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Stereospecificity and Mechanism in Cation Radical Diels–Alder and Cyclobutanation Reactions

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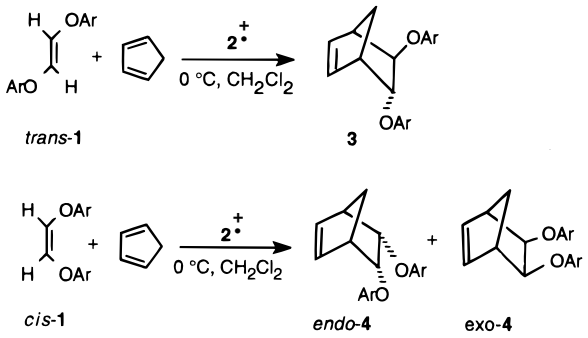
ABSTRACT



The cation radical Diels–Alder and cyclobutanation reactions of *cis*- and *trans*-1,2-(diaryloxy)ethenes with a cyclic and an acyclic diene have been found to be stereospecific, in accord with a concerted cycloaddition mechanism.

The mechanism of cation radical cycloadditions continues to elicit interest, especially the question of whether these reactions proceed in a stepwise manner involving a distonic cation radical intermediate, as originally postulated by Ledwith for cation radical cyclobutanation,[1] or via a concerted albeit highly nonsynchronous pericyclic path, as later proposed by Bauld for both cyclobutanation and Diels−Alder cycloaddition.[2] Although reaction stereochemistry is generally considered to be a key probe for the concerted vs stepwise nature of a reaction, relatively little information of this type has thus far been presented. Single examples of stereospecific cation radical Diels−Alder cycloaddition and cyclobutanation have, however, been published, and there are apparently no reported instances of nonstereospecific additions. It therefore appears highly desirable to probe more extensively the stereochemistry of cation radical cycloadditions of both the Diels−Alder and cyclobutanation type. The new electron rich substrates *cis*- and *trans*-**1** have recently been synthesized for the specific purpose of further probing the stereochemistry of cation radical cycloadditions, as well as to provide potential enediol synthetic equivalents for cation radical Diels−Alder reactions.[3]

Results and Discussion. The cycloadditions of *cis*- and *trans*-**1** were carried out under typical aminium salt conditions (CH_2Cl_2, 0 °C) using tris(4-bromophenyl)aminium hexachloroantimonate (**2**$^{\bullet+}$) as the catalyst. The cycloadditions of these substrates to 1,3-cyclopentadiene are 100% periselective, affording Diels−Alder adducts to the exclusion

(1) Bell, F. A.; Ledwith, A.; Sherrington, D. C. *J. Chem. Soc.* **1969**, 2719. Crellin, R. A.; Lambert, M. C.; Ledwith, A. *J. Chem. Soc. D* **1970**, 682. Ledwith, A. *Acc. Chem. Res.* **1972**, *5*, 133.

(2) Bauld, N. L.; Pabon, R. *J. Am. Chem. Soc.* **1983**, *105*, 633−634. Bellville, D. J.; Wirth, D.D.; Bauld, N. L. *J. Am. Chem. Soc.* **1981**, *103*, 718−720. Bauld, N. L.; Bellville, D. J.; Pabon, R.; Chelsky, R.; Green, G. *J. Am. Chem. Soc.* **1983,** *105*, 2378. Bauld, N. L. *Tetrahedron* **1989**, *45*, 5307−5363.

(3) Yang. J.; Bauld, N. L. *J. Org. Chem.*, in press.

(4) The cation radical vinylcyclobutane rearrangement has previously been found to be nonstereospecific in some instances: Reynolds, D. W.; Harirchian, B.; Chou, H.-S.; Marsh, B. K.; Bauld, N. L. *J. Phys. Org. Chem.* **1989**, *2*, 57−88.

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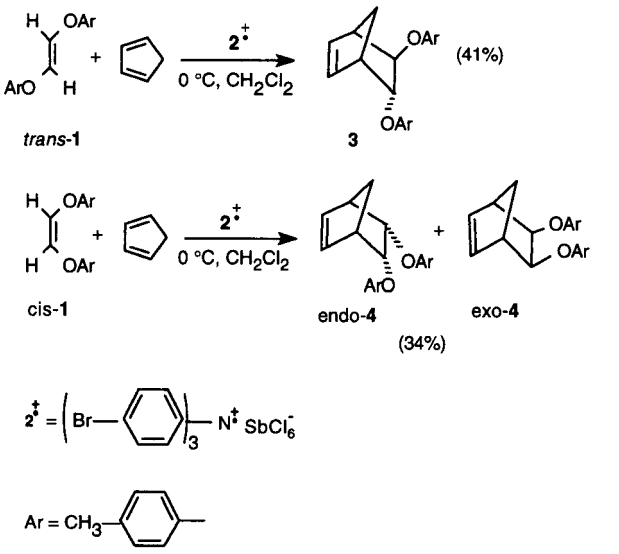
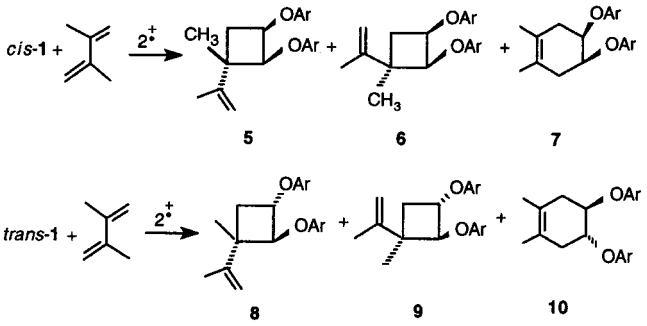
of cyclobutane adducts. In each case the adducts are formed in a highly (≥98%) *syn* stereospecific manner (Scheme 1), as indicated by TLC, ^{1}H and ^{13}C NMR, and GC. *cis*-**1** yields an approximately 1:1 mixture of the *endo* and *exo cis* adducts, while *trans*-**1** yields only the *trans* adduct. GC analysis confirmed that the reaction of *cis*-**1** is ≥99.5% stereospecific, while that of the *trans* isomer is ≥98% stereospecific. The isolated yield of the pure *trans* adduct was 41%, while the *cis* adducts were isolated in 34% total yield. It is important to note that none of the reactions described in this paper occur in the absence of the aminium salt catalyst.

Scheme 1



The cycloadditions of *cis*- and *trans*-**1** to a conformationally flexible diene (2,3-dimethyl-1,3-butadiene) were also studied. In this acyclic system, cyclobutane (CB) products, formed by the addition of **1**$^{\bullet+}$ to the *s-trans* diene conformation, are predominant, but Diels−Alder (DA) adducts are also formed as primary products in competition with cyclobutanation (CB:DA ≈ 2.5:1). Both pericyclic reaction types occur in a stereospecific manner (Scheme 2). In particular *cis*-**1** gives a CB mixture which consists of ≥96% **5** and **6** (in the ratio 1.6:1), while *trans*-**1** yields cyclobutanes which are ≥94% **8** and **9** (in a ratio of 3.1:1). The analysis of the Diels−Alder type products is complicated by the circumstance that they are formed both directly (via the *s-cis* diene) and indirectly from the cyclobutanes, via a cation

Scheme 2



radical vinylcyclobutane rearrangement. The primary Diels−Alder products (at very early reaction time) are formed stereospecifically, *cis*-**1** giving essentially only **7** (>98%) and *trans*-**1** giving **10** (>93%). Further, the vinylcyclobutane rearrangement of **5** and **6** yields ≥98% of **7**, while the rearrangement of **8** and **9** proceeds via isomerization to **5** and **6** and also results in the formation of **7**.[4]

As a consequence of these studies, there are now at least five established examples of stereospecific cation radical cycloadditions (three Diels−Alder and two cyclobutanation reactions), which stand in contrast to the absence of examples of nonstereospecific additions. Certainly, these results should not be construed as suggesting that nonstereospecific cycloaddition reactions will not be found, or even that they will prove to be rare, but rather that stereospecificity is at least a very common and very likely the more general characteristic of these reactions. Mechanistically, these results would appear to be in much better accord with a concerted/nonsynchronous mechanism than with a stepwise/distonic cation radical mechanism. The possibility of a stepwise mechanism can, however, be retained as plausible, but only to the extent that it is presumed to be a rather *general* characteristic of such distonic cation radical intermediates that they undergo cyclization to the virtual exclusion of bond rotations which would cause stereorandomization. The variety of reaction systems and types for which stereospecific reactions have now been observed would appear to render this possibility progressively less likely.

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