Tetrahedron Letters,Vol.31,No.2,pp 213-216,1990 0040-4039/90 $3.00 + .00
Printed in Great Britain Pergamon Press plc

UNUSUAL LITHIATION OF 4-(1',2'-ALKADIENESULPHINYL)-MORPHOLINES. PREPARATION OF SUBSTITUTED PROPARGYLIC SULPHINAMIDES AND THEIR HYDROLYTIC DESULPHINYLATION INTO THE CORRESPONDING ALLENES [1]

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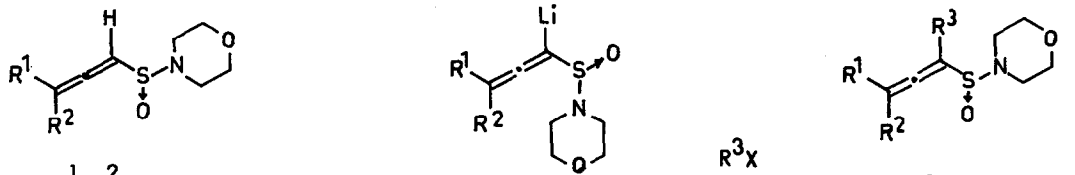
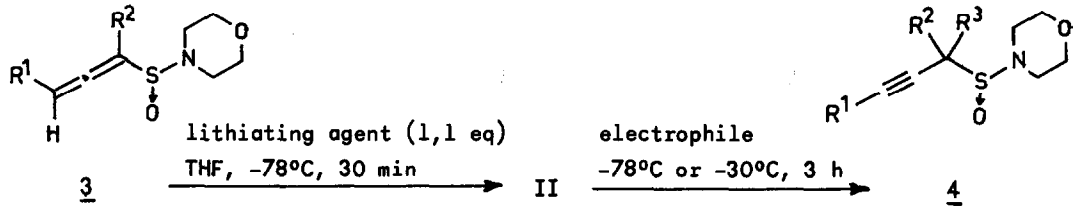
Summary: By deprotonation with methyllithium and reaction with water, deuterium oxide or alkyl halide, the γ-monosubstituted allenic sulphinamides 3 have been converted into the substituted propargylic sulphinamides 4 which were hydrolysed or deuterolysed with loss of sulphur dioxide to provide the corresponding allenes 5.

In an earlier report [1b], we have shown how the formation of the α-lithiated sulphinamides I can be achieved by treatment of γ,γ-disubstituted allenic sulphinamides 1a,b with either lithium diisopropylamide (LDA) or methyllithium in THF at -78°C for 30 min and how the reaction of these lithio-derivatives I with organic halides afford cleanly the corresponding α-alkylated products 2:



Following our interest in the deprotonation of various unsaturated sulphinyl-compounds, we had the occasion to examine the lithiation of the γ-monosubstituted allenic sulphinamides 3 (R^2=H) and the reaction of the resulting carbanions with simple electrophiles. Surprisingly, when carried out under the same conditions as for the sulphinamides 1, these reactions gave the α-substituted propargylic sulphinamides 4 in reasonable yields (Table 1) [2]. A most interesting feature of the lithiation of 3 is that the remote γ-allenic proton is removed in preference to an α-proton which is activated by an adjacent sulphinyl function and which is therefore thermodynamically more acidic. In order to be certain that the γ-deprotonations are direct reactions, we have carried out the lithiation of the α-deuteriated sulphinamide 3c and allowed the lithium reagent formed to react with water and deuterium oxide. In both cases, the α-deuterium is retained in the products 4e,f (entries 6,7). Thus these reactions do not involve an initial α-deprotonation (3 → III) [3] followed by an unexpected proton transfer.



3 → II → 4

Table 1

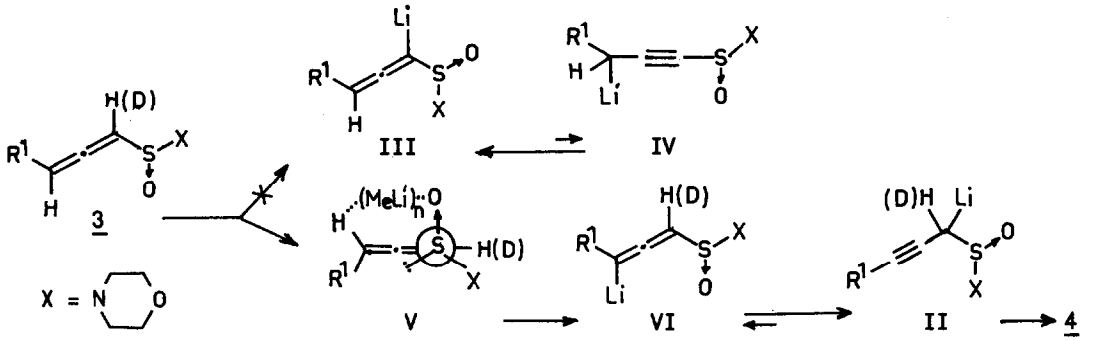
Entry	Substrate	R^1	R^2	Conditions		Yields (%)	R^2	R^3
1	3a	n.C_5H_{11}	H	LDA; H_2O, -78°C	4a	52	H	H
	3a			$(Me_3Si)_2NLi$; H_2O, -78°C	4a	59		
	3a			MeLi; H_2O, -78°C	4a	79		
2	3a	n.C_5H_{11}	H	MeLi; D_2O, -78°C	4b	74	H	D
3	3a	n.C_5H_{11}	H	MeLi; MeI (1,2 eq), -30°C	4c	67	H	Me
4	3b	n.C_7H_{15}	H	MeLi; H_2O, -78°C	4d	65	H	H
5	3b	n.C_7H_{15}	H	MeLi; D_2O, -78°C	4e	66	H	D
6	3c	n.C_7H_{15}	D	MeLi, H_2O, -78°C	4e	68	D	H
7	3c	n.C_7H_{15}	D	MeLi, D_2O, -78°C	4f	61	D	D
8	3a	n.C_5H_{11}	H	MeLi; CH_2=CH-CH_2Br (2 eq), -78°C	4g	67*	H	CH_2-CH=CH_2
9	3b	n.C_7H_{15}	H	LDA,HMPA (1,1 eq); MeI (4 eq), -78°C, 1 h	4h	71	H	Me
10	3d	n.C_7H_{15}	CH_3	MeLi; H_2O, -78°C	4h	12**	H	Me
11	3e	n.Bu	n.C_5H_{11}	LDA, 50 min; H_2O, -78°C	***			
12	3b	n.C_7H_{15}	H	MeLi; MeI (1,2 eq), -78°C; repeated once more	4i	32	Me	Me
13	3a	n.C_5H_{11}	H	MeLi; HMPA and Me_2C=CH-CH_2Br (1,2 eq), -78°C, 1 h	4j	72*	H	CH_2-CH=CMe_2
14	3f	n.$C_{11}H_{23}$	H	MeLi; H_2O, -78°C	4k	46	H	H
15	3f	n.$C_{11}H_{23}$	H	MeLi; D_2O, -78°C	4l	52	H	D
16	3a	n.C_5H_{11}	H	MeLi; p.Me-C_6H_4-CH_2-Br (1,2 eq), -78°C	4m	56*	H	CH_2-p.Tol

* A small amount of bisalkylated sulphinamide was also obtained: 4g', R^2=R^3= CH_2-CH=CH_2 (7 %); 4j', R^3=R^2=CH_2-CH=CMe_2 (2 %) and 4m', R^2=R^3= CH_2-p.Tol (trace)

** The majority of the starting material was destroyed during the reaction.

*** This reaction lead to a complete decomposition of the starting material.

Hence the observed loss of a γ-proton can be seen to indicate regiocontrol by a complex-induced proximity effect (CIPE) process [4,5]. The kinetic deprotonation of 3 to give II is tentatively interpreted to involve a transition state represented as V for the major diastereoisomer [6] leading to the carbanions VI and II:



The results of entries 10 and 11 show that two α-alkylated allenic sulphinamides 3d and 3e gave poor results, this perhaps being due to their major diastereoisomers not being able to adopt the appropriate conformation owing to $A^{(1,3)}$-strain and thus giving opportunity for reaction with base via alternative paths.

Finally, application of our usual hydrolytic procedure to the propargylic sulphinamides 4 gave the expected allenes 5 (Table 2) [2] through the intermediate propargylic sulphinic acids VII which fragmented smoothly with exclusive rearrangement. Replacing water by deuterium oxide allowed the regioselective preparation of deuterated allenes.

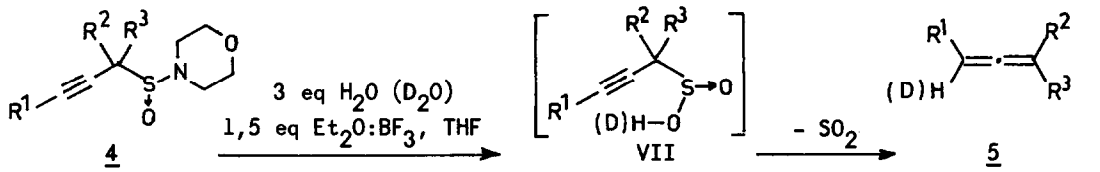


Table 2

Substrate	Conditions		Yields of allenes %	H(D)	R^1	R^2	R^3
4g	H_2O, 30 min at 0°C then 4 h at 20°C	5a	46	H	n.C_5H_{11}	H	CH_2-CH=CH_2
4h	H_2O, 15 min at 20°C then 45 min at 60°C	5b	77	H	n.C_7H_{15}	H	Me
4h	D_2O, 15 min at 20°C then 45 min at 60°C	5c	76	D	n.C_7H_{15}	H	Me
4i	H_2O, 15 min at 20°C then 45 min at 60°C	5d	52	H	n.C_7H_{15}	Me	Me
4j	H_2O, 30 min at 0°C then 3,5 h at 20°C	5e	66	H	n.C_5H_{11}	H	CH_2-CH=CMe_2
4k	D_2O, 15 min at 20°C then 45 min at 60°C	5f	70	D	n.$C_{11}H_{23}$	H	H
4l	D_2O, 15 min at 20°C then 45 min at 60°C	5g	75	D	n.$C_{11}H_{23}$	H	D
4m	H_2O, 30 min at 0°C then 1 h at 20°C	5h	58	H	n.C_5H_{11}	H	CH_2-p.Tol
4m	H_2O, 15 min at 20°C then 45 min at 60°C	5h	60				
4m	D_2O, 30 min at 0°C then 1 h at 20°C	5i	64	D	n.C_5H_{11}	H	CH_2-p.Tol

This report documents the γ-lithiation and subsequent electrophilic substitution of 4-(1',2'-alkadienesulphinyl)-morpholines thus providing a direct and simple route to the corresponding propargylic sulphinamides [7]. The hydrolytic desulphinylation of the propargylic sulphinamides represents a new synthesis of allenic compounds with possible regioselective incorporation of deuterium.

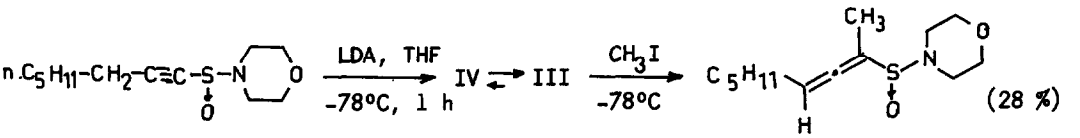
Acknowledgement: The authors thank Dr P.H. Williams for correcting the English manuscript.

REFERENCES AND NOTES

1. a) Unsaturated Sulphinamides, part VII.
   b) Part VI: Baudin J.-B., Julia S.A., Wang Y., Tetrahedron Lett., 1989, 30, 4965.

2. The identity of all new compounds reported in this communication was established by IR, ^{1}H NMR, ^{13}C NMR and MS. For most of them, the elemental compositions were determined by combustion analysis. The methyllithium (solution in diethyl ether) used was of low chloride content (Janssen).

3. In order to prove the existence of such a carbanion III, the following reaction has been carried out:



and starting material (48%)

Although this result was not optimised, it is another interesting case of CIPE process.

4. Beak P., Meyers A.I., Acc. Chem. Res., 1986, 19, 356; see also Klumpp, G.W., Recl. Trav. Chim. Pays-Bas, 1986, 105, 1.

5. Beak P., Hunter J.E., Jun, Y.M., Wallin A.P., J. Am. Chem. Soc., 1987, 109, 5403.

6. We believe that the major diastereoisomers V of the sulphinamides 3 have been formed preferentially via the least hindered conformation of the propargylic morpholinesulphenate esters, similar to that hypothesised for the (2.3)-sigmatropic rearrangement of propargylic benzenesulphenate esters: Shen G.-Y., Tapia R., Okamura W.H., J. Am. Chem. Soc., 1987, 109, 7499; see note 5 of ref. 1b.

7. This novel case of a CIPE process is applicable to γ-monosubstituted allenic sulphoxides (Dr R. Lorne, unpublished results).

(Received in France 12 October 1989)