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SUBSTITUTED 4-(1',2'-ALKADIENESULPHINYL)-MORPHOLINES; PREPARATION AND HYDROLYTIC DESULPHINYLATION INTO THE CORRESPONDING ALKYNES [1]

Jean-Bernard Baudin, Sylvestre A. Julia and Yuan Wang

Laboratoire de Chimie associé au C.N.R.S., Ecole Normale Supérieure,
24 rue Lhomond, 75231 Paris Cedex 05, France.

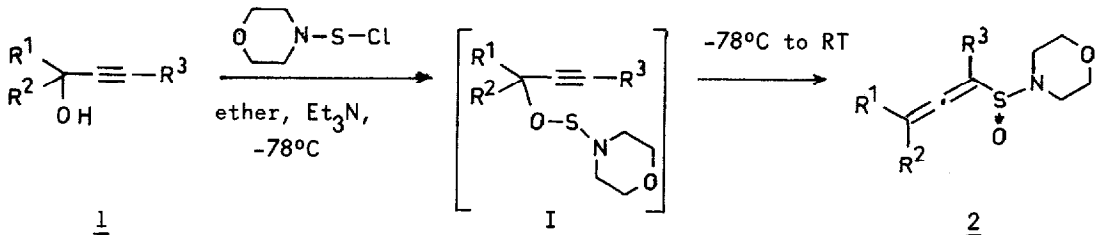
Summary: By the reaction with 4-morpholinesulphenyl chloride carried out in the presence of triethylamine, several substituted propargylic alcohols have been converted into the corresponding allenic sulphinamides 2. As a complementary method, the new allenic lithio-derivatives II have been prepared and efficiently alkylated with organic halides. The acid-catalysed hydrolysis or deuterolysis of the title sulphinamides 2 provide the corresponding alkynes.

It has been previously shown that allylic sulphinamides can be readily obtained by the reaction of allylic alcohols with 4-morpholinesulphenyl chloride in the presence of triethylamine through the remarkably facile and efficient (2,3)-sigmatropic rearrangement of the intermediate allylic 4-morpholinesulphenate esters [2].

As a reasonable continuation, it seemed very likely that this procedure would be applicable to substituted propargylic alcohols. The results in this new series demonstrate the utility of the reaction for the preparation of allenic sulphinamides 2 (Table 1) [3,4]. The (2,3)-sigmatropic rearrangements of the examined propargylic 4-morpholinesulphenate esters I are generally of low diastereoselectivity except for compounds 2k and 2l [5] and can be considered as an useful extension of the classical rearrangement of propargylic sulphenate esters to allenic sulphoxides [6].

Given the interesting results associated with synthetic applications of the lithiated methane-[7] and 2-alkene-[2b] sulphinamides, exploration of the chemistry of lithiated allenic sulphinamides II should prove fruitful. Typically, the allenic derivatives II are generated by treatment of the γ,γ-disubstituted allenic sulphinamides 2 (R^1=R^2= alkyl, R^3=H) with a slight excess (1,1 eq) of lithium diisopropylamide (LDA) or methyllithium in THF at -78°C. After 30 min, the allenic anions II were treated with some representative organic halides at -78°C or -30°C, thus affording the substituted allenic sulphinamides 2 (Table 2). The reactions were generally straightforward except for the alkylations with 1-bromo-3-methyl-2-butene which provided mixtures of the normal products 2r and 2t with small quantities of their isomeric conjugated trienic sulphinamides (see footnotes of Table 2).

When applied to γ-monosubstituted allenic sulphinamides 2 (R^1=alkyl, R^2=R^3=H), the lithiation-alkylation sequence took an unexpected course which will be the subject of a forthcoming report.



1 I 2

Table 1

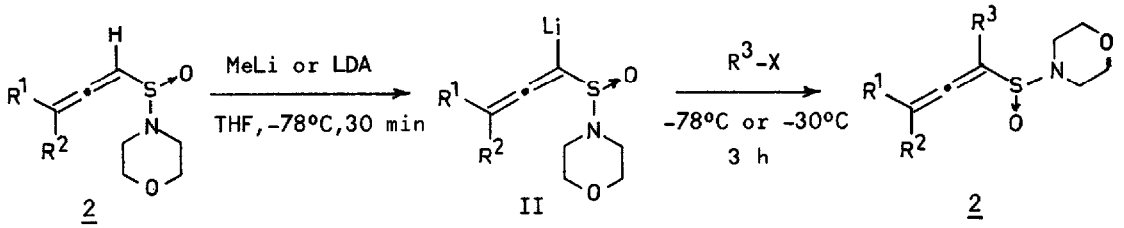
Substrate	R^1	R^2	R^3	time (h)	yields (%) of sulphinamides		ratios A:B *
1a	H	H	H	1	2a	99 **	-
1b	Me	H	H	15	2b	69 **	60:40
1c	Me	Me	H	1	2c	88	-
1d	$-(CH_2)_5-$		H	1	2d	93	-
1e	n.C_5H_{11}	H	H	1	2e	91	***
1f	$Me_2C{=}CH{-}(CH_2)_2-$	Me	H	1	2f	89	75:25
1g	n.C_7H_{15}	H	H	1	2g	90	***
1h	n.C_7H_{15}	H	D	1	2h	94	65:35
1i	p.Me-C_6H_4	H	Me	1	2i	96	55:45
1j	n.C_7H_{15}	H	Me	1	2j	75	75:25
1k	n.Bu	H	n.C_5H_{11}	1	2k	96	85:15
1l	i.Pr	H	n.C_6H_{13}	1	2l	72	90:10
1m	Ph	H	n.Bu	1	2m	79	55:45
1n	Me	Me	n.C_8H_{17}	1	2n	70	-
1o	n.C_7H_{15}	H	i.Pr	1	2o	77	75:25
1p	n.C_7H_{15}	H	t.Bu	1	2p	85	75:25

* The ratios A:B of diastereoisomers are determined by ^1H NMR.

** This compound is very unstable but can be stored in solution at -20°C.

*** The A:B ratio could not be determined by ^1H NMR.

The next task which appeared attractive was a simple hydrolysis of the substituted allenic sulphinamides 2 since the expected allenic sulphinic acids would fragment with rearrangement [8] into alkynes. Application of our previously described hydrolytic procedure [1b,9] gave the results which are summarised in Table 3. Moreover, replacing water by deuterium oxide allowed the smooth preparation of mono-deuterated alkynes (entries 4, 9, 11). The yields of alkynes were generally acceptable except for the transformations of γ,γ-disubstituted allenic sulphinamides (entries 1, 6, 7) owing to the reluctance of the γ,γ-disubstituted allene group to be protonated in the correct way to allow the loss of sulphur dioxide from the intermediate allenic sulphinic acid [10,11].

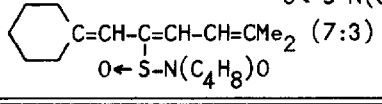


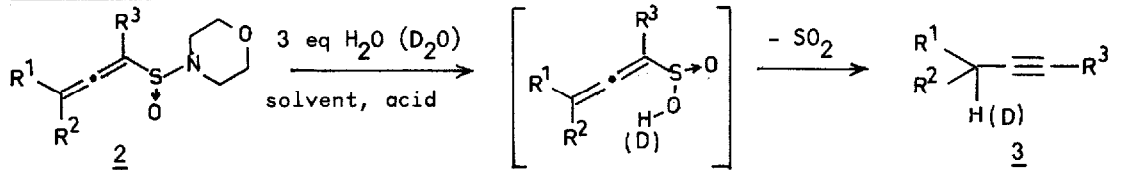
2 II 2

Table 2

substrate	R^1	R^2	conditions	yields	(%)
2d	$-(CH_2)_5-$		LDA; MeI (1,1 eq), -30°C	2q	94
2c	Me	Me	MeLi; $Me_2C=CH-CH_2-Br$ (1,2 eq), -30°C	2r	51 *
2d	$-(CH_2)_5-$		MeLi; n.BuI (1,2 eq); -30°C	2s	70
2d	$-(CH_2)_5-$		MeLi; $Me_2C=CH-CH_2-Br$ (1,2 eq), -30°C	2t	86 **
2c	Me	Me	MeLi; p.Me-$C_6H_4-CH_2-Br$ (1,2 eq), -78°C	2u	79
2c	Me	Me	LDA; n.$C_8H_{17}I$ (1,1 eq), -30°C	2n	61
			MeLi; idem		75
2d	$-(CH_2)_5-$		LDA; n.$C_8H_{17}I$ (1,2 eq), -30°C	2v	82

* The product is an unseparable mixture of 2r and $Me_2C=CH-\underset{\underset{O\leftarrow S-N(C_4H_8)O}{|}}{C}=CH-CH=CMe_2$ (8:2)

** unseparable mixture of 2t and  (7:3)



2 3

Table 3

entry	substrate	conditions			yields of alkynes 3 %	R^1	R^2	R^3	H (D)
1	2s	H_2O, THF; 1,5 eq BF_3:OEt_2;	1h,	60°C	25	$-(CH_2)_5-$		n.Bu	H
2	2k	idem ;	90 min,	60°C	62	n.Bu	H	n.C_5H_{11}	H
3	2k	H_2O, THF, leq $MeSO_3H$;	2 h,	0°C	72	n.Bu	H	n.C_5H_{11}	H
4	2k	D_2O, THF; 1,5 eq BF_3:OEt_2;	90 min,	60°C	68	n.Bu	H	n.C_5H_{11}	D
5	2l	H_2O, THF; 1 eq $MeSO_3H$;	2 h,	0°C	64	i.Pr	H	n.C_6H_{13}	H
6	2u	H_2O, THF; 1,5 eq BF_3:OEt_2;	1 h,	60°C	25	Me	Me	CH_2-p.Tol	H
7	2n	H_2O,dioxane;1,5 eq BF_3:OEt_2;	90 min,	60°C	33	Me	Me	n.C_8H_{17}	H
8	2o	H_2O,THF; 1,5 eq BF_3:OEt_2;	2 h,	20°C	69	n.C_7H_{15}	H	i.Pr	H
9	2o	D_2O, THF; idem			53	n.C_7H_{15}	H	i.Pr	D
10	2p	H_2O, THF; idem			64	n.C_7H_{15}	H	t.Bu	H
11	2p	D_2O, THF; idem			65	n.C_7H_{15}	H	t.Bu	D

The experiments described above illustrate very well the synthetic applicability of the (2,3)-sigmatropic rearrangement of the propargylic morpholinesulphenate esters, the lithiation-alkylation sequence of the γ,γ-disubstituted allenic sulphinamides and their hydrolytic desulphinylation into alkynes with incorporation of deuterium.

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REFERENCES AND NOTES

1. a) Unsaturated Sulphinamides, part VI.
b) part V: Baudin J.-B., Julia S.A., Tetrahedron Lett., 1989, 30, 1967.

2. a) Baudin J.-B., Julia S.A., ibid., 1988, 29, 3251; b) ibid., 1989, 30, 1963.

3. The procedure was the same as that previously reported (ref. 2a). The allenic sulphinamides were purified by flash chromatography and can be stored at -20°C for several weeks without appreciable decomposition.

4. The identity of all new compounds reported in this communication was established by IR, ^{1}H NMR, ^{13}C NMR and M.S. For most of them, the elemental compositions were determined by combustion analysis.

5. Other examples of diastereoselective (2,3)-sigmatropic rearrangement of some propargylic N,N-dialkylaminosulphenate esters have been found in our laboratory; further work is in progress to shed light on their stereochemistry.

6. Braverman S., in "The Chemistry of Sulphones and Sulphoxides", Ed. Patai S., Rappoport Z., Stirling Ch., J. Wiley and Sons, 1988, chapter 14, p. 736.

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8. see Chang C.-A., Cronin K.G., Crotts D.D., Dunach E., Gadek T.R., Vollhardt R.P. C., J. Chem. Soc. Chem. Commun., 1984, 1545, for sulphur dioxide-catalysed hydrogen-deuterium exchanges at the position α to the triple bond in terminal alkynes.

9. Baudin J.-B., Julia S.A., Tetrahedron Lett., 1988, 29, 3255.

10. As several similarly substituted allenic sulphinamides have been smoothly converted by methanol-boron trifluoride:etherate into the corresponding sulphinate esters with good yields (unpublished results), the hydrolysis should similarly be straightforward and the γ,γ-disubstituted allenic sulphinic acids could be expected to undergo different transformations. Indeed, the hydrolysis of sulphinamide 2c provided mainly two unstable polar compounds, one of which is the product of a simple disproportionation, i.e. $Me_2C=C=CH-SO_2-S(O)-CH=C=CMe_2$

11. When submitted to the hydrolytic procedure, the conjugated phenyl-allenic sulphinamide 2m did not afford any trace of the expected acetylenic compound.

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