Intramolecular Opening of an Activated Vinylcyclopropane: an Entry to the Bicyclo[3,3,0]octenone Series

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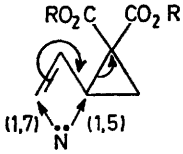
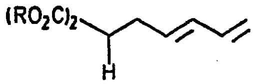
Summary Intramolecular 1,7-attack, geometric isomerization, and intramolecular homoconjugate addition have been observed for an activated vinylcyclopropane bearing an internal centre of nucleophilicity.

Diethyl 2-vinylcyclopropane-1,1-dicarboxylate undergoes intermolecular nucleophilic attack *via* S_N2 displacement[1] either exclusively (amines, RS^- in EtOH) or with very strong preference (malonate ion or RS^- in dimethoxyethane) in a 1,5-sense. [2a,b,3] Free-radical-induced openings occur in a 1,7-sense,[2] cuprate additions which may involve free radicals,[4] also occur in a 1,7-sense[5] and, finally, enamines react at *ca.* 190 °C in a 1,7 fashion,[6] but this may reflect prior opening of (**1**) to a dipolar form[1,7] followed by capture at the terminus of the allylic system. Alternatively, the product which appears to arise from 1,7-attack by carbon may, in fact, be the consequence of 1,5-attack by nitrogen followed by Cope-type rearrangement of the *N*-allylenammonium salt. Thus, none of these studies demonstrates unambiguously the feasibility of 1,7-attack in a purely nucleophilic sense. We describe here an intramolecular example of an apparent nucleophilic 1,7-attack under very mild conditions.

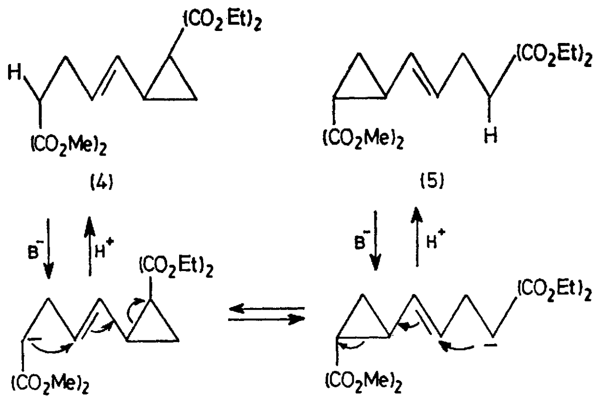
Compounds (**2**) and (**3**) were prepared by the alkylation of dimethyl and diethyl malonate with the known[8] *trans*-5-chloropenta-1,3-diene. Compounds (**4**)† (62%) and (**5**)† (70% yield) were obtained, respectively, from the copper-induced reactions of (**2**) with diethyl diazomalonate[9] and (**3**) with dimethyl diazomalonate. Similarly, the tetramethyl ester (**6**)† was obtained from the reaction of (**2**) with dimethyl diazomalonate.



(**1**)



(**2**) R = Me
(**3**) R = Et



(**4a**) (**5a**)

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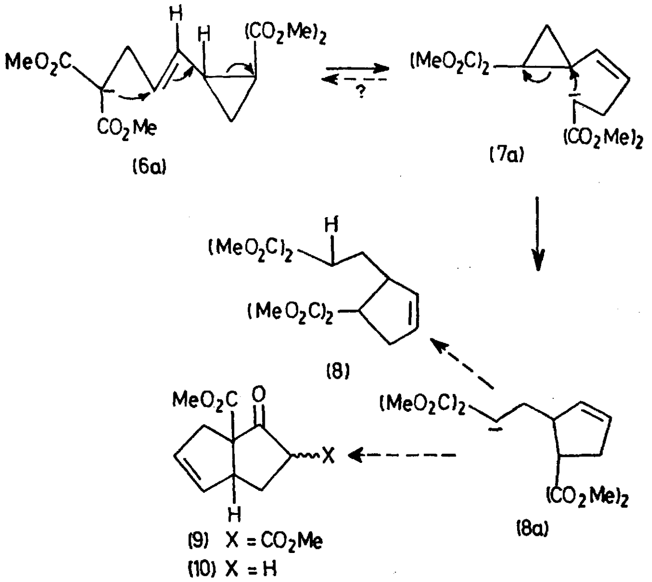
† C and H combustion analysis within 0·4% of theory as well as confirmatory i.r. n.m.r., and mass spectra were obtained for this compound.

Deprotonation of either (**4**) or (**5**) with dimsylsodium[10]–Me_2SO at room temperature resulted in a yellow solution. Upon quenching after times as short as 5 min, a mixture[‡] of (**4**) and (**5**) was obtained. Compounds (**4**) and (**5**) differ in the chemical shifts of the triplets of the 'malonyl-type' methine proton; for (**4**) τ (CCl_4) = 6·76 while for (**5**) τ (CCl_4) 6·78. A similar trend for the chemical shifts of 'malonyl' protons as a function of the alkyl group of the ester has already been noted.[11] At 250 MHz, these two triplets, separated by 5 Hz, are easily discerned in a mixture of (**4**) and (**5**). As a check on the n.m.r. analysis, mixtures of (**4**) and (**5**) produced through deprotonation and acidification were ozonized at −78 °C (CH_2Cl_2). Reductive workup (Zn–AcOH) gave a four-component mixture of dimethyl and diethyl (formylmethyl)malonate, and dimethyl and diethyl 2-formylcyclopropane-1,1-dicarboxylate, which was quantitatively analysed by g.l.p. Clearly, the mechanism of isomerization involves intramolecular 1,7-attack in a nucleophilic sense. These transformations appear to be convincing demonstrations of the concerted S_N2 type reactions,[12] though other formulations may be possible.



In the reactions of (**4a**) and (**5a**) at higher temperatures, n.m.r. analysis showed that more fundamental changes were taking place. These could be studied more easily with the tetramethyl ester (**6**). Heating compound (**6**) with dimsylsodium–Me_2SO at 50 °C for 2 h followed by quenching gave a 58% yield of the cyclopentene tetraester (**8**).† Catalytic reduction (10% Pd–C–MeOH) gave its known[13] saturated derivative.

The pathway from (**6a**) to (**8a**) must involve the intermediacy of the *cis*-isomer (**7a**). This presumably arises by intramolecular 1,7-attack on a higher energy conformer (see **6a**) in which the vicinal methine and vinylic protons are arranged in a '*s-cis*' fashion

When compound (**6**) was treated with dimsylsodium–Me_2SO at 90° for 21 h, a 71% yield of the epimeric enedi-esters (**9**) was obtained. This mixture was converted into the single compound (**10**)† by selective hydrolysis–decarboxylation (1% HCl–EtOH–H_2O, reflux). The pathway from (**8a**) to (**9**) involving Dieckmann reaction followed by demethoxycarbonylation, is well precedented.[13]

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[‡] Average ratio (**4**) : (**5**) = 2·1 : 1. The range of this ratio in 9 runs starting with either compound was 1 : 1—3·1 : 1. In no run was the ratio of (**4**) : (**5**) >1. Presumably these results arise because our experimental procedure (stability to hydrolysis, slight chromatographic separation, etc.) distorts the ratio in some way. No such deviation from unity was noted in a related previous study.[11]

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