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REGIO- AND STEREOSELECTIVITY IN ALKYLATIONS OF DIANIONS DERIVED FROM ALLYLIC DITHIOCARBONATE p-TOLUENESULFONYLHYDRAZONES

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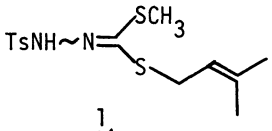
Facile generations of dianions from various dithiocarbonate tosylhydrazones including allylic ones are described. The dianions so generated were found to exhibit a high syn-stereoselectivity in their alkylations and also a high α-regioselectivity in allylic systems. The importance of the six-membered chelation of the dianionic species to the observed regio- and stereoselectivity has been evaluated.

In order to study the stereochemical course of [2,3]sigmatropic rearrangement of allylic dithiocarbenes,[1] we had needed a facile method for regioselective introduction of alkyl groups to the allylic positions of allylic dithiocarbonate p-toluenesulfonylhydrazones (tosylhydrazones). Thus we initiated studies on generations of dianions of various dithiocarbonate tosylhydrazones including allylic ones (e.g., 1) and on the role of the hydrazone stereochemistry upon both the stereoselectivity (syn vs. anti to the tosylamino moiety) and the regioselectivity (α vs. γ) in alkylations of the dianions (e.g., 2).



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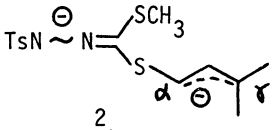
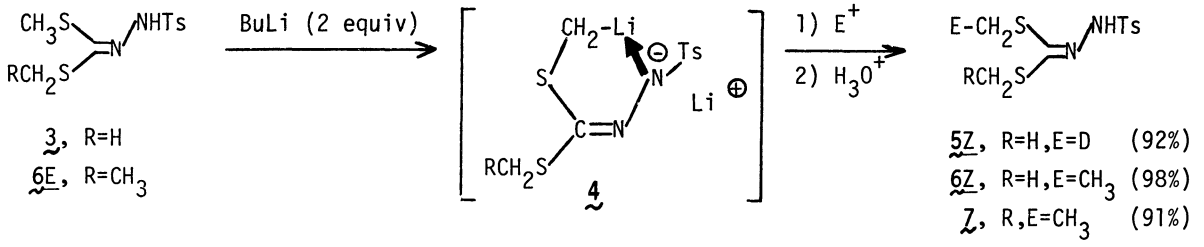


2

We now wish to report a facile generation of dianions from dithiocarbonate tosylhydrazones and to demonstrate a high syn-stereoselectivity and α-regioselectivity in alkylations at the allylic dianions, thereby accomplishing regioselective alkylations at the allylic positions by using the (Z)-isomers of allylic tosylhydrazones.

First of all, we examined the stereoselectivity (syn vs. anti) in dianion formations with simple S,S'-dialkyltosylhydrazones. Thus S,S'-dimethyl tosylhydrazone (3) was treated with 2 equiv of butyllithium (a commercial hexane solution) in tetrahydrofuran (THF) at -70~-75°C giving an orange solution. At that temperature, additions of deuterium oxide (a slightly excess) and methyl

iodide (1 equiv) to the solution followed by acidification[2] with 1N hydrochloric acid produced (Z)-S-deuteromethyl-S'-methyl (5Z)[3] and (Z)-S-ethyl-S'-methyl derivative (6Z),[4] respectively, in good yields. The assignment of the Z geometry was based on spectral comparisons with authentic samples and/or NMR analysis described in our preceding paper.[5] Similarly, methylation of the dianion derived from (E)-S-ethyl-S'-methyl tosylhydrazone (6E)[4] afforded exclusively the syn-methylation product (7).[6] The basis of the high syn-stereoselectivity in the deprotonation



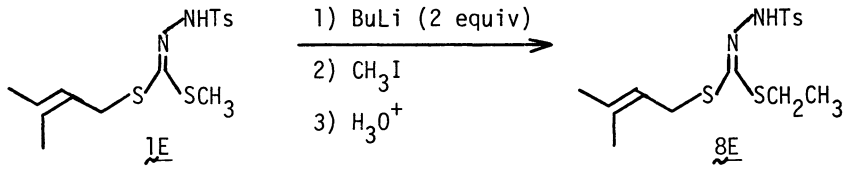
3, R=H
6E, R=CH3

4

5Z, R=H,E=D (92%)
6Z, R=H,E=CH3 (98%)
7, R,E=CH3 (91%)

reactions can be explained in terms of the six-membered chelation of the dilithium ion (4) which is similar to the five-membered chelation of the dilithium ions of ketone oximes[7] and tosylhydrazones[8] used to rationalize similar syn-stereoselectivities in alkylations of these dianions.

In an attempt to see if this stereoselective deprotonation procedure is applicable to the preparation of a primary syn carbanion in preference to an allylic anti carbanion which should be more thermodynamically stable, (E)-S-methyl-S'-prenyl tosylhydrazone (1E)[4] was treated with 2 equiv of butyllithium under the standard condition described above followed by alkylation. We found that methylation of the dianion of 1E produced cleanly the syn-methylation product, (E)-S-ethyl-S'-prenyl tosylhydrazone (8E),[9] in 95% yield. The result obviously indicates not only the

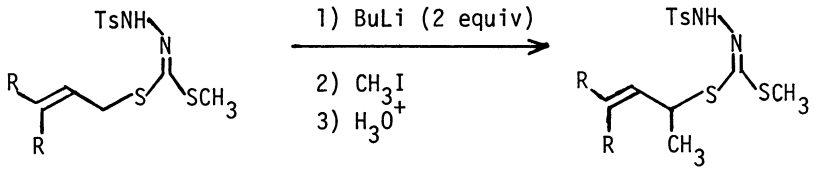


1E

8E

the absence of geometrical isomerization during the deprotonation and alkylation reactions but also a kinetic syn-preference for the dianion formation which is in direct contrast to the kinetic anti-preference recently reported for the monoanion formations from ketone N,N-dimethylhydrazones.[10]

In view of the high syn-stereoselectivity in dianion formations in our systems described above, we can easily anticipate that allylic alkylations might be embodied by using the (Z)-isomers of allylic dithiocarbonate tosylhydrazones, although the regioselectivity (α vs. γ) problem still remains unsolved. Thus (Z)-S-allyl-S'-methyl tosylhydrazone (9Z)[4] was subjected to the lithiation-methylation sequence under the standard conditions. As expected, the product thus obtained was found to be exclusively the α-methylation product (10Z).[11] Unfortunately, however, the dianion of the (Z)-S-prenyl derivative (1Z) generated by the standard procedure exhibited a much lower



9Z, R=H
1Z, R=CH3

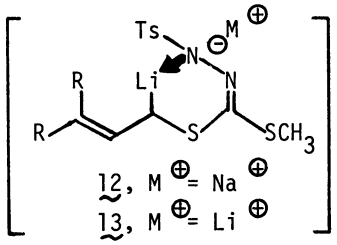
10Z, R=H (98%)
11Z, R=CH3 (60%)

α-regioselectivity (ca. 60%). Thus we studied the effect of the solvent system and the nature of the counter cations (metal ions) of the dianion on the regioselectivity in methylations of allylic systems in some details (Table 1). The results obviously indicate that the mixed ($Na^{\oplus}/Li^{\oplus}$)

Table 1. Regioselectivity in methylation of Dianions

Deprotonating Reagent	Solvent System	α-Regioselectivity	
		9Z	1Z
BuLi (2 equiv)	THF	>95%[a]	~60%
NaH (1 equiv) + BuLi (1 equiv)	THF	>95%[a]	>95%[a]
BuLi (2 equiv)	THF + TMEDA[b] (10 equiv)	80%	< 5%

[a] This means that any other isomers were not detected by NMR.
[b] N,N,N',N'-Tetramethylethylenediamine.



12, $M^{\oplus}$ = Na $^{\oplus}$
13, $M^{\oplus}$ = Li $^{\oplus}$

dianions (12) generated with sodium hydride (1 equiv) and butyllithium (1 equiv) exhibited a much higher α-regioselectivity[13] than the dilithium anions (13) and that addition of TMEDA, a powerful chelating agent, considerably decreased the α-regioselectivity.[14] These findings clearly indicate that the degree of the intramolecular chelation plays an important role in determining both the regio- and stereoselectivity in these systems.

References and Notes

1) J. E. Baldwin and J. A. Walker, J. Chem. Soc., Chem. Commun., 1972, 354; D. A. Evans, C. L. Sims, and G. C. Andrews, J. Am. Chem. Soc., 99, 5453 (1977); T. Nakai and K. Mikami, Chem. Lett., 1978, 1243.

2) In order to avoid Z-E isomerization of the products, the reaction mixture was acidified at -70~ -75°C.

3) Mp 145-146° (CCl_4); NMR ($CDCl_3$), δ 7.64 (1H, s), 7.78 and 7.28 (4H, AB, J=8Hz), 2.42 (6H, s), 2.32 (2H, s)

4) Physical and spectral properties of these tosylhydrazones have been described in our preceding paper.

5) The Z-E stereochemistry of other tosylhydrazones described in this paper was also determined by the NMR spectra in deuterochloroform and/or benzene.

6) Mp 79-80° (CCl_4); NMR ($CDCl_3$), δ 8.00 (1H, s), 7.72 and 7.20 (4H, AB, J=8Hz), 2.87 and 2.86 (4H, 2q, J=6.8Hz), 2.38 (3H, s), 1.16 and 1.14 (6H, 2t, J=6.8Hz).

7) W. G. Kofron and M.-K. Yeh, J. Org. Chem., 41, 439 (1976); M. E. Jung, P. A. Blair, and J. A. Lowe, Tetrahedron Lett., 1976, 1439.

8) R. H. Shapiro, Org. React., 23, 405 (1975); W. G. Dauben, G. T. Rivers, and W. T. Zimmerman, J. Am. Chem. Soc., 99, 3414 (1977), and references cited therein.

9) Oil; NMR ($CDCl_3$), δ 8.16 (1H, s), 7.78 and 7.35 (4H, AB, J=8Hz), 5.23 (1H, br.t, J=8Hz), 3.59 (2H, d, J=8Hz), 2.90 (2H, q, J=6.8Hz), 2.43 (3H, s), 1.67 (6H, s), 1.19 (3H, t, J=6.8Hz).

10) M. E. Jung and T. J. Shaw, Tetrahedron Lett., 1977, 3305.

11) Mp 92-93° (CCl_4-$CHCl_3$); NMR ($CDCl_3$), δ 7.95 (1H, s), 7.82 and 7.30 (4H, AB, J=8Hz), 5.75 (1H, ddd, J=12, 6.6, and 6Hz), 5.08 (1H, d, J=12Hz), 4.90 (1H, d, J=6Hz), 4.10 (1H. dq, J=7.8 and 6.6 Hz), 2.40 (6H, s), 1.28 (3H, d, J=6.6Hz).

12) Oil; NMR ($CDCl_3$), δ 7.93 (1H, s), 7.83 and 7.27 (4H, AB, J=8Hz), 5.00 (1H, br.d, J=9Hz), 4.20 (1H, dq, J=9 and 6Hz), 2.40 (6H, s), 1.69 and 1.60 (6H, 2s), 1.22 (3H, d, J=6Hz).

13) This is not unexpected since the more ionized sodium-amido nitrogen should more strongly coordinate to the α-lithium atom.

14) This is also not unexpected since an intermolecular coordination by TMEDA to the α-lithium atom should break the intramolecular chelation at least partially.

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