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REACTIVITY OF THE 1-t.BUTYLTHIO-3-METHOXY-1-ALKENES TOWARDS METALATING AGENTS, I. REGIOSELECTIVE DEPROTONATION AT EITHER ONE OF THE TWO OLEFINIC SITES OF THE Z-ISOMERS

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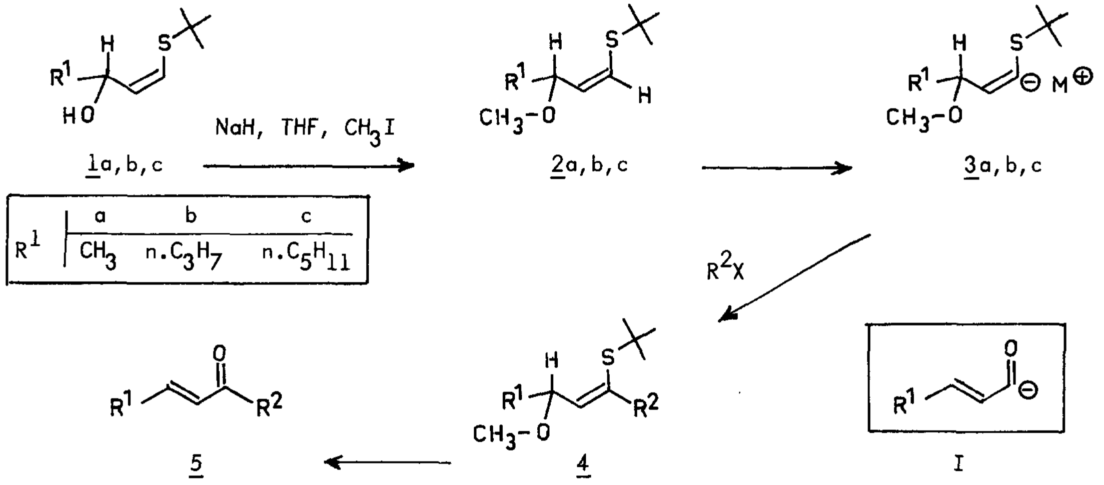
Summary: THF solutions of the title Z-isomers (with the exception of the propenyl compound) at -78° produce either (i) the 1-metalated derivatives when treated with potassium t.butoxide and n.butyllithium or (ii) the 2-lithiated derivatives when sec.butyllithium is the metalating agent. Both metalated derivatives become new equivalents of the hypothetical anions I and II respectively.

Previous work in our laboratory has shown that various 1-t.butylthio-1(Z)-alken-3-ols 1 are available through nucleophilic trans addition of 2-methyl-2-propanethiol to 1-alkyn-3-ols [1]. As these compounds 1 and other γ-hydroxy-α,β-ethylenic sulfides can be readily hydrolysed into the corresponding α,β-unsaturated aldehydes [2,3] and the acidity of the α-proton of vinyl sulfides is well known [4], it seemed worthwhile to investigate a method for converting 1 into the acyl-anion equivalents.

In a previous study, the 1-t.butylthio-3-methyl-1(Z)-buten-3-ol treated first with potassium hydride and then with n.butyllithium in THF at -78°, readily furnished the corresponding $K^{+}Li^{+}$ dianion; but the secundary 1-t.butylthio-1(Z)-alken-3-ols gave poor to moderate yields [3].

More rewarding results were obtained starting with the methoxy-derivates 2 [5]. Addition of a solution of n.butyllithium in hexane to a cooled (- 78°) solution of 2 and potassium t.butoxide [6] in THF resulted in a rapid metalation (15 min). As expected, this metalation occurred with retention of the double bond configuration, as indicated by the recovery of the unchanged Z-starting compound 2a after protonation of the carbanion 3a. Reaction of the carbanions 3a,b,c with various alkylating species (Table I) afforded the substituted compounds 4 [5]. As 4ab, 4bb and 4ca can be hydrolysed with methyl iodide in wet acetonitrile [7] at reflux to yield the ketones 5, the carbanions 3 may be viewed as the conjugated carbonyl anion equivalents I.



R^1	a	b	c
	CH_3	n.C_3H_7	n.C_5H_{11}

Table I

Substrate	R^2X	Product	Yield %*	Ketone	Yield %
2a	CH_3OH	2a	(99)		
	CH_3I	4aa	(98)		
	n.C_4H_9I	4ab	68	5aa	51
	$(CH_3)_3SiCl$	4ac	(97)		
2b	CH_3I	4ba	(98)		
	n.C_4H_9I	4bb	60	5ba	56
	$(CH_3)_3SiCl$	4bc	(96)		
2c	CH_3I	4ca	(99)	5ca	73
	$(CH_3)_3SiCl$	4cb	62		

* The values in brackets are the yields of crude products whose purity is ensured by spectral data.

When treated with sec.butyllithium in THF : HMPA (9:1) at -78° during 45 min [8] followed by methyl iodide, the vinyl sulfide 2c gave only 41 % of the alkylated compound 4ca, the remainder being the unchanged starting compound. Repeating the same experiment without HMPA during 15 min surprisingly gave the 2-substituted product 7ca (98%). In the same way, the cis vinyl sulfides 2a,b were converted into the substituted products 7 [5] in good yields. These metalations occurred also with retention of the configuration of the double bond as indicated by the recovery of the uninverted starting compound 2a *after protonation of the organolithium 6a. Some of the substituted methoxy-vinyl-sulfides*

7 have been hydrolysed with methyl iodide in aqueous acetonitrile at reflux to yield the α-substituted α,β-ethylenic aldehydes 8. Thus the lithio derivatives 6 can be viewed as the α-carbanions of α,β-unsaturated aldehydes II.

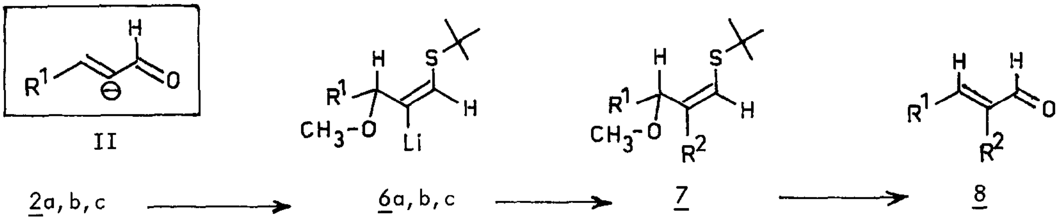
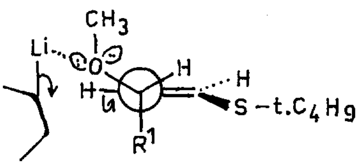


Table II

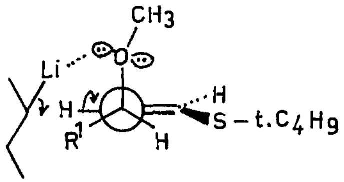
Substrate	R^2X	Product	Yield % *	Aldehyde	Yield % *
2a	CH_3OH	2a	(98)		
	CH_3I	7aa	(99)		
	$(CH_3)_2C{=}CH{-}CH_2Br$	7ab	68	8ab	55
	$(CH_3)_3SiCl$	7ac	(97)		
2b	CH_3I	7ba	(99)	8ba	67
2c	CH_3I	7ca	(98)	8ca	74

* The values in brackets are the yields of crude products whose purity is ensured by spectral data.

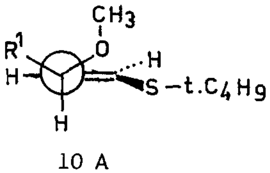
The striking formation of the lithio-derivatives 6 may have its origin in the transition states (9 A or B) of the starting Z-sulfides 2. These conformations are obviously favored over the other rotamers (10 A,B) on account of their $A^{(1,3)}$-strain. Due to its proximity to the plane of the double bond, the allylic proton (δ : 4.11-4.24 ppm) is regularly deshielded ($\Delta\delta$: 0.5 ppm) relative to the corresponding proton of the 1-t.butylthio-3-methoxy-1(E)-alkenes[9,10]. It can be assumed that the initial step in



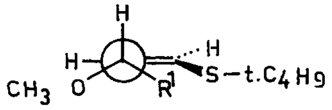
9 A



9 B



10 A



10 B

the lithiation reaction is the coordination of the metalating agent with a lone pair of the oxygen atom; the nearest available proton then suffers a protophilic attack leading to the observed lithio-derivative 6. This phenomenon can be considered as a new case of heteroatom-assisted lithiation, which is prevented in the presence of HMPA.

REFERENCES AND NOTES

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2. S. Akiyama, S. Nakatsuji, T. Hamamura, M. Kataoka, M. Nakagawa, ibid., 2809 (1979); M. Julia, Ch. Lefebvre, ibid., in press. We thank Professor M. Julia for communicating their results before publication and many stimulating discussions.
3. These results have been presented by one of us (S.A.J.) at the French Chemical Society Meeting (September 14th, 1982).
4. See the review "Heteroatom-facilitated lithiations" by H.W. Gschwend, H.R. Rodriguez in Organic Reactions, vol. 26, John Wiley & Sons Inc. (1979).
5. All new compounds exhibited the expected I.R., N.M.R. (^{1}H, ^{13}C) and Mass spectral properties.
6. By this means, some ene- and diene-sulfides have been metalated at the olefinic site next to the heteroatom: R. Muthukrishnan, M. Schlosser, Helv. Chim. Acta, 59, 13 (1976); R.H. Everhardus, R. Gräfing, L. Brandsma, Recl. Trav. Chim. Pays Bas, 97, 69 (1978).
7. This procedure has been reported for converting thioacetals into the parent carbonyl compounds: M. Fetizon, M. Jurion, J. Chem. Soc. Chem. Comm., 382 (1972); H.-L. Wang Chang, Tetrahedron Letters, 1989 (1972).
8. These conditions have been recommended for a complete and rapid conversion of 1-methylthio-1-decene into the corresponding 1-lithio derivative: K. Oshima, K. Shimoji, H. Takahashi, H. Yamamoto, H. Nozaki, J. Amer. Chem. Soc., 95, 2694 (1973).
9. O. Ruel, C. Bibang Bi Ekogha, S.A. Julia, following communication.
10. For a similar analysis of the ^{1}H NMR spectra of the two 2-$\left[(E \text{ or } Z)\text{-1-propenyl}\right]$-1,3-dithianes, see F.E. Ziegler, J.-M. Fang, C.Ch. Tam, J. Amer. Chem. Soc., 104, 7174 (1982).

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