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SYNTHESIS OF 4-ALKYL-1-TRIMETHYLSILYLBUTA-1,3-DIYNES

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Summary: Lithium trimethylsilylbutadiyne (2) is alkylated by primary alkyl halides in THF-HMPA or *via* the ethylenediamine complex (4) in THF-DMSO to give the title compounds (3) in good yield.

We have previously shown that the cleavage of bistrimethylsilylbutadiyne (1) with methyllithium-lithium bromide complex in ether at room temperature gives a quantitative yield of lithium trimethylsilylbutadiyne (2) which in turn reacts smoothly with a variety of aldehydes and ketones.[1] Stereoselective partial hydrogenation[2,3] of the non-silylated triple bond in these products offers a convenient method of preparing precursors to the 5-chloropent-3-en-1-yne side chain such as is present in the maneonenes.[4,5] The preparation of 4-alkyl-1-trimethylsilylbuta-1,3-diynes (3) by reaction of compound (2) with alkyl halides is also a highly desirable reaction, since these products can be expected to act as useful precursors to the terminal *cis*-enyne side chain present in a variety of *Laurencia*-derived species,[6] and neurotoxins such as histrionicotoxin[7] and gephyrotoxin[8]. We now report the alkylation of compound (2) with a range of alkyl halides (Table 1).

Table 1.

$$\underset{(1)}{\text{TMS}-\equiv-\equiv-\text{TMS}} \xrightarrow[\text{THF, RT, 3.5h}]{\text{MeLi-LiBr}} \underset{(2)}{\text{Li}-\equiv-\equiv-\text{TMS}} \xrightarrow{\text{RX}} \underset{(3)}{\text{R}-\equiv-\equiv-\text{TMS}}$$

RX	Conditions	Product (3)	Yield (%)
MeI	a	R = Me	65
EtI	b	R = Et	65
BuI	b	R = Bu	64
EtBr	b	R = Et	50
$C_6H_{11}CH_2Br$	b	R = $C_6H_{11}CH_2$	57
^iPrI	b	R = ^iPr	8
$C_6H_{11}Br$	b	R = C_6H_{11}	0

a. The reagent (0.65 mmole/ml) in THF was added to (2) at -78°C, the reaction mixture was warmed to RT, and stirred for 3.5h.

b. The reagent (0.5 mmole/ml) in HMPA was added to (2) at -78°C, the reaction mixture was warmed to RT, and stirred for 0.5h.

The results shown in Table 1 indicate that only methyl iodide cleanly alkylates compound (2) in THF (but not ether); all other primary alkyl halides require an excess of HMPA as cosolvent for effective alkylation to occur. The use of HMPA as cosolvent to promote alkylation of acetylides has been reported previously[9]. Alkylation of compound (2) with alkyl bromides is slightly less effective than with alkyl iodides. Secondary alkyl halides give a very poor yield of alkylation product.

In view of the well-publicised toxicity of HMPA, an alternative cosolvent was sought. Alkylated acetylenes can be prepared by the reaction of lithium acetylide ethylenediamine complex with primary alkyl halides in DMSO.[10] This reagent is prepared by treating the lithium salt of ethylenediamine with acetylene,[11] a method which would be unsuitable for the preparation of the analogous complex (4). However, addition of an equimolar quantity of ethylenediamine to compound (2) in THF at room temperature gave a white precipitate, presumed to be the complex (4), which redissolved upon addition of DMSO. This reagent reacted with various alkyl halides in acceptable yield (Table 2), although the product (3) was always accompanied by about 10% of disubstitution product (R-C≡C-C≡C-R).

Table 2.

$$\underset{(2)}{\text{Li-}\equiv\text{-}\equiv\text{-TMS}} \xrightarrow[\text{RT, 5 min}]{\text{ethylenediamine}} \underset{(4)}{\text{en.Li-}\equiv\text{-}\equiv\text{-TMS}} \xrightarrow[\text{DMSO}]{\text{RX}} \underset{(3)}{\text{R-}\equiv\text{-}\equiv\text{-TMS}}$$

RX†	Product (3)	Yield (%)	
MeI	R = Me	45	(unoptimised)
BuI	R = Bu	55	
EtBr	R = Et	39	
^{i}PrI	R = ^{i}Pr	11	

† The reagent (0.5 mmole/ml) in DMSO was added to (4) in THF-DMSO at 0°C, the reaction mixture was warmed to RT, and stirred for 0.5h.

The elaboration of compounds (3) is in hand.[12,13]

References

1. A.B. Holmes, C.L.D. Jennings-White, A.H. Schulthess, B. Akinde, and D.R.M. Walton, J.C.S. Chem. Comm., 1979, 840.
2. A.B. Holmes, R.A. Raphael, and N.K. Wellard, Tetrahedron Letters, 1976, 1539.
3. C.L.D. Jennings-White, Ph.D. Thesis, Cambridge, 1979.
4. For the isolation and structure elucidation of the maneonenes, see S.M. Waraszkiewicz, H.H. Sun, K.L. Erickson, J. Finer, and J. Clardy, J.Org. Chem., 1978, **43**, 3194.
5. C.L.D. Jennings-White, A.B. Holmes, and P.R. Raithby, J.C.S. Chem. Comm., 1979, 542.
6. P.J. Scheuer, "Marine Natural Products, Chemical and Biological Perspectives," Volume 1, Academic Press, New York, 1978.
7. J.W. Daly, I.L. Karle, C.W. Myers, T. Tokuyama, J.A. Waters, and B. Witkop, Proc. Nat. Acad. Sci. U.S.A., 1971, **68**, 1870.
8. J.W. Daly, B. Witkop, T. Tokuyama, T. Nishikawa, and I.L. Karle, Helv. Chim. Acta., 1977, **60**, 1128.
9. H. Normant, Angew. Chem. Internat. Edn., 1967, **6**, 1046; M. Schwarz and R.M. Waters, Synthesis, 1972, 567; G. Schill and U. Keller, ibid., 1972. 621; J.H.P. Tyman and J. Caplin, Chem. Ind., 1973, 40; D.N. Brattesani and C.H. Heathcock, Synth. Comm., 1973, **3**, 245; N. Gilman and B. Holland, ibid., 1974, **4**, 199; W. Beckmann, G. Doerjer, E. Logemann, C. Merkel, G. Schill, and C. Zürcher, Synthesis, 1975, 423.
10. W.N. Smith and O.F. Beumel, Synthesis, 1974, 441; R. Sood, M. Nagasawa, and C.J. Sih, Tetrahedron Letters, 1974, 423.
11. O.F. Beumel and R.F. Harris, J.Org. Chem., 1963, **28**, 2775.
12. All new compounds exhibited satisfactory spectroscopic and analytical properties.
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