Tetrahedron Letters No. 29, pp. 2783-2786, 1971. Pergamon Press. Printed in Great Britain.

THE STEREOCHEMISTRY OF THE ALDER-ENE REACTION BETWEEN 2,3,3-TRIMETHYL-1-BUTENE AND MALEIC ANHYDRIDE

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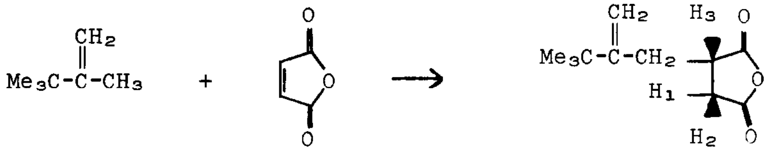
(Received in USA 24 May 1971; received in UK for publication 22 June 1971)

Most workers assume that the simple ene reaction[2] involves a concerted mechanism with the same *syn-syn* stereochemistry as the familiar Diels-Alder reaction. Actually, however, only those stepwise reactions involving initial hydrogen or proton transfer from the ene to the enophile are rigorously eliminated by the complete migration of the double bond of propene-1-C^{14} in the reaction with maleic anhydride.[3] Qualitative transfer of asymmetry from ene to adduct leads to the same general conclusion.[4] Formation of an intermediate biradical or zwitterion by initial carbon-carbon bond formation is not definitely excluded.[5,6] The absence of cyclobutane derivatives as side products[2] and the lack of skeletal rearrangements when β-pinene is used as the ene component[2,7] may simply indicate that these intermediate biradicals or zwitterions prefer to transfer hydrogen to yield the ene product rather than to ring close[8] or rearrange.

Theory predicts that both *syn-syn* and *anti-anti* concerted ene reactions are symmetry preferred.[2] These processes correspond to *cis* and *trans* addition to the enophile component, respectively. Biradical and zwitterionic intermediates similarly do not demand a unique stereochemistry of addition. We have therefore determined the stereochemistry of a simple ene reaction. Deuterium was used to mark the stereochemistry so that any preference for *cis* or *trans* addition cannot be attributed to differences in product stabilities which are reflected in the transition states for hydrogen transfer.

Reaction of 2,3,3-trimethyl-1-butene (1) with maleic anhydride for 18 hr at 210° in xylene solution gives (3,3-dimethyl-2-methylene)-butylsuccinic anhydride (2)[9] in 45% yield. 2,3,3-Trimethyl-1-butene-1,1-d_2-2-methyl-d_3[10,11] is prepared by the sequential reaction of *t*-butylmagnesium bromide[12] with acetone-d_6, followed by dehydration with $POCl_3$/pyridine.[13] Reactions of olefin 1-d_5 with maleic anhydride under a variety of conditions gave extensive intra- and intermolecular deuterium scrambling in recovered olefin 1 and adduct 2. Nmr spectra of the adducts in the multiplet region between δ2.13-3.50 show no recognizable pattern of absorption which reveals the stereochemistry of addition. After several tries, a successful experiment at 200° for 16 hr in a xylene slurry of sodium carbonate gave a useful sample of the deuterated adduct 2.[14]



1 2

The nmr spectrum of deuterated 2 shows a four-peak pattern within the δ2.13-3.50 multiplet which was proved to be an AB quartet by comparison of 60- and 100-Hz nmr spectra. The lower field doublet is assigned to H_3 in structure 2 because of its position and because it is sharper than the broader higher field doublet which must be geminally coupled to deuterium. Computer analysis of the AB quartet gives the values shown in Table 1 and 2. Related data are also shown for comparison. Both the coupling constant and chemical shift data indicate that the higher field doublet of deuterated 2 should be assigned to H_2 in a *cis* relationship to H_3. The deuterium and alkyl components of the ene, therefore, add with *cis* stereochemistry. Because of partial deuterium scrambling, a conservative limit of detectibility for the *trans* deuterated adduct **2** is *ca*. 30%. This work, therefore, establishes that the ene reaction is at least 70% stereoselective. Since there is no definite evidence for the presence of the *trans* isomer, a stereospecific *cis* addition is also permitted by the data.

TABLE 1

CIS AND *TRANS* COUPLING CONSTANTS IN SUCCINIC ANHYDRIDES

Substituent	J_{cis}, Hz	J_{trans}, Hz	DF[a]
HO[b]	8.6	6.8	
Cl[b]	9.0	5.7	
Br[b]	8.7	4.9	
Ph[c]	10.2 ± .2	6.5 ± .2	6
Me[c]	10.3 ± .3	6.6 ± .4	20
Me[d]	11.1 ± .5	5.4 ± .2	1
Deuterated **2**[c]	9.1 ± .8		1

a. Degrees of freedom. b. Ref. 16. c. This work. d. By first-order analysis of the spectrum in the presence of Eu(fod)$_3$ in a 3-fold weight excess in CCl_4(17).

TABLE II

CHEMICAL SHIFTS OF ALKYL SUBSTITUTED SUCCINIC ANHYDRIDES[a]

Substituent	H_1, Hz	H_2, Hz	H_3, Hz
Me	159	190	202
Deuterated **2**	183		198

a. Shifts are downfield from TMS at 60-MHz; see structure **2** for numbering of protons.

In conclusion, the *cis* addition of ene to enophile is consistent with either a concerted *syn*-*syn* pathway or a biradical or zwitterionic intermediate in which *cis* hydrogen transfer is kinetically preferred. In principle, the question of "concerted" versus "stepwise" mechanisms can be answered unambiguously by an extension of these labeling experiments to maleic and fumaric esters in which a stepwise reaction would lead to loss of stereochemistry.

REFERENCES

1. This work is described in the M.S. Thesis of M. Good, University of Rochester, 1971. We are pleased to acknowledge preliminary experiments by Priscilla Byrd and Susan Schneider Soloway.
2. The ene reaction is comprehensively reviewed by H. M. R. Hoffmann, *Angew. Chem.*, *81*, 597 (1969); *Int. Eng. Ed.*, *8*, 556 (1969). Alder-Ene additions to alkynes give *syn* addition, but this result does not give the stereochemistry of a simple ene reaction because of an inherent bias against *anti* addition. In effect, *anti* addition to an alkyne requires a transition state with the characteristics of a *trans* double bond in a six-membered ring. The system described in the present work is free of this bias.
3. B. S. Sublett and N. S. Bowman, *J. Org. Chem.*, *26*, 2594 (1961).
4. R. K. Hill and M. Rabinovitz, *J. Amer. Chem. Soc.*, *86*, 965 (1964).
5. R. T. Arnold and J. F. Dowdall, *ibid.*, *72*, 2950 (1948).
6. J. A. Berson, R. G. Wall and H. D. Perlmutter, *ibid.*, *88*, 187 (1966).
7. G. I. Birnbaum, *Chem. and Ind.*, 1116 (1961).
8. P. D. Bartlett, *Science*, *159*, 833 (1968).
9. Adduct **2**: mp 63-65° (petroleum ether); ir (CCl_4) 3030, 1860, 1780, 1645, 922 cm^{-1}; nmr (CCl_4) δ1.12 (s, 9 H), 2.13-3.50 (m, 5 H) 4.56 (s, 1 H), 5.00 (s, 1 H); *m/e* (75 eV) 196; satisfactory carbon hydrogen analysis.
10. Olefin **1**-d_5: ir (CCl_4) 2275, 2197, 2097, 2036, 1579, 711 cm^{-1}; nmr (CCl_4) δ1.05 (s, 176 units), 1.73 (3), 4.58 (1), 4.65 (1); mass spectrum (75 eV) mol fraction d_4 0.04, d_5 0.93, d_6 0.03.
11. H. C. Brown and C. J. Kim, *J. Amer. Chem. Soc.*, *90*, 2082 (1968).
12. C. N. Pillai and H. Pines, *ibid.*, *83*, 3274 (1961).
13. R. R. Sauers, *ibid.*, *81*, 4873 (1959).
14. Deuterated adduct **2**: mp 63.0-64.5°, mmp with **2**-d_0 63.0-65.0°; ir (CCl_4) 1846, 1771, 1585, 709 cm^{-1}; nmr (CCl_4) δ1.12 (s, 191 units), 2.13-3.50 (m, 41) 4.56 (s, 1), 5.00 (s, 1); mass spectrum (75 eV) mol fraction d_4 0.12, d_5 0.81, d_6 0.06, d_7 0.01. Recovered deuterated olefin **1**: nmr (CCl_4) δ1.05 (s, 182 units), 1.73 (s, 3), 4.58 (s, 1), 4.65 (s, 1). Recovered maleic anhydride contained no deuterium by mass spectral analysis.
15. Laocoon III: A. A. Bothner-By and S. M. Castellano in "Computer Programs for Chemistry," Vol. 1, D. F. DeTar, E., W. A. Benjamin, New York, 1968, p. 10.
16. L. E. Erickson, *J. Amer. Chem. Soc.*, *87*, 1867 (1965).
17. R. E. Rondeau and R. E. Sievers, *ibid.*, *93*, 1522 (1971).