COMPETITIVE ELECTROCYCLIC REACTION OF o-QUINODIMETHANE: SEQUENTIAL ELECTROCYCLIC-DOUBLE[3,3]SIGMATROPIC REACTIONS FOR THE CONSTRUCTION OF 4-ALKYLIDENEISOCHROMAN-3-ONES

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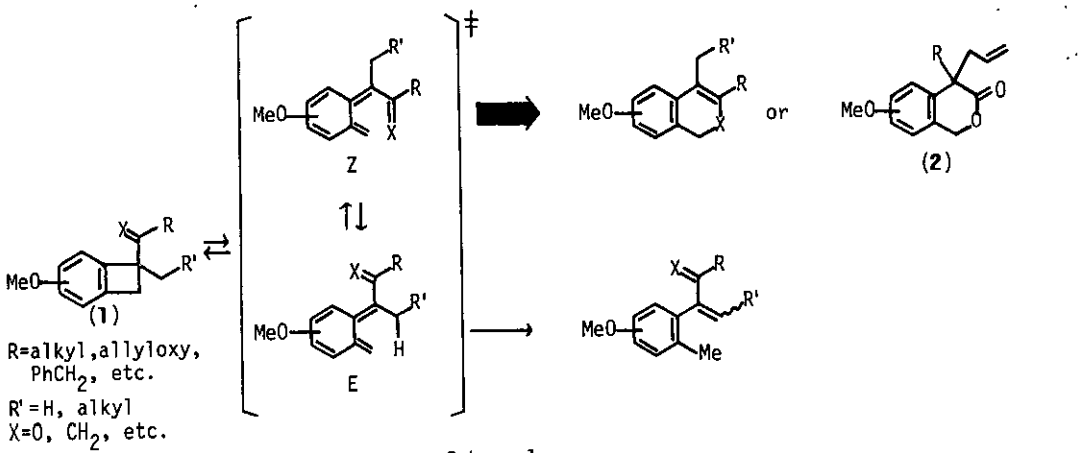
Abstract — Thermolysis of allyl 1-alkenylbenzocyclobutenyl-1-carboxylate (**5a-f**) produced a mixture of 4,4-disubstituted isochroman-3-ones (**6a-f**), dihydronaphthalenes (**8a-f**), and 4-alkylideneisochroman-3-ones (**7a-f**) in good yield. The third product (**7a-f**) was generated via an unprecedented sequential electrocyclic-double[3,3]sigmatropic reactions of Z-o-quinodimethane.

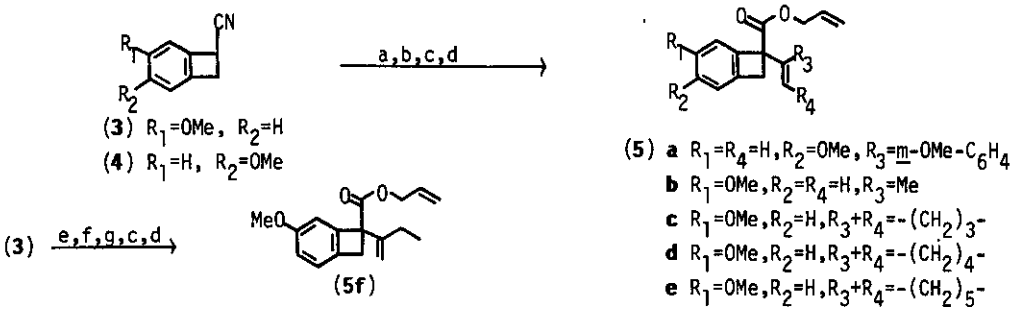
In our earlier work[1], we showed the preferential electrocyclic process through Z-o-quinodimethane, generated in situ by the thermolysis of benzocyclobutenes (**1**), over [1,5]sigmatropic process through E-transition state in the competitive reaction, as illustrated in Scheme 1. Particularly, the thermolysis of allyl 1-alkylbenzocyclobutenyl-1-carboxylate has been led to the exclusive formation of 4-alkyl-4-allylisochroman-3-one (**2**).[1b] We now report the results of two competitive



Scheme 1

electrocyclic reactions during the thermolysis of allyl 1-alkenylbenzocyclobutenyl-1-carboxylates (**5a-f**), in which an unprecedented sequential electrocyclic-double[3,3]sigmatropic reaction is included.

The substrates (5a-f) used in this study were easily prepared by combination of standard procedures starting from the 1-cyanobenzocyclobutenes (3)[2] and (4)[3], as shown in Scheme 2.



Reagents: a, LDA, HMPA, $R_3COCH_2R_4$; b, $SOCl_2$, pyridine or Burgess reagent; c, KOH, aq.EtOH; d, allyl alcohol, DCC, 4-DMAP; e, LDA, HMPA, EtCHO; f, $(COCl)_2$, DMSO, NEt_3; g, $Ph_3P{=}CH_2$.

Scheme 2

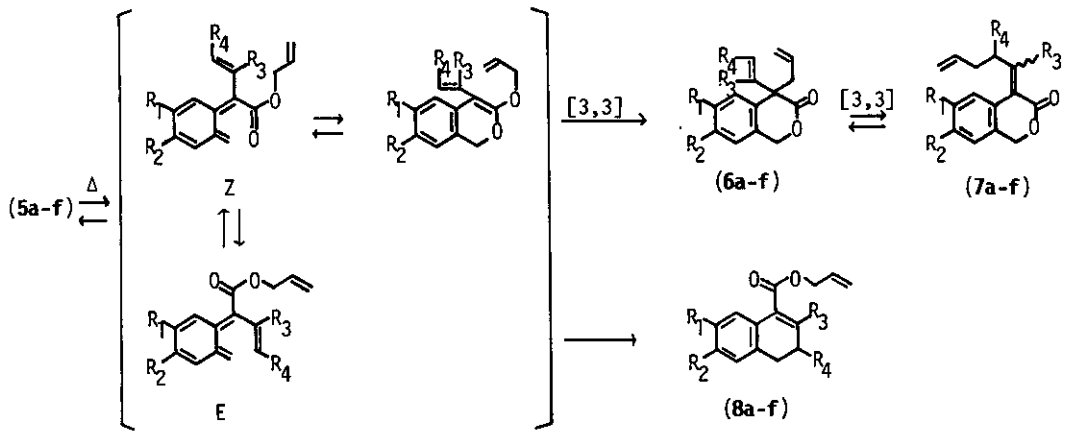
The thermolysis of a solution of the benzocyclobutenes (5a-f) in o-dichlorobenzene at 180°C for 20 min proceeded cleanly, and very high yield of the products could generally be obtained as a chromatographically easily separable mixture of three isomers. The first product thus obtained was 1-allyloxycarbonyl-3,4-dihydronaphthalenes (8a-f), produced through E-o-quinodimethane, and the second one, the major product except for (5c)[4] (Entry 4), was 4-alkenyl-4-allylisochroman-3-ones (6a-f) which might be formed by the tandem electrocyclic-[3,3]sigmatropic reaction[1b] of Z-o-quinodimethane. The third one with the smallest Rf value could be determined on the basis of the ^{1}H-nmrdata as 4-alkylidneisochroman-3-ones (7a-f), an inseparable mixture of two geometrical isomers except for (7a)[5], which would be generated from the Cope rearrangement of (6a-f). (Scheme 3) The results of the thermolysis are presented in Table 1. The validity of the triply sequential

Table 1. Thermolysis of the benzocyclobutenes (5a-f)

Entry	Substrate	% Yield (6)	% Yield (7)	% Yield (8)	Isomeric purity of (7)	Ratio of the Contribution for Z and E
1	(5a)	50	13	24	E	2.6 : 1
2*	(5a)	9	36	15	E	3.0 : 1
3	(5b)	63	11	26	mixt.	2.8 : 1
4	(5c)	20	3	64	mixt.	1 : 2.8
5	(5d)	57	2	34	mixt.	1.7 : 1
6	(5e)	50	5	44	mixt.	1.3 : 1
7	(5f)	63	11	26	mixt.	2.8 : 1

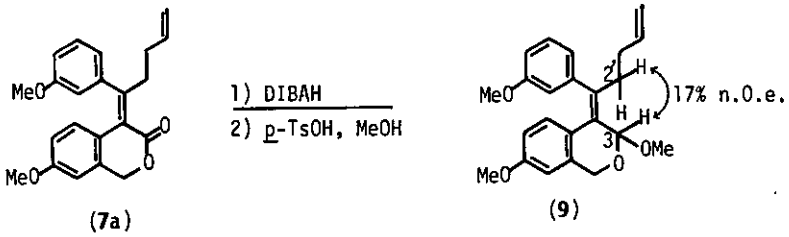
* The thermolysis was conducted at 180°C for 3.8 h.

process might be supported by the fact that the prolonged reaction time of the thermolysis of (5a) changed the product distribution as shown in Entry 2 of Table 1. It should be noted that the thermolysis of (5a) afforded (7a) as a single



Scheme 3

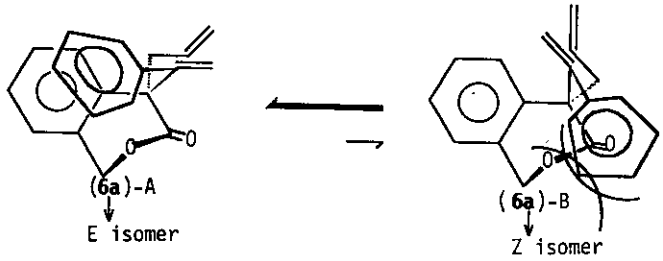
product. The olefin geometry of (**7a**) could be established as E by the n.O.e. experiment of (**9**), derived from (**7a**) by the sequential reduction with DIBAH and acetalization (irradiate C-2'(CH_2), 17 % enhancement at C-3(H)). (Scheme 4) The



Scheme 4

highly stereoselective formation of (**7a**) can be rationalized by considering the transition states (**6a**)-A and (**6a**)-B for the Cope rearrangement as illustrated in Figure 1. The stabilization due to π-stacking[6] effect of the two aromatic rings

Figure 1. Transition state for the Cope rearrangement



in (**6a**)-A leading to E-isomer makes it favorable than the alternative transition state (**6a**)-B which is sterically congested (or electronically unfavorable due to

the repulsion between the aromatic ring and the oxygen atoms of the lactone). In summary, it was clarified that the competitive electrocyclic reactions during the thermolysis of 1-alkenyl-1-allyloxycarbonyl substituted benzocyclobutenes proceeded predominantly through Z-transition state except for the case of cyclopentene as an olefin part. In addition, we could find an unprecedented sequential electrocyclic-double[3,3]sigmatropic reaction of o-quinodimethane in the course of the present study.

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4. The reverse selectivity in the competitive electrocyclic reactions may be due presumably to the strain of cyclopentene ring.
5. Colorless oil. ^{1}H-nmr (90 MHz, $CDCl_3$) δ 2.08(2H, q, J=7.1 Hz), 3.19(2H, t, J=7.1 Hz), 3.72(3H, s) 3.74(3H, s), 5.15(2H, s); ^{13}C-nmr (125 MHz, $CDCl_3$) δ 32.3(t), 33.9(t), 55.3(q), 55.4(q), 69.1(t), 109.6(d), 113.1(d), 113.7(d), 114.6(d), 115.7(t), 121.2(d), 124.5(s), 125.8(s), 129.5(d), 130.0(d), 134.5(s), 137.5(d), 142.0(s), 150.9(s), 158.7(s), 159.7(s), 168.0(s); ν_{max}($CHCl_3$)cm^{-1} 1721; λ_{max}(EtOH)nm 210 (ε=16684), 297 (ε=8115); MS (m/z) 350 (M^+, 100 %). Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 74.99; H, 6.20.
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