Simulation of Biological *C*-Ethylation using Sulphoxide Anions as Intermediates

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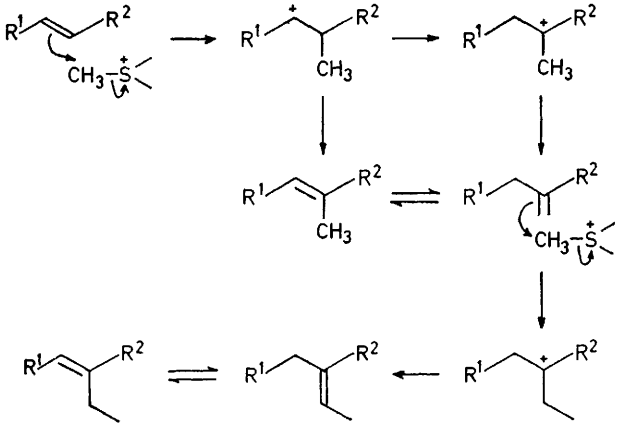
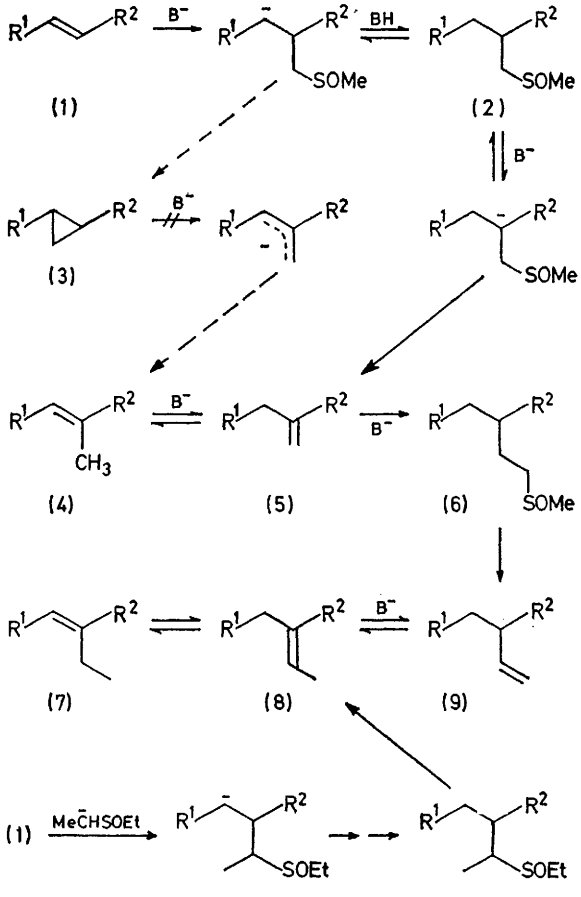
Summary Biological *C*-ethylation of C–C double bonds can be simulated *in vitro* by a double methylation sequence employing dimethyl sulphoxide anion as methyl-transfer reagent.

TRANSFER of the methyl group of L-methionine to unsaturated carbon centres leading to *C*-methyl and *C*-ethyl substituted double bonds has been demonstrated in a number of biological systems.[1] It has been postulated that these processes occur by nucleophilic attack on *S*-adenosylmethionine leading to carbonium ion intermediates which then rearrange as in Scheme 1. Direct *C*-ethylation from ethionine is not thought to be possible. We report here studies of the alkylation of C–C double bonds by sulphoxide anions which illustrate that biological *C*-ethylation can be simulated *in vitro* using dimethyl sulphoxide anion (DMSO⁻) as methyl-transfer reagent.



SCHEME 1

Methylation of (**1b**) by DMSO⁻ has been shown to lead selectively to either (**4b**) or (**4c**).[2] Sulphoxides (**2**) are intermediates in these reactions since authentic (**2b**) and



SCHEME 2

a; $R^1 = R^2 = Ph$
b; $R^1 = Ph$, $R^2 = o\text{-}MeC_6H_4$
c; $R^1 = o\text{-}MeC_6H_4$, $R = Ph$

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(**2c**) each produced (**4b**) and (**4c**) respectively by brief treatment with $DMSO^-$. The cyclopropane (**3**) however, is not implicated in the reaction schemes, since (**3a**) remained unchanged in $DMSO^-$ solution. When sulphoxide (**2c**), m.p. 119—120°; ν_{max} 1039 cm^{-1}; τ 2·78—3·1 (9H), 6·8—7·2 (5H), 7·63 (SOMe), and 7·8 (:C*Me*), was treated with $DMSO^-$ for long periods, a different sulphoxide was produced (*ca.* 70%) [ν_{max} 1040 cm^{-1}; τ 2·8—3·1 (9H), 7·1 (3H), 7·5—8·0 (4H), 7·7 (SOMe), and 7·82 (:CMe)] consistent with the homologue (**6c**). The same sulphoxide was also produced (*ca.* 75%) when both (**4c**) and (**5c**) were treated with $DMSO^-$ and is therefore probably formed from (**2c**) as outlined in Scheme 2. Thermal elimination of sulphinic acid from (**6c**) produced the butene (**9c**) (*ca.* 60%), ν_{max} 990 and 910 cm^{-1}, τ 2·7—3·1 (9H), 3·98 (ddd, *J* 9, 10, and 17 Hz, CH·C*H*:CH_2), 5·02 (1H), 5·10 (1H), 6·48 (dt, *J ca.* 9 Hz), 7·2 (2H), and 7·8 (Me Ar), which was smoothly isomerised in $DMSO^-$ to a *Z*–*E* mixture of hydrocarbons (**7c**) and (**8c**). In another series, both (**1a**) and (**4a**) similarly produced a *Z*–*E* mixture of (**7a**) and (**8a**) following treatment with $DMSO^-$ (to **6a**), thermal elimination of sulphinic acid (to **9a**), and isomerisation.

These studies thus demonstrated that transformation of (**1**) into (**7**) and (**8**) can be achieved by a double methylation sequence (see Scheme 2) employing $DMSO^-$ as methyltransfer reagent, and in this respect provide an interesting laboratory mimic of *in vivo* *C*-ethylation *via* methionine. Although methionine *S*-oxide has been found in higher plants where transfer of the methyl group of methionine has been demonstrated,[3] the anion from methionine *S*-oxide (or ylides formed from methionine sulphonium salts) is not considered to take part in *in vivo* *C*-alkylation processes.

As a corollary to these studies, *direct* *C*-ethylation of (**1**) to (**7**) and (**8**) *via* sulphoxide anion intermediates was demonstrated by reaction of (**1a**) with the anion from diethyl sulphoxide; this produced (*ca.* 45%) a similar proportion of *Z*–*E*-isomers of (**7a**) and (**8a**) to that obtained from isomerisation of (**9a**).

The *Z*- and *E*-isomers of (**7a**,**c**) and (**8a**,**c**) were separated by g.l.c. and unambiguously characterised by spectral comparison with authentic materials obtained by independent routes.

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[1] For review see E. Lederer, *Quart. Rev.*, 1969, **23**, 453.
[2] B. G. James and G. Pattenden, *Chem. Comm.*, 1971, 1015.
[3] W. E. Spittstoesser and M. Mazelis, *Phytochemistry*, 1967, **6**, 39.