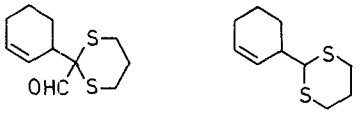
In Situ Alkylation of 2-Formyl-1,3-dithiane

S. R. Wilson, J. Mathew

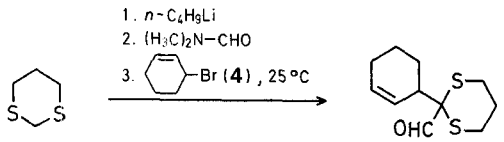
Department of Chemistry, Indiana University, Bloomington, Indiana 47405, U.S.A.

In connection with another synthetic study, it became necessary to develop a convenient synthesis of 2-(3-cyclohexenyl)-2-formyl-1,3-dithiane (**1**). 2-Alkyl-1,3-dithianes had been formylated[1,2,3] in yields ranging from 50–75%, although we were able to affect formylation of **2** in only low yield (possibly for steric reasons).



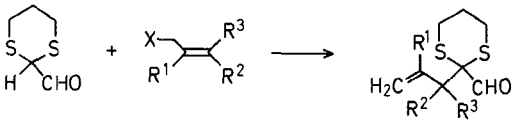
1 **2**

2-Formyl-1,3-dithiane (**5**) is known[4,5], but its alkylation chemistry has not been reported. We have found that addition of 2-lithio-1,3-dithiane to dimethylformamide at −20 °C, followed by treatment with 3-bromocyclohexene (**4**) yielded after workup 70–75% of the aldehyde **1** *directly* (Scheme **A**). This reaction has been extended (Scheme **B**) to a variety of other allylic halides.



3 **1**

Scheme **A**



5 **6 a-d** **7 a-d**

6,7	R^1	R^2	R^3	X
a	H	H	H	Br
b	CH_3	H	H	J
c	H	CH_3	H	Br
d	H	CH_3	CH_3	Br

Scheme **B**

As evident from the Table, the alkylations with unsymmetrical allylic halides **6** yield products **7** corresponding to S_N2' reaction. This is probably the result of *S*-alkylation of the lithium enolate of **5** by the allylic halides followed by a [2,3]-type rearrangement[8].

It should be noted that any unreacted 2-formyl-1,3-dithiane can be easily removed from the alkylation product by washing the crude reaction mixture with aqueous (10%) sodium hydroxide. From G.L.C. analysis it was concluded that 2-formyl-1,3-dithiane (**5**) is completely deprotonated by aqueous sodium hydroxide solution and can be extracted from ether solution. Acidification liberates **5** which can be isolated by ether extraction.

Swedish chemists[6] have reported that reaction of alkylmagnesium bromides with dialkylformamides yields enamines which, in certain cases, can be alkylated *in situ* in high yield. They report, however, that alkyllithium reagents in hexane react with dialkylformamides to form the amino-alcoholates which did not undergo elimination to form enamines.

We favor a mechanism that involves addition of 2-lithio-1,3-dithiane to dimethylformamide to yield the amino-al-

0039-7881/80/0832-0625 $ 03.00

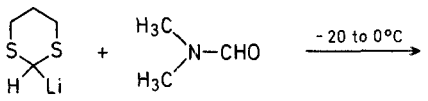
Table. *In Situ* Alkylation of 2-Formyl-1,3-dithiane (**5**)

Product	Yield[a] [%]	b.p. [°C]/ torr	Molecular formula[b]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	M.S. *m/e* (M^+)
7a[7]	50	105°/1	$C_8H_{12}OS_2$ (188.3)	9.0 (s, 1H); 5.8 (m, 1H); 5.1 (m, 2H)	—
7b	48	120°/1	$C_9H_{14}OS_2$ (202.0)	9.0 (s, 1H); 5.8 (m, 1H); 5.1 (m, 2H); 1.1 (d, 3H)	202.04831 (calc. 202.04858)
7c	69	115°/1	$C_9H_{14}OS_2$ (202.0)	9.1 (s, 1H); 4.9 (m, 2H); 1.9 (s, 3H)	202.04869 (calc. 202.04858)
7d	54	123°/1	$C_{10}H_{16}OS_2$ (216.1)	9.2 (s, 1H); 6.0 (dd, 1H); 5.1 (m, 2H); 1.1 (s, 6H)	216.06335 (calc. 216.06424)

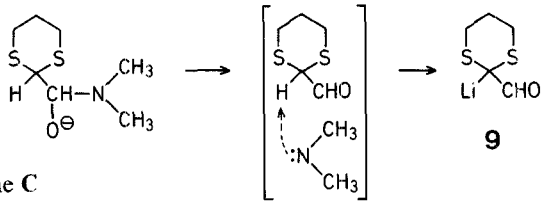
[a] Yield of isolated product of >96% purity as determined by ^{1}H-N.M.R. (220 MHz) and G.L.C. (conditions: OV 101, programmed 40–250 °C).

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.26, H ±0.26, S ±0.26).

coholate which breaks down to form the stable enolate (Scheme C).



8



Scheme C

2-(3-Cyclohexenyl)-2-formyl-1,3-dithiane (1); Typical Procedure:

A solution containing 1,3-dithiane (**3**; 1.2 g, 0.01 mol) in anhydrous tetrahydrofuran (20 ml) is cooled with stirring under nitrogen to −30 °C (Dry Ice/isopropyl alcohol) and treated dropwise with 2.4 molar *n*-butyllithium in hexane (4.2 ml, 0.01 mol). After 1 h of additional stirring, dimethylformamide (2.8 g, 0.04 mol) in tetrahydrofuran (5 ml) is added. The mixture is stirred at −20 °C for 2 h and then kept at 0 °C (refrigerator) for 12 h. To the resulting white suspension under nitrogen is added 3-bromocyclohexene (**4**; 2 ml, 3.2 g, 0.02 mol). After stirring for 16 h at 25 °C, the reaction mixture is poured into ice/water (25 ml) and extracted with ether (2 × 20 ml). The ether extract is washed with 2 normal hydrochloric acid (2 × 20 ml) and then with 10% sodium hydroxide solution (2 × 20 ml). The organic extract is finally washed with water and dried with magnesium sulfate. Evaporation of the ether gives a yellow oil (1.85 g), and distillation gives analytically pure **1**; yield: 1.7 g (72%); b.p. 135 °C/1 torr.

$C_{11}H_{16}OS_2$	calc.	C 57.89	H 7.01	S 28.07
(228.1)	found	57.60	7.05	28.43

M.S.: *m/e* = 228.06424 (M^+, calc. 228.06412).

^{1}H-N.M.R. ($CHCl_3$): δ = 9.1 (s, 1H, CHO); 5.8 ppm (m, 2H).

Received: January 11, 1980
(Revised form: February 25, 1980)

[1] D. Seebach, E. J. Corey, *J. Org. Chem.* **40**, 231 (1975).
[2] K. F. Burri, R. A. Cardone, W. Y. Chen, P. Rossen, *J. Am. Chem. Soc.* **100**, 7069 (1978).
[3] E. W. Colvin, T. A. Purcell, R. A. Raphael, *J. Chem. Soc. Chem. Commun.* **1972**, 1031.
[4] A. I. Meyers, R. C. Strickland, *J. Org. Chem.* **37**, 2579 (1972).
[5] M. Nakane, C. R. Hutchinson, *J. Org. Chem.* **43**, 3922 (1978).
[6] C. Hansson, B. Wickberg, *J. Org. Chem.* **38**, 3075 (1973).
[7] S. R. Wilson, R. N. Misra, submitted for publication.
[8] Note added: H. J. Reich, M. L. Cohen, *J. Am. Chem. Soc.* **101**, 1307 (1979).

0039-7881/80/0832-0626 $ 03.00