in obtaining and interpreting its electronic absorption spectrum,[23,24] we felt that it was highly desirable that our interpretation and analysis of UV/visible and EPR spectra not rest on the study of a single species. Thus, we placed great importance on the generation and study of a family of R^1—C≡C—C̈—C≡C—R^2 derivatives.

SCHEME 1



SCHEME 2



Skell's studies established the viability of generating diazo compound precursors to this family of carbenes.[21,22] We were not enthusiastic, however, about the prospect of reinventing these unpublished syntheses, especially as they involve potentially carcinogenic *N*-nitrosourea derivatives. Given our success in generating 1-diazo-2,4-pentadiyne from thermolysis of the lithium salt of the tosylhydrazone (Bamford–Stevens reaction,[25] Scheme 2),[3] we sought to develop procedures for the synthesis of tosylhydrazone, or trisylhydrazone, precursors for the carbenes depicted in Figure 1. At the outset, we recognized that these efforts would be complicated by the existence of *syn* and *anti* isomers of the hydrazones, the propensity of the *syn* isomer to cyclize to the pyrazole, and the instability of the requisite aldehydes or ketones from which the hydrazones are derived.

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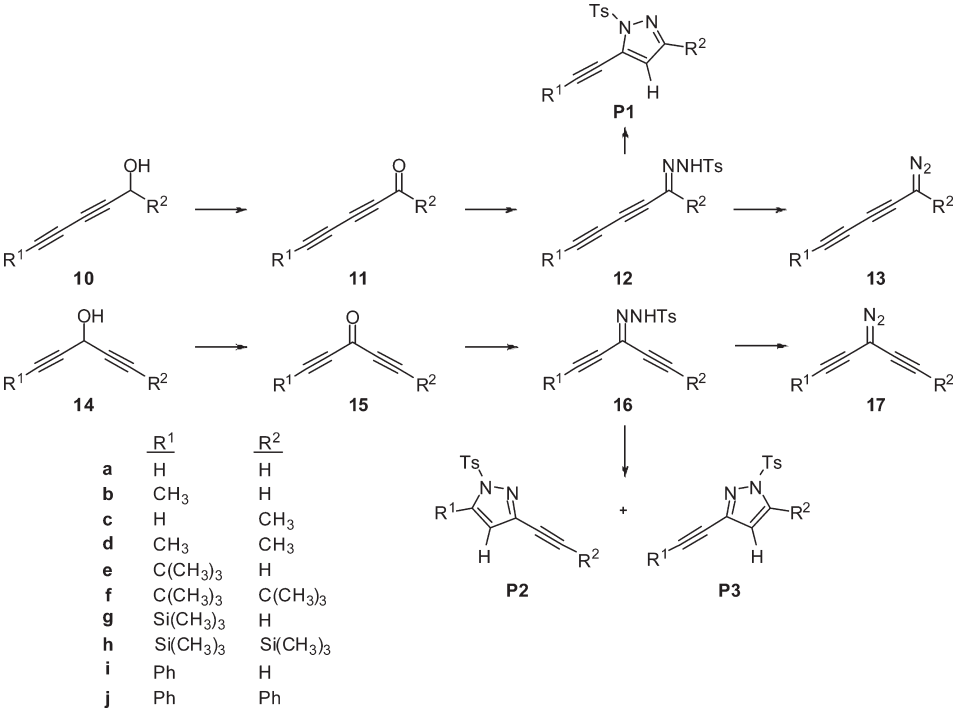
SCHEME 3



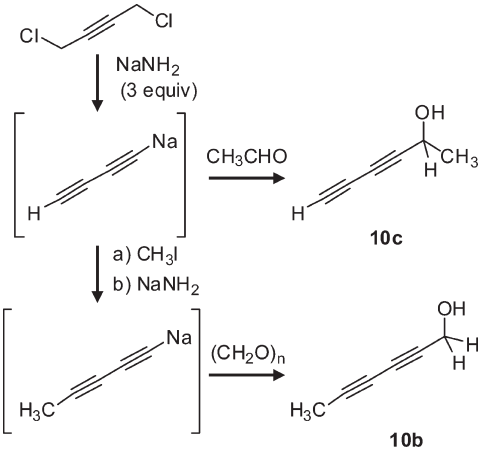
	R^1	R^2
a	H	H
b	CH_3	H
c	H	CH_3
d	CH_3	CH_3
e	$C(CH_3)_3$	H
f	$C(CH_3)_3$	$C(CH_3)_3$
g	$Si(CH_3)_3$	H
h	$Si(CH_3)_3$	$Si(CH_3)_3$
i	Ph	H
j	Ph	Ph

Results and Discussion

We envisioned generating the target $R^1C_5R^2$ carbenes (Figure 1) from either, or both, of the isomeric diazo compounds, 1-diazo-2,4-pentadiyne (**13**) or 3-diazo-1,4-pentadiyne (**17**) (Scheme 3).[3] The terminal 1-diazo-2,4-pentadiyne derivatives have turned out to be better precursors—at least for the purposes of our experiments. Although salts of symmetrically substituted tosylhydrazone **16** apparently function as precursors to 3-diazo-1,4-pentadiyne derivatives and $R^1C_5R^1$ carbenes in solution,[15,20] our attempts to utilize these precursors to prepare and isolate the diazo compounds rarely met with success. A symmetrical, dialkynyl tosylhydrazone (**16**) necessarily contains a *syn* relationship between the *N*-imino substituent and one of the alkyne moieties; this arrangement often leads to complications associated with pyrazole formation and/or other undesired decomposition pathways (Scheme 3). This geometric relationship is not intrinsic to the unsymmetrical, butadiynyl tosylhydrazones (**12**). Salts of the *anti* butadiynyl tosylhydrazones are, in our hands, the most reliable precursors for generating and isolating the corresponding diazo compounds.

Precursors to MeC_5H (2). Diazo compounds **13b**, **13c**, and **17b** represent plausible precursors to MeC_5H (**2**). We have synthesized tosylhydrazone precursors to two of them. The first route assembles the carbon skeleton using 4 + 1 methodology. Diacetylide anion, resulting from treatment of 1,4-dichloro-2-butyne with 3 equiv of sodamide, is alkylated with methyl iodide (Scheme 4). In the same pot, subsequent addition of sodamide, followed by paraformaldehyde and an acidic quench, produces hexa-2,4-diyn-1-ol (**10b**) in 64% overall yield—a marked improvement over an earlier procedure.[26] A drawback to this procedure, however, is associated with the difficulty in maintaining proper control of stoichiometry. If methylation of diacetylene is incomplete, the desired alcohol **10b** is contaminated with the nonalkylated penta-2,4-diyn-1-ol (**10a**). Neither the mixture of alcohols nor the mixture of tosylhydrazones derived from them is separable by column chromatography.

SCHEME 4



An alternate procedure avoids the formation of penta-2,4-diyn-1-ol (**10a**). This route assembles the carbon skeleton using 3 + 2 methodology (Scheme 5). Cadiot–Chodkiewicz cross coupling of propyne (**18b**) with bromopropargyl alcohol (**19a**), under the conditions suggested by Marino,[27] affords hexa-2,4-diyn-1-ol (**10b**) in 50% yield, in accord with literature precedent.[28] We found this reaction to be generally useful for the preparation of substituted penta-2,4-diyn-1-ols (Scheme 5). In the specific case of propyne, the use of a

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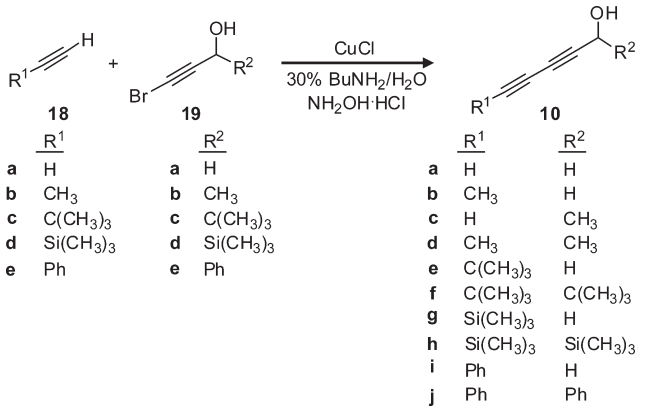
SCHEME 5



gaseous reagent in a room temperature reaction poses technical problems, and care must be taken to have an appropriate vent in order to avoid an excessive pressure build-up in the reaction flask.

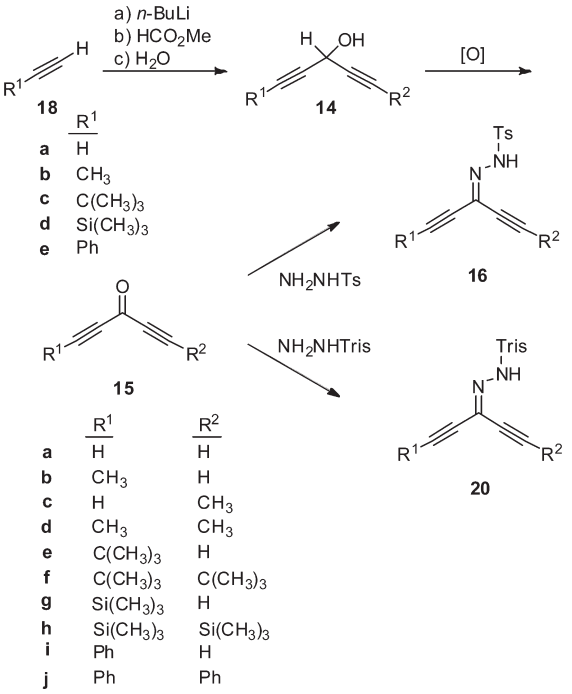
Oxidation of hexa-2,4-diyn-1-ol (**10b**) with Dess−Martin reagent[29] affords aldehyde **11b**, which did not prove to be amenable to isolation (Scheme 3). (Oxidation of alcohol **10b** may also be effected with MnO_2.[30]) The reaction mixture was filtered through silica gel (to remove the spent oxidant) directly into a flask containing *p*-toluenesulfonhydrazide. Tosylhydrazone **12b** was isolated as a mixture of *syn* and *anti* isomers (85% yield from **10b**). This procedure represents a general method that is used throughout the course of this investigation.

In the route to the isomeric tosylhydrazone **12c** (Scheme 4), 1,4-dichloro-2-butyne is again converted to the diacetylide anion upon treatment with 3 equiv of sodamide in ammonia.[26] Reaction of diacetylide with acetaldehyde, followed by an acidic quench, yields hexa-3,5-diyn-2-ol (**10c**) in 53% yield. Oxidation of diynol **10c** to diynone **11c**, with Dess−Martin reagent, and conversion to tosylhydrazone **12c** followed standard procedures (65% yield from **10c**). (Oxidation of hexa-3,5-diyn-2-ol (**10c**) may also be effected with chromic acid.[31])

By using the Bamford−Stevens reaction (Scheme 2), tosylhydrazones **12b** and **12c** may be converted to their respective diazo compounds (**13b**, **13c**). Both diazo compounds have been trapped under matrix isolation conditions and photochemically converted to MeC_5H (**2**).[32]

Precursors to MeC_5Me (3). Diazo compounds **13d** or **17d** represent plausible precursors to MeC_5Me (**3**). We have synthesized tosylhydrazone precursors to both of them, as well as the trisylhydrazone precursor to **17d**. The route to diazo compound **13d** assembles the carbon skeleton using 3 + 2 methodology. Cadiot−Chodkiewicz cross-coupling of propyne (**18b**) with bromoalkyne **19b** (Scheme 5)[27] affords

SCHEME 6



alcohol **10d** in 59% yield, in accord with literature precedent.[28] Oxidation of diynol **10d** to diynone **11d** and conversion to tosylhydrazone **12d** followed standard procedures (33% yield from **10d**).

The route to diazo compound **17d** assembles the carbon skeleton using 2 + 2 + 1 methodology. Literature procedures for generating the symmetrical alcohols **14** and ketones **15**, bearing either $-C(CH_3)_3$[33] or $-Si(CH_3)_3$[15] substituents (see below), led us to believe that these procedures could be used to prepare the corresponding tosylhydrazone **16d** bearing $-CH_3$ substituents (Scheme 6). Indeed, the addition of 2 equiv of 1-propynyllithium to methyl formate affords diynol **14d** in excellent yield (97%) after an acidic quench. The oxidation of alcohol **14d** to ketone **15d** may be accomplished by using $BaMnO_4$, PCC, or MnO_2, each giving similarly successful results. We found that stirring the ketone **15d** with tosylhydrazide in acetic acid at room temperature overnight generally leads to a higher yield of tosylhydrazone **16d** than the reflux conditions described for the $-Si(CH_3)_3$ derivative (**16h**).[15] Unfortunately, tosylhydrazone **16d** is accompanied by pyrazole **P2d** (ca. 3:1), which, in our experience, appears to be a general problem for symmetrical penta-1,4-diyn-3-one derivatives lacking bulky substituents (Scheme 3). The inability to separate the desired tosylhydrazone **16d** from pyrazole by column chromatography (silica gel; acidic or basic alumina) seemed puzzling until we established that the tosylhydrazone cyclizes during chromatography. In the hope that the bulkier trisylhydrazone derivative (trisyl = 2,4,6-triisopropylbenzenesulfonyl) would inhibit cyclization to pyrazole, we prepared trisylhydrazone **20d** from a slurry of ketone **15d** and trisylhydrazide in glacial acetic acid. The strategy was apparently successful; although yields were modest, isolation and purification of trisylhydrazone **20d**

(29) Our attempts to synthesize Dess−Martin periodinane using the combined procedures of Santagostino (Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537−4538) and Ireland (Ireland, R. E.; Lin, L. *J. Org. Chem.* **1993**, *58*, 2899) often resulted in a mixture of the desired reagent and the acetoxyiodinane oxide (Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549−7552), both of which effectively oxidize propargylic alcohols.

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were not complicated by the presence of the corresponding pyrazole.

With use of the Bamford−Stevens reaction (Scheme 2), tosylhydrazone **12d** may be converted to diazo compound **13d**. The diazo compound has been trapped under matrix isolation conditions and photochemically converted to MeC_5Me (**3**).[34]

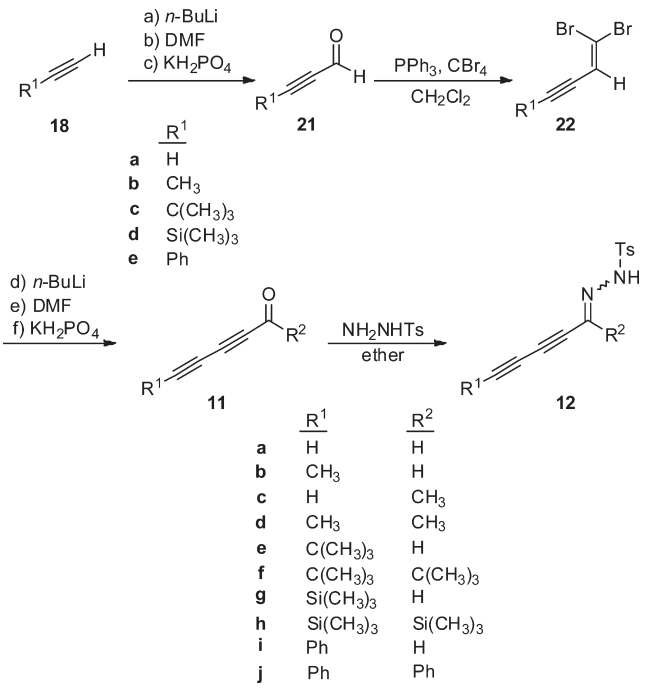
Precursors to *t*-BuC_5H (4). Although diazo compound **13e** has been utilized as a precursor to carbene *t*-BuC_5H (**4**), the synthetic procedure for the preparation of **13e** was not published.[21,22] We explored two synthetic routes to tosylhydrazone **12e**. The first employs a 3+2 cross-coupling strategy (Scheme 5). 3,3-Dimethylbutyne (*t*-butylacetylene) is an ideal substrate for the Cadiot−Chodkiewicz cross-coupling reaction because the alkyne is a liquid at room temperature. Stirring 3,3-dimethylbutyne (**18c**) and bromopropargyl alcohol (**19a**) in the presence of CuCl affords diynol **10e** in acceptable yield (45%), in accord with literature precedent.[35] (Iodopropargyl alcohol is also a suitable coupling partner for 3,3-dimethylbutyne.[36]) Oxidation of diynol **10e** to diynal **11e** and conversion to tosylhydrazone **12e** followed standard procedures (75% yield from **10e**).

An alternative route to tosylhydrazone **12e** employs a 2 + 1 + 1 + 1 chain homologation process involving formation of a dibromomethylidene intermediate (**22**) and subsequent rearrangement to extend the alkyne chain (Scheme 7).[37,38] Our interest in this reaction sequence is partially based on our desire to place a ^{13}C-label at the 3-position of these carbon chains.[39] The Cadiot−Chodkiewicz protocol does not afford a simple way to introduce the desired label, while the procedure in Scheme 7 does, through the use of isotopically enriched dimethylformamide. The synthesis begins with nucleophilic attack of lithiated 3,3-dimethylbutyne (**18c**) onto dimethylformamide, followed by an acidic quench, to generate aldehyde **21c** in 60% yield. Addition of aldehyde **21c** to a stirred mixture of PPh_3 and CBr_4 yields dibromoolefin **22c** in 81% yield. Conversion of **22c** to a vinylidene via lithiation and collapse of this unstable intermediate, followed by deprotonation, produces a *tert*-butyl-substituted diacetylide, which can attack dimethylformamide and yield aldehyde **11e** in 53% yield after acidic workup. (A similar Bouveault aldehyde synthesis of **11e** has been reported.[40]) When aldehyde **11e** is stirred with tosylhydrazide at room temperature, the desired tosylhydrazone **12e** is produced in 45% yield.

With the Bamford−Stevens reaction (Scheme 2), tosylhydrazone **12e** may be converted to diazo compound **13e**. The diazo compound has been trapped under matrix isolation conditions and photochemically converted to *t*-BuC_5H (**4**).[34]

Precursor to *t*-BuC_5-*t*-Bu (5). The preparation of bis(*tert*-butylethynyl) tosylhydrazone (**16f**)[20] utilizes the 2 + 2 + 1 methodology described previously for the dimethyl derivative (**16d**) (Scheme 6). Addition of 2 equiv of deprotonated

SCHEME 7



3,3-dimethylbutyne (**18c**) onto methyl formate affords alcohol **14f** in excellent yield (94%) after an acidic quench. Oxidation to ketone **15f** (using MnO_2, 62% yield) and formation of tosylhydrazone **16f** (35% yield) were uneventful. We have not isolated diazo compound **17f**, derived from tosylhydrazone **16f**, although previous work suggests that this transformation is facile.[20]

Precursors to Me_3SiC_5H (6). We explored four synthetic routes for the preparation of monotrimethylsilyl tosylhydrazone **12g**. In considering the application of our general 3 + 2 cross-coupling strategy for the synthesis of alcohol **10g** (Scheme 5), we rediscovered the fact that trimethylsilyl acetylene (**18d**) cannot be coupled to bromopropargyl alcohol (**19a**) by using known cross-coupling methods.[27] (Alcohol **10g** can be formed, however, through the coupling of iodotrimethylsilylacetylene and propargyl alcohol.[41]) Since the coupling of three-carbon and two-carbon fragments proved to be problematic, we pursued the coupling of four-carbon and one-carbon fragments. Monodesilylation of bis(trimethylsilyl)butadiyne (**23**), followed by formylation of the resulting carbanion **24** with dimethylformamide, has been reported as a route to the monotrimethylsilyl aldehyde **11g** (Scheme 8).[42] We encountered some difficulties with this procedure, and conjecture that it is difficult to avoid exposing the TMS-aldehyde to the strongly basic reaction conditions.[43,44] To avoid this problem, we opted to treat carbanion **24** with paraformaldehyde, rather than dimethylformamide.[3] This procedure affords alcohol **10g** (85% yield), which was subsequently oxidized to aldehyde **11g** (97% yield)

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(40) Jones, E. R. H.; Lee, H. H.; Whiting, M. C. *J. Chem. Soc.* **1960**, 3483–3489.
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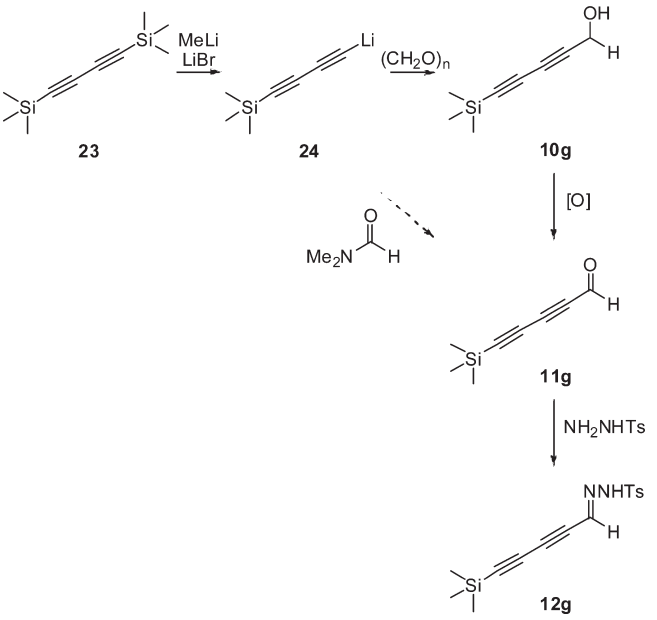
(43) At an earlier stage of our investigation, we believed that we had successfully generated aldehyde **11g**, albeit in poor yield, using the literature procedure.[42] Only with the subsequent, successful preparation of aldehyde **11g** and tosylhydrazone **12g**, did we realize that our initial characterization of **11g** was erroneous.[44]

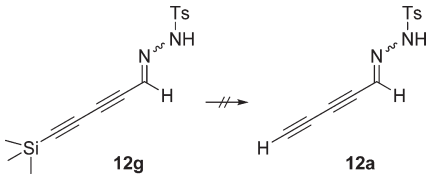
SCHEME 8



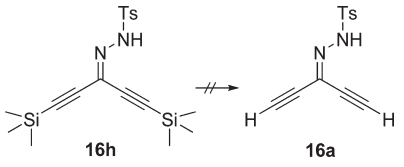
using the mild reaction conditions permitted by the Dess–Martin periodinane.[3] Conversion of aldehyde **11g** to tosylhydrazone **12g** (68% yield) was uneventful.

The 3 + 1 + 1 homologation procedure for the preparation of tosylhydrazone **12g** (Scheme 7) also suffers from the problematic generation of the aldehyde under strongly basic reaction conditions. The preparation of dibromoolefin **22d** proceeds smoothly, but conversion of **22d** to aldehyde **11g** is problematic. Attempts to convert dibromoolefin **22d** to aldehyde **11g** under a variety of conditions were unsuccessful.

In passing, we note our inability to find reaction conditions to effect the desilylation of **12g** to **12a** without predominant cyclization to pyrazole and/or other decomposition products.



Precursor to $Me_3SiC_5SiMe_3$ (7). The procedure offered by Rubin[15] for the synthesis of tosylhydrazone **16h** is quite reliable (Scheme 6). Once again, we note our inability to find reaction conditions to effect the desilylation of **16h** to **16a** without predominant cyclization to pyrazole and/or other decomposition products.



Precursor to PhC_5H (8). Diazo compounds **13i** and **17i** represent plausible precursors to PhC_5H (**8**). Our route to diazo compound **13i** assembles the carbon skeleton using 3 + 2 methodology (Scheme 5). Cadiot–Chodkiewicz cross-coupling of phenylacetylene (**18e**) with 3-bromopropargyl alcohol (**19a**) affords alcohol **10i** in 87% yield. Oxidation of diynol **10i** to diynal **11i**, and conversion to tosylhydrazone **12i** followed standard procedures (44% yield from **10i**).

Precursors to PhC_5Ph (9). Diazo compounds **13j** and **17j** represent plausible precursors to PhC_5Ph (**9**), and **13j** has been prepared, previously.[45] We have synthesized tosylhydrazone precursors to both diazo compounds. The route to diazo compound **13j** assembles the carbon skeleton using 3 + 2 methodology (Scheme 5).[45] Cadiot–Chodkiewicz cross-coupling of phenylacetylene (**18e**) with bromoalkyne **19e** affords alcohol **10j** in 74% yield. Oxidation to ketone **11j** (using $BaMnO_4$, 80% yield) and formation of tosylhydrazone **12j** (35% yield) were uneventful.

The route to diazo compound **17j** assembles the carbon skeleton using 2 + 2 + 1 methodology. The addition of 2 equiv of 2-phenylethynyllithium to methyl formate affords alcohol **14j** in 80% yield (Scheme 6). Oxidation to ketone **15j** (using $BaMnO_4$, 83% yield) and formation of tosylhydrazone **16j** (62% yield) were uneventful. Unfortunately, the symmetrical tosylhydrazone **16j** is once again accompanied by pyrazole formation (Scheme 3). We were unable to separate the desired tosylhydrazone **16j** from pyrazole by column chromatography (silica gel; acidic or basic alumina), as we determined that the tosylhydrazone cyclizes during chromatography.

Summary

Various strategies have been employed for the synthesis of a number of simple pentadiynols, -diynals, and -diynones, as well as their corresponding tosylhydrazones. The requisite five-carbon skeletons were prepared using 4 + 1, 3 + 2, 2 + 2 + 1, and 2 + 1 + 1 + 1 coupling methodologies. These compounds serve as precursors to diazo compounds, which, in turn, permit detailed studies of the photochemistry and spectroscopy of a family of dialkynyl carbenes (R^1—C≡C—C̈—C≡C—R^2).

Experimental Section

Synthetic Details for the Precursors of MeC_5H (2).

Hexa-2,4-diyn-1-ol (10b). Dry ammonia (35 mL) was condensed into a flask at −78 °C. $Fe(NO_3)_3 \cdot 9H_2O$ (50 mg) was added as the flask was warmed to −40 °C. At this temperature, small pieces of sodium (700 mg, 30.4 mmol) were slowly added. After addition of 1,4-dichloro-2-butyne (1.0 mL, 10.2 mmol), 15 mL of dry THF was added, followed immediately by 0.635 mL (10.2 mmol) of methyl iodide. This mixture was stirred for 3.5 h at −40 °C. An additional 3 equiv of sodamide in 35 mL of ammonia was added, followed by a suspension of 1.0 g (33.2 mmol) of paraformaldehyde in dry THF. The mixture was again stirred for 3.5 h at −40 °C. NH_4Cl (5.0 g) was added, followed by stirring for 15 min. The mixture was then rinsed into an Erlenmeyer flask with ether and the ammonia was allowed to evaporate. The remaining mixture was subjected to suction filtration and the precipitate was rinsed several times with ether. The filtrate was concentrated somewhat under reduced pressure, dried with $MgSO_4$, filtered, and concentrated fully to reveal a reddish oil, which crystallized in a freezer overnight. This residue was purified via flash chromatography (CH_2Cl_2, then 5%

(44) Halter, R. J. Ph.D. Thesis, University of Wisconsin, Madison, 2002.
(45) Noro, M.; Koga, N.; Iwamura, H. *J. Am. Chem. Soc.* **1993**, *115*, 4916.

EtOAc/CH_2Cl_2, then 10% EtOAc/CH_2Cl_2). The appropriate fractions were concentrated to reveal 0.617 g (6.56 mmol, 64% yield) of the desired alcohol **10b** as a reddish oil. ^{1}H NMR δ 4.31 (d, J = 5.1 Hz, 2H), 1.95 (t, J = 1 Hz, 3H), 1.56 (t, J = 5.7 Hz, 1H).

Alternative Route to Hexa-2,4-diyn-1-ol (10b). A flask was charged with CuCl (14 mg, 0.14 mmol) and 5 mL of 30% n-$BuNH_2/H_2O$ solution. This flask was equipped with a pressure equalizing dropping funnel with an aqueous $NH_2OH \cdot HCl$ solution. Propyne (**18b**) (~2.0 mL) was condensed at −78 °C into a separate flask. Propyne was transferred via cannula as it was slowly warmed. Bromopropargyl alcohol (**19a**) (1.0 g, 7.41 mmol) was added and the mixture was stirred at room temperature. Every time the solution started to turn green, a couple of drops of $NH_2OH \cdot HCl$ solution was added. Over time (~30 min), the mixture turned a rusty red color. The reaction mixture was extracted three times with 20 mL of ether. The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated to reveal an oily solid. This solid was purified via flash chromatography (5% EtOAc/CH_2Cl_2) yielding 0.350 g (3.71 mmol, 50%) of **10b** as an off-white solid. ^{1}H NMR matches that listed above.

3-Bromopropargyl Alcohol (19a). A flask was charged with 4.6 g (82.0 mmol) of KOH and 40 mL of deionized water. After the KOH pellets had dissolved, 1.19 mL (23.2 mmol) of Br_2 was added. The flask was cooled to 0 °C and covered in foil. Propargyl alcohol (1.20 mL, 20.6 mmol) was added, and the mixture was stirred at 0 °C for 3 h. The mixture was extracted twice with ether. The combined organic layers were dried with $NaSO_4$, filtered, and concentrated to reveal bromopropargyl alcohol **19a** as a light amber oil (2.33 g, 17.3 mmol, 84% yield). ^{1}H NMR ($CDCl_3$) δ 4.31 (s, 2H), 1.80 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 78.2, 51.3, 45.6.

Hexa-2,4-diyn-1-al Tosylhydrazone (12b). Hexa-2,4-diyn-1-ol (**10b**) (0.617 g, 6.56 mmol) was dissolved in 30 mL of dry CH_2Cl_2. Dess−Martin reagent[29] (4.26 g, 10.0 mmol) was added and the mixture was stirred for 4 h at room temperature, at which point oxidation was complete by TLC. Diethyl ether was added and the suspension was flushed through a short plug of silica with excess ether into a flask containing p-toluenesulfonhydrazide (1.22 g, 6.56 mmol). This mixture was stirred for 24 h at room temperature. Insoluble hypervalent iodine species were removed by filtration. The reaction mixture was concentrated somewhat at reduced pressure and washed with 50 mL of sat. aq. $NaHCO_3$ to eliminate any residual acetic acid from the Dess−Martin reagent, then sat. aq. NH_4Cl to ensure that the remaining tosylhydrazone was intact and was not the hydrazide salt. The combined aqueous layers were extracted with ether. The combined ether layers were then dried with $MgSO_4$, filtered, and concentrated to reveal an oily off-white solid mixture. After purification via flash chromatography (CH_2Cl_2, then 5% EtOAc/CH_2Cl_2, then 10% EtOAc/CH_2Cl_2), the appropriate fractions were concentrated to reveal two hexa-2,4-diyn-1-al tosylhydrazone isomers with an overall yield of 85% (1.46 g, 5.61 mmol, 35:65 *syn*:*anti* ratio).

***syn*-Hexa-2,4-diyn-1-al Tosylhydrazone (12b).** A total of 0.517 g was isolated as a white solid (R_f 0.56 in 5% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 8.67 (s, 1H), 7.83 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 6.61 (s, 1H), 2.43 (s, 3H), 2.09 (s, 3H). EIMS (70 eV) m/z M^+ 260.0 (34), 200 (41), 155 (53), 91 (100). HRMS (ESI) calcd for $C_{13}H_{12}N_2O_2SNa^+$ 283.0517, found 283.0508.

***anti*-Hexa-2,4-diyn-1-al Tosylhydrazone (12b).** A total of 0.947 g was isolated as a white solid (R_f 0.36 in 5% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 8.06 (s, 1H), 7.82 (d, J = 7.3 Hz, 2H), 7.34 (d, J = 7.3 Hz, 2H), 6.96 (s, 1H), 2.45 (s, 3H), 2.01 (s, 3H). EIMS (70 eV) m/z M^+ 260.0 (81), 196.1 (42), 91.0 (95). HRMS (ESI) calcd for $C_{13}H_{12}N_2O_2SNa^+$ 283.0517, found 283.0518.

Hexa-3,5-diyn-2-ol (10c). Approximately 50 mL of dry NH_3 was condensed into a flask at −78 °C. A catalytic quantity of $Fe(NO_3)_3 \cdot 9H_2O$ (25 mg) was added. The flask was warmed to −50 °C and 0.69 g of Na (30.0 mmol) was added slowly (in ~0.1 g chunks). After stirring for 15 min, the mixture was recooled to −78 °C and 1.0 mL of 1,4-dichloro-2-butyne (10.2 mmol) was added dropwise via syringe. Dry THF (10 mL) was added followed by acetaldehyde (0.612 mL, 10.2 mmol). After stirring for 1.5 h at −40 °C, 2.0 g of NH_4Cl was added. The mixture was stirred for 5−10 min, then rinsed into a large Erlenmeyer flask with diethyl ether. Once much of the ammonia had evaporated, the mixture was subjected to suction filtration and the precipitate was washed three times with ether. The filtrate was concentrated somewhat under reduced pressure, dried with $MgSO_4$, filtered, then concentrated completely to reveal a dark red oil. The resulting oil was purified via flash chromatography (first CH_2Cl_2, then 5% EtOAc/CH_2Cl_2). The appropriate fractions were concentrated to reveal 0.497 g (5.29 mmol, 53% yield) of **10c** alcohol as a reddish oil. ^{1}H NMR ($CDCl_3$) δ 4.58 (qdd, J = 6.5, 5.5, 1.0 Hz, 1H), 2.21 (d, J = 1 Hz, 1H), 1.85 (d, J = 5.5 Hz, 1H), 1.49 (d, J = 6.5 Hz, 3H).

Hexa-3,5-diyn-2-one Tosylhydrazone (12c). Alcohol **10c** (0.497 g, 5.29 mmol) was dissolved in 25 mL of dry CH_2Cl_2. Dess−Martin reagent[29] (3.60 g, 8.5 mmol) was added and rinsed into solution with an additional 5 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for 3 h, at which point the reaction was complete by TLC. Ether was added to the mixture and the resulting suspension was flushed through a short plug of silica gel with an excess of ether into a flask containing p-toluenesulfonhydrazide (0.985 g, 5.29 mmol). This mixture was stirred for 24 h at room temperature. The reaction mixture was concentrated somewhat at reduced pressure and washed with 50 mL of sat. aq. $NaHCO_3$ to eliminate any residual acetic acid from the Dess−Martin reagent, then sat. aq. NH_4Cl to ensure that the remaining tosylhydrazone was intact and was not the hydrazide salt. The organic phase was then dried with $MgSO_4$, filtered, and concentrated fully to reveal an off-white solid, which was purified by flash chromatography (CH_2Cl_2, then 5% EtOAc/CH_2Cl_2, then 10% EtOAc/CH_2Cl_2). The appropriate fractions were isolated to yield the desired tosylhydrazone **12c** in 65% overall yield (0.89 g, 3.42 mmol, 55:45 *syn*:*anti* ratio):

***syn*-Hexa-3,5-diyn-2-one Tosylhydrazone (12c).** A total of 490 mg was isolated as a white solid (R_f 0.48 in 5% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 8.33 (s, 1H), 7.83 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.83 (s, 1H), 2.45 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (Me_2SO) δ 143.6, 135.9, 133.7, 129.6, 127.6, 83.5, 81.2, 66.8, 66.2, 22.6, 21.1. HRMS (ESI) calcd for $C_{13}H_{12}N_2O_2SNa^+$ 283.0517, found 283.0519.

***anti*-Hexa-3,5-diyn-2-one Tosylhydrazone (12c).** A total of 400 mg was isolated as a white solid (R_f 0.24 in 5% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 2H), 7.80 (s, 1H), 7.34 (d, J = 8.4 Hz, 2H), 2.49 (s, 1H), 2.45 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (Me_2SO) δ 143.9, 136.9, 135.8, 129.8, 127.5, 77.4, 73.1, 72.1, 66.9, 21.1, 18.9. HRMS (ESI) calcd for $C_{13}H_{12}N_2O_2SNa^+$ 283.0517, found 283.0529.

Synthetic Details for the Precursors of MeC_5Me (3).

4-Bromobut-3-yn-2-ol (19b). A flask was charged with 4.60 g (82.0 mmol) of KOH pellets and 40 mL of deionized water. After the pellets had dissolved, 1.19 mL of Br_2 was added via syringe. The flask was covered with foil and cooled to 0 °C. 3-Butyn-2-ol (1.57 mL, 20.0 mmol) was added dropwise via syringe, and the solution changed from clear and yellow to milky and yellow in appearance. The mixture was allowed to stir for 3 h at 0 °C, then was extracted three times with ether. The combined organic layers were dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash column chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed the bromoalcohol **19b** (1.56 g, 10.5 mmol, 52% yield) as

a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 4.51 (q, J = 6.6 Hz, 1H), 2.91 (s, 1H), 1.43 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 82.1, 59.3, 44.5, 24.167. EIMS (70 eV) m/z M^+ 149 (11), 133 (100), 121 (6), 105 (11), 84 (8), 69 (32).

Hepta-3,5-diyn-2-ol (10d). CuCl (13.4 mg, 0.136 mmol) and 30% n-$BuNH_2$/H_2O (6.0 mL, 14.9 mmol) were added to a 25 mL round-bottom flask and the mixture was stirred under nitrogen. The cerulean blue solution was cooled to 0 °C. Propyne (**18b**) (excess) was condensed into a 10 mL round-bottom flask at −78 °C and cannula-transferred into the 25 mL round-bottomed flask until there was a visible change in volume in the 25 mL round-bottom flask. The solution turned teal in color. 4-Bromobut-3-yn-2-ol (**19b**) (0.475 g, 3.2 mmol) was added dropwise via syringe, and a fine yellow solid precipitated. The mixture was warmed to room temperature and NH_2OH/HCl was added until the solution remained a golden color and the precipitate dissolved. The mixture was poured into a separatory funnel containing water and ether. The aqueous layer was extracted three times with ether. The combined organic layers were dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash column chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed alcohol **10d** (0.202 g, 1.87 mmol, 59% yield) as a very pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 4.50 (q, J = 6.6 Hz, 1H), 2.86 (s, br, 1H), 1.89 (s, 3H), 1.41 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 77.5, 76.9, 69.2, 63.9, 58.7, 24.2, 4.4.

***anti*-Hepta-3,5-diyn-2-one Tosylhydrazone (12d).** Dry CH_2Cl_2 (25 mL) and Dess−Martin periodinane (2.7146 g, 6.40 mmol) were added to alcohol **10d** (0.4752 g, 3.1895 mmol) and allowed to stir under nitrogen at room temperature. The reaction was shown to be complete by TLC after 1 h. Diethyl ether was added and the resulting suspension was flash-filtered through a short Celite plug into a round-bottom flask containing p-toluenesulfonhydrazide (0.615 g, 3.30 mmol). The mixture was allowed to stir under nitrogen at room temperature overnight. The mixture was filtered to remove insoluble hypervalent iodine species, and the filtrate was washed with saturated sodium bicarbonate solution. The organic layer was washed with saturated ammonium chloride solution, and the combined aqueous layers were extracted with diethyl ether. The combined organic layers were dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash column chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed tosylhydrazone **12d** (0.291 g, 1.06 mmol, 33% yield) as a white powder. ^{1}H NMR ($CDCl_3$) δ 8.36 (s, br, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 2.40 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 144.4, 135.6, 133.9, 129.8, 128.0, 88.0, 87.3, 63.6, 62.9, 22.5, 21.7, 4.9. HRMS (ESI) calcd for [MH^+] 275.0854, found 275.0861.

Hepta-2,5-diyn-4-ol (14d). A flame-dried 100 mL round-bottomed flask was charged with 30 mL of dry THF and the mixture was cooled to −78 °C. n-BuLi (6.0 mL, 9.0 mmol, 1.5 M solution in hexane) was added via syringe. Propyne (**18b**) was condensed into the flask in excess (until there was a visible change in volume in the flask). After the addition of methyl formate (0.185 mL, 3.0 mmol), the mixture was stirred at −78 °C for 1 h. The mixture was allowed to warm to −40 °C and was maintained there for 45 min. Water was added and the reaction mixture was warmed to room temperature. The mixture was rinsed into a separatory funnel with H_2O and ether. The aqueous phase was extracted with ether (3 × 30 mL). The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (10% CH_3CN/CH_2Cl_2) to reveal 315 mg (2.91 mmol, 97% yield) of alcohol **14d** as a white powder. ^{1}H NMR ($CDCl_3$) δ 5.07 (doublet of septets, J = 7.2 Hz, 2.4 Hz, 1H), 2.10 (d, J = 7.2 Hz, 1H), 1.89 (d, J = 2.4 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 80.8, 77.2, 52.4, 3.7.

Hepta-2,5-diyn-4-one (15d). Method 1. A mixture of 20 mL of dry CH_2Cl_2 and $BaMnO_4$ (1.67 g, 6.50 mmol) was prepared and added to the 100 mL round-bottom flask containing alcohol **14d** (0.16 g, 1.46 mmol). After stirring under nitrogen at room temperature for 45 min, the reaction was complete by TLC. The contents of the flask were flash-filtered through a short Celite plug. The filtrate was dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash column chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed ketone **15d** (0.148 g, 1.39 mmol, 95%) as a peach-colored powder. ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 6H). ^{13}C NMR ($CDCl_3$) δ 161.3, 90.7, 81.5, 4.3. EIMS (70 eV), m/z M^+ 106 (28), 91 (11), 84 (17), 78 (42), 67 (28), 58 (100).

Method 2. A mixture of 10 mL of dry CH_2Cl_2, 1.29 g (5.98 mmol) of pyridinium chlorochromate (PCC), and a small amount of Celite was prepared in a round-bottom flask. A solution of alcohol **14b** in 10 mL of dry CH_2Cl_2 was transferred to this flask. After stirring at room temperature for 2 h, the reaction was complete by TLC. The contents of the flask was filtered, with suction, through a plug of Celite. The filtrate was concentrated under reduced pressure then purified via flash chromatography (CH_2Cl_2). Concentration of the appropriate fractions afforded 0.210 g (1.98 mmol, 78% yield) of ketone **15d** as a white powder. ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 161.3, 90.7, 81.5, 4.3.

Hepta-2,5-diyn-4-one Tosylhydrazone (16d). Glacial acetic acid (5.0 mL) and tosylhydrazide (0.413 g, 2.22 mmol) were added to a 100 mL round-bottom flask containing 0.237 g (2.24 mmol) of ketone **15d**. The mixture was stirred overnight under nitrogen, then poured into a separatory funnel containing 2:1 cold water and cold CH_2Cl_2. The organic phase was dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed 0.330 g (1.20 mmol, 54% yield) of a 3:1 ratio of tosylhydrazone **16d** to pyrazole **P2d** as a white powder. Tosylhydrazone (**16d**): ^{1}H NMR ($CDCl_3$) δ 8.81 (s, br, 1H), 7.80 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 2.38 (s, 3H), 2.04 (s, 3H), 1.91 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 144.5, 135.4, 129.8, 120.6, 101.0, 88.5, 75.4, 70.2, 4.8. HRMS (ESI) calcd for $C_{14}H_{14}N_2O_2SNa^+$ 297.0674, found 297.0681. Pyrazole **P2d**: ^{1}H NMR ($CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 6.03 (s, br, 1H), 2.48 (s, 3H), 2.37 (s, 3H), 1.96 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 145.8, 143.7, 139.5, 134.8, 130.1, 127.9, 112.7, 89.6, 71.6, 21.7, 13.1, 4.4. HRMS (ESI) calcd for $C_{14}H_{14}N_2O_2SNa^+$ 297.0674, found 297.0668.

Hepta-2,5-diyn-4-one Trisylhydrazone (20d). Method 1. Glacial acetic acid (5 mL) and trisylhydrazide (0.37 g, 1.25 mmol) were added to a 100 mL round-bottom flask containing 0.13 g (1.25 mmol) of ketone **15d**. The mixture was allowed to stir overnight under nitrogen, then poured into a separatory funnel containing 2:1 cold water and cold CH_2Cl_2. The organic phase was dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash chromatography ($CHCl_3$). Concentration of the appropriate fractions revealed 0.19 g (0.49 mmol, 39% yield) of trisylhydrazone **20d** as a white powder. ^{1}H NMR ($CDCl_3$) δ 8.71 (s, br, 1H), 7.13 (s, 2H), 4.16 (septet, J = 6.6 Hz, 2H), 2.87 (septet, J = 6.9 Hz, 1H), 2.07 (s, 3H), 1.90 (s, 3H), 1.24 (d, J = 6.6 Hz, 12 H), 1.21 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 153.7, 151.4, 131.5, 124.1, 119.7, 100.4, 88.2, 75.5, 70.3, 34.3, 30.2, 24.9, 23.7, 4.8, 4.4. HRMS (ESI) calcd for $C_{22}H_{30}N_2O_2SH^+$ 387.2101, found 387.2083.

Method 2. A flask was charged with 220 mg (2.11 mmol) of ketone **15d** and 631 mg (2.11 mmol) of trisylhydrazide. Ethanol was added dropwise with stirring until it formed a thick slurry. This mixture was stirred for 18 h at room temperature (turning into an orange homogeneous mixture). Some crystals precipitated overnight. Crystallization was further induced with cooling to 0 °C. Suction filtration afforded a yellow solid. Upon rinsing

with hexane, the solid turned white. This white powder was isolated and found to be the desired trisylhydrazone **20d** (0.181 g, 0.47 mmol, 22% yield). ^{1}H NMR ($CDCl_3$) δ 8.66 (s, 1H), 7.17 (s, 2H), 4.19 (septet, J = 6.6 Hz, 2H), 2.91 (septet, J = 6.6 Hz, 1H), 2.14 (s, 3H), 1.95 (s, 3H), 1.25−1.29 (multiplet, 18H).

Synthetic Details for the Precursors of *t*-BuC_5H (4).

6,6-Dimethylhepta-2,4-diyn-1-ol (10e). To a flask containing 7.4 mg (0.07 mmol) of CuCl and 2.5 mL of a 30% *n*-BuNH_2/H_2O solution was added 0.54 mL (4.4 mmol) of 3,3-dimethylbutyne (**18c**). The mixture was immediately cooled to 0 °C and 0.5 g (3.7 mmol) of bromopropargyl alcohol (**19a**) was added, the solution turned bright blue in color, and the ice bath was removed. When the reaction mixture turned green, $NH_2OH \cdot HCl$ crystals were added in small increments until the solution remained a rusty red color. After 30 min, the mixture was poured into a separatory funnel and washed with water. The aqueous portion was then extracted (3 × 20 mL) with ether. The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated to reveal a pale yellow oil. Purification via flash chromatography (CH_2Cl_2) yielded 0.225 g (1.66 mmol, 45% yield) of alcohol **10e** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 4.32 (d, J = 6.0 Hz, 2H), 1.53 (t, J = 6.3 Hz, 1H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 89.5, 75.0, 70.9, 63.3, 51.7, 30.6, 28.2. EIMS (70 eV) m/z M^+ 136 (86), 121 (64), 107 (29) 93 (100), 77 (98), 63 (34), 51 (26) 41 (34).

6,6-Dimethylhepta-2,4-diynal Tosylhydrazone (12e). Dry CH_2Cl_2 (25 mL) and Dess−Martin periodinane (0.85 g, 2.00 mmol) were added to **10e** (0.225 g, 1.66 mmol) and the mixture was allowed to stir under nitrogen at room temperature. The reaction was shown to be complete by TLC after 30 min. Diethyl ether was added and the resulting suspension was flash-filtered through a short Celite plug into a round-bottom flask containing *p*-toluenesulfonhydrazide (0.31 g, 1.66 mmol). The mixture was allowed to stir under nitrogen at room temperature overnight. The solution was washed with saturated sodium bicarbonate solution. The organic layer was washed with sat. aq. NH_4Cl, and the combined aqueous layers were extracted with diethyl ether. The combined organic layers were dried with $MgSO_4$, filtered, concentrated under reduced pressure, and purified with flash column chromatography (CH_2Cl_2, then 5% EtOAc/CH_2Cl_2, then 10% EtOAc/CH_2Cl_2). Concentration of the appropriate fractions revealed tosylhydrazone **12e** (0.368 g, 1.21 mmol, 74% overall yield, ca. 1:1 *syn*:*anti* ratio).

***syn*-6,6-Dimethylhepta-2,4-diynal Tosylhydrazone (12e).** A total of 0.171 g was isolated as a pale yellow solid (R_f 0.77 in 10% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 8.72 (s, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 6.59 (s, 1H), 2.43 (s, 3H), 1.29 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 144.8, 135.4, 130.0, 128.1, 124.2, 99.7, 88.2, 63.9, 62.6, 30.3, 28.8, 21.8. HRMS (ESI) calcd for $C_{16}H_{18}N_2O_2SNa^+$ 325.0987, found 325.0973.

***anti*-6,6-Dimethylhepta-2,4-diynal Tosylhydrazone (12e).** A total of 0.196 g was isolated as an off-white solid (R_f 0.62 in 10% EtOAc/CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 9.06 (s, 1H), 7.80 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.00 (s, 1H), 2.43 (s, 3H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 144.9, 135.0, 130.1, 128.2, 124.3, 95.8, 79.8, 69.9, 63.5, 30.4, 28.6, 21.9. HRMS (ESI) calcd for $C_{16}H_{18}N_2O_2SNa^+$ 325.0987, found 325.0984.

Alternative Route to 6,6-Dimethylhepta-2,4-diynal Tosylhydrazone (12e). 4,4-Dimethyl-pent-2-ynal (21c). A flask was charged with 30 mL of dry THF and 3,3-dimethylbutyne (**18c**) (1.0 mL, 8.12 mmol), then cooled to −78 °C. *n*-BuLi (3.53 mL, 8.12 mmol, 2.3 M in hexane) was added via syringe and the mixture was allowed to warm to room temperature over 15 min. The mixture was recooled to −78 °C and dimethylformamide (1.26 mL, 16.2 mmol) was added. The mixture was allowed to stir for 1 h at room temperature. The reaction mixture was poured into a vigorously stirring biphasic mixture of 10% aq KH_2PO_4 and ether precooled to 0 °C. The layers were separated and the organic phase was extracted three times with diethyl ether. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated to reveal 0.535 g (4.9 mmol, 60% yield) of aldehyde **21c** as a colorless oil. The aldehyde is rather volatile. Cooling to 0 °C when concentrating under reduced pressure is advised. ^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 1.31 (s, 9H).

1,1-Dibromo-5,5-dimethylhex-1-en-3-yne (22c). A flask was charged with 3.22 g (9.71 mmol) of CBr_4 and 20 mL of dry CH_2Cl_2 and was cooled to −20 °C. A solution of 5.25 g (20.0 mmol) of PPh_3 in 20 mL of CH_2Cl_2 was transferred to this flask and the mixture was stirred for 30 min at −20 °C. The flask was then cooled to −78 °C and a solution of 0.535 g (4.86 mmol) of aldehyde **21c** and 0.681 mL (4.86 mmol) of NEt_3 in 10 mL of CH_2Cl_2 was transferred to the flask. The mixture was stirred at room temperature overnight. After 16 h, hexane was added and the mixture was flushed through a short plug of silica with excess hexane. The colorless filtrate was dried with $MgSO_4$, filtered, and concentrated to reveal 1.05 g (3.93 mmol, 81%) of the desired dibromoenyne **22c** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 6.53 (s, 1H), 1.28 (s, 9H).

6,6-Dimethylhepta-2,4-diynal (11e). A flask was charged with 10 mL of dry THF and 1.05 g (3.93 mmol) of dibromoenyne **22c** and was cooled to −78 °C. *n*-BuLi (3.56 mL, 8.2 mmol, 2.3 M in hexane) was added dropwise via syringe, as the solution turned black. The mixture was stirred at −78 °C for 30 min, then was warmed to 0 °C for 15 min. After recooling to −78 °C, dimethylformamide (1.53 mL, 19.7 mmol) was added. The mixture was then warmed to room temperature for 1 h. After warming, the mixture was poured into a vigorously stirring biphasic mixture of 10% aq. KH_2PO_4 and ether precooled to 0 °C. The layers were separated and the organic layer was washed with water. The combined aqueous layers were extracted with diethyl ether (3 × 25 mL). The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated to reveal a black oil. This oil was purified via flash chromatography (5% EtOAc/hexane) yielding 0.280 g (2.09 mmol, 53% yield) of diynal **11e** as a dark oil. ^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 1.29 (s, 9H).

6,6-Dimethylhepta-2,4-diynal Tosylhydrazone (12e). Aldehyde **11e** (0.280 g, 2.09 mmol) was dissolved in 10 mL of diethyl ether in the presence of *p*-toluenesulfonhydrazide (0.389 g, 2.09 mmol). This mixture was stirred overnight at room temperature. After 18 h, the mixture was dried with $MgSO_4$, filtered, and concentrated to reveal a thick red oil. This oil was purified via flash chromatography (5% EtOAc/CH_2Cl_2). The appropriate fractions were combined to reveal 0.287 g (0.95 mmol, 45% yield) of tosylhydrazone **12e** as an orange solid. ^{1}H NMR ($CDCl_3$) δ 8.52 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.98 (s, 1H), 2.44 (s, 3H), 1.25 (s, 9H).[46] ^{13}C NMR ($CDCl_3$) δ 144.7, 135.3, 130.0, 128.1, 124.2, 99.7, 88.1, 63.9, 62.6, 30.2, 28.7, 21.8. HRMS (ESI) calcd for $C_{16}H_{18}N_2O_2SNa^+$ 325.0987, found 325.0973.

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Supporting Information Available: Experimental procedures for the synthesis of precursors to *t*-BuC_5-*t*-Bu (**5**), Me_3Si-C_5H (**6**), $Me_3SiC_5SiMe_3$ (**7**), PhC_5H (**8**), and PhC_5Ph (**9**) and ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(46) This spectrum seems to correlate with the *syn*-conformer obtained using the independent synthetic route. In retrospect, since the compound isolated in this procedure was the first to elute from the column, it is possible that the *anti*-conformer was simply left on the column and therefore, not isolated.