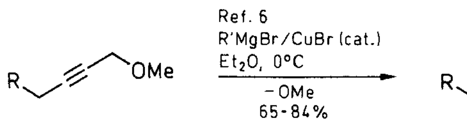
A Convenient Terminal Allene Synthesis from Propargylic Acetates

Michael H. Nantz,* Daniel M. Bender, S. Janaki
Department of Chemistry, University of California, Davis, California 95616, USA

Received 14 September 1992; revised 6 November 1992

The use of lithium butyl(phenylthio)cuprate as a reactant with propargylic acetates for the synthesis of terminal allenes is reported. Treatment of propargylic acetates with lithium butyl(phenylthio)cuprate in diethyl ether at − 78 °C yields the title compounds on workup with aqueous ammonium chloride.

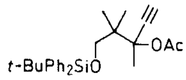
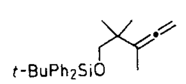
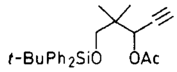
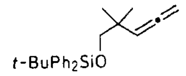
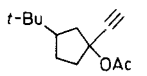
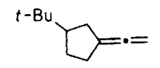
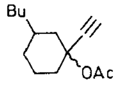
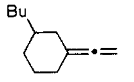
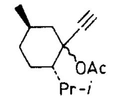
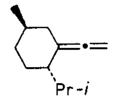
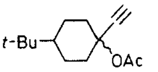
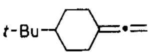
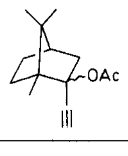
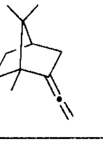
Terminal allenes, which can be prepared by various methods,[1−3] are emerging as versatile building blocks in organic synthesis.[4,5] As part of a program aimed at developing new allene transformations, we were interested in general, preparative syntheses of 1,1-dialkyl-1,2-propadienes (terminal allenes). The copper iodide catalyzed S_N2' displacement of propargylic leaving groups by Grignard reagents is an effective method for synthesis of acyclic terminal allenes.[6] However, this approach is not applicable to the synthesis of cyclic terminal allenes and is not particularly well suited for substrates having propargylic substitution capable of diminishing the S_N2'-regioselectivity.



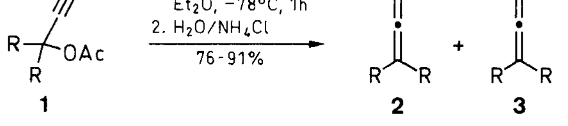
To prepare the cyclic and α-substituted terminal allenes we required, conversion of the corresponding propargylic acetates to the terminal allenes was examined using literature procedures.[3,7] Unfortunately, these syntheses were either unwieldy for large scale operation or afforded inseparable mixtures containing both terminal and alkylated allene products in low ratios. We report herein an improvement of a method previously described by Crabbé[7] for the synthesis of terminal allenes from propargylic acetates.

We have found that treatment of propargylic acetates, **1**, with lithium butyl(phenylthio)cuprate, formed by addition of equimolar amounts of (phenylthio)copper[8] and butyllithium, affords terminal allenes, **2**, along with minor amounts of the corresponding butylated allenes, **3**, on hydrolytic quench. Crabbé had reported examples of this transformation using lithium dimethylcuprate followed by a reductive workup using lithium aluminum hydride to yield mixtures of terminal to methylated allenes.[7] It has been postulated that propargylic acetates are consumed on treatment with cuprate reagents to form an intermediate species, presumably a putative copper[III] intermediate.[9] At lower temperatures, the transfer of an alkyl ligand from copper to the proximal allenic carbon is sufficiently slow that interception of this intermediate copper species on workup leads to the predominant formation of a terminal allene product. In this context, we have noted that the substitution of an alkyl group on copper with a phenylthio group gave an improved ratio of terminal to alkylated allenic products (see Table 1), an observation which suggests a relative stabilization of the intermediate copper species by the increased electron donating ability of the phenylthio ligand.

Table 1. Compounds **2** Prepared[a]

Substrate		Product **2**		Yield[b] (%)	Ratio[c] **2**/**3**
1a		**2a**		85	> 24 : 1[d]
1b		**2b**		82	11 : 1
1c		**2c**		86	> 24 : 1[d]
1d		**2d**		90	15 : 1
1e		**2e**		85 (66)[e]	7 : 1
1f		**2f**		91	> 24 : 1[d]
1g		**2g**		76	13 : 1

[a] All reactions were conducted on greater than 1 mmol scale.
[b] Isolated yield by column chromatography.
[c] Determined from the integral regions (^1H NMR, 300 MHz, $CDCl_3$) for the isolated and well separated allenic-H resonances of the crude reaction mixtures.
[d] Corresponding butylated allene **3** was not detected by ^1H NMR.
[e] Distilled (Kugelrohr) yield.



1 **2** **3**

The reactions were carried out in diethyl ether at − 78 °C and were quenched at − 78 °C by the *slow* dropwise addition of saturated aqueous ammonium chloride. This modification of Crabbé's method was found to be operationally more convenient than using lithium aluminum hydride on workup. A syringe pump[10] was routinely used to ensure a slow addition of the ammonium chloride solution and to minimize the effects of local warming during the quenching process. The effects of a temperature increase on the terminal to alkylated allene product ratio has been previously documented.[7] A final modification involved the use of butyllithium to form the mixed cuprate reagent, a choice motivated by the possibility of

Table 2. Analytical and Spectroscopic Data of Compounds **2a**–**g**

Product	bp[a] (°C)/mbar	Molecular Formula[b] or Lit. bp (°C)/mbar	R_f (TLC)[c]	IR (neat)[d] ν (cm^{-1}) C=C=C	^{1}H NMR ($CDCl_3$/TMS)[e] δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS)[f] δ Allenic Carbons[g]		
						C_s	C_i	C_t
2a	oil	$C_{24}H_{32}OSi$ (364.6)	0.25	1953	1.05 (s, 9H), 1.06 (s, 6H), 1.62 (t, 3H, J = 3.0), 3.45 (s, 2H), 4.57 (q, 2H, J = 3.0), 7.39–7.65 (m, 10H)	104.7	206.7	74.3
2b	oil	$C_{23}H_{30}OSi$ (350.2)	0.37	1955	1.03 (s, 6H), 1.05 (s, 9H), 3.38 (s, 2H), 4.71 (d, 2H, J = 6.6), 5.19 (t, 1H, J = 6.6), 7.35–7.60 (m, 10H)	98.2	207.1	76.2
2c	30/1.3	$C_{11}H_{18}$ (150.1)	0.64	1963	0.89 (s, 9H), 1.34 (m, 1H), 1.74 (m, 2H), 2.16 (m, 1H), 2.40 (m, 3H), 4.61 (m, 2H)	102.5	202.1	74.8
2d	oil	$C_{12}H_{20}$ (164.1)	0.63	1964	0.89 (t, 3H, J = 6.7), 1.00 (m, 1H), 1.26 (m, 5H), 1.35 (m, 2H), 1.62 (m, 1H), 1.73 (m, 2H), 1.91 (m, 2H), 2.27 (m, 2H), 4.53 (m, 2H)	100.8	203.6	72.3
2e	58/1.8	$C_{12}H_{20}$ (164.1)	0.64	1958	0.87 (d, 3H, J = 6.7), 0.93 (d, 3H, J = 6.5), 0.96 (d, 3H, J = 6.8), 1.20–1.80 (m, 7H), 2.28 (m, 1H), 4.65 (t, 2H, J = 3.5)	104.8	203.6	74.5
2f	oil	oil[2]	0.63	1964	0.90 (s, 9H), 1.05–1.24 (m, 3H), 1.89–2.07 (m, 4H), 2.36–2.42 (m, 2H), 4.59 (m, 2H)	100.9	203.2	72.5
2g	68/1.3	70.5/12[11]	0.65	1965	0.86 (s, 3H), 0.89 (s, 3H), 0.90 (s, 3H), 1.23 (m, 1H), 1.46 (m, 1H), 1.65 (m, 1H), 1.73 (m, 1H), 1.77 (m, 1H), 1.99 (dt, 1H, J = 15.2, 3.8), 2.52 (m, 1H), 4.70 (m, 2H)	110.5	201.2	77.2

[a] Compounds **2a**–**g** are oils; the recorded bp was obtained by Kugelrohr distillation.

[b] Satisfactory HRMS obtained: $m/z \pm 0.0006$.

[c] Silica gel (hexane).

[d] Recorded on an IBM FTIR-32 spectrometer with an IBM 9000 data system.

[e] Measuring frequency: 300 MHz.

[f] Measuring frequency: 75 MHz.

[g] C_s = substituted allenic carbon, C_i = internal allenic carbon, C_t = terminal allenic carbon.

separating the terminal allene products from any butylated contaminants by distillation. Indeed, allene **2e** (Table 1) was readily separated from the corresponding butylated allene by Kugelrohr distillation. The purity of the distilled allene was confirmed by GC analysis and determined at > 98 %.

In conclusion, we report a convenient method for the synthesis of terminal allenes from propargylic acetates using readily prepared lithium butyl(phenylthio)cuprate. The reaction is amenable to preparative scale synthesis and is accomplished with good yield (76–91 %).

PhSCu was prepared according to the literature procedure.[8] Et_2O was dried and distilled from Na/benzophenone before use. All reactions were run under an atmosphere of Ar. Analytical TLC plates and silica gel (230–400 mesh) were purchased from EM Science. GC analyses were performed on a Shimadzu Model 14A gas chromatograph fitted with a capillary column (30 m × 0.25 mm, DB-5).

4-(*tert*-Butyl)-1-vinylidenecyclohexane (2f); Typical Procedure:

A stirred suspension of PhSCu (4.41 g, 25.5 mmol) in Et_2O (100 mL) was cooled to − 35 °C and treated with a 2.47 M solution of BuLi in hexane (9.91 mL, 24.5 mmol). The mixture was allowed to warm to − 30 °C and stirred at this temperature for 20 min and then cooled to − 78 °C. A solution of acetate **1f** (2.26 g, 10.2 mmol) in Et_2O (35 mL) at − 78 °C was added dropwise to the mixture via cannula. After stirring 1 h, the reaction was quenched by the addition of sat. aq NH_4Cl (2 mL) at a rate of 0.16 mL/h using a syringe pump. After stirring at − 78 °C for 6 h, the reaction was gradually warmed to r. t. The precipitated solids were removed by filtration through a Celite pad and the collected solids were washed with additional portions of Et_2O (2 × 25 mL). The combined organic phase was washed with 1 M NaOH (2 × 50 mL) and brine (50 mL) and then dried ($MgSO_4$). The solvent was evaporated and the crude product was purified by flash chromatography over silica gel (hexane) to afford **2f**; yield 1.51 g (91 %).

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(1) Cekovic, Z.; Matovic, R. *J. Chem. Soc., Chem. Commun.* **1991**, 294.
Doyle, M.P.; Bagheri, V.; Claxton, E.E. *J. Chem. Soc., Chem. Commun.* **1990**, 46.
Pornet, J.; Damour, D.; Miginiac, L. *J. Organomet. Chem.* **1987**, *319*, 333.
Baldwin, J.E.; Adlington, R.M.; Basak, A. *J. Chem. Soc., Chem. Commun.* **1984**, 1284.
Buchwald, S.L.; Grubbs, R.H. *J. Am. Chem. Soc.* **1983**, *105*, 5490.
Salvadori, P.; Rossi, R.; Chiellini, E. *Chim. Ind. (Milan)* **1968**, *50*, 1365.
(2) Tsuji, J.; Sugiura, T.; Minami, I. *Synthesis* **1987**, 603.
(3) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 5237.
(4) Fox, D.N.A.; Lathbury, D.; Mahon, M.F.; Molloy, K.C.; Gallagher, T. *J. Am. Chem. Soc.* **1991**, *113*, 2652.
Crandall, J.K.; Ayers, T.A. *Tetrahedron Lett.* **1991**, *30*, 3659.
Larock, R.C.; Berrios-Peña, Fried, C.A. *J. Org. Chem.* **1991**, *56*, 2615.
Crandall, J.K.; Batal, D.J.; Sebesta, D.P.; Lin, F. *J. Org. Chem.* **1991**, *56*, 1153.
Trost, B.M.; Kottirsch, G. *J. Am. Chem. Soc.* **1990**, *112*, 2816.
Cazes, B. *Pure Appl. Chem.* **1990**, *62*, 1867.
(5) Schuster, H.F.; Coppola, G.M. In *Allenes in Organic Synthesis*; Wiley-Interscience: New York, 1984.
Pasto, D.J. *Tetrahedron* **1984**, *40*, 2805.
Smadja, W. *Chem. Rev.* **1983**, *83*, 263.
(6) Alexakis, A.; Commercon, A.; Villieras, J.; Normant, J.F. *Tetrahedron Lett.* **1976**, 2313.
(7) Crabbé, P.; Barreiro, E.; Dollat, J.-M.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1976**, 183.
(8) Posner, G.H.; Brunelle, D.J.; Sinoway, L. *Synthesis* **1974**, 662.
(9) For mechanistic interpretations regarding the reaction of propargylic acetates with organocuprates see:
Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J.F. *J. Am. Chem. Soc.* **1990**, *112*, 8042.
Sahlberg, C.; Claesson, A. *J. Org. Chem.* **1984**, *49*, 4120.
(10) Sage Instruments, Syringe Pump model 341A.
(11) Mattay, J.; Conrads, M.; Runsink, J. *Synthesis* **1988**, 595.