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Highly Chemoselective Triple Bond Reductions on Unsymmetrical 1,4-Diorganyl-1,3-Butadiynes.

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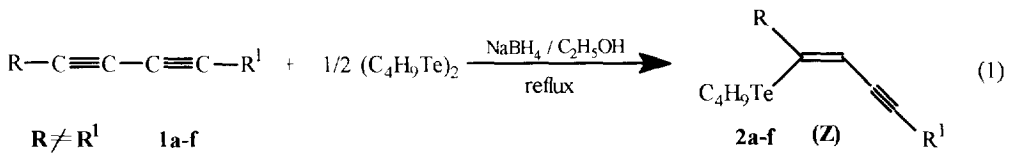
Abstract: Unsymmetrical 1,4-diorganyl-1,3-butadiynes **1a-g** undergo regio-, stereo- and chemoselective addition of butyltellurolate anion leading to (**Z**)-1-butyltelluro-1,4-bis(organyl)but-1-en-3-ynes **2a-g** in good yields. The terminal triple bond reacts faster than the propargylic triple bond (alcohol derivatives), which is more reactive than the triple bond bearing an alkyl or aryl group. Combination with removal of butyl tellurium moiety from the products obtained is equivalent to a chemoselective *trans*-hydrogenation of one triple bond of 1,3-butadiynes. Treatment of **2c** or **2f** with n-butyllithium in THF at -78 °C furnished the corresponding (**E**)-enynes free of tellurium **7a** and **7b**, respectively. Detelluration occurs with absolute retention of the double bond geometry. In this way, sequential treatment with dimethyl sulfate of enynyl lithium **8** generated *in situ* by reaction of **2b** with n-butyllithium produced the (**Z**)-enyne free of tellurium **9**. The reaction of **8** with CO_2 followed by acidification of the reaction mixture resulted in the formation of carboxylic acid **10** also with the central carbon-carbon double bond of **Z** configuration.

Hydrotelluration of terminal acetylenes and conjugated enynes is a *trans*-stereospecific process that permits the exclusive formation of compounds with **Z** double bonds bearing an organyltellurium substituent.[1-11] Vinylic tellurium species are of synthetic interest since the tellurium moiety can be replaced by different organic groups with total retention of configuration. For example, lithium-tellurium exchange reaction with n-BuLi, followed by treatment with aldehydes or ketones produced allylic alcohols.[4,12-15] Transmetalation with $Me_2Cu(CN)Li_2$ and $Bu(2\text{-}Th)Cu(CN)Li_2$ leads to the **Z**-vinylic cyanocuprates, which react with enones and epoxides furnishing 4,5-unsaturated ketones[16] or homoallylic alcohols.[17] Cross-coupling of vinylic tellurides of **Z** configuration with higher order cyanocuprates[18] or with Grignard reagents[1] catalyzed by $NiCl_2(PPh_3)_2$ afforded olefins with retention of the original geometry. Alkylation of vic-bis(phenyltelluro) alkenes with lithium dialkylcuprates (Me_2CuLi) takes place regioselectively with the removal of the phenyltelluro group bonded at the terminal carbon.[15]

In a previous paper, we have described[14] a preparative method of a series of **Z**-1-butyltelluro-1,4-bis(organyl)but-1-en-3-ynes by the addition of butyltellurolate anion to symmetrical 1,4-bis(organyl)-1,3-butadiynes and the study of Li/Te exchange reaction of these conjugated compounds with n-BuLi. Furthermore, other authors have studied the transmetalation of these tellurobutenynes with higher order cuprates.[16-18] In this paper we report the results obtained by

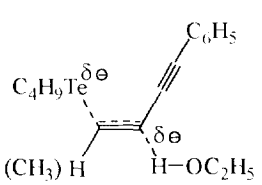
selective addition of butyltellurolate anion to one of the triple bonds of conjugated unsymmetrical diacetylenes (eq. 1). Detelluration of the products obtained by the Te/Li exchange reaction was also studied.



(1)

With the mono-substituted-1,3-butadiyne **1a**, the reaction of dibutyl ditelluride (0.5 equiv.) and sodium borohydride in ethanol, with the mixture refluxed for the time indicated in Table I (entry 1), occurs chemoselectively, with Te-H addition taking place exclusively at the terminal triple bond leading the (**Z**)-1-butyltelluro-4-phenyl-1-buten-3-yne **2a** in 75% yield (Table I, entry 1). The terminal triple bond is more reactive because of the steric hindrance caused by the phenyl group attached to the other triple bond. Evidence that steric factors are at work here was obtained by replacing the terminal hydrogen in **1a** with the larger methyl group in **1c**, since in this case the reaction is slower (2 hours). However, addition of butyl tellurolate to **1c** occurs exclusively at the methyl substituted triple bond and the product **2c** was isolated in good yield (Table I, entry 3). The last result showed that electronic factors are also important. During the attack of tellurolate anion, a negative charge is developed at adjacent carbon (C-2) and the transition state of type **3** is formed, since **3** is more stable than **4**, because the phenyl acetylenic moiety tends to stabilize the incipient carbanion by withdrawing electrons more effectively than the ethynil group of **1a** or propynil of **1c** in **4**.

In the cases of compounds **1d-f**, the propargylic triple bonds underwent addition of butyltellurolate anion more easily than triple bonds bearing an aryl (entries 4 and 5) or alkyl substituent (entry 6). This is probably due to the formation of the cyclic five members transition state of type **5** and **6** which is responsible for the intramolecular protonation of the incipient carbanion formed in C-2. For reactions of **1a-c,** ethanol acts as the proton donor as depicted in **3**. The difference in rate between reactions of **1d** (15 min) and **1e** (1 hour) is due to steric factors because when carbinolic hydrogens are replaced with two methyl groups there is an increased crowding in the transition state (compare structures **5** and **6**). However, stabilization by the electronic effect of the phenyl acetylenic group and intramolecular protonation by the formation of cyclic structure **6** are more important. Thus, **2e** is the only product formed.



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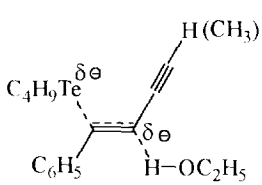

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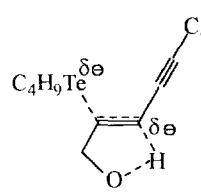

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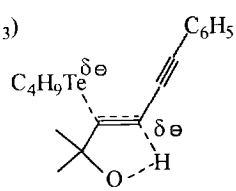
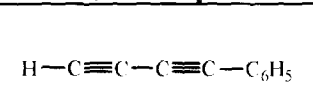
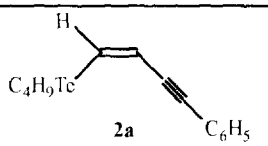
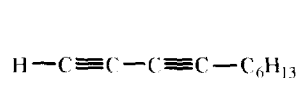
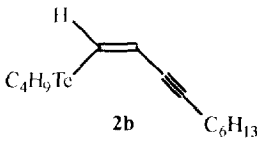
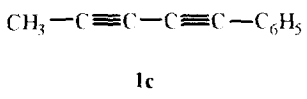
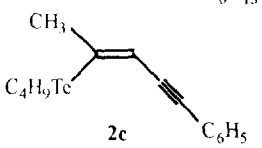
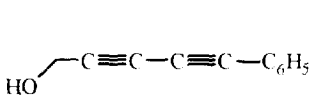
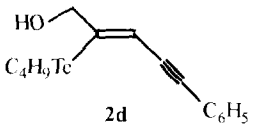
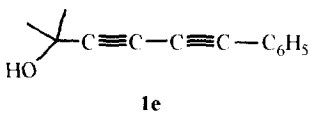
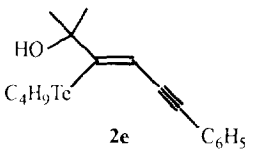
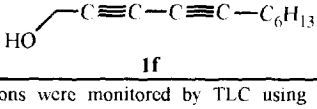
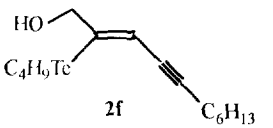


6

The structures of the compounds obtained were easily determined by ^{1}H NMR and ^{13}C NMR spectroscopy. The ^{13}C NMR spectra reveal a signal in the range of 118.6 - 137.6 ppm corresponding to the tellurium-substituted olefinic carbon (C)-1, and another signal in the range of 113.7 - 117.9 ppm due to carbon (C)-2 in accordance with results previously described for similar compounds.[14] For all compounds in Table I and separated **2g** and **2h**, only two signals (one in the range of 80.2 - 97.9 and another in the range of 94.5 - 104.7 ppm) are observed in the acetylenic region (from 80 to 110 ppm) in the ^{13}C NMR spectra, showing the presence of only one type of triple bond.

Table I. Tellurobutenynes obtained from unsymmetrical 1,3-diynes.

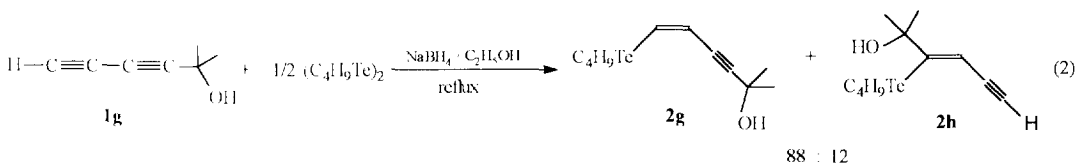
Entry	1,3-Butadiyne	Product	Reaction time[a]	Yield (%)[b]
1	 **1a**	 **2a**	10 min.	75
2	 **1b**	 **2b**	17 min	79
3	 **1c**	 **2c**	2.0 hour	80
4	 **1d**	 **2d**	15 min.	76
5	 **1e**	 **2e**	1.0 hour	82
6	 **1f**	 **2f**	35 min.	89

a. The reactions were monitored by TLC using hexane or hexane/AcOEt mixture as eluent. b.Product purified by flash chromatography using hexane or hexane/AcOEt mixture as eluent.

On the basis of the results obtained, we propose that a fundamental feature that defines the mechanism of the hydrotelluration of alkynes is that the reaction occur in a single step and hence Te-C(1) and C(2)-H bonds making and C-C triple bond-breaking occur simultaneously in a concerted fashion (as shown in transition states **3**,**4**,**5** and **6**). This feature is also supported by the **Z** geometry of

the double bond obtained which is explained by the fact that in the transition state the tellurium nucleophile is partly bonded and consequently accommodates a partial negative charge and bond C(2)-H is partly formed with the carbon accommodating a partial negative charge too. In this way, ethanol in **3** or hydroxylic moiety in **5** and **6** that are donating a proton to the incipient carbanion formed and the tellurium nucleophile should be as far apart as possible to minimize steric interactions.

In all cases studied, the reactions were 100% chemoselective (Table I), but when the 2-hydroxy-2-methyl-3,5-hexadiyne **1g** was used, a mixture of isomers **2g** and **2h** was obtained (80% yield) at a 88:12 ratio. The preferential addition on the terminal triple bond (product **2g**; eq. 2) was determined by ^{1}H NMR. These isomers were separated by flash chromatography using hexane/AcOEt (6/4) as the mobile phase.



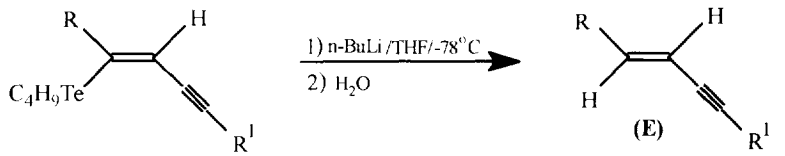
(2)

All results discussed above show that the order of reactivity of triple bonds in conjugated unsymmetrical butadiynes toward the addition of butyltellurolate anion is the following:

terminal > propargylic (alcohol derivatives) > alkyl substituted > aryl substituted

There has been increasing interest in enyne, enyne-allene and enediyne system synthesis because these structures are present in several natural products[19] and are used in generating biradicals as potential DNA-cleaving agents.[20] In this way, the versatility of the tellurobutenyne approach could be greatly enhanced if tellurium-free enynes or enediynes with diverse chemical structures could be readily synthesized from it. To this end, we have thus transformed some **Z**-tellurobutenynes obtained here into both **E** and **Z** enynes tellurium free. The same strategy can be successfully utilized for the synthesis of **Z**-iodo enynes[21a] that by sequential coupling with alkynes can lead to the enediynes with retention of configuration.[21b]

Reaction of **2c** and **2f** with n-BuLi in THF at -78°C followed by water addition produces the corresponding 5-phenyl-2-penten-4-yne **7a** in 73% and the 2-undecen-4-yne-1-ol **7b** in 69% yield, respectively (eq. 3). In the reaction of **2f** the use of 2.0 equivalents of n-butyllithium was necessary, since a hidroxyl group is present in the molecule. No other regio- or stereoisomers were detected in the reaction mixture by either GLC or spectrometric analysis. The last reactions occur with total retention of configuration,[14] confirming the assignment made for the structures of **2c** and **2f** and permiting the synthesis of compounds containing an **E** double bond directly bonded to an acetylene.



(3)

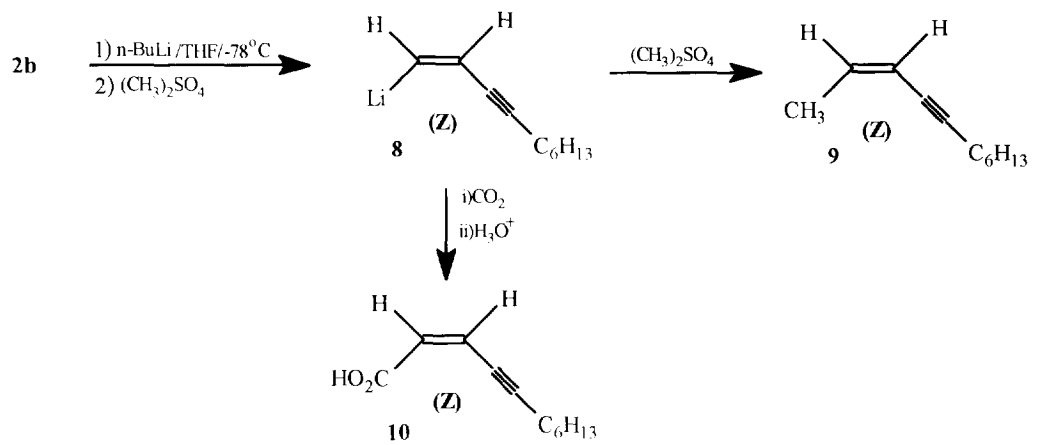
2c → **7a** R = CH_3; R^1 = C_6H_5 Yield: 73%
2f → **7b** R = CH_2OH; R^1 = C_6H_{13} Yield: 69%

The *cis*-enyne structure is present in histrionicotoxin and its derivatives[22] and is found in a wide range of natural products extracted from several sources such as compounds present in various species of the *Laurencia* red alga[19a-b,23] with the secondary metabolites and in the green variety of the Hawaiian alga, *Laurencia nidifica*.[24] **Z**-Enynes are also obtained from seahares,[25] sponges,[26] and South American "poison arrows" frogs[19d,27] and are present in the potent antitumor antibiotics[28] esperamycin/calicheamycin[29] and dynemycin[30] that are obtained from fermentation broths of soil microorganisms. The available methods for the synthesis of this types of compounds are varied; however, it should be noted that partial catalytic hydrogenation,[31] hydroboration[32] and hydroalumination[33] of unsymmetrically substituted diynes are not chemoselective. However, catalytic hydrogenation[22] and hydroalumination[34] of trimethylsilyl-protected butadiyne derivatives take place exclusively at the non-silicon bearing triple bond. Some other usual methods for obtaining unsymmetrically substituted enynes involve vinyl sulfone chemistry,[35] the coupling of a metal acetylide with cis-vinyl halides[36] or of vinyl organometallics with an acetylenic halide[36] and transition-metal-catalyzed dimerization of 1-alkynes.[37]

The chemoselective hydrotelluration of diynes developed here was also extended to the synthesis of **Z**-enynes by sequential detelluration of 1-tellurobutenyne **2b** obtained from a 1,3-diyne containing a terminal triple bond and by capture of the enynyl lithium intermediate of type **8** with electrophilic reagents as exemplified in Scheme 1.

By using dimethyl sulfate to capture the lithium intermediate **8** obtained from reaction of 1-butyltelluro-1-decen-3-yne **2b** with butyllithium, **Z**-2-undecen-3-yne **9** was obtained in 56 % yield (Scheme 1). Treatment of **2b** with butyllithium followed by reaction of **8** with CO_2 and HCl furnished the corresponding carboxylic acid conjugated with the **Z**-enyne system **10** in 60 % yield. These results clearly indicate that detelluration/alkylation proceeded stereospecifically in the retention manner. Electrophiles such as CO_2, $(CH_3)_2SO_4$, aldehydes,[14] ketones, epoxides[17] could be used instead of water in reactions of 1-butyltelluro-1,4-diorganyl-1-buten-3-ynes of type **1c-f** (see eq. 3). We[14] and others[16,17] described previously similar reactions using analogues compounds obtained from symmetrical 1,3-butadiynes. These reactions could provide an attractive route for the synthesis of enynes having trisubstituted alkene double bonds.

Scheme 1



In conclusion, this paper describes the first example of highly chemoselective reduction of triple bonds in 1,4-diorganyl-1,3-butadiynes. Combination of hydrotelluration with the Te/Li exchange reaction or other known reactions of vinylic tellurium species[1,4,12-18] thus provides a convenient sequence to obtain butenynes free of tellurium, with total control of the regio and stereochemistry. Systems containing **Z** or **E** double bonds were obtained in this manner. The development of reactions commented in this paper discloses new perspectives for challenging synthetic applications of tellurium intermediates. Applications of the reactions described here to the synthesis of some natural products are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Remarks. ^{1}H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with Brucker AC 80 (80 MHz) and AC 200 (200 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm) with respect to tetramethylsilane as an internal standard. IR spectra were obtained on neat samples and recorded with a Perkin-Elmer model 1600 spectrometer. Mass spectra (EI) were obtained at 70 eV with a Hewlett Packard EM/CG HP-5988A spectrometer. Elemental analyses were performed at the Instrumental Analysis Center of the Chemistry Institute of the São Paulo University. Reactions were conducted in oven-dried (120 °C) glassware under a nitrogen atmosphere. Analytical TLC of all reactions was performed using E. M. Merck prepared plates (silica gel 60 F-254 on aluminum). Merck silica gel (230-400 mesh) was used for flash chromatography. Ethanol 95% from Merck without purification was used and tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. The 1-alkynes and n-butyl-lithium (2.5 M in hexanes) were purchased from Aldrich Chemical Co., Inc., dibutylditelluride,[38] and the 1,3-butadiynes[39a] were prepared by the procedures in the literature: $C_6H_5C{\equiv}C\text{-}C{\equiv}CC(CH_3)_2OH$;[39b,c] $C_6H_5C{\equiv}C\text{-}C{\equiv}CH_2OH$;[39b,d] $C_6H_{13}C{\equiv}C\text{-}C{\equiv}CCH_2OH$;[39b,d] $C_6H_{13}C{\equiv}C\text{-}C{\equiv}CC(CH_3)_2OH$,[39b,c] $C_6H_5C{\equiv}C\text{-}C{\equiv}CH$;[39a,e] $C_6H_{13}C{\equiv}C\text{-}C{\equiv}CH$[39a,e,f] and $C_6H_5C{\equiv}C\text{-}C{\equiv}CCH_3$.[39a,g]

(Z)-1-Butyltelluro-4-phenyl-1-buten-3-yne (2a). A solution of 1-phenyl butadiyne (2.0 mmol) was obtained *in situ* by reaction of 2-hydroxy-2-methyl-6-phenyl-3,5-hexadiyne **1e** (0.368 g, 2.0mmol) with solid NaOH (5.0 mg) in dry xylene (2.2 mL) at reflux for 15 minutes. The temperature was then allowed to reach room temperature and 95% ethanol (20 mL) and dibutyl ditelluride (0.369g, 1.0 mmol) were added. The reaction now was run under an atmosphere of N_2 and sodium borohydride (0.09g, 2.5 mmol) was added. After disappearence of the red color, the yellow-brown mixture was refluxed for 10 minutes, diluted with ethyl acetate (70 mL) and washed with brine (4 x 30mL). After drying the organic phase over anhydrous $MgSO_4$, the solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel using hexane as mobile phase, to give the pure butyltelluro enyne **2a** as a yellow oil. 0.468 g (75%); CG/MS m/z 314 (M^+) $C_{14}H_{16}Te$, 256 ($-C_4H_9$) 128 (100.00); IR (neat, cm^{-1}) 690, 750, 1541, 1595, 2184; ^1H NMR (80 MHz) (δ in $CDCl_3$) 0.93 (t, J = 7, 3H) 1.41 (sext., J = 7, 2H) 1.85 (quint., J = 7, 2H) 2.81(t, J = 7, 2H) 6.61 (d, J = 13, 1H) 7.1-7.6 (m, 6H); ^{13}C NMR 6.2, 13.2, 24.7, 33.9, 89.5, 96.2, 117.3, 120.8, 123.0, 126.3, 128.1, 128.3, 131.1. *Anal.* Calcd. for $C_{14}H_{16}Te$: C 53.92, H 5.17; Found : C 54.33, H 5.30.

(Z)-1-Butyltelluro-1-decen-3-yne (2b). Powdered NaOH (0.11 g) was added to a two-neck round bottomed flask (250 mL) equipped with a reflux condenser, containing a solution of 2-hydroxy-2-methyl-3,5-dodecadiyne (2.064 g; 10.75 mmol) in dry xylene (11 mL) under a nitrogen atmosphere. The white mixture was slowly heated to reach reflux temperature, at this time the reaction mixture turned brown and was refluxed for 10 minutes. The solution of the 1,3-decadiyne **1b** obtained was cooled to room temperature and then dibutyl ditelluride (1.845 g; 5.0 mmol) and 95% ethanol (170 mL) were added. $NaBH_4$ (0.463 g; 12.5 mmol) was cautiously added dropwise and gas evolution was observed during addition. After the red-brown color disappearance, the yellow mixture was refluxed for 17 minutes, cooled at room temperature, diluted with ethyl acetate (70 mL) and washed with brine (5 x 40 mL). After drying the organic phase over anhydrous $MgSO_4$, the solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel using hexane as mobile phase, to give the pure butyltelluro enyne **2b** as a yellow oil. 2.53 g (79 %); CG/MS m/z 322 (M^+) $C_{14}H_{24}Te$, 195 (100.00), 135 ($-C_4H_9Te$); IR (neat, cm^{-1}) 690, 1546, 2206; ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.8-1.0 (m, 6H), 1.2-1.6 (m, 10H), 1.80 (quint., J = 7.5 Hz, 2H), 2.34 (td, J = 6.7 Hz, J = 2 Hz, 2H), 2.74 (t, J = 7.5 Hz, 2H), 6.34 (dt, J = 10 Hz, J = 2 Hz, 1H), 7.15 (d, J = 10 Hz, 1H); ^{13}C NMR 5.8, 13.4, 14.1, 19.7, 22.6, 25.0, 28.6, 28.7, 31.4, 34.4, 80.9, 97.9, 118.0, 118.2. *Anal.* Calcd. for $C_{14}H_{24}Te$: C 52.56, H 7.56. Found : C 52.85, H, 7.30.

(Z)-2-Butyltelluro-5-phenyl-2-penten-4-yne (2c). To a solution of **1c** (0.878 g; 6.27 mmol) and dibutyl ditelluride (1.15 g; 3.13 mmol) in 95% ethanol (100 mL) under N_2, $NaBH_4$ (0.28 g; 8 mmol) was added at room temperature. After the disappearance of the red color, the yellow mixture was refluxed for 15 min., allowed to reach room temperature, work-up and purification as above gave the pure compound **2c** as a yellow oil. Yield: 1.632 g (80%); CG/MS m/z 328 (M^+) $C_{15}H_{18}Te$, 141 (100.00; $-C_4H_9Te$); IR (neat, cm^{-1}) 690, 750, 1562, 1595, 2184; ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.90 (t, J = 7.27 Hz, 3H), 1.41 (sext., J = 7.5 Hz, 2H), 1.77 (quint., J = 7.5 Hz, 2H), 2.27 (d, J = 1.5 Hz, 3H), 2.80 (t, J = 7.5 Hz, 2H), 6.17 (q, J = 1.5 Hz, 1H), 7.2-7.3 (m, 3H), 7.4-7.5 (m, 2H); ^{13}C NMR 5.3, 13.4, 25.1, 27.4, 34.4, 89.5, 94.5, 113.7, 123.4, 128.0, 128.2, 131.2, 132.4. *Anal.* Calcd. for $C_{15}H_{18}Te$: C 55.28, H 5.57. Found : C 55.19, H 5.30.

(Z)-2-Butyltelluro-5-phenyl-2-penten-4-yne-1-ol (2d). The same procedure as for **2c** was followed using 5-phenyl-2,4-pentadiyn-1-ol **1d** (0.312g, 2.0 mmol) and dibutylditelluride (0.369g, 1.0 mmol) in ethanol (40 mL) and $NaBH_4$ (0.09g; 2.5 mmol). After 15 minutes of reflux and the usual work-up, the residue was purified by flash chromatography using a mixture of hexane/ethyl acetate (7/3) to afford the pure compound **2d**. Yield: 0.519g (76%). CG/MS m/z 344 (M^+) $C_{15}H_{18}TeO$, 158 (-C_4H_9Te), 140 (-H_2O and -C_4H_9Te), 128 (100.00) ($Te^{\cdot+}$); IR (neat, cm^{-1}) 1579 (m), 2191(w), 3352 (s); ^1H NMR (80 MHz) (δ in $CDCl_3$) 0.88 (t, J = 6.7 Hz, 3H), 1.40 (sext., J = 6.7, 2H), 1.79 (quint., J = 6.7 Hz, 2H), 2.35 (broad s, 1H), 2.94 (t, J = 6.9 Hz, 2H), 4.35 (d, J ≅ 1.3 Hz, 2H), 6.55 (t, J ≅ 1.3 Hz, 1H), 7.2-7.6 (m, 5H); ^{13}C NMR 5.6, 13.4, 24.8, 34.2, 69.0, 89.2, 96.1, 115.1, 123.3, 128.3, 131.4, 135.1. *Anal.* Calcd. for $C_{15}H_{18}$ TeO : C 52.69, H 5.31. Found : C 52.61, H 5.30.

(Z)-2-Methyl-3-Butyltelluro-6-phenyl-3-hexen-5-yne-1-ol (2e). The same procedure as for **2c** was followed using 2-hydroxy-2-methyl-6-phenyl-3,5-hexadiyne **1e** (0.368g, 2.0 mmol) and dibutylditelluride (0.369g, 1.0 mmol) in ethanol (40 mL) and $NaBH_4$ (0.09g; 2.5 mmol). After 1 hour of reflux and the usual work-up, the residue was purified by flash chromatography using a mixture of hexane/ethyl acetate (7/3) to afford the pure compound **2e**. Yield: 0.606g (82%). CG/MS m/z 372 (M^+) $C_{17}H_{22}TeO$, 315 (-C_4H_9), 185 (-C_4H_9Te), 167 (100.00) (-H_2O and -C_4H_9Te); IR (neat, cm^{-1}) 1576 (m), 2194 (w), 3369 (br., m); ^1H NMR (80 MHz) (δ in $CDCl_3$) 0.83 (t, J = 6.7 Hz), 1.1-2.0 (m, 4H), 1.48 (s, 6H), 3.05 (t, J = 7 Hz, 2H), 6.67 (s, 1H), 7.1-7.6 (m, 5H); ^{13}C NMR 8.5, 13.1, 24.7, 29.5, 33.4, 75.3, 89.6, 95.1, 116.6, 123.1, 127.9, 128.0, 130.7, 145.7. *Anal.* Calcd. for $C_{17}H_{22}TeO$: C 55.19, H 5.99. Found : C 55.06, H 5.96.

(Z)-2-Butyltelluro-2-undecen-4-yn-1-ol (2f). The same procedure as for **2c** was followed using 2,4-undecadiyne-1-ol **1f** (0.328g, 2.0 mmol) and dibutylditelluride (0.369g, 1.0 mmol) in ethanol (40 mL) and $NaBH_4$ (0.09g; 2.5 mmol). After 35 minutes of reflux and the usual work-up, the residue was purified by flash chromatography using a mixture of hexane/ethyl acetate (9/1) as mobile phase to afford the pure compound **2f**. Yield: 0.622g (89%). CG/MS m/z 352 (M^+) $C_{15}H_{26}TeO$, 294 (-C_4H_9), 225 (100.00) $C_6H_8TeO^{\cdot+}$; IR (neat, cm^{-1}) 1573, 2206, 3351; ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.89 (t, J = 6.6 Hz, 3H), 0.92 (t, J = 7 Hz, 3H), 1.2-1.6 (m, 10H), 1.76 (quint., J = 7 Hz, 2H), 2.36 (td, J = 6 Hz, J = 1.7 Hz, 2H), 2.87 (t, J = 7.5 Hz, 2H), 3.1 (br s, 1H), 4.25 (s, 2H), 6.27 (t, J = 1.7 Hz, 1H); ^{13}C NMR 4.9, 13.5, 14.1, 19.7, 22.6, 25.1, 28.7, 31.4, 31.7, 34.3, 68.7, 80.2, 97.8, 115.7, 132.2. *Anal.* Calcd. for $C_{15}H_{26}TeO$: C 51.48, H 7.49. Found : C 51.60, H 7.25.

(Z)-1-Butyltelluro-5-methyl-1-hexen-3-yn-5-ol (2g). The same procedure as for **2c** was followed using 2-methyl-2-hydroxy-3,5-hexadiyne **1g** (0.432g, 4.0 mmol) and dibutylditelluride (0.738g, 2.0 mmol) in ethanol (80 mL) and $NaBH_4$ (0.18g; 5.0 mmol). After 10 minutes of reaction and the usual work-up, the residue contained a mixture of **2g** and **2h** and dibutyl telluride as determined by ^1H NMR. After purification by flash chromatography using a mixture of hexane/ethyl acetate (6/4) as mobile phase, compound **2g** was isolated in a pure form. Yield: 0.823g (70%). MS m/z 296 (M^+) $C_{11}H_{18}TeO$, 258 (Te_2), 221 (C_7H_8Te), 109 (-C_4H_9Te), 91 (100.00) (-H_2O and -C_4H_9Te), IR (neat, cm^{-1}) 1548 (m), 2219 (w); 3378 (br, s); ^1H NMR (80 MHz) (δ in $CDCl_3$) 0.93 (t, J = 6.6 Hz, 3H), 1.0-2.0 (m, 4H), 1.57 (s, 6H), 2.78 (t, J = 7.5 Hz, 2H), 3.14 (br s, 1H), 6.37 (d, J = 10.4 Hz, 1H), 7.32 (d, J = 10.4 Hz, 1H); ^{13}C NMR 6.2, 13.4, 24.9, 31.5, 34.3, 65.6, 82.2, 101.2, 117.0, 120.6. *Anal.* Calcd. for $C_{11}H_{18}TeO$: C 44.96, H 6.17. Found : C 45.29, H 6.18.

(Z)-2-Methyl-2-hydroxi-3-butyltelluro-3-hexen-5-yne (2h). Compound **2h** was obtained in pure form after separation by flash chromatography from the mixture described above. Yield: 0.117g (10%). MS m/z 296 (M^+) $C_{11}H_{17}TeO$, 221 (C_7H_8Te), 109 (-C_4H_9Te), 91 (-H_2O and -C_4H_9Te), 57 (100.00); ^1H NMR (80 MHz) (δ in $CDCl_3$) 0.93 (t, J = 6.6 Hz, 2H), 1.0-2.0 (m, 4H), 1.48 (s, 6H), 2.45 (br s, 1H), 3.02 (t, J = 7.5 Hz, 2H), 3.32 (d, J = 2.6 Hz, 1H), 6.47 (d, J = 2.6 Hz, 1H); ^{13}C NMR 9.0, 29.6, 31.0, 32.5, 33.7, 68.6, 83.6, 104.7, 116.2, 137.6. *Anal.* Calcd. for $C_{11}H_{18}TeO$: C 44.96, H 6.17. Found : C 45.13, H 6.05.

(E)-5-Phenyl-2-penten-4-yne (7a) by reaction of 2c with n-BuLi. To a solution of **2c** (0.887g, 2.73 mmol) in THF (16 mL) at -78°C under N_2, butyllithium (1.5 mL, 3.0mmol, 2.0 M in hexane) was added at once and the reaction stirred for 15 min. The cooling bath was removed and the mixture treated with saturated solution of ammonium chloride (5 mL), diluted with ethyl acetate (40 mL) and washed with brine (20 mL x 3). After drying the organic phase over anhydrous $MgSO_4$, the solvent was removed under reduced pressure. The residue containing dibutyl telluride and **7a** was diluted with petroleum ether and sulfuryl chloride (~1mL) was added dropwise at 0 °C until the yellow color turned white. The product **7a** was separated from the dibutyl tellurium dichloride by horizontal distillation in a Kugelrohr oven. Fraction distilled at 52-55 °C/ 0.25 mmHg was the pure (E)-enyne **7a** obtained as a colorless liquid. Yield: 0.283g (73%). CG/MS m/z 143 (M^+), 141(M-1) (100.00), 115 (-C_2H_2), 102 ($C_6H_5C{\equiv}C$); IR (neat, cm^{-1}) 690, 750, 946, 1590, 1655, 2184; ^1H NMR (200 MHz) (δ in $CDCl_3$) 1.80 (dd, J = 6.8 Hz J = 1.7 Hz, 3H), 5.69 (d.quart., J = 15.75 J = 1.7 Hz, 1H), 6.22 (d.quart., J = 15.75 Hz J = 6.8 Hz, 1H), 7.1-7.3 (m, 3H), 7.3-7.5 (m, 2H); ^{13}C NMR 18.7, 88.3, 110.8, 123.6, 127.8, 128.2, 131.4, 131.9, 139.8. *Anal.* Calcd. for $C_{11}H_{10}$: C 92.91, H 7.09. Found : C 92.58, H 6.78.

(E)-2-Undecen-4-yn-1-ol (7b) by reaction of 2f with n-BuLi. The same procedure as above was followed using compound **2f** (0.741g, 2.12 mmol), THF (12 mL) and 2.2 equiv. of n-BuLi (2.33 mL, 4.66 mmol, 2.0 M in hexanes). After work up and solvent removal, the residue was purified by column chromatography using hexane to remove the dibutyl telluride and compound **7b** was then eluted with a mixture of hexane/ethyl acetate (9/1) as mobile phase. Yield: 0.242g (69%). CG/MS m/z 166, 123 (-$C_3H_7{\cdot}^+$), 109 (-$C_4H_9{\cdot}^+$), 105 (-H_2O and $C_3H_7{\cdot}^+$), 95 (100.00) (-$C_5H_9{\cdot}^-$), 81 (-$C_6H_{13}{\cdot}^-$); IR (neat, cm^{-1}) 951, 1459, 1628, 2217, 3319; ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.89 (t, J = 6.7 Hz, 3H), 1.2-1.6 (m, 8H), 2.28 (t, J = 6.7 Hz, 2H), 2.82 (br s, 1H), 4.13 (d, J = 5 Hz, 2H), 5.69 (d quart., J = 15.8 Hz, J = 1.6 Hz, 1H), 6.13 (dt, J = 15.8 Hz J = 5.4 Hz, 1H); ^{13}C NMR 14.1, 19.4, 22.6, 28.6, 28.7, 31.4, 62.8, 78.4, 91.3, 111.6, 140.3. *Anal.* Calcd. for $C_{11}H_{18}O$: C 79.46, H 10.91. Found : C 79.42, H 10.61.

(Z)-2-Undecen-4-yne (9) from 2b. To a solution of **2b** (0.8016 g; 2.5 mmol) in THF (15 mL) at -78 ° C under N_2, n-butyllithium (1.37 mL; 2.75 mmol; 2.0 M in hexanes) was added at once and the reaction stirred for 15 min. Then Me_2SO_4 (0.6 mL, 6.25 mmol) was added dropwise and the stirring was continued at -78 °C for an additional half hour. After this time, the cooling bath was removed and the reaction stirred overnight. After work-up and solvent removal as above, the residue was diluted in petroleum ether and the yellow solution treated dropwise with sulfuryl chloride (~1mL) at 0 °C. The solvent was evaporated from the resulting mixture and **9** was distilled in a Kugelrohr apparatus at 55° C/0.25 mmHg and repurified by filtration in a silica gel column using hexane as solvent to separate

from the remaining dimethyl sulfate. Yield: 0.21 g (56 %). CG/MS m/z 150 (M^+), 135 (-CH_3), 121 (-C_2H_5), 107 (-C_3H_7), 93 (-C_4H_9), 79 (-C_5H_{11}) (100.00); ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.82(t, J = 6.7 Hz, 3H), 1.1-1.5 (m, 9H), 1.78 (dd, J = 9.2 Hz, J = 1.6 Hz, 3H), 2.27 (dt, J = 7Hz, J = 2.1 Hz, 2H), 5.39 (dq, J = 10.7 Hz, J = 1.7 Hz, 1H), 5.81 (dq, J = 10.7 Hz, J = 6.7 Hz, 1H); ^{13}C NMR 14.0, 15.7, 19.5, 22.6, 28.6, 28.9, 31.3, 95.0, 110.4, 125.4, 136.8. *Anal.* Calcd. for $C_{11}H_{18}$: C 87.93, H 12.07 Found: C 87.31, H 11.99.

(Z)-2-Undecen-4-yne-1-oic (10) from 2b. To a solution of **2b** (0.897 g; 2.8 mmol) in THF at -78 °C under N_2, n-BuLi (1,54 mL; 3.08 mmol; 2.0 M in hexanes) was added at once and the reaction mixture was stirred for 15 minutes. Then CO_2 (evaporated dry ice) was bubbled into the resulting solution at -78 °C for 15 minutes and the cooling bath was removed. After the reaction mixture reach room temperature (~15 min.) a 10% H_2SO_4 solution (4 mL) was added and allowed to stand for additional 5 minutes. The reaction mixture was diluted with diethyl ether (30 mL) and washed with H_2O (10 mL portions) until neutral pH. After drying the organic phase over anhydrous $MgSO_4$, the solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel using a mixture of hexane:ethyl acetate (9:1) to remove impurities and ethyl acetate to remove compound **10** wich was distilled in a Kugelrohr apparatus at 250°C/0.3 mmHg to obtain an analitically pure sample. Yield: 0.304 g (60 %); CG/MS m/z 180 (M), 152 (-CO), 135 (-CO_2H), 123 (-C_4H_9), 95 (-C_6H_{13}) (100.00); IR (neat, cm^{-1}) 815 (s), 1437 (s), 1606 (s), 1683 (s) 1693 (s), 2206 (s), 3100 (bs); ^1H NMR (200 MHz) (δ in $CDCl_3$) 0.85 (t, J = 6.7 Hz, 3H), 1.2-1.6 (m, 8H), 2.40 (dt, J = 6.7 Hz, J = 2.2 Hz, 2H), 6.02 (d, J = 11.4 Hz, 1H), 6.22 (dt, J = 11.4 Hz, J = 2.3 Hz, 1H), 11.11 (bs, 1H); ^{13}C NMR 14.0, 20.0, 22.4, 28.1, 28.4, 31.2, 77.6, 106.3, 126.1, 126.6, 170.2; *Anal* Calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95. Found: C 73.36, H 8.67.

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References and Notes:

1. Uemura, S., Fukuzawa, S. *Tetrahedron Lett.*, **1982**, 1181.
2. Dabdoub, M. J., Dabdoub, V. B., Comasseto, J. V., Petragnani, N. *J. Organomet. Chem.*, **1986**, *308*, 211.
3. Dabdoub, M. J., Comasseto, J. V. *Organometallics*, **1988**, *7*, 84.
4. Barros, S. M., Dabdoub, M.J., Dabdoub, V. B., Comasseto, J. V. *Organometallics*, **1989**, *8*, 1661.
5. Buzilova, S. R., Vereshchagin, L. I., Sadekov, I. D., Minkin, V. I. *Zh. Obshch. Khim.*, **1976**, *46*, 932.
6. Buzilova, S. R., Sadekov, I. D., Lipovich, T. V., Filipova, T. M., Vereshchagin, L. I. *Zh. Obshch. Khim.*, **1977**, *47*, 1999.
7. Uemura, S., Fukuzawa, S., Patil, S. R. *J. Organomet. Chem.*, **1983**, *243*, 9.
8. Detty, M. R., Murray, B. J., Smith, D. L., Zumbulyadis, N. *J. Amer. Chem. Soc.*, **1983**, *105*, 875.
9. Takahashi, H., Ohe, K., Uemura, S., Sugita, N. *Nippon Kagaku Kaishi*, **1987**, 1508.

10. Ohe, K., Takahashi, H., Uemura, S., Sugita, N. *J. Org. Chem.*, **1987**, *52*, 4859.
11. Ohe, K., Takahashi, S., Uemura, S., Sugita, N. *J. Organomet. Chem.*, **1987**, *326*, 35.
12. Hiiro, T., Kambe, N., Ogawa, A., Miyoshi, N., Murai, S., Sonoda, N. *Angew. Chem. Intl. Ed. Engl.*, **1987**, *26*, 1187.
13. Barros, S. M., Comasseto, J. V., Berriel, J. N. *Tetrahedron Lett.*, **1989**, *30*, 7353.
14. Dabdoub, M. J., Dabdoub, V. B., Comasseto, J. V. *Tetrahedron Lett.*, **1992**, *33*, 2261.
15. Ogawa, A., Tsuboi, Y., Obayashi, R., Yokoyama, K., Ryu, I., Sonoda, N. *J. Org. Chem.*, **1994**, *59*, 1600.
16. Tucci, F. C., Chieffi, A., Comasseto, J. V. *Tetrahedron Lett.*, **1992**, *33*, 5721.
17. Marino, J. P., Tucci, F. C., Comasseto, J. V. *Synlett.*, **1993**, 761.
18. Chieffi, A., Comasseto, J. V. *Tetrahedron Lett.*, **1994**, 35, 4063.
19. (a) Moore, R. E. In *Marine Natural Products*, Scheuer, P.J.; Ed.; Academic Press: New York; **1978**, Vol. 1, Ch 2, p.43. (b) Erickson, K.L. In *Marine Natural Products*, Scheuer, P.J.; Ed.; Academic Press: New York; **1983**, Vol. 5, Ch. 4, p. 131. (c) Guella, G.; Pietra, F. *Helv. Chim. Acta* **1991**, *74*, 47. (d) Daly, J.W.; Spande, T.F. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S.W.; Ed.; Wiley Interscience: New York; **1986**, Vol. 4, Ch. 1, p. 1.
20. Nicolaou, K. C.; Dai, W. M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387 and references cited therein.
21. a) Dabdoub, M. J., Begnini, M. L., Guerrero, P. Jr. Results to be published. b) Wang, Z.; Wang, K. K. *J. Org. Chem.* **1994**, *59*, 4738.
22. Holmes, A. B.; Raphael, R. A.; Wellard, N. *Tetrahedron Lett.*, **1976**, *17*, 1539 and references cited therein.
23. (a) Faulkner, D. J. *Nat. Prod. Rep.*, **1984**, *1*, 251. (b) Faulkner, D. J. *Nat. Prod. Rep.*, **1984**, *1*, 551. (c) Faulkner, D. J. *Nat. Prod. Rep.*, **1986**, *3*, 1. (d) Faulkner, D. J. *Nat. Prod. Rep.*, **1987**, *4*, 539. (e) Faulkner, D. J. *Nat. Prod. Rep.*, **1988**, *5*, 613. (f) Faulkner, D. J. *Nat. Prod. Rep.*, **1990**, *7*, 269. (g) Faulkner, D. J. *Nat. Prod. Rep.*, **1991**, *8*, 97. (h) Brandes, A., Hoffmann, H. M. R. *Tetrahedron*, **1995**, *51*, 145.
24. Holmes, A. B.; Jennings-White, C. L. D.; Kendrick, D. A. *J. Chem. Soc. Chem. Commun.*, **1983**, 415 and references cited therein.
25. (a) McDonald, F. J.; Campbell, D. C.; Vanderah, D. J.; Schmitz, F. J.; Washecheck, D. M.; Burks, J. E.; van der Helm, D. *J. Org. Chem.*, **1975**, *40*, 665. (b) Shulte, G. R.; Chung, M. C. H.; Scheuer, P. J. *J. Org. Chem.*, **1981**, *46*, 3870. (c) Gopichand, Y.; Schmitz, F. J.; Shelly, J.; Rahman, A.; van der Helm, D. *J. Org. Chem.*, **1981**, *46*, 5192.
26. (a) Rotem, M.; Kashan, Y. *Tetrahedron Lett.*, **1979**, *31*, 3193. (b) Guella, G.; Mancini, I.; Pietra, F. *J. Chem. Soc., Chem. Commun.*, **1986**, 77. (c) Guella, G.; Mancini, I.; Pietra, F. *Helv. Chim. Acta*, **1987**, *70*, 1050. (d) Fusetani, N.; Sugano, M.; Matsuaga, S.; Hashimoto, K. *Tetrahedron Lett.*, **1987**, *28*, 4311. (e) Hirsh, S.; Carmely, S.; Kashman, Y. *Tetrahedron*, **1987**, *43*, 3257. (f) Cimino, G.; DeGiulio, A.; DeRosa, S.; DiMarzo, V. *Tetrahedron Lett.*, **1989**, *30*, 3563. (g) Guella, G.; Pietra, F. *Helv. Chim. Acta.*, **1991**, *74*, 47.
27. (a) Tokuyama, T.; Uenoyama, K.; Brown, G.; Daly, J. W.; Witkop, B. *Helv. Chim. Acta*, **1974**, *57*, 2597. (b) Daly, J. W.; Witkop, B.; Tokuyama, T.; Nishikawa, T.; Karle, I. L. *Helv. Chim.*

Acta, **1977**, *60*, 1128. (c) Tokuyama, T.; Yamamoto, J.; Daly, J. W.; Highet, R. J. *Tetrahedron*, **1983**, *39*, 49. (d) Tokuyama, T.; Nishimori, N.; Karle, I. L.; Edwards, M. W.; Daly, J. W. *Tetrahedron*, **1986**, *42*, 3453. (e) Tokuyama, T.; Tsujita, T.; Shimada, A.; Garrafo, H. M.; Spande, T. F.; Daly, J. W. *Tetrahedron*, **1991**, *47*, 5401.

28. (a) For a review of enediyne antibiotics see: Nicolaou, K. C.; Dai, W. M. *Angew. Chem., Int. Ed. Engl.*, **1991**, *30*, 1387. (b) Skrydstrup, T.; Ulibarri, A. G.; Grierson, D. S. *Tetrahedron Lett.*, **1992**, *33*, 4563.
29. (a) Magnus, P.; Annoura, H.; Harling, J. *J. Org. Chem.*, **1990**, *55*, 1709 and references cited therein. (b) Lee, M. D.; Dunne, T. S.; Chang, C. C.; Siegel, M. M.; Morton, G. O., Ellestad, G. A.; McGahren, W. J.; Borders, D. B. *J. Am. Chem. Soc.*, **1992**, *114*, 985.
30. Konishi, M.; Ohkuma, H.; Matsumoto, K.; Tsuno, T.; Kamei, H.; Miyaki, T.; Oki, T.; Kawaguchi, H.; Van Duyne, G.; Clardy, J. *J. Antibiot.*, **1989**, *42*, 1449.
31. Shakhovskoi, B. G.; Stadnichuk, M. D.; Petrov, A. A. *Zh. Obshch. Khim.*, **1964**, *34*, 2625; *J. Gen. Chem.* USSR, **1964**, *34*, 2646.
32. Zweifel, G.; Polston, N. L. *J. Am. Chem. Soc.*, **1970**, *92*, 4068.
33. Zweifel, G.; Lynd, R. A.; Murray, R. E. *Synthesis*, **1977**, 52.
34. (a) Miller, J. A.; Zweifel, G.; *J. Am. Chem. Soc.*, **1983**, *105*, 1383. (b) Miller, J. A.; Leong, W.; Zweifel, G. *J. Org. Chem.*, **1988**, *8*, 1839.
35. Holmes, A. B.; Pooley, G. R. *Tetrahedron*, **1992**, *48*, 7775.
36. Paley, R. S.; Lafontaine, J. A.; Paz Ventura, M. *Tetrahedron Lett.*, **1993**, 34, 3663 and References cited in Ref. 35.
37. Ohshita, J.; Furumori, K.; Matsuguchi, A.; Ishikawa, M. *J. Org. Chem.*, **1990**, *55*, 3277 and references cited therein.
38. Cava, M.; Engman, L. *Synth. Commun.*, **1972**, *12*, 163.
39. a) 1,3-Butadiynes are available by a wide variety of procedures. for a comprehensive discussion see: Shostakovskii, Bogdanova, A. V. In "*The Chemistry of Diacetylenes*" John Wiley & Sons, New York, **1974**. b) Brandsma, L. In "*Preparative Acetylenic Chemistry*" pp. 212-213 Elsevier, Amsterdam, **1988**. c) Volkov, A. N.; Skvortsov, Y. M.; Danda, L. I.; Shostakovskii, M. F.; Russ. *J. Org. Chem.*, **1970**, 903. d) Curtis, R. F.; Taylor, J. A.; *J. Chem. Soc.* (C), **1971**, 186. e) Kende, A. S.; Smith, C. A.; *J. Org. Chem.*, **1988**, *53*, 2655. f) Brandsma, L. In "*Preparative Acetylenic Chemistry*" pp. 60 Elsevier, Amsterdam, **1988**. g) Taniguchi, H.; Mathai, I. M.; Miller, S. I. *Org. Synth.*, **Coll. Vol**. 6, **1988**, 925.

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