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THE COMPETITION BETWEEN ELECTROCYCLIC REACTION AND [1,5]SIGMATROPIC REACTION IN THE THERMOLYSIS OF 1,1-DISUBSTITUTED BENZOCYCLOBUTENES

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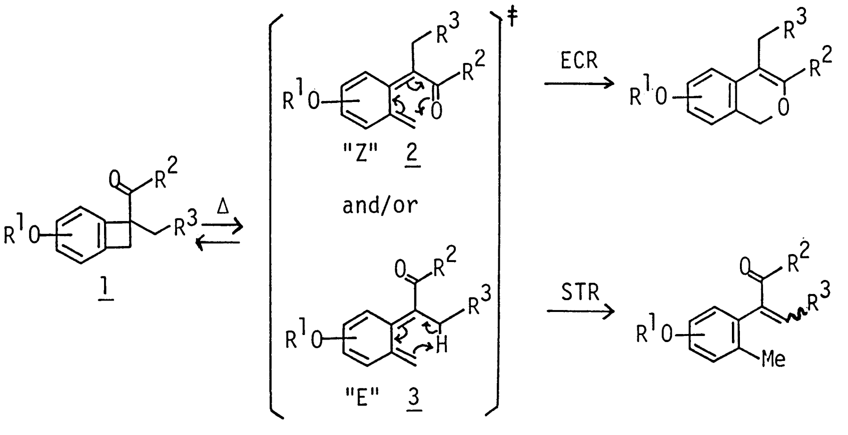
Thermolysis of 1-acyl-1-alkylbenzocyclobutenes was found to give predominantly the corresponding isochromenes *via* Z-conformer of the *o*-quinodimethane in the transition state.

In recent years the versatility of benzocyclobutenes[1] in organic synthesis has been demonstrated by many groups including our laboratory. However, much attention has mainly been focused on the [4+2]cycloaddition reaction using benzocyclobutenes as a diene moiety for constructing polycyclic natural products.[2]

As part of programme utilizing benzocyclobutenes in organic synthesis we planned to investigate the reactivity in the thermolysis of 1-acyl-1-alkylbenzocyclobutenes (1), which would undergo two possible reactions, namely electrocyclic reaction (ECR) and [1,5]sigmatropic reaction (STR), depending upon the geometry of the *o*-quinodimethane (2, 3) in the transition state.



Scheme 1.

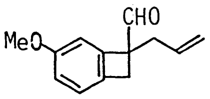
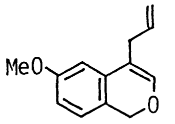
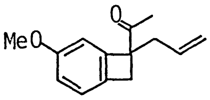
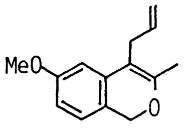
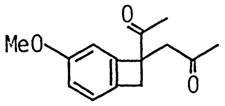
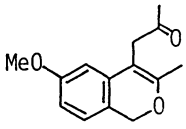
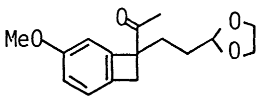
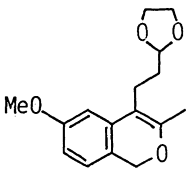
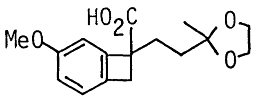
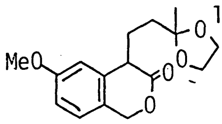
Although ECR,[3,4] STR,[5,7] and competitive reaction between ECR[6,8] or STR[7,8] and [4+2] cycloaddition in the thermolysis of 1-substituted or 1,1-disubstituted benzocyclobutenes have been reported so far, the systematic investigations about a competition between ECR and STR are few.[9] We report here the results of a thermolysis of various 1-acyl-1-alkylbenzocyclobutenes.

First of all, simple 1,1-disubstituted benzocyclobutenes, readily prepared from 1-cyano-5-methoxybenzocyclobutene[10] by standard manipulations, were thermolized at 180 °C. The results are summarized in Table 1. The reactions were cleanly completed within 15 minutes except for the case of the carboxylic acid (entry 5), and all of the cases gave a single product, the isochromenes (entries 1-4) and the lactone (entry 5), in good yield by ECR *via* Z-conformer of the *o*-quinodimehtane (e.g. 2).

Next we examined the thermolysis of spiro-systems, also prepared from 1-cyanobenzocyclobutenes, as shown in Table 2. The cyclohexanone (entry 3) afforded exclusively the isochromene product via ECR, although in the cyclohexenones (entries 1 and 2) and the δ-lactam (entry 4) cases the competition between ECR and STR could be observed. In the former cases ECR was predominant and in the latter the reverse selectivity was observed.

The occurrence of biaryls in the thermolysis of spiro-benzocyclobutenes (entries 1 and 2 in Table 2) prompted us to develop a general procedure for synthesizing unsymmetrical biaryls which would be difficult to obtain by standard methods, e.g. Ullmann reaction.[11] As substrates we chose two spiro-cyclohexenones (Table 3; entries 1 and 2), which have no possibility of undergoing ECR, they were thermolyzed at the conditions as depicted in Table 3 to give the expected biaryls in 90% and 67% yields, respectively. The prolonged reaction time and higher temperature in entry 2 seem to be attributed to an increase of activation energy ($\Delta G^{\ddagger}$) by non-conjugation of the π-system of o-quinodimethane in the transition state. This would be supported by the fact that the thermolysis of the cyclohexanone in entry 3 gave the 3-arylcyclohexenone in analogous reaction conditions as shown.

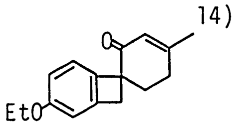
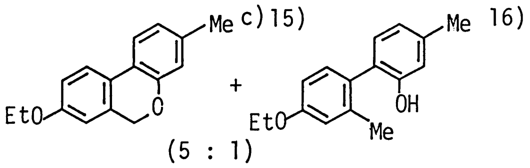
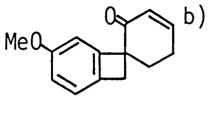
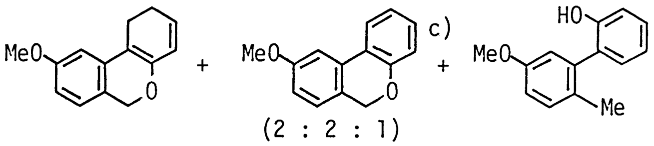
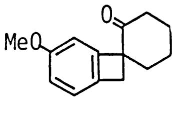
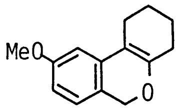
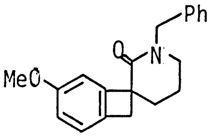
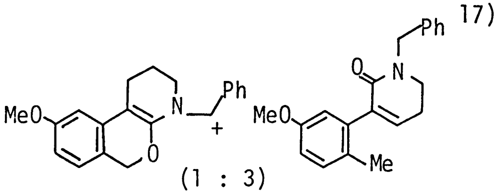
Table 1. Thermolysis[a] of 1,1-disubstituted benzocyclobutenes

Entry	Substrate	Time	Product[21]	Yield/%
1		10 min		60
2		15 min		76
3		5 min	 [12]	95
4		15 min		78
5		2 h	 [13]	100

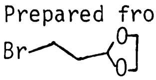
a) Substrate (1 mmol) in o-dichlorobenzene (ca. 30 ml) was stirred at 180 °C under nitrogen.

In summary, it was found that the thermolysis of 1-aryl-1-alkylbenzocyclobutenes proceeded predominantly via Z-conformer of o-quinodimethane in the transition state to afford the isochromenes except for the case of spiro-lactam (entry 4 in Table 2). Moreover, a new and general synthetic method for assembling unsymmetrical biaryls could be developed.

Table 2. Thermolysis[a)] of spiro-benzocyclobutenes

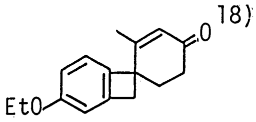
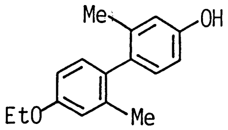
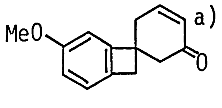
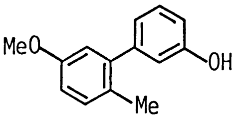
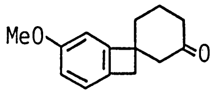
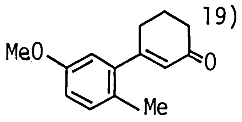
Entry	Substrate	Time/h	Product (Ratio)	Yield/%
1	 14)	6	 c)15) + 16) (5 : 1)	71
2	 b)	14.5	 + + c) (2 : 2 : 1)	56
3		5.3		53
4		9.3	 + 17) (1 : 3)	33

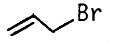
a) Reaction was conducted at 180 °C.

b) Prepared from 1-cyano-5-methoxybenzocyclobutene by the following treatment, i) LDA,  ii) Li, MeI, ultrasound[20)] iii) H_3O^+.

c) Resulted from spontaneous aromatization of the initial product.

Table 3. Thermolysis of spiro-benzocyclobutenes

Entry	Substrate	Temp/°C	Time/h	Product	Yield/%
1	 18)	180	15		90
2	 a)	200	216		67
3		220	200	 19)	48

a) Prepared from the corresponding 1-cyanobenzocyclobutene by the sequential treatment, i) LDA,  ii) DIBAH then H_3O^+ iii) $NaBH_4$ iv) MsCl, NEt_3 v) NaCN vi) DIBAH then H_3O^+ vii) $PdCl_2$, Cu^{II}, O_2, DMF, H_2O viii) KOH, aq. dioxane.

References

1) For reviews, see W. Oppolzer, Angew. Chem., Int. Ed. Engl., 16, 10 (1977); Synthesis, 1978, 793.
2) T. Kametani and K. Fukumoto, Kagaku No Ryoiki Zokan, 125, 81 (1980).
3) For a review, see T. Kametani and K. Fukumoto, Heterocycles, 3, 29 (1975).
4) R. Hug, H.-J. Hansen, and H. Schmid, Helv. Chim. Acta, 55, 10 (1972); M. R. Decamp, R. H. Levin, and M. Jones, Tetrahedron Lett., 1974, 3575; T. Kametani, Y. Enomoto, K. Takahashi, and K. Fukumoto, J. Chem. Soc., Perkin Trans. 1, 1979, 2836.
5) T. Kametani, Y. Shiratori, H. Inoue, M. Ihara, K. Fukumoto, and F. Satoh, J. Indian Chem. Soc., 55, 1219 (1978).
6) T. Kametani, K. Suzuki, and H. Nemoto, J. Org. Chem., 47, 2331 (1982).
7) T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, H. Nemoto, M. Ihara, K. Fukumoto, F. Satoh, and H. Inoue, J. Org. Chem., 42, 2672 (1977).
8) cf. W. Oppolzer, D. A. Roverts, and T. G. C. Bird, Helv. Chim. Acta, 62, 2017 (1979).
9) B. J. Arnold, P. G. Sammes, and T. W. Wallace, J. Chem. Soc., Perkin Trans. 1, 1974, 415.
10) T. Kametani, M. Kajiwara, and K. Fukumoto, Chem. Ind. (London), 1973, 1165; Tetrahedron, 30, 1053 (1974).
11) For a review, see P. E. Fanta, Synthesis, 1974, 9.
12) Pale yellow oil; NMR ($CDCl_3$), δ 1.98 (3H, s), 2.16 (3H, s), 3.43 (2H, s), 3.77 (3H, s), 4.93 (2H, s).
13) Colorless oil; IR ($CHCl_3$), 1740 cm^{-1}; NMR ($CDCl_3$, 100 MHz), δ 1.25 (3H, s), 3.50 (1H, m), 3.74 (3H, s), 3.85 (4H, s), 5.12 (1H, d, J = 15 Hz), 5.27 (1H, d, J = 15 Hz).
14) Colorless oil; IR ($CHCl_3$), 1665 cm^{-1}; NMR ($CDCl_3$), δ 2.00 (3H, s), 5.77 (1H, br.s).
15) Colorless prisms, mp 101 - 103 °C; NMR ($CDCl_3$), δ 2.31 (3H, s), 5.03 (2H, s), 6.60 - 7.64 (6H, m).
16) Pale yellow oil; IR ($CHCl_3$), 3550 cm^{-1}; NMR ($CDCl_3$), δ 2.16 (6H, s), 4.68 (1H, br.s, disappeared by the addition of D_2O), 6.68 - 7.36 (6H, m).
17) Pale brown oil; NMR ($CDCl_3$, 100 MHz), δ 2.08 (3H, s), 2.36 (2H, m), 3.35 (2H, t, J = 7 Hz), 4.60 (2H, s), 6.37 (1H, t, J = 5 Hz).
18) Pale yellow oil; IR ($CHCl_3$), 1665 cm^{-1}; NMR (CCl_4), δ 1.73 (3H, s), 5.76 (1H, br.s).
19) Pale yellow oil; IR (neat), 1660 cm^{-1}; NMR ($CDCl_3$), δ 2.21 (3H, s), 5.99 (1H, br.s).
20) cf. J.-L. Luche and J.-C. Damiano, J. Am. Chem. Soc., 102, 7926 (1980).
21) All new compounds gave satisfactory spectral and analytical (combustion and/or high resolution mass spectral) data consistent with the structures shown.

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