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THE STEREOSELECTIVITY OF REPRESENTATIVE CYCLOBUTENES IN (4+2)π CYCLOADDITION REACTIONS (1)

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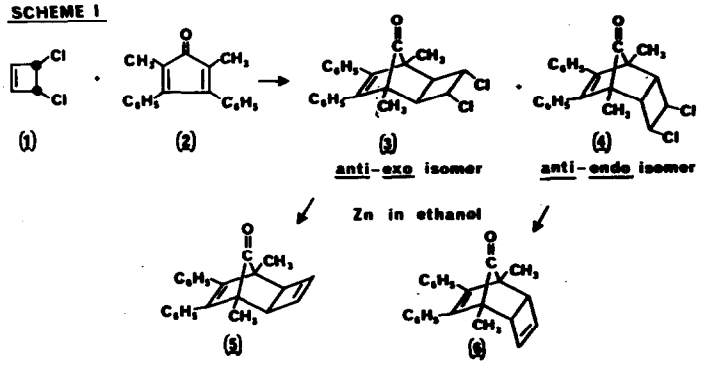
Previous reports from our own laboratory (*1,2*) as well as others (*3,4*) have demonstrated that cyclobutenes are effective dienophiles. Little is reported, however, on the stereochemistry of these adducts. Our present results pertain to the dienophilic stereoselectivity of two cyclobutenes (1 and 12) in the (4+2)π cycloadditions with 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (2). Two facts emerge from this study: a) *exo*-addition is the favoured mode of addition and b) the present methods, namely cycloaddition followed by either dechlorination with (1) or *retro* Diels-Alder reaction with (12), can be used to synthetic advantage for the introduction of the cyclobutene moeity (C_4H_4) into alicyclic systems. This serves as an alternative and complementary method to that involving cyclobutadiene (*5*), which specifically forms *endo*-cyclobutenes.

SCHEME 1



Reaction of *cis*-3,4-dichlorocyclobutene (1) with dienone (2) (generated *in situ* from its dimer in refluxing chloroform) yields a mixture (>85% yield) of the *anti-exo* isomer (3), and the *anti-endo* isomer (4)‡ in the ratio 4:1 (see

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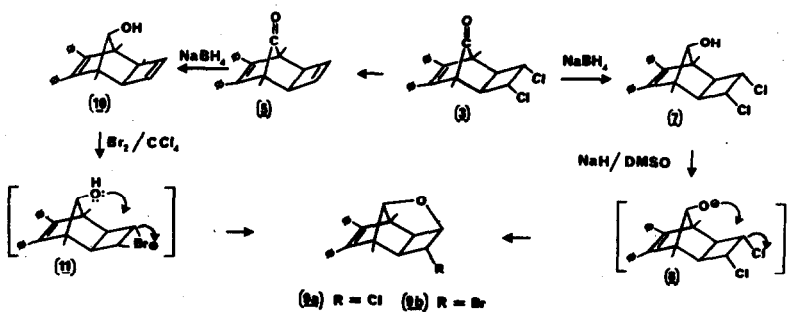
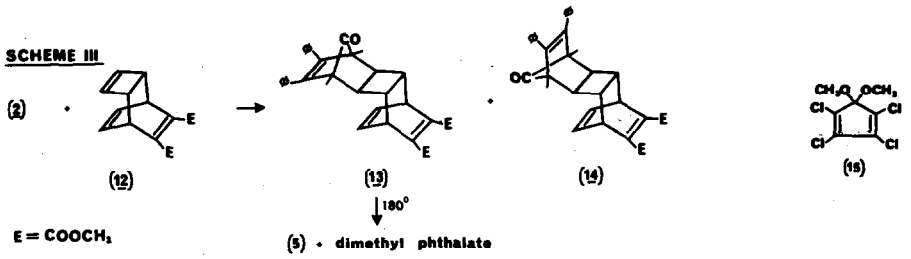
‡ See footnote next page

SCHEME II



Scheme I). This is the kinetic product ratio as no evidence for isomer interconversion is observed (decarbonylation occurs at higher temperature, $k_{endo} > k_{exo}$.) The structural assignment of these adducts depends on analytical and spectroscopic data (*6*) together with the following chemical evidence a) dechlorination with zinc in ethanol to the cyclobutenes (5) and (6) respectively and b) the reaction sequences outlined in Scheme II. The key step in this sequence is the SN2 displacement of chloride ion in the conversion of alcohol (7) to cyclic ether (9a), which fully delineates the *exo*-ring fusion of the cyclobutene in (3) as well as the *anti*-relationship of the *cis*-chlorine atoms.‡

SCHEME III

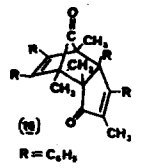


The related dienophile (12) also undergoes a similar cycloaddition with dienone (2) to form (>90% yield) the *exo*- and *endo*-isomers, (13) and (14) respectively (Scheme III). Once again the *exo*-isomer (13) predominates (*ca.* 6:1) and its stereochemistry is determined by controlled pyrolysis (180°) to form the *exo*-cyclobutene (5) in high yield. We have previously reported (*2a*) that (12) reacts with the ketal (15) to form only the *endo*-adduct (*vide infra*).

In view of the small number of reactions which kinetically favour *exo*-add-

‡ The *anti*-stereochemistry of the *cis*-chlorine atoms is assigned after consideration of the relative ease of dechlorination of (3) and (4), and of the resistance of the *syn-endo* isomer (17) to similar treatment (*3*).

ition, a separate study has been carried out on the dienone (2) with other dienophiles (7). This shows that the dienone dimer (16) as well as the *p*-benzoquinone adduct have the *endo*-configuration (2b), and these results parallel those of cyclopentadiene in related reactions (8). More recently Woodward *et al.* (9) have demonstrated that (6+4)π cycloadditions involving tropone and either cyclopentadiene or the dienone (2) are completely stereospecific and exhibit the same symmetry controlled mode of cycloaddition. In view of these findings it seems unlikely that the dienone (2) is exceptional in its orbital symmetry requirements.



It is difficult to account for the present stereoselectivity without taking recourse to steric arguments similar to those reviewed by Hill and Martin (8), although Herndon and Hall have been critical of this "rather nebulous" effect (10). While the mechanistic speculation relating to these results must remain, a qualitative evaluation of the results does seem merited (11). Clearly the proportion of adducts formed in cycloaddition reactions (of the same order) reflects the relative free energy of activation ($\Delta G^{\ddagger}$) of the respective transition states (T.S.). Steric interaction between diene and dienophile can raise the $\Delta G^{\ddagger}$ of either the *exo*- or *endo*-T.S., whereas only the *endo*-T.S. is subject to stabilisation by orbital symmetry contributions (9). These steric effects on $\Delta G^{\ddagger}_{exo}$ are most pronounced in cyclopentadienes containing 5-substituents and this accounts for the *endo*-adduct formed between (12) and the ketal (15) (*vide supra*). Substituents (particularly those capable of out-of-plane conformations) in the 2,3-position of the diene (or the equivalent 3,4-positions of the dienone) increase the $\Delta G^{\ddagger}_{endo}$ and account for the formation of (13) and (14). $\Delta G^{\ddagger}_{endo}$ is decreased when β-orbital stabilization is possible and accounts for the stereochemical preference for (16) and related adducts. Reactions of *cis*-3,4-dichlorocyclobutene are more interesting as the chlorine atoms in the dienophile appear able to exhibit secondary orbital stabilization (11c) arising from the lone pair electrons on the chlorine atom, as well as the more obvious steric contribution. This stabilization is insufficient to overcome the bad steric interaction of the 3,4-substituents in the dienone (2) [or the related 1,4-dimethyl-2,3-diphenylcyclopentadiene (12)] and so both *exo*- and *endo*- adducts are observed. Again attack from the least hindered side of the

dienophile occurs to form (3) and (4). In the case of cyclopentadiene however, steric effects are considerably reduced, and now the orbital contribution is dominant. This leads not only to *endo*-stereochemistry, but to the *syn-endo* isomer (17)(*3*). Other types of cycloaddition onto (1) have recently been reported to give varied stereochemical results (*13*).

(17)

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6. Pure samples were obtained for all compounds in the *exo*-series: melting points (Kofler Hot-bar): (3), 221°; (5), 136°; (7), 184°; (9a), 103°; (9b), 117°; (10), 112°; (13), 203°. The *endo*-isomers (4), (6), (14) have only been obtained as enriched mixtures with varying amounts of the *exo*-isomer. Consistent spectroscopic data supported assignments in both series.

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12. This also forms two major adducts which readily dechlorinate to form two different symmetrical cyclobutenes, p.m.r. studies again support the *exo*-isomer as the major product.

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