Evidence for *syn* Stereochemistry in Intramolecular S_N' Reaction of Allylic Acetates

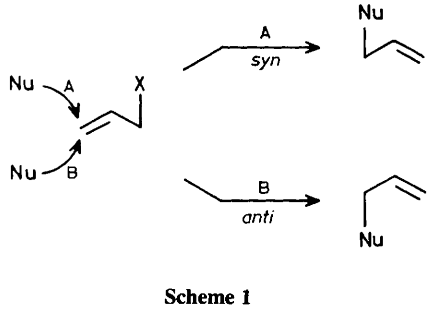
J. E. Bäckvall,*[a] **J. O. Vågberg,**[a] **and J. P. Genêt***[b]

[a] *Department of Organic Chemistry, Royal Institute of Technology, 100 44 Stockholm, Sweden*

[b] *Laboratoire de Synthèse Organique et Organometallique Associé au CNRS, Université Pierre et Marie Curie, 75005 Paris, France*

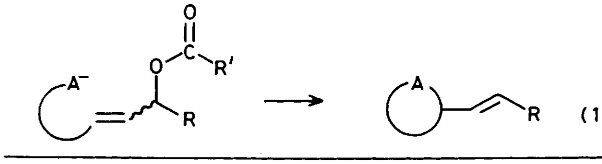
Reaction of the anion of the (R^*,R^*) and (R^*,S^*) isomers of dimethyl (E-5-acetoxyhex-3-en-2-yl)malonate [(R^*,R^*)-(**1**) and (R^*,S^*)-(**1**)] in refluxing dimethoxyethane results in an intramolecular S_N' reaction, where the displacement of the acetate by the carbanion proceeds with *syn* stereochemistry (94—96% *syn*).

The mechanism of the S_N2' reaction has been the matter of some controversy since its discovery.[1—3] Stereochemical studies have shown both *syn*- and *anti*-displacement by the nucleophile (Scheme 1), and a number of arguments have been invoked to account for the results. Although the *inter*-molecular S_N2' reactions often take place by *syn*-displacement[1,2] the corresponding *intra*-molecular S_N' reaction of allylic carboxylates [reaction (1)] has recently been shown to proceed *anti* with both a sulphur and a stabilized carbon nucleophile in acyclic systems.[4] During our studies on stereoselective vinylcyclopropane formation[5] we observed *syn*-stereoselectivity in a related intramolecular S_N' reaction. In this communication we report that *syn*-attack is highly favoured over *anti*-attack in an intramolecular vinylogous displacement of an allylic acetate by a stabilized carbon nucleophile to give a cyclopropane derivative.



Scheme 1

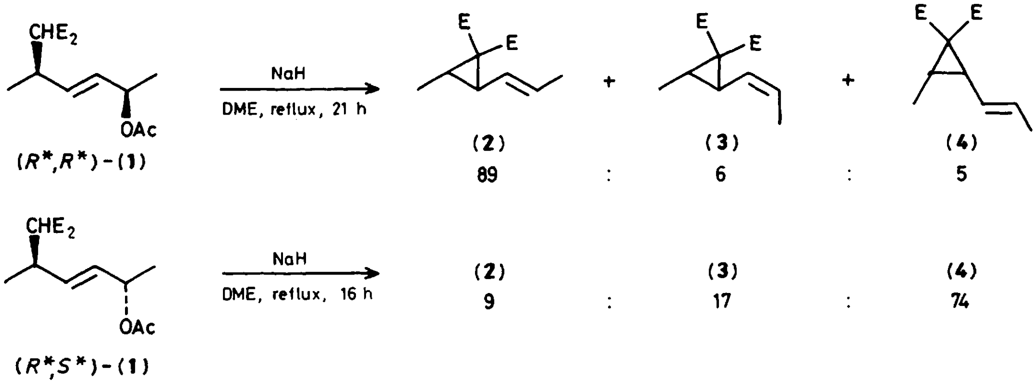
The compounds (R^*,R^*)-(**1**) and (R^*,S^*)-(**1**), readily available from (E, E)-hexa-2,4-diene and (E, Z)-hexa-2,4-diene in two steps,[6] were used as substrates for the stereochemical studies. The diastereoisomeric purity of the starting materials was 95% in both cases. Reaction of (R^*, R^*)-(**1**) with 1 equiv. of sodium hydride and subsequent heating of the anion in 1,2-dimethoxyethane (DME) for 21 h afforded the vinylcyclopropane (**2**) as the major isomer together with small amounts of (**3**) and (**4**) (Scheme 2).† The isomer (**2**), which is



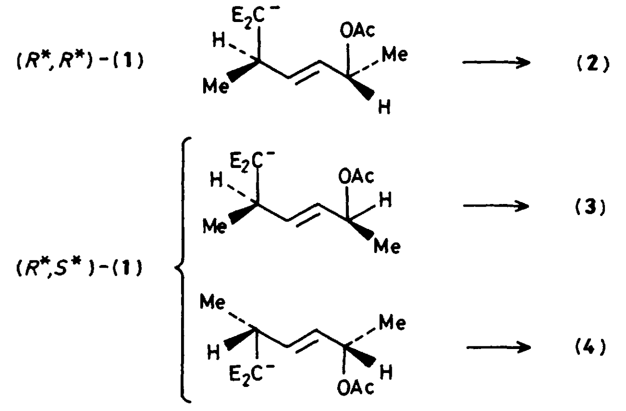
(1)

---

† The reaction was carried out at a concentration of 0.25 M. The crude yield of cyclopropane product was 65—70%.



Scheme 2. E = CO_2Me



Scheme 3. E = CO_2Me

formed in a relative yield of 89%, is the one expected from a *syn*-displacement (Scheme 3). The analogous reaction of (*R**, *S**)-(**1**) gave (**4**) (74%) as the major product together with (**2**) (9%) and (**3**) (17%).† In this case (**3**) and (**4**) are formed by a *syn*-displacement *via* two different conformations (Scheme 3). The relative yields of *syn*-products from (*R**, *R**)-(**1**) and (*R**, *S**)-(**1**) are therefore 89 and 91%, respectively. Since the diastereoisomeric purity of (*R**, *R**)-(**1**) and (*R**, *S**)-(**1**) is 95%, the corrected stereoselectivities for *syn*-attack are 94 and 96%, respectively. It is interesting to note that the conformation of (*R**, *R**)-(**1**) in which both methyl groups are *gauche* to the double bond does not give any detectable amount of product (*i.e.* that with *Z* double bond and *cis*-cyclopropane).

The structures of products (**2**), (**3**), and (**4**) were unambiguously assigned from their ^1H n.m.r. spectra.‡ To confirm the assignments an authentic sample of (**2**) was prepared by a known method.[7]

It has often been argued that the *syn*-stereochemistry in S_N2' reactions would be a result of an interaction between the nucleophile and the departing leaving group.[3,8] In the reaction of (*R**, *R**)-(**1**) and (*R**, *S**)-(**1**) such an interaction is excluded because of the *transoid* relationship between the nucleophilic centre and the leaving group. The fact that both (*R**, *R**)-(**1**) and (*R**, *S**)-(**1**) give the same stereochemical result rules out the possibility that conformational preferences would favour *syn*-attack.

The present results are in contrast with the stereochemistry reported by Stork for analogous S_N' reactions in acyclic systems.[4] He observed that the intramolecular S_N' displacement of an allylic carboxylate takes place *anti* when the displacing group is a carbanion (malonate) or a sulphide ion. There is one report of intramolecular *syn* S_N' displacement in an acyclic system but in this case the departing oxygen function was part of an epoxide.[9]

Received, 26th September 1986; Com. 1379

References

1 R. M. Magid, *Tetrahedron*, 1980, **36**, 1901.
2 G. Stork and A. F. Kreft, *J. Am. Chem. Soc.*, 1977, **99**, 3850; R. M. Magid and O. S. Fruchey, *ibid.*, 1979, **101**, 2107; A. A. Dobbie and K. H. Overton, *J. Chem. Soc., Chem. Commun.*, 1977, 722.
3 T. Oritani and K. H. Overton, *J. Chem. Soc., Chem. Commun.*, 1978, 454.
4 G. Stork and A. F. Kreft, *J. Am. Chem. Soc.*, 1977, **99**, 2851; G. Stork and A. R. Schoofs, *ibid.*, 1979, **101**, 5081.
5 J. E. Bäckvall, J. O. Vågberg, J. P. Genêt, D. Alexis, and C. Zercher, manuscript in preparation; see also F. Colobert and J. P. Genêt, *Tetrahedron Lett.*, 1985, **26**, 2779.
6 J. E. Bäckvall, J. E. Nyström, and R. E. Nordberg, *J. Am. Chem. Soc.*, 1985, **107**, 3676.
7 P. H. Mazzocchi and J. I. Tamburin, *J. Org. Chem.*, 1973, **38**, 2221.
8 R. H. DeWolfe and W. G. Young in 'The Chemistry of Alkenes,' ed. S. Patai, Interscience, New York, 1964, ch. 10.
9 J. Martel, A. D. Blade-Font, C. Marie, M. Vivat, E. Toromanoff, and J. Buendia, *Bull. Soc. Chim. Fr. II*, 1978, 131.

---

‡ The J_{HH} values of the cyclopropane protons in (**2**), (**3**), and (**4**) are 7.5, 7.5, and 9.7 Hz respectively. The J_{HH} values of the olefinic protons in (**2**), (**3**), and (**4**) are 15.0, 11.0, and 15.0 Hz respectively.