An Alternative Approach for the Conversion of Aldehydes to Terminal Alkynes

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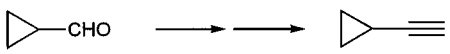
Received April 13, 1999

Efavirenz (Sustiva, DMP 266) is a nonnucleoside reverse transcriptase inhibitor of the HIV-1 virus developed by our company for the treatment of AIDS. This compound demonstrates superior antiretroviral activity and has been approved for use as an anti-HIV agent in the U.S. Our enantioselective synthesis of Efavirenz[1] employs cyclopropylacetylene (**1**), which is expensive and difficult to obtain. The existing preparations of **1** require either 5-chloro-1-pentyne[2] or cyclopropyl methyl ketone[3] as starting materials. These syntheses proceed in only moderate overall yields from limited starting materials or under inefficient reaction conditions. We anticipated that the most efficient synthesis of **1** would occur from cyclopropylcarboxaldehyde via a one-carbon homologation. These expectations were based upon the knowledge that cyclopropylcarboxaldehyde is easily and cheaply prepared by sequential thermal rearrangements of butadiene monoxide on ton scale.[4]



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The reactions of Corey−Fuchs,[5] Wittig/Horner−Emmons,[6] and Gilbert−Seyferth[7] and its modifications[8] are the most frequently used methods for the conversion of aldehydes to terminal alkynes. However, the need for phosphorus reagents limits the appeal of these applications as a result of toxicity, exothermicity, and voluminous waste streams, particularly for large scale preparations. As an extension of our new preparation of **1**, we present an alternative approach for the conversion of aldehydes to terminal alkynes through a three-step reaction sequence: addition of dihalomethyllithium to aldehydes **2** to form dihalo alcohols **3**, transformation of **3** into dihalosulfonates **4**, and finally, elimination of chloride and tosylate followed by elimination of HX to generate the desired alkynes **5** (Scheme 1). This reaction sequence works remarkably well for our target, cyclopropylacetylene. We have brought this chemistry up to the scale of 0.2−0.4 kg of cyclopropylacetylene in 65−70% overall yield. It is furthermore an efficient and general synthesis for the preparation of several terminal alkynes (Table 1).

Dihalomethyllithiums are versatile synthons that are thermolabile to varying degrees. They can be formed at low temperature in excellent yield employing lithium dicyclohexylamide as a base to react with dihalomethane.[9] We wished to develop conditions to generate either dichloro- or dibromomethyllithiums at temperatures above −50 °C and to react these species with aldehydes to form the desired 1,1-dihalo-2-hydroxy alkanes **3**. During the course of our study, we demonstrated that in situ generation of dichloro- or dibromomethyllithiums in the presence of aldehydes utilizing LDA as a base offered a good solution to our needs. The treatment of a mixture of an aldehyde and dichloromethane (2 equiv) with LDA (1.5 equiv) in THF at −78 °C afforded the desired dichlorocarbinol in 82−90% yield and did not require further purification for conversion to tosylate **4** (Table 1). When dibromomethane was substituted for dichloromethane, the reaction proceeded well at −30 °C, although a slight improvement in yield and purity of the adduct was observed at reaction temperatures of −50 to −78 °C.

The dichlorocarbinols resulting from the above procedure were easily converted to their corresponding sulfonate esters in 68−93% yields by treatment with 1 equiv of either *p*-toluenesulfonyl chloride or methanesulfonyl chloride in the presence of triethylamine (Table 1). Yields of the dibromo analogues determined over two steps from the aldehyde were 56−64%. Of greater practicality, the addition reaction and the sulfonation reaction can be conducted sequentially in one vessel. Namely, the desired sulfonates can be obtained by treatment of the reaction mixture derived from the addition reaction at 0 °C with 1 equiv of alkyl or arylsulfonyl chloride, followed by warming to 25 °C and aqueous workup. Further purifications of the dihalosulfonates are achieved, if necessary, by recrystallization from ethyl acetate/heptane.

The dihalosulfonates can be converted to their corresponding terminal alkynes through elimination utilizing strong bases, for example, methyllithium or sodamide. The eliminations were monitored by GC, which revealed that a mixture of E/Z vinylhalides (in approximate 2/1 ratio by GC, the structures confirmed by both MS and ^{1}H NMR spectroscopy) were formed as intermediates. This indicated that the elimination reaction proceeded via a stepwise mechanism. Initially, one chloride was lithiated to form a carbenoid species, RCH(OTS)−CH(Li)Cl, which lost lithium tosylate to form a vinylhalide

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(1) Pierce, M. E.; Parsons, R. L.; Radesca, L. A.; Lo, Y. S.; Silverman, S.; Moore, J. R.; Islam, Q.; Choudhury, A.; Fortunak, J. M.; Nguyen, D.; Luo, C.; Morgan, S. J.; Davis, W. P.; Confalone, P. N.; Chen, C.; Tillyer, R. D.; Frey, L.; Tan, L.; Xu, F.; Zhao, D.; Thompson, A. S.; Corley, E. G.; Grabowski, E. J. J.; Reamer, R.; Reider, P. J. *J. Org. Chem*. **1998**, *63*, 8536.

(2) Corley, E. G.; Thompson, A. S.; Huntington, M. *Org. Synth*., submitted for publication.

(3) Schoberth, W.; Hanack, M. *Synthesis* **1972**, 703.

(4) (a) Liang, S.; Price, T. W.; Nolen, D. B.; Attride, D. C. U.S. Patent 5,502,257, 1996; *Chem. Abstr*. **1996**, *125*, 10231. (b) Torihara, M.; Minagawa, Y. Japan Patent Application, H08-233884, **1996**.

(5) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett*. **1972**, 3769.

(6) (a) Corey, E. J.; Achiwa, K.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 4318. (b) Horner, L.; Hoffmann, H.; Wippel, H. G. *Chem. Ber*. **1958**, 61. (c) Horner, L.; Hoffmann, H.; Wippel, H. G.; Klaher, G. *Chem. Ber*. **1959**, 2499. (d) Wadsworth, W. S., Jr.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733. (e) Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1975**, 458.

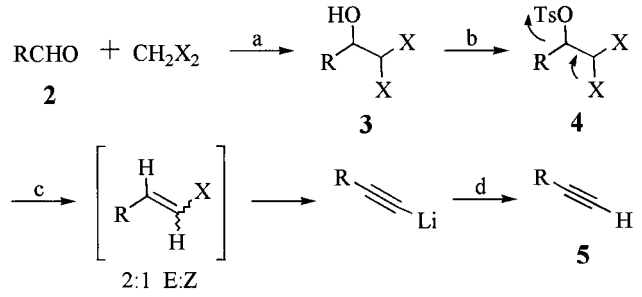
(7) Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem*. **1982**, *47*, 1837.

(8) Muller, S.; Liepold, B.; Roth, G. J.; Bestman, H. J. *SynLett* **1996**, 521.

(9) (a) Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010. (b) Taguchi, H.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn*. **1977**, *50*, 8.

10.1021/jo990623z CCC: $18.00
Published on Web 08/14/1999

Scheme 1. General Method for 1-Alkyne Preparation[a]



[a] Reagents: (a) LDA/THF, −78 °C; (b) TsCl/TEA/CH_2Cl_2, 25 °C; (c) 3.5 eq MeLi/THF, −10 °C; (d) H_3O^+.

Table 1. Reaction Temperatures and Yields of Dihalocarbinols 3, Alkylsulfonates 4, and Acetylenes 5

			yield, %		
entry	RCHO	temp, °C	**3a−g**	**4a−i**[a]	**5a−g**
a	cyclopropyl	−78	90	80	94[b]
b	cyclohexyl	−78	90	93	91
c	iso-butyl	−78	90	79	92[b]
d	*n*-octyl	−78	82	74	93
e	*tert*-butyl	−78	87	68[c]	78[b]
f	phenyl	−78	95	84	93
g	2-phenylethyl	−78	89	82	97
h	cyclopropyl	−30	*d*	64[e]	67[b]
i	phenyl	−30	*d*	56[e]	80[b]

[a] Yield of pure compound after recrystallization based on the dihalocarbinols unless otherwise stated. [b] Product isolated as THF/ether/hexane solution; yield determined by GC. [c] Mesylate was produced instead of tosylate. [d] Dibromomethane used as dihalomethane. Dihalocarbinol intermediate was not isolated but converted directly to the tosylate. [e] Yield of pure compound based on aldehyde. This compound is the dibromo analogue of **4**.

intermediate. The vinyl halides underwent further elimination of hydrogen halide to generate the desired acetylenes, which were in turn deprotonated under the strongly basic conditions to form lithium acetylides. The desired acetylenes were obtained after aqueous workup and were either isolated by distillation or partially concentrated to produce a concentrated solution. Interestingly, when the dihalosulfonate was treated with 1.5 equiv of potassium *tert*-butoxide, a new intermediate, the vinyldihalide ($RCH{=}CX_2$), was the only product observed. This indicated that tosic acid was eliminated initially, at least when a base that would not lead to metalation was used. To determine if the vinyldihalide was the common intermediate, we applied less than 1 equiv of methyllithium or sodamide/DMSO as base. We did not detect the vinyldihalide intermediate. This observation supports the mechanism described in Scheme 1.

In summary, we have developed an efficient procedure for the conversion of aldehydes to terminal alkynes. It is also a practical method, as the multistep conversion requires only two reactors. Of particular importance to us is a commerically viable preparation of cyclopropylacetylene, a key component of Sustiva.

Experimental Section

General. All NMR spectra were recorded in $CDCl_3$. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 mHz, respectively.GC analysis was conducted using a J&W DB-1 column (0.32 mm × 30 m). Oils were purified by flash chromatography,[10] typically by ethyl acetate/heptane on silica gel. Crude yields are reported unless stated otherwise. Combustion analyses were performed by Quantitative Technologies, Inc., Bound Brook, NJ.

Preparation of Dichlorocarbinols (3a−g). The following procedure for cyclopropyl dichlorocarbinol **3a** is representative.

α-(Dichloromethyl)cyclopropanemethanol (3a). To a stirred solution of cyclopropane carboxaldehyde (30 mL, 0.39 mol) and dichloromethane (63 mL, 1.19 mol) in THF (660 mL) at −78 °C was added dropwise LDA (2 M in THF/heptane/ethylbenzene, 0.59 mol) over 20 min. The reaction mixture was stirred for an additional 2 h at −78 °C and quenched with water (150 mL). After dilution with *tert*-butyl methyl ether and separation of layers, the organic phase was washed with 0.5 M HCl, water, saturated $NaHCO_3$, and finally with brine. The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude **3a** was obtained as an orange oil (55.20 g, 90%). No additional purification was required for further reaction (bp 37−43 °C/2 mmHg): ^1H NMR δ 0.52 (m, 2H), 0.65 (m, 2H), 1.08−1.20 (m, 1H), 3.33 (dd, J = 4.2, 4.8 Hz, 1H), 5.80 (d, J = 5.2 Hz, 1H); ^{13}C NMR δ 4.05, 5.32, 12.2, 72.0, 88.0.

α-(Dichloromethyl)cyclohexanemethanol (3b): oil; yield 90%; ^1H NMR δ 1.05−1.40 (m, 5H), 1.65−1.90 (m, 5H), 1.95 (m, 1H), 3.91 (dd, J = 8.7, 8.7 Hz, 1H), 5.85 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 21.8, 25.7, 25.9, 28.0, 28.2, 29.9, 39.9, 88.8.

1,1-Dichloro-4-methyl-2-pentanol (3c): oil; yield 90%; ^1H NMR δ 0.88 (d, J = 10.2 Hz, 3H), 0.98 (d, J = 10.0 Hz, 3H), 1.54 (m, 1H), 1.95 (m, 2H), 2.62 (m, 1H), 5.64 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 21.0, 21.8, 23.1, 23.7, 35.9, 80.7.

1,1-Dichloro-2-decanol (3d): oil; yield 82%; ^1H NMR δ 0.88 (t, J = 6.4, 6.6 Hz, 3H), 1.20−1.53 (m, 12H), 1.80−1.90 (m, 2H), 3.84 (m, 1H), 5.22 (d, J = 7.2, 1H); ^{13}C NMR δ 14.0, 21.9, 22.1, 25.5, 29.6, 29.7, 29.8, 29.9, 31.8, 89.20.

1,1-Dichloro-3,3-dimethyl-2-butanol (3e): oil; yield 87%; ^1H NMR δ 1.02 (s, 9H), 2.72 (s broad, 1H), 3.65 (d, J = 4.0 Hz, 1H), 6.03 (d, J = 4.0 Hz, 1H); ^{13}C NMR δ 28.2 (3C), 37.8, 87.9.

α-(Dichloromethyl)benzenemethanol (3f): oil; yield 95%; ^1H NMR δ 3.20 (s broad, 1H), 4.94 (d, J = 10.0 Hz, 1H), 5.80 (d, = 9.9 Hz, 1H), 7.22−7.46 (m, 5H); ^{13}C NMR δ 21.9, 84.0, 127.8, 127.9, 128.0, 128.2, 128.5, 129.6.

α-(Dichloromethyl)benzenepropanol (3g): oil; yield 89%; ^1H NMR δ 2.18−2.30 (m, 2H), 2.62−2.75 (m, 2H), 4.38 (dd, J = 4.8, 4.8 Hz, 1H), 5.94 (d, J = 5.8 Hz, 1H), 7.17−7.25 (m, 5H); ^{13}C NMR δ 21.9, 31.8, 34.0, 80.2, 127.3, 127.9, 128.4, 128.6 128.9, 132.0.

Preparation of dichlorotosylates (4a−d, f, and g) and dichloromesylate (4e). The following procedure for cyclopropyl tosylate derivative **4a** is representative.

α-(Dichloromethyl)cyclopropanemethanol 4-Methylbenzenesulfonate (4a). *p*-Toluenesulfonyl chloride (25.55 g, 0.134 mol) was added in one portion to a stirred solution of **3a** (20.77 g, 0.134 mol) and triethylamine (20.34 g, 0.201 mol) in dichloromethane (250 mL) at 25 °C. (In the case of **3e**, methanesulfonyl chloride (0.13 mol) was used instead.) The solution was stirred for 1.5 h and quenched with water (60 mL), and the layers were separated. The organic layer was washed with 5 M HCl, water, 2 M NaOH (240 mL), water, and brine. The solution was dried over $MgSO_4$, filtered, and concentrated to 39.38 g of crude **4a** as a solid. This was recrystallized from 4/1 hexane/ethyl acetate to produce white crystals (33 g, 80%): mp 92−93 °C; ^1H NMR δ 0.36 (m, 1H), 0.55−0.62 (m, 2H), 0.71−0.82 (m, 1H), 1.33 (m, 1H), 2.43 (s, 3H), 4.15 (dd, J = 7.8, 7.8 Hz, 1H), 5.85 (d, J = 6.8 Hz, 1H), 7.37 (d, J = 10.9 Hz, 2H), 7.82 (d, J = 10.9 Hz, 2H); ^{13}C NMR δ 4.05, 5.32, 11.2, 40.4, 72.0, 88.0, 127.8 (2C), 129.9 (2C), 134.3, 144.6; MS 310. Anal. Calcd for $C_{12}H_{14}Cl_2O_3S$: C, 46.61; H, 4.56; S, 10.37. Found: C, 46.63; H, 4.54; S, 10.32.

α-(Dichloromethyl)cyclohexanemethanol 4-Methylbenzenesulfonate (4b): white crystals; yield 93%; mp 68−69 °C; ^1H NMR δ 1.05−1.37 (m, 5H), 1.55−1.87 (m, 5H), 1.93−2.04 (m, 1H), 2.43 (s, 3H), 4.62 (dd, J_1 = 7.3, 7.3 Hz, 1H), 5.83 (d, J = 8.9 Hz, 1H), 7.35 (d, J = 11.0 Hz, 2H), 7.82 (d, J = 11.0 Hz, 2H); ^{13}C NMR δ 21.8, 25.7, 25.9, 26.0, 26.1, 28.0, 39.9, 70.0, 88.0, 127.8, 127.9, 129.8, 129.9, 134.0, 145.2. Anal. Calcd for $C_{15}H_{20}Cl_2O_3S$: C, 51.29; H, 5.74; S, 9.13. Found: C, 51.30; H, 5.75; S, 9.11.

(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

1,1-Dichloro-4-methyl-2-pentanol 4-Methylbenzenesulfonate (4c): white crystals; yield 79%; mp 62−63 °C; ^{1}H δ NMR 0.74 (d, J = 10.0 Hz, 3H), 0.91 (d, J = 10.0 Hz, 3H), 1.45−1.65 (m, 2H), 1.80−1.87 (m, 1H), 2.45 (s, 3H), 4.77 (dd, J_1 = 5.2, 5.0 Hz, 1H), 6.0 (d, J = 5.8 Hz, 1H) 7.35 (d, J = 10.1 Hz, 2H), 7.82 (d, J = 10.1 Hz, 2H); ^{13}C NMR δ 21.0, 21.8, 23.0, 23.7, 36.2, 71.0, 80.9, 127.8, 128.9, 129.7, 129.8, 133.2, 145.7. Anal. Calcd for $C_{13}H_{18}Cl_2O_3S$: C, 48.00; H, 5.58; S, 9.85. Found: C, 48.03; H, 5.58; S, 9.84.

1,1-Dichloro-2-decanol 4-Methylbenzenesulfonate (4d): oil; yield 74%; ^{1}H NMR δ 0.88 (t, J = 9.8, 10.0 Hz, 3H), 1.19−1.55 (m, 12H), 1.80−1.91 (m, 2H), 2.42 (s, 3H), 4.48 (m, 1H), 5.87 (d, J = 6.4 Hz, 1H), 7.35 (d, J = 10.8 Hz, 2H), 7.80 (d, J = 10.8 Hz, 2H); ^{13}C NMR δ 14.0, 21.9, 22.1, 24.2, 27.2, 28.0, 29.4, 29.6, 31.92, 72.0, 81.0, 128.4, 128.5, 129.8, 129.9, 133.0, 145.3.

1,1-Dichloro-3,3-dimethyl-2-butanol 4-Methanesulfonate (4e): white crystals; yield 68%; mp 70−71 °C; ^{1}H δ NMR 1.17 (s, 9H), 3.32 (s, 3H), 5.07 (d, J = 4.8 Hz, 1H), 6.10 (d, J = 4.6 Hz, 1H); ^{13}C NMR δ 28.2, 28.5 (3C), 39.0, 40.0, 94.0.

α-(Dichloromethyl)benzenemethanol 4-Methylbenzenesulfonate (4f): white crystals; yield 84%; mp 85−86 °C; ^{1}H NMR δ 2.37 (s, 3H), 5.63 (d, J = 8.3 Hz, 1H), 5.84 (d, J = 8.7 Hz, 1H), 7.14 (d, J = 10.4 Hz, 2H), 7.22−7.30 (m, 5H), 7.63 (d, J = 10.4 Hz, 2H); ^{13}C NMR δ 21.9, 71.7, 84.0, 127.7, 127.8, 127.9, 127.9, 128.0, 128.1, 128.3, 128.4, 129.7, 132.5, 133.2, 145.6. Anal. Calcd for $C_{15}H_{14}Cl_2O_3S$: C, 52.18; H, 4.07; S, 9.29. Found: C, 52.15; H, 4.09; S, 9.30.

α-(Dichloromethyl)benzenepropanol 4-Methylbenzenesulfonate (4g): white solids; yield 82%; mp 58−59 °C; ^{1}H NMR δ 2.18−2.30 (m, 2H), 2.31−2.44 (m, 1H), 2.42 (s, 3H), 2.60−2.70 (m, 1H), 4.71 (dd, J_1 = 4.8, 4.6 Hz, 1H), 5.92 (d, J = 5.2 Hz, 1H), 7.17 (d, J = 10.0 Hz, 2H), 7.12−7.30 (m, 3H), 7.34 (d, J = 9.8 Hz, 2H), 7.82 (d, J = 10.0 Hz, 2H); ^{13}C NMR δ 21.9, 29.9, 30.9, 71.7, 82.0, 126.9, 128.0, 128.2, 128.3, 128.4, 128.5, 129.2, 129.8, 130.2, 133.6, 139.8, 145.5. Anal. Calcd for $C_{17}H_{18}Cl_2O_3S$: C, 54.76; H, 4.86; S, 8.60. Found: C, 54.78; H, 4.84; S, 8.58.

Preparation of Dibromotosylates (4h,i). The following procedure for the cyclopropyl tosylate derivative **4h** is representative for the preparation of the dibromotosylates and the method for proceeding without isolation of the carbinol intermediate **3** for both the dichloro and dibromo series.

α-(Dibromomethyl)cyclopropanemethanol 4-Methylbenzencesulfonate (4h). A solution of lithium diisopropylamide (105 mmol) in THF/hexane (∼70 mL) was added to a stirred solution of cyclopropylcarboxaldehyde (4.5 g, 68 mmol) and dibromomethane (20.0 g, 114 mmol) in THF (30 mL) at −30 °C over 1 h. The mixture was stirred another 20 min at −20 °C, and *p*-toluenesulfonyl chloride (10.0 g, 52 mmol) was charged over 10 min. The reaction was aged 1.5 h at −15 °C and quenched with water (60 mL). The organic phase was separated, and the aqueous layer was re-extracted with toluene. The combined organic phase was washed with water and dried ($MgSO_4$). The solution was filtered, the filtrate was concentrated, and the product was crystallized by the addition of heptane at 50 °C followed by cooling to 25 °C. The crystals were collected by filtration, washed with heptane, and dried under vacuum to produce white crystals (16.3 g, 64%): mp 80−81 °C; ^{1}H NMR δ 0.40 (m, 1H), 0.60 (m, 2H), 0.80 (m, 1H), 1.40 (m, 1H), 2.45 (s, 3H), 4.13 (dd, J = 0.3, 0.9 Hz, 1H), 5.80 (d, J = 0.3 Hz, 1H), 7.38 (d, J = 0.8 Hz, 2H), 7.80 (d, J = 0.8 Hz, 2H); ^{13}C NMR δ 3.5, 5.9, 12.9, 21.7, 44.6, 87.6, 127.8, 129.8, 133.7, 145.2. Anal. Calcd for $C_{12}H_{14}Br_2O_3S$: C, 36.21; H, 3.54; S, 8.04. Found: C, 36.49; H, 3.32; S, 8.13.

α-(Dibromomethyl)benzenemethanol 4-Methylbenzenesulfonate (4i): white solids; yield 56%; mp 64−66 °C; ^{1}H NMR δ 2.37 (s, 3H), 5.6−5.8 (m, 2H), 7.17 (d, J = 8.1 Hz, 2H), 7.2−7.4 (m, 5H), 7.63 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 21.6, 44.1, 84.8, 127.9, 127.9, 128.2, 129.51, 129.55, 133.2, 133.7, 144.9. Anal. Calcd for $C_{15}H_{14}Br_2O_3S$: C, 41.50; H, 3.25; S, 7.39; Br, 36.81. Found: C, 41.47; H, 3.38; S, 7.56, Br, 36.57.

Preparation of Acetylenes (5a−g). The following procedure for cyclopropyl acetylene **5a** is representative for the conversion of both dichloro- and dibromosulfonates using methyllithium.

Ethynylcyclopropane (5a). A solution of 1.4 M MeLi in ether (72.8 mL, 101.9 mmol) was added dropwise to a stirred solution of **4a** (9.00 g, 29.1 mmol) in THF (290 mL) at −30 °C (typically, −10 °C was sufficient). The solution was warmed to 0 °C over 1 h and quenched with saturated aqueous ammonium chloride (120 mL). The mixture was diluted with hexane and the layers were separated. (If the product was not hexane soluble, methyl *tert*-butyl ether was used instead throughout this experiment.) The aqueous phase was extracted with hexane. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. This produced 1.81 g of **5a** within 720 g of THF/ether/hexane solution (94% solution yield). Neat **5a** (99.2 GC area %) could be isolated as an oil by vacuum distillation (1.78 g, 93%): bp 53−55 °C; ^{1}H NMR δ 1.75 (d, J = 6.1, 1H), 1.24 (m, 1H), 0.78 (m, 2H), 0.72 (m, 2H); ^{13}C NMR δ 87.6, 63.3, 8.0, −0.88.

The following procedure for cyclopropyl acetylene **5a** is representative for the conversion of dibromosulfonates using sodamide. Solid **4h** (30.0 g, 75.3 mmol) was added over 1 h at 15−20 °C to a solution of sodium amide (14.7 g, 376.8 mmol) in DMSO (90 mL). After 1 h, the reaction was quenched with water (15 mL). Methylcyclohexane was charged as a cosolvent, and the mixture was distilled. The distillate was collected at 50−80 °C to produce a 29 wt % solution of **5a** (11.0 g, 67%).

Acetylenes of higher boiling point were stripped of most of their solvents, and the purity was either measured by GC versus dilutions of the known standard or stated as GC area %. Acetylenes that were distilled are listed as such. All acetylenes are known compounds.

Ethynylcyclohexane[11] **(5b):** oil; yield 91%; 98.0 GC area %.

4-Methylpentyne[12] **(5c):** oil; yield 92%; 92.2 wt %.

***n*-Octyne**[13] **(5d):** oil (distilled); yield 93%; 97.1 GC area %.

3,3-Dimethyl-1-butyne[14] **(5e):** oil; yield 78%; 81.0 wt %.

Ethynylbenzene[15] **(5f):** oil (distilled); yield 93%; 98.3 GC area %. Ethynylbenzene (**5f**) derived from **4i** (dibromo analog): yield 80%; 1.5 wt % solution.

3-Butynylbenzene[16] **(5 g):** oil; yield 97%; 98.8 GC area %.

Acknowledgment. We are grateful to the Chemical Process Analytical Group for their support of this work and to Barbara W. Dotts, Cristina Gebreyesus, and Latasha R. Jones for deriving some of the nomenclature.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **4d** and **4e**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO990623Z

(11) (a) Preparation: Theus, V.; Schinz H. *Helv. Chem. Acta* **1956**, *39*, 1290. (b) Proton and carbon spectra: Aithen, R. A.; Atherton, J. I. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1281.

(12) (a) Preparation: Miller, H. N.; Greenlee, K. W.; Derfer, J. M.; Boord, C. E. *J. Org. Chem.* **1954**, *19*, 1882. (b) Proton spectrum: Bernadou, F.; Mesnard, D.; Miginiac, L. *J. Chem. Res., Miniprint* **1978**, *1*, 1501. (c) Carbon spectrum: Dubois, J. E.; Doucet, J. P. *J. Chem. Res., Miniprint* **1980**, *3*, 1101.

(13) (a) Preparation: Vaughn, T. H.; Vogt, R. R.; Nieuwland, J. A. *J. Am. Chem. Soc.* **1934**, *56*, 2120. (b) Proton spectrum: Vinczer, P.; Kovacs, T.; Novak, L. *Org. Prep. Proced. Int.* **1989**, *21*, 232. (c) Carbon spectrum: Bernassau, J. M.; Bertranne, M.; Collongues, C.; Fetizon, M. *Tetrahedron* **1985**, *41*, 3063.

(14) (a) Preparation and proton spectrum: Bock, H.; Rittmeyer, P.; Stein, U. *Chem. Ber.* **1986**, *119*, 3766. (b) Carbon spectrum: Fraenkel, G.; Pramanik, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1527.

(15) a) Proton and carbon spectrum: Aithen, R. A.; Atherton, J. I. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1281.

(16) (a) Preparation: Johnson, J. R.; McEwen, W. L. *J. Am. Chem. Soc.* **1926**, *48*, 469. (b) Proton and carbon spectra: Maercker, A.; Fischenich, J. *Tetrahedron* **1995**, *37*, 10209.