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Intramolecular Diels−Alder Reactions of Ester Linked 1,3,9-Decatrienes: Cis/Trans Selectivity in Thermal and Lewis Acid Promoted Reactions of Ethylene-Tethered and Benzo-Tethered Systems

Emma L. Pearson,[†] Laurence C. H. Kwan,[†] Craig I. Turner,[†] Garth A. Jones,[‡]
Anthony C. Willis,[†] Michael N. Paddon-Row,*[,‡] and Michael S. Sherburn*[,†]

Research School of Chemistry, Australian National University, Canberra, ACT 0200, Australia, and School of Chemistry, The University of New South Wales, Sydney, NSW 2052, Australia

sherburn@rsc.anu.edu.au; m.paddonrow@unsw.edu.au

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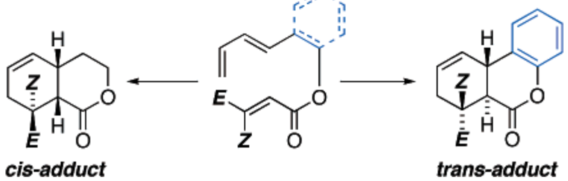

High cis (i.e., endo) diastereoselectivities are witnessed in heat-promoted intramolecular Diels−Alder (IMDA) reactions of ethylene-tethered hexadienyl acrylates. The cis stereoselectivity is improved by promotion with Et_2AlCl. The first examples of Et_2AlCl *catalyzed* intramolecular Diels−Alder reactions of ester-activated dienophiles are reported. In contrast, the corresponding benzo-tethered hexadienyl acrylates undergo moderately trans (i.e., exo) selective IMDA reactions. Very high trans stereoselection is obtained upon promotion with ATPH. The outcomes of these reactions are essentially insensitive to dienophile (C10) geometry and substitution. DFT (B3LYP/6-31+G(d)) computed cis/trans product distributions—based on Boltzmann transition structure populations—are in good agreement with the experimental results. These computational investigations provide useful insights into the origins of stereoselection in these systems. The stereoselectivity exhibited by the ethylene-tethered hexadienyl acrylates is ascribed to stabilizing secondary orbital interactions at play in the cis-transition structures (TSs). In the benzo-tethered series, this effect is overridden by stabilizing π-conjugative interactions, between the benzo moiety and the 1,3-diene component, which are stronger in trans TSs, compared to the cis TSs. The computed TS geometries generally exhibit advanced peripheral bond forming asynchronicity, with the tether carbonyl group in conjugation with the dienophile. Such TS features significantly weaken the stereodirecting influence of terminal dienophile substituents.

Introduction

The intramolecular version of the Diels−Alder cycloaddition (IMDA) is a powerful reaction since two rings, two covalent bonds, and up to four contiguous stereocenters are generated in a concerted event.[1] We are focusing efforts on the prediction and rationalization of the stereochemical outcome of this synthetically important reaction. In recent papers, we presented experimental and computational studies of the IMDA reactions of pentadienyl acrylates **1** (Scheme 1) bearing substituents at C1 and C9.[2,3] These reactions can furnish two distinct diastereoisomeric products (**P**), namely *cis*-**1P** and *trans*-**1P**, which differ in the stereochemistry about the ring fusion. Whereas terminal diene (C1) substituents have little influence upon the stereochemical outcome of the reaction, there is a marked stereochemical dependence upon both the nature of the dienophile (C9) substituent and the dienophile geometry. Experiments show that the C9-unsubstituted acrylate derivative is quite strongly cis selective (trans/cis = 25:75).[4] The 9-*E*-CH_3 analogue also shows *cis*-IMDA selectivity whereas the 9-*Z*-CH_3 gives equal amounts of the two isomers. The two 9-CO_2Me derivatives exhibit trans selectivity, the selectivity being marked in the case of the *Z*-ester analogue. These intriguing results were explained in terms of competing conformational, electronic, and

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[†] Australian National University.
[‡] University of New South Wales.

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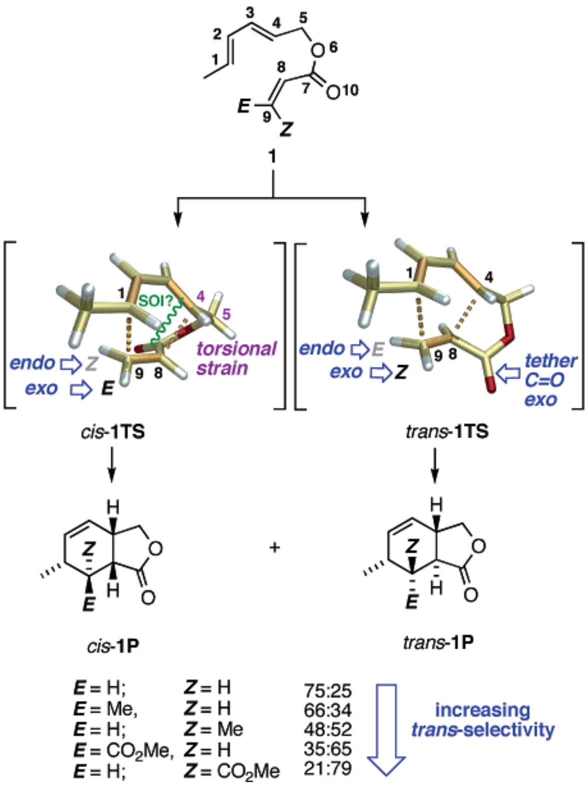
SCHEME 1. Pentadienyl Acrylate IMDA Reaction Cis and Trans Transition Structures (TS) and Bicyclic Products (P)



steric effects operating in the two competing diastereomeric TSs. For example, the cis preference exhibited by C9-unsubstituted pentadienyl acrylates is the result of two *opposing* influences in the cis TS, namely *destabilizing* torsional strain about the C4−C5 bond and (slightly stronger) *stabilizing* attractive electrostatic and/or Singleton-type [4 + 3] secondary orbital interactions (SOIs)[5,6] between the endo-oriented tether carbonyl group and atoms C4 and possibly C3 of the diene unit.[4]

Whereas cis/trans selectivity for IMDA reactions involving 9-*E*-substituted pentadienyl acrylates generally follows the normal pattern found for the corresponding intermolecular DA reactions, the 9-*Z*-substituted stereoisomers generally displayed trans selectivity that was much stronger than can be attributed to effects of the isolated substituent. This is strikingly so with unsaturated electron withdrawing substituents (e.g., CO$_2$Me) whose endo selectivities, displayed in intermolecular DA reactions, are reversed in the IMDA reactions of pentadienyl acrylates. The origin of this so-called anomalous *Z*-effect was ascribed to destabilizing structural changes in the cis TS—namely, amplification of twist-mode asynchronicity, resulting from out-of-plane twisting of the tether carbonyl group—caused by repulsive interactions between the 9-*Z*-substituent and the tether carbonyl group, which lead to diminished SOIs involving the tether carbonyl and to the 9-*Z* substituent being driven further into the endo region of the diene where electrostatic repulsion prevail over SOIs (Figure 1).

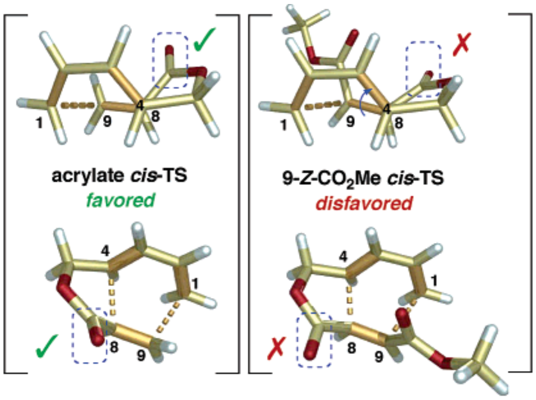


FIGURE 1. The presence of the 9-*Z*-CO$_2$Me group (right-hand TS) in pentadienyl acrylate cis TSs is accompanied by increased twist-mode asynchronicity (blue arrow) and increased out-of-plane twisting of the tether carbonyl group (blue dashed box).

The aims of the present study are to investigate the stereochemical outcomes of IMDA reactions of the higher homologue of the system depicted in Scheme 1, ethylenoxycarbonyl-tethered 1,3,9-decatrienes **2**, along with their benzo-tethered analogues **3** (Scheme 2). A major objective of this work was to develop an understanding of the origins of stereoselection of these reactions by the location and examination of computed transition structures. Would a similar stereochemical dependence upon dienophile substitution be witnessed in these systems? Pentadienyl acrylates **1** suffer decomposition through C5−O6 bond heterolysis upon treatment with Lewis acids.[7] A further goal of the present study was to investigate both the enhancement and reversal of inherent thermal stereoselectivities in IMDA reactions of **2** and **3**, by way of Lewis acid promotion.

The importance of IMDA reactions of ester linked decatrienes **2** in total synthesis is well documented. The natural products

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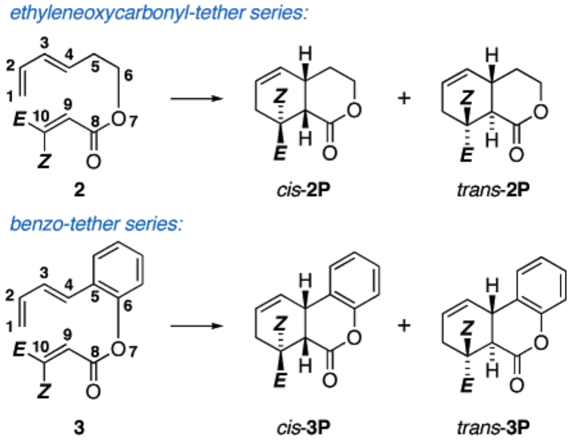
SCHEME 2. IMDA Reactions under Scrutiny



gibberellic acid,[8] mellein and ramulosin,[9] stenine,[10] and lycorine[11] have all been prepared using an IMDA reaction of this class as a key step, and no less than four groups have described the results of preliminary investigations into the total synthesis of eleutherobin.[12] In agreement with Corey's observations with a precursor containing a semicyclic diene and a chloroacrylate dienophile,[8] Martin demonstrated that the parent ester linked decatriene **2** (Scheme 2, $E = Z = \mathrm{H}$) undergoes a strongly (90%) cis-selective cycloaddition under thermal conditions.[13] Subsequent investigations with more highly substituted precursors under both thermal[14−16] and Lewis acid-mediated[17−19] conditions have confirmed high cis stereoselectivity as the norm for substrates **2** where $E = Z = \mathrm{H}$ and E = substituent; $Z = \mathrm{H}$.[20] A computational investigation by Tantillo, Houk, and Jung[21] into the IMDA reaction of the 3,5-dimethyl analogue of *E*-crotonate **2** (Scheme 2, $E = \mathrm{Me}$; $Z = \mathrm{H}$) highlighted the preference for a boatlike-TS tether conformation[22] and identified its origins but apparently did not offer an explanation of the cis preference of the reaction. Despite the significant number of publications describing IMDA reactions of trienes **2**, no investigation into the influence of dienophile substitution has been reported. Recent findings by Roush in the decatrienone series demonstrate an intriguing cis−trans stereoselectivity reversal with *E*- and *Z*-dienophile congeners of otherwise identical triene precursors,[23] a result which is similar to that witnessed with pentadienyl acrylates.[2] We felt that a systematic computational−experimental investigation into compounds of type **2**, carrying representative *E*- and *Z*-substituents, was warranted.

Despite the ease of access to benzo-precursors **3** depicted in Scheme 2 and the synthetic potential of their cycloadducts, we have been able to locate only three previous examples of IMDA reactions of this type in the literature. One describes a trans-selective double IMDA reaction of a cross-conjugated thia-triene with acrylate dienophiles,[24] and another describes a trans-selective IMDA reaction of triene **3** ($E = Z = \mathrm{H}$).[25] The third paper describes our preliminary investigations with the *E*-crotonate **3** (Scheme 2, $E = \mathrm{Me}$; $Z = \mathrm{H}$), in which we erroneously reported a transposed experimental cis 73:27 trans ratio from the thermal IMDA reaction.[16] This experimental error led us to the incorrect conclusions that DFT is inferior to MP theory and that DFT failed in this case. Herein we clarify the experimental selectivities and elucidate their origins with a detailed computational−experimental investigation into compounds of type **3**.

Results and Discussion

Heat-Promoted IMDA Reactions. Triene IMDA precursors **4**−**13**, differing in the nature of the dienophile (C10) substituent and dienophile geometry, were accessed in two or three straightforward steps as described in the Supporting Information (SI). Heat-promoted IMDA reactions were carried out in common aromatic solvents (Table 1). The order of reactivity of the five non-benzo substrates toward IMDA reaction is as follows: fumarate **6** > maleate **8** > acrylate **4** > *E*-crotonate **5** > *Z*-crotonate **7**. A very similar order of reactivity was witnessed within the benzo series, with the only difference being that the acrylate precursor **9** underwent IMDA reaction more readily than the maleate precursor **13**. A substrate containing an aromatic ring invariably cyclizes more readily than its ethylene tether analogue. The reactions of the crotonates were considerably slower than those of the other three substrates, with some decomposition being witnessed under conditions required to induce thermal cycloaddition of *Z*-crotonate **7**. The reactions

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[20] To our knowledge, only one example of an IMDA reaction of a *Z*-substituted precursor **2**, the carboxylic acid ($E = \mathrm{H}$; $Z = \mathrm{CO_2H}$) has been reported. Cyclization of this substrate was promoted by $\mathrm{In(OTf)_3}$ in an aqueous solvent.[18d] No thermal cycloaddition results were disclosed.

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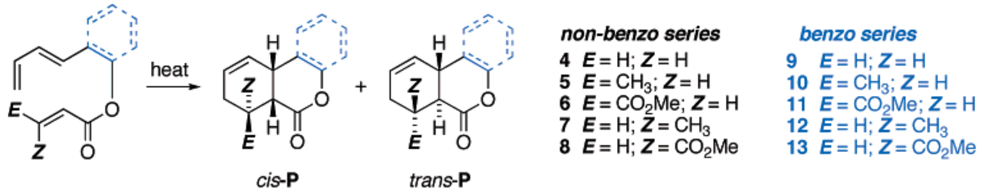
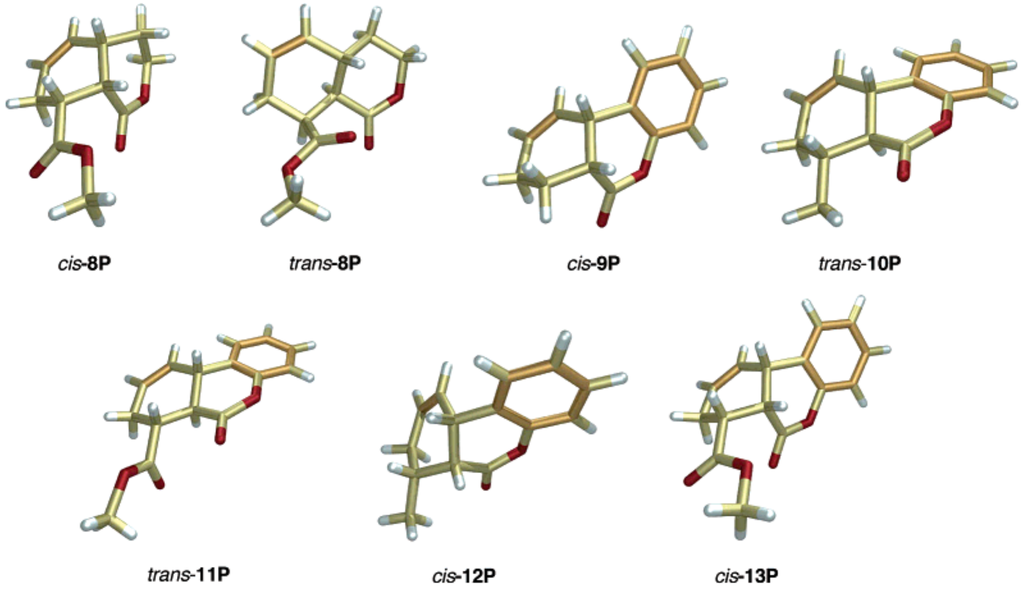
TABLE 1. Thermal Intramolecular Diels–Alder Reactions



structure	C10-substituent	T (°C)	t (h[a])	Y (%)	cis/trans$_{\text{exptl}}$[b]	cis/trans$_{\text{DFT}}$[c]	E_{rel}[c]
4[d]	H	132[e]	47	70	*92*:8	*85*:15	*c*5.85
5	*E*-Me	180[f]	113	76	*88*:12	*81*:19	*c*5.54
6[g]	*E*-CO_2Me	110[h]	22	82	*83*:17	*79*:21	*c*4.20
7	*Z*-Me	180[h]	120	54	*85*:15	*74*:26	*c*3.94
8	*Z*-CO_2Me	132[e]	72	90	*70*:30	*60*:40	*c*1.38
9[i]	H	110[h]	12	92	26:*74*	13:*87*	*t*5.94
10	*E*-Me	180[f]	2.2	100	27:*73*[j]	21:*79*	*t*4.96
11	*E*-CO_2Me	110[h]	0.5	96	29:*71*	31:*69*	*t*2.51
12	*Z*-Me	180[f]	21	92	24:*76*	9:*91*	*t*8.76
13	*Z*-CO_2Me	110[h]	28.5	87	22:*78*	6:*94*	*t*9.01

[a] Time taken for >95% conversion of starting triene. [b] The mean of the ratios measured from HPLC of the crude reaction mixture, ^{1}H NMR of the crude reaction mixture, and the isolated yields after purification. The difference between the three sets of ratios was at most ±5%. [c] DFT = B3LYP/6-31+G(d). Relative energies (kJ mol^{-1}) refer to 0 K and include ZPVE corrections. For **4**–**8**, the boatlike conformation is always more stable—between 6 and 20 kJ mol^{-1}—than the chairlike conformation and E_{rel} refers only to the boatlike conformations. The cis/trans$_{\text{DFT}}$ ratios are the Boltzmann populations of the cis and trans TSs at the experimental temperatures; both chairlike and boatlike TSs were included in the calculations. All 10-CO_2Me TSs have the ester group adopting the cisoid conformation; inclusion of those TSs having the transoid conformation had no effect on the Boltzmann distributions. [d] Previously reported to give a 90:10 mixture of *cis*-**4P**/*trans*-**4P** in 42% yield (sealed tube, 210 °C, 5 h).[13] [e] Chlorobenzene. [f] 1,2-Dichlorobenzene. [g] Previously reported to give a 78:22 mixture of *cis*-**6P**/*trans*-**6P** in 67% yield (xylene, reflux, 5 h).[10] [h] Toluene. [i] Previously reported to give a 30:70 mixture of *cis*-**6P**/*trans*-**6P** (no yield, experimental details, or characterization data provided).[25] [j] Erroneously reported to give a 73:27 mixture of *cis*-**10P**/*trans*-**10P** in an earlier communication.[16]


cis-**8P** *trans*-**8P** *cis*-**9P** *trans*-**10P**

trans-**11P** *cis*-**12P** *cis*-**13P**

FIGURE 2. IMDA product molecular structures from single-crystal X-ray analyses.

of the non-benzo substrates **4**–**8** exhibit strong cis kinetic[26] stereoselectivities, whereas the IMDA reactions of the five benzo-tethered analogues all exhibit marked trans kinetic[26] stereoselectivities. Single-crystal X-ray analyses of *cis*-**8P**, *trans*-**8P**, *cis*-**9P**, *trans*-**10P**, *trans*-**11P**, *cis*-**12P**, and *cis*-**13P** (Figure 2) augmented NMR analyses in securing the stereochemical assignments of cycloadducts (see SI for full details).

The thermal IMDA reactions of substrates **4**–**13** were modeled computationally in order to answer the following questions: (1) Why are the stereochemical outcomes of these thermal IMDA reactions not influenced by the dienophile geometry and the nature of the dienophile terminal substituent? (cf. pentadienyl acrylates, Scheme 1.) (2) Why do the non-benzo precursors undergo cis-selective thermal IMDA reactions, and (3) why do the benzo precursors give trans cycloadducts?

Computational Methods. Gas-phase transition structures (TSs) for intramolecular Diels–Alder reactions were optimized using the B3LYP functional[27] and the 6-31+G(d) basis set.[28] Harmonic vibrational frequencies (at the same level of theory) were employed to characterize optimized geometries as either first-order saddle structures (one negative Hessian eigenvalue) or minima (all frequencies real), and to provide—after scaling

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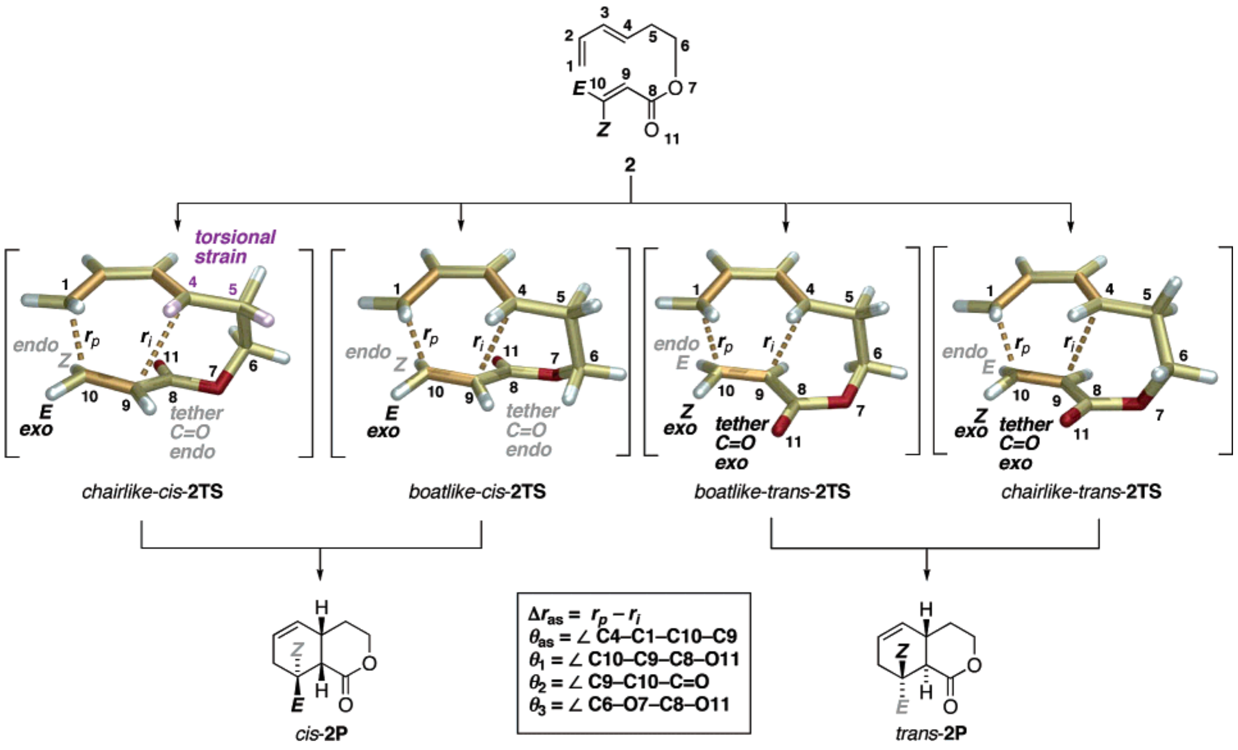
[26] All cycloadducts reported in this study were found to be stable towards the reaction conditions used to form them.

SCHEME 3. Schematic of Cis and Trans Boatlike and Chairlike IMDA TSs for the Non-Benzo Hexadienyl Acrylate, Depicting the Numbering Conventions and Relevant Geometrical Parameters



by 0.9614[29]—zero-point vibrational energies (ZPVEs) and enthalpies and free energies. ZPVE (0 K) corrected TS relative energies ($E_{\text{rel}}^{\text{TS}}$) were calculated using the electronic energies from optimized cis- and trans-IMDA TS isomers (i.e., $E_{\text{rel}}^{\text{TS}} = E_{\text{cis TS}} - E_{\text{trans TS}}$). The relative enthalpies and free energies of the cis and trans TSs, $H_{\text{rel}}^{\text{TS}}$ and $G_{\text{rel}}^{\text{TS}}$, respectively, were calculated at the experimental temperatures. The cis and trans TS populations (which are equated to the cis/trans product ratios) were calculated using three different methods. First, and least rigorously, TS Boltzmann populations were calculated from the ZPVE-corrected electronic energies for each IMDA reaction, using the experimental temperature. Second and third, the TS populations were calculated from the TS enthalpies and free energies, respectively, the latter being the most sound procedure to follow. Interestingly, the cis/trans product ratios, determined from electronic energies (i.e., the first method) have been shown to give similar results to those based on enthalpies and free energies.[4] Indeed, both electronic energy and enthalpy calculations give almost identical cis/trans selectivities for the current series of systems, **4**−**13**. With one exception, the free energy-calculated cis/trans selectivities are very similar to those calculated using electronic energies. The single exception is **8**, for which the free energy calculation incorrectly predicts predominant trans selectivity, whereas both electronic energy and enthalpy calculations are in agreement with the experimental finding of predominant cis selectivity. Salient TS ZPVE-corrected relative energies and cis/trans populations, calculated using the electronic energies, are presented in Table 1. The corresponding cis/trans selectivities, based on enthalpy and free energy calculations, are given in Supporting Information (SI) (Table S2). Geometrical parameters (Schemes 3 and 4) are summarized in Tables S3 and S4 (SI). The Gaussian 98[30] and 03[31] program packages were used throughout. Optimized geometries (in Cartesian coordinate form) and their energies are provided as Supporting Information.

Justification of the Theoretical Model. The B3LYP functional, in conjunction with either the 6-31G(d) or 6-31+G(d) basis sets, is known to give acceptable relative energies and geometries for a broad variety of Diels−Alder reactions.[3−5,21,32,33] Importantly, we have shown that the B3LYP/6-31+G(d) method correctly predicts cis/trans ratios for the IMDA reactions of several 9-substituted pentadienyl acrylates, often with an accuracy of 1 kJ/mol.[2] This level of theory is, therefore, adequate for this study. In this work we focus exclusively on the influence

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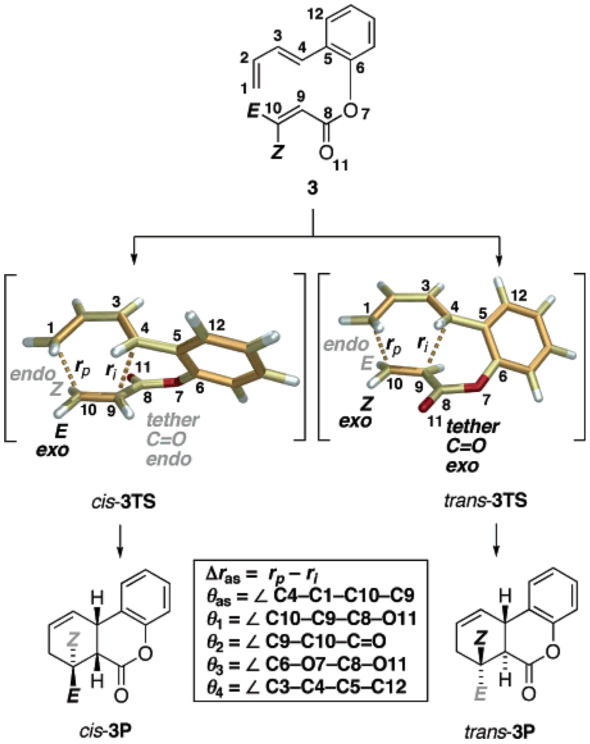
SCHEME 4. Schematic of Cis- and Trans-IMDA TSs for the Benzo Hexadienyl Acrylate, Depicting the Numbering Conventions and Relevant Geometrical Parameters



of electronic, strain, and steric factors on cis/trans selectivities of IMDA reactions, without considering solvent effects; consequently, we have used gas-phase DFT calculations. The excellent agreement found between gas-phase B3LYP/6-31+G(d) predicted IMDA cis/trans ratios and the experimental ratios, obtained using toluene, chlorobenzene, or 1,2-dichlorobenzene as solvent, suggests that weakly polar solvents, which are often used in IMDA reactions, have no significant influence on cis/trans selectivities.[3]

Transition Structure Geometries and Salient Parameters. The good agreement between synthetic and calculated stereoselectivities for the heat-promoted reactions (Table 1) allows the experimental findings to be explained through interpretation of the TS geometries. As noted previously by Tantillo, Houk, and Jung,[21] the diene-dienophile linkers of ethylene-tethered hexadienyl acrylates adopt two distinct conformations in IMDA TSs, namely the chairlike and boatlike conformations. In the benzo-analogues, the linker adopts a single flattened boatlike conformation. The cis and trans cycloaddition modes are feasible for each tether conformation type. Thus, four discrete TSs are located for the non-benzo system (Scheme 3) and two for the benzo system (Scheme 4). Referring to Schemes 3 and 4, there are eight significant geometrical parameters associated with the IMDA TS: the peripheral and internal forming bonds, r_p and r_i, respectively; the bond forming asynchronicity, Δr_{as} ($= r_p - r_i$); the twist-mode asynchronicity dihedral angle, θ_{as} (= the dihedral angle C4−C1−C10−C9); the dihedral angle, θ_1, made between the tether carbonyl group and the dienophile double bond; the dihedral angle, θ_2, made between the C10 carbonyl group (when present) and the dienophile double bond; the ester group dihedral angle, θ_3, made between the tether carbonyl group and the alkoxy (aryloxy) substituent; the dihedral angle, θ_4, which gives the degree of conjugation between the diene and the aromatic ring in benzo-TSs. Values for developing bond length parameters and dihedral angles for all TSs are given in Tables S3 and S4, respectively.

Before we offer explanations of stereoselectivities in these reactions, it should be noted that boatlike TS are more stable than chairlike TSs in hexadienyl acrylate IMDA reactions. Consistent with findings on tether-substituted systems by Tantillo, Houk, and Jung,[21] the ester group of the tether exhibits an energetically costly 55−72° out-of-plane conformation in chairlike TSs (Table S4, dihedral θ_3). In comparison, ester tethers of boatlike TSs are significantly closer to the preferred in-plane conformation (154−170°). The preference for boatlike TSs in IMDA reactions of decatrienone systems was proposed in earlier studies by Roush and Coe,[21] who identified more subtle conformational influences at play in IMDA TSs. Indeed, such influences can be seen in hexadienyl acrylate TSs (Scheme 3, pink hydrogens). The chairlike-cis TS for the IMDA reaction of **4**, for example, contains an unfavorable eclipsed arrangement about the C4−C5 bond (H4−C4−C5−H5 dihedral angle = 10°) which is much weaker in the boatlike-cis TS (H4−C4−C5−H5 dihedral angle = 45°). Nevertheless, a comparison of the trans TSs leads us to believe that the stronger ester overlap in the boatlike TSs of the ester tethered system is the dominant TS feature. Thus, the torsional strain associated with the H4−C4−C5−H5 angle is about the same magnitude in both chairlike-trans TS and boatlike-trans TS, H4−C4−C5−H5 dihedral angles = 75° and 41°, respectively, and yet the boatlike-trans TS is more stable than the chairlike-trans TS (by 7.4 kJ mole^{-1}), albeit, to a lesser extent than in the corresponding cis TSs in which the boatlike-cis TS is 9.4 kJ mole^{-1} more stable than the chairlike-cis TS.

Because we find that the boatlike TS is always significantly more stable (by 6 to 20 kJ mol^{-1}) than the corresponding chairlike TS for all IMDA reactions studied, the sections of the following discussion involving cis/trans stereoselectivities in hexadienyl acrylates will be restricted to the consideration of boatlike TSs. The ensuing sections offer possible answers to the three questions posed earlier.

**Why Are the Stereochemical Outcomes of these Thermal IMDA Reactions *Not* Influenced by the Dienophile Geometry

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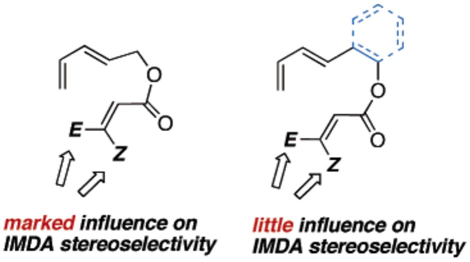

FIGURE 3. Diverging outcomes from related Diels−Alder reactions.

and the Nature of the Dienophile Terminal Substituent (Figure 3)? In all but 2 of the 28 hexadienyl acrylate TSs located, the peripheral (C1−C10) bond r_p is shorter than the internal (C4−C9) bond r_i. This result contrasts markedly with the corresponding pentadienyl acrylate system, which exhibits advanced internal TS bond formation.[3] Advanced internal bond formation is linked to the "*Z*-effect",[3] whereby *Z*-substituted dienophiles exhibit anomalously trans-selective IMDA reactions (Scheme 1, Figure 1). A significant consequence of advanced peripheral bond formation in hexadienyl acrylates is the lack of an anomalous *Z*-effect, that is, the consistently high cis stereoselection for **4**−**8** (Table 1).

The anomalous *Z*-effect is most apparent in the IMDA reaction of pentadienyl maleate precursor (Scheme 1, **1**, E = H; Z = CO_2Me), which undergoes a trans-selective IMDA reaction (cis/trans = 21:79), while the corresponding hexadienyl maleate **8** shows no such behavior and remains cis selective (Table 1, cis/trans = 62:38).[34] Not only is twist-mode asynchronicity modest in boatlike *cis*-**8TS**, amounting to 5° (Table S4), but it takes place about the shorter C1−C10 forming bond[35] and in the exo direction, away from the diene. Thus, the 10-*Z*-CO_2Me group in boatlike *cis*-**8TS** does not experience the energetically costly displacement in the endo direction, as suffered by the 9-*Z*-substituted pentadienyl acrylates (Figure 1).[3] The main reason for the smaller magnitude of twist-mode asynchronicity in the cis-*Z* IMDA TSs of the hexadienyl acrylates, compared to that found in the TSs for the pentadienyl acrylates is that, in the TSs for the latter systems, the developing five-membered lactone ring forces the tether carbonyl group out-of-plane, with respect to the dienophile double bond (Figure 1); the presence of a 9-*Z*-CO_2Me group forces the tether carbonyl group further out-of-plane which, in the cis TS, results in driving the 9-*Z*-CO_2Me group further in the endo direction. Free from any ring-forming constraints, the 9-*Z*-CO_2Me group is able to remain coplanar with respect to the dienophile C═C bond, thereby preserving conjugative stabilization. In contrast, the developing, less strained, six-membered ring in the TSs for the hexadienyl acrylates allows the tether carbonyl to remain coplanar with respect to the dienophile double bond, even in the presence of the 10-*Z*-CO_2Me group. In this case, the repulsive interaction between the 10-*Z*-ester substituent and the tether carbonyl group in the endo TS is ameliorated by the out-of-plane twisting of the ester substituent by 71° (Figure 4); because the 10-*Z*-ester is not part of the tether, out-of-plane twisting of this group has a negligible effect on the magnitude of twist-mode asynchronicity. Consequently, no significant destabilization of the cis-*Z* TS is to be expected.

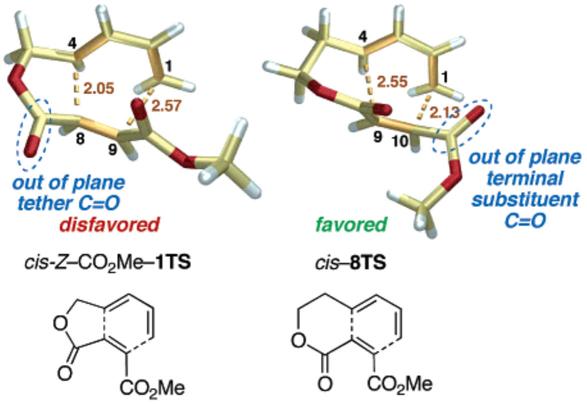

FIGURE 4. B3LYP/6-31+G(d) optimized pentadienyl maleate (left) and hexadienyl maleate (right) TSs. Note the advanced internal bond formation in the former and the advanced peripheral bond formation in the latter. Distances are in angstroms.

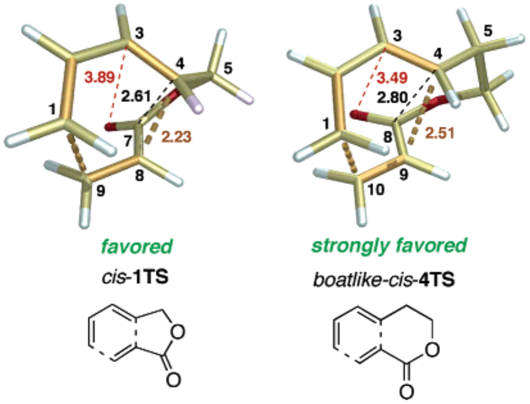

FIGURE 5. B3LYP/6-31+G(d) optimized pentadienyl acrylate (left) and hexadienyl acrylate (right) TSs. Note the essentially coplanar C10═C9−C8═O arrangement in the latter and the severely twisted C9═C8−C7═O arrangement in the former. This results in the C3═C4 bond being much more closely aligned in the right-hand TS. Distances are in angstroms.

Why Do the Non-Benzo Precursors Undergo Cis-Selective Thermal IMDA Reactions? It is noteworthy that the favored conformation of the forming six-membered lactone ring in all boatlike TSs has the tether carbonyl group nearly coplanar with the dienophile double bond (Table S4, $\theta_1 = 4-13°$). Coplanarity between tether carbonyl and dienophile cannot take place in the pentadienyl acrylate TSs, even in the absence of a 9-*Z*-substituent (θ_1 = ca. 30−40° in pentadienyl acrylates[3]). That the hexadienyl acrylate TSs (a) tolerate an essentially coplanar tether carbonyl group, and (b) have a shorter developing internal C4−C9 bond has a consequence for the cis TSs, namely, that they bring the tether carbonyl group into better alignment with C3 and C4 of the diene, perhaps promoting SOIs (Figure 5). Indeed, C4···C8 distances (2.76−2.83 Å) and C3···O distances (3.42−3.68 Å) are remarkably similar throughout the five boatlike-cis TSs.

It is noteworthy that the cis selectivity—both experimentally observed and computationally predicted—is more pronounced in the hexadienyl acrylates **4**−**8** than in the pentadienyl acrylates **1**. For example, the cis IMDA TS for the 9-unsubstituted pentadienyl acrylate **1** (Scheme 1; $E = Z =$ H) is 1.9 kJ mol^{-1} more stable than the trans TS,[2] whereas, for the 10-unsubstituted hexadienyl acrylate **4**, the cis TS is 5.9 kJ mol^{-1} more stable

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(34) This reaction was erroneously reported to give *exclusive* formation of the cis product in ref 2.

(35) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2297−2300.

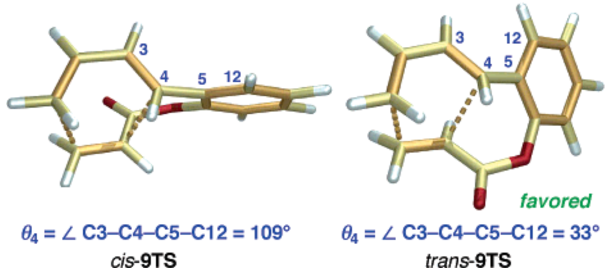

FIGURE 6. B3LYP/6-31+G(d) optimized *cis*- and *trans*-**9TS**. Note the essentially orthogonal diene−arene arrangement in the former. The latter enjoys significantly more stabilizing π-conjugative interactions. Distances are in angstroms.

than the trans TS (Table 1). The smaller cis selectivity found for the pentadienyl acrylates, compared to the hexadienyl acrylates, is probably due to two effects: (1) there may be weakened SOIs in the pentadienyl acrylate cis TSs, owing to the less favorable alignment of the tether carbonyl group with the diene (the tether carbonyl group is twisted out-of-plane in the TS (vide supra)) and (2) there is greater torsional strain about the C4−C5 bond in the pentadienyl acrylate cis TSs (i.e., the H4−C4−C5−H5 dihedral angle = 3° for the cis TS of **1** (*E*, *Z* =H)),[2,3] compared to that in the hexadienyl acrylate cis TSs (i.e., the H4−C4−C5−H5 dihedral angle = 45° for the cis TS of **4**) (Figure 5, eclipsed protons highlighted).

Why Do the Benzo Precursors Give Trans Cycloadducts? The benzo-tethered trienes **9**−**13** undergo trans-selective IMDA reactions. Interestingly, the same stabilizing SOIs seen between C8=O and C3=C4 are evident here in the cis TSs. The alignment between these two π-bonds is similar to that witnessed in the non-benzo cis TSs, with little variation in both C4···C8 distances (2.70−2.77 Å) and C3···O distances (3.31−3.50 Å). Evidently, some other factor is operative in the benzo TSs to override this cis-TS stabilization.

The preference for the trans isomer can be traced to conjugation effects between the diene and the aromatic ring of the tether. Values for the dihedral angle, θ_4, which gives the degree of conjugation between the diene and the aromatic ring in the benzo TSs, for optimized cis and trans TSs for the IMDA reaction of **3** (Scheme 4) are listed in Table S4. Whereas the cis TSs suffer roughly perpendicular diene-arene angles of 103−111°, the trans TSs benefit from substantially more conjugation between these two groups, with dihedral angles in the 29−33° range (Figure 6).

The relative energies of the two conformations of 1-phenyl-1,3-butadiene were calculated to estimate the magnitude of the stabilization enjoyed by the benzo trans TSs over the cis TSs. The dihedral angle between the phenyl and diene groups were set at 30° in one conformation (quasi-trans) and 112° in the other (quasi-cis). The B3LYP/6-31+G(d) method favors the quasi-trans conformation of 1-phenyl-1,3-butadiene over the quasi-cis conformation by 11.7 kJ mol^{-1}. Thus, there is substantially more conjugative stabilization between the benzene and diene groups in the trans TS than in the cis TS. The fact that the calculated trans selectivities for **9**−**13** are generally greater than the experimental values suggests that the DFT calculations may be overestimating the benzo−diene conjugative interaction energy; indeed, it is known that DFT methods tend to overestimate the stability of conjugated systems.[36,37]

Et$_2$AlCl-Promoted and Et$_2$AlCl-Catalyzed IMDA Cycloadditions of Esters. The stereoselectivities listed for substrates **4**−**13** in Table 1 are clearly synthetically useful. Nevertheless, we were intrigued by the potential for stereoselectivity enhancement or reversal in IMDA reactions by way of Lewis acid promotion.

It has been known for many years that Lewis acids impact upon the rate and stereoselectivity of IMDA reactions.[38] Simple Lewis acids generally lead to an improvement in the stereoselectivity of an IMDA process in the same manner observed for intermolecular Diels−Alder reactions, that is, they promote the formation of the product resulting from an endo disposition of the coordinating carbonyl group of the dienophile.[39] Aluminum-based compounds are among the most frequently used promoters, and the relatively mild Lewis acid Et$_2$AlCl is a particularly common reagent. In seminal investigations into IMDA reactions in the 1980s, Roush observed that stoichiometric quantities of Et$_2$AlCl and related Lewis acids are required for complete conversions of ester-substituted trienes.[40] This result was ascribed to the stronger Lewis basicity of the cycloadducts (saturated esters) than the precursor trienes (α,β-unsaturated esters), which form more stable complexes. Interestingly, MeAlCl$_2$ and EtAlCl$_2$ have been shown to catalyze IMDA reactions of α,β-unsaturated ketones[41] and aldehydes,[42] and important competition experiments performed by Keay demonstrated that the unconjugated carbonyl groups of cycloadducts derived from these functionalities are weaker Lewis bases than their conjugated counterparts.[43] Our own studies (vide infra) demonstrate that IMDA reactions involving α,β-unsaturated ester precursors can be catalyzed by Et$_2$AlCl.

Under optimized reaction conditions, Et$_2$AlCl was effective in enhancing the rate and modifying the stereochemical outcome of the IMDA reactions of all 10 hexadienyl acrylate precursors (Table 2).[44] Under Et$_2$AlCl promotion, trienes undergo IMDA reaction at temperatures ca. 100 °C lower than the purely thermal process. Under high dilution conditions (10 mM triene concentrations), stoichiometric amounts of the reagent were needed for complete conversions; with the fumarate precursors **6** and **11** and maleate precursor **8**, 1.9 equiv of Et$_2$AlCl was optimal. Unexpectedly, benzo maleate precursor **13** suffered decomposition when exposed to the same reaction conditions. All five non-benzo precursors **4**−**8** exhibit stronger cis selectivity under Et$_2$AlCl promotion than under purely thermal conditions. Regarding the benzo-tethered precursors, all of which are inherently trans selective, three substrates display a shift in stereoselectivity toward the cis cycloadduct on promotion with

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[36] Choi, C. H.; Kertesz, M.; Karpfen, A. *J. Chem. Phys.* **1997**, *107*, 6712−6721.

[37] Choi, C. H.; Kertesz, M.; Karpfen, A. *Chem. Phys. Lett.* **1997**, *276*, 266−268.

[38] (a) First report of significant rate and product selectivity improvement upon the intermolecular Diels−Alder reaction by Lewis acid: Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, *82*, 4436−4437. (b) First report of significant rate and product selectivity improvement upon the intramolecular Diels−Alder reaction by Lewis acid: Roush, W. R.; Gillis, H. R. *J. Org. Chem.* **1980**, *45*, 4267−4268.

[39] For an excellent discussion on Lewis acid promotion of IMDA reactions, see ref 1f.

[40] Roush, W. R.; Gillis, H. R.; Ko, A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269−2283.

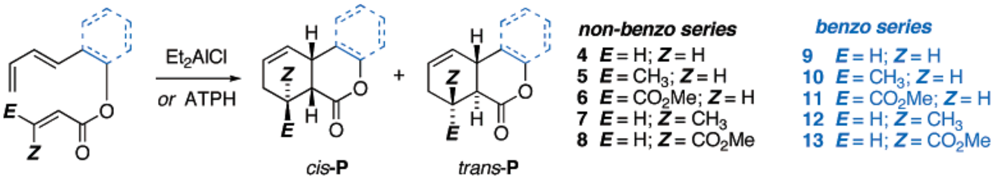
[41] Rogers, C.; Keay, B. A. *Tetrahedron Lett.* **1991**, *32*, 6477−6480.

[42] Marshall, J. A.; Audia, J. E.; Grote, J. *J. Org. Chem.* **1984**, *49*, 5277−5279.

[43] Hunt, I. R.; Rogers, C.; Woo, S.; Rauk, A.; Keay, B. A. *J. Am. Chem. Soc.* **1995**, *117*, 1049−1056.

[44] The Supporting Information contains the yields and stereoselectivities of IMDA reactions of acrylate precursor **9** promoted by seven common Al-based Lewis acid catalysts.

TABLE 2. Lewis Acid Promoted and Catalyzed Intramolecular Diels−Alder Reactions[a]



	IMDA reaction cis/trans ratio (isolated yield)			
substrate	thermal	Et$_2$AlCl-promoted	Et$_2$AlCl-catalyzed	ATPH-promoted
4	92:8 (70%)	>99:1 (72%)	>99:1 (68%)	77:23 (71%)
5	88:12 (76%)	98:2 (86%)	98:2 (71%)	58:42 (60%)
6	83:17 (82%)	96:4 (79%)	96:4 (72%)	54:46 (80%)
7	85:15 (54%)	94:6 (50%)	85:15 (63%)	77:23 (70%)
8	70:30 (90%)	>99:1 (71%)	>99:1 (60%)	93:7 (90%)
9	26:74 (92%)	47:53 (72%)	60:40 (48%)	3:97 (73%)
10	27:73 (100%)	63:37 (89%)	52:48 (81%)	4:96 (75%)
11	29:71 (96%)	23:77 (89%)	22:78 (66%)	5:95 (72%)
12	24:76 (92%)	80:20 (40%)	88:12 (28%)	62:38 (60%)
13	22:78 (87%)	decomposes	79:21 (35%)	78:22 (70%)

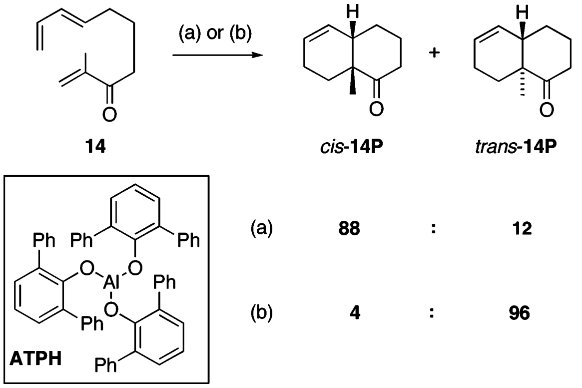
[a] Reaction conditions: (a) 0.01 M substrate concentration in PhMe, Et$_2$AlCl (0.95 equiv per substrate carbonyl group); (b) 0.5−1.0 M substrate concentration in PhMe or PhCl, Et$_2$AlCl (0.2 equiv); (c) 0.1−0.5 M substrate concentration in PhMe or PhCl, ATPH (1.5 equiv per substrate carbonyl group). For reaction temperatures and times, see SI.

Et$_2$AlCl. The stereochemical switch is most dramatic in the case of *Z*-crotonate **12** (thermal: 76% trans; Et$_2$AlCl-promoted: 80% cis). Interestingly, fumarate **11** exhibits an essentially unaltered trans selectivity upon promotion with Et$_2$AlCl.

Attempts to catalyze these IMDA reactions with Et$_2$AlCl at 10 mM initial substrate concentrations were unsuccessful, with incomplete consumption of starting triene being witnessed. Consistent with previous findings[40] were our observations that conversion rates of precursors invariably reflected the amount of reagent added. Complete conversions of precursors can be realized with substoichiometric amounts of Et$_2$AlCl, however, if high concentrations are employed. Routinely, 0.5 M substrate concentrations and temperatures a little higher than those used for the stoichiometric Et$_2$AlCl-promoted process are necessary.[45] Et$_2$AlCl-catalyzed IMDA reactions of esters generally compare favorably with those from Et$_2$AlCl-promoted runs. Evidently, α,β-unsaturated esters *can* compete with their saturated counterparts for aluminum-based Lewis acids in concentrated solutions. In the case of the maleate precursor **13**, Et$_2$AlCl is effective in promoting the IMDA reaction when present in catalytic amounts in high concentration solutions, yet the same reagent (1.9 equiv) leads to substrate decomposition at high dilution![46] It is noteworthy that four of the five benzo-tethered precursors display a shift in stereoselectivity toward the cis cycloadduct on catalysis of the IMDA process with Et$_2$AlCl, as compared to the heat-promoted reaction.

ATPH-Promoted IMDA Cycloadditions. Yamamoto and co-workers have described a very different stereochemical outcome in the promotion of Diels−Alder reactions by the sterically hindered Lewis acids methyl aluminum di(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) and aluminum tris(2,6-diphenylphenoxide) (ATPH), which encourage exo-selective intermolecular Diels−Alder reactions.[47,48] One example of an IMDA reaction was also described in this elegant investigation, detailing a dramatic switch from cis to trans stereoselectivity with 1,3,9-decatrienone **14** (Scheme 5). These very unusual outcomes are rationalized in terms of a destabilization of the endo TS upon carbonyl group complexation to Al in the deep binding pocket of these promoters. The need for a stoichiometric quantity of these bulky Lewis acid promoters is curious in light of the relative Lewis base strengths of cycloadducts and precursor (vide supra).[49] To our knowledge, no other reports of ATPH, or MAD-promoted IMDA reactions are present in the literature.

SCHEME 5. Cis/Trans IMDA Stereocontrol by Lewis Acid Promoters According to Yamamoto[47a]



[a] Reaction conditions: (a) Me$_3$Al (unspecified amount), CH$_2$Cl$_2$, −78 to −20 °C, 75%; (b) ATPH (1.1 equiv), CH$_2$Cl$_2$, −78 to −20 °C, 69%.

As can be seen by inspection of Table 2, with the non-benzo substrates of common structure **2**, ATPH generally causes a modest shift in stereoselection toward the trans-fused product, when compared to the thermal process.[50] Unfortunately, the switch to the trans isomer is of insufficient magnitude for the

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(45) Control experiments demonstrated that under the conditions employed, triene conversion by way of the thermal (uncatalyzed) IMDA reaction is negligible.

(46) These findings are consistent with an unstable **13**·2Et$_2$AlCl complex.

(47) Maruoka, K.; Imoto, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 12115−12116.

(48) For reviews, see the following: (a) Saito, S.; Yamamoto, H. *Chem. Commun.* **1997**, 1585−1592. (b) Saito, S. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1, pp 189−306.

(49) We presume that ligand exchange at aluminum is either an associative or S$_N$2-type process, since neither would be possible with these complexes.

process to be synthetically useful. Non-benzo maleate **8** behaves differently to the four other substrates in that ATPH inexplicably promotes a more cis selective reaction of this precursor. With the benzo substrates of common structure **3**, ATPH reinforces the inherent thermal stereoselectivity to deliver a very strongly trans-selective IMDA reaction for unsubstituted **9** and *E*-substituted trienes **10** and **11**. Conversely, *Z*-substituted trienes **12** and **13** exhibit cis-selective IMDA reactions upon exposure to ATPH. The results with **8**, **12**, and **13** are intriguing in that inherently exo-selective processes are being made endo-selective by ATPH, i.e., a reversal of its known function.[47]

Whereas a detailed analysis of the experimental findings from Lewis acid mediated IMDA reactions are the subject of ongoing investigations, a brief discussion is offered here. In reactions employing Et_2AlCl as catalyst or promoter, IMDA reaction cis selectivity is enhanced because of the known endo preference for a Lewis acid-complexed carbonyl group, in these cases the carbonyl group of the tether. The Et_2AlCl−mediated IMDA reactions of the two fumarate substrates **6** and **11** are interesting since the former non-benzo analogue **6** shows enhanced cis selectivity, whereas the latter benzo analogue **11** exhibits enhanced trans selectivity. Presumably, productive complexation of the non-benzo fumarate substrate **6** occurs readily at the tether carbonyl, thus promoting the formation of the cis isomer, in line with the other substrates. The enhanced trans selectivity for benzo substrate **11** can be explained by productive Et_2AlCl complexation at the C10 ester carbonyl group; in this case the tether carbonyl is less Lewis basic owing to ester conjugation with the aromatic ring. With ATPH as promoter, Yamamoto's steric argument holds for 7 of the 10 substrates. Of the three exceptions, two (**8** and **13)** involve the maleate dienophile. Perhaps the maleates do not follow the standard reactivity pattern because, owing to repulsions between the C10 and C8 carbonyls, several different conformations of similar energy are adopted upon complexation with ATPH. A more detailed analysis of these intriguing experimental findings will be presented in a forthcoming report from our group.

Concluding Remarks

The first systematic survey of IMDA reactions of ester linked decatrienes has demonstrated that substrates of general structure **2** (Scheme 2) undergo cis-selective thermal reactions, while their benzannulated cousins of general structure **3** undergo trans-selective thermal reactions. In most cases, the application of Lewis acid promoters enhance the thermal process to furnish one diastereomer in ≥94% stereoselectivity: with substrates of general structure **2,** a suitable Lewis acid is Et_2AlCl, whereas substrates of general structure **3** require ATPH. Under high concentration conditions, Et_2AlCl has been shown to catalyze intramolecular Diels−Alder reactions of ester-containing substrates for the first time.

The analysis of intramolecular Diels−Alder reaction transition structures using DFT methods continues to provide important new insights. We reaffirm the validity of the DFT method in this paper. With substrates of general structure **2**, stabilizing secondary orbital interactions between the tether carbonyl group and the diene operate to stabilize the transition structure leading to the cis isomer. Conversely, with substrates of general structure **3**, π-conjugative interactions between the diene and the aromatic ring of the tether stabilize the transition structure leading to the trans isomer.

Major reviews of the IMDA reaction explain stereoselectivities on the basis of the location of dienophile activating groups and their influence on bond length asynchronicities in TSs: an activating group at the internal position was thought to give rise to advanced peripheral bond formation and a cis-selective IMDA reaction, whereas an activating group at the peripheral position was thought to give rise to advanced internal bond formation and a trans-selective IMDA reaction.[1e,f] In the present study and in our earlier studies with pentadienyl acrylates[3] we find no such correlation between bond length asynchronicity and cis/trans stereoselectivity of intramolecular Diels−Alder reactions.

Experimental Section

General Procedure for Thermal IMDA Reactions. A stirred 5−10 mM concd solution of the triene substrate and BHT (0.05−0.10 equiv) in PhMe, PhCl, or 1,2-$Cl_2C_6H_4$ under Ar or N_2 was heated to reflux until ^1H NMR analysis of the reaction mixture indicated >95% conversion of the starting material. The solvent was removed under reduced pressure, and product ratios were determined by GC and/or ^1H NMR analysis. The products were separated by flash chromatography or HPLC of the crude reaction mixture.

General Procedure for Et_2AlCl-Promoted IMDA Reactions. To a stirred 10 mM concd solution of the triene substrate in PhMe under Ar or N_2 at the temperature specified in the SI (range: 0−110 °C) was added Et_2AlCl (1.8 M solution in PhMe, 0.95 or 1.90 equiv). Stirring was continued at the same temperature until analysis indicated >95% conversion of the starting material. Saturated aq NH_4Cl was added, and the organic layer was collected, then washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and product ratios were determined by GC and/or ^1H NMR analysis. Products were separated by flash chromatography or HPLC of the crude reaction mixture.

General Procedure for Et_2AlCl-Catalyzed IMDA Reactions. To a degassed 0.5 or 1.0 M concd stirred solution of the triene substrate in PhMe or PhCl under Ar or N_2 at the temperature specified in the SI (range: 80−132 °C) was added Et_2AlCl (1.8 M solution in PhMe, 0.2 equiv). Stirring was continued at the same temperature until ^1H NMR analysis indicated complete consumption of the starting material. After the mixture was diluted with CH_2Cl_2, saturated aq NH_4Cl was added, and the organic layer was collected, then washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and product ratios were determined by GC and/or ^1H NMR analysis. Products were separated by flash chromatography or HPLC of the crude reaction mixture.

General Procedure for ATPH Promoted IMDA Reactions. After Yamamoto et al.,[51] to a degassed, stirred solution of 2,6-diphenylphenol (3.0 equiv) in PhMe or PhCl at room temperature under Ar or N_2 was added dropwise $AlMe_3$ (2.0 M in toluene, 1.0 equiv). Methane gas was immediately evolved. The resulting yellow solution was stirred at room temperature for 1 h. To this 0.1 −0.5 M solution of ATPH (1.5 or 3.0 equiv) in PhMe or PhCl under Ar or N_2 at the temperature specified in the SI (range: 80−132 °C) was added dropwise the triene precursor (1.0 equiv). Stirring was continued at the same temperature until ^1H NMR analysis indicated complete consumption of the starting material. After the mixture was diluted with CH_2Cl_2, saturated aq NH_4Cl was added. The organic layer was collected, washed with brine, and dried over

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(50) Exposure of fumarate **6** to $(PhO)_3Al$ under conditions otherwise identical to those used for the ATPH mediated reactions delivered a cis 85:15 trans ratio of cycloadducts; i.e., there was essentially no change from the ratio observed for the thermal IMDA reaction.

(51) Saito, S.; Nagahara, T.; Shiozawa, M.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6200−6210.

$MgSO_4$. The solvent was removed under reduced pressure, and product ratios were determined by GC and/or ^{1}H NMR analysis. Products were separated by flash chromatography or HPLC of the crude reaction mixture.

Representative Thermal IMDA Reaction of 2((*E*)-Buta-1,3-dienyl)phenyl Acrylate (9). According to the general procedure, a solution of **9** (176 mg, 0.88 mmol) and BHT (10.0 mg, 0.04 mmol) in toluene (100 mL) was heated at reflux for 12 h. Flash chromatography (15 g silica gel, 1:1 CH_2Cl_2-hexane) gave a mixture of the two diastereomeric adducts *cis*-**9P** and *trans*-**9P** as a colorless oil (162 mg, 0.81 mmol, 92%, *cis*-**9P**/*trans*-**9P** = 26:74). Separation was performed using preparative HPLC (EtOAc−hexane 5:95).

***rel* 6a*R*,7,8,10a*S*-Tetrahydro-6*H*-dibenzo[b,d]pyran-6-one.** Compound *cis*-**9P** was recrystallized from CH_2Cl_2−hexane as colorless rhombs: mp 72−77 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21−7.26 (2H, m), 7.11−7.16 (1H, m), 7.03 (1H, dd, $J = 8.4$, 1.4 Hz), 5.77−5.84 (1H, m), 5.61 (1H, ddd, $J = 10.3$, 4.4, 2.2 Hz), 3.68 (1H, ddd, $J = 6.3$, 3.2, 3.0 Hz), 3.04−3.09 (1H, m), 2.27−2.41 (2H, m), 2.06−2.17 (1H, m) and 1.75−1.86 (1H, m) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 150.9, 128.9, 128.5, 128.2, 126.4, 125.9, 124.8, 117.0, 37.6, 36.3, 21.9 and 21.6 ppm. IR (thin film): υ 1759, 1230, 1132, 751 cm^{-1}. MS (55 eV, EI) *m*/*z* (%): 200 (100) $[M]^+$, 171 (44), 144 (88), 131 (45). HRMS (200 eV, EI): calcd for $C_{13}H_{12}O_2$ $[M]^+$, 200.0837; found, 200.0835.

***rel* 6a*R*,7,8,10a*R*-Tetrahydro-6*H*-dibenzo[b,d]pyran-6-one.** Compound *trans*-**9P** was recrystallized from CH_2Cl_2−hexane as colorless needles: mp 85−88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25−7.35 (2H, m), 7.08−7.19 (2H, m), 6.25 (1H, ddd, $J = 10.2$, 4.2, 1.8 Hz), 5.97−6.04 (1H, m), 3.55 (1H, d, $J = 13.2$ Hz), 2.12−2.49 (4H, m) and 1.76 (1H, ddd, $J = 25.2$, 12.3, 6.3 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 151.5, 129.9, 128.2, 126.9, 124.5, 123.9, 123.0, 117.1, 40.6, 34.9, 24.7 and 22.0 ppm. IR (thin film): υ 1775, 1455, 1221, 1140, 755 cm^{-1}. MS (200 eV, EI) *m*/*z* (%): 200 (100) $[M]^+$, 185 (31), 172 (41), 171 (44), 144 (86), 131 (44). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.84; H, 6.08.

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Supporting Information Available: Synthetic procedures and characterization details, ^{1}H and ^{13}C NMR spectra, thermal ellipsoid plots for compounds *cis*-**8P**, *trans*-**8P**, *cis*-**9P**, *trans*-**10P**, *trans*-**11P**, *cis*-**12P**, and *cis*-**13P**, the Cartesian coordinates of B3LYP/6-31+G(d) optimized TS geometries, cis/trans ratios and energy differences from electronic energies, enthalpies and free energies, and geometric parameters for transition structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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