1,2-Carbonyl Migration along the Allylic Framework: Synthesis of Alkenylnaphthoquinones

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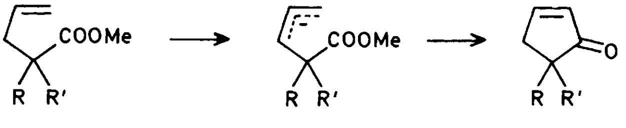
Instead of undergoing a cyclopentenone annulation, the allylmalonate anion derived from the dicarboxylate (**7**) rearranges to vinylsuccinate (**5**), an application of which has led to a convenient synthesis of vinylnaphthoquinones (**10**).

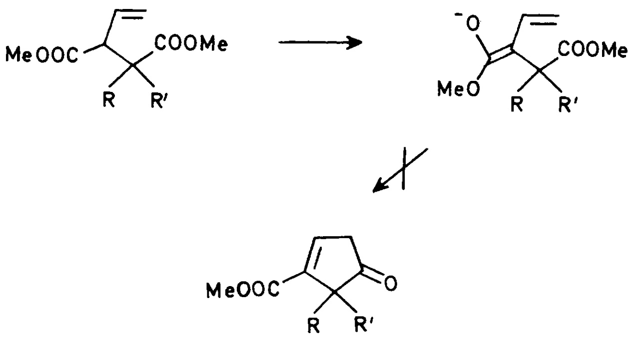
Base catalysed cyclisation of allylic esters to yield cyclopentenones (Scheme 1) has been used as the key step in the synthesis of various α-methylene cyclopentenones, including the antibiotics methylenomycin B and sarkomycin.[1,2] The method is easy to manipulate and affords high yields of products.[3] Further study of the nature and scope of reaction has revealed a significant feature of the cyclisation, *i.e.*, attachment of an ester group to the α-position of the allylic function results in inhibition of the process (Scheme 2),[4] possibly due to unfavourable strain in the transition state.

Here we investigate the course of the reaction with other diesters, in particular that derived from Meldrum's acid, which, unlike the open-chain monoester in Scheme 1, presents a restricted geometry where both ester carbonyl groups are locked in a ring.

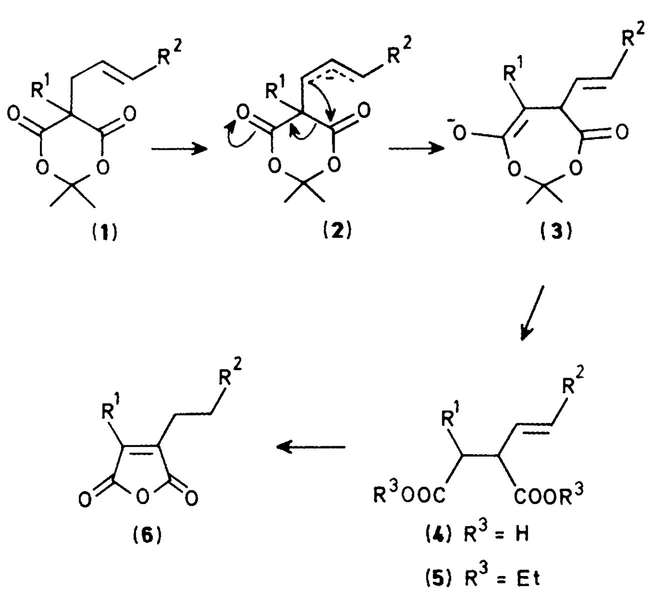
Compounds (**1a**—**f**) were prepared by direct allylation of commercially available Meldrum's acid and subjected to cyclisation [lithium di-isopropylamide (LDA), THF/tetramethylethylenediamine (TMEDA), 0°, 3 h]. After conventional saturated aqueous ammonium chloride work-up, saturated succinic acids (**4**) (identified as their ethyl esters) were obtained. Thus (**1a**—**f**) yielded (**5a**—**f**) respectively as 1:1 mixtures of two separable but unassigned stereoisomers (silica gel; 5% ethyl acetate in hexane) in low overall yields (32—46%). The possibility of incomplete product recovery during work-up was subsequently eliminated using a modified procedure. Acidification of the reaction mixture with 10% aqueous hydrochloric acid followed by evaporation to dryness, then bulb to bulb distillation (bath temp. 150 °C; 0.1 mmHg), afforded pure disubstituted maleic anhydrides



Scheme 1. R = alkyl, R' = aryl.

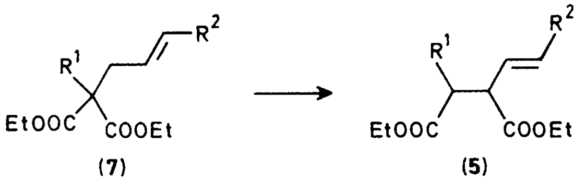


Scheme 2



a; R^1 = Me, R^2 = H
b; R^1 = R^2 = Me
c; R^1 = Me, R^2 = Ph
d; R^1 = Ph, R^2 = H
e; R^1 = Ph, R^2 = Me
f; R^1 = R^2 = Ph

Scheme 3



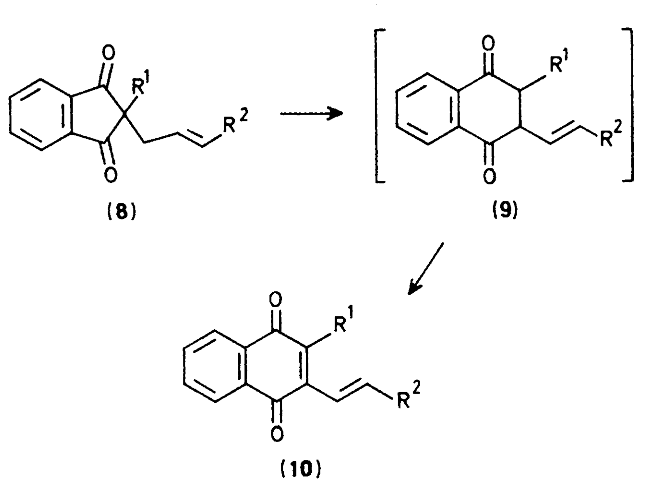
	% of (**5**)
a; R^1 = Me, R^2 = H	71
b; R^1 = R^2 = Me	73
c; R^1 = Me, R^2 = Ph	65
d; R^1 = Ph, R^2 = H	65
e; R^1 = Ph, R^2 = Me	78
f; R^1 = R^2 = Ph	83

Scheme 4

(**6a**—**f**) in 69, 66, 73, 75, 69, and 64% yields respectively. Again, these compounds were converted to the corresponding diethyl maleate derivatives for additional characterization.

Formation of the diacids indicates that the reaction path is different from that observed in Scheme 1. It appears that the allyl anion (**2**) undergoes intramolecular 1,2-carbonyl migration, which can be rationalized in terms of attack of the ester carbonyl by the anion at the latter's α-carbon, followed by C–C bond cleavage to result in ester enolate (**3**), and finally, upon work-up, acid (**4**). Subsequent transformation in which (**4**) condenses with migration of the double bond to yield the stable anhydride (**6**) takes place during distillation and is not unusual (Scheme 3).

It turns out that this 1,2-carbonyl migration along the allylic framework is not restricted to cyclic diesters but proceeds also with the open-chain analogues. The reaction, therefore, has good potential in organic synthesis. For example, under the above reaction conditions substituted allylmalonic esters (**7**) yield succinic esters (**5**) in moderate to good yields (Scheme 4).†



	% of (**10**)
a; R^1 = Et, R^2 = Ph	26
b; R^1 = R^2 = Ph	65
c; R^1 = 4-OMe-C_6H_4, R^2 = Ph	45
d; R^1 = 4-Cl-C_6H_4, R^2 = Ph	51
e; R^1 = CH_2Ph, R^2 = Ph	41

Scheme 5

Application of this rearrangement is exemplified in the following synthesis of naphthoquinones. Readily available[5] indane-1,3-diones (**8**) are easily converted to (**9**) which, upon work-up, are further air-oxidized to give vinylnaphthoquinones (**10**) (Scheme 5).[6] It should be mentioned that acyl migration to the benzylic position is not observed in the case of (**8e**), and that yields drop sharply when R^1 is not an aryl group.

Although reaction yields are not exceptionally high, the ready availability of starting materials and the simple experimental procedures involved make this 1,2-acyl migration along the allylic framework a very attractive way to construct many otherwise difficult-to-prepare compounds.

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References

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6 This type of ring expansion has already been observed when $-CH_2CO_2CH_2Me$ is the substituent instead of the allyl group in (**8**), *cf.* C. F. Koelsch and D. J. Byers, *J. Am. Chem. Soc.*, 1940, **62**, 560. Quinones (**10**) were reductively-acetylated (Zn—AcOH) for further identification.

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† In the same manner as they were obtained from the reaction of (**1**), compounds (**5**) were here obtained as mixtures of equal amounts of two separable diastereoisomers, to which no attempt was made to assign the stereochemistry. All compounds described gave satisfactory spectroscopic data as well as elemental analyses. All yields indicated are isolated yields.