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STEREOCHEMICAL FEATURES OF THE [2,3]SIGMATROPIC REARRANGEMENT OF DITHIOCARBENES

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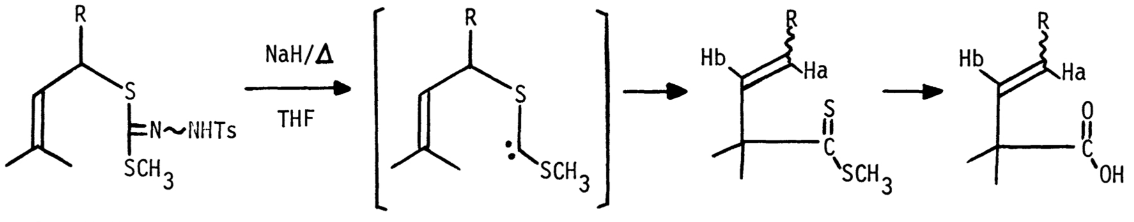
The [2,3]sigmatropic rearrangement of dithiocarbenes has been demonstrated to proceed with high level of stereoselectivity favoring the trans geometry of the newly formed double bond and with low level of asymmetric induction across the convex face of cyclohexylidene ring system.

Over the years numerous variants of the [2,3]sigmatropic rearrangement have been reported and the stereochemistry of each of these concerted rearrangements has been the subject of much current interest, particularly from the standpoint of synthetic utility.[1] Baldwin and Walker[2] have recently reported the [2,3]sigmatropic variant of dithiocarbene generated from the allylic dithiocarbonate tosylhydrazone (**1**) (eq 1) which should have obvious applications in organic synthesis.[3] However, no study on the stereochemistry of the particular sigmatropic variant has been reported except for the stereochemistry across the convex face of cis-fused hydrindane system within the context of natural product synthesis.[1c,4] In this communication, we wish to report intriguing stereochemical features of the carbenic [2,3]sigmatropic rearrangement.

First, we have examined the stereospecificity about the newly formed double bond employing α-substituted allylic systems (**2**). The requisite tosylhydrazones (**2a** and **2b**) were prepared in more than 90% yields via reactions of the dianion derived from (*Z*)-**1**[5] with methyl iodide and trimethylsilyl chloride according to the procedure recently developed in our laboratory.[6,7] When the sodium salt of (*Z*)-**2a** thus obtained was heated in THF at 60-70°C for 6 h , we obtained



(1)

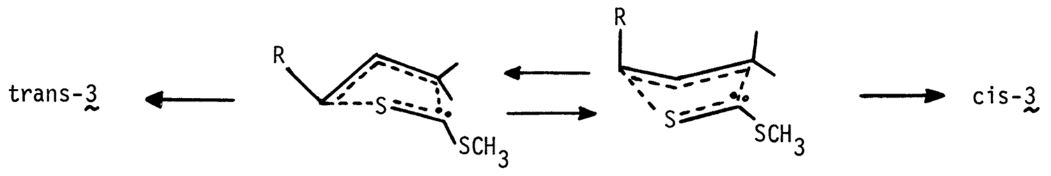
1 , R=H
2a, R=CH_3; **2b**, R=$Si(CH_3)_3$

3

4

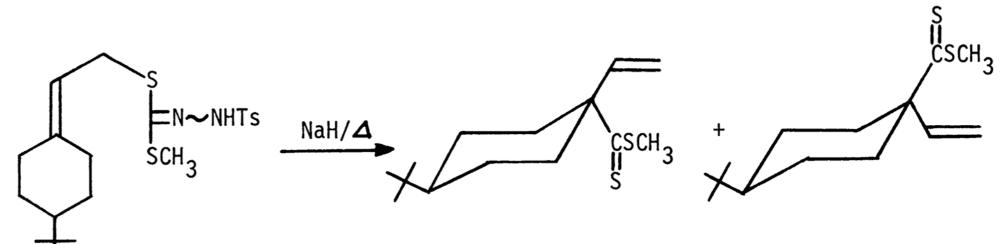
the trans isomer of the rearranged dithioester (**3**, R=CH_3) as a single product in 85% yield. The trans geometry was unambiguously assigned on the basis of careful spectral (ir and nmr) analysis of both the dithioester and its hydrolytic product (**4**).[8] In a similar experiment, (*Z*)-**2b** afforded only the trans isomer of the dithioester (**3**, R=$Si(CH_3)_3$)[9] in 81% yield.

The stereochemical outcome obviously indicates that the alkyl groups introduced regiospecifically at the allylic position eventually end up trans to the substituent bearing the dithioester moiety in the product. The basis of the high trans selectivity can be explained by essentially the same argument used to rationalize the comparable stereoselectivity in related [2,3]sigmatropic processes of sulfoxides[1b] and sulfonium ylides[10]; the "folded envelope" conformer **5** is favored over **6** which leads to the cis isomer because the alkyl group should preferentially occupy the pseudoequatorial orientation.



5 **6**

Secondly, we have examined the stereoselectivity with respect to the newly formed quaternary center. Thus 4-t-butylcyclohexylidene ring system (**7**) was chosen for study which would provide valuable data on the level of stereoselectivity across the convex face of the cyclohexane ring system (eq 2). When the sodium salt of (*E*)-**7**[11] was heated in THF, we obtained a



(2)

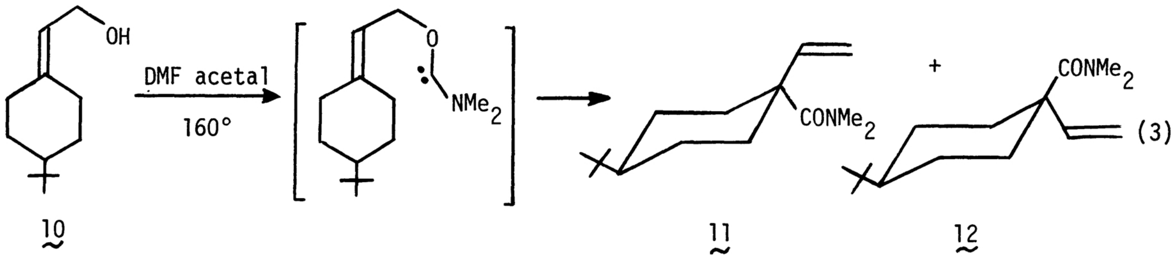
7 **8** **9**

55 : 45 (indicated by nmr) of the diastereomeric isomers **8** and **9**,[12] respectively, in 88% yield. The stereochemical assignments were determined by comparisons of both their relative rates of hydrolysis (10% methanolic sodium hydroxide) and their vpc retention times (10% SE 30, 190°C); the isomer which had the larger rate ($t_{1/2} \leq 4$ h) and the larger retention time (8.5 min) was assigned to the equatorial dithioester (**8**) whereas the isomer which had the smaller rate

($t_{1/2} \gg 8$ h) and the smaller retention time (6.5 min) was assigned to 9.[13] We have also found that a similar rearrangement in benzene in the presence of $Cu(acac)_2$ (0.1 equiv) gave almost the same isomeric ratio (65 : 35) (68% yield).

This low stereoselectivity across the convex face of the cyclohexylidene ring system is in stark contrast to great preferences (>90%) for equatorial entry in the same ring system recently reported for the related [2,3]sigmatropic processes of sulfoxides,[1c,14] sulfonium ylides,[1c,14] and ammonium ylides[15] as well as the exclusive formation of the pseudoequatorial isomer in the [2,3]sigmatropic process of dithiocarbene across the convex face of cis-fused hydrindane system.[1c,4]

In order to ascertain general levels of asymmetric induction in carbenic [2,3]sigmatropic processes of the cyclohexylidene ring system, we have further evaluated the stereoselectivity in a different carbenic variant (eq 3).[16] When a mixture of the allylic alcohol (10) and DMF acetal



(6 equiv) was heated in or without xylene at 160°C for 20 h , we obtained a 55 : 45 mixture (indicated by nmr) of the rearranged amides 11 and 12, respectively, in 21-28% yields. Structures of these amides were determined by ir and nmr spectra and vpc comparison.[17]

To the best of our knowledge these carbenic rearrangements are the first two examples of [2,3]sigmatropic processes exhibiting low stereoselectivity across the cyclohexylidene ring system. Although factors which are responsible for the low stereoselectivities are still not completely clear at present, the stereochemical results of this work point out that the nature of the migrating terminus appears to play a more pronounced role in defining the level of asymmetric induction in a given [2,3]sigmatropic process than has previously been considered.[1c] We are now investigating the specific role of the migrating terminus dictating the level of asymmetric induction in these and related [2,3]sigmatropic rearrangements.

Finally, it should be noted that the overall characteristics of these carbenic [2,3]-sigmatropic rearrangements described above are similar to those of the Claisen ([3,3]sigmatropic) rearrangements recently reported by House and co-workers.[18]

References and Notes

1) For pertinent reviews, see (a) B. M. Trost and L. S. Melvin, Jr., "Sulfur Ylides," Academic Press, New York, 1975, Ch.7;(b)D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974). For leading more recent references, consult (c) D. A. Evans, C. L. Sims, and G. C. Andrews, *J. Am. Chem. Soc.*, **99**, 5453 (1977);(d) W. C. Still and A. Mitra, *ibid.*, **100**, 1927 (1978).

2) J. E. Baldwin and J. A. Walker, *J. Chem. Soc., Chem. Commun.*, **1972**, 354.

3) T. Nakai and K. Mikami, *Chem. Lett.*, **1978**, 1243.

4) D. A. Evans and C. L. Sims, *Tetrahedron Lett.*, **1973**, 4691.

5) For the stereoselective synthesis of (*E*)- and (*Z*)-tosylhydrazones and the *Z*-*E* assignments, see T. Nakai and K. Mikami, *Chem. Lett.*, **1979**, 465.

6) For the regio- and stereochemistry of reactions of dianions derived from (*E*)- or (*Z*)-**1**, see T. Nakai and K. Mikami, *Chem. Lett.*, **1979**, 469.

7) For (*Z*)-**2a**, see ref 6. (*Z*)-**2b**, oil; nmr ($CDCl_3$) δ0.07 (s, 9H), 1.65 (s, 3H), 1.75 (s, 3H), 2.42 (s, 3H), 2.46 (s, 3H), 3.80 (d, J=12Hz, 1H), 4.95 (d, 1H), 7.23 and 7.77 (AB, J=8.0 Hz, 4H), 8.14 (s, 1H).

8) **3a**(R=CH_3), ir(neat) 965 cm^{-1}(s, trans C=C); nmr (CCl_4) δ1.46 (s, 6H), 1.72 (d, J=5.3Hz, 3H), 2.47 (s, 3H), 5.17-6.00 (m, 2H); **4a**(R=CH_3), ir(neat) 1700 (CO) and 970 cm^{-1}(trans C=C); nmr (CCl_4) δ1.30 (s, 6H), 1.67 (d, J=4.8Hz, 3H), 5.23-5.76 (m. 2H); J_{ab}=15.0 Hz (by decoupling).

9) **3b**(R=$SiMe_3$), ir(neat) 990 cm^{-1}(s, trans C=C); nmr (CCl_4) δ0.10(s, 9H), 1.47 (s, 6H), 2.43 (s,3H), 5.81 (d, J_{ab}=18.0Hz, 1H), 6.32 (d, 1H); **4b**(R=$SiMe_3$), ir (neat) 1700 and 990 cm^{-1}; nmr(CCl_4) δ0.03 (s, 9H), 1.23 (s, 6H), 5.66 (d, J=18.3Hz, 1H), 6.14 (d, 1H), 10.64 (s, 1H).

10) P. A. Grieco, D. Boxler, and K. Hiroi, *J. Org. Chem.*, **38**, 2572 (1973).

11) (*E*)-**7**, nmr ($CDCl_3$) δ0.86 (s, 9H), 2.30 (s, 3H), 2.40 (s, 3H), 0.9-2.8 (m, 9H), 3.54 (d, J=7.5 Hz, 2H), 5.07 (t, 1H), 7.30 and 7.83 (AB, J=8.7Hz, 4H), 8.2 (s, 1H).

12) **8**, nmr (CCl_4) δ0.81 (s, 9H), 0.9-2.8 (m, 9H), 2.50 (s, 3H), 5.20 (dd, J=16.8 and 1.32 Hz, 1H), 5.34 (dd, J=10.2 and 1.32, 1H), 5.84 (dd, 1H); **9**, nmr δ0.81 (s, 9H), 0.9-2.8 (m. 9H), 2.57 (s, 3H), 4.91 (dd, J=10.2 and 1.32Hz, 1H), 5.03 (dd, J=16.8 and 1.32Hz, 1H), 5.80 (dd, 1H).

13) Generally an equatorial ester group on 4-t-butylcyclohexane ring is more easily hydrolyzed and more strongly absorbed on the vpc column as compared with the axial ester: E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, Ch.8.

14) G. C. Andrews and D. A. Evans, *Tetrahedron Lett.*, **1972**, 5121.

15) L. N. Mander and J. V. Turner, *J. Org. Chem.*, **38**, 2915 (1973).

16) G. Büchi, M. Cushman, and H. Wüest, *J. Am. Chem. Soc.*, **96**, 5563 (1975). This particular [2,3]-variant has been established to be highly stereoselective for the newly formed double bonds.

17) **11**, Rt (10% SE30, 190°C)=5.6 min; ir(neat) 1620 cm^{-1}; nmr (CCl_4) δ0.84 (s, 9H), 0.9-2.2(m, 9H), 2.87 (s, 6H), 5.00 (d, 1H), 5.17 (d, 1H), 6.06 (dd, J=17.7 and 11.1Hz, 1H); **12**, Rt=3.9 min;nmr(CCl_4) δ 0.83 (s, 9H), 0.9-2.2 (m, 9H), 2.90 (s, 6H), 4.93 (d, 1H), 4.97 (d, 1H), 5.83 (dd, J=18.0 and 11.4Hz, 1H).

18) H. O. House, J. Lubinkowski, and J. J. Good, *J. Org. Chem.*, **40**, 86 (1975).

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