# Enantioselective isothiourea catalysed Michael-Michael-Lactonisation cascade; synthesis of δ-lactones and 1,2,3,4-substituted cyclopentanes

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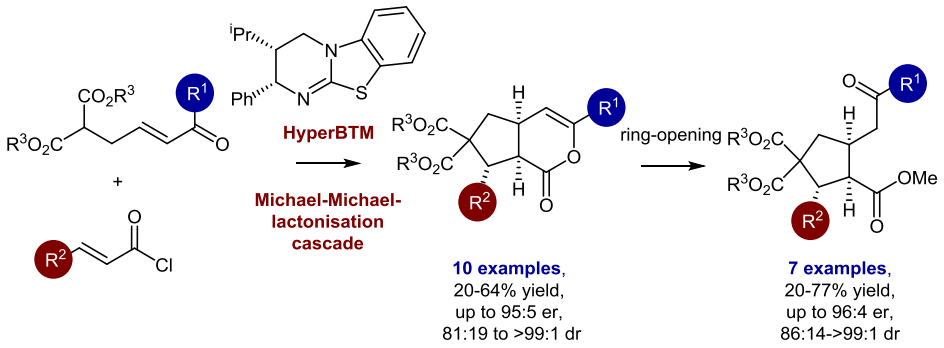
Dedicated to Professor Dieter Enders on the occasion of his 70th birthday




Received:
Accepted:
Published online:
DOI:

**Abstract** This manuscript describes the application of α,β-unsaturated acyl ammonium intermediates in a Michael-Michael-lactonisation cascade process to furnish δ-lactones. Generation of α,β-unsaturated acyl ammonium intermediates was achieved upon addition of isothiourea catalyst HyperBTM into α,β-unsaturated acid chlorides. Subsequent reaction with enone-malonates gave access to δ-lactones in 20-64% yield, 72.5:27.5 to 95:5 er and 81:19 to >95:5 dr. Additionally, application of a ring-opening protocol yielded 1,2,3,4-substituted cyclopentanes in 28-77% yield, 76:24 to 98:2 er and 86:14 to >95:5 dr. Interestingly, highest er was observed at high reaction temperatures, with 70˚C proving optimal. This effect was investigated by conducting an Eyring analysis, which indicated that differential activation entropy rather than differential activation enthalpy is responsible for enantiodiscrimination in this process.

**Key words** Lewis base catalysis, α,β-unsaturated acyl ammonium intermediates, isothiourea catalysis, cascades, enantioselective catalysis

The use of cascade sequences in enantioselective organic synthesis has long been considered a "gold standard" in the field, as complex product architectures can be elegantly and efficiently built up from simple, achiral starting materials.[1,2] Historically, the development of organocatalysis was driven by a desire to mimic the chemistry of enzyme catalysis using small molecules, and since many complex biosyntheses are facilitated by enzyme-catalysed cascade processes[3] the development of organocatalyzed cascades is of great interest to the synthetic community.[4] Lewis base catalysis is a versatile way of achieving cascade reactions, and many examples that exploit the interconnected nature of enamine and iminium intermediates are known.[5]

Recent advances in this area have shown that α,β-unsaturated acyl ammonium and azolium species can be used as intermediates in cascade reactions.[6] An early example was reported by Studer *et al.* in 2011, who applied a Michael-Michael-lactonisation approach to the NHC-catalysed synthesis of functionalised indanes. Enantioselective addition of dicarbonyl nucleophiles to an α,β-unsaturated acyl azolium species (generated in-situ under oxidative NHC catalysis) containing a tethered enone, followed by subsequent Michael addition and lactonisation allowed a cascade approach to these valuable products to be accessed (Approach A).[7] An alternative approach to cascade cyclisation was adopted by Romo *et al.* who employed malonates with a tethered ketone functionality

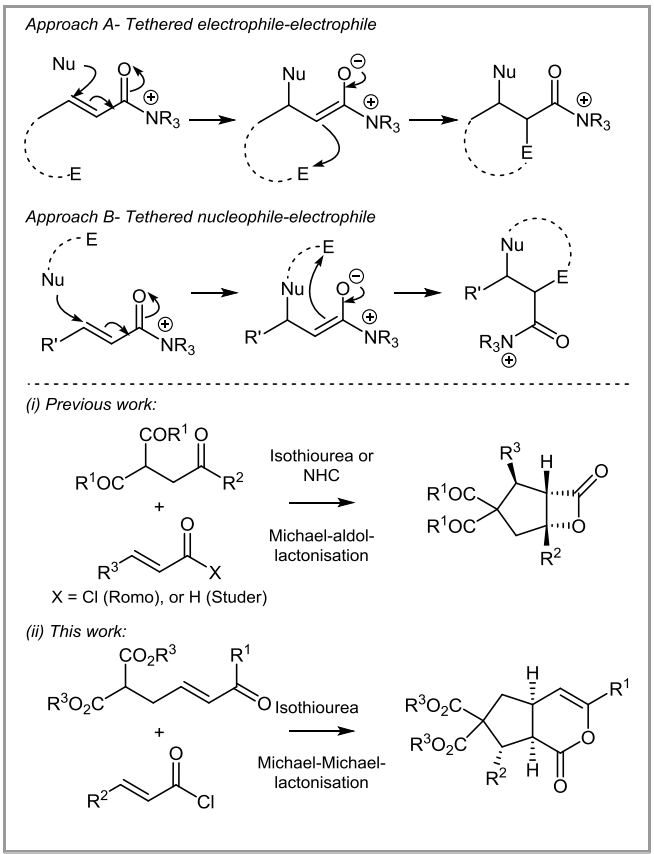



**Figure 1** Proposed Michael-Michael lactonisation cascade reaction

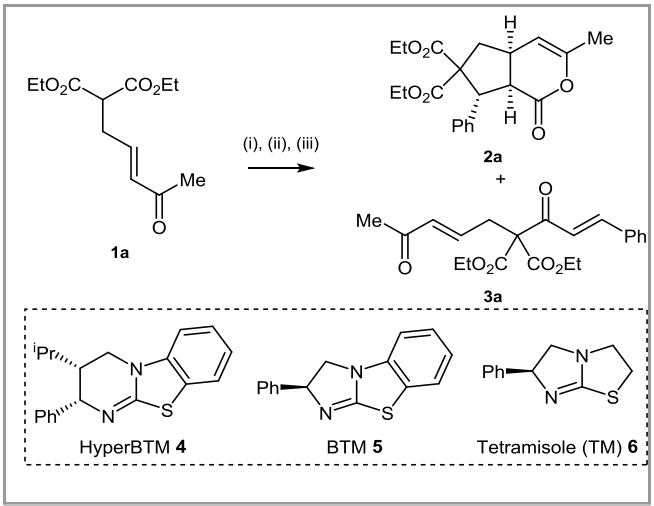
as a dual Michael donor-electrophile in the synthesis of β-lactones via a Michael-aldol-lactonisation reaction (Approach B). This strategy relies on the in-situ catalytic generation of an α,β-unsaturated acyl ammonium intermediate (Figure 1(i)), with Michael addition, followed by an aldol-lactonisation

reaction of the resultant ammonium enolate generating the desired products.[8] The same product architectures have also been accessed in analogous NHC-catalysed processes by the groups of Lupton[9] and Studer,[10] respectively. Building upon this work, and our own expertise in the utility of isothioureas[11] in enantioselective catalysis,[12] we looked to further the utility of α,β-unsaturated acyl ammonium intermediates[13] by applying them in a Michael-Michael-lactonisation cascade. In this process, the use of Michael donor-acceptor substrates containing a malonate and a tethered enone and their reaction with a catalytically generated α,β-unsaturated acyl ammonium intermediate was envisaged (Figure 1(ii), Approach B). Since embarking on this work, three independent but related NHC-catalysed processes that also target these substrates in an analogous strategy using an in-situ generated α,β-unsaturated acyl azolium species under oxidative catalysis have been published.[14,15,16] Our approach differs in that oxidative catalysis is not employed, with the α,β-unsaturated acyl ammonium species being generated directly at the carboxylic acid oxidation level from an acid chloride.

## Results and Discussion

### Optimisation

Initial screening of the proposed Michael-Michael-Lactonisation (MML) reaction utilised enone-malonate **1a** as the model nucleophile-electrophile component, and cinnamoyl chloride as the α,β-unsaturated acyl ammonium precursor (Table 1). LiHMDs was added to enone-malonate **1a** at 0 °C in THF. After stirring for 10 minutes, $^{i}Pr_2NEt$ and isothiourea catalyst HyperBTM **4** were added, and the resultant mixture was allowed to stir at 0 °C for a further 10 minutes. Cinnamoyl chloride was then added as a solution in $CH_2Cl_2$, and the reaction was stirred and allowed to warm to rt overnight, giving a 76:24 mixture of two products, **2a** and **3a**, which were isolated in 31% and 13% yield, respectively. The expected product of this cascade reaction **2a** was formed in 69:31 er, with the observation of **3a** postulated to be due to competitive 1,2-addition of malonate **1a** to cinnamoyl chloride. To probe the observed chemoselectivity of initial malonate addition and enantioselectivity of the process, further studies were performed at 0% and 100% catalyst loading (Table 1). With no catalyst present (0 mol%), an 87:13 ratio of 1,2-addition product **3a** and 1,4-addition product **2a** was generated. Alternatively, at 100 mol% catalyst loading the reaction proceeded to form only the cascade reaction product **2a**, that is initiated by 1,4-addition, in 72.5:27.5 er. These observations suggest that (i) the undesired product **3a** arises from direct 1,2-addition to the acid chloride; (ii) the isothiourea-catalysed reaction results in excellent selectivity for the product arising from 1,4-addition; (iii) the poor enantioselectivity observed under these conditions is in part due to competitive generation of this product in racemic form from direct reaction with the acid chloride. Alternative isothiourea catalysts were also trialled. Reaction in the presence of 20 mol% of either BTM **5** or tetramisole (TM) **6** proceeded to 87 and 85% conversion respectively (with respect to **1a**), with the 1,2-addition product **3a** predominating. For the BTM **5** catalysed reaction, a 33:67 mixture of 1,4-addition product **2a** (79:21 er) and 1,2-addition product **3a** was isolated. Similarly, reaction with TM **6** gave an 18:82 mixture of **2a** (72.5:27.5 er) and 1,2-addition product **3a**. All subsequent optimisation utilised HyperBTM **4**, as this catalyst gave superior conversion to desired product **2a**.

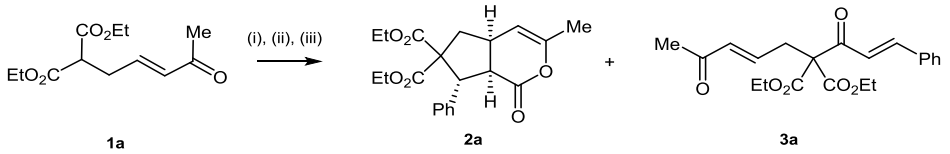



**Scheme 1** *Reagents and conditions*: (i) LiHMDS (1.1 equiv.), THF, 0 °C, 10 min; (ii) $^{i}Pr_2NEt$ (1.4 equiv.), catalyst (see Table XX), $CH_2Cl_2$, 0 °C, 10 min; (iii) cinnamoyl chloride (1.4 equiv.), $CH_2Cl_2$, 0 °C to rt, 18 h.

| catalyst | catalyst loading (mol%) | conv. | 2a | 3a | er |
|---|---|---|---|---|---|
| 4 | 20 | 100% | 76 | 24 | 69:31 |
| | 0 | 75% | 13 | 87 | - |
| | 100 | 100% | 100 | 0 | 72.5:27.5 |
| 5 | 20 | 87% | 33 | 67 | 79:21 |
| 6 | 20 | 85% | 18 | 82 | 72.5:27.5 |

**Table 1** Initial reaction screen.

Further reaction optimisation began with a solvent screen (Table 2). Mixtures of $CH_2Cl_2$ and THF have been reported to give high enantioselectivity in Romo's related Michael-Aldol-Lactonisation protocol (Figure 1),[8] thus an investigation into the relationship between solvent mixture composition and selectivity was analysed (Table 2). In general, the higher the proportion of $CH_2Cl_2$ in the reaction solvent, the lower the enantioselectivity, and the lower the proportion of 1,4-addition product **2a** (entries 1-5). In contrast, increased selectivity for the 1,4-addition product was generally observed at higher THF content. The best enantioselectivity was obtained at 90-100% THF content (entries 4 and 5), with a 84:16 ratio of **2a** (74.5:25.5 er):**3a** afforded in 100% THF. The effect of temperature upon the reaction manifold was explored next. Decreasing the reaction temperature to −78 °C gave 82% conversion to a 43:57 mixture of **2a** and **3a**. Interestingly, **2a** was almost racemic, with an er of 51:49. Conversely, as the reaction temperature was increased, the enantioselectivity of the process also increased, with the highest selectivity observed at 70 °C. At this temperature, 85% conversion to a 54:46 mixture of **2a** and **3a** was observed, and desired 1,4-addition product **2a** was formed in 87:13 er. Attempts to further improve the enantioselectivity by heating the solvent above its boiling point in a sealed tube, resulted in reduced material recovery, presumably due to degradation of the starting material under these conditions. Similarly, using dioxane as solvent/co-solvent resulted in lower conversion to the desired product **2a**.




**Scheme 2** *Reagents and conditions*: (i) LiHMDS (1 equiv.), solvent (see table), 0 °C, 10 min; (ii) base 2 (1.4 equiv., see table), HyperBTM **4** (20 mol%), 0 °C, 10 min; (iii) cinnamoyl chloride (1.4 equiv.), %), solvent (see table), temperature (see table).

**Table 2** Reaction optimisation

| Entry | $CH_2Cl_2$ (%) | THF (%) | Temperature ( °C) | base 2 | conv. | 2a | 3a | er |
|---|---|---|---|---|---|---|---|---|
| 1 | 80 | 20 | 0 °C to rt | $^iPr_2NEt$ | 100% | 59 | 41 | 54:46 |
| 2 | 40 | 60 | 0 °C to rt | $^iPr_2NEt$ | 100% | 63 | 37 | 62.5:37.5 |
| 3 | 30 | 70 | 0 °C to rt | $^iPr_2NEt$ | 100% | 76 | 24 | 69:31 |
| 4 | 10 | 90 | 0 °C to rt | $^iPr_2NEt$ | 100% | 58 | 42 | 74.5:25.5 |
| 5 | 0 | 100 | 0 °C to rt | $^iPr_2NEt$ | 88% | 84 | 16 | 74.5:25.5 |
| 6 | 0 | 100 | -78 | $^iPr_2NEt$ | 82% | 43 | 57 | 51:49 |
| 7 | 0 | 100 | 0 | $^iPr_2NEt$ | 89% | 63 | 37 | 75.5:24.5 |
| 8 | 0 | 100 | 20 | $^iPr_2NEt$ | 91% | 70 | 30 | 80:20 |
| 9 | 0 | 100 | 40 | $^iPr_2NEt$ | 85% | 67 | 33 | 85:15 |
| 10 | 0 | 100 | 70 | $^iPr_2NEt$ | 85% | 54 | 46 | 87:13 |
| 11 | 0 | 100 | 70 | - | 42% | 57 | 43 | 91:9 |
| 12 | 0 | 100 | 70 | $Cs_2CO_3$ | 62% | 67 | 33 | 88:12 |

[a] Insert table footnotes here.

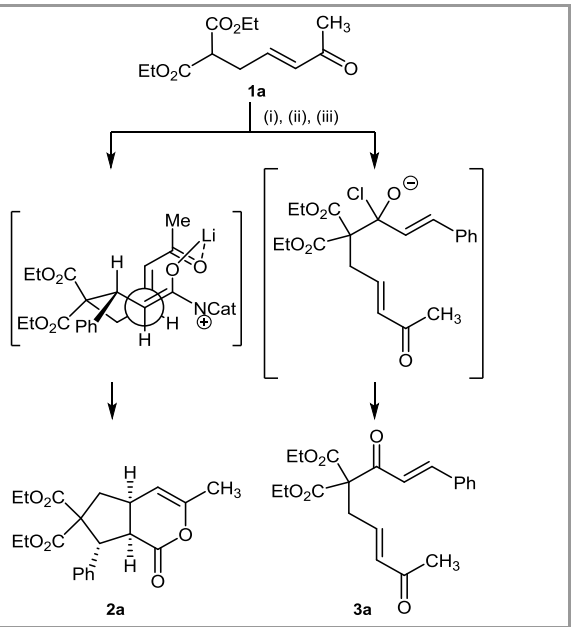



**Figure 2** Proposed influence of Lithium cation chelation on the ratio of 1,4- and 1,2-addition products.

Further optimisation varied the base and probed its effect on product ratio and er. Carrying out the reaction without $^iPr_2NEt$ gave low (42%) conversion of starting material, suggesting that this second base may be important for catalyst turnover. $Cs_2CO_3$ was also a suitable base for this function, giving a 67:33 ratio of **2a** (88:12 er) and **3a**, albeit with reduced 62% conversion. Earlier studies had indicated that LiHMDS was crucial to achieve a high ratio of 1,4-addition to 1,2-addition products.[17] This observation is consistent with chelation by the lithium counter-ion being required to aid pre-organisation of the transition state of the intramolecular Michael addition, thus leading to preferential 1,4-addition over the 1,2-addition that is favoured in the absence of $Li^+$(Figure 2).

The unusual dependence of the enantioselectivity of this reaction with temperature prompted us to conduct a kinetic analysis using an Eyring plot. The rate of formation of (4*S*,7*R*,7a*R*)-**2a**, relative to its enantiomer (4*R*,7*S*,7a*S*)-**2a**, is related to the differential activation enthalpy ($\Delta\Delta H^‡$) and differential activation entropy ($\Delta\Delta S^‡$) according to equation 1.[18]

$$\ln\left(\frac{K_{(S,R,R)}}{K_{(R,S,S)}}\right) = \frac{-\Delta\Delta H^‡}{RT} + \frac{\Delta\Delta S^‡}{R}$$

**Equation 1** Differential Eyring equation

The natural logarithm of the enantiomeric ratio of (4*S*,7*R*,7a*R*)-**2a**, measured from reactions conducted at a range of temperatures, was plotted as a function of reciprocal temperature,[19] to give a straight line with a good correlation coefficient (0.984). This is consistent with a single mechanism operating over this temperature range, in which the same step is responsible for determining enantioselectivity.[21,22,23] The activation parameters $\Delta\Delta H^‡$ and $\Delta\Delta S^‡$ are accessible from the Eyring plot, and determination of these values indicated that the $\Delta\Delta S^‡$ term (+4.42 $Jmol^{-1}K^{-1}$) is dominant over the $\Delta\Delta H^‡$ term (−0.865 $kJmol^{-1}$) in the enantiodiscrimination of this reaction. Entropically controlled enantioselectivity may suggest that the origin of this temperature effect is conformational flexibility in the diastereomeric transition states. A similar effect has previously been observed in other systems where chelation is expected to play a key role in determining enantioselectivity, accounting for sensitivity to changes in temperature.[23]

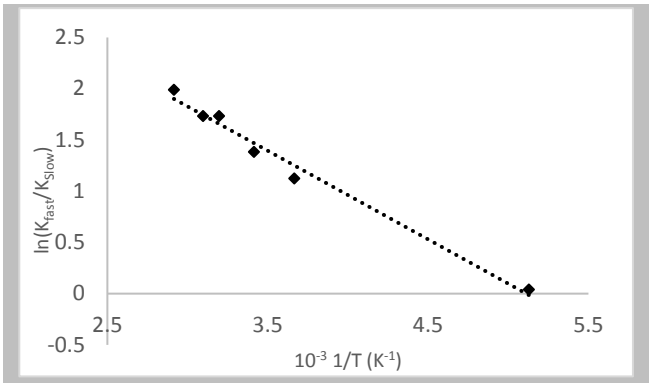
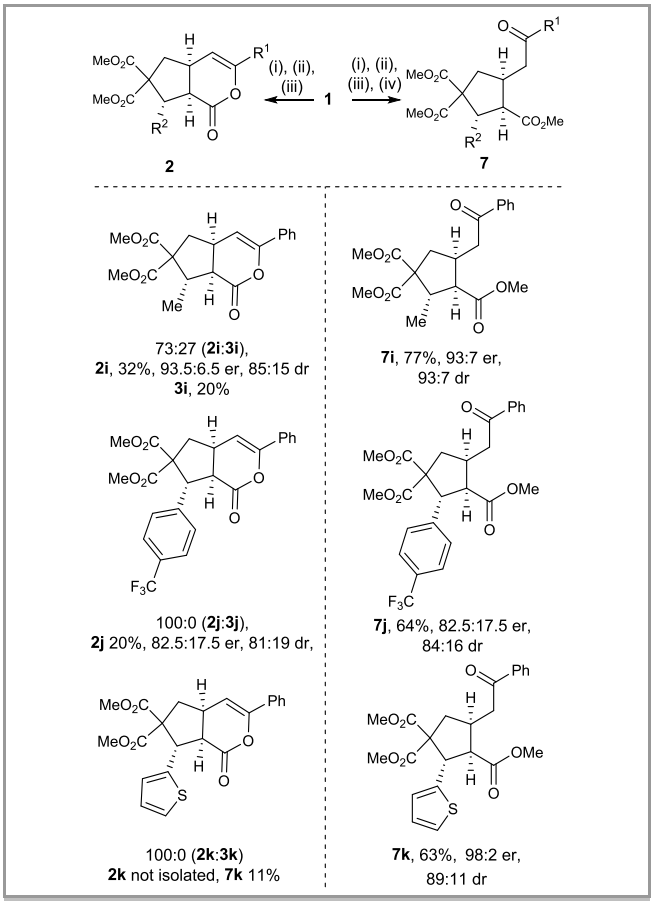



**Figure 3** Linear Eyring plot of the enantiomeric ratios obtained in the Michael-Michael lactonisation cascade reaction.

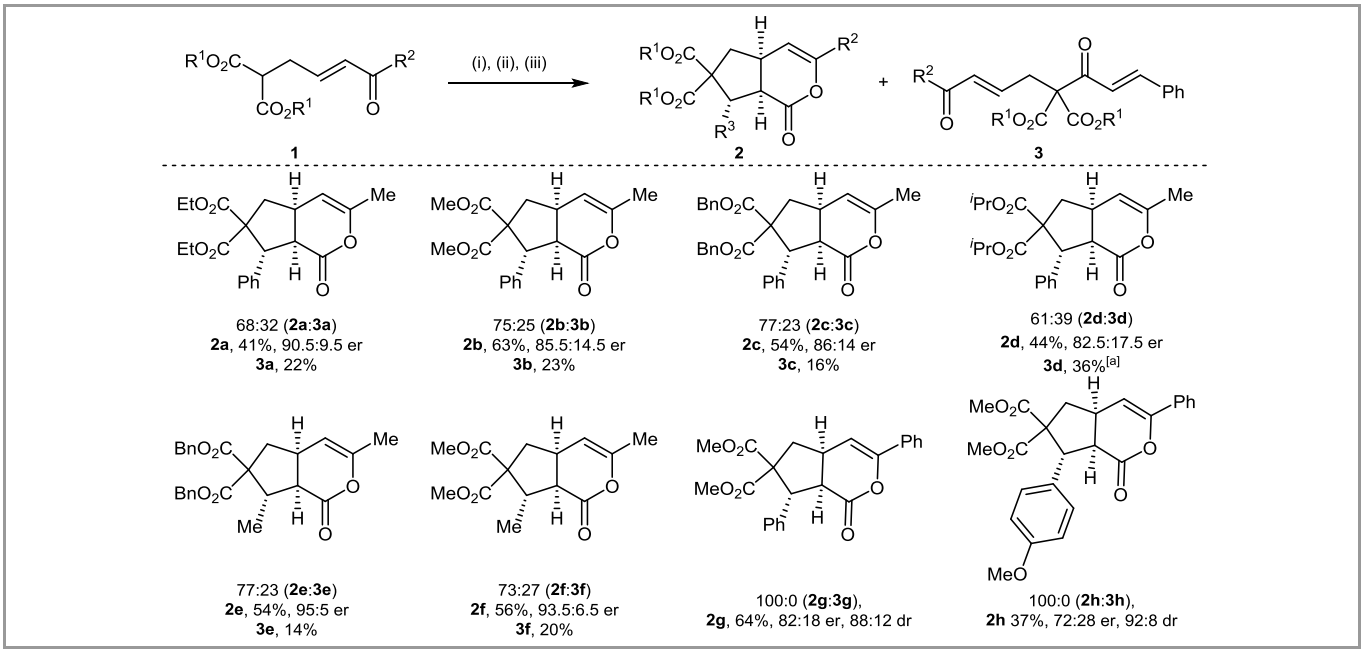
Under optimised conditions and upon scale-up of the reaction, a 70:30 ratio of **2a** to **3a** was achieved, enabling isolation of **2a** as a single diastereoisomer in 41% yield and 90.5:9.5 er (Scheme 3). The relative configuration of the major diastereoisomer was determined via NOE analysis, and the absolute configuration was confirmed via comparison of its specific rotation value with that of a known compound {$[\alpha]_D^{20}$ +33.0 (*c*1.0 in $CHCl_3$), 82% ee; {lit.[15] *for enantiomer* $[\alpha]_D^{20}$ −48.0 (*c*1.6 in $CHCl_3$), 90% ee}.

**Scope and Limitations**

With this optimised condition set in hand, investigations into the scope of the developed reaction were undertaken. Initially the nucleophilic malonate component was varied (Scheme 3). Upon annulation with cinnamoyl chloride, the ratio of the constitutional isomer products B:C derived from 1,4- and 1,2-addition varies between 61:39 to 77:23. Use of dimethyl malonate led to increased 1,4-:1,2-addition ratio (75:25 **2b**:**3b**) and gave an increased 63% yield of 1,4-addition product **2b** in 85.5:14.5 er. Benzyl substitution was also well tolerated, giving a 77:23 mixture of **2c** and **3c**, from which **2c** was isolated in 54% yield and 86:14 er. In most cases the starting material was fully converted during the reaction time, however the use of bulky isopropyl substituted enone-malonate gave a slower reaction, which afforded 1,4-product **2d,** 1,2-product **3d** and starting material **1d** in a 51:22:16 crude mixture. Upon purification, this afforded **2d** in 44% yield and 82.5:17.5 er. Extending the reaction time increased degradation products and did not increase the yields of either 1,4- or 1,2-addition products.




**Scheme 4 Variation of acid chloride component**: *Reagents and conditions*: (i) LiHMDS (1.1 equiv.), THF, 0 °C, 10 min; (ii) $^iPr_2NEt$ (1.4 equiv.), HyperBTM **4** (20 mol%), 0 °C, 10 min; (iii) acid chloride (1.4 equiv.), THF, 70 °C, 2 h.



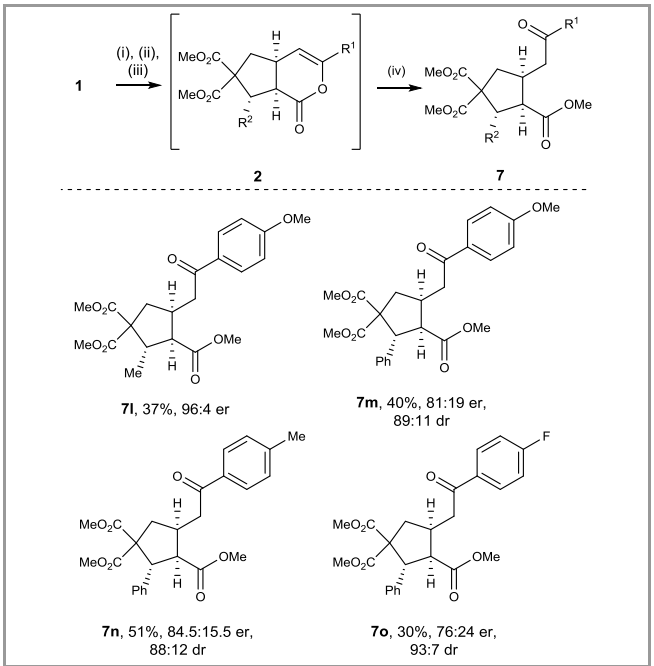

Scheme 3– Reaction scope: Variation of malonate component:

*Reagents and Conditions*: (i) LiHMDS (1 M in THF, 1.1 equiv), THF, 0 °C, 10 min; (ii) $^{i}Pr_2NEt$ (1.4 equiv, HyperBTM **2** (20 mol%),0 °C, 10 min; (iii) acid chloride (1.4 equiv), THF, 70 °C, 2 h. [a]Isolated as a mixture of 1,2 (**3d**)-addition product **3d** and starting material **1d** (7:3, inseparable by chromatography)

The scope with respect to substitution on the acid chloride component was investigated next. Reaction between dibenzyl malonate **1c** and commercially available crotonoyl chloride ($R^2$ = Me) gave a 77:23 mixture of **2e** and **3e**, from which **2e** was isolated in 54% yield and 95.0:5.0 er. Reaction with dimethyl malonate **1b** gave a 73:27 mixture of 1,4- and 1,2-addition products, enabling isolation of **2f** in 56% yield and 93.5:6.5 er. Aromatic substitution of the acid chloride was also investigated, using a dimethyl malonate/phenyl enone coupling partner. Reaction with cinnamoyl chloride gave **2g** in 64% yield, 82.0:18.0 er and 88:12 dr.[24] Electron rich aromatics showed a pronounced reduction in enantioselectivity, but increase in diastereoselectivity, giving *p*-OMe substituted **2h** in 37% yield, 72.0:28.0 er and 92:8 dr.

For some of the acid chlorides trialled, the corresponding lactones were obtained in poor isolated yields. Upon reaction of **1g** with crotonyl chloride, lactone **2i** was obtained in 32% yield, 93.5:6.5 er and 85:15 dr (Scheme 4). Similarly, incorporation of an electron withdrawing *p*-$CF_3$ substituent within the acid chloride component gave lactone **2j** in just 20% yield, and 82.5:17.5 er and 81:19 dr. Synthesis of heteroaromatic lactones was also attempted: thiophene substituted derivative **2k** was obtained in high 85% NMR yield, but upon attempted chromatographic isolation ring opening of this lactone was observed, and cyclopentane **7k** was instead isolated in 11% yield. To overcome these isolation issues, an alternative ring-opening protocol was adopted (Scheme 4). The crude reaction mixture was treated with MeOH and DMAP to facilitate ring-opening, resulting in products that it was hoped would be more stable to chromatographic purification. Following this approach, reaction of **1g** with crotonoyl chloride, with subsequent ring-opening, gave **7i** in an enhanced 77% yield, 93.0:7.0 er and 93:7 dr. Similarly, p-$CF_3$ substituted substrate **7j** was obtained in 64% yield, 82.5:17.5 er and 84:16 dr, whilst thiophene derivative **7k** was isolated in a much improved 63% yield, 98:2 er and 89:11 dr.

The substituent at the electrophilic enone component was varied next (Scheme 5). Electron rich *p*-OMe aromatic enone **1l** was reacted with both crotonoyl and cinnamoyl chloride. Upon reaction with crotonoyl chloride with subsequent ring-opening, **7l** was obtained in 37% yield and 96:4 er and as a single diastereoisomer. Isolation of the corresponding lactone was also attempted, but this did not improve the yield. Reaction with cinnamoyl chloride saw a reduction in stereoselectivity, giving **7m** in 40% yield, 81:19 er and 89:11 dr. Introducing a *p*-Me substituent into the aromatic enone gave **7n** in 51% yield, 84.5:15.5 er and 88:12 dr upon reaction with cinnamoyl chloride, whereas *p*-F substituted enone gave **7o** in 30% yield, 76:24 er and 93:7 dr. Incorporation of electron withdrawing aromatic substitutents on the enone portion gave a significant reduction in reactivity, and thus were not investigated further.




**Scheme 5 Variation of enone component**: *Reagents and Conditions*: (i) LiHMDS (1 M in THF, 1.1 equiv), THF, 0 °C, 10 min; (ii) $^{i}Pr_2NEt$ (1.4 equiv, HyperBTM **4** (20 mol%),0 °C, 10 min; (iii) acid chloride (1.4 equiv), THF, 70 °C, 2 h.

It is postulated that the mechanism of this cascade reaction begins with acylation of the isothiourea catalyst **4** by the requisite acid chloride. Anion **9** could then add in either a 1,2- or a 1,4-fashion, yielding either **3a** or **2a** respectively. In the case of 1,4-addition, turnover from intermediate **11** is achieved via lactonisation, giving rise to product **2a** and regenerating catalyst **4**. Product of 1,2-addition **3a** could also be formed via direct attack of anion **9** on the acid chloride, consistent with the high proportion of this product observed in the background reaction (Figure 4). The observed stereochemical outcome is proposed to arise from an initial Michael addition onto the *Re*-face of α,β-unsaturated acyl ammonium **8**, which is conformationally locked due to a stabilising non-bonding O–S interaction ($n_O$ to $\sigma^*_{C\text{-}S}$),[25,26] with the *Si*-face effectively blocked by the stereodirecting groups on the isothiourea catalyst.

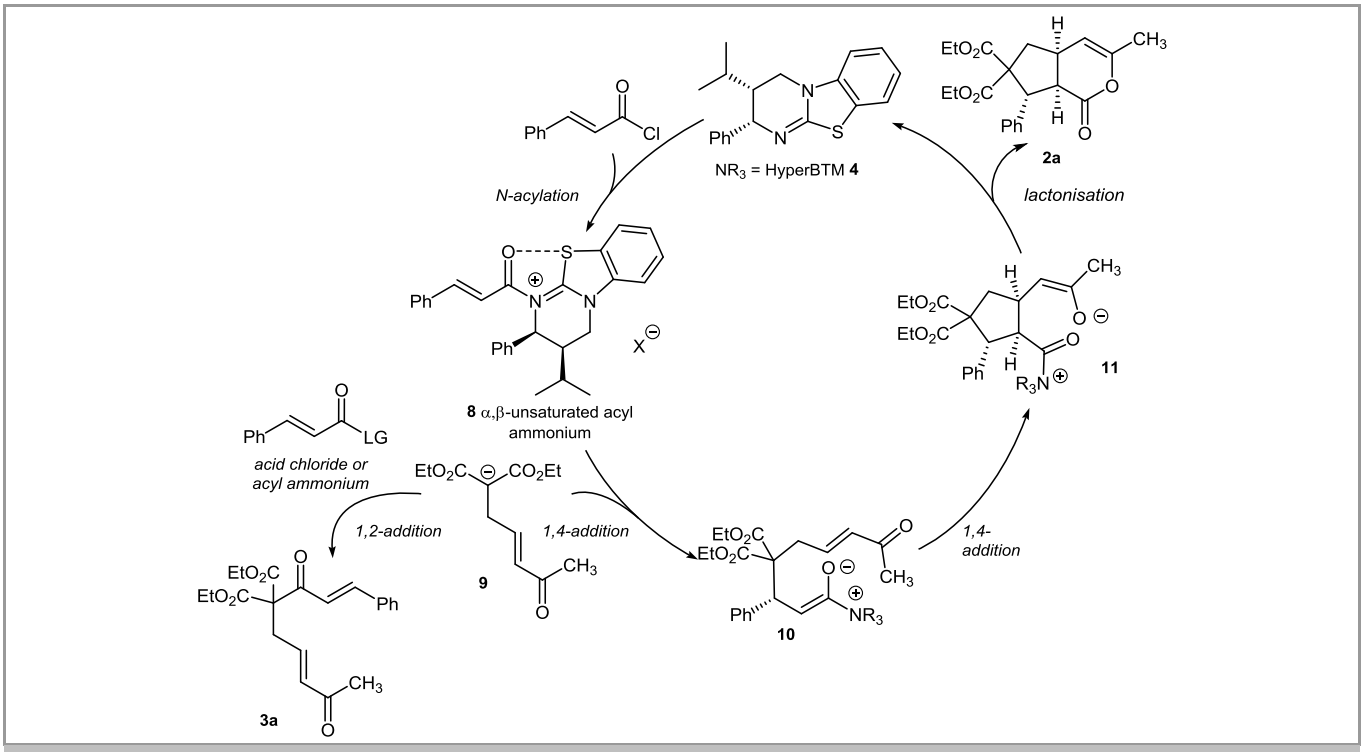



**Figure 4** Proposed mechanism for the developed Michael-Michael Lactonisation cascade process.

## Conclusion

In conclusion, as part of our efforts to explore the chemistry of α,β-unsaturated acyl ammonium intermediates we have demonstrated the first isothiourea-catalysed Michael-Michael-lactonisation process, utilising enone-malonates as Michael donor-acceptor species alongside α,β-unsaturated acyl ammonium intermediates, generated *in situ* from addition of HyperBTM **4** into α,β-unsaturated acid chlorides. Under the optimised conditions stereodiscrimination is governed by differential reaction entropy rather than enthalpy, accounting for the enhanced enantioselectivity observed at elevated temperatures. This reaction has been applied to a range of enone-malonates, affording 10 δ-lactones in 20-64% yield, 72.5:27.5 to 95:5 er and 81:19 to >95:5 dr and 7 1,2,3,4-substituted cyclopentanes in 28-77% yield, 76:24 to 98:2 er and 86:14->95:5 dr. Research into further applications of α,β-unsaturated acyl ammonium intermediates in enantioselective organocatalysis is ongoing within our laboratory.

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Reactions were performed in flame-dried glassware under an Ar or $N_2$ atmosphere unless otherwise stated. Anhydrous $CH_2Cl_2$, $Et_2O$, THF and toluene were obtained from an MBraun SPS-800 system. Petrol is defined as petroleum ether 40–60 °C. All other solvents and commercial reagents were used as received without further purification unless otherwise stated. Room temperature (rt) refers to 20–25 °C. Temperatures of 0 °C and −78 °C were obtained using ice/water and $CO_2$(s)/acetone baths respectively.

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 $F_{254}$ silica). Plates were visualised under UV light (254 nm) or by staining with either phosphomolybdic acid or $KMnO_4$ followed by heating. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated under a positive pressure of compressed air or on a Biotage® IsoleraTM 4, using Biotage® Snap Ultra or Biotage® KP Sil columns under the solvent system stated.

Melting points were recorded on an Electrothermal 9100 melting point apparatus. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at 20 °C.

HPLC analyses were obtained on a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatography SIL-20AHT autosampler, CMB-20A communications bus module, SPDM20A diode array detector and a CTO-20A column oven that allows the temperature to be set from 25–40 °C. Separation was achieved using Chiralcel columns.

Infrared spectra ($\nu_{max}$) were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50 and only characteristic peaks are reported.

$^1$H, $^{13}$C{$^1$H}, and $^{19}$F{$^1$H} NMR spectra were recorded on Bruker Avance 500 MHz, Bruker Avance 400 MHz and Bruker Avance 300 MHz NMR spectrometers. In $CDCl_3$, $^1$H and $^{13}$C{$^1$H} NMR chemical shifts are reported relative to $CHCl_3$ at 7.27 ppm and 77.0 ppm, respectively. Coupling constants (*J*) are reported in Hertz (Hz). Multiplicities are indicated by: br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet).

Mass spectrometry (*m/z*) data were acquired by electrospray ionisation (ES) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI MS on a Thermofisher LTQ Orbitrap XL spectrometer.

**General Procedures**

***General Procedure A: Enone-Malonate Synthesis via Cross Metathesis:*** Allylation procedure from Han and Widenhoefer.[27] NaH (60% in mineral oil, 1 equiv) was suspended in DMF (0.35 M) at 0 °C. A solution of dicarbonyl (1 equiv) in DMF (1 M) was added and the flask stirred at 0 °C for 2 h. A solution of allylbromide (1 equiv) in DMF (1 M) was added dropwise and the flask stirred at 0 °C to rt for 16 h. Water (xx mL) was added and the mixture extracted with $Et_2O$ (xx mL × 2). The combined organic layers were washed with brine (xx mL × 3), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude allyl ester (used without further purification). The allyl ester was dissolved in a solution of methyl vinyl ketone (3 equiv) in $CH_2Cl_2$ (0.5 M) in a sealable tube and the solution degassed by sparging with argon for 10 minutes. Metathesis catalyst M2 (2 mol%) was added, the tube sealed and heated at 50 °C for 48 h. After cooling to rt the solution was concentrated *in vacuo* and purified by silica chromatography (passed through silica twice to remove Ru residues) to afford enone malonates.

***General procedure B: Synthesis of enone malonates via Wittig reaction:*** Dimethyl 2-(2-oxoethyl)malonate and the requisite ylid were stirred at rt in $CHCl_3$ for 24 h, then concentrated *in vacuo*. The crude product was purified by column chromatography in the solvent system specified.

***General Procedure C: Acid Chloride Synthesis:*** Thionyl chloride (2 equiv) was added dropwise to the requisite carboxylic acid (1 equiv) in dry $CH_2Cl_2$ (1.1 M) and DMF (few drops) at 0 °C, and the resultant mixture was stirred at reflux for 3 h. The solution was cooled to rt and the solvent was concentrated *in vacuo* to afford the product(s) which was used directly without further purification.

***General Produre D: Michael-Michael-Lactonisation:*** LiHMDS (1 M in THF, 1.1 equiv) was added to a solution of the requisite enone malonate (1 equiv) in dry THF (0.05 M) at 0 °C. After 5 minutes $^iPr_2NEt$ (1.4 equiv) and HyperBTM **4** (20 mol%) were added then a reflux condenser added to the setup and the flask warmed to 70 °C. A solution of the requisite acid chloride (1.4 equiv) in THF (1 M) was added and the flask heated at 70 °C for 2 h. The solution was cooled to room temperature, diluted with EtOAc and washed sequentially with 0.1 M HCl and saturated aq $NaHCO_3$ solution, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, in the solvent system specified, to afford the product(s).

***General Procedure E: Ring-opened products:*** LiHMDS (1 M in THF, 1.1 equiv) was added to a solution of the requisite enone malonate (1 equiv) in dry THF (0.05 M) at 0 °C. After 5 minutes $^iPr_2NEt$ (1.4 equiv) and HyperBTM **4** (20 mol%) were added and the flask warmed to 70 °C. A solution of acid chloride (1.4 equiv) in dry THF (1 M) was added and the flask heated at 70 °C for 2 h. The solution was cooled to room temperature, diluted with EtOAc and washed sequentially with 1 M HCl, saturated aq $NaHCO_3$ solution and brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The obtained crude residue was dissolved in MeOH, and DMAP (20 mol%) was added. The reaction mixture was stirred at rt for 2 h. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel, in the solvent system specified, to afford the product.

**Experimental Procedures**

**Diethyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate 1a:** Following *General Procedure A*, diethylmalonate (2.30 mL, 15.0 mmol in DMF, 15 mL), allylbromide (1.30 mL, 15.0 mmol in DMF, 15 mL) and NaH (60% in mineral oil, 0.60 g, 15.0 mmol) were reacted in DMF (40 mL). Aqueous work-up afforded crude allylmalonate which was dissolved in $CH_2Cl_2$ (40 mL), and methyl vinyl ketone (3.65 mL, 45.0 mmol) and M2 (285 mg, 0.3 mmol) were subsequently added. The residue was purified by silica chromatography (20% EtOAc/hexane) to afford **1a** as a pale yellow oil (820 mg, 23%), with spectroscopic data in accordance with the literature.[28] $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.26 (6H, t, *J* 7.1, 2 × $CO_2CH_2CH_3$), 2.22 (3H, s, $COCH_3$), 2.79 (2H, td, *J* 7.2, 1.5, $CH_2CH$=CH), 3.49 (1H, t, *J* 7.3, $CHCO_2Et$), 4.20 (4H, qd, *J* 7.1, 2.2, 2 × $CO_2CH_2CH_3$), 6.11 (1H, dt, *J* 15.9, 1.5, $CH_2CH$=CH), 6.73 (1H, dt, *J* 16.0, 7.0, $CH_2CH$=CH).

**Dimethyl *(E)*-2-(4-oxopent-2-en-1-yl)malonate 1b:** Following *General Procedure A*, dimethylmalonate (1.14 mL, 10.0 mmol in DMF, 10 mL), allylbromide (0.87 mL, 10.0 mmol in DMF, 10 mL) and NaH (60% in mineral oil, 0.40 g, 10.0 mmol) were reacted in DMF (40 mL). Aqueous work-up afforded crude allylmalonate which was dissolved in $CH_2Cl_2$ (20 mL), and methyl vinyl ketone (2.43 mL, 30.0 mmol) and M2 (190 mg, 0.2 mmol) were subsequently added. The residue was purified by silica chromatography (10-30% EtOAc/hexane) to afford **1b** as an orange oil (522 mg, 23%), with spectroscopic data in accordance with the literature.[14,16] $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.20 (3H, s, $COCH_3$), 2.78 (2H, td, *J* 7.1, 1.5, $CH_2$), 3.52 (1H, t, *J* 7.3, $CHCO_2CH_3$), 3.72 (6H, s, 2 × $OCH_3$), 6.09 (1H, dt, *J* 16.0, 1.5, CH=$CHCOCH_3$), 6.69 (1H, dt, *J* 16.0, 7.0, $CH$=$CHCOCH_3$).

**Dibenzyl *(E)*-2-(4-oxopent-2-en-1-yl)malonate 1c:** Following *General Procedure A*, dibenzylmalonate (2.50 mL, 10.0 mmol in DMF, 10 mL), allylbromide (0.87 mL, 10.0 mmol in DMF, 10 mL) and NaH (60% in mineral oil, 0.40 g, 10.0 mmol) were reacted in DMF (40 mL). Aqueous work-up afforded crude allylmalonate which was dissolved in $CH_2Cl_2$ (20 mL), and methyl vinyl ketone (2.43 mL, 30.0 mmol) and M2 (190 mg, 0.2 mmol) were subsequently added. The residue was purified by silica chromatography (10→20% EtOAc/hexane) to afford **1c** as a pale orange oil (683 mg, 19%), with spectroscopic data in accordance with the literature.[15] $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.07 (3H, s, $COCH_3$), 2.77 (2H, td, *J* 7.2, 1.5, $CH_2$), 3.55 (1H, t, *J* 7.3, $CHCO_2Bn$), 5.09 (4H, s, 2 × $CO_2CH_2Ph$), 5.99 (1H, dt, *J* 16.0, 1.5, CH=$CHCOCH_3$), 6.60 (1H, dt, *J* 16.0, 7.0, $CH$=$CHCOCH_3$), 7.14 – 7.35 (10H, m, Ar*H*).

**Diisopropyl *(E)*-2-(4-oxopent-2-en-1-yl)malonate 1d:** Following *General Procedure A*, diisopropylmalonate (1.90 mL, 10.0 mmol in DMF, 10 mL), allylbromide (0.87 mL, 10.0 mmol in DMF, 10 mL) and NaH (60% in mineral oil, 0.40 g, 10.0 mmol) were reacted in DMF (40 mL). Aqueous work-up afforded crude allylmalonate which was dissolved in $CH_2Cl_2$ (20 mL), and methyl vinyl ketone (2.43 mL, 30.0 mmol) and M2 (190 mg, 0.2 mmol) were subsequently added. The residue was purified by silica chromatography (10→20% EtOAc/hexane) to afford **1d** as a pale yellow oil (526 mg, 19%); $\nu_{max}$ (film)/cm$^{-1}$ 2982 (C-H), 2938 (C-H), 1724 (C=O), 1676 (C=O), 1632 (C=C); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.24 (12H, dd, *J* 6.2, 1.5, 2 × $CH(CH_3)_2$), 2.23 (3H, s, $COCH_3$), 2.78 (2H, td, *J* 7.2, 1.6, $CH_2$), 3.43 (1H, t, *J* 7.3, $CHCO_2{}^iPr$), 5.06 (2H, hept, *J* 6.3, $CH(CH_3)_2$), 6.12 (1H, dt, *J* 16.0, 1.5, CH=$CHCOCH_3$), 6.75 (1H, dt, *J* 16.0, 7.0 $CH$=$CHCOCH_3$); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 21.7 (2 × $CH(CH_3)_2$), 27.1 ($COCH_3$), 31.3 ($CH_2$), 51.1 ($CHCO_2{}^iPr$), 69.5 (2 × $CH(CH_3)_2$), 133.2 (CH=$CHCOCH_3$), 143.2 ($CH$=$CHCOCH_3$), 168.0 (2 × $CO_2{}^iPr$), 198.2 ($COCH_3$); *m/z* (NSI$^+$)288 ([M+NH$_4$]$^+$, 100%), 271 ([M+H]$^+$, 55%); HRMS (NSI$^+$)$C_{14}H_{23}O_5$ ([M+H]$^+$) requires 271.1540, found 271.1543.

**Dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate 1g:** Dimethyl (*E*)-2-(4-hydroxy-4-phenylbut-2-en-1-yl)malonate (1 equiv, 3.68 mmol, 1.02 g) was dissolved in $CH_2Cl_2$ (27 mL) and activated $MnO_2$ (20 equiv, 73.58 mmol, 6.4 g) added. The flask was stirred at rt for 16 h then filtered through celite and concentrated *in vacuo*. Purification via column chromatography ($CH_2Cl_2$→ EtOAc/$CH_2Cl_2$ 1:50) gave **1g** as a pale yellow oil (686 mg, 2.48 mmol, 67%), with spectroscopic data in accordance with the literature.[14,16] $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.97-2.92 (2H, m, C(2)$H_2$), 3.63 (1H, t, *J* 7.4, C(1)*H*), 3.78 (6H, s, 2 × $CO_2CH_3$), 7.03 – 6.90 (2H, m, 2 ×

C*H*=CH), 7.53-7.45 (2H, m, 2 × *Ph*), 7.63-7.55 (1H, m, *Ph*), 7.98-7.89 (2H, m, 2 × *Ph*).

**Dimethyl (*E*)-2-(4-(4-methoxyphenyl)-4-oxobut-2-en-1-yl)malonate 1l:** Following *General Procedure B*, dimethyl 2-(2-oxoethyl)malonate (977 mg, 5.61 mmol) and 1-(4-methoxyphenyl)-2-(triphenyl-λ$^5$-phosphanylidene)ethan-1-one[29] (2.53 g, 6.17 mmol) were reacted in $CHCl_3$ (16 mL). Purification via column chromatography on silica gel (petrol/EtOAc, 3:1) gave **1l** as a pale yellow sold (615 mg, 36%, >95:5 dr), with spectroscopic data in accordance with the literature.[14,16] mp 55-58 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.91 (2H, t, *J* 7.5, C(1)$H_2$), 3.60 (1H, t, *J* 7.5, C*H*($CO_2$Me)$_2$), 3.76 (6H, s, $CO_2$*Me*), 3.88 (3H, s, O*Me*), 6.83-7.06 (4H, m, C(2)*H*, C(3)*H*, *Ar*), 7.93 (2H, d, *J* 8.9, *Ar*).

**Dimethyl (*E*)-2-(4-oxo-4-(*p*-tolyl)but-2-en-1-yl)malonate 1n:** Following *General Procedure B*, dimethyl 2-(2-oxoethyl)malonate (1.48 g, 8.49 mmol) and 1-(*p*-tolyl)-2-(triphenyl-λ$^5$-phosphanylidene)ethan-1-one[29] (3.68 g, 9.34 mmol) were reacted in $CHCl_3$ (24 mL). Purification via column chromatography on silica gel (petrol/EtOAc, 4:1) gave **1n** as an orange oil (806 mg, 33%, >95:5 dr), with spectroscopic data in accordance with the literature.[16] $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.41 (3H, s, *Me*), 2.90 (2H, t, *J* 7.5, C(1)$H_2$), 3.60 (1H, t, *J* 7.5, C*H*($CO_2$Me)$_2$), 3.75 (6H, s, $CO_2$*Me*), 6.85-7.04 (2H, m, C(2)*H*, C(3)*H*), 7.26 (2H, d, *J* 8.2, *Ar*), 7.82 (2H, d, *J* 8.2, *Ar*).

**Dimethyl (*E*)-2-(4-(4-fluorophenyl)-4-oxobut-2-en-1-yl)malonate 1o:** Following *General Procedure B*, dimethyl 2-(2-oxoethyl)malonate (1.30 g, 7.76 mmol) and 1-(4-fluorophenyl)-2-(triphenyl-λ$^5$-phosphanylidene)ethan-1-one[29] (3.27 g, 8.21 mmol) were reacted in $CHCl_3$ (21 mL). Purification via column chromatography on silica gel (petrol/EtOAc, 4:1) gave **1o** as a pale yellow oil (706 mg, 32%, >95:5 dr), with spectroscopic data in accordance with the literature.[14,16] $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.88-2.95 (2H, m, C(1)$H_2$), 3.61 (1H, t, *J* 7.4, C*H*($CO_2$Me)$_2$), 3.76 (6H, s, $CO_2$*Me*), 6.90-6.97 (2H, m, C(2)*H*, C(3)*H*), 7.08-7.20 (2H, m, *Ar*), 7.88-8.01 (2H, m, *Ar*); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) $\delta_F$: −105.3 (C(4')*F*).

**Diethyl (4a*S*,7*R*,7a*R*)-3-methyl-1-oxo-7-phenyl-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2a and diethyl 2-cinnamoyl-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3a:** Following *General Procedure D*, diethyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (121 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) and cinnamoyl chloride (117 mg, 0.7 mmol) were reacted in THF (10 mL) to give a 68:32 mixture of **2a** and **3a** in 68:32. The mixture was purified by chromatography on silica gel (20% EtOAc/hexane) to afford **2a** as a pale yellow oil (76 mg, 41%) and **3a** as a pale yellow oil (40 mg, 22%). **2a:** $[\alpha]_D^{20}$+51.9 (*c* 1.07 in $CH_2Cl_2$); $[\alpha]_D^{20}$+33.0 (*c* 1.0 in $CHCl_3$); {lit.[15] *for enantiomer* $[\alpha]_D^{20}$ −48.0 (*c* 1.6 in $CHCl_3$), 90% ee}; chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*R*,7a*R*): 14.8 min, $t_R$ (4a*R*,7*S*,7a*S*): 16.5 min, 90.5:9.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 3032 (C-H), 2982 (C-H), 1717 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 0.75 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.25 (3H, t, *J* 7.0, $CO_2CH_2CH_3$), 1.88 (3H, dd, *J* 2.2, 1.1, C(3)C$H_3$), 2.16 (1H, dd, *J* 13.9, 4.0, C(5)$H_A$), 3.03 (1H, dd, *J* 13.9, 7.3, C(5)$H_B$), 3.29 – 3.46 (3H, m, $CO_2CH_AH_BCH_3$, C(4a)*H*, C(7a)*H*), 3.73 (1H, dq, *J* 10.7, 7.1, $CO_2CH_AH_BCH_3$), 4.15 – 4.29 (2H, m, $CO_2CH_2CH_3$), 4.63 (1H, d, *J* 9.4, C(7)*H*), 4.77 (1H, dt, *J* 3.1, 1.2, C(4)*H*), 7.20 – 7.25 (1H, m, *p*-*Ph*), 7.25 – 7.30 (2H, m, 2 × *m*-*Ph*), 7.31 – 7.36 (2H, m, 2 × *o*-*Ph*); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) $\delta_C$: 13.4 ($CO_2CH_2CH_3$), 14.1 ($CO_2CH_2CH_3$), 18.9 (C(3)$CH_3$), 36.3 (*C*(4a)H), 41.3 (*C*(5)$H_2$), 47.7 (*C*(7a)H), 53.4 (*C*(7)H), 61.6 ($CO_2CH_2CH_3$), 61.9 ($CO_2CH_2CH_3$), 65.0 (*C*(6)), 102.4 (*C*(4)H), 127.7 (*p*-*Ph*), 128.2 (2 × *Ph*), 129.0 (2 × *Ph*), 137.6 (*i*-*Ph*), 148.5 (*C*(3)$CH_3$), 169.1 (*C*(1)), 170.0 ($CO_2$Et), 171.4 ($CO_2$Et); *m/z* (NSI$^+$) 390 ([M+$NH_4$]$^+$, 100%), 373 ([M+H]$^+$, 50%); HRMS (NSI$^+$)$C_{21}H_{24}O_6$ ([M+H]$^+$) requires 373.1646, found 373.1650. **3a:** $\nu_{max}$ (film)/cm$^{-1}$ 2982 (C-H), 2934 (C-H), 1728 (C=O), 1676 (C=O), 1609 (C=C); $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.27 (6H, t, *J* 7.1, 2 × $CO_2CH_2CH_3$), 2.22 (3H, s, COC$H_3$), 3.08 (2H, dd, *J* 7.3, 1.4, C$H_2$CH=CH), 4.27 (4H, q, *J* 7.1, 2 × $CO_2CH_2CH_3$), 6.09 (1H, dt, *J* 15.9, 1.4, $CH_2CH$=C*H*), 6.83 (1H, dt, *J* 16.0, 7.3, $CH_2CH$=CH), 7.05 (1H, d, *J* 15.6, C*H*=CHPh), 7.33 – 7.45 (3H, m, *Ph*), 7.51 – 7.59 (2H, m, *Ph*), 7.72 (1H, d, *J* 15.6, CH=C*H*Ph); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta_C$: 14.2 (2 × $CO_2CH_2CH_3$), 26.7 (CO*C*H$_3$), 35.2 ($CH_2$CH=CH), 62.7 (2 × $CO_2CH_2CH_3$), 70.0 (C($CO_2$Et)$_2$), 122.5 (*C*H=CHPh), 128.8 (2 × *Ph*), 129.1 (2 × *Ph*), 131.1 (*p*-*Ph*), 134.3 (*i*-*Ph*), 134.7 ($CH_2$CH=*C*H), 142.5 ($CH_2$*C*H=CH), 144.5 (CH=*C*HPh), 167.1 (2 × *C*O$_2$Et), 189.3 (*C*OCH=CHPh), 198.5 (*C*OMe); *m/z* (NSI$^+$) 390 ([M+$NH_4$]$^+$, 40%), 373 ([M+H]$^+$, 100%); HRMS (NSI$^+$)$C_{21}H_{24}O_6$ ([M+H]$^+$) requires 373.1646, found 373.1652.

**Dimethyl (4a*S*,7*R*,7a*R*)-3-methyl-1-oxo-7-phenyl-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2b and dimethyl 2-cinnamoyl-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3b:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (107 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) and cinnamoyl chloride (117 mg, 0.7 mmol) were reacted in THF (10 mL) to give a 75:25 mixture of **2b** and **3b**. The mixture was purified by chromatography on silica gel (20%→30% EtOAc/hexane) to afford **2b** as a pale yellow oil (108 mg, 63%) and **3b** as a pale yellow oil (40 mg, 23%). **2b:** $[\alpha]_D^{20}$ +38.0 (*c* 1.50 in $CH_2Cl_2$); chiral HPLC analysis, ChiralPak AS-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*R*,7a*R*): 13.2 min, $t_R$ (4a*R*,7*S*,7a*S*): 23.6 min, 85.5:14.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2953 (C-H), 1749 (C=O), 1727 (C=O), 1699 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.89 (3H, dd, *J* 2.0, 1.1, C(3)C$H_3$), 2.14 (1H, dd, *J* 13.9, 4.0 C(5)$H_A$), 3.02 (1H, dd, *J* 14.1, 7.0, C(5)$H_B$), 3.12 (3H, s, $CO_2CH_3$), 3.29 – 3.50 (2H, m, C(4a)*H*, C(7a)*H*), 3.75 (3H, s, $CO_2CH_3$), 4.63 (1H, d, *J* 9.0, C(7)*H*), 4.75 – 4.80 (1H, m, C(4)*H*), 7.00 – 7.48 (5H, m, Ar*H*); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 18.8 (C(3)*C*H$_3$), 36.2 (*C*(4a)H), 41.2 (*C*(5)H$_2$), 47.4(*C*(7a)H), 52.3 ($CO_2CH_3$), 53.0 ($CO_2CH_3$), 53.6 (*C*(7)H), 65.1 (*C*(6)), 102.3 (*C*(4)H), 127.7 (*p*-*Ph*), 128.2 (*Ph*), 128.8 (*Ph*), 137.4 (*i*-*Ph*), 148.5 (*C*(3)), 168.9 (*C*(1)), 170.3 (*C*O$_2$CH$_3$), 171.8 (*C*O$_2$CH$_3$); *m/z* (NSI$^+$) 367 ([M+Na]$^+$, 100%), 345 ([M+H]$^+$, 65%); HRMS (NSI$^+$) $C_{19}H_{21}O_6$ ([M+H]$^+$) requires 345.1333, found 345.1329. **3b:** $\nu_{max}$ (film)/cm$^{-1}$ 2955 (C-H), 1732 (C=O), 1674 (C=O), 1607 (C=C); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.22 (3H, s, COC$H_3$), 3.08 (2H, dd, *J* 7.3, 1.4, C$H_2$), 3.80 (6H, s, 2 × $CO_2CH_3$), 6.09 (1H, dt, *J* 16.0, 1.4, CH=C*H*COCH$_3$), 6.81 (1H, dt, *J* 16.0, 7.3, C*H*=CHCOCH$_3$), 7.00 (1H, d, *J* 15.6, C*H*=CHPh), 7.41 (3H, qd, *J* 2.9, 1.1, *Ph*), 7.50 – 7.61 (2H, m, *Ph*), 7.73 (1H, d, *J* 15.6, CH=C*H*Ph); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 26.8 (CO*C*H$_3$), 35.3 (*C*H$_2$), 53.5 (2 × $CO_2CH_3$), 70.1 (*C*($CO_2CH_3$), 122.1 (*C*H=CHPh), 128.9 (2 × *Ph*), 129.1 (2 × *Ph*), 131.2 (*p*-*Ph*), 134.2 (i-*Ph*), 134.7 (CH=*C*HCOCH$_3$), 142.1 (*C*H=CHCOCH$_3$), 145.0 (CH=*C*HPh), 167.5 (2 × *C*O$_2$CH$_3$), 189.0 (*C*OCH=CHPh), 198.4 (*C*OCH$_3$); *m/z* (NSI$^+$) 367 ([M+Na]$^+$, 100%), 345 ([M+H]$^+$, 20%); HRMS (NSI$^+$) $C_{19}H_{21}O_6$ ([M+H]$^+$) requires 345.1333, found 345.1330.

**Dibenzyl (4a*S*,7*R*,7a*R*)-3-methyl-1-oxo-7-phenyl-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2c and dibenzyl 2-cinnamoyl-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3c:** Following *General Procedure D*, dibenzyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (183 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) and cinnamoyl chloride (117 mg, 0.7 mmol) were reacted in THF (10 mL) to give a 77:23 mixture of **2c** and **3c**. The mixture was purified by chromatography on silica gel (20% EtOAc/hexane) to afford **2c** as a pale yellow oil (135 mg, 54%) and **3c** as a pale yellow oil (41 mg, 16%). **2c:** $[\alpha]_D^{20}$ +24.6 (*c* 3.42 in $CH_2Cl_2$); chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*R*,7a*R*): 35.6 min, $t_R$ (4a*R*,7*S*,7a*S*): 38.4 min, 86.0:14.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 3034 (C-H),

1749 (C=O), 1724 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.84 (3H, dd, *J* 2.1, 1.1, C$H_3$), 2.21 (1H, dd, *J* 13.9, 3.9, C(5)$H_A$), 3.07 (1H, dd, *J* 13.9, 7.2, C(5)$H_B$), 3.29 – 3.42 (1H, m, C(4a)*H*), 3.43 – 3.48 (1H, m, C(7a)*H*), 4.20 (1H, d, *J* 12.3, $CO_2CH_AH_BPh$), 4.64 – 4.71 (2H, m, C(4)*H*, C(7)*H*), 4.75 (1H, d, *J* 12.3, $CO_2CH_AH_BPh$), 5.06 (1H, d, *J* 12.1, $CO_2CH_AH_BPh$), 5.17 (1H, d, *J* 12.1, $CO_2CH_AH_BPh$), 6.85 – 6.91 (2H, m, *Ph*), 7.16 – 7.39 (13H, m, *Ph*); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 18.8 (C(3)$CH_3$), 36.3 (*C*(4a)H), 41.3 (*C*(5)$H_2$), 47.7 (*C*(7a)H), 53.7 (*C*(7)H), 65.2 (*C*(6)), 67.4 ($CO_2CH_2$Ph), 67.8 ($CO_2CH_2$Ph), 102.3 (*C*(4)H), 127.8 (*p-Ph*), 128.0 (2 × *Ph*), 128.2 (*p-Ph*), 128.4 (2 × *Ph*), 128.4 (2 × *Ph*), 128.4 (2 × *Ph*), 128.5 (*p-Ph*), 128.6 (2 × *Ph*), 129.0 (2 × *Ph*), 134.7 (*i-Ph*), 135.2 (*i-Ph*), 137.3 (*i-Ph*), 148.6 (*C*(3)), 168.9 (*C*(1)), 169.7 (*C*O$_2$Bn), 171.0 (*C*O$_2$Bn); *m/z* (NSI$^+$) 497 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{31}H_{29}O_6$ ([M+H]$^+$) requires 497.1959, found 497.1944. **3c:** $\nu_{max}$ (film)/cm$^{-1}$ 3032 (C-H), 1730 (C=O), 1676 (C=O), 1608 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.11 (3H, s, C$H_3$), 3.12 (2H, dd, *J* 7.4, 1.3, C$H_2$), 5.23 (4H, d, *J* 2.0, 2 × $CO_2CH_2$Ph), 6.02 (1H, dt, *J* 16.0, 1.3, CH=C*H*COCH$_3$), 6.76 (1H, dt, *J* 15.9, 7.3 C*H*=CHCOCH$_3$), 6.90 (1H, d, *J* 15.6, C*H*=CHPh), 7.23 – 7.33 (10H, m, *Ph*), 7.33 – 7.40 (5H, m, *Ph*), 7.69 (1H, d, *J* 15.6, CH=C*H*Ph); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 26.6 (*C*H$_3$), 35.2 (*C*H$_2$), 68.3 (4 × $CO_2CH_2$Ph), 122.6 (*C*H=CHPh), 128.5 (*Ph*), 128.7 (*Ph*), 128.7 (*Ph*), 128.8 (*Ph*), 128.9 (*Ph*), 129.0 (*Ph*), 131.1 (*Ph*), 134.1 (*i-Ph*), 134.6 (2 × *i-Ph*), 134.8 (CH=*C*HCOCH$_3$), 142.1 (*C*H=CHCOCH$_3$), 144.8 (CH=*C*HPh), 166.8 (2 × *C*O$_2$Bn), 188.7 (*C*OCH=CHPh), 198.4 (*C*OCH$_3$); *m/z* (NSI$^+$) 497 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{31}H_{29}O_6$ ([M+H]$^+$) requires 497.1959, found 497.1946.

**Diisopropyl (4a*S*,7*R*,7a*R*)-3-methyl-1-oxo-7-phenyl-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2d and diisopropyl 2-cinnamoyl-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3d:** Following *General Procedure D*, diisopropyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (135 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) in THF and cinnamoyl chloride (117 mg, 0.7 mmol) were reacted in THF (10 mL) to give a 61:39 mixture of **2d** and **3d**.The mixture was purified by chromatography on silica gel (10%→20% EtOAc/hexane) to afford **2d** as a pale yellow oil (87 mg, 44%) and **3d** as a pale yellow oil (isolated as a 7:3 mixture of **3d** to enone-malonate **1d**, 71 mg, 36%). **2d:** $[\alpha]_D^{20}$ +51.0 (*c* 0.58 in $CH_2Cl_2$); chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*R*,7a*R*): 10.2 min, t$_R$ (4a*R*,7*S*,7a*S*): 12.0 min, 82.5:17.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2980 (C-H), 2924 (C-H), 1763 (C=O), 1719 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.48 (3H, d, *J* 6.3, CH(CH$_3$)(C*H*)$_3$), 1.01 (3H, d, *J* 6.2, CH(CH$_3$)(C*H*)$_3$), 1.24 (3H, d, *J* 6.3, CH(CH$_3$)(C*H*)$_3$), 1.28 (3H, d, *J* 6.2, CH(CH$_3$)(C*H*)$_3$), 1.89 (3H, dd, *J* 2.1, 1.1 C(3)C$H_3$), 2.19 (1H, dd, *J* 13.9, 3.5, C(5)$H_A$), 3.03 (1H, dd, *J* 13.9, 7.1, C(5)$H_B$), 3.26 – 3.48 (2H, m, C(4a)*H*, C(7a)*H*), 4.46 (1H, p, *J* 6.3, C*H*(CH$_3$)$_2$), 4.62 (1H, d, *J* 9.0, C(4)*H*), 4.75 (1H, dq, *J* 2.9, 1.1, C(7)*H*), 5.09 (1H, p, *J* 6.2, C*H*(CH$_3$)$_2$), 7.19 – 7.38 (5H, m, *Ph*); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 18.9 (C(3)*C*H$_3$), 20.7 (CH(CH$_3$)(*C*H$_3$)), 21.4, (CH(CH$_3$)(*C*H$_3$)) 21.6 (CH(CH$_3$)(*C*H$_3$)), 21.8 (CH(CH$_3$)(*C*H$_3$)), 36.3 (*C*(4a)H), 41.6 (*C*(5)$H_2$), 48.4 (*C*(7a)H), 53.4 (*C*(7)H), 65.0 (*C*(6)), 69.4 (*C*H(CH$_3$)$_2$), 69.5 (*C*H(CH$_3$)$_2$), 102.4 (*C*(4)H), 127.7 (*p-Ph*), 128.3 (2 × *Ph*), 129.2 (2 × *Ph*), 137.9 (*i-Ph*), 148.6 (*C*(3)), 169.1 (*C*(1)), 169.5 (*C*O$_2^i$Pr), 171.0 (*C*O$_2^i$Pr); *m/z* (NSI$^+$) 401 ([M+H]$^+$, 100%), 423 ([M+Na]$^+$, 65%); HRMS (NSI$^+$) $C_{23}H_{29}O_6$ ([M+H]$^+$) requires 401.1959, found 401.1949. **3d:** $\nu_{max}$ (film)/cm$^{-1}$ 2982 (C-H), 1724 (C=O), 1676 (C=O), 1609 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.25 (12H, d, *J* 6.3, 2 × CH(C$H_3$)$_2$), 2.21 (3H, s, COC$H_3$), 3.05 (2H, dd, *J* 7.3, 1.4, C$H_2$), 5.12 (2H, p, *J* 6.3, 2 × C*H*CH$_3$)$_2$), 6.09 (1H, dt, *J* 16.1, 1.4, CH=C*H*COCH$_3$), 6.83 (1H, dt, *J* 16.0, 7.3, C*H*=CHCOCH$_3$), 7.06 (1H, d, *J* 15.7, C*H*=CHPh), 7.39 (3H, dd, *J* 5.1, 1.9, *Ph*), 7.48 – 7.59 (2H, m, *Ph*), 7.70 (1H, d, *J* 15.7, CH=C*H*Ph); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 21.7 (CH(*C*H$_3$)$_2$), 21.7 (CH(*C*H$_3$)$_2$), 26.6 (COC$H_3$), 35.1 (*C*H$_2$), 70.6 (2 × *C*H(CH$_3$)$_2$), 122.8 (*C*H=CHPh), 128.7 (2 × *Ph*), 129.1 (2 × *Ph*), 131.0 (*p-Ph*), 134.4 (*i-Ph*), 134.7 (CH=*C*HCOCH$_3$), 142.7 (*C*H=CHCOCH$_3$), 144.0 (CH=*C*HPh), 166.6 (2 × *C*O$_2^i$Pr), 189.6 (*C*OCH=CHPh), 198.5 (*C*OCH$_3$); *m/z* (NSI$^+$) 401 ([M+H]$^+$, 30%), 423 ([M+Na]$^+$, 100%); HRMS (NSI$^+$) $C_{23}H_{29}O_6$ ([M+H]$^+$) requires 401.1959, found 401.1949.

**Dibenzyl (4a*S*,7*S*,7a*R*)-3,7-dimethyl-1-oxo-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2e and dibenzyl 2-((*E*)-but-2-enoyl)-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3e:** Following *General Procedure D*, dibenzyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (183 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) and crotonoyl chloride (67 µL, 0.7 mmol) were reacted in THF (10 mL) to give a 77:23 mixture of **2e** and **3e**. The mixture was purified by chromatography on silica gel (20% EtOAc/hexane) to afford **2e** as a pale yellow oil (118 mg, 54%) and **3e** as a pale yellow oil (30 mg, 14%). **2e:** $[\alpha]_D^{20}$ +84.2 (*c* 1.55 in $CH_2Cl_2$); chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 21.4 min, t$_R$ (4a*R*,7*R*,7a*S*): 23.2 min, 95.0:5.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 2955 (C-H), 1748 (C=O), 1722 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.15 (3H, d, *J* 6.9, C(7)C$H_3$), 1.79 (3H, dd, *J* 2.3, 1.1, C(3)C$H_3$), 2.06 (1H, dd, *J* 14.0, 4.3, C(5)$H_A$), 2.73 (1H, ddd, *J* 11.1, 8.8, 0.9, C(7)*H*), 2.81 (1H, dd, *J* 13.9, 8.2, C(5)$H_B$), 2.99 – 3.08 (1H, m, C(7a)*H*), 3.08 – 3.16 (1H, m, C(4a)*H*), 4.59 (1H, dp, *J* 2.1, 1.1, C(4)*H*), 4.98 – 5.19 (4H, m, 2 × $CO_2CH_2$Ph), 7.19 – 7.27 (4H, m, *Ph*), 7.29 – 7.37 (6H, m, *Ph*); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta_C$: 15.3 (C(7)*C*H$_3$), 18.8 (C(3)*C*H$_3$), 34.9 (*C*(4a)H), 41.2 (*C*(5)$H_2$), 44.2 (*C*(7)H), 48.4 (*C*(7a)H), 62.4 (*C*(6)), 67.5 ($CO_2CH_2$Ph), 67.5 ($CO_2CH_2$Ph), 103.1 (*C*(4)H), 128.3 (2 × *Ph*), 128.4 (2 × *Ph*), 128.5 (*p-Ph*), 128.6 (*p-Ph*), 128.6 (2 × *Ph*), 128.7 (2 × *Ph*), 135.0 (*i-Ph*), 135.4 (*i-Ph*), 147.1 (*C*(3)), 169.6 (*C*(1)), 170.5 (*C*O$_2$Bn), 170.9 (*C*O$_2$Bn); *m/z* (NSI$^+$) 436 ([M+Na]$^+$, 30%), 435 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{26}H_{27}O_6^+$ ([M+H]$^+$) requires 435.1802, found 435.1798. **3e:** $\nu_{max}$ (film)/cm$^{-1}$ 2967 (C-H), 1728 (C=O), 1694 (C=O), 1676 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.79 (3H, dd, *J* 7.0, 1.7, CH=CHC$H_3$), 2.06 (3H, s, COC$H_3$), 3.01 (2H, dd, *J* 7.3, 1.4, C$H_2$), 5.18 (4 H, d, *J* 1.4, 2 × $CO_2CH_2$Ph), 5.95 (1H, dt, *J* 16.0, 1.4, CH=C*H*COCH$_3$), 6.29 (1H, dq, *J* 15.2, 1.7, C*H*=CHCH$_3$), 6.67 (1H, dt, *J* 16.0, 7.3, C*H*=CHCOCH$_3$), 6.98 (1H, dq, *J* 15.2, 7.0, CH=C*H*CH$_3$), 7.19 – 7.30 (4H, m, *Ph*), 7.30 – 7.35 (6H, m, *Ph*); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta_C$: 18.4 (CH=CH*C*H$_3$), 26.5 (COC$H_3$), 35.1 (*C*H$_2$), 68.2 (2 × $CO_2CH_2$Ph), 69.6 (*C*(CO$_2$Bn)$_2$), 127.7 (*C*H=CHCH$_3$), 128.6 (4 × *Ph*), 128.8 (4 × *Ph*), 128.8 (2 × *Ph*), 134.7 (2 × *i-Ph*), 134.8 (CH=*C*HCOCH$_3$), 142.1 (*C*H=CHCOCH$_3$), 145.6 (CH=*C*HCH$_3$), 166.8 (2 × *C*O$_2$Bn), 188.5 (*C*OCH=CH), 198.4 (*C*OCH$_3$); *m/z* (NSI$^+$) 457 ([M+Na]$^+$, 100%); HRMS (NSI$^+$) $C_{26}H_{26}NaO_6^+$ ([M+Na]$^+$) requires 457.1622, found 457.1610.

**Dimethyl (4a*S*,7*S*,7a*R*)-3,7-dimethyl-1-oxo-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2f and dimethyl 2-((*E*)-but-2-enoyl)-2-((*E*)-4-oxopent-2-en-1-yl)malonate 3f:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxopent-2-en-1-yl)malonate (107 mg, 0.5 mmol), LiHMDS (1 M in THF, 0.55 mL, 0.55 mmol), HyperBTM **4** (30.8 mg, 0.10 mmol), $^i$Pr$_2$NEt (0.12 mL, 0.7 mmol) and crotonoyl chloride (67 µL, 0.7 mmol) were reacted in THF (10 mL) to give a 73:27 mixture of **2f** and **3f**. The mixture was purified by chromatography on silica gel (20%→30% EtOAc/hexane) to afford **2f** as a pale yellow oil (79 mg, 56%) and **3f** as a pale yellow oil (28 mg, 20%). **2f:** $[\alpha]_D^{20}$+117.4 (*c*0.98 in $CH_2Cl_2$); chiral HPLC analysis, ChiralPak AS-H (2.5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 9.3 min, t$_R$ (4a*R*,7*R*,7a*S*): 15.8 min, 93.5:6.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2955 (C-H), 1726 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.14 (3H, d, *J* 6.9, C(7)C$H_3$), 1.81 (3H, dd, *J* 2.3, 1.1, C(3)C$H_3$), 2.00 (1H, dd, *J* 14.0, 4.3, C(5)C$H_A$), 2.71 (1H, ddd, *J* 11.2, 8.7, 0.8, C(7)*H*), 2.77 (1H, dd, *J* 14.0, 8.2, C(5)$H_B$), 2.90 – 3.08 (1H, m, C(7a)*H*), 3.06 – 3.17 (1H, m, C(4a)*H*), 3.71 (6H, d, *J* 3.0, 2 × $CO_2CH_3$), 4.65 (1H, dp, *J* 2.3, 1.2, C(4)*H*); $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$) $\delta_C$: 15.2

(C(7)*C*H$_3$), 18.8 (C(3)*C*H$_3$), 34.8 (*C*(4a)H), 41.1 (*C*(5)H$_2$), 44.1 (*C*(7)H), 48.2 (*C*(7a)H), 52.6 (CO$_2$*C*H$_3$), 52.8 (CO$_2$*C*H$_3$), 62.2 (*C*(6)), 103.2 (*C*(4)H), 147.0 (*C*(3)), 169.6 (*C*(1)), 171.2 (*C*O$_2$CH$_3$), 171.7 (*C*O$_2$CH$_3$); *m/z* (NSI$^+$) 283 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{14}H_{19}O_6^+$ ([M+H]$^+$) requires 283.1176, found 283.1177. **3f:** $\nu_{max}$ (film)/cm$^{-1}$ 2957 (C-H), 1732 (C=O), 1676 (C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta_H$: 1.92 (3H, dd, *J* 7.0, 1.7, CH=CHC*H*$_3$), 2.21 (3H, s, COC*H*$_3$), 3.00 (2H, dd, *J* 7.4, 1.4, C*H*$_2$), 3.78 (6H, s, 2 × CO$_2$C*H*$_3$), 6.05 (1H, dt, *J* 16.0, 1.4, CH=C*H*COCH$_3$), 6.39 (1H, dq, *J* 15.1, 1.6, C*H*=CHCH$_3$), 6.77 (1H, dt, *J* 16.0, 7.3, C*H*=CHCOCH$_3$), 7.05 (1H, dq, *J* 15.2, 7.0, CH=C*H*CH$_3$); $^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$) $\delta_C$: 18.6 (CH=CH*C*H$_3$), 26.7 (COC*H*$_3$), 35.2 (*C*H$_2$), 53.4 (2 × CO$_2$*C*H$_3$), 69.7 (*C*(CO$_2$CH$_3$)$_2$), 127.4 (*C*H=CHCH$_3$), 134.7 (CH=*C*HCOCH$_3$), 142.2(*C*H=CHCOCH$_3$), 145.9 (CH=*C*HCH$_3$), 167.5 (2 × *C*O$_2$CH$_3$), 188.7 (*C*OCH=CH), 198.5 (*C*OCH$_3$); *m/z* (NSI$^+$) 283 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{14}H_{19}O_6^+$ ([M+H]$^+$) requires 283.1176, found 283.1177.

**Dimethyl 1-oxo-3,7-diphenyl)-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1*H*)-dicarboxylate 2g:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (70 mg, 0.25 mmol), LiHMDS (1 M in THF, 0.28 mL, 0.28 mmol), HyperBTM **4** (16 mg, 0.05 mmol), $^i$Pr$_2$NEt (62 µL, 0.35 mmol) and cinnamoyl chloride (59 mg , 0.35 mmol) were reacted in THF (5.35 mL) to give **2g** in 84:16 dr. The mixture was purified by chromatography on silica gel (EtOAc/Hexane 1:5) to afford **2g** as a yellow oil in 93:7 dr (64.7 mg, 64%). **2g:** $[\alpha]_D^{20}$ −17.0 (c 1.1 in CHCl$_3$); chiral HPLC analysis, ChiralPak IA (2% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 23.5 min, t$_R$ (4a*R*,7*R*,7a*S*): 32.9 min, 82.0:18.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 2951 (C-H), 2849 (C-H), 1759 (C=O), 1748 (C=O), 1724 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 2.30 (1H, dd, *J* 14.0, 4.4, C(5)*H*$_A$), 3.18-3.12 (4H, m, CO$_2$C*H*$_3$, C(5)*H*$_B$), 3.60-3.55 (1H, m, C(7a)*H*), 3.65-3.60 (1H, m, C(4a)*H*), 3.74 (3H, s, CO$_2$C*H*$_3$), 4.73 (1H, d, *J* 8.9, C(7)*H*), 5.60 (1H, d, *J* 2.5, C(4)*H*), 7.30-7.25 (1H, m, *Ph*), 7.35-7.30 (4H, m, 4 × *Ph*), 7.43-7.37 (3H, m, 3 × *Ph*), 7.66-7.60 (2H, m, 2 × *Ph*); $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) $\delta_C$: 36.7 (*C*(4a)H), 41.2 (*C*(5)H$_2$), 47.6 (*C*(7a)H), 52.3 (CO$_2$*C*H$_3$), 53.1 (CO$_2$*C*H$_3$), 53.6 (*C*(7)H), 65.0 (*C*(6)), 102.2 (*C*(4)H), 124.8 (2 × *Ph*), 127.8 (*p-Ph*), 128.3 (2 × *Ph*), 128.6 (2 × *Ph*), 128.7 (2 × *Ph*), 129.2 (*p-Ph*), 132.1 (*i-Ph*), 137.3 (*i-Ph*), 149.2 (*C*(3)), 168.4 (*C*(1)), 170.2 (*C*O$_2$CH$_3$), 171.6 (*C*O$_2$CH$_3$). Selected data for minor diastereomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 4.54 (1H, d, *J* 11.8, C(7)*H*), 6.12 (1H, d, *J* 2.1, C(4)*H*).

**Dimethyl 7-(4'-methoxyphenyl)-1-oxo-3-phenyl)-4a,5,7,7a tetrahydrocyclopenta[c]pyran- 6,6(1*H*)-dicarboxylate 2h:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (70 mg, 0.25 mmol), LiHMDS (1 M in THF, 0.28 mL, 0.28 mmol), HyperBTM **4** (16 mg, 0.05 mmol), $^i$Pr$_2$NEt (62 µL, 0.35 mmol) and 4-methoxycinnamoyl chloride (70 mg , 0.35 mmol) were reacted in THF (5.4 mL) to give **2h** in 92:8 crude dr. The mixture was purified by chromatography on silica gel (Toluene/CH$_2$Cl$_2$ 1:5→CH$_2$Cl$_2$) to afford **2h** as a yellow oil in 97:3 dr (40 mg, 37%). **2h:** $[\alpha]_D^{20}$−21.7 (c 1.0 in CHCl$_3$); chiral HPLC analysis, ChiralPak AS-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 32.2 min, t$_R$ (4a*R*,7*R*,7a*S*): 48.2 min, 72.0:28.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 2951 (C-H), 2839 (C-H), 1724 (C=O), 1748 (C=O), 1610 (C=C), 1250 (C-O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 2.30 (1H, dd, *J* 14.0, 3.9, C(5)*H*$_A$), 3.16-3.13 (1H, m, C(5)*H*$_B$), 3.23 (3H, s, CO$_2$C*H*$_3$), 3.57-3.52 (1H, m, C(7a)*H*), 3.62-3.56 (1H, m, C(4a)*H*), 3.73 (3H, s, CO$_2$C*H*$_3$), 3.80 (3H, s, OC*H*$_3$), 4.63 (1H, d, *J* 9.6, C(7)*H*), 5.57 (1H, d, *J* 3.2, C(4)*H*), 6.88-6.83 (2H, m, 2 × *Ar*), 7.30-7.25 (2H, m, 2 × *Ar*), 7.43-7.36 (3H, m, 3 × *Ph*), 7.64-7.60 (2H, m, 2 × *Ph*); $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) $\delta_C$: 36.4 (*C*(4a)H), 41.1 (*C*(5)H$_2$), 47.6 (*C*(7a)H), 52.5 (CO$_2$*C*H$_3$), 53.0, 53.1 (*C*(7)H, CO$_2$*C*H$_3$), 55.2 (OCH$_3$), 64.8 (*C*(6)), 102.4 (*C*(4)H), 113.6 (2 × *Ar*), 124.8 (2 × *Ar*), 128.5 (2 × *Ar*), 128.9 (*Ar*), 129.2 (*Ar*), 129.9 (2 × *Ar*), 132.2 (*C*(1')H), 149.0 (*C*(3)), 159.0 (*C*(4')OMe), 168.4 (*C*(1)), 170.4 (*C*O$_2$CH$_3$), 171.7 (*C*O$_2$CH$_3$); *m/z* (ESI$^+$) 459 ([M+Na]$^+$, 100%); HRMS $C_{25}H_{24}NaO_7^+$ [M+Na]$^+$ found 459.1401, requires 459.14. Selected data for minor diastereomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 4.48 (1H, d, *J* 11.7, C(7)*H*).

**Dimethyl (4a*S*,7*S*,7a*R*)-7-methyl-1-oxo-3-phenyl-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1H)-dicarboxylate 2i and dimethyl 2-((*E*)-but-2-enoyl)-2-((*E*)-4-oxo-4-phenylbut-2-en-1-yl) malonate 3i:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (40.6 mg, 0.15 mmol), LiHMDS (1 M in THF, 0.15 mL, 0.15 mmol), HyperBTM **4** (9.1 mg, 0.03 mmol), EtN(*i*Pr)$_2$ (36 µL, 0.21 mmol) and crotonyl chloride (20 µL , 0.21 mmol) were reacted in THF (3.2 mL) to give a 73:27 mixture of **2i** and **3i**, and **2i** in 85:15 crude dr. The mixture was purified by chromatography on silica gel (EtOAc/Hexane 1:4) to afford **2i** as a yellow oil in >95:5 dr (15.9 mg, 32%) and **3i** as a yellow oil (10.2 mg, 20%). **2i:** $[\alpha]_D^{20}$ +11.4 (*c* 0.6 in CHCl$_3$); chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 21.9 min, t$_R$ (4a*R*,7*R*,7a*S*): 40.5 min, 93.5:6.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2953 (C-H), 1728 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 1.25 (3H, d, *J* 6.9, C(7)C*H*$_3$), 2.22 (1H, dd, *J* 14.1, 4.4, C(5)*H*$_A$), 2.96-2.89 (2H, m, C(5)*H*$_B$, C(7a)*H*), 3.12 (1H, dq, *J* 11, 6.9, C(7)*H*), 3.44-3.37 (1H, m, C(4a)*H*), 3.74 (3H, s, CO$_2$C*H*$_3$), 3.78 (3H, s, CO$_2$C*H*$_3$), 5.50 (1H, d, *J* 2.1, C(4)*H*), 7.41-7.35 (3H, m, 3 × *Ph*), 7.62-7.58 (2H, m, 2 × *Ph*); $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) $\delta_C$: 15.3 (*C*H$_3$), 35.2 (*C*(4a)H), 41.1 (*C*(5)H$_2$), 44.2 (*C*(7)H), 48.4 (*C*(7a)H), 52.6 (CO$_2$*C*H$_3$), 52.8 (CO$_2$*C*H$_3$), 62.2 (*C*(6)), 103.1 (*C*(4)), 124.7 (2 × *Ph*), 128.5 (2 × *Ph*), 129.1 (*p-Ph*), 132.2 (*i-Ph*), 147.8 (*C*(3)), 169.0 (*C*(1)), 171.1 (*C*O$_2$CH$_3$), 171.5 (*C*O$_2$CH$_3$); *m/z* (ESI$^+$) 367 ([M+Na]$^+$, 100%); HRMS $C_{19}H_{20}NaO_6$ [M+Na]$^+$ found 367.1152, requires 367.1152. **3i:** $\nu_{max}$ (film)/cm$^{-1}$ 2953 (C-H), 2922 (C-H), 1732 (C=O), 1624 (C=C). $^1$H NMR (400 MHz, CDCl$_3$) $\delta_H$: 1.94 (3H, dd, *J* 7.0, 1.7, C*H*$_3$), 3.14 (2H, d, *J* 6.5, C*H*$_2$), 3.82 (6H, s, 2 × CO$_2$C*H*$_3$), 6.45 (1H, dq, *J* 15.2, 1.7, C*H*=CHCH$_3$), 7.02-6.87 (2H, m, C*H*=C*H*COPh), 7.08 (1H, dq, *J* 15.2, 7.0, CH=C*H*CH$_3$), 7.53-7.45 (2H, m, 2 × *Ph*), 7.62-7.54 (1H, m, *Ph*), 7.94-7.87 (2H, m, 2 × *Ph*). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) $\delta_C$: 18.5 (*C*H$_3$), 35.4 (*C*H$_2$), 53.3 (2 × CO$_2$*C*H$_3$), 127.3 (*C*H=CHCH$_3$), 128.6 (2 × *Ph*), 128.7 (2 × *Ph*), 130.0 (CH=*C*HCOPh), 132.8 (*p-Ph*), 142.9 (*C*H=CHCOPh), 145.6 (*i-Ph*), 167.5 (2 × CO$_2$*C*H$_3$), 188.7 (C=O), 190.6 (C=O); *m/z* (ESI$^+$) 367 ([M+Na]$^+$, 100%); HRMS $C_{19}H_{20}NaO_6$ [M+Na]$^+$ found 367.1146, requires 367.1152.

**Dimethyl 1-oxo-3-phenyl-7-(4'-(trifluoromethyl)phenyl)-4a,5,7,7a-tetrahydrocyclopenta[c]pyran-6,6(1*H*)-dicarboxylate 2j:** Following *General Procedure D*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (60 mg, 0.22 mmol), LiHMDS (1 M in THF, 0.24 mL, 0.24 mmol), HyperBTM **4** (14 mg, 0.04 mmol), $^i$Pr$_2$NEt (53 µL, 0.30 mmol) and 3-(4-trifluoromethyl-phenyl)acryloyl chloride (72 mg , 0.30 mmol) were reacted in THF (4.7 mL) to give **2j** in 81:19 crude dr. The mixture was purified by chromatography on silica gel (Toluene/CH$_2$Cl$_2$ 1:5) to afford **2j** as a yellow oil in 87:13 dr (20 mg, 0.04 mmol, 20%). **2j:** $[\alpha]_D^{20}$ −16.8 (*c* 1.0 in CHCl$_3$); chiral HPLC analysis, ChiralPak AS-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), t$_R$ (4a*S*,7*S*,7a*R*): 12.6 min, t$_R$ (4a*R*,7*R*,7a*S*): 43.1 min, 82.5;17.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2954 (C-H), 1726 (C=O), 1111 (C-F); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$: 2.31 (1H, dd, *J* 14, 4.6, C(5)*H*$_A$), 3.16-3.13 (1H, m, C(5)*H*$_B$), 3.18 (3H, s, CO$_2$C*H*$_3$), 3.62-3.56 (1H, m, C(7a)*H*), 3.69-3.63 (1H, m, C(4a)*H*), 3.76 (3H, s, CO$_2$C*H*$_3$), 4.74 (1H, d, *J* 9.7, C(7)*H*), 5.61 (1H, d, *J* 3.2, C(4)*H*), 7.44-7.38 (3H, m, 3 × *Ar*), 7.52-7.46 (2H, m, 2 × *Ar*), 7.64-7.55 (4H, m, 4 × *Ar*); $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) $\delta_C$: 36.5 (*C*(4a)H), 41.3 (*C*(5)H$_2$), 47.2 (*C*(7a)H), 52.4 (*C*(7)H), 53.2 (2 × CO$_2$*C*H$_3$), 64.9 (*C*(6)), 102.1 (*C*(4)H), 124.1 (q, $^1J_{CF}$ 272.9, *C*F$_3$), 124.8 (2 × *Ar*), 125.2 (q, $^3J_{CF}$ 3.9, *C*(3')H, *C*(5')H), 128.6 (2 × *Ar*), 129.4 (2 × *Ar*), 129.9 (*p-Ph*), 130.0 (q, $^2J_{CF}$ 32.6, *C*(4')CF$_3$), 131.9 (*Ar*), 141.2 (*Ar*), 149.2 (*C*(3)), 168.0 (*C*(1)), 170.0 (*C*O$_2$CH$_3$), 171.3 (*C*O$_2$CH$_3$); $\delta_F$ (376 MHz, CDCl$_3$) −62.7 (C*F*$_3$); *m/z* (ESI$^+$) 497 ([M+Na]$^+$, 100%); HRMS $C_{25}H_{21}F_3NaO_6$ [M+Na]$^+$ found 497.1182, requires 497.1182. Selected data for minor

diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.08 (1H, dd, *J* 14.1, 5.8, C(5)$H_2$), 4.66 (1H, d, *J* 10.7, C(7)*H*), 7.96-7.92 (2H, m, 2 × Ph*H*).

**Trimethyl 2-methyl-4-(2-oxo-2-phenylethyl)cyclopentane-1,1,3-tricarboxylate 7i:** Following *General Procedure E*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (70 mg, 0.25 mmol), LiHMDS (1 M in THF, 0.28 mL, 0.28 mmol), HyperBTM **4** (16 mg, 0.05 mmol), $^i$Pr$_2$NEt (62 µL, 0.35 mmol) and crotonyl chloride (34 µL , 0.35 mmol) were reacted in THF (5.5 mL). Subsequent ring-opening with MeOH (2.3 mL) and DMAP (6.1 mg, 0.05 mmol) gave **7i** in 91:9 crude dr. The mixture was purified by chromatography on silica gel (EtOAc/Hexane 1:4) to afford **7i** as a yellow oil in 99:1 dr (49.9 mg, 0.16 mmol, 64%). **7i**: $[\alpha]_D^{20}$ +11.8 (c 1.0 in $CHCl_3$); ChiralPak IC (10% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 254 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 28.7 min, $t_R$ (4a*R*,7*R*,7a*S*): 36.2 min, 93.0:7.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 2953 (C-H), 2849 (C-H), 1724 (C=O), 1684 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.10 (3H, d, *J* 6.8, C$H_3$), 1.91 (1H, dd, *J* 13.9, 7.4, C(5)$H_A$), 2.79 (1H, dd, *J* 13.9, 7.7, C(5)$H_B$), 3.01-2.86 (2H, m, C(3)*H*, C$H_A$H$_B$COPh), 3.19-3.05 (2H, m, C(2)*H*, CH$_A$$H_B$COPh), 3.34-3.22 (1H, m, C(4)*H*), 3.60 (3H, s, CO$_2$C$H_3$), 3.73 (3H, s, CO$_2$C$H_3$), 3.75 (3H, s, CO$_2$C$H_3$), 7.50-7.44 (2H, m, 2 × *Ph*), 7.60-7.53 (1H, m, *Ph*), 7.94-7.88 (2H, m, 2 × *Ph*); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta_C$: 15.1 (*C*H$_3$), 34.7 (*C*(4)H), 40.8 (*C*(5)H$_2$), 40.9 (*C*H$_2$COPh), 43.0 (*C*(2)H), 51.7 (CO$_2$*C*H$_3$), 52.3 (CO$_2$*C*H$_3$), 52.6 (CO$_2$*C*H$_3$), 53.0 (*C*(3)H), 62.4 (*C*(1)), 127.9 (2 × *Ph*), 128.6 (2 × *Ph*), 133.1 (*p-Ph*), 136.8 (*i-Ph*), 171.4 (*C*O$_2$CH$_3$), 172.0 (*C*O$_2$CH$_3$), 174.1 (*C*O$_2$CH$_3$), 198.5 (*C*OPh); *m/z* (ESI$^+$) 399 ([M+Na]$^+$, 100%); HRMS $C_{20}H_{24}NaO_7$ [M+Na]$^+$ found 399.1412, requires 399.1414. Selected data for minor diastereomer: $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.07 (3H, d, *J* 6.8, C$H_3$), 3.71 (3H, s, CO$_2$C$H_3$), 8.00-7.95 (2H, m, 2 × Ph*H*).

**Trimethyl (2*S*,3*R*,4*S*)-4-(2-oxo-2-phenylethyl)-2-(4'-(trifluoromethyl)phenyl)cyclopentane-1,1,3-tricarboxylate 7j:** Following *General Procedure E*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (60 mg, 0.22 mmol), LiHMDS (1 M in THF, 0.24 mL, 0.24 mmol), HyperBTM **4** (14 mg, 0.04 mmol), $^i$Pr$_2$NEt (53 µL, 0.30 mmol) and 3-(4-trifluoromethyl-phenyl)acryloyl chloride (72 mg, 0.30 mmol) were reacted in THF (4.7 mL). Subsequent ring-opening with MeOH (2 mL) and DMAP (5.4 mg, 0.04 mmol) gave **7j** in 84:16 crude dr. The mixture was purified by chromatography on silica gel (EtOAc/Hexane 1:4) to afford **7j** as a yellow oil in 83:17 dr (70 mg, 64%). **7j**: $[\alpha]_D^{20}$ −6.7 (c 1.1 in $CHCl_3$); ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 25.8 min, $t_R$ (4a*R*,7*R*,7a*S*): 33.3 min, 82.5:17.5 er; $\nu_{max}$ (film)/cm$^{-1}$ 2953 (C-H), 2849 (C-H), 1726 (C=O), 1686 (C=O), 1114 (C-F); $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.07 (1H, dd, *J* 14.1, 5.8, C(5)$H_A$), 3.10-2.97 (2H, m, C(5)$H_B$, C$H_A$H$_B$COPh), 3.22-3.14 (4H, m, CO$_2$C$H_3$, CH$_A$$H_B$COPh), 3.58-3.48 (4H, m, CO$_2$C$H_3$, C(4)*H*), 3.65-3.78 (4H, m, CO$_2$C$H_3$, C(3)*H*), 4.67 (1H, d, *J* 4.67, C(2)*H*), 7.53-7.44 (4H, m, 4 × *Ar*), 7.64-7.53 (3H, m, 3 × *Ar*), 7.98-7.92 (2H, m, 2 × *Ar*); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta_C$: 36.1 (*C*(4)H), 40.1 (*C*H$_2$COPh), 40.7 (*C*(5)H$_2$), 51.5 (*C*(3)H), 51.8 (*C*(2)H), 51.9 (CO$_2$*C*H$_3$), 52.1 (CO$_2$*C*H$_3$), 52.9 (CO$_2$*C*H$_3$), 64.5 (*C*(1)), 124.1 (q, $^1J_{CF}$ 272.0, *C*F$_3$), 125.0 (q, $^3J_{CF}$ 3.6, *C*(3')H, *C*(5')H), 128.0 (2 × *Ar*), 128.7 (2 × *Ar*), 129.0 (2 × *Ar*), 129.6 (q, $^2J_{CF}$ 32.4, *C*(4')CF$_3$), 133.3 (*Ar*), 136.8 (*Ar*), 142.3 (*Ar*), 170.6 (*C*O$_2$CH$_3$), 172.2 (*C*O$_2$CH$_3$), 172.9 (*C*O$_2$CH$_3$), 198.1 (*C*OPh); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) $\delta_F$: −62.6 (C*F*$_3$); *m/z* (ESI$^+$) 529 ([M+Na]$^+$, 100%); HRMS $C_{26}H_{25}F_3NaO_7$ [M+Na]$^+$ found 529.1443, requires 529.1445. Selected data for minor diastereomer: $^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$: 3.77 (3H, s, CO$_2$C$H_3$), 4.52 (1H, d, *J* 12.2, C(2)*H*), 8.03-7.98 (2H, m, 2 × Ph*H*).

**Trimethyl 4-(2-oxo-2-phenylethyl)-2-(thiophen-2'-yl)cyclopentane-1,1,3-tricarboxylate 7k:** Following *General Procedure E*, dimethyl (*E*)-2-(4-oxo-4-phenylbut-2-en-1-yl)malonate (91 mg, 0.33 mmol), LiHMDS (1 M in THF, 0.37 mL, 0.37 mmol), HyperBTM **4** (21 mg, 0.07 mmol), $^i$Pr$_2$NEt (81 µL, 0.46 mmol) and 3-(2-thienyl)acrylic chloride (80 mg , 0.46 mmol) were reacted in THF (7 mL). Subsequent ring-opening with MeOH (3 mL) and DMAP (8 mg, 0.07 mmol) gave **7k** in 91:9 crude dr. The mixture was purified by chromatography on silica gel (EtOAc/Hexane 1:4) to afford **7k** as a yellow oil in 92:8 dr (92.3 mg, 0.21 mmol, 63%). **7k**: $[\alpha]_D^{20}$ -1.1 (c 1.0 in $CHCl_3$); chiral HPLC analysis, ChiralPak IB (2.5% *i*-PrOH:hexane, flow rate 1.5 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 11.6 min, $t_R$ (4a*R*,7*R*,7a*S*): 15.4 min, 73.0;24.0 er; $\nu_{max}$ (film)/cm$^{-1}$ 2951 (C-H), 2846 (C-H), 1724 (C=O), 1684 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.00 (1H, dd, *J* 14.2, 5.8, C(5)$H_A$), 2.97 (1H, dd, *J* 17.5, 7.9, C$H_A$H$_B$COPh), 3.06 (1H, dd, *J* 14.2, 7.6, C(5)$H_B$), 3.18 (1H, dd, *J* 17.5, 6.6, CH$_A$$H_B$COPh), 3.36 (3H, s, CO$_2$C$H_3$), 3.52-3.46 (1H, m, C(4)*H*), 3.55 (3H, s, CO$_2$C$H_3$), 3.69 (1H, dd, *J* 11.4, 8.5, C(3)*H*), 3.75 (3H, s, CO$_2$C$H_3$), 4.78 (1H, d, *J* 11.4, C(2)*H*), 6.92 (1H, dd, *J* 5.1, 3.5, C(3')*H*), 7.00-6.96 (1H, m, C(5')*H*), 7.17 (1H, dd, *J* 5.1, 1.1, C(4')*H*), 7.52-7.46 (2H, m, 2 × *Ph*), 7.62-7.56 (1H, m, *Ph*), 7.96-7.91 (2H, m, 2 × *Ph*); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) $\delta_C$: 35.2 (*C*(4)H), 40.5 (*C*H$_2$COPh), 40.6 (*C*(5)H$_2$), 47.7 (*C*(2)H), 52.0 (CO$_2$*C*H$_3$), 52.5 (CO$_2$*C*H$_3$), 52.8 (CO$_2$*C*H$_3$), 52.9 (*C*(3)), 64.5 (*C*(1)), 124.6 (*C*(5')), 125.8 (*C*(4')), 126.5 (*C*(3')H), 128.0 (2 × *Ph*), 128.7 (2 × *Ph*), 133.3 (*p-Ph*), 136.7 (*i-Ph*), 140.6 (*C*(2')), 170.7 (*C*O$_2$CH$_3$), 172.0 (*C*O$_2$CH$_3$), 172.8 (*C*O$_2$CH$_3$), 198.1 (*C*OPh); *m/z* (ESI$^+$) 467 ([M+Na]$^+$, 100%); HRMS $C_{23}H_{24}NaO_7S$ [M+Na]$^+$ found 467.1125, requires 467.1135. Selected data for minor diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 3.32 (3H, s, CO$_2$C$H_3$), 3.62 (3H, s, CO$_2$C$H_3$), 4.68 (1H, d, *J* 12, C(2)*H*), 8.02-7.98 (2H, m, 2 × *Ph*). $^{13}$C{$^1$H} NMR (126 MHz, $CDCl_3$) $\delta_C$: 49.1 (*C*(2)), 124.7 (*C*(5')), 140.1 (*C*(2')), 198.4 (*C*OPh).

**Trimethyl 4-(2'-(4''-methoxyphenyl)-2-oxoethyl)-2-methylcyclopentane-1,1,3-tricarboxylate 7l:** Following *General Procedure E*, dimethyl (*E*)-2-(4-(4-methoxyphenyl)-4-oxobut-2-en-1-yl)malonate (100 mg, 0.31 mmol), LiHMDS (1 M in THF, 0.34 mL, 0.34 mmol), HyperBTM **4** (19 mg, 0.06 mmol), $^i$Pr$_2$NEt (76 µL, 0.44 mmol) and crotonyl chloride (42 µL , 0.44 mmol) were reacted in THF (6.2 mL). Subsequent ring-opening with MeOH (3 mL) and DMAP (8 mg, 0.06 mmol) gave **7l** in >95:5 crude dr. Purification via column chromatography on silica gel (Petrol/EtOAc, 3:1) gave **7l** as a pale yellow oil (40 mg, 28%); $[\alpha]_D^{20}$ +10.5 (*c*1.0 in $CHCl_3$); chiral HPLC analysis, ChiralPak IA (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 36.1 min, $t_R$ (4a*R*,7*R*,7a*S*): 51.6 min, 96.0;4.0 er $\nu_{max}$ (ATR)/cm$^{-1}$ 2953 (C–H), 1724, 1724, 1674, 1599 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 1.07 (3H, d, *J* 6.8, C(2)*Me*), 1.87 (1H, dd, *J* 14.0, 7.3, C(5)$H_A$), 2.75 (1H, dd, *J* 14.0, 7.7, C(5)$H_B$), 2.82 (1H, dd, *J* 17.1, 8.0, C(1')$H_A$), 2.94 (1H, dd, *J* 10.8, 9.2, C(3)*H*), 3.00-3.11 (2H, m, C(2)*H*, C(1')$H_B$), 3.20-3.29 (1H, m, C(4)*H*), 3.57 (3H, s, C(3)CO$_2$*Me*), 3.71 (3H, s, C(1)CO$_2$*Me*), 3.72 (3H, s, C(1)CO$_2$*Me*), 3.85 (3H, s, O*Me*), 6.91 (2H, d, *J* 8.9, C(3'')*H*, C(5'')*H*), 7.87 (2H, d, *J* 8.9, C(2'')*H*, C(6'')*H*); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) $\delta_C$: 15.2 (C(2)*Me*), 35.0 (*C*(4)), 40.6 (*C*(1')), 40.8 (*C*(5)), 43.0 (*C*(2)), 51.8 (C(3)CO$_2$*CMe*), 52.4, 52.7 (C(1)(CO$_2$*Me*)$_2$), 53.1 (*C*(3)), 55.6 (O*Me*), 62.6 (*C*(1)), 113.8 (*C*(3''), *C*(5'')), 130.0 (*C*(1'')), 130.4 (*C*(2''), *C*(6'')), 163.6 (*C*(4'')), 171.6, 172.2 (C(1)(*C*O$_2$Me)$_2$), 174.2 (C(3)*C*O$_2$Me), 197.1 (*C*(2')); *m/z* (ESI$^+$) 429 ([M+Na]$^+$, 100%); HRMS $C_{21}H_{26}O_8$ [M+Na]$^+$ found 429.1519, requires 429.1520.

**Trimethyl 4-(2-(4-methoxyphenyl)-2-oxoethyl)-2-phenylcyclopentane-1,1,3-tricarboxylate 7m:** Following *General Procedure E*, dimethyl (*E*)-2-(4-(4-methoxyphenyl)-4-oxobut-2-en-1-yl)malonate (100 mg, 0.31 mmol), LiHMDS (1 M in THF, 0.34 mL, 0.34 mmol), HyperBTM **4** (19 mg, 0.06 mmol), $^i$Pr$_2$NEt (76 µL, 0.44 mmol) and cinnamoyl chloride (72 mg , 0.44 mmol) were reacted in THF (6.2 mL). Subsequent ring-opening with MeOH (3 mL) and DMAP (8 mg, 0.06 mmol) gave **7m** in 83:17 dr. Purification via column chromatography on silica gel (Petrol/EtOAc, 3:1) gave **7m** as a pale yellow oil (58 mg, 40%, 91:9 dr); $[\alpha]_D^{20}$ +11.0 (*c*1.0 in $CHCl_3$); chiral HPLC analysis, ChiralPak IB (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 17.0 min, $t_R$ (4a*R*,7*R*,7a*S*): 20.0 min, 81.0;19.0 er; $\nu_{max}$ (ATR)/cm$^{-1}$ 2951 (C–H), 1724, 1724, 1674, 1599 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.03 (1H, dd,

*J* 14.1, 5.7, C(5)$H_A$), 2.93 (1H, dd, *J* 17.2, 7.9, C(1')$H_A$), 3.01 (1H, dd, *J* 14.1, 7.2, C(5)$H_B$), 3.07 (1H, dd, *J* 17.2, 6.7, C(1')$H_B$), 3.12 (3H, s, C(1)$CO_2Me$), 3.43-3.50 (1H, m, C(4)*H*), 3.48 (3H, s, C(3)$CO_2Me$), 3.65 (1H, dd, *J* 10.5, 8.0 C(3)*H*), 3.69 (3H, s, C(1)$CO_2Me$), 3.87 (3H, s, O*Me*), 4.62 (1H, d, *J* 10.5, C(2)*H*), 6.96 (2H, d, *J* 9.0, C(3")*H*, C(5")*H*), 7.16-7.33 (5H, m, *Ph*), 7.94 (2H, d, *J* 9.0, C(2")*H*, C(6")*H*); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) $\delta_C$: 36.4 (*C*(4)), 39.6 (*C*(1')), 40.7 (*C*(5)), 51.7 (C(3)$CO_2CMe$), 51.8 (*C*(3)), 51.9 (*C*(2)), 52.1, 52.8 (C(1)$(CO_2Me)_2$), 55.5 (O*Me*), 64.6 (*C*(1)), 113.8 (*C*(3"), *C*(5")), 127.3 (*p-Ph*), 128.1 (*m-Ph*), 128.3 (*o-Ph*), 129.9 (*C*(1")), 130.3 (*C*(2"), *C*(6")), 138.1 (*i-Ph*), 163.6 (*C*(4")), 170.8, 172.5 (C(1)$(CO_2Me)_2$), 173.3 (C(3)$CO_2Me$), 196.8 (*C*(2')); *m/z* (ESI$^+$) 491 ([M+Na]$^+$, 100%); HRMS $C_{26}H_{28}NaO_8^+$ [M+Na]$^+$ found 491.1661, requires 491.1676. Selected data for minor diastereoisomer: $^1H$ NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.49 (1H, dd, *J* 14.2, 10.3, C(5)$H_A$), 2.66 (1H, dd, *J* 14.2, 8.5, C(5)$H_B$), 3.41-3.35 (2H, m, C(1')$H_2$), 3.56 (3H, s, *Me*), 3.76 (3H, s, *Me*), 4.48 (1H, d, *J* 12.0, C(2)*H*), 6.86 (2H, d, *J* 8.0, *Ar*), 7.04-7.12 (3H, m, *Ph*), 7.37 (2H, d, *J* 8.2, *Ph*), 7.99 (2H, d, *J* 8.0, *Ar*); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) $\delta_C$: 40.3 (*C*(5)), 42.0 (*C*(1')), 53.5 (*C*(2)), 107.7 (*Ar*), 122.0, 122.1 (*Ph*), 130.4 (*Ar*).

**trimethyl 4-(2-oxo-2'-(4"-tolyl)ethyl)-2-phenylcyclopentane-1,1,3-tricarboxylate 7n:** Following *General Procedure E*, dimethyl (*E*)-2-(4-oxo-4-(*p*-tolyl)but-2-en-1-yl)malonate (90 mg, 0.31 mmol), LiHMDS (1 M in THF, 0.34 mL, 0.34 mmol), HyperBTM **4** (19 mg, 0.06 mmol), $^iPr_2NEt$ (76 µL, 0.44 mmol) and cinnamoyl chloride (72 mg , 0.44 mmol) were reacted in THF (6.2 mL), MeOH (3 mL) and DMAP (8 mg, 0.06 mmol) gave **7n** in 88:12 dr. Purification via column chromatography on silica gel (Petrol/EtOAc, 5:1) gave **7n** as a pale yellow oil (73 mg, 51%, 88:12 dr); $[\alpha]_D^{20}$ −4.3 (*c* 1.0 in $CHCl_3$); chiral HPLC analysis, ChiralPak AD-H (5% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 41.1 min, $t_R$ (4a*R*,7*R*,7a*S*): 47.2 min, 84.5:15.5 er; $\nu_{max}$ (ATR)/cm$^{-1}$ 2951 (C–H), 1728, 1728, 1682, 1607 (C=O); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.03 (1H, dd, *J* 14.0, 5.8, C(5)$H_A$), 2.41 (3H, s, C(4")*Me*), 2.95 (1H, dd, *J* 17.4, 7.2, C(1')$H_A$), 3.01 (1H, dd, *J* 14.0, 7.2, C(5)$H_B$), 3.07-3.15 (1H, m, C(1')$H_B$), 3.12 (3H, s, C(1)$CO_2Me$), 3.44-3.51 (1H, m, C(4)*H*), 3.48 (3H, s, C(3)$CO_2Me$), 3.65 (1H, dd, *J* 10.4, 8.0 C(3)*H*), 3.69 (3H, s, C(1)$CO_2Me$), 4.62 (1H, d, *J* 10.4, C(2)*H*), 7.15-7.33 (7H, m, *Ph*, *Ar*), 7.83 (2H, d, *J* 8.2, C(2")*H*, C(6")*H*); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta_C$: 21.7 (*Me*), 36.4 (*C*(4)), 39.9 (*C*(1')), 40.7 (*C*(5)), 51.8 (C(3)$CO_2CMe$), 51.8 (*C*(3)), 51.9 (*C*(2)), 52.1, 52.8 (C(1)$(CO_2Me)_2$), 64.6 (*C*(1)), 127.3 (*p-Ph*), 128.1 (*m-Ph*), 128.1 (*C*(2"), *C*(6")), 128,5 (*o-Ph*), 129.3 (*C*(3"), *C*(5")), 134.4 (*C*(1")), 138.1 (*i-Ph*), 144.0 (*C*(4")), 170.8, 172.5 (C(1)$(CO_2Me)_2$), 173.3 (C(3)$CO_2Me$), 197.9 (*C*(2')); *m/z* (ESI$^+$) 475 ([M+Na]$^+$, 100%); HRMS $C_{26}H_{28}O_7$ [M+Na]$^+$ found 475.1725, requires 475.1727. Selected data for minor diastereoisomer: $^1H$ NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.49 (1H, dd, *J* 14.2, 10.3, C(5)$H_A$), 2.67 (1H, dd, *J* 14.2, 8.5, C(5)$H_B$), 3.19-3.28 (1H, m, C(1')$H_A$), 3.42 (1H, dd, *J* 17.3, 4.3, C(1')$H_B$), 3.53 (3H, s, *Me*), 3.73 (3H, s, *Me*), 4.49 (1H, d, *J* 12.0, C(2)*H*), 7.90 (2H, d, *J* 8.0, *Ar*); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) $\delta_C$: 37.4 (*C*(4)), 40.3 (*C*(5)), 42.7 (*C*(1')), 53.2 (*C*(2)), 53.5 (*C*(3)), 64.3 (*C*(1)), 128.2 (*Ar*), 134.2 (*C*(1")), 137.5 (*i-Ph*), 171.7, 172.0 (C(1)$CO_2$Me), 173.1 (C(3)$CO_2$Me), 198.0 (*C*(2')).

**Trimethyl 4-(2'-(4"-fluorophenyl)-2-oxoethyl)-2-phenylcyclopentane-1,1,3-tricarboxylate 7o:** Following *General Procedure E*, (*E*)-2-(4-(4-fluorophenyl)-4-oxobut-2-en-1-yl)malonate (92 mg, 0.31 mmol), LiHMDS (1 M in THF, 0.34 mL, 0.34 mmol), HyperBTM **4** (19 mg, 0.06 mmol), EtN(*i*Pr)$_2$ (76 µL, 0.44 mmol) and cinnamoyl chloride (72 mg , 0.44 mmol) were reacted in THF (6.2 mL), MeOH (3 mL) and DMAP (8 mg, 0.06 mmol) gave **7o** in 91:9 dr. Purification via column chromatography on silica gel (Petrol/EtOAc, 5:1) gave **7o** as a pale yellow oil (43 mg, 30%, 91:9 dr); $[\alpha]_D^{20}$ −4.0 (*c* 1.0 in $CHCl_3$); chiral HPLC analysis, ChiralPak IB (2% *i*-PrOH:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C), $t_R$ (4a*S*,7*S*,7a*R*): 16.0 min, $t_R$ (4a*R*,7*R*,7a*S*): 20.2 min, 76.0:24.0 er; $\nu_{max}$ (ATR)/cm$^{-1}$ 2953 (C–H), 1724, 1724, 1684, 1597 (C=O); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.02 (1H, dd, *J* 14.3, 5.7, C(5)$H_A$), 2.94 (1H, dd, *J* 17.5, 7.5, C(1')$H_A$), 3.03 (1H, dd, *J* 14.0, 7.3, C(5)$H_B$), 3.11-3.17 (1H, m, C(1')$H_B$), 3.12 (3H, s, C(1)$CO_2Me$), 3.48 (3H, s, C(3)$CO_2Me$), 3.43-3.50 (1H, m, C(4)*H*), 3.65 (1H, dd, *J* 10.5, 7.9, C(3)*H*), 3.70 (3H, s, C(1)$CO_2Me$), 4.61 (1H, d, *J* 10.5, C(2)*H*), 7.10-7.17 (2H, m, C(3")*H*, C(5")*H*), 7.23-7.33 (5H, m, *Ph*), 7.92-7.99 (2H, m, C(2")*H*, C(6")*H*); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta_C$: 36.3 (*C*(4)H), 40.0 (C(1')), 40.7 (*C*(5)), 51.7 (C(3)$CO_2Me$), 51.8 (*C*(3)), 52.0 (*C*(2)), 52.1 (C(1)$CO_2Me$), 52.9 (C(1)$CO_2Me$), 64.6 (*C*(1)), 115.8 (d, *J* 21.9, *C*(3"), *C*(5")), 127.4 (*p-Ph*), 128.1 (*m-Ph*), 128.5 (*o-Ph*), 130.6 (d, *J* 9.3, *C*(2"), *C*(6")), 138.0 (*i-Ph*), 165.8 (d, *J* 255.0 *C*(4")), 170.8, 172.5 (C(1)$CO_2$Me), 173.3 (C(3)$CO_2$Me), 196.7 (*C*(2')); *m/z* (ESI$^+$) 479 ([M+Na]$^+$, 100%); HRMS $C_{25}H_{25}FNaO_7^+$ [M+Na]$^+$ found 479.1464, requires 479.1477.

## Acknowledgments

We thank the EPSRC (ERTR – grant code EP/J500549/1; ABF - grant code EP/J018139/1), the Spanish government for a FPU Fellowship and the University of Seville (V Plan Propio de Investigación) for financial support (PER). This work was supported by the European Research Council under the European Union's Seventh Framework Programme (FP7/2007–2013) ERC grant agreement no. 279850. ADS thanks the Royal Society for a Wolfson Research Merit Award. We also thank the EPSRC UK National Mass Spectrometry Facility at Swansea University.

## Supporting Information

YES (this text will be updated with links prior to publication)

## Primary Data

YES (this text will be updated with links prior to publication)

Primary data is available via the following link:
http://dx.doi.org/10.17630/08eb25ec-9059-4b5e-86a0-9d9106dc34ad

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