Controlling *cis*/*trans*-selectivity in intramolecular Diels–Alder reactions of benzo-tethered, ester linked 1,3,9-decatrienes†

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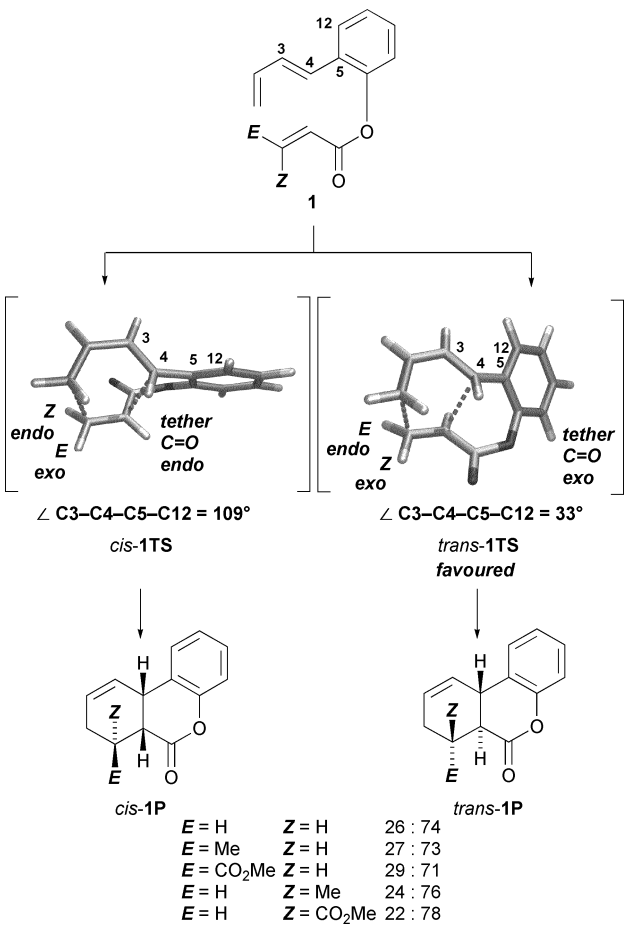
Predictions from DFT (B3LYP/6-31 G(d))-computed stereoisomer product distributions for *intra*molecular Diels–Alder (IMDA) reactions have been successfully replicated in the laboratory. Benzo-tethered hexadienyl acrylates generally undergo moderately *trans*-selective IMDA reactions which, as suggested by DFT calculation, arise from two opposing transition structure (TS) features: stabilising secondary orbital interactions, which are stronger in the *cis*-TSs, and stabilising π-conjugative interactions between the benzo moiety and the 1,3-diene component – which are stronger in *trans*-TSs. Substrates carrying a removable substituent (*i.e.* Br or TMS) at C3 of the diene or C12 of the aromatic ring are predicted to undergo highly *cis*-selective thermal IMDA reactions by steric destabilisation of the *trans*-TS. A substrate carrying a two atom tether between C3 and C12 is predicted to undergo a highly *trans*-selective intramolecular cycloaddition by destabilisation of the *cis*-TS. These calculations are borne out experimentally.

Introduction

In a recent paper, we presented experimental and computational studies of the intramolecular Diels–Alder[1] (IMDA) reactions of a series of hexadienyl acrylates **1** (Scheme 1) bearing substituents at the dienophile terminus.[2] These reactions can furnish two distinct diastereoisomeric products (**P**), namely *cis*-**1P** and *trans*-**1P**, which differ in the stereochemistry about the ring fusion. Of interest was the observation that, whereas the IMDA reaction of the cognate system possessing the ethylene tether (–$CH_2CH_2OC(=O)$–) displays strong *cis* stereoselectivity, the IMDA reactions of the benzo-tethered systems exhibit moderate *trans* selectivity. Moreover, this *trans* selectivity is not markedly influenced by the terminal dienophile substituent, an observation in stark contrast to earlier work with pentadienyl acrylates, which showed a clear stereochemical dependence upon both the nature of the dienophile (C9) substituent *and* the dienophile geometry.[3,4]

The preference for the *trans*-isomer was traced – by means of B3LYP/6-31 + G(d) calculations – to conjugation effects between the diene and the aromatic ring of the tether, as reflected in the magnitude of the dihedral angle θ between the diene and the aromatic ring in the *cis* and *trans* IMDA TSs for **1**. Whereas the *cis*-TSs suffer nearly perpendicular diene–arene dihedral angles of 103–111°, the *trans*-TSs benefit from substantially increased



Scheme 1 Benzo-tethered hexadienyl acrylate IMDA reaction *cis*- and *trans*-B3LYP/6-31 + G(d) transition structures (TS)[2] and bicyclic products (P).

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† Electronic supplementary information (ESI) available: Cartesian coordinates, imaginary frequencies, energies, enthalpies and free energies of the *cis* and *trans* IMDA TSs for **2–7**, anisotropic thermal ellipsoid plots for *cis*-**3P**, *cis*-**4P**, *cis*-**5P**, *cis*-**6P** and *trans*-**7P**, and ^{1}H and ^{13}C NMR spectra. See DOI: 10.1039/b716910h

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conjugation between these two groups, with dihedral angles in the 29–33° range.

These markedly different dihedral angles between the aromatic ring and the C3-C4 double bond in the TSs for the IMDA reaction of **1** suggested ways of tuning the *cis* : *trans* product ratio from these reactions (Fig. 1). Thus, the placement of a sufficiently large group at either C3 or C12[5] should disfavour the *trans* TS relative to the *cis* TS. Furthermore, linking C3 to C12 by a short tether should disfavour the *cis* TS, while having only a minor effect on the *trans* TS energy. The aims of the present study are to investigate these predictions, both computationally and experimentally. Fumarate esters **2–7** (Fig. 1) were selected for the present study since they represent the more reactive triene precursors towards heat-promoted cycloadditions.

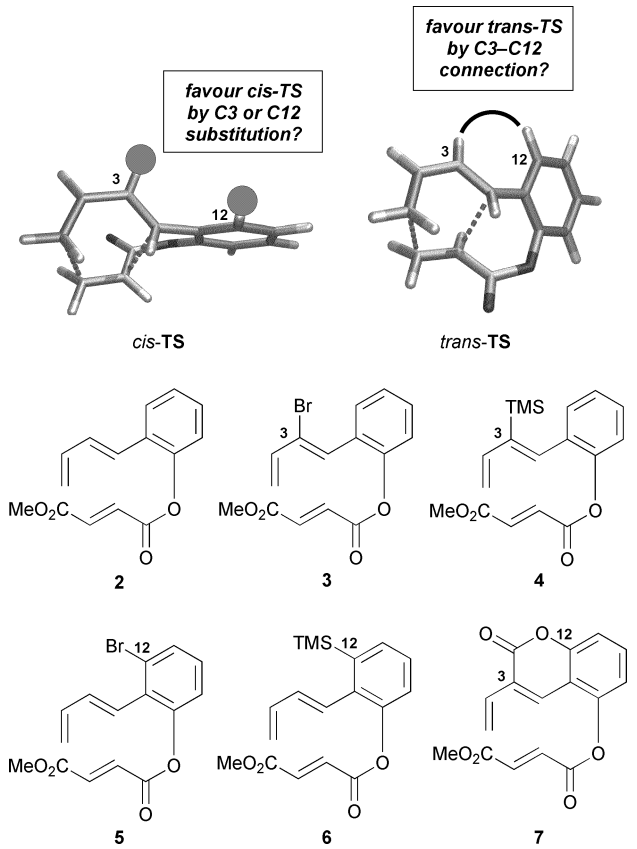


Fig. 1 IMDA reaction precursors under scrutiny.

Results and discussion

DFT-predicted *cis*/*trans* stereoselectivities

Gas phase *cis* and *trans* IMDA TSs for the 10-*E*-CO_2Me-substituted molecules **2**, **3**, **4**, **5**, **6** and **7** were computed at the B3LYP/6-31G(d) level (see Experimental Section) and their relative enthalpies $\Delta H^{\ddagger}_{CT}$ [$=H^{\ddagger}(cis) - H^{\ddagger}(trans)$], free energies $\Delta G^{\ddagger}_{CT}$ [$=G^{\ddagger}(cis) - G^{\ddagger}(trans)$] and *cis* : *trans* product ratios (calculated from the $\Delta G^{\ddagger}_{CT}$ values) are given in Table 1.

For **2**, which lacks substituents at either C3 or C12 positions, the *trans* product is moderately preferred, with a predicted *cis* : *trans* ratio of 25 : 75 at 298.15 K which is in accord with the experimental value of 29 : 71 (383 K) and with the earlier B3LYP/6-31 + G(d) predicted ratio of 31 : 69.[2] The dihedral angle, θ, in the *trans* TS is 29°, compared to 109° in the *cis* TS. Placement of bulky substituents at either C3 or C12, should, by dint of destabilising steric interactions between the C3 and C12 groups in the *trans* TS, lead to strong *cis* selectivity. Indeed, the calculations confirm this analysis. Thus, greater than 95% *cis* selectivity is predicted for **3–6**, which possess either Br or TMS at the aforementioned positions. Despite the presence of a significant steric clash between the Br/TMS group and the C3/C12 proton, the *trans* TSs for **3–6** don't reveal any marked geometric changes from that for **2**, although there is a 4–7° increase in the magnitude of θ (Fig. 2). As expected, connecting C3 and C12 with a two atom oxycarbonyl bridge, to give **7**, leads to a predicted 100% *trans* selectivity, the $\Delta G^{\ddagger}_{CT}$ being a massive 55 kJ mol^{-1}. In this case, the *cis*-TS must endure a large energetic penalty to accommodate the oxycarbonyl tether.

Table 1 B3LYP/6-31 G(d) relative enthalpies, $\Delta H^{\ddagger}_{CT}$, and free energies, $\Delta G^{\ddagger}_{CT}$, for *cis* and *trans* IMDA transition structures (kJ mol^{-1}, 298.15 K, gas phase, 1 atm) and *cis* : *trans* product ratios

	Reactant	$\Delta H^{\ddagger}_{CT}$[a]	$\Delta G^{\ddagger}_{CT}$[b]	*cis* : *trans*
	2	3.98	2.68	25 : 75
	3	−7.29	−7.27	95 : 5
	4	−8.77	−13.2	99.5 : 0.5
	5	−8.62	−9.88	98 : 2
	6	−15.6	−15.6	100 : 0
	7	56.5	55.4	0 : 100

[a] $\Delta H^{\ddagger}_{CT} = H^{\ddagger}(cis) - H^{\ddagger}(trans)$. [b] $\Delta G^{\ddagger}_{CT} = G^{\ddagger}(cis) - G^{\ddagger}(trans)$.

Experimental verification of predicted *cis*/*trans* selectivities

IMDA precursors 3 and 4, substituted at C3 of the diene

C3-Diene-substituted precursors were prepared from the TBS ether of salicylaldehyde, **9**[6] (Scheme 2). Ramirez dibromoolefination[7] of aldehyde **9** gave 1,1-dibromoalkene **10**, which underwent a selective[8] Negishi coupling[9] with vinylzinc bromide to give *Z*-bromodiene **11**. Deprotection of the TBS group with TBAF gave phenol **12**, which was esterified with methyl fumaroyl chloride **13** in the presence of DBU to give bromotriene IMDA precursor **3**. Bromotriene **3** cyclises slowly at room temperature; the IMDA reaction is complete within 3 h at 80 °C to furnish a mixture rich in the *cis*-cycloadduct, *cis*-**3P**. Following separation, the identity of the major diastereomer was confirmed through single crystal X-ray analysis (Table 2).

We initially envisaged a construction of the C3-TMS precursor **4** through lithium–halogen exchange of bromide **11** with *n*-BuLi followed by trapping of the 2-lithio-1,3-butadiene intermediate with TMSCl to give **14** (Scheme 2). In the event, this procedure led to product **15**, in which the TBS and TMS groups are transposed relative to compound **14**. The mechanism for the formation of **15** presumably involves a retro-1,5-Brook rearrangement[10,11] of the TBS group, followed by trapping of the resulting phenoxide with TMSCl. After some experimentation with unsuccessful routes, we elected to take advantage of the rearrangement. Following the conversion of phenol **12** into the corresponding TMS ether **14**, exposure to *n*-BuLi followed by the addition of methyl fumaroyl chloride delivered *cis*-fused tricycle *cis*-**4P** directly. Neither the

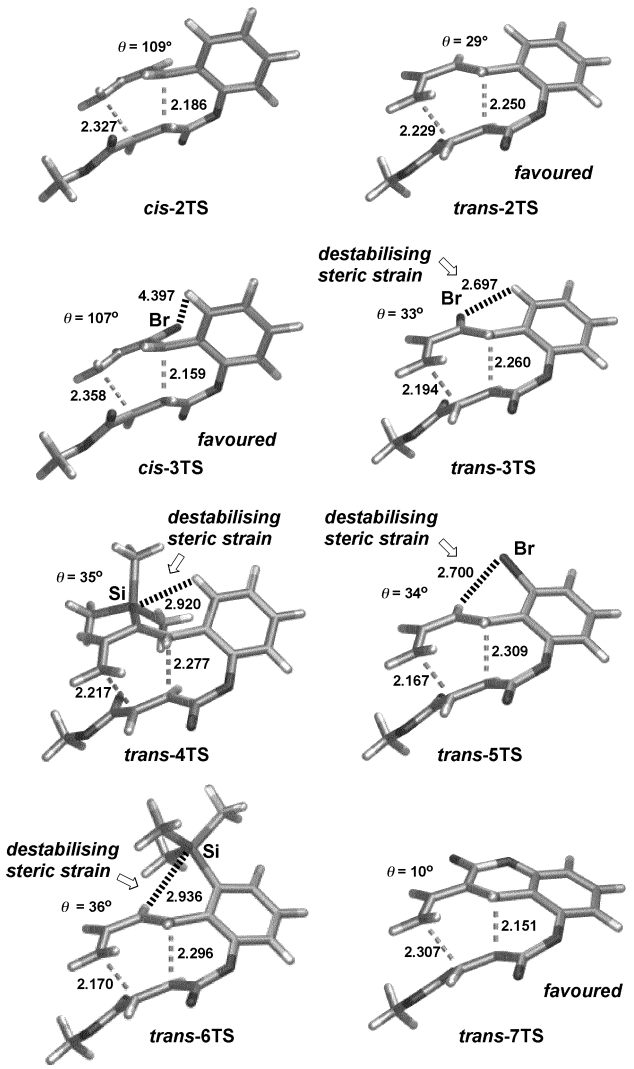


Fig. 2 Selected B3LYP/6-31G(d) optimised TSs. Distances are in Å.

triene IMDA precursor **4** nor diastereomeric cycloadduct *trans*-**4P** were detected in the product mixture. The rapid cyclisation of IMDA precursor **4** can be rationalised on both steric and electronic grounds: the TMS group would stabilise the s-*cis* diene conformer relative to its s-*trans* congener and silicon's electropositive characteristic would electronically activate the 1,3-butadiene towards cycloaddition with electron deficient dienophiles. The stereochemistry of *cis*-**4P** was secured through single crystal X-ray analysis of the purified product (Table 2).

IMDA precursors 5 and 6, substituted at the aromatic ring

Triene IMDA precursors **5** and **6**, carrying bromine and trimethylsilyl groups at aromatic ring position C12 were prepared from 3-bromosalicylaldehyde **17**,[12,13] according to the sequence depicted in Scheme 3. A Wittig reaction between aldehyde **17** and the ylide derived from allyltriphenylphosphonium bromide gave diene **18** with high *E*-selectivity. Esterification with methyl fumaroyl chloride gave C12-bromo precursor **5** in modest yield. Lithium–bromine exchange of the lithium phenoxide of **18** with *n*-BuLi followed by the introduction of trimethylsilyl chloride and acidic work-up gave phenol **19**, which was esterified to C12-TMS precursor **6** in a similar yield to the bromine-containing substrate. IMDA reactions of **5** and **6** proceeded smoothly with complete stereocontrol – within the limits of detection – to give *cis*-**5P** and *cis*-**6P**, respectively. Once again, the identities of these compounds were secured through single crystal X-ray analyses (Table 2).

The C3–C12 tethered IMDA precursor 7

C3–C12 lactone-tethered IMDA precursor **7** was prepared in four steps from **20**, the mono-MOM ether of 2-formyl resorcinol[14] (Scheme 4). The *E*-crotonyl ester of phenol **20**, namely compound **21**, was prepared easily but underwent ester hydrolysis on attempted purification, presumably due to neighbouring group participation from the aldehyde. Nevertheless, treatment of unpurified **21** with DBU instigated the desired intramolecular aldol condensation[15] to furnish diene **22**. Acidic hydrolysis of the MOM ether gave phenol **23** cleanly. The limited solubility of **23** in common organic solvents prompted the use of DMF as solvent for the esterification to IMDA precursor **7**. Interestingly, intramolecular cycloaddition of **7** required significantly higher temperatures than the other IMDA precursors examined in this study. Nevertheless, only one diastereomer, *trans*-**7P**, could be detected upon ^{1}H NMR spectroscopic analysis of the crude product mixture, the structure and stereochemistry of which was confirmed by a single crystal X-ray analysis (Table 2).

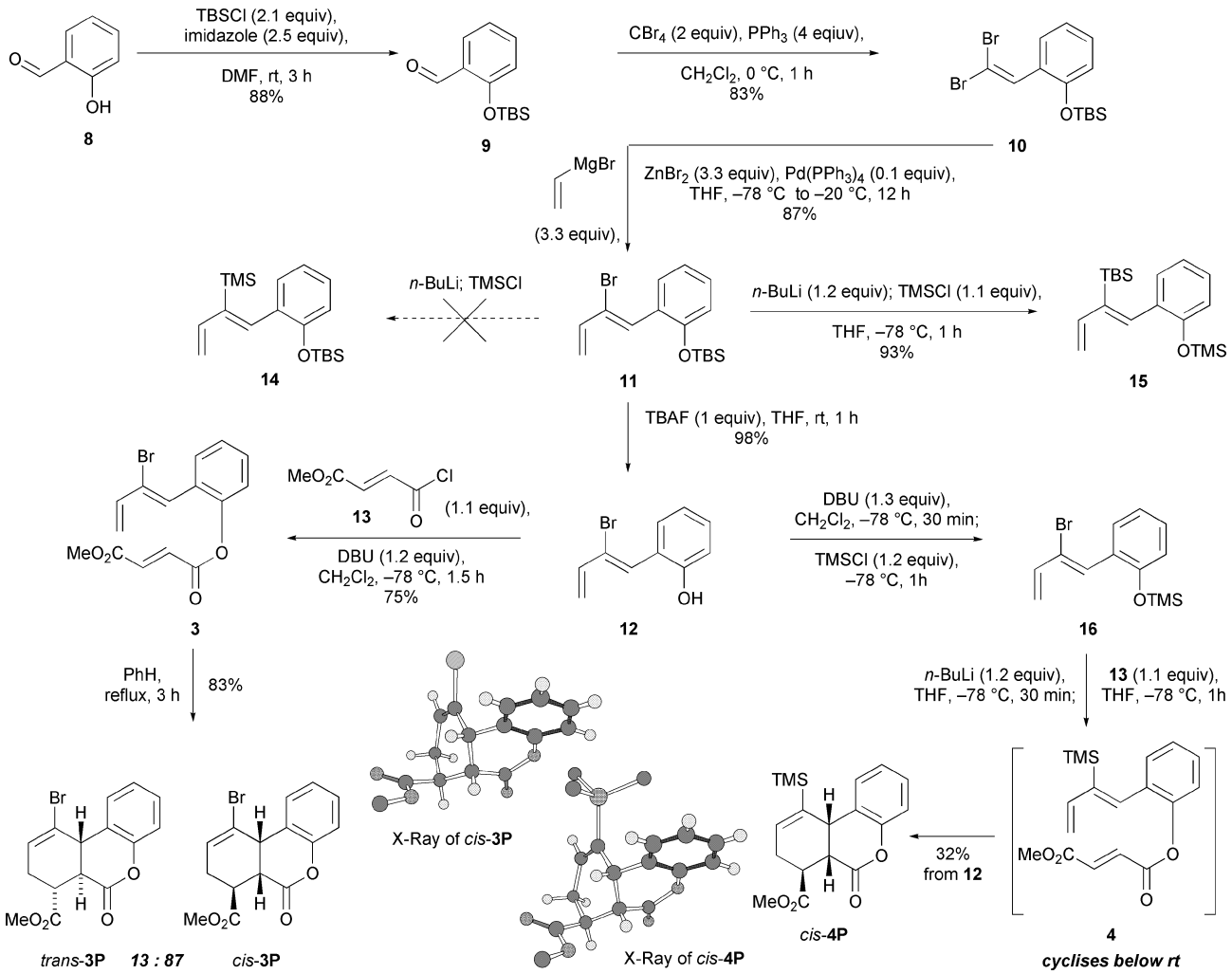
Concluding remarks

This work has shown that an analysis of the geometries of transition structures of intramolecular Diels–Alder reactions can lead to the development of new methods for stereochemical control. Importantly, this work also demonstrates that IMDA stereocontrol methods can be confirmed firstly through computational investigations before being subjected to experimental testing. In the present study, the recognition that the *cis*- and *trans*-IMDA TSs of benzo-tethered trienes **1** (Scheme 1) place the C3 and C12 hydrogens apart and in close proximity, respectively, has allowed the development of reactions with very high levels of selectivity *for either diastereomer.* Thus, whereas the C3/C12 unsubstituted precursor **2** undergoes a weakly *trans*-selective reaction (*trans* : *cis* ratio = 71 : 29), precursors carrying a removable bromine or trimethylsilyl group at one of these positions, namely **3**, **4**, **5** and **6**, undergo strongly *cis*-selective reactions. In these cases, the steric clash between the proximate C3 and C12 substituents in the *trans*-TSs leads to destabilisation relative to the *cis*-TS. In contrast, linking the C3 and C12 positions with a two-atom tether, as in system **7**, places enormous strain on the *cis*-TS and consequently, the reaction is completely *trans*-selective. In the case of the *cis*-selective reactions, we emphasise the use of readily removable C3 or C12 substituents. In the case of the *trans*-selective reaction, whereas the C3/C12 tether is not readily removable, the oxycarbonyl group offers the opportunity for further elaboration.[16]

Experimental section

Computational methods

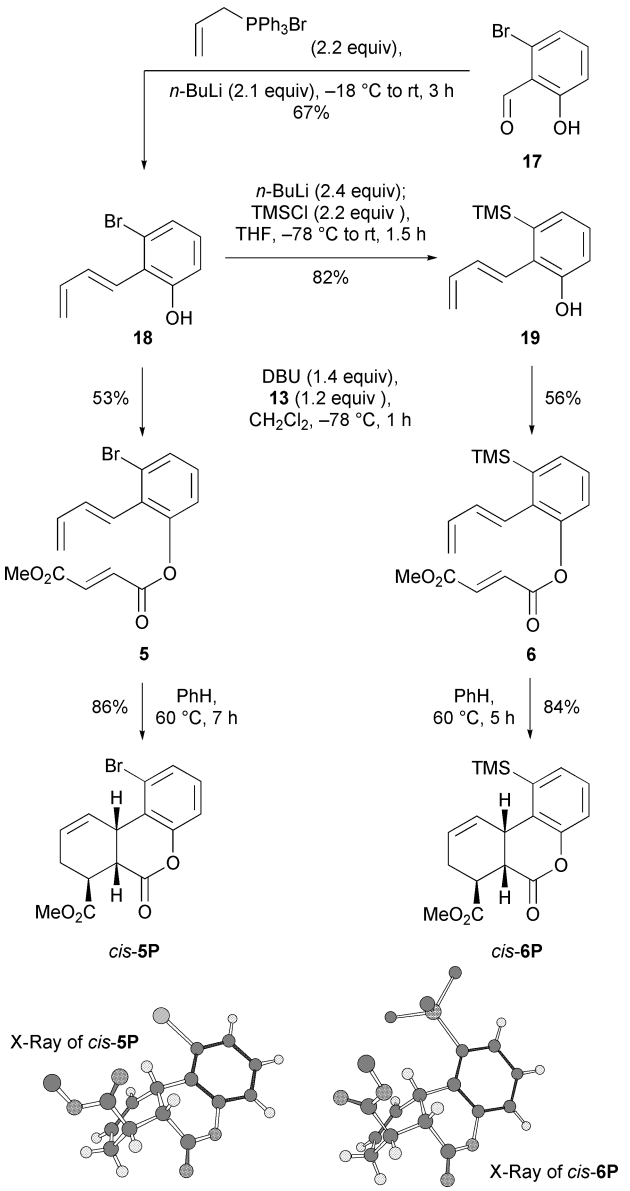
Gas phase transition structures (TSs) for intramolecular Diels–Alder reactions were optimised using the B3LYP functional[17] and



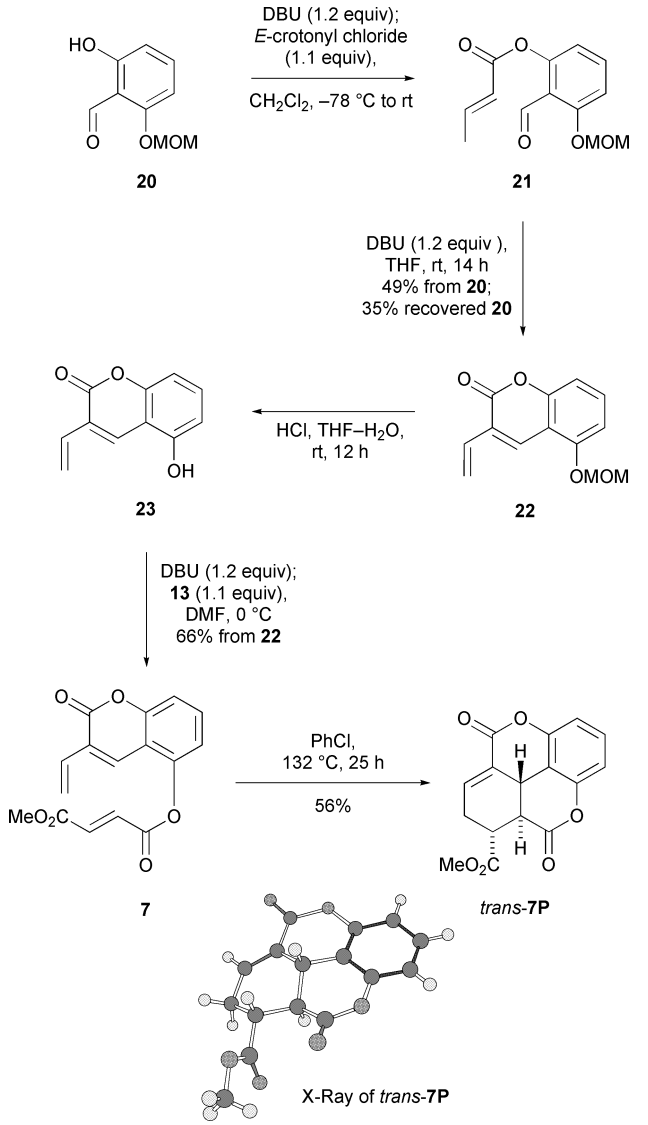
Scheme 2 Synthesis and IMDA reactions of precursors **3** and **4**, substituted at C3 of the diene. Methyl group hydrogens are omitted from X-ray molecular structures for clarity.

Table 2 X-ray crystallographic data for compounds *cis*-**3P**, *cis*-**4P**, *cis*-**5P**, *cis*-**6P** and *trans*-**7P**

	cis-**3P**	*cis*-**4P**	*cis*-**5P**	*cis*-**6P**	*trans*-**7P**
CCDC No.	664829	664830	664831	664832	664833
Formula	$C_{15}H_{13}BrO_4$	$C_{18}H_{22}O_4Si$	$C_{15}H_{13}BrO_4$	$C_{18}H_{22}O_4Si$	$C_{16}H_{12}O_6$
M	337.17	330.46	337.17	330.46	300.27
Crystal system	triclinic	monoclinic	monoclinic	triclinic	orthorhombic
Space group	$P\bar{1}$	$C2/c$	$P2_1/c$	$P\bar{1}$	$Pna2_1$
a/Å	6.7091(2)	44.1595(17)	9.3080(2)	9.3794(2)	11.7777(5)
b/Å	8.0770(2)	6.5892(2)	10.1060(2)	9.9026(2)	5.4798(1)
c/Å	13.7233(4)	30.3735(11)	14.4185(3)	10.4159(2)	20.1905(6)
α/°	103.9603(17)	—	—	86.4869(12)	—
β/°	93.8881(18)	127.2050(11)	95.7272(12)	66.0202(13)	—
γ/°	109.0036(18)	—	—	79.5571(15)	—
V/Å^3	673.62(3)	7039.2(4)	1349.53(5)	869.21(3)	1303.08(7)
Z	2	16	4	2	4
T/K	200	200	200	200	200
Measured reflections	11941	48216	29685	19510	14752
Independent reflections	3101	6112	3094	3968	1527
Reflections in refinement	2507 [$I>3\sigma(I)$]	3703 [$I>2\sigma(I)$]	1922 [$I>3\sigma(I)$]	3031 [$I>3\sigma(I)$]	1370 [$I>2\sigma(I)$]
R	0.0272	0.039	0.0208	0.0353	0.026
Rw	0.0321	0.041	0.0233	0.0371	0.031
S	1.0615	1.15	1.1202	1.0878	1.15



Scheme 3 Synthesis and IMDA reactions of precursors **5** and **6**, substituted at the aromatic ring. Methyl group hydrogens are omitted from X-ray molecular structures for clarity.



Scheme 4 Synthesis and IMDA reaction of C3–C12 tethered precursor **7**. Methyl group hydrogens are omitted from X-ray molecular structure for clarity.

the 6-31G(d) basis set.[18] Harmonic vibrational frequencies (at the same level of theory) were employed to characterise the TSs as first order saddle points (one negative Hessian eigenvalue) and to provide thermal corrections for calculating the enthalpies and free energies of the TSs at 298.15 K and 1 atm pressure. The Gaussian 03[19] program package was used throughout. Optimised geometries (in Cartesian coordinate form) and their energies are provided as Electronic Supplementary 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.[2–4,20–22] Importantly, we have shown that the B3LYP/6-31G(d) method correctly predicts *cis* : *trans* ratios for the IMDA reactions of a sizable number of substituted pentadienyl- and hexadienyl-acrylates, often with an accuracy of 1 kJ mol^{-1}.[2–4,22] This level of theory is, therefore, adequate for this study. Although the DFT calculations ignored solvent effects, we do not expect such effects to markedly influence *cis* : *trans* product ratios because the experimental IMDA reactions carried out in this study employed weakly polar aprotic solvents (benzene and chlorobenzene). This expectation was confirmed by carrying out a polarised continuum model (PCM) calculation[23] on the IMDA reaction of **2**, using toluene as solvent. The PCM calculation gave a *cis* : *trans* product ratio of 22 : 78, which is similar the gas phase ratio of 25 : 75 (Table 1).

Synthesis – General

NMR spectra were recorded at 298 K using a Varian INOVA 300 or Varian INOVA 500 spectrometer. Residual protio-chloroform (δ 7.26 ppm), benzene (δ 7.15 ppm), and methanol (δ 3.31 ppm)

were used as internal references for ^{1}H NMR spectra measured in these solvents. The ^{13}C NMR resonance of chloroform (δ 77.1 ppm), benzene (δ 128.1 ppm) and methanol (δ 49.0 ppm) were used as internal references for ^{13}C NMR spectra measured in these solvents. Assignment of proton signals was assisted by ^{1}H–^{1}H COSY and NOESY experiments when necessary; assignment of carbon signals was assisted by DEPT experiments, HSQC and HMBC experiments were employed when necessary. IR spectra were recorded on a Perkin-Elmer Spectrum One spectrometer as neat films on NaCl plates for oils or as KBr disks for solid products. Mass spectra were recorded by the Mass Spectrometry Facility of the Research School of Chemistry, Australian National University, Canberra on a VG Autospec M series sector (EBE) MS for EI, VG Quattro II triple quadrupole MS for LR ESI and Bruker Apex3 4.7T FTICR-MS for HR ESI. Micro analyses were performed at the Microanalytical Laboratory, Research School of Chemistry, Australian National University, Canberra. Melting points were measured on a Reichert hot stage melting point apparatus or an Optimelt automated melting point apparatus and are uncorrected. Analytical TLC was performed with Merck (A.T. 5554) silica gel 60 F_{254} (0.2 mm) plates, precoated on aluminium sheets. Flash chromatography employed Merck Kiesegel 60 (230–400 mesh) silica gel. Reactions were conducted under a positive pressure of dry argon or nitrogen. Diethyl ether, toluene and THF were dried over sodium wire and distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Commercially available chemicals were purified by standard procedures or used as purchased.

{2-[2,2-Dibromovinyl]phenoxy}(*tert*-butyl)dimethylsilane (10)

To a solution of triphenylphosphine (12.4 g, 47.2 mmol, 4 equiv.) in CH_2Cl_2 (40 mL) at 0 °C was added dropwise over 15 min a solution of carbon tetrabromide (7.0 g, 23.6 mmol, 2 equiv.) in CH_2Cl_2 (15 mL). The resulting solution was allowed to warm to rt and stirred for 30 min before being cooled back to 0 °C. To this mixture was added dropwise a solution of TBS protected salicylaldehyde (**9**)[6] (2.8 g, 11.8 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred for 30 min at 0 °C after which time the solution was diluted slowly (with vigorous stirring) with hexanes (70 mL). Stirring was continued for a further 15 min then the resulting precipitate was removed by filtration. The solvent was removed *in vacuo* to leave a brown oil which was purified by silica gel chromatography (200 g silica gel, 1 : 99 EtOAc–hexane) to afford the *title compound* **10** (3.8 g, 9.8 mmol, 83%) as a pale yellow oil; δ_H (300 MHz, $CDCl_3$) 7.63 (1H, dm, J = 7.3 Hz), 7.59 (1H, s), 7.24 (1H, ddm, J = 7.4, 7.4 Hz), 7.00 (1H, ddm, J = 8.5, 8.5 Hz), 6.82 (1H, dm, J = 7.2 Hz), 1.05 (9H, s) and 0.22 (6H, s) ppm; δ_C (75 MHz, $CDCl_3$) 153.0, 134.0, 129.7, 129.2, 127.3, 121.0, 119.5, 89.7, 25.7, 18.2 and −4.4 ppm; IR (thin film) 2956, 1597, 1479, 1253 cm^{-1}; MS (70 eV, EI): m/z (%) 392 (23) $[M]^+$, 333 (52), 255 (65), 136 (100); HRMS: calcd for $C_{14}H_{20}O^{79}Br_2Si$ $[M]^+$: 389.9650; found: 389.9653.

{2-[(*Z*)-2-Bromobuta-1,3-dienyl]phenoxy}(*tert*-butyl)dimethylsilane (11)

To a stirred mixture of anhydrous zinc bromide (4.7 g, 21.0 mmol, 3.3 equiv.) in THF (25 mL) at rt was added dropwise vinyl magnesium bromide (22.4 mL, 0.94 M in THF, 21.0 mmol, 3.3 equiv.). The resulting mixture was stirred for 20 min at rt then cooled to −78 °C before the dropwise addition of a solution of dibromide **10** (2.5 g, 6.4 mmol) and tetrakis(triphenylphosphine)palladium(0) (737 mg, 0.6 mmol, 0.1 equiv.) in THF (10 mL). The reaction was stirred at −78 °C for 1 h then allowed to warm to −20 °C overnight. The reaction mixture was poured into hexanes (200 mL), filtered and the solvent was removed *in vacuo* to leave a yellow oil. Purification of the residue by silica gel chromatography (200 g silica gel, hexane) gave the *title compound* **11** (1.9 g, 5.6 mmol, 87%) as a colourless oil; δ_H (300 MHz, $CDCl_3$) 7.90 (1H, dd, J = 7.8, 1.2 Hz), 7.22 (1H, ddd, J = 8.0, 8.0, 1.8 Hz), 7.16 (1H, s), 7.02 (1H, ddd, J = 7.4, 7.4, 1.1 Hz), 6.84 (1H, dd, J = 8.1, 1.0 Hz), 6.52 (1H, dd, J = 16.2, 10.3 Hz), 5.73 (1H, d, J = 16.2 Hz), 5.33 (1H, d, J = 10.3 Hz), 1.02 (9H, s) and 0.20 (6H, s) ppm; δ_C (75 MHz, $CDCl_3$) 153.9, 137.3, 130.5, 129.6, 129.2, 127.7, 124.6, 120.9, 119.4, 118.7, 25.9, 18.4 and −4.2 ppm; IR (thin film) 2930, 1497, 1251 cm^{-1}; MS (70 eV, EI): m/z (%) 339 (10) $[M]^+$, 281 (36), 136 (100); HRMS: calcd for $C_{16}H_{23}O_2{}^{81}BrSi$ $[M]^+$: 338.0702; found: 338.0708.

Synthesis of dienylsilane 15 through retro-1,5-Brook rearrangement

To a solution of bromodiene **11** (1.00 g, 3.0 mmol) in THF (12 mL) at −78 °C was added *n*-BuLi (2.2 mL, 1.59 M in hexanes, 3.5 mmol, 1.2 equiv.). The resulting mixture was stirred at this temperature for 30 min then TMSCl (352 mg, 3.2 mmol, 1.1 equiv.) was added and the mixture was allowed to warm slowly to rt over 1 h. After this time Et_2O (50 mL) was added and the mixture was washed with H_2O (30 mL), brine (30 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to afford dienylsilane **15** (950 mg, 2.8 mmol, 93%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 7.33 (1H, s), 7.19 (1H, d, J = 7.6 Hz), 7.15 (1H, dd, J = 7.6, 7.6 Hz), 6.87 (1H, dd, J = 7.6, 7.6 Hz), 6.75 (1H, d, J = 7.6 Hz), 6.62 (1H, dd, J = 16.8, 10.3 Hz), 5.25 (1H, dd, J = 16.8, 2.0 Hz), 4.93 (1H, dd, J = 10.3, 2.0 Hz), 0.93 (9H, s), 0.24 (9H, s) and −0.15 (6H, s) ppm; δ_C (125 MHz, $CDCl_3$) 153.6, 144.1, 141.5, 139.8, 131.6, 130.9, 128.8, 120.5, 119.3, 112.8, 27.8, 18.2, 0.7 and −3.5 ppm; IR (thin film) 2957, 1479, 1252 cm^{-1}; MS (70 eV, EI): m/z (%) 332 (5) $[M]^+$, 275 (21), 187 (84), 73 (100); HRMS: calcd for $C_{19}H_{32}OSi_2$ $[M]^+$: 332.1992; found: 332.1987.

2-(2-Bromo-1*E*,3-butadienyl)phenol (12)

To a solution of bromodiene **11** (0.88 g, 2.59 mmol) in THF (12 mL) at rt was added TBAF (2.59 mL, 1.0 M in THF, 2.59 mmol, 1 equiv.). The resulting solution was allowed to stir at rt for 1 h before the addition of saturated aqueous NH_4Cl (20 mL). The mixture was extracted with Et_2O (2 × 20 mL) and the ethereal layers were combined and washed with H_2O (15 mL), brine (15 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave a yellow oil which was purified by silica gel chromatography (70 g silica gel, 1 : 9 EtOAc–hexane) to give the *title compound* **12** (0.53 g, 2.54 mmol, 98%) as a pale yellow solid, mp = 42–45 °C; δ_H (300 MHz, $CDCl_3$) 7.66 (1H, dd, J = 7.7, 1.7 Hz), 7.23 (1H, dd, J = 8.0, 8.1 Hz), 7.10 (1H, s), 6.97 (1H, dd, J = 7.4, 7.5 Hz), 6.85 (1H, dd, J = 8.1, 1.0 Hz), 6.56 (1H, dd, J = 16.2, 10.3 Hz), 5.76 (1H, d, J = 16.2 Hz), 5.38 (1H, d, J = 10.3 Hz) and 5.16 (1H, s) ppm; δ_C (75 MHz, $CDCl_3$) 153.1, 136.6, 130.2, 129.9, 127.4, 127.3, 123.2, 120.6, 119.9 and 115.8 ppm; IR (thin film) 3401,

1594, 1453, 1247 cm^{-1}; MS (70 eV, EI): *m/z* (%) 224 (41) $[M]^+$, 145 (100), 127 (35), 115 (66); HRMS: calcd for $C_{10}H_9O^{79}Br$ $[M]^+$: 223.9837; found: 223.9842.

Methyl 2-(2-bromo-1*E*,3-butadienyl)phen-1-yl 2*E*-butendioate (3)

To a solution of bromodiene **12** (50 mg, 0.24 mmol) in CH_2Cl_2 (3 mL) at −78 °C was added DBU (43, mg, 0.29 mmol, 1.2 equiv.). The resulting solution was allowed to stir at this temperature for 20 min before the addition of methyl fumaroyl chloride **13** (39 mg, 0.26 mmol, 1.1 equiv.). The reaction mixture was stirred for a further 1 h at this temperature before being diluted with Et_2O (30 mL) and warmed to rt. The ethereal mixture was washed with saturated aqueous $NaHCO_3$ (20 mL), water (20 mL), brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave a colourless oil which was purified by flash chromatography (5 g silica gel, 1 : 9 EtOAc–hexane) to give the *title compound* **3** (60 mg, 0.18 mmol, 75%) as a colourless oil; δ_H (300 MHz, $CDCl_3$) 7.81 (1H, dd, $J = 7.8$, 1.8 Hz), 7.38 (1H, ddd, $J = 7.8$, 7.8, 2.1 Hz), 7.30 (2H, $J = 7.5$, 7.5, 1.5 Hz), 7.16 (1H, dd, $J = 8.1$, 1.2 Hz), 7.05 (1H, s), 6.85 (1H, s), 6.49 (1H, ddd, $J = 16.5$, 10.7, 0.9 Hz), 5.75 (1H, d, $J = 16.5$ Hz), 5.37 (1H, d, $J = 10.7$ Hz) and 3.85 (3H, s) ppm; δ_C (75 MHz, $CDCl_3$) 165.2, 163.0, 148.1, 136.4, 135.3, 132.7, 130.7, 129.5, 128.9, 127.6, 126.5, 126.1, 122.0, 120.4 and 52.6 ppm; IR (thin film) 1730, 1294, 1141 cm^{-1}; MS (70 eV, EI): *m/z* (%) 337 (64) $[M]^+$, 276 (77), 197 (80), 113 (100); HRMS: calcd for $C_{15}H_{13}O_4{}^{79}Br$ $[M]^+$: 335.9997; found: 335.9993.

Thermal IMDA reaction of methyl 2-(2-trimethylsilyl-1*E*,3-butadienyl)phen-1-yl 2*E*-butendioate (3)

A solution of the IMDA precursor **3** (50 mg, 0.15 mmol) in C_6D_6 (2 mL) was heated at reflux for 3 h. After this time the reaction mixture was cooled to rt and the solvent was removed *in vacuo* to leave a yellow oil (*cis*-**3P** : *trans*-**3P** = 87 : 13 by δ_H analysis). Purification by flash chromatography (5 g silica gel, 1 : 1 CH_2Cl_2–hexane) gave *cis*-**3P** (41 mg, 0.12 mmol, 81%) as a colourless solid and *trans*-**3P** (1 mg, 0.03 mmol, 2%) as a colourless oil.

***cis*-3P.** White solid (EtOAc–hexane); mp = 76–77 °C; δ_H (300 MHz, $CDCl_3$) 7.41–7.34 (2H, m), 7.18 (1H, ddd, $J = 7.3$, 7.3, 0.8 Hz), 7.08 (1H, dd, $J = 8.1$, 0.8 Hz), 6.24–6.20 (1H, m), 3.98 (1H, m), 3.79 (3H, s), 3.63 (1H, dd, $J = 5.9$, 3.4 Hz), 3.58 (1H, ddd, $J = 6.5$, 3.4, 3.4 Hz) and 2.72–2.68 (2H, m) ppm; δ_C (75 MHz, $CDCl_3$) 173.0, 168.0, 150.3, 131.7, 129.9, 129.5, 124.1, 122.4, 119.6, 116.8, 52.6, 41.0, 39.4, 37.2 and 25.9 ppm; IR (thin film) 2920, 1762, 1735, 1237, 1148 cm^{-1}; MS (70 eV, EI): *m/z* (%) 337 (29) $[M]^+$, 276 (100), 197 (87); Anal. Calcd for $C_{15}H_{13}O_4Br$: C 53.43, H 3.89. Found: C 53.61, H 3.95.

***trans*-3P.** Colourless oil; δ_H (500 MHz, $CDCl_3$) 7.92 (1H, d, $J = 7.8$ Hz), 7.33 (1H, dd, $J = 7.8$, 7.8, Hz), 7.20 (1H, dd, $J = 7.8$, 7.8 Hz), 7.14 (1H, d, $J = 7.8$ Hz), 6.45 (1H, ddd, $J = 7.2$, 2.0, 2.0 Hz), 3.92 (1H, brd, $J = 13.9$ Hz), 3.76 (3H, s), 3.10 (1H, dd, $J = 11.9$, 11.9 Hz), 2.91 (1H, ddd, $J = 11.9$, 5.0, 5.0 Hz), 2.56–2.49 (1H, m) and 2.33–2.22 (1H, m) ppm; δ_C (125 MHz, $CDCl_3$) 174.1, 169.1, 151.2, 132.7, 128.7, 127.2, 125.1, 124.8, 117.9, 117.5, 52.6, 45.9, 41.3, 38.8 and 30.8 ppm; IR (thin film) 2921, 1771, 1735, 1455, 1172, 1105 cm^{-1}; MS (70 eV, EI): *m/z* (%), 337 (55) $[M]^+$, 276 (67), 197 (100); HRMS: calcd for $C_{15}H_{13}O_2{}^{79}Br$ $[M]^+$: 335.9997; found: 335.9993.

Synthesis and thermal IMDA reaction of TMS-diene precursor (4)

To a solution of bromodiene **12** (50 mg, 2.4 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added DBU (47 mg, 3.1 mmol, 1.3 equiv.). The resulting yellow solution was allowed to stir at this temperature for 30 min before the addition of TMSCl (31 mg, 2.9 mmol, 1.2 equiv.) dropwise *via* syringe. The reaction was stirred at this temperature for 1 h before being diluted with Et_2O (50 mL) and warmed to rt. The ethereal solution was washed with H_2O (20 mL), brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave crude TMS ether **16** as a colourless oil which was dried *via* azeotropic removal of THF (3 × 2 mL of THF) and taken up in THF (1 mL). The solution was cooled to −78 °C and *n*-BuLi (180 μL, 1.59 M in hexane, 2.9 mmol, 1.2 equiv.) was added dropwise *via* syringe. The reaction mixture was allowed to stir at this temperature for 30 min after which time methyl fumaroyl chloride (39 mg, 2.6 mmol, 1.1 equiv.) was added. The reaction mixture was stirred for a further 1 h at this temperature before being partitioned between a mixture of saturated aqueous NH_4Cl (10 mL) and Et_2O (20 mL). The layers were separated and the ethereal layer was washed with brine and dried ($MgSO_4$). The solvent was removed *in vacuo.* The presence of *trans*-**4P** could not be detected by ^1H NMR analysis of the residue, which was purified by flash chromatography (5 g silica gel, 2 : 8 EtOAc–hexane) to give *cis*-**4P** (25 mg, 0.8 mmol, 32%) as a white solid (CH_2Cl_2–heptane), mp = 91–93 °C; δ_H (500 MHz, $CDCl_3$) 7.30 (2H, dd, $J = 7.5$, 7.5 Hz), 7.14 (1H, ddd, $J = 7.5$, 7.5, 1.0 Hz), 7.05 (1H, d, $J = 7.5$ Hz), 6.11 (1H, dd, $J = 6.3$, 3.0 Hz), 3.75 (3H, s), 3.70 (1H, ddd, $J = 5.0$, 5.0, 2.5 Hz), 3.44 (1H, dd, $J = 5.0$, 4.0 Hz), 3.33 (1H, dd, $J = 5.5$, 5.0 Hz), 2.65 (2H, ddd, $J = 6.3$, 6.3, 3.0 Hz) and 0.21 (9H, s) ppm; δ_C (125 MHz, $CDCl_3$) 174.2, 169.7, 151.6, 137.6, 136.8, 129.5, 129.0, 126.7, 124.5, 117.2, 52.5, 41.2, 37.2, 36.0, 25.2, and −0.9 ppm; IR (thin film) 2952, 1766, 1735, 1139 cm^{-1}; MS (70 eV, EI): *m/z* (%) 330 (82) $[M]^+$, 269 (100), 73 (98); Anal. Calcd for $C_{18}H_{22}O_4Si$: C 65.42, H 6.71. Found: C 65.09, H 6.84.

2-(1*E*,3-Butadienyl)-3-bromophenol (18)

To a vigorously stirred suspension of allyl triphenylphosphonium bromide[24] (2.10 g, 5.49 mmol, 2.2 equiv.) in THF (15 mL) at −18 °C under Ar was added dropwise a solution of *n*-BuLi (1.56 M in hexanes, 3.35 mL, 5.23 mmol, 2.1 equiv.). After stirring for 30 min, a solution of 3-bromosalicylaldehyde **17**[12] (0.50 g, 2.49 mmol) in THF (5 mL) at −18 °C under Ar was added dropwise *via* cannula and the resulting mixture stirred at this temperature for 1 h. The solution was warmed to rt and stirring was continued for a further 3 h. Saturated aqueous NH_4Cl (15 mL) was added and the reaction mixture was concentrated *in vacuo.* The residue was extracted with CH_2Cl_2 (3 × 20 mL) and the organic layers were combined, washed with brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave an orange oil which was purified by flash chromatography (200 g silica gel, 1 : 9 EtOAc–hexane) to give **18** (0.37 g, 1.67 mmol, 67%) as a colourless oil; δ_H (300 MHz, $CDCl_3$) 7.16 (1H, dd, $J = 4.5$, 0.6 Hz), 7.00 (1H, dd, $J = 5.0$, 5.0 Hz), 6.86 (1H, d, $J = 5.0$ Hz), 6.73 (1H, dd, $J = 10.2$, 6.0 Hz), 6.62–6.53 (2H, m), 5.41 (1H, s), 5.40 (1H, d, $J =$

10.2 Hz) and 5.29 (1H, d, $J = 6.0$ Hz) ppm; δ_C (75 MHz, $CDCl_3$) 154.0, 136.8, 136.2, 129.3, 128.2, 125.0, 124.5, 124.4, 119.8, and 115.1 ppm; IR (thin film) 3258, 1569, 1443, 1009 cm^{-1}; MS (70 eV, EI): *m/z* (%) 224 (32) $[M]^+$, 209 (29), 145 (100); HRMS: calcd for $C_{10}H_9O^{79}Br$ $[M]^+$: 223.9837; found: 223.9838.

Methyl 2-(1*E*,3-butadienyl)-3-bromophen-1-yl 2*E*-butendioate (5)

To a solution of phenol **18** (50 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) at −78 °C was added DBU (47 mg, 0.31 mmol, 1.4 equiv.). The resulting solution was allowed to stir at this temperature for 20 min before the addition of methyl fumaroyl chloride (36 mg, 0.24 mmol, 1.1 equiv.). The reaction mixture was stirred for a further 1 h at this temperature before being diluted with Et_2O (30 mL) and warmed to rt. The ethereal mixture was washed with saturated aqueous $NaHCO_3$ (20 mL), water (20 mL), brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave a colourless oil which was purified by flash chromatography (5 g silica gel, 1 : 9 EtOAc–hexane) to give the *title compound* **5** (33 mg, 0.12 mmol, 53%) as a colourless oil; δ_H (500 MHz, C_6D_6) 7.14 (1H, dd, $J = 8.0$, 1.0 Hz), 6.92 (1H, d, $J = 15.8$ Hz), 6.87 (1H, d, $J = 15.8$ Hz), 6.71 (1H, d, $J = 8.0$ Hz), 6.57–6.44 (3H, m), 6.19 (1H, ddd, $J = 17.2$, 10.0, 10.0 Hz), 5.02 (1H, d, $J = 17.2$ Hz), 4.89 (1H, d, $J = 10.0$ Hz) and 3.18 (3H, s) ppm; δ_C (125 MHz, C_6D_6) 164.4, 162.6, 148.8, 137.1, 137.0, 135.1, 132.2, 131.4, 130.9, 128.5, 127.0, 124.9, 122.2, 119.3 and 51.7 ppm; IR (thin film) 1727, 1319, 1299, 1145 cm^{-1}; MS (70 eV, EI): *m/z* (%) 337 (13) $[M]^+$, 144 (35), 113 (100); HRMS: calcd for $C_{15}H_{13}O_4{}^{79}Br$ $[M]^+$: 335.9997; found: 336.0000.

Thermal IMDA reaction of 2-(1*E*,3-butadienyl)-3-bromophen-1-yl 2*E*-butendioate (5)

A solution of **5** (35 mg, 0.10 mmol) in C_6D_6 (3 mL) was heated to 60 °C for 5.5 h. After this time the reaction was allowed to cool to rt and the solvent was removed *in vacuo.* The presence of *trans*-**5P** could not be detected by ^1H NMR analysis of the residue, which was purified by flash chromatography (3 g silica gel, 1 : 9 EtOAc–hexane) to give *cis*-**5P** (30 mg, 0.09 mmol, 86%) as a white solid. Recrystallisation from CH_2Cl_2–heptane gave colourless cubes, mp = 148–150 °C; δ_H (300 MHz, $CDCl_3$) 7.38 (1H, dd, $J = 8.0$, 1.2 Hz), 7.15 (1H, dd, $J = 8.0$, 8.0 Hz), 7.01 (1H, dd, $J = 8.0$, 1.2 Hz), 5.80–5.75 (1H, m), 5.53 (1H, dm, $J =$ 10.1 Hz), 4.12–4.07 (1H, m), 3.77 (3H, s), 3.62 (1H, ddd, $J = 6.8$, 1.8, 1.8 Hz), 3.49 (1H, dd, $J = 6.8$, 2.7 Hz) and 2.74–2.50 (2H, m) ppm; δ_C (75 MHz, $CDCl_3$) 173.4, 168.1, 151.1, 129.4, 128.9, 127.2, 124.6, 124.0, 123.5, 116.3, 52.4, 38.3, 37.4, 33.8 and 22.5 ppm; IR (thin film) 2950, 1765, 1726, 1450, 1221, 1147 cm^{-1}; MS (70 eV, EI): *m/z* (%) 337 (20) $[M]^+$, 278 (100), 197 (75), 115 (43); Anal. Calcd for $C_{15}H_{13}O_4Br$: C 53.43, H 3.89. Found: C 53.47, H 3.92.

2-(1*E*,3-Butadienyl)-3-trimethylsilylphenol (19)

To a stirred solution of 2-(1*E*,3-butadienyl)-3-bromophenol **18** (0.16 g, 0.69 mmol) in THF (5 mL) at −78 °C under Ar was added dropwise *n*-BuLi (1.06 mL, 1.57 M in hexanes, 1.66 mmol, 2.4 equiv.) and the resulting solution was stirred for 30 min. Chlorotrimethylsilane (165 mg, 1.52 mmol, 2.2 equiv.) was added and the mixture allowed to warm to rt over 1 h. Aqueous HCl (5.0 mL, 1 M) was added and the resulting mixture was stirred for a further 1 h. The reaction mixture was diluted with diethyl ether (15 mL), washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by flash chromatography (10 g silica gel, 5 : 95 EtOAc–hexane) to give the *title compound* **19** (0.12 g, 0.57 mmol, 82%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 7.17 (1H, dd, $J =$ 7.5, 7.5 Hz), 7.09 (1H, dd, $J = 7.5$, 1.0 Hz), 6.95 (1H, dd, $J =$ 7.5, 1.0 Hz), 6.69 (1H, d, $J = 15.5$ Hz), 6.63–6.51 (2H, m), 5.41 (1H, s), 5.35 (1H, dm, $J = 10.5$ Hz), 5.28 (1H, dm, $J = 8.5$ Hz) and 0.28 (9H, s) ppm; δ_C (125 MHz, $CDCl_3$) 152.7, 140.7, 136.7, 136.1, 129.6, 129.0, 128.2, 126.6, 119.2, 116.8 and 0.23 ppm; IR (thin film) 3524, 2955, 1249 cm^{-1}; MS (70 eV, EI): *m/z* (%) 218 (84) $[M]^+$, 203 (61), 187 (64), 144 (77), 73 (100); HRMS: calcd for $C_{13}H_{18}OSi$ $[M]^+$: 218.1127; found: 218.1131.

Methyl 2-(1*E*,3-butadienyl)-3-trimethylsilylphen-1-yl 2*E*-butendioate (6)

To a solution of phenol **19** (20 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) at −78 °C was added DBU (20 mg, 0.13 mmol, 1.4 equiv.). The resulting solution was allowed to stir at this temperature for 20 min before the addition of methyl fumaroyl chloride (16 mg, 0.11 mmol, 1.2 equiv.). The reaction mixture was stirred for a further 1 h at this temperature before being diluted with Et_2O (20 mL) and warmed to rt. The ethereal mixture was washed with saturated aqueous $NaHCO_3$ (10 mL), water (10 mL), brine (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave a colourless oil which was purified by flash chromatography (1 g silica gel, 5 : 95 EtOAc–hexane) to give the *title compound* **6** (17 mg, 0.05 mmol, 56%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 7.43 (1H, dd, $J = 7.6$, 1.3 Hz), 7.27 (1H, dd, $J = 7.6$, 7.6 Hz), 7.08 (1H, dd, $J = 7.6$, 1.3 Hz), 7.05 (1H, d, $J = 15.5$ Hz), 7.00 (1H, d, $J = 15.5$ Hz), 6.55 (1H, d, $J = 15.3$ Hz), 6.46–6.37 (2H, m), 5.24 (1H, d, $J = 15.3$ Hz), 5.17 (1H, d, $J = 9.5$ Hz), 3.85 (3H, s) and 0.30 (9H, s) ppm; δ_C (125 MHz, $CDCl_3$) 165.4, 163.6, 147.7, 141.9, 137.0, 136.1, 135.9, 134.8, 133.1, 132.7, 128.7, 127.6, 123.2, 118.7, 52.6 and 0.36 ppm; IR (thin film) 2954, 1732, 1295, 1139 cm^{-1}; MS (70 eV, EI): *m/z* (%) 330 (29) $[M]^+$, 113 (79), 73 (100); HRMS: calcd for $C_{18}H_{22}O_4Si$ $[M]^+$: 330.1287; found: 330.1287.

Thermal IMDA reaction of methyl 2-(1*E*,3-butadienyl)-3-trimethylsilylphen-1-yl 2*E*-butendioate (6)

A solution of IMDA precursor **6** (16 mg, 0.05 mmol) in C_6D_6 (2 mL) was heated to 60 °C for 5 h. After this time the reaction mixture was allowed to cool to rt and the solvent was removed *in vacuo.* The presence of *trans*-**6P** could not be detected by ^1H NMR analysis of the residue, which was purified by flash chromatography (2 g silica gel, 5 : 95 EtOAc–hexane) to give *cis*-**6P** (14 mg, 0.04 mmol, 84%) as a white solid. Recrystallisation from CH_2Cl_2–heptane gave colourless cubes mp = 103–104 °C; δ_H (300 MHz, $CDCl_3$) 7.32 (1H, dd, $J = 7.4$, 1.5 Hz), 7.26 (1H, dd, $J = 7.4$, 7.4 Hz), 7.06 (1H, dd, $J = 7.4$, 1.5 Hz), 5.76 (1H, ddd, $J =$ 10.1, 6.9, 3.6 Hz), 5.45 (1H, dm, $J = 10.1$ Hz), 3.95–3.88 (1H, m), 3.76 (3H, s), 3.62 (1H, ddd, $J = 5.5$, 1.6, 1.6 Hz), 3.44 (1H, ddd, $J = 5.5$, 2.9, 0.8 Hz), 2.72–2.54 (2H, m) and 0.33 (9H, s) ppm; δ_C (75 MHz, $CDCl_3$) 173.8, 168.2, 150.9, 139.5, 131.1, 130.6, 128.0, 127.2, 126.2, 118.1, 52.3, 39.3, 37.7, 32.9, 22.8 and 0.3 ppm; IR (KBr disk) 2953, 1766, 1739, 1179, 1140 cm^{-1}; MS (70 eV, EI):

m/z (%) 330 (90) $[M]^+$, 255 (96), 211 (87), 73 (100); Anal. Calcd for $C_{18}H_{22}O_4Si$: C 65.42, H 6.71. Found: C 65.50, H 6.83%.

2-Hydroxy-6-(methoxymethoxy)benzaldehyde (20)

2,6-Bis(methoxymethoxy)benzaldehyde[25] (110 mg, 0.49 mmol) was dissolved in a solution of 3% HCl in THF (1 mL). The resulting mixture was stirred at rt under N_2 for 12 h before being diluted with Et_2O (10 mL) and washed with H_2O (2 × 5 mL) and brine (5 mL). The ethereal solution was dried ($MgSO_4$) and the solvent was removed *in vacuo* to leave a yellow oil which was purified by flash chromatography (10 g silica gel, 1 : 9 EtOAc–hexane) to give the *title compound* **20** (76 mg, 0.42 mmol, 86%) as a white solid, mp = 50–51 °C; δ_H (300 MHz, $CDCl_3$) 11.89 (1H, s), 10.36 (1H, s), 7.38 (1H, dd, J = 8.3, 8.3 Hz), 6.57 (2H, dd, J = 8.3, 8.3 Hz), 5.25 (2H, s) and 3.50 (3H, s) ppm; δ_C (75 MHz, $CDCl_3$) 194.3, 163.3, 160.0, 138.3, 111.2, 110.6, 104.0, 94.5 and 56.5 ppm; IR (KBr Disk) 3111, 2906, 1642, 1613, 1459 cm^{-1}; MS (70 eV, EI): *m/z* (%) 182 (59) $[M]^+$, 45 (100); Anal. Calcd for $C_9H_{10}O_4$: C 59.34, H 5.53. Found: C 59.55, H 5.71%.

5-(Methoxymethoxy)-3-vinyl-2*H*-chromen-2-one (22)

To a solution of 2-hydroxy-6-(methoxymethoxy)benzaldehyde **20** (1.0 g, 5.5 mmol) in CH_2Cl_2 (20 mL) at −78 °C was added DBU (1.0 g, 6.6 mmol, 1.2 equiv.). The resulting yellow solution was allowed to stir at this temperature for 15 min before the addition of crotonyl chloride (630 mg, 6.0 mmol, 1.1 equiv.) dropwise *via* syringe. The reaction mixture was stirred at −78 °C for 1.5 h after which time Et_2O (100 mL) was added, the mixture was warmed to rt and H_2O (50 mL) was added immediately. The layers were separated and the aqueous was extracted with Et_2O (50 mL). The ethereal layers were combined and washed with H_2O (2 × 80 mL) and brine (80 mL), dried ($MgSO_4$) and the solvent was removed *in vacuo.* The crude crotonate product **21** was taken up in THF (20 mL) and the solution was cooled to 0 °C before the addition of DBU (1.0 g, 6.6 mmol, 1.2 equiv.). The resulting mixture was allowed to warm slowly to rt and stirred at this temperature for 14 h. The reaction mixture was diluted with Et_2O (100 mL) and washed with aqueous HCl (2 × 50 mL, 2M), H_2O (50 mL) and brine (50 mL) before being dried ($MgSO_2$). The solvent was removed *in vacuo* to leave a yellow oil which was purified by flash chromatography (80 g silica gel 5 : 95 to 2 : 8 EtOAc–hexane) to give recovered phenol **20** (340 mg, 1.9 mmol, 35%) as a white solid and the *title compound* **22** (630 mg, 2.7 mmol, 49%) as a white solid, mp = 250 °C (decomp.); δ_H (500 MHz, $CDCl_3$) 8.10 (1H, s), 7.39 (1H, dd, J = 7.8, 7.8 Hz), 6.96 (2H, d, J = 7.8 Hz), 6.74 (1H, dd, J = 17.5, 11.5 Hz), 6.20 (1H, dd, J = 17.5 Hz), 5.47 (1H, d, J = 11.5 Hz), 5.32 (2H, s) and 3.53 (3H, s) ppm; δ_C (125 MHz, $CDCl_3$) 160.3, 154.1, 153.9, 132.9, 132.0, 130.9, 123.6, 119.2, 110.9, 109.9, 108.6, 95.0 and 56.7 ppm; IR (thin film) 2917, 1726, 1605, 1053 cm^{-1}; MS (70 eV, EI): *m/z* (%) 232 (60) $[M]^+$, 45 (100); HRMS: calcd for $C_{13}H_{12}O_4$ $[M]^+$: 232.0736; found: 232.0737.

5-Hydroxy-3-vinyl-2*H*-chromen-2-one (23)

MOM ether **22** (20 mg, 0.9 mmol) was dissolved in a solution of 7% concentrated aqueous HCl in THF (1 mL) and the resulting solution was stirred at rt under N_2 for 14 h. The mixture was diluted with EtOAc (60 mL) and washed with H_2O (20 mL) and brine (20 mL) then dried ($MgSO_4$). The solvent was removed *in vacuo* to give the *title compound* **23** (17 mg, 0.9 mmol, 99%) as a white solid, mp = 230 °C (decomp.); δ_H (500 MHz, CD_3OD) 8.18 (1H, s), 7.33 (1H, dd, J = 8.3, 8.3 Hz), 6.77–6.67 (3H, m), 6.16 (1H, d, J = 17.7 Hz), 5.41 (1H, d, J = 11.3 Hz) and 4.93 (1H, brs) ppm; δ_C (125 MHz, CD_3OD) 161.0, 155.3, 154.2, 134.1, 132.3, 131.0, 122.0, 117.5, 109.6, 109.3 and 106.6 ppm; IR (KBr disk) 3209, 2392, 1672, 1608, 1472 cm^{-1}; MS (70 eV, EI): *m/z* (%) 188 (100) $[M]^+$; HRMS: calcd for $C_{11}H_8O_3$ $[M]^+$: 188.0473; found: 188.0474.

Methyl 2-oxo-3-vinyl-2*H*-chromen-5-yl fumarate (7)

To a solution of phenol **23** (17 mg, 0.9 mmol) in DMF (2 mL) at 0 °C under N_2 was added DBU (16 mg, 1.0 mmol, 1.2 equiv.). The resulting bright orange solution was allowed to stir at this temperature for 15 min before the addition of methyl fumaroyl chloride (14 mg, 0.95 mmol, 1.1 equiv.) dropwise *via* syringe. The reaction mixture was immediately quenched by the addition of a mixture of Et_2O (30 mL) and saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and ethereal layer was washed with brine (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave a colourless oil which was purified by flash chromatography (2 g silica gel, 2 : 8 EtOAc–hexane) to afford the *title compound* **7** (17 mg, 0.57 mmol, 66%) as a white solid, mp = 137–176 °C; δ_H (500 MHz, $CDCl_3$) 7.65 (1H, s), 7.50 (1H, dd, J = 8.3, 8.3 Hz), 7.23 (1H, d, J = 8.3 Hz), 7.16–7.09 (3H, m), 6.68 (1H, dd, J = 17.6, 11.4 Hz), 6.21 (1H, d, J = 17.6 Hz), 5.51 (1H, d, J = 11.4 Hz) and 3.87 (3H, s) ppm; δ_C (125 MHz, $CDCl_3$) 164.8, 162.7, 159.2, 153.5, 146.2, 136.1, 131.7, 131.1, 130.9, 130.3, 125.4, 120.7, 117.3, 114.4, 113.0 and 52.6 ppm; IR (KBr disk) 3073, 1725, 1324, 1159 cm^{-1}; MS (70 eV, EI): *m/z* (%) 300 (62) $[M]^+$, 188 (33), 113 (100); Anal. Calcd for $C_{16}H_{12}O_6$: C 64.00, H 4.03. Found: C 63.79, H 4.14%.

Thermal IMDA reaction of methyl 2-oxo-3-vinyl-2*H*-chromen-5-yl fumarate (7)

A solution of IMDA precursor **7** (40 mg, 0.13 mmol) and BHT (3 mg, 0.01 mmol, 0.1 equiv.) in PhCl (60 mL) under N_2 was heated to reflux for 25 h. The reaction mixture was cooled to rt and the solvent was removed *in vacuo* to leave a colourless oil. The presence of *cis*-**7P** could not be detected by ^1H NMR analysis of the residue, which was purified by flash chromatography (2 g silica gel, 1 : 99 EtOAc–CH_2Cl_2) to give *trans*-**7P** (24 mg, 0.80 mmol, 61%) as a white solid. Recrystallisation from EtOAc–CH_2Cl_2 gave colourless needles, mp = 186–198 °C; δ_H (300 MHz, CD_3CN) 7.40 (1H, ddd, J = 9.4, 8.3, 1.0 Hz), 7.16 (1H, dd, J = 7.0, 3.7 Hz), 6.98–6.91 (2H, m), 4.05 (1H, dm, J = 13.1 Hz), 3.76 (3H, s), 3.18–2.91 (3H, m) and 2.59–2.45 (1H, m) ppm; δ_C (75 MHz, $CDCl_3$–CD_3OD) 173.5, 166.7, 160.0, 150.6, 149.1, 142.1, 130.2, 122.7, 112.5, 112.3, 107.6, 52.3, 41.1, 38.3, 30.5 and 30.2 ppm; IR (KBr disk) 2950, 1769, 1745, 1725, 1473 cm^{-1}; MS (70 eV, EI): *m/z* (%) 300 (100) $[M]^+$, 240 (74), 113 (59); Anal. Calcd for $C_{16}H_{12}O_6$: C 64.00, H 4.03. Found: C 64.27, H 3.35%.

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