INTRAMOLECULAR CYCLOADDITION OF ALLENECARBOXYLATE. AN EFFECT OF ORBITAL OVERLAP REQUIREMENT OF THE ESTER LINKAGE

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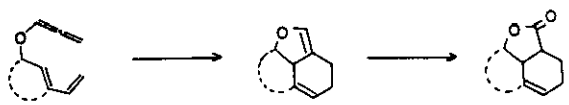
Abstract - The intramolecular cyclizations of the allenecarboxylates have been examined and two types of the cycloadditions are observed. The periselectivity in these reactions was discussed on the basis of the effect of orbital overlap requirements of the ester linkage in the transition state.

Previously, we have demonstrated a new approach of the stereocontrolled syntheses of tricyclic lactones via allenyl ether intramolecular cycloaddition followed by hydration and oxidation of the resulting adducts as outlined in Scheme 1.

Scheme 1

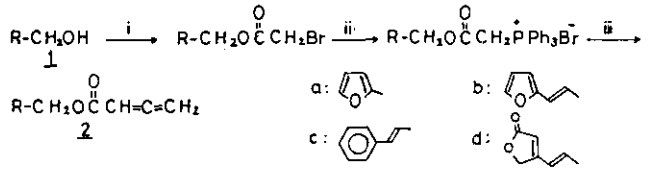


This unique lactone synthesis has been characterized by a very facile and stereospecific formation of polycyclic ring system under the mild reaction conditions and bears a potentially utility for the synthesis of the basic skeletons of some naturally occurring terpenes possessing lactone moiety.[1]

On the other hand, incorporation of an ester linkage into the chain often has an adverse effect on the intramolecular Diels-Alder reaction. In some cases, the intramolecular cyclizations of the esters are reported to be unsuccessful.[2] In continuation of our work on the chemistry of allene, we have investigated the intramolecular cycloaddition of the allenecarboxylates. It was now found that the allene esters undergo the intramolecular cycloadditions of [4+2]- and/or [2+2] type manner, which are strongly affected by the conformational differences of the substrates in the transition state.

The required allenecarboxylates (2a-d) for the thermal reaction were prepared from readily available alcohols (1a-d) by the following three steps. Acetylation by bromoacetyl bromide, preparation of Wittig reagent(Ph_3P) and allenylation by acetyl chloride-Et_3N afforded the corresponding esters (2a-d) in moderate yield.

Scheme 2



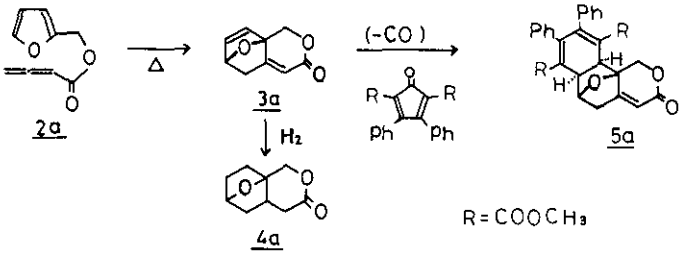
i $BrCH_2COBr$, Et_3N in CH_2Cl_2 at 0°C

ii PPh_3 in benzene, room temp.

iii $2Et_3N$, CH_3COCl in CH_2Cl_2 at 0°C → room temp.

A solution of the allene (2a) (440 mg, 2.68 mmol) in o-xylene (70 ml) was heated at 150°C for 13 h. After removal of the solvent, the residue was purified by column chromatography on silica gel with hexane-ethyl acetate (4:1) as an eluent to afford the cycloadduct (3a) as colorless crystals (mp 64-65°C, 68%). The structural assignment of compound (3a) was accomplished by the spectral inspection. The mass spectrum displayed a molecular ion peak at m/z 164. The ^{1}H-nmr spectrum showed two kinds of methylene protons at δ 4.85 (1H, d, J=10 Hz) and 4.6 (1H, d, J=10 Hz), and 2.79 (1H, m) and 2.24 (1H, dd, J=16 and 2 Hz) as each AB pattern, the methine proton at δ 5.2 (1H, m), and the three olefinic protons at δ 6.53 (2H, m) and 5.85 (1H, m). These assignments were fully confirmed by spin-decoupling experiments. Thus these spectral features were compatible with the [4+2] adduct. Compound (3a) was confirmatively converted to the tetrahydro derivative (4a) (H_2, 10% Pd-C, THF; 90%) as well as to the cycloadduct (5a).

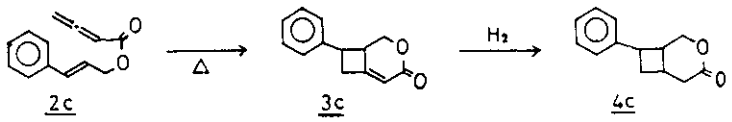
Scheme 3



Similar treatment of (2c) afforded the cycloadduct (3c) as colorless oil (51%). The mass spectrum displayed a molecular ion peak at m/z 200. The ^{1}H-nmr spectrum showed the aromatic protons at δ 7.26 (5H, m) and the olefinic proton

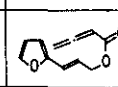
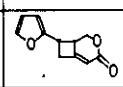
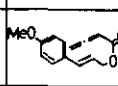
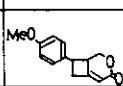
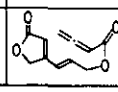
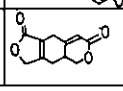
at δ 5.78 (1H, m). The ^{13}C-nmr spectrum exhibited two signals for methylene carbons at δ 72 and 39, and two signals for methin carbons at δ 45 and 42. These spectral features were compatible with the [2+2] adduct. Furthermore, compound (3c) was converted to the dihydro derivative (4c) as colorless needles (mp 58-60°C , H_2, 10% Pd-C , THF , 87%). Table 1 summarizes the results with other heterocyclic compounds.

Scheme 4



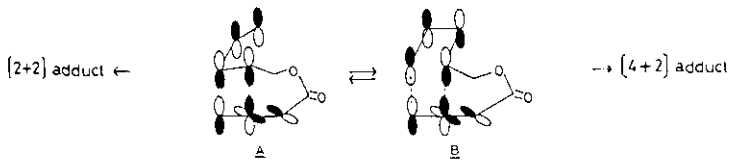
2c 3c 4c

Table 1

Comp. No.	Substrate	Condition	Product	Yield	^{a}c-nmr -CH-,-CH$_2$-,-CH$_3$
2b		Xylene 150°C 6 h		24%	69(t) 29(t) 42(d) 40(d)
2d		Xylene 150°C 22 h		50%	72(t) 39(t) 46(d) 41(d) 55(q)
2e		Xylene 150°C 20 h		25%	71(t) 69(t) 28(t) 27(t) 32(d)

From the experimental results, it is suggested that the allene ester linkage with one methylene into chain is in existence of two possible conformational isomers in transition state as illustrated in Scheme 5.

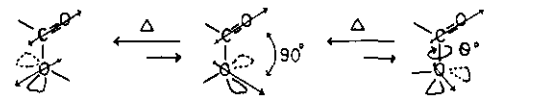
Scheme 5



A B

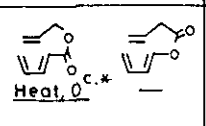
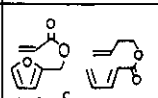
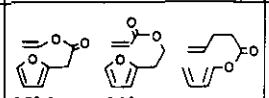
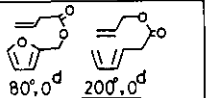
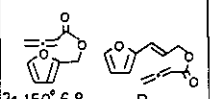
In this connection, the reduced reactivity for the intramolecular cycloaddition of ester has been attributed to preference for the transoid form and a relatively high barrier for interconversion of the two rotamers, or, in some cases, loss of ester resonance in the transition state.[3] Furthermore, it is to be noted that the twist angle of the dipole in the ester group nearly corresponds with the grade of possibility to cyclize as illustrated in Scheme 6.

Scheme 6



When the twist angle extends, the reactivity is seemed to be reduced by degree. An examination of stereomodels of the various ester compounds supports this assumption for the intramolecular cyclization as shown in Table 2, and the successful examples are few known in some cases.[3,4] In fact, the [2+2] adducts were obtained in spite of thermally disadvantage.

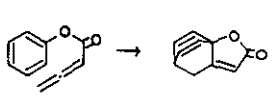
Table 2 The Intramolecular Cyclization of the Ester Compounds

θ[a]	0 − 15°	15 − 30°	30 − 45°	> 45°
	Heat, 0[c,*] —  A, 150°, 24 2f, 150°, 63	 80°, 0[c] Heat, 0	 25°, 0 80°, 0 —	 80°, 0[d] 200°, 0[d]  2a, 150°, 68 B

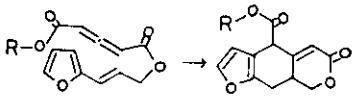
a : The twist angle of the C-O bond by inspection of molecular model.
b : A dash (-) in the column listing the reaction condition (°C) and yields (%). A zero (0) means that the reaction did not proceed under the condition listed.
c : A second activating group could be necessary. [3,4]
d : Failure to cyclize even if a second group activated. [3,4]
* : Efficient intramolecular Diels-Alder reaction of 2-pyrones was reported. M.Noguchi, S.Kakimoto, H.Kawakami, and S.Kajigaeshi, Heterocycles, 1985, 23, 1085.

Thus, the conformational isomer [A] is more advantage than [B]. However, this geometrical advantage could not make the allene esters to proceed the [2+2] cycloaddition beyond the aromaticity of furan. Interestingly, the thermolysis of aryl allencarboxylate (2f) has recently reported to afford the [4+2] adduct in a good yield.[5] On the other hand, the analogous allene diester (2g) was reported to give the [4+2] adducts in poor yield (5%) and a lot of polymer was obtained.[6]

Scheme 7



2f



2g

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