The Intramolecular Diels–Alder Reaction with Allenic Ester Dienophiles

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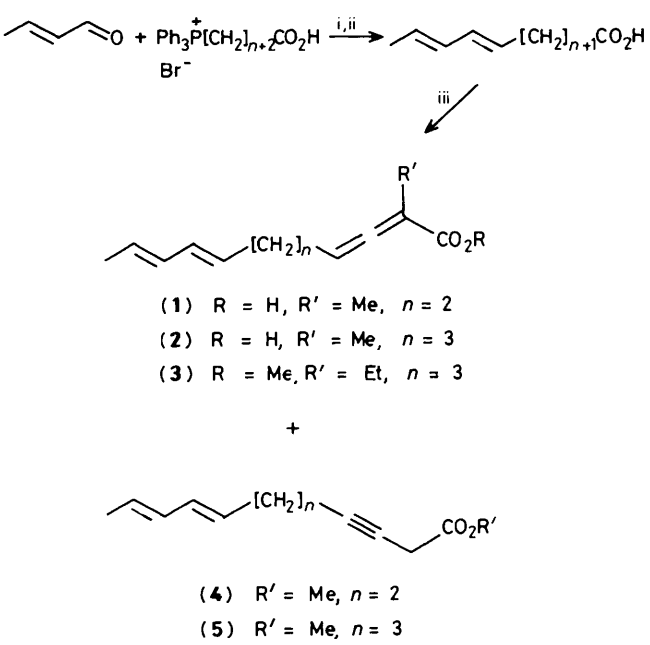
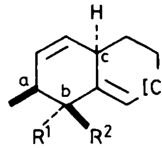
Methyl (*E,E*)-dodeca-2,3,8,10-tetraenoate and (*E,E*)-undeca-2,3,7,9-tetraenoate have been prepared and shown to undergo intramolecular Diels-Alder reactions, the latter spontaneously at ambient temperature.

The intramolecular Diels–Alder reaction has been extensively developed over the past 15 years and shown to be a powerful method for stereocontrolled synthesis.[1] Although α,β-unsaturated esters have been widely used as dienophiles in the intramolecular reaction, allenic esters have not (to our knowledge) been so used, though they do undergo intermolecular Diels–Alder reactions.[2] It seemed that the allenic esters might offer some advantages, not least being the potential of using pure enantiomers.

The allenic esters were prepared as shown in Scheme 1. Wittig condensation of the appropriate phosphorane with but-2-enal gave a mixture of diene acids which was isomerised



Scheme 1. i, Bu^nLi/Me_2SO; ii, I_2/CCl_4; iii, $(COCl)_2$, then Ph_3PCRCO_2R'/Et_3N.



(6) $n = 0$, $R^1 = CO_2Me$, $R^2 = H$
(7) $n = 0$, $R^1 = H$, $R^2 = CO_2Me$
(8) $n = 1$, $R^1 = CO_2Me$, $R^2 = H$
(9) $n = 1$, $R^1 = H$, $R^2 = CO_2Me$
(10) $n = 1$, $R^1 = CO_2Et$, $R^2 = Me$
(11) $n = 1$, $R^1 = Me$, $R^1 = CO_2Et$

with I_2/CCl_4 to give predominantly the (*E*,*E*)-diene acid. The acids were converted into the allenes using the Lang–Hansen procedure.[3] In the case of the undecatetraenoate (**1**) the compound could be detected after a short reaction time, but a longer exposure led to the Diels–Alder reaction products (**6**) and (**7**) and the alkyne (**4**). The major product, δ_H 6.07 (1H, m), 5.66 (2H, m), 3.72 (3H, s), 3.53 (1H, m), 3.15 (1H, m), 2.78 (1H, m), 2.40 (2H, m), 2.16 (1H, m), 1.34 (1H, m), and 0.87 (3H, d, *J* 6.5 Hz), was shown to be the *endo*-isomer (**7**) by decoupling to establish that H_a, H_b, and H_c resonated at δ_H 2.78, 3.53, and 3.15, respectively, with $J(H_a,H_b)$ 6 Hz, followed by the demonstration of the nuclear Overhauser effects summarised in Figure 1. The *exo*-isomer (**6**) showed δ_H 6.69 (1H, m), 6.64 (1H, m), 6.59 (1H, ddd, *J* 10, 5, and 2 Hz), 3.66 (3H, s), 3.25 (1H, m), 3.20 (1H, s), 2.84 (1H, m), 2.38 (2H, m), 2.23 (1H, m), 1.39 (1H, m), and 0.97 (3H, d, *J* 7 Hz), and $J(H_a,H_b)$ was shown by decoupling to be *ca.* 0 Hz. Both isomers were equilibrated to a 78 : 22 *exo* : *endo* mixture with 1,8-diazabicyclo[5.4.0]undec-7-ene/CH_2Cl_2, and a mixture of the same composition was obtained from the alkyne under these conditions, presumably by isomerisation of the alkyne to allene, Diels–Alder reaction, and further isomerisation.

Table 1. Cyclisation reactions.[a]

Compound	Conditions	Yield (%)	*exo* : *endo*[b]
(1)	T	49	27 : 73
(2)	T	87	65 : 35
(2)	L	65	13 : 87
(3)	T	83	66 : 34
(3)	L	49	13 : 87

[a] Conditions: T PhMe, 111 °C; L Et_2AlCl/CH_2Cl_2, 0 °C. Yields are of isolated material. [b] Determined by capillary g.l.c.

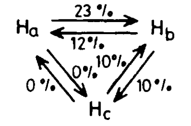


Figure 1. Nuclear Overhauser enhancements in (**7**).

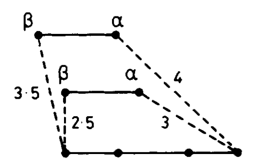


Figure 2. Diene–dienophile distances (Å).

Methyl dodeca-2,3,8,10-tetraenoate (75%) (**2**) was prepared as in Scheme 1 and was accompanied by the isomeric alkyne (**5**). The provenance of the alkyne is likely to be the 82 : 18 equilibrium between the allene (**2**) and the alkyne (**5**) established in the presence of Et_3N/CH_2Cl_2. On heating in PhMe the allene is rapidly converted into the *exo*-adduct (**9**), δ_H 5.62 (1H, m), 5.55 (1H, m), 5.46 (1H, dd, *J* 9 and 2.5 Hz), 3.63 (3H, s), 2.88 (1H, s), 2.82 (1H, m), 2.75 (1H, m), 2.06 (2H, m), 1.80 (1H, m), 1.76 (1H, m), 1.59 (1H, m), 1.07 (1H, m), and 0.94 (3H, d, *J* 7 Hz), and the *endo*-adduct (**8**), δ_H 5.70 (2H, m), 5.43 (1H, dd, *J* 10 and 2.6 Hz), 3.67 (3H, s), 3.40 (1H, m), 2.76 (1H, m), 2.60 (1H, m), 2.06 (2H, m), 1.88 (1H, m), 1.74 (1H, m), 1.50 (1H, m), 1.13 (1H, m), and 0.98 (3H, d, *J* 6 Hz). In the *exo*-isomer $J(H_a,H_b)$ was *ca.* 0 Hz and in the *endo*-isomer 5 Hz. The results of Et_2AlCl-catalysed cyclisation together with the thermal and Lewis acid catalysed cyclisation of methyl 2-methyldodeca-2,3,8,10-tetraenoate [to (**10**) and (**11**)] are summarised in Table 1.

The Roush group[4] have carried out extensive work on the intramolecular Diels–Alder reaction using α,β-unsaturated esters as dienophiles: their results show that *trans*-perhydroindans and *cis*-decalins are preferentially formed from deca-2,7,9-trienoates and undeca-2,8,10-trienoates, respectively; the *endo*- or *exo*-orientation of the ester group is not of prime importance in thermal reactions. It was convincingly postulated that the stereochemical outcome of reaction was dominated by conformational effects in the saturated ring being formed. The *endo* : *exo* ratios observed by us are remarkably similar to those reported for the analogous α,β-unsaturated esters, though the reactions occur at significantly lower temperatures. It is unlikely that a variant of the Roush proposal can explain our results, since the same ring system is being formed for each isomer and would require the methoxycarbonyl group to influence the transition state conformation of the bridging atoms; there appears to be no convincing rationale for this and the transition state conformations of the bridging atoms may well be the same in the *endo* and the *exo* reactions.

From Drieding molecular models it is apparent that the conventional overlap model for the Diels–Alder reaction cannot be attained in either ester. It is instructive to examine the conformations when the reacting π-bonds are parallel (Figure 2). In the undecatetraenoate (**1**) both α and β C–C distances are well within the distance for bonding and rehybridisation,† whereas in the dodecatetraenoate (**2**) the β C–C distance is about the van der Waals distance and the α beyond that. Although it is not possible to propose accurate trajectories for the reactions it is clear that whatever they are the β interaction must predominate initially and that the α interaction will be more effective in (**1**) than in (**2**) or (**3**) at distances leading to the transition state.

From these results it appears that the use of an allenic ester instead of an α,β-unsaturated ester can offer certain advantages. It is notable that, in the α-methylated compound (**3**), Lewis acid catalysis is successful with the allenyl compound but not with the alkene, though Marshall[5] has shown that replacement of the ester with an aldehyde function does lead to successful reaction.

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† The van der Waals distance for the π-bond is *ca.* 1.7 Å and the transition state bond length calculated for the symmetrical Diels–Alder reaction is 2.2 Å.[6]

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