Thermal Isomerization of *cis*- and *trans*-Dimethyl Epoxymethylsuccinate to Dimethyl α-Oxoglutarate

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Summary An unusual rearrangement of the methyl substituted epoxides, *cis*- and *trans*-dimethyl epoxymethylsuccinate, to the straight-chain ketone, dimethyl α-oxoglutarate, is described together with the partially analogous rearrangements of the *cis*- and *trans*-dimethyl 1-methylcyclopropane-1,2-dicarboxylates into dimethyl α-methyleneglutarate and *cis*- and *trans*-dimethyl 1,2-dimethylaziridine-2,3-dicarboxylates into methyl 1-methoxycarbonyl(methyl)acrylate.

TRANSFORMATION of unactivated methyl into more highly functionalized carbon occurs widely in biochemical reactions but is rare in synthetic chemistry, the Barton reaction being one of the few examples known.[1]

We describe a novel rearrangement of methyl substituted epoxy-esters,[2] which results in methyl insertion. When heated at 360° for 2—3 h in a base-washed Pyrex tube sealed *in vacuo*, *cis*- or *trans*-dimethyl epoxymethylsuccinate (I) rearranges to dimethyl α-oxoglutarate (II). Pure dimethyl α-oxoglutarate (20%) was collected by preparative g.l.c.† The lowest temperature at which the rearrangement will take place is 270°.

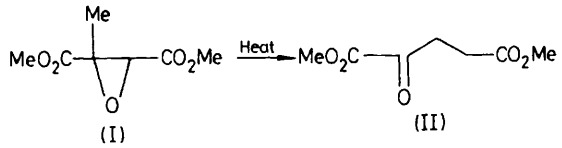
There are two major mechanistic possibilities for this ring opening: (i) direct abstraction of a methyl hydrogen by a methoxycarbonyl group concomitant with ring opening[3] or (ii) prior opening to a carbonyl ylide[4] followed by internal hydrogen transfer.‡ Since heating interconverts the epoxides to a 40:60 *cis–trans* equilibrium mixture and the equilibration occurs more rapidly than the carbon skeleton rearrangement, it is not possible to draw mechanistic conclusions based on the stereochemistry of the starting epoxides.

We have also examined the analogous cyclopropane and aziridine compounds. *trans*-Dimethyl 1-methylcyclopro-

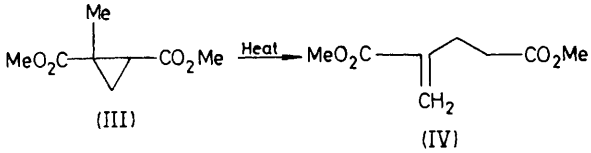
† Yields are calculated on the basis of recovered starting material (*ca.* 40%). In addition to starting material, the reaction mixture contains dimethyl mesaconate and dimethyl citraconate, and small amounts of unidentified products having short retention times.

‡ Both mechanisms lead to an intermediate enol ether $MeO_2CC(:CH_2)OCH_2CO_2Me$. Preliminary studies on a closely related system indicate that such enol ethers rearrange readily by a formal 1,3-shift to the corresponding ketones. At present, the latter appears to be an intermolecular free-radical reaction.

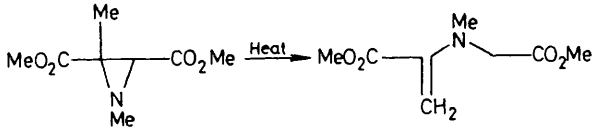
pane-1,2-dicarboxylate (III) rearranges smoothly to dimethyl α-methyleneglutarate (IV) on heating to 300°. The *cis*-isomer reacts more slowly, and, at least in part, by prior



(I) (II)



(III) (IV)



(V) (VI)

isomerization into the *trans*-compound (III), since substantial amounts of *trans*-(III) can be detected by g.l.c. On this basis and in accord with the results of others,[3] we conclude that the cyclopropane opening occurs, in the main, by a cyclic mechanism involving abstraction of hydrogen by the carbonyl group of the ester *cis* to the methyl.

By contrast, not only do the corresponding *cis*- and *trans*-aziridines rearrange under milder conditions (refluxing benzene for 24 h for complete reaction), but the *cis*-dimethyl 1,2-dimethylaziridine-2,3-dicarboxylate (V) rearranges *ca.* 1·5 times faster than its *trans*-isomer. Both give satisfactory first-order plots with $k_{cis} = 2{\cdot}00 \pm 0{\cdot}05 \times 10^{-5}\ s^{-1}$ and $k_{trans} = 1{\cdot}46 \pm 0{\cdot}11 \times 10^{-5}\ s^{-1}$ at 70 °C in benzene. No interconversion between the *cis*- and *trans*-aziridines takes place under these conditions. Clearly, the aziridines behave quite differently from the cyclopropanes and the epoxides; the involvement of the ring nitrogen is very evident in the low temperature required for rearrangement and the slight preference for *cis*- over *trans*-isomer in rate.[5] The difference in rate between the two isomers appears too small to warrant detailed comment yet, but we suggest that the aziridine may open to the 1,3 dipole[4] prior to transfer of hydrogen.

The aziridines differ in an additional respect in that the enamine (VI)§ is formed (85%). Conditions under which the 1,3 migration will take place in the nitrogen series have not yet been found; only decomposition has been observed in attempts to force this reaction.

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§ This structure was proved spectroscopically and by hydrogenation to *N*-methyl-*N*-methoxycarbonylmethylalanine methyl ester, an authentic sample of which was prepared by sequential alkylation of alanine methyl ester with methyl chloroacetate and methyl iodide.

[1] D. H. R. Barton and J. M. Beaton, *J. Amer. Chem. Soc.*, 1961, **83**, 750; M. Akhtar and D. H. R. Barton, *ibid.*, 1962, **84**, 1496; M. Akhtar, *Adv. Photochem.*, 1964, **2**, 263.

[2] P. Dowd and C. S. Nakagawa, *Proc. Nat. Acad. Sci. U.S.A.*, 1972, **69**, 1173; E. Corre and A. Foucaud, *Chem. Comm.*, 1971, 10; see also M. C. Flowers and R. M. Parker, *Internat. J. Chem. Kinetics*, 1971, **3**, 443.

[3] D. E. McGreer, V. W. K. Chin, and R. S. McDaniel, *Proc. Chem. Soc.*, 1964, 415; R. J. Ellis and H. M. Frey, *ibid.*, 1964, 221; G. Ohloff, *Tetrahedron Letters*, 1965, 3795; M. J. Jorgenson and A. F. Thatcher, *ibid.*, 1969, 4651; W. R. Roth and J. Konig, *Annalen*, 1964, **688**, 28; E. J. Corey, H. Yamamoto, D. K. Herron, and K. Achiwa, *J. Amer. Chem. Soc.*, 1970, **92**, 6635.

[4] R. Huisgen, *J. Org. Chem.*, 1968, **33**, 2291; H. Hamberger and R. Huisgen, *Chem. Comm.*, 1971, 1190; W. J. Linn, O. W. Webster, and R. E. Benson, *J. Amer. Chem. Soc.*, 1965, **87**, 3651; A. Robert, J. J. Pomneret, and A. Faucaud, *Compt. rend.*, 1970, **270C**, 1739.

[5] *Cf.* A. Padwa, D. Dean, A. Mazzu, and E. Vega, *J. Amer. Chem. Soc.*, 1973, **95**, 7168.